ROC PRIMED

Manual of Operations

Updated October 26, 2009

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Overview

1.1 ROC PRIMED Trial Summary

A Factorial Design of An Active Impedance Threshold Valve versus Sham Valve and Analyze Later versus Analyze Early

Specific Aims:

The main aims of this trial are to compare survival to hospital discharge with an acceptable neurologic status, between standard CPR plus active impedance threshold valve/device (ITD) compared to standard CPR plus sham (non-active) ITD in patients with out-of-hospital cardiac arrest. These same comparisons will be made using a strategy of Analyze Early consisting of early rhythm analysis (30 seconds of CPR) versus a strategy of Analyze Later (consisting of 3 minutes of CPR), followed by rhythm analysis. A selection of mental and functional status scores at hospital discharge, and at 1, 3 and 6 months post-discharge will be performed on the above patients.

Study Population

Except for some specific situations, the inclusion and exclusion criteria for both ITD and Analyze Later protocols will be the same.

Inclusion Criteria

All persons of local age of consent or older who suffer non-traumatic cardiopulmonary arrest outside of the hospital in the study communities with defibrillation and/or delivery of chest compressions provided by participating ROC EMS providers dispatched to the scene and do not meet any of the exclusion criteria below.

Common Exclusion Criteria

-- Less than the age of consent
– Do not attempt resuscitation (DNAR) orders;
– Arrest due to traumatic cause (blunt, penetrating, or burn-related injury);
– Patients with exsanguinations;
– Known prisoners;
– Known pregnancy.

ITD Exclusion Criteria

– Tracheostomy present;
– Mechanical CPR device used;
--Ventilated by a mechanical device;
-- Non-ROC vehicle applied pads or began CPR (and no agreement in place to get time call received data)

Analyze Later Exclusion Criteria

– ROC EMS witnessed arrests;
– Non-EMS rhythm analysis (AED placed by police or lay responder);
– Non-ROC EMS agency/provider on scene and placed pads or began CPR.

Description of Impedance Threshold Device
The ITD (Figure 1a) is designed to be inserted easily between a facemask or advanced airway (e.g., ET tube, Combitube, or LMA) and a manual resuscitation bag (Figure 1b). In addition to an advanced airway, the ITD can be attached to any pediatric or adult facemask (Figure 1c) taking care to provide a continuously good seal around the nose and mouth (Figure 1d). As such, the device can be easily used by rescuers trained at both basic and advanced life support levels and moved quickly from any facemask once the patient is intubated.

Figure 1a

Figure 1b

Figure 1c

Figure 1d

The ITD contains ventilation timing assist lights, which flash at 12/minute at 1 second/flash to help promote the proper ventilation rate and duration for the patient with an advanced airway.
The LED lights are controlled by an ON/OFF switch on the device.
The ITD contains a filter that is rated at >99% filtration efficiency (at 0.10 micron or larger bacteria size) to help minimize contamination of the ventilation source.
The ITD is latex free and disposable (intended for single use only).

For this trial, ITDs will be specially manufactured in an opaque color so that active (functional) and sham (non-functional placebo) devices will appear externally identical.

Sham Devices:
Sham devices will be manufactured with the inspiratory impedance components eliminated, thus the device will function essentially as a hollow conduit. They will contain ventilation timing assist lights and appear externally identical to active devices. As with the active devices, there will be insignificant resistance to patient exhalation or rescuer ventilation.

All investigational devices (active and sham) will have a unique number to facilitate device accountability and tracking. They will look like the pictures above with the exception that the body will be opaque and there will be no pad printed labeling. Packaging will have the label "CAUTION: Investigational Device – Limited by Federal Law to investigational use."

ITD Use:
Training will emphasize that rescuers will use the ITD during initial airway management (either facemask or advanced airway).

Analyze Later Arm:
For the EMS providers allocated to Analyze Later, defibrillator analysis will not be initiated until the chest compression count reaches 3 minutes, after which a rescue shock will be administered, if indicated.

Analyze Early Arm:
For the EMS providers allocated to Analyze Early, defibrillation pads will be placed and defibrillator analysis will be initiated as soon as possible which should be when the chest compression count reaches approximately 50 (e.g., 30-60 seconds), or as soon thereafter as possible, after which a rescue shock will be administered if indicated. The rescuers will note the compression count that has been reached by the rescuer assigned to CPR. After the initial analysis, the standard resuscitation protocol will be followed.

Both Early and Later Arms
Chest Compressions: Initiation of chest compressions will not be delayed. Recognition that a patient is in cardiac arrest will immediately prompt one rescuer to initiate and count chest compressions. If the scene is first attended by two EMS rescuers, chest compressions will be performed by one while the second will set up the monitor/defibrillator and place the defibrillator pads. Then ventilation with the ITD will proceed. If three rescuers are present, ventilation and defibrillation readiness can proceed simultaneously. The start time for the compression count begins with the first compression by any organized EMS responder.

Minimum Interruptions: Training will emphasize that chest compressions should not be interrupted, except for required ventilations. If endotracheal intubation or other advanced airway procedures are deemed medically necessary, the providers should proceed, but continue chest compressions with minimum interruption. However, training will emphasize that interruption of chest compressions while securing the airway may dilute the theoretical benefit of the initial intervention. Interruption of chest compressions for airway manipulations will be documented when feasible.

Arrival of Additional EMS Personnel
In tiered response systems, or when backup EMS crews arrive on scene, first-responders delivering the chest compressions consistent with assignment prior to initial ECG analysis

should complete this intervention even if paramedics arrive on scene, and, if the subject has defibrillation pads in place, continue using the first crew's equipment until the first ECG analysis (and shock, if indicated).
Additional personnel are encouraged to assist with ongoing activities that do not interrupt chest compressions or initial rhythm analysis. For example, airway management, rotation of chest compressions, and placement of AED/monitor electrodes may benefit from additional personnel. If sufficient personnel arrive, they may also begin attempts at IV access.

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2.1 Protocol

Resuscitation Outcomes Consortium Prehospital Resuscitation using an IMpedance valve and Early vs Delayed analysis (ROC PRIMED) Trial

FDA APPROVED PROTOCOL dated 5/11/2006
PROTOCOL AMENDMENT 1 dated 12/28/2006

Title: A Factorial Design of An Active Impedance Threshold Valve versus Sham Valve and Analyze Later versus Analyze Early

Abbreviations commonly used in this protocol:

ACLS	advanced cardiac life support
AED	automated external defibrillator
CPR	cardiopulmonary resuscitation
DCC	data coordinating center
ED	emergency department
EMS	emergency medical services
EMT	emergency medical technicians
ICU	intensive care unit
PEA	pulseless electrical activity
RCC	regional coordinating center
ROC	Resuscitation Outcomes Consortium
ROSC	resumption of spontaneous circulation
VF	ventricular fibrillation

IDE G980125/S52

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1. Factorial Study Summary

Background

Little is known about how to optimize resuscitation for patients with out-of-hospital cardiac arrest. This is evident from the very low survival rates that are currently reported. The advent of automatic external defibrillators (AEDs) and their potential for wide-spread use by less highly trained emergency medical service (EMS) providers and lay persons has not resulted in the substantial increased survival rates anticipated. This has led to speculation that more and sooner circulation of oxygenated blood to the brain and heart may be important. Resuscitation Outcomes Consortium (ROC) Investigators propose a large clinical trial, using a partial factorial design, to test two strategies to increase blood flow. One strategy involves the impedance threshold device (ITD), which enhances venous return and cardiac output by increasing the degree of negative intrathoracic pressure during decompression. The second involves initiating resuscitation with a period of manual compressions and ventilations (Analyze Later), rather than attempting defibrillation immediately (Analyze Early).

Rationale

The rationale for the partial factorial design is based on several arguments.

- Most importantly, both interventions are worthy of study in their own right. Both interventions were proposed by several of the participating ROC sites in their initial applications.
- A number of ROC EMS agencies currently use cardiopulmonary resuscitation (CPR) first (i.e., Analyze Later) as their standard protocol, whereas others analyze the rhythm and shock as required before initiating CPR (i.e. Analyze Early.) Thus, if the ITD intervention were to be studied alone, we would be faced with an uncontrolled heterogeneity of practice, possibly changing during the course of the trial. This would necessitate, at a minimum, stratifying by the EMS protocol.
- We anticipate no substantial interactive effect between these two interventions. One relates to when assisted circulation takes place, compared with when the defibrillatory attempt takes place. The other has to do with the quantity of flow during assisted circulation. Both include some blood flow prior to any defibrillation attempt.
- The infrastructures to conduct the two trials are virtually identical, thus assuring substantial efficiencies in costs, and virtually cutting in half the number of patients and the time needed to study the two interventions sequentially, providing there are no interactions between the interventions.
- A partial factorial design, as opposed to a full factorial design, is necessary because eligibility criteria for the two interventions are not identical. Current medical standards would dictate that the Analyze Later strategy is inappropriate for patients whose cardiac arrest was witnessed by EMS, but some such patients might have an ITD or sham device applied during their resuscitation. Similarly, some patients on either the Analyze Later or Analyze Early arm might achieve resumption of spontaneous circulation (ROSC) prior to the application of the ITD or sham device. Further, because a greater sample size is required to achieve the desired statistical power to detect the anticipated effect of the ITD than that required to detect the effect of the Analyze Later strategy, the ROC investigators have allowed for the inclusion of one agency (Seattle Medic One) that would participate only in the ITD/sham comparison and not the Analyze Later vs Analyze Early comparison. We anticipate that of all

cardiac arrests treated by participating ROC agencies during the course of the study, approximately 85% will be judged evaluable for both the ITD/sham and Analyze Later/Analyze Early comparisons.

Challenges

The partial factorial design poses three challenges:

- Implementation of two interventions may be difficult for the persons who must conduct these interventions; the emergency medical technicians and paramedics, who must perform their efforts under the duress of life-threatening emergent conditions. This potential challenge has been mitigated by adopting cluster randomization for the Analyze Later protocol, whereby each cluster will be randomized to either always doing CPR first (Analyze Later) or always doing rhythm analysis first (Analyze Early). These clusters will consist of geographic areas or monitor/defibrillators within the EMS agencies. EMS personnel will place an active or sham ITD on all patients meeting criteria. Hence, EMS providers will always follow the same procedures: a) place an active or sham ITD on all patients, and b) analyze the rhythm either early or later consistently according to cluster randomization. No on-the-spot decisions regarding randomization will be required for use of either intervention.
- The cluster randomization will require that all out-of-hospital cardiac arrest events be accounted for. This requirement is actually beneficial, in that it provides additional motivation for the implementation of a comprehensive epidemiologic database of all life-threatening out-of-hospital events (what we have termed the ROC Registry). Whether the trial benefits from the Registry or the Registry benefits from the trial is unclear at this point and will depend in part upon the timing of various funding mechanisms.
- When a factorial design is used, there is an almost irresistible temptation to test for an interactive effect (i.e., risk difference for one factor depends on the level of the other factor). While a factorial design is the only reasonably efficient way of testing for an interaction between several interventions, to power the trial for the specific interaction effect generally requires a substantially increased sample size. As noted previously, we do not anticipate any substantial interaction between these two therapies. Nonetheless, potential interactions will be assessed by the DSMB at interim analyses and the sample size adjusted accordingly.

Potential Advantage

It should be noted that the intervention of Analyze Later probably cannot be appropriately compared by randomizing individual episodes. The issues with compliance caused by the confusion of having an EMS provider alternate between the basic concept of aggressively doing CPR initially versus assiduously assessing rhythm and defibrillating initially can be easily appreciated. The choice of the cluster will vary depending upon the realities of training and the fluidity of personnel within an agency. All clusters will be encouraged, and large clusters will be required, to switch from Analyze Later to Analyze Early or vice versa at midpoint, or more often through the trial, thus serving as their own control.

Outcomes

The trials share a common primary outcome, namely survival to hospital discharge with modified Rankin score $\leq$3, and common secondary outcomes, namely survival to discharge as well as functional status at discharge and at 1, 3 and 6 months after discharge as well as depression at 3 and 6 months.

Design

The trial will be partial factorial with one intervention based on a double-blind randomization of individuals through the use of an active versus a sham ITD (identical to the user), and the other intervention based on non-blinded randomized clusters.

Setting

The trial will be conducted in all EMS agencies participating in the Resuscitation Outcomes Consortium.

Sample Size and Analysis

Since we are not testing for an interaction, sample size for each intervention will be based on the traditional significance levels of .05 for two-sided and .025 for one-sided and a power of 0.9. Each will require approximately 16-18 months of enrollment. The specific inclusion criteria, sample size, and analytic techniques are defined with each of the specific interventions.

CPR Performance

Critical to understanding both interventions is the monitoring of CPR performance. All sites will implement procedures to attempt to collect 100% of data sources needed to assess CPR performance. Three performance measures will be abstracted: the ventilation rate, the compression rate, and the CPR fraction as defined in Appendix 2. It is known, based on the longstanding effort in Seattle, as well as more recent efforts in Chicago and Norway, that the data sources will be missing or incomplete in approximately 25% of episodes. Details for the CPR performance monitoring are dealt with in Section 4, since the process is applicable to both interventions.

Run-in Phase

After personnel have been trained in use of the ITD and the methods for Analyze Later vs. Analyze Early according to their cluster randomization, they will initiate a run-in phase. Evidence of compliance with the protocol and completion and submission of the data will be required before the site can enroll in the active phase of the trial.

Anticipated Clinical Impact

If the ITD demonstrates the hypothesized improvement in survival, we estimate that the premature death of approximately 2,700 victims of cardiac arrest[1] per year would be averted in North America compared to standard CPR. If the Analyze Later approach demonstrates the hypothesized improvement in survival, we estimate approximately 4,000 lives will be saved per year in North America. By implementing a factorial study design, these benefits to clinical practice can be achieved more efficiently and faster than otherwise would be the case.

Remainder of This Protocol

The remainder of this protocol is split into three parts. The second section contains the materials specific to the ITD intervention. The third section contains the materials specific to the Analyze

[1] Number of treatable cardiac arrests X Proportion of cases with non VF initial rhythm or VF that does not respond to initial shock X Absolute difference in survival i.e. (US population 295,483,056 X 0.53 per 1000 population (52) + Canadian population 31,127,234 X 0.57 per 1000 population (53)) X Absolute difference

Later intervention. The fourth section contains materials common to both interventions and/or specific to the partial factorial design of the study.

2. Impedance Threshold Device Trial

Comparison of Standard CPR Plus Active Impedance Threshold Device Versus Standard CPR Plus Sham Impedance Threshold Device In Patients With Out-Of-Hospital Cardiac Arrest

Study Summary

Background: Most patients with out-of-hospital cardiac arrest do not survive to hospital discharge. Survival after cardiac arrest is correlated with the time from its onset to the circulation of oxygenated blood to the brain and heart. Compression of the chest during cardiopulmonary resuscitation (CPR) increases intrathoracic pressure and compresses the heart. Decompression of the chest results in negative intrathoracic pressure, which enhances venous return and cardiac output. Collectively these actions circulate blood to the brain and heart. The impedance threshold device (ITD) is a novel respiratory device intended to increase the degree of negative intrathoracic pressure during decompression. Studies in animal models of cardiac arrest or small randomized trials in humans demonstrate that the ITD improves hemodynamics and short-term outcomes but it remains unclear whether ITD improves survival to discharge or neurological outcome. Therefore we propose a large clinical trial to test whether standard CPR supplemented by active ITD is effective compared to standard CPR supplemented by sham ITD.

Aims: The primary aim of the trial is to compare survival to hospital discharge with modified Rankin score $\leq$3 between standard CPR plus active ITD versus standard CPR plus sham ITD in patients with out-of-hospital cardiac arrest. The secondary aims of the trial are to compare survival to discharge, functional status at discharge and at 1, 3 and 6 months as well as depression at 3 and 6 months.

Hypotheses: The null hypothesis is that survival to hospital discharge with modified Rankin score $\leq$3 is identically distributed with use of standard CPR plus active ITD versus standard CPR plus sham ITD in patients with cardiac arrest. The secondary null hypotheses are that survival to discharge, functional status at discharge and at 1, 3 and 6 months after discharge as well as depression at 3 and 6 months will be identically distributed with use of standard CPR plus active ITD versus standard CPR plus sham ITD in patients with cardiac arrest.

Design: Double-blind randomized controlled trial.

Population: Patients with non-traumatic out-of-hospital cardiac arrest, presumed to be local age of consent or greater and treated by EMS providers.

Setting: EMS systems participating in the Resuscitation Outcomes Consortium.

Sample Size: Based on a one-sided significance level of 0.025, power = 0.90, a survival with modified Rankin score $\leq$ 3 to discharge rate of 5.33% with standard CPR and sham ITD, and two interim analyses, a maximum of 14,742 evaluable patients are needed to detect a 6.69% absolute survival with modified Rankin score $\leq$ 3 to discharge with standard CPR and active ITD.

Anticipated Clinical Impact: If this trial demonstrates a significant improvement in survival with use of the ITD, we estimate that the premature deaths of approximately 2,700 victims of cardiac arrest per year would be averted annually in North America alone.

Specific Aims

Primary Aim: The primary aim of the trial is to compare survival to hospital discharge with modified Rankin score $\leq$3 between standard CPR plus active ITD versus standard CPR plus sham ITD in patients with out-of-hospital cardiac arrest.

Hypothesis: The null hypothesis is that survival to hospital discharge with modified Rankin score $\leq$3 is identically distributed with use of standard CPR plus active ITD versus standard CPR plus sham ITD in patients with cardiac arrest.

Secondary Aims: The secondary aims of this trial are to compare survival to discharge, functional status scores at discharge and at 1, 3 and 6 months as well as depression at 3 and 6 months between standard CPR plus active ITD versus standard CPR plus sham ITD in patients with out-of-hospital cardiac arrest.

Hypotheses: The null hypotheses are that survival to discharge, functional status scores at discharge and at 1, 3 and 6 months as well as depression score at 3 and 6 months are identically distributed with use of standard CPR plus active ITD versus standard CPR plus sham ITD in patients with cardiac arrest.

Prespecified Subgroup Analyses: These include assessment of treatment effect by:

a) First recorded cardiac arrest rhythm before application of the ITD.
b) Observational status of an arrest (e.g., witnessed versus unwitnessed).
c) EMS response time interval of <10 minutes and $\geq$10 minutes from 911 call to initiation of CPR by EMS.

Background and Significance

Conceptual Framework for ITD

Despite the widespread availability of basic and advanced life support for patients with out-of-hospital cardiac arrest, few survive to hospital discharge.(1-3) In the most efficient EMS systems, less than 15% of all patients with out-of-hospital cardiac arrest are discharged from the hospital with intact neurological function.(1-3) Furthermore, the median published survival to hospital discharge after out-of-hospital cardiac arrest is only 6.4%.(4)

While there are many variables that impact on the potential for a patient in cardiac arrest to survive, the timely circulation of oxygenated blood to the heart and brain is considered critical.(2) An airway device such as a facemask or an endotracheal tube is commonly used to assist in oxygenating and ventilating the patient. However, the inherent mechanical inefficiencies of standard CPR limit the ability to circulate blood by even the most highly skilled rescuers.(5)

The purpose of CPR is to pump blood from the chest to the vital organs. Blood flow to the vital organs is highly dependent on the amount of blood return to the chest after each compression phase.(6, 7) During standard CPR, chest compression results in an elevation of intrathoracic pressure and direct cardiac compression. Both of these mechanisms result in forward blood flow out of the chest to perfuse the brain and other vital organs. When the chest

recoils, intrathoracic pressures decrease relative to extrathoracic pressures, enhancing venous return to the right heart. Blood flow back to the chest is highly dependent on the degree of chest wall recoil.(8)

Blood flows through the coronary arteries predominantly during the chest decompression phase. The pressure gradient generated between the aorta and the right atrium during the decompression phase of CPR has been termed the coronary perfusion pressure.(9) The pressure gradient between the aorta and left ventricular cavity is also a fundamental determinant of blood flow to the heart during CPR. During standard CPR, the coronary perfusion pressures are only marginally adequate, resulting in inadequate venous return during the chest wall recoil phase.(10, 11)

Since the description of standard CPR by Kouwenhoven and colleagues in 1960,(12) several new CPR techniques have been described. These include circumferential vest CPR,(13, 14) interposed abdominal counterpulsation CPR, (15-19) and phased abdominal counter-pulsation CPR.(20) These techniques are not widely applied as they have not been shown to significantly improve survival to discharge or other long-term outcomes compared with standard CPR in patients with out-of-hospital cardiac arrest.

This trial is focused on evaluating the ITD (see Appendix 1 for detailed information regarding the ITD). This novel device is designed to increase the coronary perfusion pressure during the decompression phase of CPR, thereby enhancing delivery of oxygenated blood to the heart. The concept of the ITD was discovered while evaluating the mechanism of another new method of CPR termed active compression decompression (ACD) CPR.(21) ACD CPR is performed with a hand-held suction device. When measuring intrathoracic pressures in patients undergoing ACD CPR, investigators realized that if the endotracheal tube was transiently occluded during the active decompression phase, intrathoracic pressures became markedly more negative. This led to the concept of impeding inspiratory gas exchange during the chest wall decompression phase of CPR to create a greater pressure differential between the thorax and the rest of the body, thereby enhancing venous return to the heart. As such, the impedance valve harnesses the kinetic energy of the chest wall recoil, thereby augmenting the “bellows-like” action of the chest with each compression-decompression cycle.(22)

The ITD is based on the principle that this impedance leads to a greater negative intrathoracic pressure, creating a small vacuum within the thorax relative to the rest of the body, leading to increased venous blood return to the heart and increased cardiac output. This concept has been evaluated in animals undergoing standard CPR (22) or active compression decompression (ACD) CPR,(6) as well as in human patients with prolonged cardiac arrest undergoing standard manual CPR (23-25) and ACD CPR.(7)

Preliminary Studies

Initial studies to test the impedance valve concept were performed in a pig model of cardiac arrest.(6) Two positive end expiratory valves (PEEP) were coupled together and placed in reverse in the respiratory circuit. These were designed to prevent respiratory gases from entering the lungs during the chest decompression phase of CPR. The pigs were ventilated by overcoming the 40 cm H20 resistance of the PEEP valves. After four minutes of cardiac arrest, the combination of this impedance valve combined with ACD CPR significantly improved vital organ blood flow compared with ACD CPR alone ($p < 0.05$). Brain blood flow increased to greater than baseline values (normal = 0.35 ml/min/gm) ($p < 0.05$) and blood flow to the heart increased to greater than 50% of baseline values (normal = 1.2ml/min/gm) ($p < 0.05$).(6) This enhanced myocardial perfusion was associated with lower energy requirements to defibrillate the animals at the end of that study. Use of the active ITD resulted in a marked improvement in coronary perfusion pressures compared to sham valve. These studies led to the development of the current ITD.

The first controlled animal studies of the ITD with standard CPR utilized a four-minute period of cardiac arrest followed by standard CPR with an automated compression device.(22) Standard CPR was performed with and without the ITD in an alternating fashion. Each time the ITD was removed from the respiratory circuit, the coronary perfusion pressures and vital organ perfusion decreased; and each time the ITD was added back, perfusion pressures stabilized or increased. A similar study evaluated active ITD versus sham ITD for 11 minutes after a six-minute period of cardiac arrest without CPR.(5) A sham ITD was used in the control group and an active ITD in the other.

After 6 minutes of cardiac arrest and 6 minutes of standard CPR, radiolabeled microspheres were injected to measure vital organ blood flow. The active ITD increased left ventricular flow by 100%, and nearly normalized blood flow to the brain compared to the sham ITD (Figures 1 and 2).

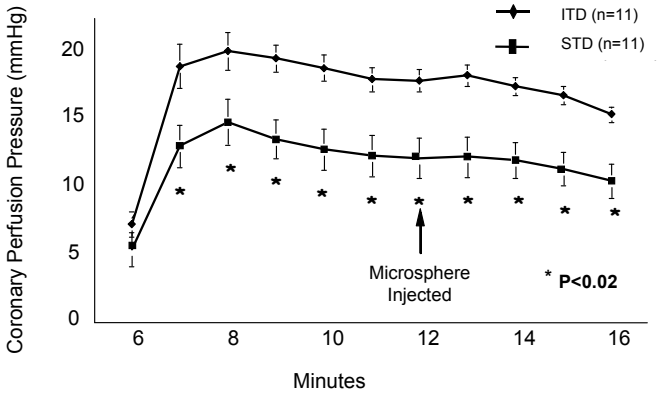


Figure 1

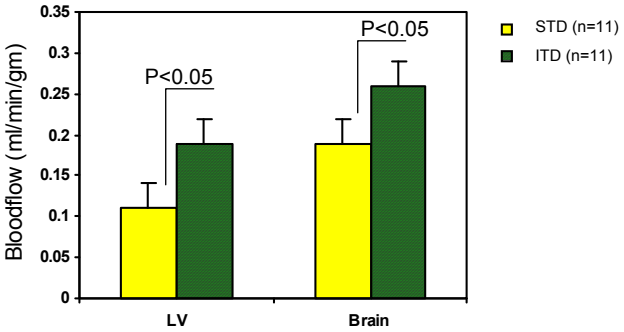


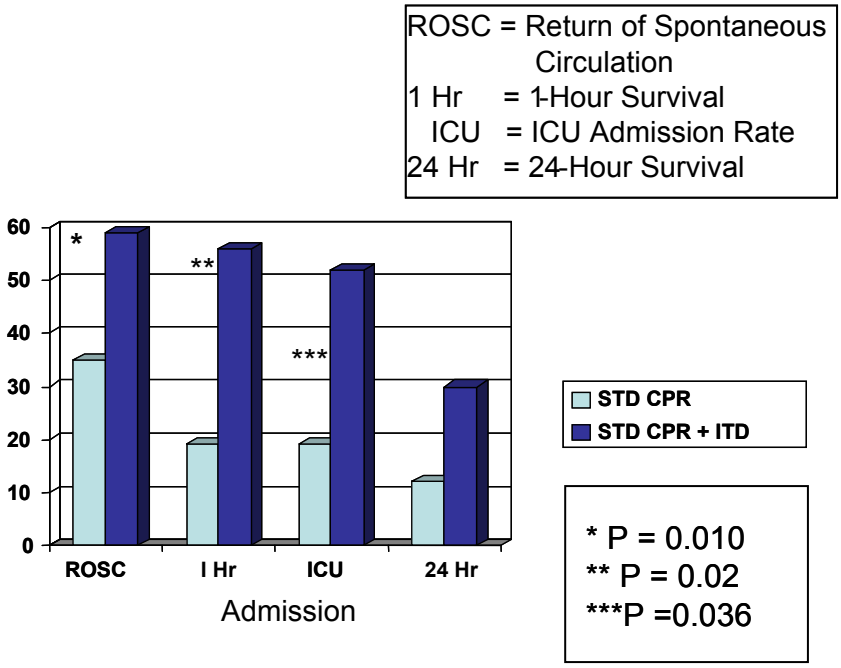
Figure 2

After a total of 17 minutes of ventricular fibrillation and 11 minutes of CPR, 3/11 pigs in the sham ITD group and 6/11 pigs in the active ITD group were resuscitated by direct current shock. In many ways, this six-minute arrest time prior to start of CPR more closely resembles clinical field experience where the time from arrest to the start of CPR in the United States ranges between 4-8 minutes in cities with highly efficient emergency medical services systems.

The Milwaukee ROC investigators recently randomized 230 adults who had protected airways after out-of-hospital cardiac arrest to receive standard CPR and sham ITD versus standard CPR and active ITD.(23, 24) The primary outcome of this study was admittance to ICU. Femoral arterial blood pressures were also evaluated by the research team during standard CPR at the scene of cardiac arrest in 22 other patients using the same protocol.

ICU admissions for all patients were not significantly different with use of the active ITD versus sham ITD (25% vs. 17%, respectively, P=NS). However, there was significantly increased ICU admissions in patients presenting in pulseless electrical activity (PEA) with use of active ITD, 19% (5 of 26) vs. 52% (14 of 27) (P = 0.02; not significant when corrected for comparisons in three rhythm groups-.05/3=.017) (Figure 3). In the hemodynamic study, systolic blood pressure was significantly increased with the active ITD versus the sham ITD: 85.1 $\pm$ 28.9 mmHg (n = 10) versus 42.9 $\pm$ 15.1 mmHg (n = 12), respectively; P < 0.001. Collectively these findings imply that by increasing venous return, and thus cardiac output, the ITD provides a novel means to increase circulation during standard CPR and cardiac arrest.

Figure 3: Outcomes Presenting in Patients with PEA



In a secondary analysis of the same study, the Milwaukee ROC investigators found that paramedics and EMTs ventilated patients in cardiac arrest an average of 30 ± 3 breaths per minute, nearly twice that recommended by the American Heart Association.(26) Subsequent studies in pigs demonstrated that excessive ventilation rates (similar to that observed in the clinical setting) significantly decreased coronary perfusion pressures and survival rates.(26) Two other studies demonstrated excessive ventilation rates delivered by healthcare professionals during in-hospital cardiac arrest.(27, 28) However a recent study demonstrated ventilation at the recommended rate during resuscitation by paramedics or nurse anesthetists in a different out-of-hospital setting.(29) Most chest compressions were too shallow and nearly half the time, chest compressions were not delivered at all.

In another analysis of the Milwaukee pilot study, rescuers were observed to maintain some residual and continuous pressure on the chest wall during the decompression phase of CPR, preventing full chest wall recoil.(8) Airway pressures were consistently positive during those periods. When this incomplete chest wall decompression was reproduced in a porcine model of ventricular fibrillation cardiac arrest, it was associated with significantly increased intrathoracic pressure and significantly decreased coronary and cerebral perfusion pressures. When monitoring CPR performance of professional EMS rescuers using a recording manikin, only 16.3% of decompressions were associated with complete recoil. A slight modification in the technique of manual CPR increased the frequency of complete chest recoil to 95.0% (OR: 129.0; CI: 43.4-382.0, $P < 0.0001$).(8)

The ITD in combination with conventional manual CPR was evaluated in a case-control study in large EMS system in Staffordshire, England. Survival to emergency department admittance was significantly greater among patients with any initial rhythm who received the ITD

(61/181 [34%]) compared with historical controls (180/808 [22%]) ($p<0.01$). No device-related adverse effects were observed.(25)

In summary, these studies demonstrate that the ITD improves hemodynamics and short-term outcomes but may be associated with poor performance of other components of CPR. In-field monitoring facilitates identification of such poor performance and provides opportunities for corrective feedback to EMS personnel.

Choice of Intervention

The investigators chose to evaluate the ITD alone rather than in combination with ACD CPR for several reasons. While the results with simultaneous use of ACD CPR and the ITD are promising,(6, 7, 30) use of the ACD CPR device requires more energy than standard CPR to perform it correctly.(6, 7, 30) Also, the sample size required to assess the effect of ACD CPR, ITD, combined therapy or standard CPR upon survival to discharge is impractical. Furthermore, a double-blind trial of ACD-CPR with or without ITD is not feasible, so the treatment effect from such a trial would be susceptible to bias. Therefore we propose a large clinical trial to assess the effect of standard CPR plus active ITD versus standard CPR plus sham ITD.

Summary of Rationale

Survival after out-of-hospital cardiac arrest is poor. Studies in animal models of cardiac arrest demonstrate enhanced myocardial perfusion and vital organ blood flow when using the ITD. Studies in humans with out-of-hospital cardiac arrest demonstrated that the ITD increased systolic blood pressure and tended to improve short-term clinical outcomes without any adverse effects. A large trial is required to demonstrate whether ITD significantly improves survival and functional status. Evaluation of the effect of ITD requires monitoring whether CPR process is consistent with currently recommended methods of resuscitation.

Research Design and Methods

Experimental Design

This randomized trial will evaluate manual CPR with either an active or sham ITD in adult patients with out-of-hospital cardiac arrest. Randomization will occur through use of a study ITD that is constructed such that the sham and active valves are indistinguishable. The intervention will be implemented by the first qualified provider to arrive at the scene of cardiac arrest and continued by subsequent providers in all ROC sites. The first qualified providers will most often be EMT-certified responders but will also include responders able to mechanically ventilate the patient using either a bag-mask or an advanced airway. Ventilation rates will be consistent with AHA guidelines.

Study Episodes

Episodes attended by EMS will be included if a study device was taken from its sealed container. All such episodes will be followed for purposes of safety evaluation.

Study Population

Inclusion Criteria

Persons aged 18 years or more (or local age of consent) who suffer non-traumatic cardiopulmonary arrest outside of the hospital in the study communities who receive defibrillation and/or chest compressions by EMS providers dispatched to the scene and do not meet any of the exclusion criteria below. Note: The etiology will be presumed to be non-

traumatic in origin unless the apparent cause is due to trauma, drowning, strangulation, electrocution, or exsanguination.

Exclusion Criteria

– Do not attempt resuscitation (DNAR) orders;
– Blunt, penetrating, or burn-related injury;
– Patients with exsanguinations;
– Known prisoners;
– Known pregnancy;
– Tracheostomy present;
– CPR performed with any mechanical compression device (e.g. AutoPulse, LUCAS, Thumper).
– Ventilated with a mechanical device (e.g. automated transport ventilator) Note: a bag-mask is not considered a mechanical ventilation device.
– A non-ROC EMS agency/provider, for whom time call received at dispatch cannot be obtained, began CPR or placed pads.

Primary Comparison Population

The ITD is conjectured to provide an improvement in the rate of neurologically intact (MRS $\leq$ 3) survival to hospital discharge in those patients experiencing OOHCA of cardiac origin and treated by EMS within 15 minutes of initial call to 911. There is, however, no contraindication to the use of the ITD in the relatively few patients whom experience OOHCA due to such noncardiac events as strangulation, drowning, or electrocution. In the emergency setting, unnecessarily introducing a need for EMS providers to evaluate eligibility criteria could potentially delay the institution of appropriate life saving treatments. Furthermore, if the ITD is proven effective and adopted widely, the eventual use of the device may include patients for whom the cardiac origin of OOHCA could not be accurately determined. Hence, this study protocol allows for the evaluation of the safety of the ITD device in some patients for whom the indication of the ITD could not be firmly established in the emergency setting. On the other hand, efficacy of the device will be analyzed in only those patients who are determined to meet the criteria defining the pre-hospital conditions for which the use of ITD is conjectured to be of benefit.

Efficacy Population: Analysis of primary and secondary efficacy outcomes will be conducted on a modified intent-to-treat basis. In order to be included in the efficacy analyses, patients must meet the inclusion/exclusion criteria for the ITD/sham device intervention. Furthermore, they must also meet the following criteria

- Not have experienced cardiac arrest secondary to drowning, electrocution, or strangulation;
- Have a response time (time from 911 call to time of arrival of ROC EMS providers at scene) less than 15 minutes, and
- Have the device actually applied.

With the exception of the criterion regarding actual application of the device, determination of whether patients meet these criteria or not will be made on the basis of data available prior to randomization (i.e., available prior to opening of the bag containing the device). In every case, the determination of whether a patient belongs in the efficacy population will be made in a blinded fashion (without knowledge of whether the device bag opened was an active ITD or a sham device). Within the efficacy population, analyses will be conducted on an intent-to-treat basis. Hence in the rare event that first and second responders in a tiered

response system might both open a bag containing a device, the patient will be analyzed according to the treatment arm corresponding to the first arriving vehicle.

In the event that the Analyze Late vs Analyze Early (ALvE) intervention is terminated early due to demonstrated superiority of one rhythm analysis strategy over the other, the efficacy population for the ITD/sham device comparison will be restricted to those subjects treated under the rhythm analysis strategy found to be superior. The number of subjects accrued to the study will be increased to achieve the planned maximal sample size in the superior rhythm analysis strategy arm.

Safety Population: Evaluation of the safety of the ITD will be made using all data from patients who were treated with a device, regardless of whether they are a member of the efficacy population or not.

In the event that the Analyze Late vs Analyze Early (ALvE) intervention is terminated early due to demonstrated superiority of one rhythm analysis strategy over the other, the safety of the ITD will also be evaluated separately in subgroups defined by the rhythm analysis strategy arm (AL or AE).

Intervention

Upon arrival of EMS providers at a patient with cardiac arrest, CPR will be initiated. Defibrillation will be performed consistent with local practice and cluster assignment. For subjects who are being ventilated with bag-mask or advanced airway (e.g., Combitube, laryngeal mask airway [LMA], or endotracheal tube) and receiving chest compressions, EMS providers will insert a study valve between the bag and the mask/airway, whichever is available. Training will target use of the ITD with initial management of the airway to assure the earliest placement of the ITD during CPR. To assure correct ventilation rate, the rescuers will turn on the ventilation timing assist lights on the device once an advanced airway has been established. The providers will be instructed to immediately remove the valve if the patient has return of spontaneous circulation or is breathing spontaneously, to facilitate rapid elimination of inspiratory impedance in a resuscitated patient. (The ITD has a safety check valve that opens if the pressure in the airway is <16 cm H2O in the event the rescuer does not recognize that the patient is able to breathe on their own). The providers will be instructed to immediately reapply the mask if such a patient ceases to have spontaneous circulation or to breath spontaneously (i.e., has recurrent cardiac arrest).

The EMS providers will be instructed to remove the ITD from the advanced airway if the valve fills with fluid; removing this fluid by forcing air through the device with the ventilation bag, suctioning the patient, and reapplying the ITD. If the device fills with fluid a second time, EMS personnel will be instructed to remove the ITD completely and continue resuscitative efforts without use of the device.

Use of the ITD will be discontinued on arrival to the hospital.

All other resuscitative measures will follow common guidelines (Appendix 3).

Random Allocation

Study devices will be randomly allocated in a proportion of 1:1 active vs. sham, with distribution determined by the CTC based on permuted blocks of concealed size within strata defined by participating site and within site by participating agency or subagency. Devices will be packaged with a flexible connector to facilitate adjunct equipment such as CO2 monitoring. A mask will also be provided to facilitate achievement of a good seal between the patient's face and the ventilatory circuit so as to maintain the intrathoracic pressure. These will be placed at each base station where they can be retrieved by the medic. One device will be kept on each

EMS vehicle. Study site personnel will keep inventory records for each EMS site and conduct EMS site visits to confirm inventory status. When a base station has less than three ITDs remaining, an additional set will be distributed. Each ITD package will have several stickers denoting its number. These will be placed on the medic report and emergency care record. Each site must establish a notification process with their EMS system and emergency department to notify study personnel of patient enrollment. In this manner, the subjects, investigators, study coordinators and all persons caring for the patient will be blinded to the treatment assignment. Note that active and sham devices will not be distinguishable visually even when removed from the opaque packaging. Patients will be considered to have been randomized as soon as the ITD package has been opened. In the event that two bags are opened for the same patient during the same arrest episode, the patient will be assigned to the treatment group of the device used by the first-arriving vehicle.

Intervention–Compliance

The location and number of devices supplied to each EMS rig and station for appropriate distribution will vary with the structure of the system. When an ITD is used, ambulance personnel will document the unique number of the device on their run report by using pull-off labels located within the packaging of the device. Following use, EMS providers will be encouraged to place the used device at a predetermined location and replace the used device with a new valve. After each use, the research team will be notified and will replace the used device. The coordinating center will maintain a record of where each device is distributed, and track their use.

Outcome Measures

Primary

The primary outcome is survival to hospital discharge with MRS $\leq$ 3. Patients who are transferred to another acute care facility (e.g., to undergo ICD placement) will be considered to be still hospitalized. Patients transferred to a non-acute ward or facility will be considered discharged.

Secondary

The secondary outcomes are survival to discharge; MRS at 3 and 6 months following hospital discharge; Adult Lifestyle and Function (ALFI) version of the Mini-Mental Status Exam (MMSE) at 1, 3 and 6 months;(31, 32) as well as Health Utilities Index III (HUI3) score(33) and Geriatric Depression Scale (T-GDS)(34) score at 3 and 6 months (details in Section 4 and Appendix 4).

Exploratory

Cerebral Performance Category (CPC) will be assessed at discharge, 3 and 6 months following hospital discharge.

In-Hospital Morbidity

Number of hospital days and time interval from 911 call to patient death will be described for all hospitalized patients as measures of morbidity after resuscitation.

Prespecified Subgroup Analyses

a) First recorded cardiac arrest rhythm prior to valve application (VF/VT vs. PEA vs. asystole vs. not obtained before device implementation);
b) Observational status of arrest (Witnessed by EMS vs. witnessed by bystanders vs. unwitnessed);
c) In witnessed cardiac arrests, response time interval from call to initiation of CPR by ROC EMS (<10 vs. ≥ 10 minutes);(30)
d) Analyze Early vs. Analyze Later vs. not participating in ALvE cohorts.

Expected Adverse Events

The following will be considered major adverse events if they occur during the resuscitative effort or the hospital stay:

Pulmonary Edema- *The presence of pulmonary edema in patients who survive long enough to receive a hospital-based chest x-ray (first emergency department or ICU chest x-ray).* This will be defined as formal radiographic interpretation as consistent with the presence on x-ray of alveolar pulmonary edema, interstitial pulmonary edema, bilateral pleural effusions, cardiomegaly (cardiothoracic ratio > 0.5 on posteroanterior projection), or pulmonary venous congestion (upper-zone flow redistribution on posteroanterior projection).(35, 36) This will be monitored because failure to remove the ITD immediately following successful resuscitation will require the patient to generate more than 16 cm of H_2O negative intrathoracic pressure before initiating inhalation. This may result in increased work of respiratory effort during the initial stages of successful resuscitation. This may result in secondary respiratory failure or pulmonary edema and the need for continuing to support the patient's respiration. Similarly, in the out-of-hospital setting, if the valve fills with fluid twice (indicating possibly significant pulmonary edema), its use will be discontinued.

All incidences where the valve fills with fluid will be reported to the DSMB. Additionally, all cases of pulmonary edema who did not survive, will have the field report individually reviewed for evidence of failure to remove the ITD valve and these cases will be presented to the DSMB.

Pulmonary edema is commonly observed after resuscitation from cardiac arrest.((37) and Unpublished Data, ASPIRE Investigators) However device-related pulmonary edema has not been observed in previous published studies of ITD. We anticipate that pulmonary edema associated with use of the ITD would be unlikely except if the device were left on a patient who is breathing spontaneously. Since the rate of pulmonary edema in the control group is unknown, we shall monitor the incidence of pulmonary edema in sham and active ITD groups and assess whether there is a significant difference between treatment groups.

Device Failure- *Mechanical failure (i.e., the device breaks).* Malfunctions are unlikely due to the simple construction and durable materials of the device. There have been no instances of the ITD breaking in the Milwaukee feasibility study, ongoing European studies or during clinical use in Europe.

Other- The following are commonly observed in patients who experience cardiac arrest or resuscitative efforts after its onset, and may or may not be attributable to specific resuscitation therapies. These will be monitored and reported but not classified as major adverse events. *Vomiting During CPR.* Vomiting during CPR is a common and anticipated complication of any method of CPR. Immediate clearing of the airway is necessary to prevent complications from aspiration. Rescuers are experienced in handling this type of complication and have portable and stationary suction available to them. The occurrence of vomiting during the application of

the ITD will be recorded from the prehospital clinical record. *Clinical diagnoses of cerebral bleeding, stroke, seizures, bleeding requiring transfusion or surgical intervention, rearrest, pulmonary edema, serious rib fractures, sternal fractures, internal thoracic or abdominal injuries as well as any other major medical or surgical outcomes* will be recorded as noted in the hospital discharge summary. Since the treating physicians will be blinded as to whether the patient received active or sham ITD, there is unlikely to be a treatment-related bias in identifying these events.

Unexpected Adverse Device Events (UADE)

These will be defined as any serious unexpected adverse effect on health or safety or any unexpected life-threatening problem caused by, or associated with, a device, if that effect or problem was not previously identified in nature, severity, or degree of incidence in the investigation plan or application (including a supplementary plan or application), or any other unexpected serious problem associated with a device that relates to the rights, safety or welfare of subjects. The death or neurological impairment of an individual patient is not considered an adverse event in this study.

Analyses

Primary Efficacy Analysis

The primary analysis of treatment efficacy will be based on a comparison across treatment arms active and sham ITD of the observed proportion of patients in the efficacy population (see page 12 for definition of efficacy population) with neurologically intact (MRS ≤ 3) survival to hospital discharge. We assume that ITD would not be implemented if it were associated with worse neurologically-intact survival to discharge. A one-sided level 0.025 hypothesis test will be used to test the null hypothesis of equal rates of such favorable events (H_0: $\pi_{ITD} = \pi_{SHAM}$) versus the alternative hypothesis that patients on the active ITD arm have a higher probability of neurologically intact survival to hospital discharge than do patients on the sham device arm (H_1: $\pi_{ITD} > \pi_{SHAM}$). The test statistic comparing those proportions will be a one-sided version of Pearson's chi squared statistic: the Z statistic defined as the difference of the proportions (ITD arm minus sham device arm) divided by its estimated standard error computed assuming the null hypothesis of equality of proportions.

$$Z = \frac{\left(\hat{\pi}_{ITD} - \hat{\pi}_{SHAM}\right)}{\sqrt{\hat{\pi}_{Null}\left(1-\hat{\pi}_{Null}\right)\left(\frac{1}{n_{ITD}} + \frac{1}{n_{SHAM}}\right)}} \quad \text{with } \hat{\pi}_{Null} = \frac{n_{ITD}\hat{\pi}_{ITD} + n_{SHAM}\hat{\pi}_{SHAM}}{n_{ITD} + n_{SHAM}}$$

The fixed sample P value corresponding to that Z statistic will be compared to the boundaries of the protocol defined group sequential stopping rule when expressed on the fixed sample P value scale. At the end of the study, analysis results will be summarized using point estimates of the difference in probability of favorable events, 95% confidence intervals, and P values adjusted for the true sampling distribution imposed by the group sequential stopping rule. (See the discussion of the group sequential monitoring plan below.)

This analytic approach assumes unbiased random allocation of patients to treatment group and relies on the sample size being large enough for asymptotic theory to provide good distributional approximations. With the exception of the inclusion criterion regarding actual application of the device, determination of whether patients meet study criteria or not will be made on the basis of data available prior to randomization (i.e., available prior to opening of the bag containing the device) (see p. 12 for more detail).

Secondary Efficacy Analyses

All secondary analyses of efficacy endpoints are directed toward finding supporting evidence for the findings of the primary efficacy analysis. As such, they will not be used as the primary basis for establishing benefit of the ITD relative to the sham device, nor will they be used as the primary basis for obtaining regulatory approval of the ITD. Hence, there is no plan to make any statistical adjustment for the multiple comparisons inherent in the secondary efficacy analyses, which include:

Modified Rankin Score (MRS) at hospital discharge. The mean MRS at hospital discharge will be compared across treatment groups using the t test which allows for unequal variances across groups. For the purposes of this analysis, patients dying before admission to the hospital will be treated the same as admitted patients dying before hospital discharge and will be assigned an MRS of 6.

Survival to hospital discharge. This secondary analysis of treatment efficacy will be based on a comparison across treatment arms of the observed proportion of patients in the efficacy population with survival to hospital discharge. This analysis shall proceed in a manner entirely analogous to that for the primary efficacy endpoint. The test statistic comparing those proportions will be a one-sided version of Pearson's chi squared statistic: the Z statistic as defined for the primary analysis.

Neurologically intact survival to hospital discharge adjusted for prognostic variables. A secondary analysis of the primary endpoint will adjust for those pre-randomization variables which might reasonably be expected to be predictive of favorable outcomes. Generalized linear models will be used to model the proportion of subjects with neurologically intact (MRS $\leq$ 3) survival to hospital discharge by ITD/sham device group adjusted for site (dummy variables modeling the 11 ROC sites), patient sex, patient age (continuous variable), witness status (dummy variables modeling the three categories of unwitnessed arrest, non-EMS witnessed arrest, and EMS witnessed arrest), location of arrest (public versus non-public), time or response (continuous variable modeling minutes between call to 911 and arrival of EMS providers on scene), presenting rhythm (dummy variables modeling asystole, PEA, VT/VF, or unknown), and treatment assignment in the Analyze Late vs. Analyze Early intervention. The test statistic used to assess any benefit of the ITD relative to the sham device will be computed as the generalized linear model regression coefficient divided by the estimated "robust" standard error based on the Huber-White sandwich estimator(38, 39) in order to account for within group variability which might depart from the classical assumptions. Statistical inference will be based on one-sided P values and 95% confidence intervals which adjust for the stopping rule used for the primary analysis.

Post-discharge neurological function, quality of life, and depression. Surviving patients will be contacted post-discharge to obtain consent for additional follow-up via telephone with consenting patients or their proxies regarding cognition, quality of life, and depression. Analyses of each of these outcomes at each time point will be compared across treatment groups by using the t test which allows for unequal variances. Analyses will first be conducted conditional on survival to the relevant time point by using only data from those patients offering consent, as well as using data imputed from discharge data for those surviving patients refusing consent. The data missing due to lack of consent for follow-up will be multiply imputed using measurements of patient age, sex, length of hospital stay, incidence of major adverse outcomes

during hospitalization, MRS at hospital discharge, and whether the patient was discharged to home or a nursing facility. Additional analyses of neurological function and quality of life will then incorporate measurements for patients dying prior to hospital admission, during hospitalization, or within 3 or 6 months post discharge. Dead patients will be assigned the worse category of neurological function and quality of life for each measurement.

Morbidity. As a measure of morbidity during hospitalization, the number of days hospitalized conditional upon survival to discharge will be compared across treatment groups using the t test which allows unequal variances. A similar analysis will also be conducted comparing the days of hospitalization for patients admitted to the hospital, but dying prior to hospital discharge. Finally, treatment groups will also be compared with respect to the number of days alive post hospital discharge during the first 6 months post OOHCA in order to incorporate information about both dead and surviving patients. In this analysis, data missing due to lack of consent for follow-up will be multiply imputed using data available at hospital discharge, and patients dying before hospital admittance or prior to hospital discharge will be scored as 0.

Safety Analyses

The incidence of adverse events will be recorded for all patients in the safety population and presented by treatment arm (ITD vs. sham device) to the DSMB for their review during the conduct of the study, as well as summarized and compared across treatment arms in the final report of study results. Assessment of the statistical significance of differences in the incidence of safety endpoints plays a lesser role, due to the need to be cautious in the introduction of new treatments in a human population. Hence, emphasis is placed on the presentation of results, with statistical tests provided for guidance on the precision of estimates as indicated. Specific measures that may reflect the safety of the ITD include:

Delay of treatment. The process of opening and applying the device could delay treatment and/or potentially cause harm in patients other than those for whom the device is conjectured to provide benefit, as well as in the evaluable patient population. The distribution of time from EMS arrival to initiation of CPR will be described using mean, standard deviation, minimum, 25th, 50th, and 75th percentiles, and maximum. When indicated, statistical tests comparing the distribution of times to initiation of CPR will be effected using the t test which allows for unequal variances. Similar analyses will be conducted for the time between EMS arrival and first assessment for defibrillation, stratified within Analyze Late vs. Analyze Early clusters.

Complications of treatment. The incidence of vomiting during CPR, device filling with fluid, mechanical failure of the device, and any UADE will be reported by treatment arm and compared as indicated using Pearson's chi squared statistic.

Serious adverse events. The incidence of each serious adverse event, along with other major adverse medical or surgical outcomes identified during review of hospital records, will be tabulated by treatment arm and compared when indicated using Pearson's chi squared test. In order to facilitate the identification of differences in rates of such events that might be due to greater survival to hospital admission and/or hospital discharge on one of the treatment arms, the incidence of any of the above specific events and/or death (either prehospital or during hospitalization) will be reported in a combined fashion and compared as indicated by using Pearson's chi squared statistic.

Subgroup Analyses

Analyses will be performed in each subgroup, along with tests for statistically significant interactions. However, it is recognized that the study is not powered adequately to detect interactions, and thus all subgroup analyses are judged exploratory.

Exploratory Analyses

Data from the clinical trial will also be used to explore two hypotheses unrelated to the treatment effect of ITD on neurologically intact survival post OOHCA.

Correlation between MRS and other measures of cognition and quality of life. Analyses will evaluate the correlation between simultaneous measures using the MRS, ALFI-MMSE, HUI or GDS at 3 and 6 months using linear regression analyses and standard errors computed using the Huber-White sandwich estimator. Additional analyses will evaluate the value of MRS at hospital discharge as a surrogate variable for the ALFI-MMSE and HUI at 6 months post hospital discharge. In this latter analysis, the effect of treatment with ITD vs. sham device on the 6 month cognitive function and quality of life measures will be analyzed both without and with adjustment for MRS at hospital discharge. A descriptive measure of the usefulness of the MRS at hospital discharge as a surrogate for the later validated measures will be based on the difference in the estimates of treatment effect between the unadjusted and adjusted analyses.

Cerebral Performance Category To assess the validity of the Cerebral Performance Category for use in future studies, CPC scores at discharge as well as three and six months after discharge will be analyzed in a manner similar to the analyses of post-discharge neurologic function described above in the secondary efficacy analyses. However the results of any analysis of CPC scores will not be used to make labeling claims for ITD.

Association between use of hypothermia and neurologically intact survival. Some patients may be treated with hypothermia according to local standards of best medical care. Data will be collected on both the pre-hospital and in-hospital use of hypothermia. In order to explore any association between the use of hypothermia and the probability of survival to hospital discharge proportional hazards regression models will be fit using use of hypothermia as a binary time-varying covariate, adjusted for treatment with ITD vs. sham device. Test statistics will be based on the estimated hazard ratio for the hypothermia covariate and the Wald statistic computed from the regression parameter divided by the “robust” standard error computed using the Huber-White sandwich estimator. Comparisons of neurologic function will use measures derived from the MRS, ALFI-MMSE, HUI and GDS over time in a generalized estimating equation (GEE) analysis restricted to patients surviving to hospital discharge and incorporating the multiple measurements made on each patient. Test statistics will be based on the Wald test using the regression parameter estimate for the hypothermia covariate and its “robust” standard error computed using the Huber-White sandwich estimator.

Sample Size and Study Duration

The sample size for the factorial trial is driven by the power analysis for the ITD intervention. These calculations are based on the estimated probability of survival to hospital discharge averaged over the participating ROC sites, which is then adjusted to reflect the estimated probability of survival to hospital discharge with acceptable neurological status (MRS ≤ 3).

Patients with OOHCA who are treated by participating agencies and subagencies and who meet the inclusion/exclusion criteria will be randomized to the ITD or sham device, unless resuscitated prior to the placement of such a device. This latter possibility may tend to occur with patients who present in VT/VF and who initially achieve ROSC following a first, early defibrillation as might be applied under the AE strategy. Thus, in computing sample sizes for the ITD intervention, we must consider the distribution of patients by presenting rhythm and their assignment to the AE or AL treatment strategies. We also must consider the number of patients who have EMS witnessed CA, because all such patients will be treated using an AE strategy, regardless of the cluster randomization of the responding unit to the AL vs. AE intervention.

It is estimated that approximately 50% of patients accrued to the factorial study will present in asystole, 25% of patients will present with pulseless electrical activity (PEA), and the remaining 25% will present in VT/VF. It is also estimated that approximately 10% of all EMS treated OOHCA will involve EMS witnessed arrest. In the ASPIRE trial, the presenting rhythm of EMS witnessed arrest occurred in the ratio of 2.20 asystole: 2.57 PEA : 4.74 VT/VF.
The anticipated distribution of patients by presenting rhythm and whether CA was EMS witnessed or not was estimated based on these assumptions (Table 1).

Table 1: Proportion of all EMS treated OOHCA patients according to presenting rhythm and EMS Witness status

Presenting Rhythm	EMS Witnessed	EMS Unwitnessed	Total
Asystole	0.0231	0.4769	0.500
Pulseless Electrical Activity (PEA)	0.0270	0.2230	0.250
VT/VF	0.0499	0.2001	0.250
TOTAL	0.1000	0.9000	1.000

Eligibility criteria for the ITD intervention excludes subjects for whom no device (ITD or sham) was used, and it is anticipated that approximately 30% of the patients presenting in VT/VF will not have a device placed when treated under the AE strategy, On the other hand, it is anticipated that all such patients would have a device placed when treated under the Analyze Later (AL) strategy. Taking into account that patients with OOHCA that is not witnessed by EMS will be randomized (by cluster) in a 1:1 ratio to the AE or AL strategies at all participating agencies except Seattle Medic One (which is projected to accrue approximately 2.7% of all patients—see Table 9), the expected distribution of patients to the various treatment strategies by presenting rhythm was estimated (Table 2).

Table 2: Proportion of all EMS treated OOHCA patients randomized to treatment combinations according to presenting rhythm and EMS Witness status

Initial Rhythm	EMS Witnessed CA or Seattle Medic One (AL vs. AE Ineligible)			Analyze Early			Analyze Late		Total ITD/Sham Randomized	
	No Device	Sham	ITD	No Device	Sham	ITD	Sham	ITD	Sham	ITD
Asystole	0.000	0.018	0.018	0.000	0.116	0.116	0.116	0.116	0.250	0.250
PEA	0.000	0.017	0.017	0.000	0.054	0.054	0.054	0.054	0.125	0.125
VT/VF	0.015	0.020	0.020	0.029	0.034	0.034	0.049	0.049	0.103	0.103
TOTAL	0.015	0.055	0.055	0.029	0.204	0.204	0.219	0.219	0.478	0.478

Based on ranges of estimates in published data and results of the ASPIRE trial, and allowing for 1-5% improvement due to better CPR process in the clinical trial setting, It is

estimated that in the absence of an ITD and when managed according to the Analyze Early (AE) strategy, the probability of survival to hospital discharge would be 1.05% for patients presenting with asystole, 4.02% for patients presenting with PEA, and 20.2% for VT/VF. These assumptions lead to an estimated probability of survival to hospital discharge of 0.0600 when treated under the AE strategy with a sham valve. We assume that 88.9% of such survivors would have acceptable neurological status (MRS $\leq$ 3) based on a combination of observed rates from the ASPIRE and PAD trials where 35 of 45 and 42 of 45 survivors had CPC scores $\leq$ 2. Therefore we estimate a rate of 0.0533 for neurologically intact survival to hospital discharge under treatment with the AE strategy and a sham valve.

Under the alternative hypothesis used for sample size calculations, the effect of the ITD on neurologically intact survival is presumed to vary by presenting rhythm. Because a more substantial relative benefit is presumed for those patients receiving CPR for a longer period of time, neurologically intact survival is presumed to be 1.4 fold higher for patients treated with the ITD if their presenting rhythm was asystole or PEA. For patients presenting in VT/VF a relative benefit of 1.20 is hypothesized to account for a lesser benefit for those patients who would respond well to early defibrillation. Applying these hypothesized effects to the numbers given above results in an estimated probability of survival to hospital discharge of 0.0753 for patients treated with an ITD under the AE strategy, with a corresponding hypothesized rate of 0.0669 for neurologically intact survival to discharge. Details of these calculations are provided below (Table 3).

Table 3: Estimated proportions of all EMS treated OOHCA patients surviving to discharge and surviving to discharge with MRS ≤ 3 by ITD/sham treatment arm and presenting rhythm.

Presenting Rhythm	Stratum Weight	Sham Device Probability of Survival to Discharge	ITD / Sham Relative Benefit	ITD Probability of Survival to Discharge
Asystole	0.5231	0.0105	1.40	0.0147
PEA	0.2616	0.0420	1.40	0.0588
VT/VF	0.2153	0.2020	1.20	0.2424
Probability of Survival to Discharge (weighted average)		0.0600		0.0753
Probability of Neurologically Intact Survival to Discharge (88.9% of patients surviving to hospital discharge)		0.0533		0.0669

The number of patients to be accrued to the ITD vs. sham device comparison is based on the ability of a one-sided level 0.025 test to reject a null hypothesis that the probability of neurologically intact survival to hospital discharge is 0.0533 on both treatment arms. Sample size computations are based on a two-sample test of binomial proportions using Pearson's chi squared statistic. The test should have approximately 90% statistical power to reject the null hypothesis when the ITD treatment arm would have a 0.0669 probability of neurologically intact survival.

The clinical trial will be conducted using a group sequential stopping rule based on up to three evenly spaced analyses (two interim analyses and the final analysis). The stopping rule corresponds to a Pampallona and Tsiatis design(40) as described in more detail under the monitoring plan. Using that stopping rule, a sample size of 14,154 evaluable patients will provide 90% power to reject the null hypothesis under the conjectured treatment effect.

However, it is anticipated that approximately 4% of accrued patients will be judged nonevaluable due to non-cardiac origin of cardiac arrest or response time in excess of 15 minutes. Hence, a maximum of 14,742 patients will be potentially treated with the ITD or sham device in order to obtain 14,154 evaluable patients for testing the effect of ITD on the primary endpoint of neurologically intact survival to hospital discharge.

The 11 participating ROC sites are estimated to have approximately 10,000 OOHCA treatable by EMS each year, so it is estimated that accrual of 16,542 patients (up to 1,800 during the run-in phase, 14,742 during the actual trial) will require 20 months.

In the event that the Analyze Late vs. Analyze Early (ALvE) intervention is terminated early due to demonstrated superiority of one rhythm analysis strategy over the other, the number of subjects accrued to the study will be increased to achieve the planned maximal sample size in the superior rhythm analysis strategy arm. The primary analyses of the effectiveness of the ITD will then be evaluated in just those patients who were treated with the rhythm analysis strategy deemed to be superior. The stopping rule will be applied to the data in the efficacy population restricted to that superior ALvE treatment arm.

Human Subjects

Risks to Subjects

Population

This study will enroll approximately 16,542 adult patients who have sustained a nontraumatic out-of-hospital cardiac arrest and are known or presumed to be at the local age of consent.

Potential Risks

ITD administration during standard manual CPR has been tested in three animal studies(5, 22, 41) and three human studies(23-25) with no serious device-related adverse effects reported. ITD increases negative intrathoracic pressure and coronary perfusion pressure, which has raised a concern for potential increased pulmonary edema. However previous studies have not observed device-related adverse events.

Other potential concerns are mechanical failure of the device. We will report any evidence of pulmonary edema, or device failure as a serious adverse event. If failure of the device or pulmonary edema occurs (the device fills with fluid twice) in the out-of-hospital setting, application of the device will be immediately stopped and appropriate clinical management undertaken. As part of the training of the prehospital providers for the study, potential signs and symptoms of serious adverse events will be clearly described.

Potential Benefits to Subjects and Society

There are several potential benefits to subjects who receive an active ITD. These include increased venous return, coronary perfusion pressure, cardiac output and admittance to intensive care with the use of the ITD during standard CPR in humans. We contend that use of the ITD may significantly increase survival to hospital discharge. The efficacy of this device can only be assessed by performing clinical studies such as the one proposed in this application.

Inclusion of Women or Minorities

There will be no exclusion on the basis of gender, race or ethnicity. Known pregnant women and prisoners will be excluded. Since this is the first large human trial using the ITD with

standard CPR, there is no available evidence to determine whether or not there is a clinically important sex/gender and/or race/ethnicity difference with its use. Investigators will compare primary and secondary study outcomes between the treatment and control groups broken down by sex/gender and race/ethnicity categories.

Inclusion of Children

The ITD has not been applied during standard CPR in humans < 21 years of age. For this reason, clinical equipoise has not been established in the pediatric population. Therefore the ROC Investigators believe that it is inappropriate to first use the ITD during standard CPR in children in a randomized trial such as that proposed in this protocol. Accordingly, victims of cardiac arrest less than the local age of consent (which varies from 17 to 21 years in ROC sites) will not be entered in the study.

3. Analyze Later versus Analyze Early

Analyze Later Trial - Comparison of a Strategy of Analyze Later Combined with CPR Early Versus a Strategy of Analyze Early Combined with CPR Later in Patients With Out-Of-Hospital Cardiac Arrest

Study Summary

Background: While patients with the shockable rhythms of VF and pulseless VT (PVT) have the best chance of survival of amongst out-of-hospital cardiac arrest victims, the vast majority of such patients do not survive to hospital discharge. The traditional approach to these patients has been to analyze the cardiac rhythm and deliver defibrillatory shocks as quickly as possible with the onset of CPR delayed. Recent thinking suggests three phases for VF cardiac arrest: a) an early “electrical” phase where rapid defibrillation is effective, b) an intermediate phase where “priming” the heart with CPR enhances the effectiveness of defibrillation, and c) a late phase where defibrillation is rarely effective. Some now advocate delaying electrical shocks and providing early CPR in cases of VF where defibrillation cannot be carried out immediately. Three clinical studies have each attempted to evaluate this hypothesis of early CPR and delayed analysis. While two studies supported early CPR and one did not, none were definitive and all had important limitations. We believe there is an urgent need for a large and definitive clinical trial to determine the optimal strategy for rhythm analysis and CPR in patients with out-of-hospital cardiac arrest.

Aims: The primary aim of the trial is to compare survival to hospital discharge with modified Rankin score $\leq$ 3 between a strategy of Analyze Later consisting of CPR first followed by rhythm analysis versus a strategy of Analyze Early consisting of early rhythm analysis in patients with out-of-hospital cardiac arrest. The secondary aims of the trial are to compare survival to discharge, functional status at discharge and at 1, 3 months and 6 months as well as depression at 3 and 6 months.

Hypotheses: The null hypothesis is that survival to hospital discharge with modified Rankin score $\leq$ 3 is identically distributed between Analyze Later versus Analyze Early in patients with cardiac arrest. The secondary null hypotheses are that survival to discharge, functional status at discharge and at 1, 3 months and 6 months as well as depression at 3 and 6 months will be

identically distributed between Analyze Later versus Analyze Early in patients with cardiac arrest.

Design: Cluster randomized trial with cluster units defined by geographic region, or monitor/defibrillator machine.

Population: Patients with non-traumatic out-of-hospital cardiac arrest, known or presumed to be local age of consent or greater and treated by EMS providers.

Setting: EMS systems participating in the Resuscitation Outcomes Consortium and agreeing to cluster randomization to the Analyze Later/Analyze Early intervention in a crossover fashion.

Sample Size: Based on a two-sided significance level of 0.05, a maximum of 13,239 evaluable patients will allow statistical power of 0.996 to detect an improvement in the probability of survival to discharge with modified Rankin score $\leq$ 3 rate from 5.41% after Analyze Early to 7.45% after Analyze Later.

Anticipated Clinical Impact: If this trial demonstrates a significant improvement in survival with a strategy of Analyze Later, we estimate that the premature death of 4,000 victims of cardiac arrest per year would be averted annually in North America alone.

Specific Aims

Primary Aim: The primary aim of this study is to compare survival to hospital discharge with modified Rankin score $\leq$3 in a variety of communities in patients with out-of-hospital cardiac arrest between a protocol of compressions equivalent to approximately 3 minutes prior to cardiac rhythm analysis (Analyze Later) compared with cardiac rhythm analysis as soon as possible after 50 compressions (Analyze Early).

Hypothesis: The null hypothesis is that survival to hospital discharge with modified Rankin score $\leq$3 is identically distributed with use of Analyze Later versus Analyze Early in patients with cardiac arrest.

Secondary Aims*:* The secondary aims of this trial are to compare survival to discharge, functional status scores at discharge and at 1, 3 and 6 months as well as depression at 3 and 6 months between Analyze Later versus Analyze Early in patients with out-of-hospital cardiac arrest.

Hypotheses: The null hypotheses are that survival to discharge, functional status at discharge and at 1, 3 and 6 months as well as depression at 3 and 6 months are identically distributed with use of Analyze Later versus Analyze Early in patients with cardiac arrest.

Prespecified Subgroup Analyses: These include assessment of treatment effect by:

a) Rhythm immediately post electrode placement: VF/VT, PEA, asystole, and not obtained.
b) Response time from 911 call to initiation of EMS CPR <4 minutes and $\geq$ 4 minutes.
c) CPR being performed by bystanders.

Background and Significance

Conceptual Framework for Analyze Later

Our current paradigm of cardiac arrest defines VF as “shockable,” with the optimal therapeutic approach being immediate direct countershock.(42) Integral to this approach is the concept that defibrillation attempts should occur without delay upon recognition of VF, either by prehospital personnel or the analysis software contained within AEDs, which can then be applied by first responders with limited training or even laypersons.(43) This approach has defined current Advanced Cardiac Life Support (ACLS) algorithms and shaped the development of EMS systems, with prehospital providers that can rapidly respond to victims of cardiac arrest, and the placement of AEDs in public areas for use by non-medical personnel. (44-48) The ability to provide early defibrillation has resulted in improved survival for cardiac arrest victims with an initial rhythm of VF in some EMS systems and has defined the current standard of care. (4, 49)

One of the major limitations to this cardiac arrest paradigm is its consideration of VF as homogenous, without regard for variability in VF morphology or elapsed time since the arrest. In contrast, experimental models of VF arrest support three distinct phases, each with a different optimal therapeutic approach.(50) The early moments following arrest define an “electrical phase” during which little ischemic injury has occurred and rapid defibrillation attempts appear to be most efficacious. After some time period, probably around 3-4 min, the optimal therapeutic approach no longer appears to be immediate countershock but instead includes a period of chest compressions prior to defibrillation attempts. It is unclear whether this is related to a “priming” effect with the delivery of substrate necessary for successful return of spontaneous circulation (ROSC) or the removal of toxic metabolites that have accumulated during the ischemic period. Effective chest compressions, traditionally held to provide approximately 30% of normal cardiac output during the first several minutes of CPR, may provide sufficient myocardial perfusion and improve the metabolic state of those myocytes in patients with ventricular fibrillation. Immediate defibrillation attempts during the circulatory phase may be unsuccessful due to persistent or recurrent VF or may result in terminal PEA or asystole. Interestingly, outcomes in patients”shocked” into PEA or asystole are significantly worse than when these are the presenting rhythms. (51)

After some additional elapsed time period, even chest compressions prior to defibrillation attempts do not appear to change outcome. This may be due to the initiation of irreversible ischemic changes that ultimately lead to substantial myocyte and neuronal cell death. This “metabolic phase” is thought to start after about 10 min of total arrest duration, with no currently available therapies demonstrating efficacy once this phase is reached.

Preliminary Studies

The effect of early rhythm analysis versus later rhythm analysis has been evaluated in animal and human studies. Animal models demonstrate improved ROSC and neurological outcomes with delayed countershock following a period of chest compressions in VF of moderate duration.(52-55) Several investigators have utilized this period of chest compressions as a therapeutic window in which to deliver various pharmacological agents designed to increase the likelihood of successful ROSC and improve neurological outcomes. Yakaitis et al compared immediate countershock to delayed defibrillation following administration of epinephrine and 5 min of chest compressions in a dog model of VF.(52) Immediate defibrillation was superior with VF of 1- or 3-min duration, while the delayed approach was optimal with VF of 5- or 9-min duration. Niemann et al observed improved outcomes with delayed countershock following administration of epinephrine and 5 min of chest compressions alone with a VF duration of 7.5 min but not 5 min in a swine model.(53) Menegazzi et al observed substantially higher ROSC and better neurological outcomes with administration of a pharmacologic “cocktail” followed by chest compressions alone prior to defibrillation attempts versus immediate countershock in a swine model of VF of 8-min duration.(54, 55)

Other parameters besides duration of ischemia may better indicate the likelihood of successful defibrillation in VF arrest victims. Various VF morphologic features have been identified as potentially useful in predicting successful defibrillation in animal models of VF.(56-58) Limited human data exist to support morphological analysis of VF/PVT as a predictor of successful ROSC.(58-60) In addition, animal and human data suggest that chest compressions alone can modulate these morphological features to a more favorable configuration for successful ROSC. (57-59) Berg et al used a swine model of VF to demonstrate that CPR alone can modulate VF median frequency to a value predictive of successful defibrillation; improvements in ROSC and cardiac function at 1 hour were also observed with CPR prior to defibrillation attempts.(57) Eftestol et al demonstrated improvements in spectral flatness measure, centroid frequency, and amplitude spectrum relationship. Improvement in ROSC was also observed in patients with at least 3 min of chest compressions prior to countershock. None of these morphological features have demonstrated adequate predictive value to justify their clinical use; however, these data further support the therapeutic value of chest compressions prior to defibrillation in VF of moderate duration. Finally, the duration between cessation of chest compressions and direct countershock appears to influence success of ROSC and ultimate survival.(61, 62) This suggests that prehospital providers should attempt to minimize delays after chest compressions due to rhythm analysis or ventilation prior to defibrillation attempts.

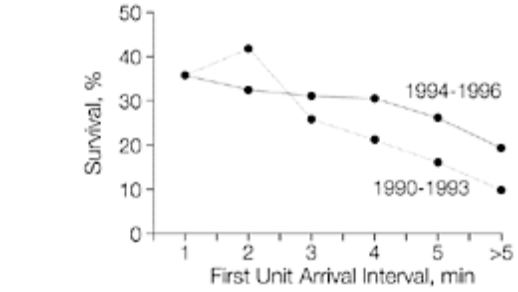
Clinical Studies

Three clinical studies have compared outcomes from out-of-hospital cardiac arrest due to VF when a period of CPR has or has not been prescribed prior to the first attempts at defibrillation.(63-65)

Cobb et al. conducted an observational, population-based study(63) of 639 patients treated for out-of-hospital VF at a time when AED application and use was given the highest priority compared with 478 patients for whom 90 seconds of chest compressions and ventilation (CPR) were mandated before AED application and use. An a priori hypothesis was that the survival benefit would be most evident in those cases with the greater delay from collapse to delivery of the first shock. Survival to hospital discharge and favorable neurological status at discharge (defined as full or nearly full neurological recovery, or requiring some but not complete dependence upon others for assistance in activities of daily living) were the primary outcomes of the study.

Survival to hospital discharge was greater during the intervention period (mandated CPR prior to shock) than in the preintervention period (high priority for AED use): 30% vs. 24% ($p=0.04$). There was a non-significant trend toward a more favorable neurological outcome observed during the intervention period (79% of patients with mandated CPR versus 71% of patients in whom AED use was prioritized, $p=0.11$). A significant interaction also described a relatively greater survival benefit for CPR before defibrillation as the response interval of the first arriving unit increased, particularly in cases in which the response interval of the first arriving unit was 4 minutes or longer ($p=0.04$) (Figure 4).

Figure 4: Survival versus Response Time Interval With and Without Initial CPR



1990-1993, No. (n=639)	22	91	205	164	86	71
1994-1996, No. (n=478)	14	80	164	114	65	41

Although its hypotheses were prospectively defined, this study was observational, and hence subject to the influence of factors, including the potential biases inherent in non-randomized studies that tend to overestimate treatment effects. For example, a change in the *sequence* of CPR could have been accompanied by an unconscious change in *emphasis* of CPR over shock or even over other interventions during resuscitation. As the authors themselves stated, their "observations represent an encouraging pilot study and that the development of randomized clinical trials be considered to evaluate further the influence of CPR before the delivery of a shock for patients who have a significant delay prior to treatment".

Wik et al. (64) conducted a randomized trial of 200 patients with out-of-hospital cardiac arrest due to VF to compare standard care with immediate defibrillation (n=96) or 3 minutes of basic CPR prior to defibrillation (n=104). In both treatment groups, if three sequential defibrillations were unsuccessful, 1 minute of CPR was given for VF/VT or three minutes for other rhythms before a new rhythm analysis. Based on the report by Cobb et al that was published subsequent to the start of the study but before analysis of outcomes, the authors hypothesized that survival benefit would be most evident in cases with longer response intervals, and analyzed subgroups with response times either up to or longer than 5 minutes.

The primary outcome of survival rate to hospital discharge did not differ significantly between the two treatment arms of the study (22% in those randomized to CPR-first versus 15% in the standard group, p=0.17). Nor were there significant differences in ROSC, 1 year survival, "good neurological recovery" at hospital discharge or 1 year after cardiac arrest between treatment groups. For those with a response time interval (time from dispatch to arrival of first EMS provider) of 5 minutes or less, there were no significant differences in ROSC, survival to hospital discharge, 1 year survival, or neurological outcome of survivors. Among 119 patients with response times longer than 5 minutes, more patients in the CPR first than in the standard group achieved ROSC (58% vs. 38%, p=0.04), survived to hospital discharge (22% vs. 4%, p=0.006) and survived to 1 year (20% vs. 4% p=0.01).

However the criterion for statistical significance in this trial ($p<0.05$) was not adjusted for sequential monitoring performed at six, 18 and 30 months, nor for subgroup analysis. The reported confidence intervals surrounding the estimated benefit were also wide. Hence the findings of this study have to be interpreted with caution, and the observed results not interpreted as definitive of benefit from a CPR first strategy. Moreover, this study had a long interval from collapse to EMS arrival (approximately 12 minutes), limiting the generalizability of the conclusions.

Jacobs et al. conducted a prospective prehospital randomized trial performed in Western Australia which randomized 256 patients to a strategy of 90 seconds of CPR before defibrillation versus immediate defibrillation.(65) Survival to hospital discharge was not significantly different in the CPR first group, 4.2%, compared with 5.1% in the immediate

defibrillation group. There was no significant difference in survival to hospital discharge among patients with a response interval of ≤5 versus >5 minutes (12% in the CPR first group, compared with 0% in the immediate defibrillation group among patients with a response interval ≤5 minutes (p= 0.24); and 3.5% vs. 4.9%, respectively, among patients with a response interval of >5 minutes (p=0.7). Unfortunately this trial was underpowered due to failure to recruit a total sample size of 390 patients, lower than expected baseline survival rates, and exclusion of 41 eligible cases. Notably, the overall low survival rate and longer response intervals observed in this trial should have favored a greater benefit from CPR before defibrillation if the interactions observed by Wik and Cobb et al. between survival and benefit from CPR hold true.

Summary of Rationale

Survival after cardiac arrest is poor. The most treatable arrhythmias immediately following cardiac arrest are VF and PVT. Current ACLS algorithms emphasize the importance of immediate defibrillation attempts in these patients. While it has been recognized for many years that chest compressions on OOH-CA patients who received "bystander CPR" result in positive outcomes,(66) this impact has been relegated to a secondary or even tertiary role in resuscitation sequencing. Small randomized or observational studies suggest that CPR before defibrillation may increase survival but the results to date are inconclusive. Although there is some evidence that favors immediate defibrillation in cases where the response time is ≤ 2 minutes, such response times are rare and the frequent delay in recognition of the OOH-CA and calling 911, as well as the complexity of the resuscitation protocol, convince us that response time should not be used as an intervention modifier. We believe that there is clinical equipoise with regard to the competing strategies of Analyze Early vs. Analyze Later. A large, randomized clinical trial is needed to examine the impact of delayed defibrillation on survival to hospital discharge in patients who are presumed to be without circulation for several minutes. Since the only cost of the intervention is training or retraining providers, the proposed study has the potential to have substantial impact upon prevention of premature cardiac death at comparatively little cost.

Research Design and Methods

Study Design Overview

This protocol will be a single-blinded (i.e. blinded to data management team) cluster randomized crossover controlled trial with two intervention groups: a) an Analyze Early group, and b) Analyze Later group. Subjects in the Analyze Early group will be assigned to receive 50 (or more) compressions of CPR prior to early ECG analysis and defibrillation shocks if indicated and those in the Analyze Later group will receive compressions equivalent to approximately 3 minutes of CPR prior to ECG analysis and rescue defibrillation. The intervention will be implemented by the first qualified provider to arrive at the scene of cardiac arrest and continued by subsequent providers in all ROC sites. Qualified providers are defibrillation-capable first-responders, emergency medical technicians (EMTs), and paramedics.

We will include all out-of-hospital locations within the participating study communities within the Resuscitation Outcomes Consortium and served by an EMS agency participating in the Analyze Later/Analyze Early intervention (the Seattle Medic One EMS agency is participating only in the ITD/sham device intervention of the partial factorial ROC PRIMED study). Outcomes will be assessed in the field and at the receiving hospitals.

Study Population

Inclusion Criteria

All persons of local age of consent or older who suffer non-traumatic cardiopulmonary arrest outside of the hospital in the study communities with defibrillation and/or delivery of chest compressions provided by defibrillation equipped EMS providers dispatched to the scene and do not meet any of the exclusion criteria below.

Exclusion Criteria

– Do not attempt resuscitation (DNAR) orders;
– Blunt, penetrating, or burn-related injury;
– Patients with exsanguinations;
– Known prisoners;
– Known pregnancy;
– EMS-witnessed arrests;
– Non-EMS rhythm analysis (AED placed by police or lay responder is an exclusion but CPR by lay or other non-EMS responders is not);
– Non-ROC EMS agency/provider on scene and CPR begun or pads placed.

EMS responders will generally provide CPR according to the cluster randomization even for patients with exclusions. Those with a clear exclusion will not be included in the primary analysis. However, all eligible patients are considered enrolled into the Analyze Later protocol regardless of how they are treated and will be included in the primary analysis.

Primary Comparison Populations

The Analyze Late treatment strategy is conjectured to provide an improvement in the rate of neurologically intact (MRS $\leq$ 3) survival to hospital discharge in those patients experiencing OOHCA of cardiac origin unwitnessed by EMS and not previously defibrillated. EMS witnessed OOHCA should be treated by an Analyze Early strategy. There is, however, no contraindication to the use of either Analyze Late or Analyze Early in the relatively few patients experiencing OOHCA due to such noncardiac events as strangulation, drowning, or electrocution. In the emergency setting, unnecessarily introducing a need for EMS providers to evaluate eligibility criteria and randomize individual patients could potentially delay the institution of appropriate life saving treatments. Furthermore, if either the Analyze Late or Analyze Early strategy is proven superior to the other and therefore adopted widely, the eventual use of the superior treatment strategy would likely be applied to all OOHCA unwitnessed by EMS. Hence, this study protocol uses cluster randomization and allows for the evaluation of the safety of the treatment strategies in some patients for whom there is no conjecture of clear benefit. On the other hand, efficacy of the treatment strategies will be analyzed in only those patients who are determined to meet the criteria defining the pre-hospital conditions for which the Analyze Late strategy is conjectured to be of benefit.

Efficacy Population: Analysis of primary and secondary efficacy outcomes will be conducted on a modified intent-to-treat basis. In order to be included in the efficacy analyses, patients must meet the inclusion/exclusion criteria for the Analyze Late vs. Analyze Early intervention. In particular, they must not have DNAR orders, have blunt or penetrating traumatic injury or burns, be visibly pregnant, a prisoner, a minor, or have had OOHCA witnessed by EMS. Furthermore, in order to be evaluable, they must also have not have experienced cardiac arrest secondary to drowning, electrocution, or strangulation.

Safety Population: Evaluation of the safety of the Analyze Late versus Analyze Early strategies will be made using all data from patients who were treated, regardless of whether

they are a member of the efficacy population or not. This will include patients who were defibrillated by ROC EMS providers but did not receive CPR from ROC EMS providers.

Random Allocation

The intervention will be randomly allocated according to the cluster assignment (i.e., Analyze Later or Analyze Early). Each ROC site has been subdivided into multiple clusters (see Sample Size section below) by various means. We believe that randomization by event or by individual patient is not feasible because the intervention is a psychomotor skill and there would be a significant risk of carryover effect from event to event. In addition, randomization by event would add unacceptable complexity for EMS providers who already must deal with randomization of the ITD protocol. Each RCC will be subdivided into a goal of at least 20 clusters by the following means: a) according to EMS agency or geographical boundaries, or b) according to individual defibrillator devices, rig, or station.

The randomization of clusters will be stratified by site. Within each site, clusters will be organized in blocks of varying size (hidden from investigators) according to the number of patients expected to be treated over the course of the study in that cluster. Within each block, clusters will be assigned in equal numbers to order of treatment. All clusters will crossover between intervention assignments at least once (i.e. have at least two distinct treatment periods). Some clusters will crossover more than once (e.g. have four or more distinct treatment periods). There will always be an even number of treatment periods. Among clusters having a single crossover, equal numbers will be assigned to Analyze Late first and Analyze Early second as are assigned to Analyze Early first and Analyze Late second. Among clusters having four treatment periods, equal numbers within each block will be assigned to each of the following four orders of treatment: Late-Early-Late-Early, Late-Early-Early-Late, Early-Late-Late-Early, and Early-Late-Early-Late. Randomization assignment will be performed at the Data Coordinating Center prior to the start of the study. Clusters will not be informed as to which group they are assigned until it is time to crossover to another intervention. Responders will, however, know that each intervention will be tested in the first two periods, and each intervention will be tested in the last two periods in each cluster.

Intervention

Detailed descriptions and algorithms demonstrating the sequence of action for Analyze Early versus Analyze Later with use of an ITD are presented in Section 4. For those clusters allocated to Analyze Later, defibrillator analysis will not be initiated until after delivery of compressions equivalent to approximately 3 minutes of CPR, after which a rescue shock will be administered, if indicated. For those clusters allocated to Analyze Early, defibrillator analysis will not be initiated until the chest compression count reaches 50 (e.g., 30-60 seconds), or as soon thereafter as possible, after which a rescue shock will be administered if indicated.

Both Early and Later Arms

Chest Compressions: Initiation of chest compressions will not be delayed. Recognition that a patient is in cardiac arrest will immediately prompt one rescuer to initiate and count chest compressions. If the scene is first attended by two EMS rescuers, chest compressions will be performed by one while the second will set up the monitor/defibrillator and place the defibrillator pads. Then ventilation with the ITD will proceed. If three rescuers are present, ventilation and defibrillation readiness can proceed simultaneously (see Appendix 3 for Resuscitation Standards).

Minimum Interruptions: Training will emphasize that chest compressions should not be interrupted, except for required ventilations. If endotracheal intubation or other advanced airway procedures are deemed medically necessary, the providers should proceed, but continue chest compressions with minimum interruption. However, training will emphasize that interruption of chest compressions while securing the airway may dilute the theoretical benefit of the initial intervention. Interruption of chest compressions for airway manipulations will be documented when feasible.
ITD Use: Training will emphasize that rescuers will use the ITD during initial airway management (either facemask or advanced airway).

Analyze Later Arm

AED analysis will not be initiated until the chest compression count reaches 300, after which a rescue shock will be administered if indicated.

Analyze Early Arm

Analysis will be initiated as soon as defibrillation pads are in place and 50 compressions have occurred and a rescue shock will be administered if indicated. The rescuers will note the compression count or time that has been reached by the rescuer assigned to CPR. After the initial analysis, the standard resuscitation protocol will be followed.

Arrival of Additional EMS Personnel

In tiered response systems, or when backup EMS crews arrive on scene, first-responders delivering the chest compressions consistent with cluster assignment prior to initial ECG analysis should complete this intervention even if paramedics arrive on scene, and, if the subject has defibrillation pads in place, continue using the first crew's equipment until the first ECG analysis (and shock, if indicated).

Additional personnel are encouraged to assist with ongoing activities that do not interrupt chest compressions or initial rhythm analysis. For example, airway management, rotation of chest compressions, and placement of AED/monitor electrodes may benefit from additional personnel. If sufficient personnel arrive, they may also begin attempts at IV access.

Adherence to Protocol

Personnel will be discouraged from terminating the protocol prematurely. As intention-to-treat principles apply, any breach of protocol will not alter the study group to which a patient has been assigned.

Intervention – Compliance

The time interval from power-on to first ECG analysis (power-to-analysis interval) and to first rescue shock (power-to-shock) will be calculated from the time stamps on the electronic record. Explicit criteria will be used to define successful delivery of the intended therapy and this information will later be fed back to the EMS providers (Table 4).

Table 4: Intervention Compliance Time Intervals

	Power-to-analysis interval	Power-to-shock interval
Analyze Early	30-60 seconds	<90 seconds
Analyze Later	180-200 seconds	180-220 seconds

Outcome Measures

Primary

The primary outcome is survival to hospital discharge with modified Rankin score ≤ 3. Patients who are transferred to another acute care facility (e.g., to undergo ICD placement) will be considered to be still hospitalized. Patients transferred to a non-acute ward or facility will be considered discharged.

Secondary Outcomes

The secondary outcomes are survival to discharge; MRS at 3 and 6 months following hospital discharge; Adult Lifestyle and Function (ALFI) version of the Mini-Mental Status Exam (MMSE) at 1, 3 and 6 months;(31, 32) Health Utilities Index III (HUI3) score(33) at 3 and 6 months following hospital discharge; and Geriatric Depression Scale (T-GDS)(34) score at 3 and 6 months (details in Section 4 and Appendix 4).

Exploratory

Cerebral Performance Category (CPC) will be assessed at discharge, 3 and 6 months following hospital discharge.

In-Hospital Morbidity

Number of hospital days and time interval from 911 call to patient death will be described for all hospitalized patients as measures of morbidity after resuscitation.

Analyses Methods

Primary Efficacy Analysis

The primary analysis of treatment efficacy will be based on a comparison across treatment arms of the observed proportion of patients in the efficacy population with neurologically intact (MRS ≤ 3) survival to hospital discharge. A two-sided level 0.05 hypothesis test will be used to test the null hypothesis of equal rates of such favorable events (H_0: $\pi_{AE} = \pi_{AL}$) versus the alternative hypothesis that patients on the Analyze Late arm have a different probability of neurologically intact survival to hospital discharge than do patients on the Analyze Early arm (H_1: $\pi_{AE} \neq \pi_{AL}$). The data will be analyzed in the context of a generalized linear mixed effects model which includes a fixed effect for treatment arm and random effects for each randomization cluster. The test statistic comparing treatment arms will be the Wald statistic computed as the regression parameter estimate for the treatment indicator divided by its estimated standard error. The fixed sample upper one-sided P value corresponding to that Z statistic will be compared to the boundaries of the protocol defined group sequential stopping rule when expressed on the fixed sample P value scale. At the end of the study, analysis results will be summarized using point estimates of the difference in probability of favorable events, 95% confidence intervals, and P values adjusted for the true sampling distribution imposed by the group sequential stopping rule. (See the discussion of the group sequential monitoring plan below.)

Secondary Efficacy Analyses

All secondary analyses of efficacy endpoints are directed toward finding supporting evidence for the findings of the primary efficacy analysis. As such, they will not be used as the primary basis for establishing superiority of one treatment strategy over the other. Hence, there is no plan to make any statistical adjustment for the multiple comparisons inherent in the secondary efficacy analyses, which include:

Modified Rankin Score (MRS) at hospital discharge. The mean MRS at hospital discharge will be compared across treatment groups using a general linear mixed model including the binary variable indicating AL vs. AE assignment and random effects for the randomization clusters. For the purposes of this analysis, patients dying before admission to the hospital will be treated the same as admitted patients dying before hospital discharge and will be assigned an MRS of 6.

Survival to hospital discharge. This secondary analysis of treatment efficacy will be based on a comparison across treatment arms of the observed proportion of patients in the efficacy population with survival to hospital discharge. This analysis shall proceed in a manner entirely analogous to that for the primary efficacy endpoint.

Neurologically intact survival to hospital discharge adjusted for prognostic variables. A secondary analysis of the primary endpoint will adjust for those pre-randomization variables which might reasonably be expected to predictive of favorable outcomes. Generalized linear mixed models will be used to model the proportion of subjects with neurologically intact (MRS $\leq$ 3) survival to hospital discharge by AL vs. AE group adjusted for randomization cluster (random effect), site (dummy variables modeling the 11 ROC sites), patient sex, patient age (continuous variable), witnessed arrest (binary variable), location of arrest (public versus non-public), time of response (continuous variable modeling minutes between call to 911 and arrival of EMS), presenting rhythm (dummy variables modeling asystole, PEA, VT/VF, or unknown), and treatment assignment in the ITD/sham device intervention. The test statistic used to assess any benefit of one strategy over the other will be computed as the generalized linear mixed model regression coefficient for the AL vs. AE treatment assignment divided by the estimated standard error. Statistical inference will be based on one-sided P values and 95% confidence intervals which adjust for the stopping rule used for the primary analysis.

Post-discharge neurological function, quality of life, and depression. Surviving patients will be contacted post-discharge to obtain consent for additional follow-up via telephone with consenting patients or their proxies regarding cognition, quality of life, and depression. Primary emphasis will be placed on analysis of outcomes at 6 months post hospital discharge, though additional analyses will also compare these secondary endpoints 3 months after hospital discharge. Analyses of each of these outcomes at each time point will be compared across treatment groups using a general linear mixed model including the binary variable indicating AL vs. AE assignment and random effects for the randomization clusters. Analyses will first be conducted conditional on survival to the relevant time point by using only data from those patients offering consent, as well as using data imputed from discharge data for those surviving patients refusing consent. The data missing due to lack of consent for follow-up will be multiply imputed using measurements of patient age, sex, length of hospital stay, incidence of major adverse outcomes during hospitalization, MRS at hospital discharge, and whether the patient was discharged to home or a nursing facility. Additional analyses of neurological function and quality of life will then incorporate measurements for patients dying prior to hospital admission, during hospitalization, or within 3 or 6 months post discharge. Dead patients will be assigned the worse category of neurological function and quality of life for each measurement.

Morbidity As a measure of morbidity during hospitalization, the number of days hospitalized conditional upon survival to discharge will be compared across treatment groups using the t test which allows unequal variances. A similar analysis will also be conducted comparing the days of hospitalization for patients admitted to the hospital, but dying prior to hospital discharge. Finally, treatment groups will also be compared with respect to the number of days alive post hospital

discharge during the first 6 months post OOHCA in order to incorporate information about both dead and surviving patients. In this analysis, data missing due to lack of consent for follow-up will be multiply imputed using data available at hospital discharge, and patients dying before hospital admittance or prior to hospital discharge will be scored as 0.

Safety Analyses

The incidence of adverse events will be recorded for all patients in the safety population and presented by treatment arm (AL vs. AE) to the DSMB for their review during the conduct of the study, as well as summarized and compared across treatment arms in the final report of study results. Statistical significance of differences in the incidence of safety endpoints plays a lesser role, due to the need to be cautious in the introduction of new treatments in a human population. Hence, emphasis is placed on the presentation of results, with statistical tests provided for guidance on the precision of estimates as indicated.

Since both interventions, Analyze Early and Analyze Late, are in current use, there is no anticipation that the study itself will present any safety issue, for example, because of new or difficult procedures. Indeed, one would expect a study benefit in any treatment arm because of the increased training and monitoring of CPR performance. Nevertheless specific measures that will be monitored include:

Delay of treatment. Witnessed episodes of cardiac arrest with response times (911 call to arrival) of less than 4 minutes might be expected to respond to early defibrillation. This subgroup of patients will be carefully monitored for potential harm from an Analyze Later strategy. The Data and Safety Monitoring Board will be asked to make recommendation concerning protocol modification, should any safety issue appear.

Compliance with protocol. Patients with EMS witnessed arrest are to be treated with early analysis for defibrillation regardless of cluster randomization to AL or AE. The adherence of EMS providers to this aspect of the protocol will be closely monitored. In addition, sites will be monitored with respect to adherence to the guidelines for either the Analyze Late or Analyze Early strategies according to the cluster randomization scheme. In particular, adherence to protocol will be monitored and reported separately for times immediately preceding and following sites' crossover from one strategy to the other. The Data and Safety Monitoring Board will be asked to make recommendation concerning protocol modification, should any safety issue related to protocol adherence appear.

Serious adverse events. The incidence of each serious adverse event, along with other major adverse medical or surgical outcomes identified during review of hospital records, will be tabulated by treatment arm and compared when indicated using Pearson's chi squared test. In order to facilitate the identification of differences in rates of such events that might be due to greater survival to hospital admission and/or hospital discharge on one of the treatment arms, the incidence of any of the above specific events and/or death (either prehospital or during hospitalization) will be reported in a combined fashion and compared as indicated using Pearson's chi squared statistic.

Subgroup Analyses

Analyses will be performed in each subgroup, along with tests for statistically significant interactions. However, it is recognized that the study is not powered adequately to detect interactions, and thus all subgroup analyses are judged exploratory.

Sample Size, and Study Duration

The sample size for the factorial trial is driven by the power analysis for the ITD intervention. A full description of the assumptions that were used to estimate the sample size required for that intervention is given in section 2. The anticipated distribution of patients by presenting rhythm and whether arrest was EMS witnessed or not was estimated based on these assumptions (Table 5.)

Table 5: Proportion of all EMS treated OOHCA patients according to presenting rhythm and EMS Witness status

Presenting Rhythm	EMS Witnessed	EMS Unwitnessed	Total
Asystole	0.0231	0.4769	0.500
Pulseless Electrical Activity (PEA)	0.0270	0.2230	0.250
VT/VF	0.0499	0.2001	0.250
TOTAL	0.1000	0.9000	1.000

Eligibility criteria for the AL vs. AE intervention excludes subjects for whom the arrest was witnessed by EMS. The distribution of patients to the various treatment strategies by presenting rhythm was estimated by taking into account that patients with EMS Unwitnessed OOHCA will be randomized (by cluster) in a 1:1 ratio to the AE or AL strategies (Table 6).

Table 6: Proportion of all EMS treated OOHCA patients randomized to treatment combinations according to presenting rhythm and EMS Witness status

Initial Rhythm	EMS Witnessed CA or Seattle Medic One (AL vs. AE Ineligible)			Analyze Early			Analyze Late		Total AE vs AL Randomized	
	No Device	Sham	ITD	No Device	Sham	ITD	Sham	ITD	AE	AL
Asystole	0.000	0.018	0.018	0.000	0.116	0.116	0.116	0.116	0.232	0.232
PEA	0.000	0.017	0.017	0.000	0.054	0.054	0.054	0.054	0.109	0.109
VT/VF	0.015	0.020	0.020	0.029	0.034	0.034	0.049	0.049	0.097	0097
TOTAL	0.015	0.055	0.055	0.029	0.204	0.204	0.219	0.219	0.438	0.438

Based on ranges of estimates in published data and results of the ASPIRE trial, and allowing for 1-5% improvement due to greater quality control on CPR process in the clinical trial setting, It is estimated that in the absence of an ITD and when managed according to the Analyze Early (AE) strategy, the probability of survival to hospital discharge would be 1.05% for patients presenting with asystole, 4.02% for patients presenting with PEA, and 20.20% for VT/VF. These assumptions lead to an estimated probability of survival to hospital discharge of 0.0609 when treated under the AE strategy with a sham valve. Assuming that 88.9% of such survivors would have acceptable neurological status (MRS $\leq$ 3), we thus estimate a rate of 0.0541 for neurologically intact survival to hospital discharge under treatment with the AE strategy and a sham valve.

Under the alternative hypothesis used for power calculations, the effect of the Analyze Late strategy on neurologically intact survival is presumed to vary by presenting rhythm. While patients with initial rhythms of asystole and PEA cannot expect to benefit from an Analyze Early versus Analyze Later protocol in the sense of potentially obtaining early defibrillation, they could benefit from the Analyze Later strategy by having fewer delays in blood circulation due to taking time for early analysis. We therefore hypothesize a 3% relative increase in survival for patients in the AL arm over the AE arm for these two rhythms. A relative benefit of 1.50 is hypothesized

for those patients in the VT/VF, with the benefit occurring primarily in patients who would not respond rapidly to early defibrillation, though that group cannot be identified *a priori.* Applying these hypothesized effects to the numbers given above results in an estimated probability of survival to hospital discharge of 0.0838 for patients treated with an AL strategy in the absence of an ITD, with a corresponding hypothesized rate of 0.0745 for neurologically intact survival to discharge. Details of these calculations are provided below (Table 7).

Table 7: Estimated proportions of all EMS treated OOHCA patients surviving to discharge and surviving to discharge with MRS ≤ 3 by AL vs. AE treatment arm and presenting rhythm

Presenting Rhythm	Stratum Weight	Analyze Early Probability of Survival to Discharge	AL / AE Relative Benefit	AL Probability of Survival to Discharge
Asystole	0.5299	0.0105	1.03	0.0108
PEA	0.2478	0.0420	1.03	0.0433
VT/VF	0.2224	0.2020	1.50	0.3030
Probability of Survival to Discharge (weighted average)		0.0609		0.0838
Probability of Neurologically Intact Survival to Discharge (88.9% of patients surviving to hospital discharge)		0.0541		0.0745

In the process of accruing 14,154 evaluable patients to the ITD/sham device intervention, it is estimated that approximately 15,423 patients with OOHCA will be treated by EMS at one of the participating ROC sites, with approximately 13,509 of these patients eligible to participate in the Analyze Late or Analyze Early interventions. Estimating that 98% of these patients will be judged evaluable, 13,239 patients will be used for the comparison of Analyze Late versus Analyze Early strategies. We therefore consider the ability of a two-sided level 0.05 test with 13,239 subjects to reject a null hypothesis that the probability of neurologically intact survival to hospital discharge is 0.0541 on both treatment arms, with statistical power computed under the alternative hypothesis that the AL arm would instead have a 0.0745 probability of neurologically intact survival. The data will be analyzed in the context of a generalized linear mixed effects model which includes a fixed effect for treatment arm and random effects for each randomization cluster. The test statistic comparing treatment arms will be the Wald statistic computed as the regression parameter estimate for the treatment indicator divided by its estimated standard error. Power computations are based on formulas appropriate for a two-sample test of binomial proportions using Pearson's chi squared statistic. We incorporate into those computations an assumed 5% loss of efficiency due to the cluster randomization with crossover.

The clinical trial will be conducted using a two-sided level 0.05 group sequential stopping rule based on up to three analyses (two interim analyses and the final analysis) after accruing approximately one-third, two-thirds, and all of the maximal sample size. The stopping rule corresponds to an O'Brien-Fleming design as described in more detail under the monitoring plan. Using that stopping rule, a sample size of 13,239 evaluable patients will provide approximately 99.6% power to reject the null hypothesis under the conjectured treatment effect.

The 11 participating ROC sites are estimated to have approximately 10,000 OOHCA treatable by EMS each year, so it is estimated that accrual of 13,239 evaluable patients for the Analyze Late versus Analyze Early comparison will require 20 months.

Effect of Clustering and Crossover Upon Required Sample Size

It is anticipated that the number of cardiac arrest episodes in each cluster will vary, as the underlying size of the geographic area and population served are variable. Some sites will cross a large geographic area over from one intervention to the other during the trial to reduce the expected number of episodes; others will cross monitor/defibrillators from one intervention to the other. Most cluster designs assume equal-sized clusters, but the presence of unequal cluster size has implications for sample size (Appendix 5).

The clusters and annual expected number of cardiac arrests episodes in each site are shown below (Table 8). Since most clusters employ crossover, and those that do not have small expected numbers, the effective sample size of each cluster should be at least 95% efficient compared to individual randomization. This is a conservative assumption since utilizing the crossover design is actually more efficient then even individual randomization.

Having close to 20 or more clusters at each site with no overly large cluster, as well as using crossover and randomizing so that each intervention is being used by half of the clusters at any time will provide reasonable balance between temporal factors, as well as system and patient factors.

We can think of no likely crossover effect except that compliance might be compromised by habit or forgetfulness at the time of crossover. We will be monitoring compliance, and if non-compliance is $\geq$2-fold higher in the 2 weeks following crossover than in the several months before at a site level, then all episodes from that 2-week period at that site will be dropped from the primary analysis. Of course, measures would be taken by the local site to address the "crossover compliance" issue.

Other designs were taken into consideration, particularly individual episode randomization. Devices (AEDs) are not currently capable of being programmed to randomize individual episodes and then provide correct prompts. Other forms of individual randomization (e.g. envelope) would therefore result in expecting EMS providers to ignore existing prompts. The consensus of the ROC investigators was that this would create serious compliance issues and individual randomization was not seen as a viable option. The simplest design is to invoke cluster design without crossover. This method is less efficient then crossover, or individual, randomization. Therefore clustering design with crossover is seen as the most efficient design from the choice of feasible and practical designs.

Table 8: Summary of ROC Site Cluster Plans

	Pop Served (#)	Annual CA Treated (#)	Cluster Type	# of Clusters
Toronto	**2,456,800**	**1,777**	geographic, agency, station	**214**
Alabama	**1,278,936**	**485**	rig	**75**
Portland	**1,444,219**	**604**	agency, station defib	**166**
Pittsburgh	**670,911**	**690**	rig	**124**

Seattle/King Co	**1,191,204**	**555**	agency, geographic	**31**
Dallas	**2,023,705**	**1,331**	rig	**151**
Ottawa	**3,000,000**	**1,468**	geographic, agency, defib	**246**
Milwaukee	**928,018**	**794**	station	**61**
BC	**3,115,331**	**1,364**	geographic	**32**
San Diego	**2,900,000**	**2,161**	rig	**334**
Iowa	**956,188**	**875**	geographic	**15**
Totals	19,965,312	12,104		1449

4. Factorial Implementation of Both Protocols

Summary

The background, significance, aims, and hypotheses of the ITD and Analyze Later versus Analyze Early trials have been previously described. Investigators intend to implement these studies simultaneously (though staggered start and stop times may occur because of resource/regulatory logistics), capitalizing on the common infrastructure necessary to accomplish the studies, thereby improving efficiency and speed of their completion. The following describes study issues common to both the ITD and Analyze Later versus Analyze Early studies including Study Setting, Study Population, Resuscitation Guidelines, Monitoring of CPR Process, Outcome Measures, Data Collection, Training, Data Safety Monitoring Strategy (DSMB), and Human Subjects.

Setting

The Resuscitation Outcomes Consortium (ROC) includes ten Regional Clinical Centers. These ROC sites are served by approximately 200 EMS agencies. The baseline characteristics of these ROC sites are summarized in Table 9. Of greater than 12,000 cardiac arrest episodes among the sites, annually, approximately 10,000 are treatable by EMS.

Table 9: Distribution of Initial Cardiac Rhythm and Outcome for Cardiac Arrest Episodes Among ROC Sites

	Dallas	Iowa	Milwaukee	Ottawa	Ottawa	Pittsburgh	Portland	Seattle	Seattle	Alabama	Toronto	San Diego	Total
EMS System	Biotel			OPALS	BC			King County	Seattle EMS				
Year Reported	2003	2003	2004	2002	2003	Average of 1998-2002	2003	2003	2003	2004	2002	2004	
Population Served	2M	956k	928k	3M	3.1M	671k	1.4M	1.2M	600k	1.3M	2.5M	2.9M	20.6M
VF or PVT	297	294	162	470	431	235	151	158	95	106	462	648	3509

Survived to discharge	50	44	32	62	74	33	37	44	29	24	39	97	565
Received <=1 shock	178	217	158	281	258	141	112	116	70	73	120	427	2151
Asystole	676	349	437	601	577	289	211	235	147	285	817	1102	5726
Survived to discharge	14	5	10	5	12	12	3	6	0	5	7	33	112
PEA	358	232	195	397	356	166	242	162	91	94	498	411	3202
Survived to discharge	25	12	18	9	7	10	15	16	12	6	12	21	163
													Totals
Cardiac arrests	1331	875	794	1468	1364	690	604	555	333	485	1777	2161	12437
Survived to discharge	89	61	60	76	93	55	55	66	41	35	58	151	840

Note: Shaded numbers are estimated

Study Population

Except for some specific situations, the inclusion and exclusion criteria for both ITD and Analyze Later protocols will be the same.

Inclusion Criteria

All persons of local age of consent or older who suffer non-traumatic cardiopulmonary arrest outside of the hospital in the study communities with defibrillation and/or delivery of chest compressions provided by EMS providers dispatched to the scene and do not meet any of the exclusion criteria below.

Common Exclusion Criteria

– Do not attempt resuscitation (DNAR) orders;
– Blunt, penetrating, or burn-related injury;
– Patients with exsanguinations;
– Known prisoners;
– Known pregnancy.

ITD Exclusion Criteria

– Tracheostomy present;
– CPR performed with any mechanical compression device (e.g. AutoPulse, Thumper, ACD-CPR).
– Ventilated with a mechanical device (e.g. automated transport ventilator). Note: a bag-mask is not considered a mechanical ventilator device.
– A non-ROC EMS agency/provider, for whom time call received at dispatch cannot be obtained, began CPR or placed pads.

Analyze Later Exclusion Criteria

– EMS witnessed arrests;
– Non-EMS rhythm analysis (AED placed by police or lay responder);
– Non-ROC EMS agency/provider on scene and began CPR or placed pads.

Resuscitation Guidelines

The ROC Investigators have developed and will disseminate consensus guidelines on how the patient with cardiac arrest should be treated in the prehospital, emergency department and hospital setting (see Appendix 3).

Monitoring of CPR Process

A long-term goal of the Resuscitation Outcome Consortium (ROC) is for all participating first EMS responders and ALS providers to have technology on, or adjunctive to, their automated (AED) and/or manual monitor/defibrillators that can monitor individual components of resuscitation. These data will serve as the basis for regular, systematic monitoring and review of the CPR process for purposes of quality improvement at each ROC site before and during clinical trials. Such processes will assure the safety of CPR performance in the field. Also feedback of this knowledge is essential to care delivery since improved quality assurance has been associated with improved outcomes after resuscitation.(67) Finally, it is essential to efficient trial conduct since low baseline rates of survival are associated with larger sample sizes to detect a clinically important difference.

Rationale

Recent studies have demonstrated that CPR is frequently not performed according to evidence-based guidelines in the out-of-hospital and in-hospital setting.(28, 29) Although these studies lacked power to detect a significant relationship between CPR process and patient outcome, a related study demonstrated that a greater rate of chest compressions was associated with a greater likelihood of achieving restoration of spontaneous circulation.(68) The importance of monitoring and improving CPR process was confirmed by the observation of potentially deleterious hyperventilation in the Milwaukee pilot study of ITD.(26)

A variety of evolving technologies offer the ability to monitor CPR process either directly or indirectly through AEDs. These include chest impedance (69) (used to monitor chest compression rate and ventilation rate(70)), chest acceleration(71) (used to monitor chest compression rate, depth, release, and duty cycle), and audio recording (used to monitor audible events during resuscitation). Each of these measures has advantages and limitations. For example, a recent prehospital study reported that even when obtaining data related to CPR process was emphasized, technical and signal quality limitations prevented its analysis in more than 25% of episodes(29). In addition, there is also considerable site heterogeneity across the Consortium that precludes the use of a single manufacturer or a single CPR monitoring technology. Accordingly, the Consortium has defined and will monitor a minimal data set pertinent to the CPR process but allow each participating site to individually specify and implement the means by which such data will be obtained. Please see Appendix 2 for a list of how each EMS Agency will monitor CPR process.

Method of Monitoring CPR Process

Overview- In preparation for the start of formal CPR process monitoring and the proposed ROC cardiac arrest trial, an educational program will be developed and implemented at each site to refresh provider skills on chest compression and ventilation, with emphasis on uninterrupted chest compressions, minimizing of "hands-off" intervals, and avoidance of hyperventilation.

All ROC clinical trial sites will implement a high-quality system for monitoring individual components of CPR, to include, at a minimum, the rate of chest compressions, the rate of ventilation, and the proportion of pulseless resuscitation time during which chest compressions are provided (i.e. CPR fraction). Recent studies show no significant differences in these parameters during the first five minutes of resuscitation as compared with the entire resuscitation episode.(28, 29) It is anticipated that during the initial period interruption of CPR

due to rhythm analysis or other procedures is more likely than throughout the resuscitation episode. After insertion of an advanced airway and initiation of ventilation that is asynchronous with chest compressions, hyperventilation is more likely than during the early resuscitation period. Therefore CPR process will be quantified during the first analyzable five minutes for 100% resuscitations as well as ventilations throughout the resuscitation episode in those who receive an advanced airway, until a sustained return of spontaneous circulation or resuscitation efforts are terminated. Sites will be encouraged to monitor the entire episode.

Sites will be required to demonstrate an ability to adequately acquire and analyze these CPR process data, identify and attempt to correct any observed deficiencies, and meet minimum performance standards (Appendix 2 CPR Process Monitoring: CPR Performance Standards) before being eligible to enroll patients in the present trial. In addition, ongoing monitoring and review of CPR process, will be used throughout the conduct of the trial.

Monitoring Devices- A range of monitoring/defibrillator devices will be deployed across the ROC sites that have capabilities to monitor CPR process. These devices and their capabilities are summarized in Appendix 2 CPR Process Monitoring: CPR Process Monitoring Devices.

Specific Methods- BLS and ALS providers will be trained to turn on the power of their AED or monitor immediately upon recognition of a subject in cardiac arrest. Monitoring hardware will be applied to the patient as soon as possible. This power-on event will initiate the recording by the device, and serve as a surrogate marker for "time zero" of initiating CPR. Each site will make efforts to maintain synchronization of monitor clocks with a common time standard (e.g. atomic clock time).

At the completion of every resuscitation attempt, the electronic record from the BLS and ALS devices used during the call will be obtained by the investigators. All electronic records will be reviewed manually by using the commercial software specific to the device, assisted where available, by proprietary automated analysis software. The record will be annotated from the time of power-on ("zero time"), and the parameters of resuscitation quantified during these periods (Appendix 2). Determination of whether a resuscitation effort meets minimally acceptable CPR performance standards for the Consortium will be based on whether it meets acceptable chest compression rate, ventilation rate and CPR fraction criteria as defined in Appendix 2.

Use of immediate (real-time) feedback software will be at the discretion of individual ROC sites and EMS agencies. Depending on system configuration, providers may be prompted by such software to modify the rate or depth of chest compressions, and to minimize interruptions in the provision of CPR. When such feedback is deployed, prompts will conform to the same target ranges specified in ROC CPR performance standards. Regardless of whether or not real-time feedback is provided, all resuscitations will be reviewed for adherence to the same performance standards, and a mechanism in place for remediation, if necessary. CPR process data derived from resuscitations during which real-time feedback was provided will be designated by an appropriate identifier. These sites may separately examine the impact of using real-time feedback in their systems.

Outcome Measures

Primary

The primary outcome for both studies is survival to hospital discharge with modified Rankin score $\leq$ 3. Patients who are transferred to another acute care facility (e.g., to undergo

ICD placement) will be considered still hospitalized. Patients transferred to a non-acute ward or facility will be considered discharged.

Secondary

Note that additional background information, rationale for selection, and details about specific functional status measures are given in Appendix 4. An interesting methodological issue is how to measure post-discharge outcomes. Physician and neuropsychological evaluations are considered the gold standard for the diagnosis of cognitive impairment. However such methods are unlikely to be feasible and likely to be associated with a high proportion of missing data in a population that resides in such a diverse geographic area as that participating in the Resuscitation Outcomes Consortium. For example, data from the ROC EMS structures serve demonstrates that participating EMS agencies (72% reporting) serve a total catchment area of 78,521 square miles. If the pattern of missingness is informative (e.g. patients from rural areas with delayed resuscitation less likely to be interviewed), then the post-discharge outcome data are susceptible to bias. Therefore all post-discharge outcome assessments will be made by using measures validated for phone administration to increase the response rate. All assessments will be made by trained interviewers.

Our criteria for choosing particular instruments to measure neurological status include prior data about reliability and reproducibility, availability of instruments suitable for a multicenter trial, and prior data in cardiac arrest survivors. The **Modified Rankin Scale (MRS)** has face validity and can be determined via review of the clinical record, in person or over the telephone.(72, 73) MRS has concurrent validity with other measures of neurological recovery after stroke and brain injury.(74, 75) MRS has prior use in a cohort of neurosurgical patients with in-hospital cardiac arrest(76) and in a cohort of survivors of out-of-hospital cardiac arrest.(77)

We are aware that CPC is less validated compared to some other measures that will be utilized in this study. CPC will be assessed by using a structured questionnaire via telephone administration (Appendix 4 of protocol). These latter questions were developed based on experience assessing outcomes after discharge in the OPALS study, PAD trial and ASPIRE trial. However it should be recognized that these questions have not been validated in their current format.

The **Health Utilities Index (HUI)** is a generic measure of health-related quality of life. (33) It has reliable interview, telephone, and proxy instruments with extensive validation in a multiple populations, including two cohort studies of survivors of cardiac arrest.(84, 85) HUI was positively correlated with bystander CPR, suggesting construct validity for measuring neurological injury incurred during cardiac arrest.(85)

The Adult Lifestyle and Function (ALFI) version of the Mini-Mental Status Exam (MMSE) is a measure of cognitive status.(31, 32) ALFI-MMSE correlates with severity of cognitive impairment as measured by the Clinical Dementia Rating Scale class.(31) Compared to the brief neuropsychiatric screening test, which is a weighted score of the Trailmaking A,(86) Word Fluency,(87) Weschler Memory Scale-Mental Control and Logical Memory,(88) ALFI-MMSE had a sensitivity of 68% and specificity of 100% for mild cognitive impairment. The corresponding MMSE values were 67% and 100%.(31)

The telephone version of the Geriatric Depression Scale (T-GDS)(34) detects the presence or absence of depression. Using a cutoff of 10/11T-GDS has a sensitivity of 86% and

specificity of 70% for detecting depression compared to a comprehensive assessment by a geriatric psychiatrist.

Table 10: Timing and Content of Secondary and Exploratory Outcome Measures

	Discharge	1 Month	3 Months	6 Months
MRS	X		X	X
CPC	X		X	X
ALFI-MMSE		X	X	X
HUI			X	X
GDS			X	X

Exploratory Outcome

Consensus statements recommend use of the **Cerebral Performance Category (CPC)** to assess functional outcomes after resuscitation from cardiac arrest.(78, 79) CPC is a five-point scale that was adapted from the Glasgow Outcome Scale.(80, 81) CPC had limited discrimination between mild and moderate brain injury, and only moderate correlation with a generic measure of health-related quality of life in a small study that was limited by a high rate of loss to follow-up.(82) However, CPC predicts long-term survival after resuscitation from cardiac arrest.(83)

Method of Assessing Post Discharge Outcomes

All post-discharge assessments will be performed by using instruments that will be made available in English and Spanish. Study coordinators will be trained to administer these instruments prior to study implementation by using didactic instruction, standardized patients and mock interview of each other according to current standards.(89) Spanish-language translators will be used as required. Interviewers will be instructed to speak clearly and articulate distinctly; ascertain the interviewee's ability to hear a spoken language at a conversational volume; try to ensure no one other than a proxy and the interviewee are present; if a precise answer is not given, probe for the correct response; exercise judgment about allowing sufficient time to answer a question before proceeding on to the next question; record the interviewee's last response as their answer to each question. Only research staff that completed this training successfully will be allowed to perform post-discharge assessments.

We are aware that some patients may be too impaired to complete an interview. Therefore, the ALFI-MMSE will be the instrument administered first during the three month interview. Patients who score $\geq$17 will be asked to complete the interview by self-report. Patients who score < 17 will be assessed further by interview of a proxy. We and others used a similar approach to assessment of post-discharge outcomes in the Public Access Defibrillation (PAD) trial. Contact details for the patient and their proxy will be identified at the time of notification of participation in hospital. Consent will be sought from the patient and their proxy for interview after discharge.

In-Hospital Morbidity

Number of hospital days and time interval from 911 call to patient death will be described for all hospitalized patients as measures of morbidity after resuscitation.

Other Outcomes

Other surrogate outcomes will be collected for descriptive purposes:

i) Return of Spontaneous Circulation: (ROSC) defined as the documented presence of a measurable pulse and blood pressure at any time after initiation of resuscitative efforts. There is no minimum duration for this return of spontaneous circulation.

ii) Admission to Hospital.

iii) Survival to 24 Hours.

iv) Process Outcomes: a) Number of Shocks Required: The total number of defibrillatory shocks; b) Duration of Pulselessness: The duration of pulselessness (from 911 to ROSC).

Data Collection

Data Forms

Appendix 6 contains draft data forms for both protocols.

Source of Data Collection

Data will be collected prospectively as patient care progresses. This will include a review of all the EMS patient care report(s), EMS dispatch times, EMS/fire/first responder electronic ECGs, emergency and hospital records. No additional studies or patient contact (except for notification of study participation) will be required for collection of this data up to hospital discharge.

Data Common to Both Protocols

Out-of-Hospital

Demographics, EMS response times (call receipt to arrival, arrival at patient side, etc.), witnessed arrest, bystander CPR, location of arrest, CPR process monitoring measures (ventilation rate, compression rate, CPR fraction), cause of arrest (cardiac vs. non cardiac), EMS therapies (drugs, shocks, advanced airway, hypothermia), first ECG rhythm, disposition, return of spontaneous circulation, potential adverse events.

Emergency and Hospital

Major procedures, possible complications of intervention, admittance to the hospital, cause of arrest, ICU days, date of awakening, disposition at discharge, withdrawal of care (DNR status) as well as MRS and CPC at hospital discharge.

Follow-up

Patients will be contacted by study personnel at 1 month after discharge and will have the ALFI-MMSE applied by telephone interview. They will be contacted by study personnel at 3 months and 6 months to have the MRS, CPC, ALFI-MMSE, HUI and GDS applied by telephone interview.

Initial ECG Rhythm

The initial ECG tracing will be analyzed off-line. The individuals performing this analysis will be blind to the interpretation that was performed in real-time by the AED and/or rescuers. The entire tracing that is available for analysis will be provided, and three possible ECG rhythms will be defined.

Asystole will be defined as background electrical activity less than 0.2 mV in amplitude with ≤10 beats per minute average rate (e.g., a 6-second strip without ventricular complexes).

VF will be defined as irregular, disorganized ventricular electrical activity of variable amplitude exceeding 0.2 mV.

Pulseless electrical activity (PEA) will be defined as electrical activity with R-waves of any width at an average rate of >10 beats per minute (e.g., organized ventricular electrical activity with R waves of any width that occur more than once over a 6-second period). The rate of PEA will be recorded as well.

Items Specific to ITD Protocol

Items specific to the ITD protocol will generally deal with events surrounding the use of the device; approximate time ITD attached, vomit with ITD, attachment of ITD to bag-mask or advanced airway, adverse/unusual events (device fills with fluid twice, device failure, patient complications) and protocol adherence.

Items Specific to Analyze Later Protocol

Items specific to the Analyze Later protocol will generally deal with events surrounding the compliance with the assigned cluster. Each event will be reviewed to determine whether the assigned protocol was followed.

Data Entry

The DCC will provide web-based HTML forms to collect necessary information from the RCCs. Web entry forms will have dynamic features such as immediate checks on data and relationships within a form and between forms. Details and clarification about data items will be provided using pop-up windows and links to appropriate sections of the on-line version of the Manual of Operations. Data encryption and authentication methods will be used. The DCC will build additional features into the web entry forms including: forms transmission history, access to past forms, tracking of data corrections, and the capability to save and re-load incomplete forms.

Database Management

The DCC will use a two-tiered database structure. A front-end database serves the web entry needs, using a database management system well-suited to handling updates from multiple interactive users. The data from this database will be transferred periodically (e.g. bi-weekly) to a “warehouse” database, on which data queries for analyses and monitoring will be run. Various versions of this database are kept as needed, e.g. for quarterly or DSMB reports. The “warehouse” database management system was selected for its ability to manage large quantities of data, to merge data from multiple databases as required, to handle complex and possibly changing relationships, and to produce analysis datasets that can be imported into a variety of statistical analysis packages.

Training

Overview

The training objectives include the following (each detailed below): review of optimal CPR performance, scientific basis for and review of study protocols, practicum/”hands-on” session, and post-test. It is anticipated that approximately 2 hours of didactic instruction and 1 hour of practicum will be required.

Optimal CPR Performance

The purpose of this component is to provide training in optimal chest compression and ventilation skills for all participating EMS personnel and to standardize the performance of CPR

across all ROC sites as much as possible. This training component will be implemented either as part of the protocol training or as a separate training module prior to specific study training. Key concepts include: optimal chest compression rate (100/min) and depth (38-51 mm), correct hand position on the distal sternum, complete chest wall recoil with each compression, minimizing "hands-off" intervals, avoiding hyperventilation (target rate 10-12/min), and proper breath duration (<2 seconds for an unprotected airway and 1 second for a protected airway). Training will also emphasize maintaining a continuously tight facemask seal with the "E-C" hand technique (one airway rescuer) or two-handed technique (two airway rescuers) when using the ITD and the use of ventilation timing assist lights with advanced airways (e.g., Combitube, laryngeal mask airway [LMA], or endotracheal tube).

Scientific Basis for ITD and Analyze Later Protocols

Level-appropriate presentation of the scientific principles underlying the ITD and Analyze Early versus Analyze Later studies will increase provider investment and improve protocol adherence. This should include presentation of prior work in both animals and humans and justification for a randomized clinical trial, including discussion as to why these approaches require further investigation prior to widespread implementation.

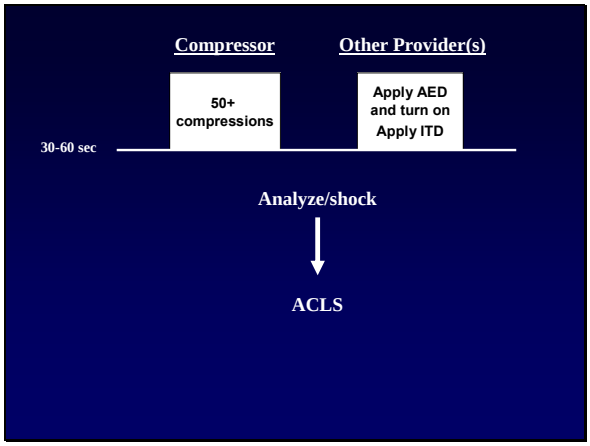
Study Protocols

This section will include the following: overall study design, inclusion and exclusion criteria, the process of exception to informed consent under emergency circumstances, and the study protocol. While the overall factorial design makes the analytic methodology somewhat complex, the operational protocol has been simplified for the purposes of training and actual trial implementation. From the provider perspective, there are only two arms to the study, as an ITD will be applied to all eligible patients but the group assignment (active or sham device) will be unknown to the providers. This creates an Analyze Early arm and an Analyze Later arm, both with ITD application existing as part of the study protocol. The training will mandate that one of the providers be designated the "compressor"; this designation should occur prior to the patient encounter to avoid confusion about role assignments once an arrest is recognized. The two study arms are then defined by the number of compressions delivered by the "compressor" before a pause for rhythm analysis and defibrillation attempts when indicated. In the Analyze Later arm, a number of compressions equivalent to approximately 3 minutes (e.g. 300 if the local CPR protocol is 100 compressions per minute with ventilations interposed, 180 if the local protocol is a compression:ventilation ratio of 15:2) will be delivered, while in the Analyze Early arm a minimum of 50 compressions will be delivered (see schematics below). The "compressor" should count the number of compressions out loud to alert the other providers as to the ongoing duration of chest compressions and to maintain an accurate count. Visual reminders (such as a colored tag on the AED/defibrillator) designating "300" or "50" compressions will be used to enhance protocol compliance, especially with a crossover design. In addition, crews will be encouraged to review their designated number of compressions as part of the daily checklist. The use of the term "compressor" should be encouraged, not only to enhance protocol compliance but also to underscore the importance of chest compressions during resuscitation.

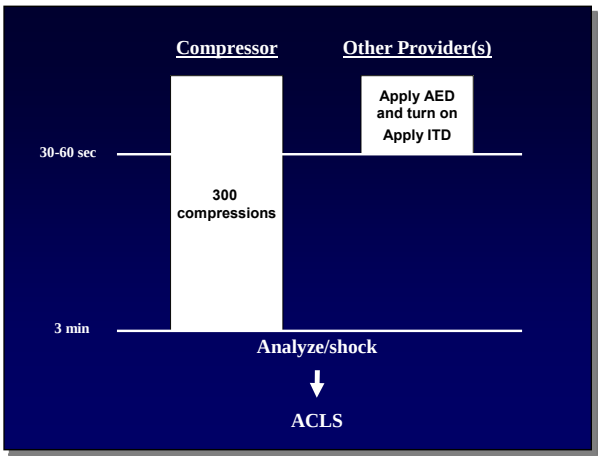
Training will define two tasks for the remaining provider(s): a) placement of the monitor/defibrillator pads and preparation for analysis/defibrillation, and b) proper application of the ITD/facemask, including maintenance of a continuously adequate seal during chest compressions and ventilations. The first priority following initiation of chest compressions by the "compressor" is the rapid placement of defibrillator pads; the monitor/defibrillator should be "powered-up" immediately upon recognition of pulselessness or sooner. The ITD and facemask should then be attached to the resuscitation bag and oxygen canister and a continuously tight

seal maintained. When additional personnel are available, the two tasks should be performed simultaneously. Training will emphasize immediate use of the ITD with initial airway management and continued use throughout the resuscitation while chest compressions are being performed as well as dedication of a single individual to maintaining adequate mask seal using a two-handed facemask technique whenever possible. Upon completion of rhythm analysis and defibrillation when indicated, standard ACLS procedure will ensue. Providers will receive specific training to transfer the ITD to the advanced airway and activate the ventilation assist timing lights on the ITD (both sham and active) once tube confirmation has occurred. Asynchronous ventilations should be performed using the assist timing lights as a guide. The proper ITD "clearing" procedure, indications for discontinuation of the ITD, and completion of study protocol will also be covered, including turnover report to ED personnel and retrieval of the ITD.

Figure 5: Training Scheme



Analyze Early Schema



Analyze Late Schema

Protocol Practicum

Providers will be given the opportunity to practice to proficiency each component of the protocol. The number of providers used during these rehearsals should simulate actual clinical practice whenever possible. The use of an AED or ALS defibrillator should also be dictated by clinical practice, using the identical brand and technology that will be available during the trial. Various permutations of the study protocol should be presented, including each of the study arms as discussed above. Specific assessment goals should emphasize inclusion/exclusion criteria, role assignment, correct number of compressions, maintenance of continuous tight facemask seal during CPR using "E-C" hand technique or two-handed technique, transfer of ITD to advanced airway and performance of optimal CPR (minimal "hands-off" time). All EMS personnel need to demonstrate proficiency in adequately managing a factorial study cardiac arrest patient. See Appendix 7 for a list of training proficiency goals.

Cognitive post-test

A cognitive post test will cover key enrollment procedures and may be completed online or as a written or verbal component of the training sessions. A record of training completion will be maintained by each site or EMS agency

Run-in Phase

After personnel have been formally trained, they will receive additional training through feedback during a run-in phase. Compliance with the protocol and completion and submission of the data will be required before the DCC will notify the site that that agency is now in the active phase of the trial. Compliance monitoring includes: correct inclusion/exclusion criteria, adherence to study protocol, CPR process measures reported, and correct completion of data elements including reporting of adverse events.

DSMB and Monitoring Strategy

Data Safety and Monitoring Committee

An independent data safety and monitoring committee will help ensure the safety of the trial by monitoring adverse outcomes throughout the trial and by reviewing outcome data for possible harm. In addition, the committee will review the results of the interim analyses. The committee must review and approve the protocol before the study can commence. The DSMB will evaluate the rate of adverse events between the treatment and control arms at intervals to be determined by the DSMB, expected to be approximately semi-annually and anticipated to correspond roughly to patient enrollment of one-third and two-thirds of total enrollment. The DSMB will also monitor primary and secondary study outcomes between the treatment and control groups. The DCC will forward DSMB reports to study investigators, the Institutions Research Board, the Food and Drug Administration, and the NIH in accordance with federal regulations 45 CFR Part 46 Subpart A and 21 CFR 312 and the IDE regulations, as well as appropriate Canadian oversight bodies.

Safety and Data Monitoring

The plans for monitoring protocol implementation/compliance, and data collection/quality are detailed elsewhere. Clinical centers will report all potential adverse events to the DCC as soon as possible. These will be collected in both a structured (standard form) and open (describing any difficulties encountered) form. All potentially serious adverse events will be reviewed by an events committee of ROC Investigators blinded as to treatment arm and further classified by: a) Severity (life-threatening, serious, non-serious); and b) Expected vs. unexpected; and c) Relation to study device. For serious adverse events, the DCC will notify the DSMB as well as appropriate regulatory agencies, sites, and NIH promptly.

The DCC will tabulate and report compliance, data quality, and non-serious adverse events on a regular basis.

Proposed Interim Monitoring Plan

Each factor will be monitored independently by the DSMB and either study could be terminated, without terminating the other. However, interactions will be evaluated. Interim analyses will be conducted after accrual of 1/3 and 2/3 of the sample size target (Appendix 8).

Proposed Interaction and Extension Monitoring Plan

We are aware that some may believe that the ITD will be ineffective for patients who receive Analyze Early care. Others may believe that this is not a realistic scenario. If it were true, it would require twice the duration to have the same power for observing the hypothesized effect in the Analyze Later cohort. The outcome will be observed during the course of the study by the independent DSMB as described in Appendix 9.

In the event that the Analyze Late vs Analyze Early (ALvE) intervention is terminated early due to demonstrated superiority of one rhythm analysis strategy over the other, the efficacy population for the ITD/sham device comparison will be restricted to those subjects treated under the rhythm analysis strategy found to be superior. The number of subjects

accrued to the study will be increased to achieve the planned maximal sample size in the superior rhythm analysis strategy arm.

In the event that the ITD/sham device intervention is terminated early, future patients will receive no device, and the efficacy population for the ALvE treatment comparison will be otherwise unchanged.

Human Subjects

Protection Against Risks

In accordance with the FDA, we will develop an adverse event reporting system to identify and treat any potential adverse events. We intend to closely monitor the clinical course of all patients enrolled in this trial to identify any expected or unexpected adverse events. Data regarding adverse events will be collected in both a structured (standard form) and open (describing any difficulties encountered) format. In accordance with the regulations 21 CFR 312.32, we have outlined the expected serious and non-serious adverse events, our plans to identify these and the time line for reporting them to the FDA, IRB and DMSB and other overseeing agencies.

An additional risk to subjects in this proposal pertains to the potential for a breach in patient confidentiality. All study personnel involved in data collection and analysis will be required to sign a confidentiality agreement as required by the institutional review board. In addition, subjects will be identified in the database by a study number and links to specific identifiers will be kept in a separate secure location. Database files will be maintained on a password protected computer in a secure location.

Recruitment and Informed Consent

This study qualifies for exception from informed consent required for emergency research as outlined in FDA regulation 21CFR50.24. The study intervention needs to be administered quickly following the onset of cardiac arrest. In this uncontrolled setting the patient is unconscious. As a result, the patient is unable to provide consent for study enrollment. Legal next-of-kin are often not immediately available at the scene, nor is it practical for the prehospital provider to explain the study and receive consent while caring for a patient in cardiac arrest. Taken together, these issues provide sufficient support for an exception from consent in order to evaluate an intervention that may have significant outcome benefits to this patient population. We have outlined below each criterion stipulated in the regulations for this exception and how our study design applies to these criteria.

Sec. 50.24 Exception from informed consent requirements for emergency research
(1) The human subjects are in a life-threatening situation, available treatments are unproven or unsatisfactory, and the collection of valid scientific evidence, which may include evidence obtained through randomized placebo-controlled investigations, is necessary to determine the safety and effectiveness of particular interventions.

The proposed trial is a factorial trial of use of either an active of sham ITD supplemented by either of two resuscitation strategies (Analyze Later and Analyze Early) in patients with nontraumatic out-of-hospital cardiac arrest. These patients are in an immediate life-threatening situation with a mortality approaching 95%. The standard of care for prehospital management of these patients includes the timely provision of CPR and advanced life support including airway management.

As reviewed in this proposal, previous studies of ITD have suggested a short-term survival advantage with this device but have not been definitive. These studies attest to the safety of ITD in the cardiac arrest population and to the practicality of using them in the prehospital environment. The major limitations of previous studies are their lack of focus on the

specific intervention and their lack of sufficient size to detect significant clinical differences in outcome. Also, in contrast to the previous human studies, the present trial will evaluate the device in patients with unprotected airways in which case potentially harmful hyperventilation is less common. Thus, critical evaluation of this intervention in humans has not been undertaken.

Animal and human data demonstrate the safety of Analyze Later. Studies in animal models of cardiac arrest indicate that a period of artificial circulation prior to the initial rescue shock can increase the likelihood of successful defibrillation when VF and circulatory arrest lasts more than 3-4 minutes. Small randomized trials in humans with cardiac arrest show that an initial period of CPR may or may not improve survival. However, the prior studies lacked concurrent control groups or were too small to detect meaningful differences in survival. Therefore, no study has adequately answered the question of whether an EMS provider, upon reaching a subject who has already developed cardiac arrest, should a) deploy a defibrillator and administer an immediate rescue shock or b) perform CPR for an interval prior to deploying the defibrillator and rescue shock.

We propose a large randomized trial focused on evaluation of these two interventions in the out-of-hospital cardiac arrest population, with sufficient statistical power to detect changes in outcome. Furthermore, an emphasis on the neurological outcome of resuscitated cardiac arrest patients will define the clinical utility of this resuscitation approach for these patients.

(2) Obtaining informed consent is not feasible because:

(i) The subjects will not be able to give their informed consent as a result of their medical condition;

(ii) The intervention under investigation must be administered before consent from the subjects' legally authorized representatives is feasible; and

(iii) There is no reasonable way to identify prospectively the individuals likely to become eligible for participation in the clinical investigation.

The study interventions need to be administered as an early intervention after the onset of cardiac arrest (see discussion of therapeutic window below). In this uncontrolled setting the patient is unconscious and unable to provide consent for study enrollment. Legal next-of-kin are often not immediately available at the scene, nor is it practical for the prehospital provider to explain the study and receive consent while caring for the cardiac arrest patient. Since we are studying out-of-hospital cardiac arrest, which is frequently the first manifestation of cardiovascular disease, there is no way to prospectively identify individuals who are likely to become eligible for this trial.

(3) Participation in the research holds out the prospect of direct benefit to the subjects because:

(i) Subjects are facing a life-threatening situation that necessitates intervention;

(ii) Appropriate animal and other preclinical studies have been conducted, and the information derived from those studies and related evidence support the potential for the intervention to provide a direct benefit to the individual subjects; and

(iii) Risks associated with the investigation are reasonable in relation to what is known about the medical condition of the potential class of subjects, the risks and benefits of standard therapy, if any, and what is known about the risks and benefits of the proposed intervention or activity.

(i) As defined, these patients with cardiac arrest are facing a life-threatening situation that requires immediate intervention.

(ii) Previous animal and human studies have been conducted, and suggest the potential for a direct benefit to individual subjects in cardiac arrest via improved hemodynamics and short-term survival advantage.

(iii) ITD administration has been tested in three previous clinical trials no serious adverse effects reported. Both Analyze Early and Analyze Late are currently used strategies. Three studies give inconsistent results, but no adverse effects have been noted. As discussed above, there are potential risks to subjects that may have not been observed in previous trials. We contend that these risks are reasonable in light of the potential benefits outlined in this proposal and the current poor outcome for patients with out-of-hospital cardiac arrest.

(4) The clinical investigation could not practicably be carried out without the waiver.

This study could not be conducted without the waiver of consent due to the need to administer the interventions as early as possible after the onset of cardiac arrest.

(5) The proposed investigational plan defines the length of the potential therapeutic window based on scientific evidence, and the investigator has committed to attempting to contact a legally authorized representative for each subject within that window of time and, if feasible, to asking the legally authorized representative contacted for consent within that window rather than proceeding without consent. The investigator will summarize efforts made to contact legally authorized representatives and make this information available to the IRB at the time of continuing review.

There have been three clinical studies of ITD use during standard manual CPR for the treatment of patients with out-of-hospital cardiac arrest. These demonstrated a potential survival benefit for patients treated with ITD vs. standard CPR. Animal models of cardiac arrest suggest that the ITD may increase venous return during the decompression phase of CPR. Based on these data, coupled with the previous clinical trials, the therapeutic window for this agent is for the time of initial resuscitation, which occurs when CPR is administered by prehospital care providers, up to hospital discharge.

It is well established that the probability of rescue shock success declines quickly during cardiac arrest.(49, 90) The decay in the probability of rescue shock success occurs over minutes, and approaches zero by 10-12 minutes. Therefore, the Analyze Early vs. Analyze Late intervention must be performed within the first few minutes of treatment in order to be meaningful.

Since this is an immediately life-threatening situation, it will not be possible to contact legal representatives at the time of study entry. We will make every effort to contact legal representatives after admission to the hospital to notify them that the patient was enrolled in a randomized trial. Requiring consent to review a hospital chart to determine the presence or absence of serious adverse events is likely to be associated with a biased estimate of the safety and efficacy of the intervention. Therefore we propose to use exception from informed consent for emergency consent, public notification, community consultation, patient notification of enrollment, and waiver of documented informed consent to review clinical records.

If legal representatives are not immediately available, research personnel will attempt to contact the subject's legal representative as soon as feasible and a summary of these efforts will be documented in the patient's chart. If the subject becomes competent during the study period then he/she will be approached by research personnel for notification of enrollment.

(6) The IRB has reviewed and approved informed consent procedures and an informed consent document consistent with Sec. 50.25. These procedures and the informed consent document are to be used with subjects or their legally authorized representatives in situations where use of such procedures and documents is feasible. The IRB has reviewed and approved procedures and information to be used when providing an opportunity for a family member to object to a subject's participation in the clinical investigation consistent with paragraph (a)(7)(v) of this section.

All procedures and consent forms will be approved by the Institutional Review Board (IRB) of the regional study site (or Research Ethics Boards (REBs) in Canada) prior to the onset of the trial.

(7) Additional protections of the rights and welfare of the subjects will be provided, including, at least:

(i) Consultation (including, where appropriate, consultation carried out by the IRB) with representatives of the communities in which the clinical investigation will be conducted and from which the subjects will be drawn;

(ii) Public disclosure to the communities in which the clinical investigation will be conducted and from which the subjects will be drawn, prior to initiation of the clinical investigation, of plans for the investigation and its risks and expected benefits;

(iii) Public disclosure of sufficient information following completion of the clinical investigation to apprise the community and researchers of the study, including the demographic characteristics of the research population, and its results;

(iv) Establishment of an independent data monitoring committee to exercise oversight of the clinical investigation; and

(v) If obtaining informed consent is not feasible and a legally authorized representative is not reasonably available, the investigator has committed, if feasible, to attempting to contact within the therapeutic window the subject's family member who is not a legally authorized representative, and asking whether he or she objects to the subject's participation in the clinical investigation. The investigator will summarize efforts made to contact family members and make this Information available to the IRB at the time of continuing review

(i) In U.S, centers, community consultation as outlined by the local IRB will be undertaken prior to IRB approval. Similarly, the Canadian centers will follow the requirements of their local REBs. Since the population eligible for enrollment includes all citizens in the study regions it will not be possible to target any particular small group. The community consultation plan for each study site will have to be individualized to fit the IRB requirements. Attached is an example of a proposed plan for community consultation, which has been used in a prior ITD trial (Appendix 10). Feedback from the community will be obtained by research personnel regarding any concerns they may have about potential enrollment. If requested, bracelets will be made available that could be worn by members of the community who do not want to participate.

(ii) & (iii) Public disclosures will be performed both prior to study enrollment and at the completion of the study in the form of multimedia press releases organized by the Resuscitation Outcomes Consortium. These will include plans for the study including potential risks and benefits and a summary of the results of the study upon completion. In the event that the press releases are not widely circulated, advertisements will also be placed in local papers describing the study.

(iv) An independent data monitoring committee will exercise oversight of the study as described below.

(v) We expect that all patients who meet the enrollment criteria will be unconscious. Any delay in medical care that would be required for the paramedic to attempt to obtain consent from the patient's legal guardian would be life threatening. Thus it will not be feasible to attempt to obtain informed consent during the initial therapeutic window.

Once enrolled in an emergency research trial, patients die in the field, die in the hospital or survive the event. Review of the clinical record is important to ascertain adverse events and important outcomes such as hospital discharge status. This does not require further participation of the patient.

The local ROC investigator will provide information about the emergency research study to the patient or their representative at the earliest feasible opportunity after administration of the intervention. Since in many cases this will be while the patient is still hospitalized, this will not include a request for consent for further participation/intervention, but will provide the patient/representative contact names/numbers for purposes of obtaining further information if desired. Since only patients who survive several months after discharge will be asked for further participation (in the form of telephone administered functional status measures at 3 months and 6 months), the timing of the request for consent for this participation will be determined by the local IRBs. However, we suggest that it should be during the first month after discharge so that patients who die before that time are not inconvenienced with a decision and so that those who have not died have had time to recover sufficiently to make a reasoned decision.

In summary, we shall notify patients enrolled under waiver of consent for emergency research as quickly as feasible, and seek consent from those who survive to discharge for ongoing participation.

Please see Appendix 10 for a sample Exception to Consent plan.

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3.1 Appendices

Table of Contents

FDA APPROVED APPENDICES dated 5/11/2006 THESE APPENDICES INCLUDE CHANGES TO APPENDIX 8-9 SENT INTO THE FDA JAN. 2007.

Appendix 1: Description of Impedance Threshold Device

The ITD (Figure 1a) is designed to be inserted easily between a facemask or advanced airway (e.g., ET tube, Combitube, or LMA) and a manual resuscitation bag (Figure 1b). In addition to an advanced airway, the ITD can be attached to any pediatric or adult facemask (Figure 1c) taking care to provide a continuously good seal around the nose and mouth (Figure 1d). As such, the device can be easily used by rescuers trained at both basic and advanced life support levels and moved quickly from any facemask once the patient is intubated.

Figure 1a

Figure 1b

Figure 1c

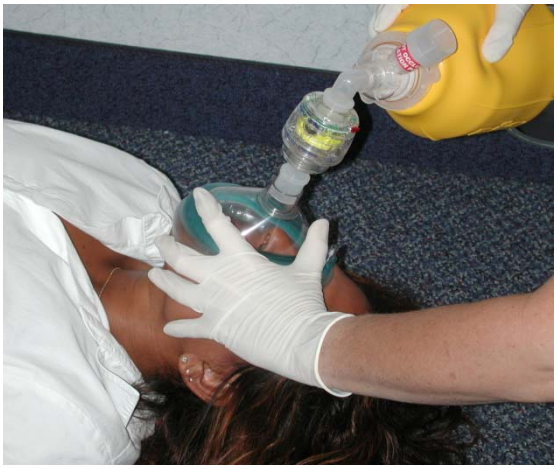


Figure 1d

The ITD contains ventilation timing assist lights, which flash at 10/minute at 1 second/flash to help promote the proper ventilation rate and duration for the patient with an advanced airway. The LED lights are controlled by an ON/OFF switch on the device.

The ITD is latex free and disposable (intended for single use only).

For this trial, ITDs will be specially manufactured in an opaque color so that active (functional) and sham (non-functional placebo) devices will appear externally identical.

Sham Devices:

Sham devices will be manufactured with the inspiratory impedance components eliminated, thus the device will function essentially as a hollow conduit. They will contain ventilation timing assist lights and appear externally identical to active devices. As with the active devices, there will be insignificant resistance to patient exhalation or rescuer ventilation.

All investigational devices (active and sham) will have a unique serial number to facilitate device accountability and tracking. They will look like the pictures above with the exception that the body will be opaque and there will be no pad printed labeling. Packaging will have the label "CAUTION: Investigational Device – Limited by Federal Law to investigational use."

ITD Function:

The ITD has a one-way valve that closes only during the decompression phase of CPR. When closed, the valve impedes inspiratory gas exchange when the chest wall recoils, thereby creating a lower intrathoracic pressure within the chest relative to the rest of the body. The lower intrathoracic pressure generates a small vacuum within the thorax and thereby increases blood flow back into the chest during the decompression. During chest compression, the one-way valve is open and does not cause any resistance to exhalation. When the resuscitation bag is squeezed during active rescuer ventilation, the one way valve remains open and does not cause any resistance to gas exchange. In this manner, the ITD functions to lower intrathoracic pressure only during the decompression phase of CPR, thereby enhancing the overall pumping efficiency of CPR without compromising patient ventilation.

As shown in Figure 2, the ITD consists of a valve body, a one-way pressure sensitive silicone valve, timing assist lights, and a safety check valve.

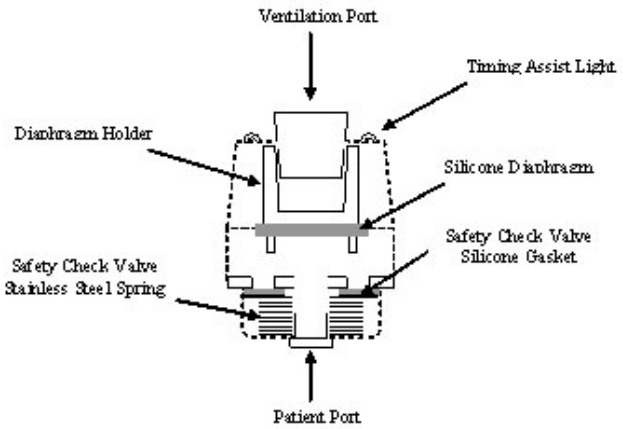
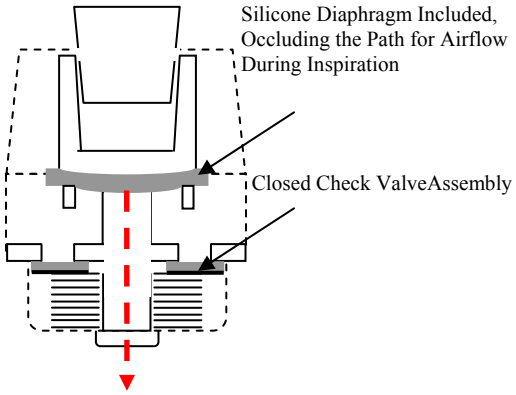


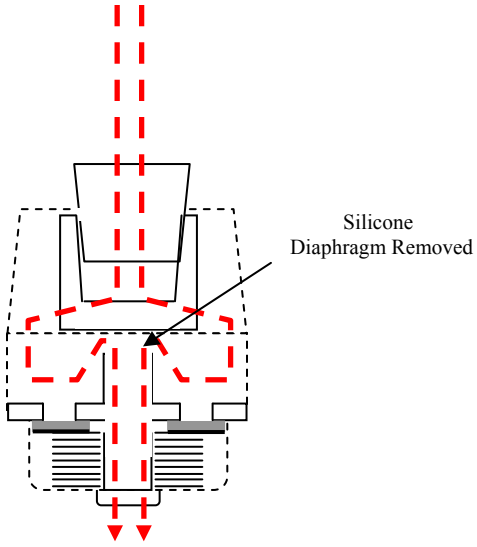
Figure 2

With chest compression, pressure in the chest rises and respiratory gases pass unimpeded through the ITD into the atmosphere. During the chest decompression phase, the natural chest wall recoil causes the pressure within the chest to fall below atmospheric pressure, and the one-way valve within the active ITD closes, thereby blocking inspiration of respiratory gases (Figure 3). With the sham ITD, inspiration of respiratory gases is unimpeded. When a rescuer actively ventilates the patient with a resuscitator bag, the respiratory gases push the one-way valve out of the way and gases pass unimpeded into the patient's lungs. In this manner, the rescuer can actively ventilate the patient without resistance from the ITD. This enables the rescuer to feel the natural compliance of the lungs during active ventilation. Because the ITD is a one-way valve, it has been equipped with a safety check valve set to open if the pressure in the chest falls below a critical value. This could happen if the patient begins to breathe spontaneously during the resuscitation effort.

Figure 3. Airflow through Active and Sham ITD during Decompression (Chest Wall Recoil)



Impeded Airflow
Being Drawn Through
Modified Active ITD Model
0902 During Chest Wall Recoil



Unimpeded Airflow
Being Drawn Through
Modified Sham ITD Model
0902 During Chest Wall Recoil

The opening pressure of the check valve is set to –16 cmH_20 based on previous study results, demonstrating that adequately negative intrathoracic pressures could be developed with –16 cmH_20 opening pressures on the check valve. Should the patient begin to breathe spontaneously, the safety check valve will open and respiratory gases will flow into the patient's lungs. If a patient begins to breathe spontaneously, the ITD should be removed immediately from the respiratory circuit. The safety check valve serves as a precautionary measure to prevent negative pressure pulmonary edema, potential barotrauma, and enable the patient to breath if there is a return of spontaneous ventilation. It is important to note that if the patient's initial spontaneous respiratory efforts go unnoticed, the rescuer will continue to provide ventilation for the patient.

In the event that the patient develops significant pulmonary edema and the valve becomes filled with fluid, the ITD will no longer be capable of impeding inspiratory gas exchange during CPR. However, patients can be actively ventilated and expiratory gases enter and exit without difficulty, despite the presence of fluid in the valve. In this setting, the valve functions as a conduit and cannot impede respiratory gases or fluids. Thus, although all efforts should be made to keep the ITD free of secretions, should the valve fill with fluid during resuscitation efforts, it will still function as a conduit to provide ventilatory gas exchange as necessary during active ventilation. Any fluid that does collect inside the ITD can be easily removed by first disconnecting the valve from the endotracheal tube and then rapidly compressing the bag-valve resuscitator. Use of the ITD will not interfere with routine suctioning and airway support. Three ventilation timing assist lights have been added, which blink on and off at a rate of 10/minute to help guide rescuers to ventilate at the appropriate rate when the patient is intubated. A switch turns the lights on and off. The ITD does not contain latex. It is disposable. It is anticipated that a new valve will be used for each patient in this study.

Sham valves will have the silicone diaphragm removed. These sham valves thus become a hollow conduit, providing no inspiratory impedance to patients serving as the control group. In the active valves, the silicone diaphragm will not be removed, and the ITD will function as intended to provide impedance to inspiratory flow during the decompression or relaxation phase of CPR. The sham and active valves will be made of an opaque plastic and will look identical from the outside, enabling the investigators and healthcare providers to perform a double-blinded study.

Appendix 2: CPR Process Monitoring

CPR Process Monitoring Devices

ALS Devices (see Table below)

LP-12 (Medtronic Emergency Response Systems, Inc): This device measures chest compression, ventilation and calculates CPR fraction based on changes in impedance; audio recording is available as an option. Measuring ventilation rate using impedance, when superimposed on chest compressions, can be problematic and requires adjunctive approaches such as use of audio recording to overhear ventilations, particularly the provider verbalizes when a breath is delivered or the sound of the ventilation event can be augmented. Capnometry is optional. Data download is performed via a cable computer link, landline modem, or GSM cellular transmission. At the present time, immediate (real-time) feedback to providers is not available.

MRx (Philips Inc and Laerdal, Inc): This device combines information obtained from an accelerometer and chest impedance to measure chest compression, ventilation and calculates CPR fraction. Capnometry is optional. An audio recording feature is available. Data download is performed via a removable memory card. Software for immediate (real-time) feedback to CPR providers is included with the device.

M Series ALS (Zoll, Inc): This device combines information obtained from an accelerometer measure chest compression calculates CPR fraction. A separate impedance channel and audio recording are in development and will reportedly soon be available. Capnometry is optional. Data download is performed via a removable memory card. Software for immediate (real-time) feedback to providers is incorporated in the device.

BLS Devices (see Table below)

LifePak 500 AED (Medtronic Emergency Response Systems, Inc): This device offers audio recording and limited impedance measurement (suitable for chest compressions only), allowing for measurement of chest compression rate and CPR fraction. Measuring ventilation rate via changes in impedance is difficult with this device because of its limited frequency response and requires adjunctive approaches such as use of audio recording to overhear ventilations, particularly if the sound of the ventilation event can be augmented, or the provider verbalizes when a breath is delivered. Data download is performed via a cable computer link, landline modem, or GSM cellular transmission. At the present time, immediate (real-time) feedback to providers is not available.

Heartstart Home and Onsite AED (Philips, Inc and Laerdal, Inc): These devices offer audio recording and a high resolution impedance channel suitable for recording chest compression rate, ventilation (with the limitations specified above), and allow for calculation of CPR fraction. A version of the MRx defibrillator is also presently in development, that incorporates the same CPR process monitoring technology as the ALS MRx defibrillator (including real-time feedback), but does not include other ALS features (such as capnometry). Data download is performed via a removable memory card.

AED Pro BLS (Zoll, Inc): This device incorporates the same CPR monitoring features available in the M Series ALS device, but does not include other ALS features

(such as capnometry). Real-time feedback for chest compression is incorporated into the device. Data download is performed via a removable memory card.

Table: Available CPR Process Monitoring Devices

Device	Chest Compression Measurement Technology	Ventilation Measurement Technology	Other Features	CPR Process Measures Available via Device	Data Download	Data Analysis	Immediate Feedback
ALS Devices							
LP-12*	High resolution impedance	High resolution impedance	Audio optional, capnometry optional	Chest compression rate, ventilation rate, CPR fraction	Computer cable link, landline modem or GSM cellular transmission	Manual review	Not available
MRx^	Accelerometer	High resolution impedance	Audio in development; capnometry optional	Chest compression rate, ventilation rate, CPR fraction	Removable memory card	Manual review and semi-automated software	Software included
M Series ALS§	Accelerometer	Impedance in development	Audio in development; capnometry optional	Chest compression rate, CPR fraction; ventilation (in development)¶	Removable memory card	Manual review and semi-automated software	In development
BLS Devices							
LifePak 500 AED *	Low resolution impedance	Audio recording		Chest compression rate, CPR fraction; ventilation¶	Computer cable link, landline modem or GSM cellular transmission	Manual review	Not available
Heartstart Home and Onsite AED^	High resolution impedance	High resolution impedance	Audio recording	Chest compression rate, ventilation rate, CPR fraction	Removable memory card	Manual review	Not available
MRx for BLS^	Accelerometer	High resolution impedance	Audio in development	Chest compression rate, ventilation rate, CPR fraction	Removable memory card	Manual review and semi-automated software	Software included
AED Pro BLS§	Accelerometer	Impedance in development	Audio in development	Chest compression rate, CPR fraction; ventilation (in development)¶	Removable memory card	Manual review and semi-automated software	In development

*Medtronic Emergency Response Systems Inc^ Philips, Inc and Laerdal, Inc§ Zoll, Inc¶ Ventilation rate may also be estimated from pauses in compression, or from overheard sounds (breath sounds or vocalized ventilation efforts) during audio recording.

CPR Performance Standards

The following table defines the CPR performance standards for the trial:

Parameter	Target	Minimum Acceptable	Maximum Acceptable	Criterion for Remediation/Retraining
Ventilation	8-10 breaths/minute^	6 per minute	16	Above maximum or below minimum parameters in >20% of resuscitations
Chest compression	100/minute*	80	120	Above maximum or below minimum parameters in > 20% of resuscitations
CPR fraction$^{\infty}$	0.85	0.5	-	Below minimum parameter in >20% of resuscitations

^ interrupt chest compressions to give ventilation via bag-mask, or give uninterrupted chest compressions with ventilation via protected airway

* refers to speed of compressions rather than actual number of compressions per minute

∞ CPR fraction will be the defined as = (Total seconds with chest compressions)÷(Total seconds with interpretable signal and no evidence of spontaneous circulation).

Definitions

Compressions will be defined as an accelerometer deflection, an impedance deflection or an ECG artifact accompanied by audio evidence of a compression, and refers to the speed of compressions per minute rather than the actual number of compressions. During the provision of BLS care (i.e. during synchronous chest compression-ventilation in patients with an unprotected airway), a presumed ventilation pause will be defined as a pause in compressions of 4-10 seconds without any other confirmation of ventilation. Recognition of a presumed ventilation pause will be enhanced when CPR employs a set synchronous compression: ventilation ratio in patients without a protected airway. A confirmed ventilation event will be a defined as having ancillary evidence of ventilation with or without a pause (e.g., ETCO2 waveform changes, characteristic chest impedance change, and/or audio confirmation of ventilation). To define CPR fraction, it will also be necessary to count the number of seconds that have an interpretable signal (leads connected and obscuring artifact absent) when there is no evidence of spontaneous circulation. Total seconds with compressions will be defined as the number of seconds during which there are countable compression events. CPR fraction will be the defined as = (Total seconds with compressions)÷(Total seconds with interpretable signal and no evidence of spontaneous circulation).

Determination of whether a resuscitation effort meets minimally acceptable CPR performance standards for the Consortium will be based on the number of one minute epochs having an acceptable chest compression rate, ventilation rate and CPR fraction (as defined in the table above), compared to the total number of interpretable epochs available from that resuscitation. A one-minute epoch will be defined as not meeting performance standards if any CPR process parameter within it falls outside the specified acceptable range. The first-minute epoch will be defined as not meeting performance standards if the time interval from device on to attachment of leads to the patient exceeds 1 minute. A resuscitation will be defined as overall not meeting CPR performance standards if the majority of its analyzed one-minute epochs (e.g. 3 or more

out of 5) fall outside the specified acceptable range. Retraining or other suitable remediation will be initiated if more than 20% of resuscitations at any ROC site do not meet CPR performance standards.

Monitoring by Site

run date: 8/17/2005

CPR Process Monitoring -- Alabama

Agency name	technology				compression rate			handsoff time			ventilation rate				data capture				data analysis	
	Medtronic	Philips/Laerdahl	Zoll	Other	Software	Impedance	Other	Software	Impedance	Other	Capnography	Software	Impedance	Other	Run report	ECG channel	Audio channel	Other	Agency staff	ROC personnel
	☐	☐	☑	☐	☑ With a manual over read	☐	☑	☑ With a manual over read	☐	☑	☐	☑ With a manual over read. May add capnography	☐	☑	☑	☑	☐	☐	☐	☑ 45 min. per case
RPS Walker Co																				
	☑	☐	☐	☐	☑ With a manual over read	☐	☑	☑ With a manual over read	☐	☑	☐	☑ With a manual over read. May add capnography	☐	☑	☑	☑	☐	☐	☐	☑ 45 min. per case
Bessemer Fire																				
Birmingham Fire																				
Centerpoint Fire																				
Homewood Fire																				
Hoover Fire																				
Pelham Fire																				
Trussville Fire																				
Vestavia Fire																				

run date: 8/17/2005

CPR Process Monitoring -- Dallas

Agency name	technology				compression rate			handsoff time			ventilation rate				data capture				data analysis	
	Medtronic	Philips/Laerdahl	Zoll	Other	Software	Impedance	Other	Software	Impedance	Other	Capnography	Software	Impedance	Other	Run report	ECG channel	Audio channel	Other	Agency staff	ROC personnel
	☑	☐	☐	☐	☑	☐	☐	☑	☐	☐	☑	☑	☐	☐	☐	☑	☐	☐	☐	☑
																				45 min. per case
Carrollton Fire Department																				
Lancaster Fire Department																				
	☑	☐	☐	☐	☑	☐	☐	☑	☐	☐	☑	☑	☐	☐	☐	☑	☐	☑	☐	☑
																and capnography channel				30 min. per case
Dallas Fire Dispatch Center																				
DeSoto Fire Dept																				
Duncanville Fire Dept																				
Farmers Branch Fire Dept																				
Garland police & fire comunications																				
Highland Pk Dpt of Pub. Safety																				
Irving Fire communications ctr																				
Mesquite Communications Center																				
University Park Fire Dept.																				
Wills Point Fire Dept																				

run date: 8/17/2005

CPR Process Monitoring -- Iowa

Agency name	technology				compression rate			handsoff time			ventilation rate				data capture				data analysis	
	Medtronic	Philips/Laerdahl	Zoll	Other	Software	Impedance	Other	Software	Impedance	Other	Capnography	Software	Impedance	Other	Run report	ECG channel	Audio channel	Other	Agency staff	ROC personnel
	☐	☐	☑	☐	☑	☐	☐	☑	☐	☐	☐	☑	☐	☐	☐	☐	☐	☑	☐	☑
																		Impedance channel/software		30 min. per case
Cedar Rapids Area Ambulance Service																				
Cedar Rapids Fire First Response																				
Dallas Co EMS																				
Dubuque Fire Dept																				
Mt. Pleasant Henry Co. EMS																				
Waterloo Fire EMS																				
West Des Moines EMS																				
	☑	☐	☐	☐	☑	☐	☐	☑	☐	☐	☐	☑	☐	☐	☐	☐	☐	☑	☐	☑
																		Impedance channel		60 min. per case
Davenport Fire EMS First Response																				
Davenport Medic EMS																				
Iowa City Johnson Co. EMS																				
Sioux City Fire Dept. First Response																				
Sioux City Siouxland Paramedics																				
	☑	☐	☐	☐	☑	☐	☐	☑	☐	☐	☐	☑	☐	☐	☐	☑	☑	☑	☐	☑
																		Impedance channel		60 min. per case
Bettendorf Fire EMS First Response																				
Des Moines Fire EMS																				

run date: 8/17/2005

CPR Process Monitoring -- Milwaukee

Agency name	technology				compression rate			handsoff time			ventilation rate				data capture				data analysis	
	Medtronic	Philips/Laerdahl	Zoll	Other	Software	Impecance	Other	Software	Impecance	Other	Capnography	Software	Impecance	Other	Run raport	ECG channel	Audic channel	Other	Agency staff	ROC personnel
	☐	☐	☑	☐	☑	☐	☐	☑	☐	☐	☑	☑	☐	☐	☑	☐	☐	☑	☐	☑
															RescueNet					60 min. per case
Milwaukee County EMS																				

run date: 8/17/2005

CPR Process Monitoring -- Ottawa / OPALS

Agency name	technology				compression rate			handsoff time			ventilation rate				data capture				data analysis	
	Medtronic	Philips/Laerdahl	Zoll	Other	Software	Impedance	Other	Software	Impedance	Other	Capnography	Software	Impedance	Other	Run report	ECG channel	Audio channel	Other	Agency staff	ROC personnel
	☐	☐	☑	☐	☐	☐	☐	☑	☐	☐	☐	☑	☐	☐	☐	☑	☐	☐	☐	☑
																				60 min. per case
Ottawa Paramedic Service																				
Sudbury Emergency Medical Services																				
Thames Emergency Medical Services																				
Thunder Bay Emergency Medical Services																				
Waterloo Regional Emergency Medical Services																				
	☐	☐	☑	☑	☑	☐	☐	☑	☐	☐	☐	☑	☐	☐	☐	☑	☐	☐	☐	☑
	may switch to Laerdal																			60 min. per case
Halton Emergency Medical Services																				
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																				60 min. per case
Essex-Windsor Emergency Medical Services																				
Kingston Regional Ambulance Service																				
Lambton County Emergency Medical Services																				
Niagara Emergency Medical System																				
North Umberland Emergency Medical Service																				
Peterborough Emergency Medical System																				
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																				60 min. per case
Kawartha Lakes Emergency Medical Services																				

run date: 8/17/2005

CPR Process Monitoring -- Pittsburgh

Agency name	technology				compression rate			handsoff time			ventilation rate				data capture				data analysis	
	Medtronic	Philips/Laerdahl	Zoll	Other	Software	Impedance	Other	Software	Impedance	Other	Capnography	Software	Impedance	Other	Run report	ECG channel	Audio channel	Other	Agency staff	ROC personnel
	☐	☐	☑	☐	☑	☐	☑	☑	☐	☐	☐	☐	☑	☐	☐	☑	☐	☐	☐	☑
					Manual review of audio/ECG															60 min. per case
Fayette EMS																				
	☐	☑	☐	☐	☑	☐	☑	☑	☐	☑	☐	☐	☑	☐	☐	☑	☐	☐	☐	☑
					Manual review of audio/ECG			Manual review of audio/ECG												90 min. per case
Ambulance and Chair																				
City of Pittsburgh																				
City of Pittsburgh Fire																				
Mutual Aid																				

run date: 8/17/2005

CPR Process Monitoring -- Portland

Agency name	technology				compression rate			handsoff time			ventilation rate				data capture				data analysis	
	Medtronic	Philips/Laerdahl	Zoll	Other	Software	Impedance	Other	Software	Impedance	Other	Capnography	Software	Impedance	Other	Run report	ECG channel	Audio channel	Other	Agency staff	ROC personnel
	☐	☐	☐	☑	☑	☐	☐	☑	☐	☐	☑	☐	☐	☐	☐	☑	☐	☐	☐	☑
	Changing machines, unsure at this time. Currently Medtronic																		90 min. per case	
Lake Oswego Fire Department																				
	☐	☐	☑	☐	☑	☐	☐	☑	☐	☐	☑	☐	☐	☐	☐	☑	☐	☐	☐	☑
																			60 min. per case	
Clackamas County Fire Dist. #1																				
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																			60 min. per case	
MetroWest Ambulance																				
Tualatin Valley																				
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																			60 min. per case	
AMR: Clark, Clackamas, Multnomah																				
Camas Fire Dept.																				
Clark County Fire District #6																				
Gresham Fire																				
Hillsboro Fire Department																				
North Country, WA																				
Port of Portland																				
Portland Fire and Rescue																				
Vancouver Fire																				

run date: 8/17/2005

CPR Process Monitoring -- San Diego

Agency name	technology				compression rate			handsoff time			ventilation rate				data capture				data analysis	
	Medtronic	Philips/Laerdahl	Zoll	Other	Software	Impedance	Other	Software	Impedance	Other	Capnography	Software	Impedance	Other	Run report	ECG channel	Audio channel	Other	Agency staff	ROC personnel
	☐	☐	☑	☐	☑	☐	☐	☑	☐	☐	☑	☐	☐	☐	☑	☑	☐	☐	☐	☑
																			60 min. per case	
Barona Fire Department																				
Borrego Springs Fire Protection District																				
City of San Diego - ALS																				
Coronado Fire Department																				
Lakeside Fire Department - ALS																				
Mercy Air																				
Oceanside Fire Dept. - ALS																				
Poway Fire Dept. - ALS																				
Ramona Fire Dept. (CDF) - ALS																				
Valley Center ALS																				

run date: 8/17/2005

CPR Process Monitoring -- San Diego

Agency name	technology				compression rate			handsoff time			ventilation rate				data capture				data analysis	
	Medtronic	Philips/Laerdahl	Zoll	Other	Software	Impedance	Other	Software	Impedance	Other	Capnography	Software	Impedance	Other	Run report	ECG channel	Audio channel	Other	Agency staff	ROC personnel
	☑	☐	☐	☐	☑	☐	☐	☑	☐	☐	☑	☐	☐	☐	☑	☑	☐	☐	☐	☑
																				30 min. per case
Alpine Fire Protection District																				
Bonita/Sunnyside Fire Protection																				
Carlsbad Fire Department																				
Deer Springs																				
Del Mar Fire Department																				
El Cajon Fire Department - ALS																				
Encinitas Fire Protection District																				
Escondido Fire Department - ALS																				
Grossmont Rural - ALS/AMR																				
Imperial Beach																				
Julian-Cuyamaca Fire Dept. - ALS																				
La Mesa																				
North County Fire - ALS																				
Rancho Santa Fe																				
San Marcos Fire Dept. - ALS																				
San Miguel Fire Dept. - ALS																				
Santee Fire Dept. - ALS																				
Solana Beach Fire Department																				
Sycuan Fire Dept. - ALS																				
Vista Fire Dept. - ALS																				

run date: 8/17/2005

CPR Process Monitoring -- Seattle / King Count

Agency name	technology				compression rate			handsoff time			ventilation rate				data capture				data analysis	
	Medtronic	Philips/Laerdahl	Zoll	Other	Software	Impedance	Other	Software	Impedance	Other	Capnography	Software	Impedance	Other	Run report	ECG channel	Audio channel	Other	Agency staff	ROC personnel
	☐	☐	☑	☐	☑	☐	☑	☑	☐	☑	☐	☐	☐	☑	☑	☑	☑	☐	☐	☑
					online review			online review			to be determined									30 min. per case
Auburn F.D																				
Federal Way Fire KCFD #39																				
North Highline FD KCFD #11																				
Tukwila F.D.																				
	☐	☑	☐	☐	☑	☐	☐	☑	☐	☐	☐	☑	☐	☐	☑	☑	☑	☐	☐	☑
																				45 min. per case
Bothell FD																				
City of Kirkland FD KCFD 41																				
City of Snoqualmie Fire Division 17M17																				
Duvall FD - KCFPD 45																				
Eastside Fire & Rescue																				
Northshore/Kenmore FD-KCFPD #16																				
Ravensdale-KCFDD #47																				
Redmond Fire Dept																				
Woodinville F.D. KCFD #36																				

run date: 8/17/2005

CPR Process Monitoring -- Seattle / King Count

Agency name	technology				compression rate			handsoff time			ventilation rate				data capture				data analysis	
	Medtronic	Philips/Laerdahl	Zoll	Other	Software	Impedance	Other	Software	Impedance	Other	Capnography	Software	Impedance	Other	Run report	ECG channel	Audio channel	Other	Agency staff	ROC personnel
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											unknown									45 min. per case
Black Diamond KCFD 17																				
Burien FD KCFD #2																				
City of Renton F.D.																				
Des Moines FD #26																				
Enumclaw FD KCFPD 28																				
Fall City F.D. KCFPD #27																				
Maple Valley Fire & Life Safety KCFPD #43																				
Renton-KCFD #40																				
SeaTac Fire Dept																				
Seattle Fire Dept.																				
South King Co Medic 1																				
	☑	☑	☐	☐	☑	☐	☐	☑	☐	☐	☐	☑	☐	☐	☑	☑	☑	☐	☐	☑
																				45 min. per case
Bellevue FD																				
Kent Fire Dept																				
Mercer Is - FD																				
Shoreline FD-KCFD #4																				
Skykomish F.D-KCFD #50																				
Vashon Is. Fire & Rescue - KCFD #13																				

run date: 8/17/2005

CPR Process Monitoring -- Toronto

Agency name	technology				compression rate			handsoff time			ventilation rate				data capture				data analysis	
	Medtronic	Philips/Laerdahl	Zoll	Other	Software	Impedance	Other	Software	Impedance	Other	Capnography	Software	Impedance	Other	Run report	ECG channel	Audio channel	Other	Agency staff	ROC personnel
	☐	☐	☐	☑	☑	☐	☐	☑	☐	☐	☐	☑	☐	☐	☑	☑	☐	☐	☐	☑
	undecided																			45 min. per case
Durham EMS																				
Durham Fire																				
Hamilton EMS																				
Hamilton Fire																				
Muskoka EMS																				
Muskoka Fire																				
Peel EMS																				
Peel Fire																				
Simcoe EMS																				
Simcoe Fire																				
Toronto EMS																				
Toronto Fire																				
York EMS																				
York Fire																				

run date: 8/17/2005

CPR Process Monitoring -- Vancouver / B.C.

Agency name	technology				compression rate			handsoff time			ventilation rate				data capture				data analysis	
	Medtronic	Philips/Laerdahl	Zoll	Other	Software	Impedance	Other	Software	Impedance	Other	Capnography	Software	Impedance	Other	Run report	ECG channel	Audio channel	Other	Agency staff	ROC personnel
	☑	☐	☐	☐	☑	☐	☐	☑	☐	☐	☑	☐	☐	☐	☑	☑	☑	☐	☑	☑

90 min. per case

BC Ambulance Service

Appendix 3: Resuscitation Guidelines

Cardiac Arrest Treatment Guidelines

The purpose of these guidelines is to present a consensus among ROC Investigators of how the patient with cardiac arrest usually would be treated. Guidelines are helpful to reduce variability in practice within a research study, and to provide a means by which to account for variability between subjects. This page describes the global approach. Reference is provided to more detailed guidelines that follow.

1. In the Field and Emergency Department

A. PRIOR to regaining pulses:

Resuscitation from puleseless state according to the ACLS guidelines (CA1)

B. AFTER regaining pulses:

Consider acute coronary event – 12 lead ECG +/- intervention (CA2)
Support blood pressure as needed – norepinephrine / dobutamine
Mechanically ventilate / maintain oxygenation

2. In the Intensive Care Unit

A. Ongoing neurological evaluation and treatment (CA8)

Serial Glasgow coma scale (GCS), pupil response and corneal reflexes
Maximal rate of recovery occurs over first 3 days.
Fever is detrimental over first 24-48 hours

B. Cardiovascular evaluation and treatment

Serial ECG, cardiac enzymes
Echocardiogram
If appropriate, percutaneous coronary intervention (PCI) or thrombolytics (CA2)
Initial myocardial dysfunction may improve over 24 hours

C. Supportive care

Ventilator and metabolic management

3. Post- Intensive Care Unit

A. Cardiovascular evaluation

Electrophysiology evaluation
Coronary artery disease evaluation
Consider catheterization, implantable defibrillator
Optimize medical management

B. Rehabilitation

CA1: Clinical Protocol for Cardiac Resuscitation

Resuscitation of individuals in cardiac arrest must honor local protocols. There are extensive evidence-based reviews of the topic embodied in the AHA/ILCOR scientific statements. Therefore, this clinical protocol is not written to be prescriptive (attempting to change practice). Instead it is written to provide explicit guidelines by which to judge whether the resuscitation of a particular subject was consistent with usual practice or deviated in some manner (for example, unusually high or low drug use, prolonged difficulty in securing airway, etc.). These deviations may be important for understanding variance in outcome data.

IMMEDIATE TREATMENT

1. Chest compressions delivered at 80-100 per minute. Goal will be no interruptions > 10 seconds.

2. Ventilate with oxygen (bag-mask) at a rate not greater than 10 per minute. Pauses in chest compressions for ventilation should not exceed 5 seconds.

3. Continuous ECG monitoring established as soon as possible. Benchmark will be automated or manual ECG monitoring within 2 minutes after arrival.

4. Establish intravenous line or intraosseous line. Benchmark will be intravenous access within 5 minutes after arrival of advanced life support.

5. Protect airway as soon as feasible with endotracheal tube, laryngeal mask airway or Combitube. Benchmark will be airway protected within 2 minutes after arrival of advanced life support.

6. Titrate epinephrine to 1-2.5 mg/5 minutes (0.015-0.03 mg/kg/5min).

7. Alternatively, titrate vasopressin to 0.3 to 0.6 IU/kg/10 min.

8. Rescue shocks should be administered for ventricular fibrillation or pulseless ventricular tachycardia (VF/VT). Benchmark will be 2-4 J/kg rescue shocks delivered at 0.5-2.0 per minute of VF/VT unless otherwise dictated by study protocol.

9. Consider pacing for pulseless organized rhythm with rate<50 complexes per minute.

10. Consider rescue shocks for pulseless organized rhythm with rate>180 complexes per minute.

11. Other drugs used as per recommended guidelines:
    a. Atropine (<2 mg; <0.03 mg/kg)
    b. Bicarbonate (1-2 mEq/kg)
    c. Lidocaine (<4 mg/kg)
    d. Amiodarone (5 mg/kg)
    e. Magnesium (<4 gm)

AFTER RESTORATION OF SPONTANEOUS CIRCULATION

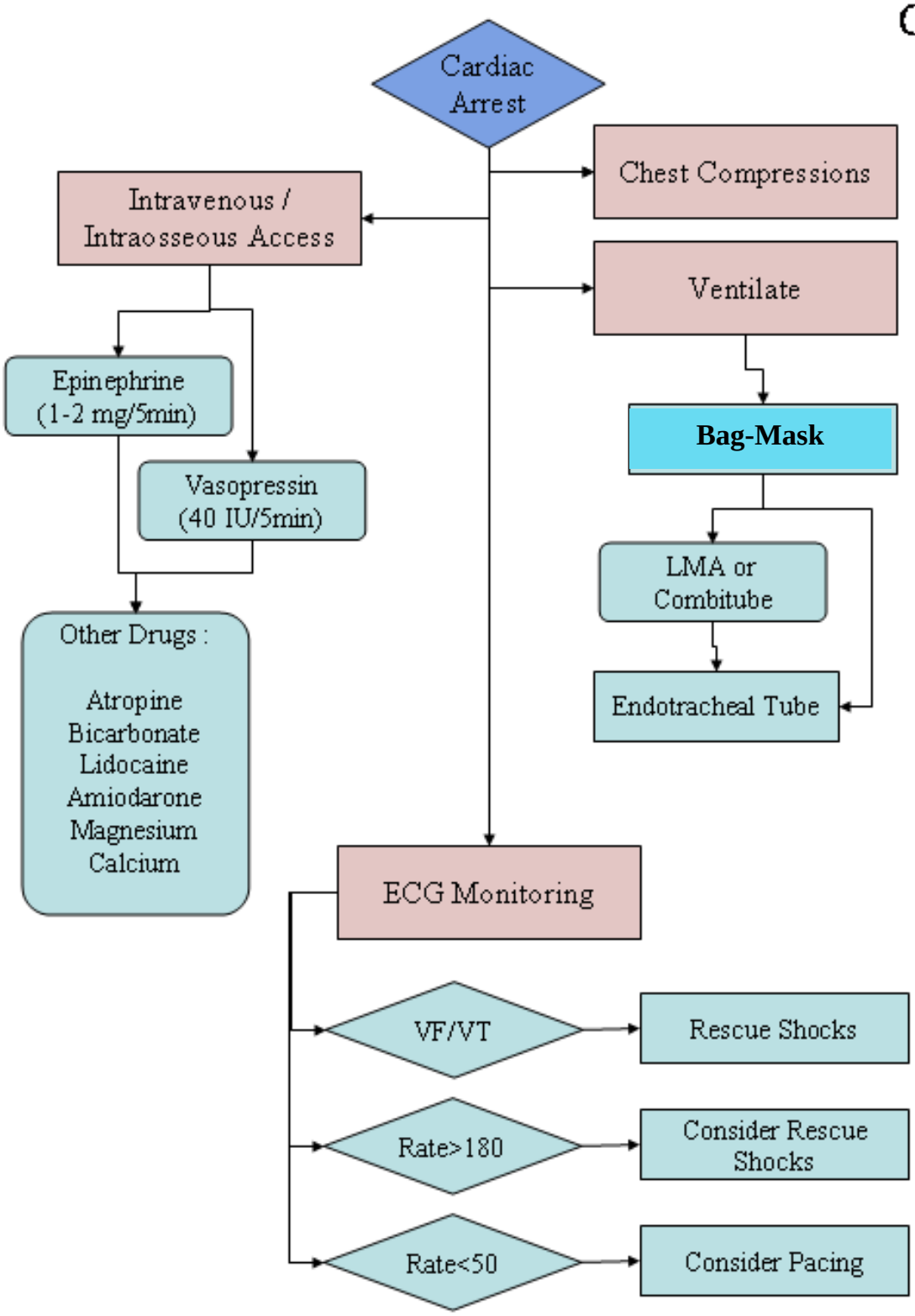
12. Initiate mechanical ventilation.
    a. Titrate FiO2 to keep PaO2= 55 - 80 mmHg or SaO2=92-100%.
    b. Titrate rate and tidal volume to achieve pH=7.35 – 7.45.

13. Initiate vasopressors and inotropic drips as needed to keep SBP>110 mmHg or MAP>90 mmHg. Note that most patients will require some inotropic support after more than momentary cardiac arrest.
    a. Arterial catheterization for blood pressure monitoring is recommended.
    b. Consider central venous pressure (CVP) monitoring or pulmonary artery catheter to optimize preload and cardiac index. Cardiac performance and optimal pressures are expected to be highly variable in this population and are likely to change over time after reperfusion.
    c. Initiate norepinephrine for hypotension. (Expect little response to dopamine if endogenous catecholamines were depleted during resuscitation.)
    d. Initiate dobutamine to increase cardiac output.

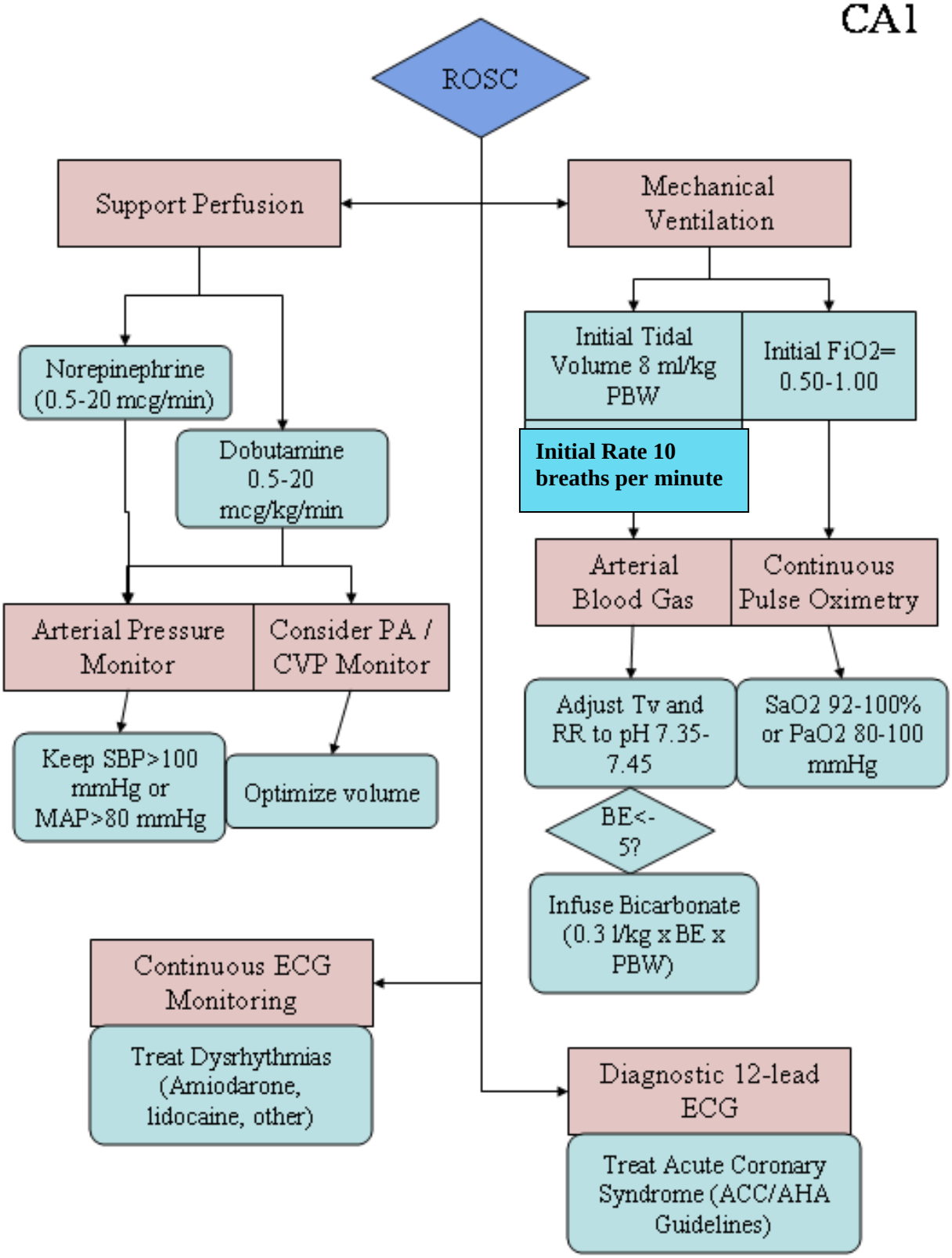
14. Treat metabolic acidosis (BE<-5 mEq/l) with bicarbonate (0.3 l/kg x weight in kg x BE) infused as bolus or drip.

15. Obtain 12-lead ECG as soon as possible after restoration of spontaneous circulation, and consider whether acute cardiac intervention is required.

CA1


Cardiac Arrest
Chest Compressions
Intravenous / Intraosseous Access
Ventilate
Epinephrine (1-2 mg/5min)
Bag-Mask
Vasopressin (40 IU/5min)
LMA or Combitube
Other Drugs :
Atropine
Bicarbonate
Lidocaine
Amiodarone
Magnesium
Calcium
Endotracheal Tube
ECG Monitoring
VF/VT
Rescue Shocks
Rate>180
Consider Rescue Shocks
Rate<50
Consider Pacing

CA1


ROSC
Support Perfusion
Mechanical Ventilation
Norepinephrine (0.5-20 mcg/min)
Dobutamine 0.5-20 mcg/kg/min
Initial Tidal Volume 8 ml/kg PBW
Initial FiO2= 0.50-1.00
Initial Rate 10 breaths per minute
Arterial Pressure Monitor
Consider PA / CVP Monitor
Arterial Blood Gas
Continuous Pulse Oximetry
Keep SBP>100 mmHg or MAP>80 mmHg
Optimize volume
Adjust Tv and RR to pH 7.35-7.45
SaO2 92-100% or PaO2 80-100 mmHg
BE<-5?
Infuse Bicarbonate (0.3 l/kg x BE x PBW)
Continuous ECG Monitoring
Treat Dysrhythmias (Amiodarone, lidocaine, other)
Diagnostic 12-lead ECG
Treat Acute Coronary Syndrome (ACC/AHA Guidelines)

CA2: Acute Cardiac Interventions

The purpose of this protocol is to determine criteria for recognizing the subject who would be eligible for acute cardiac interventions. Local care will be affected by availability of resources and by individual patient decisions concerning invasive procedures. Therefore, these guidelines are not prescriptive, requiring specific action, but are advisory, allowing the provider to recognize when the decision whether or not to intervene should be made.

Coronary artery occlusion has been identified in 48% of subjects undergoing angiography immediately after resuscitation from out-of-hospital cardiac arrest (Spaulding, Joly et al. 1997). Likewise, 51% of resuscitated subjects exhibit cardiac enzyme elevation or ECG evidence of acute myocardial infarction (Bulut, Aengevaeren et al. 2000). Among subjects receiving out-of-hospital CPR, troponin T is elevated in 40% (Lai, Hostler et al. 2004). These data suggest that at least one-half of subjects with out-of-hospital cardiac arrest are experiencing acute coronary syndromes. Early angioplasty or reperfusion therapy is associated with improved survival and outcome (Spaulding, Joly et al. 1997; Ornato, Peberdy et al. 2001; Keelan, Bunch et al. 2003). Guidelines for treatment of patients with acute coronary syndromes have been developed (Braunwald, Antman et al. 2002; Braunwald, Antman et al. 2002).

1. Obtain 12-lead ECG as soon as possible after restoration of spontaneous circulation.

2. Initiate medical therapy for acute cardiac ischemia, unless clear non-cardiac cause is evident (for example, drowning or collapse secondary to asthma).
    a. Nitrates (IV nitroglycerin)
    b. Beta-blockade (target heart rate 50-60)
    c. Anticoagulation (heparinoid)
    d. Consider IABP for hemodynamic instability, poor LV function of large area of myocardium at risk.

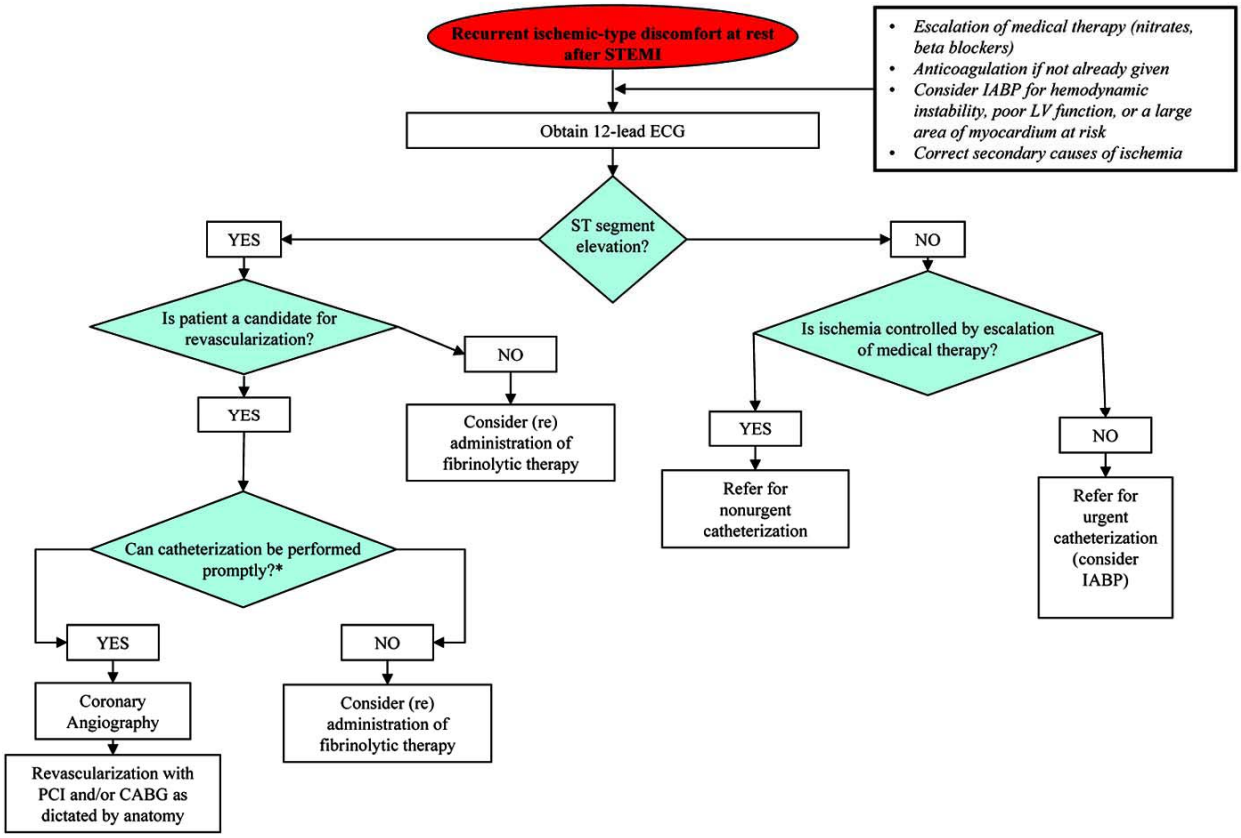
3. Monitor serum troponin or CPK-MB levels at 6-8 hour intervals over the first 24 hours after resuscitation.

4. If there is ST segment elevation AND patient is candidate for percutaneous cardiovascular intervention (PCI),
    a. Consider coronary angiography and revascularization (PCI or CABG)
    b. If angiography unavailable, consider fibrinolytic therapy

5. If there is ST segment elevation AND patient is not a candidate for angiography,
    a. Consider fibrinolytic therapy

6. If there is no ST elevation,
    a. Consider coronary angiography with timing dictated by condition

ACC/AHA Acute MI Guidelines



CA8: Neurological Prognostication / Withdrawal of Care

Assessment of neurological prognosis after resuscitation becomes increasingly reliable over the first three days of recovery (Levy, Caronna et al. 1985; Edgren, Hedstrand et al. 1994; Zandbergen, de Haan et al. 1998). A burst-suppression pattern or an isoelectric EEG during the first week after resuscitation is associated with poor neurological prognosis (Zandbergen, de Haan et al. 1998). Recovery of longer latency event related potentials and of evoked potentials (EPs) potentials is associated with awakening (Madl, Kramer et al. 2000; Gendo, Kramer et al. 2001; Zingler, Krumm et al. 2003). Absence of early somatosensory EPs is very specific for poor neurological outcome (Zandbergen, de Haan et al. 1998).

Therefore, neurological prognostication should include the following at a minimum.

1. Daily neurological assessment of subject
    a. Corneal reflexes
    b. Pupillary reflexes
    c. Motor response to pain (GCS motor)
    d. Response to verbal stimuli (GCS verbal)
2. Two complete assessments at least 24 hours apart

The following tests can be considered, but are not essential

1. Somatosensory evoked potentials
    a. P100 or P200 (thalamic) potentials
2. Electroencephalogram (EEG)
    a. Isoelectric
    b. Burst-suppression pattern
    c. Other
3. Cerebral blood flow studies
    a. Xenon clearance
    b. Transcranial dopplers

When death occurs in the hospital, these broad categories should be noted.

1. Subject is physiologically unstable, and continued life support is impossible or futile.
    a. Multi-system organ failure
    b. Second cardiac arrest with unsuccessful resuscitation
    c. Intractable shock

2. Subject has brain-death criteria, resulting in withdrawal of care and cardiovascular death.

3. Subject is physiologically stable or continued life-support is possible. Because of other non-neurological considerations, care is withdrawn or limited resulting in death.
    a. Underlying terminal illness (metastatic cancer, for example)
    b. Preexisting advanced directives or living will

    c. Family or surrogate representation of subject's wishes

4. Subject is deemed to have poor neurological prognosis, and care is withdrawn or limited resulting in death.
    a. No improvement in neurological status over 3 days
    b. Ominous EEG or evoked potential evaluations

These categorizations are important, because categories #1 and #2 represent mortality at discrete times, whereas categories #3 and #4 represent censoring of the outcomes with an artifactual time of death. Subjects in category #4, in particular, might be supported longer or shorter times because of caregiver, family or institutional differences that are external to the physiology of the disease. These differences could skew estimation of outcomes if not distinguished (Niemann and Stratton 2001)

Appendix 4: Functional Status Measures

NOTE: FUNCTIONAL STATUS QUESTIONNAIRES IN APPENDIX 4 SUPERCEDE THOSE IN DATAFORMS.

Background

Assessment of neurological recovery is an important component of evaluating the effects of resuscitation interventions. Neurological injury after cardiac arrest contributes to in-hospital death often because of withdrawal of care.(Niemann and Stratton 2001; Booth, Boone et al. 2004) Some surviving patients have decrements in cognitive function,(Yarnell 1976; Roine, Kajaste et al. 1993; van Alem, de Vos et al. 2004) although most surviving patients enjoy good quality of life.(Nichol, Stiell et al. 1999; van Alem, Waalewijn et al. 2004) Neurological status varies over time with large improvements during the first few days after resuscitation.(Edgren, Hedstrand et al. 1994; Booth, Boone et al. 2004) Detailed neuropsychiatric testing reveals that most improvement occurs during the first 3 months after resuscitation, (Roine, Kajaste et al. 1993; Edgren, Hedstrand et al. 1994) with only small clinical changes during rehabilitation in those with severe anoxic brain injury.(Fertl, Vass et al. 2000; Pusswald, Fertl et al. 2000) These studies suggest that it is possible to reliably measure neurological status three months after resuscitation.

Criteria for choosing an instrument to measure neurological status include prior data about reliability and validity, availability of instruments suitable for a multicenter trial, and application to prior cardiac arrest survivors. The **Modified Rankin Scale (MRS)** will be assessed from the clinical record prior to discharge and by interview after discharge. It has face validity and can be determined in person or over the telephone. MRS has concurrent validity with other measures of neurological recovery after stroke and brain injury.(Hop, Rinkel et al. 2001; Weimar, Kurth et al. 2002) Use of a structured interview in a recent study of stroke patients improved the weighted kappa from 0.71 to 0.91 (Wilson, Hareendran et al. 2005). The only previous published applications of MRS to survivors of cardiac arrest evaluated a cohort of neurosurgical patients with in-hospital cardiac arrest (Rabinstein, McClelland et al. 2004) and a cohort of survivors of out-of-hospital cardiac arrest.(van Alem, de Vos et al. 2004)

The **Cerebral Performance Category (CPC)** will be assessed from the clinical record prior to discharge and by interview after discharge. Consensus statements recommend use of the CPC to assess functional outcomes after resuscitation from cardiac arrest.(Cummins, Chamberlain et al. 1991; Jacobs, Nadkarni et al. 2004) CPC is a five-point scale that was adapted from the Glasgow Outcome Scale.(Jennett and Bond 1975; The Brain Resuscitation Clinical Trial II Study Group 1991) CPC has limited discrimination between mild and moderate brain injury. A small study with incomplete follow-up of survivors demonstrated only moderate correlation with other measures of health-related quality of life.(Hsu, Callaham et al. 1996) However, CPC at discharge predicts long-term survival. (Herlitz, Ekstrom et al. 1995)

An interesting question is whether simple MRS or CPC scores at discharge correlate with more detailed assessments post discharge. However our primary intended application of MRS or CPC scores is at discharge, since patient contact after discharge

makes assessment of more detailed measures feasible. A limitation to the post-discharge assessment of MRS or CPC scores is that there is no well-validated instrument for either measure. Also proxy respondents tend to overestimate patient burden,(Sneeuw, Sprangers et al. 2002) and may or may not be available for interview.

Therefore, we shall assess MRS or CPC at discharge based on review of the clinical record, and after discharge based on interview at three and six months. MRS will be assessed after discharge by using an instrument validated for telephone administration.(Wilson, Hareendran et al. 2005) CPC will be assessed by using a structured questionnaire via telephone administration. These latter questions were developed based on experience assessing outcomes after discharge in the OPALS study, PAD trial and ASPIRE trial as well as previous work by others to develop a structured phone interview to assess the related Glasgow Outcome Score (Wilson et al, 1998). However it should be recognized that these questions have not been validated in their current format.

Generic health-related quality of life (Feeny, Furlong et al. 1995; Torrance, Furlong et al. 1995) will be measured three and six months after discharge by administering the Health Utilities Index Mark 3 HUI system.(Feeny, Furlong et al. 2002) The interview-administered version of HUI3 requires completion of a maximum of 39 questions.(www.healthutilities.com accessed on October 14, 2005) The HUI3 consists of eight attributes of health (vision, hearing, speech, mobility, dexterity, emotion, cognition, and pain) with 5 or 6 levels per attribute. For each attribute, no or mild impairment in health has been defined as better than level 3 function (or level 4 function in the cognitive attributes). For each respondent, health status is described as a vector that combines the levels of each attribute. The health status information is then converted into a utility score of health-related quality of life on a scale from perfect health (1.0) to death (0).(Torrance, Zhang et al. 1992; Feeny, Furlong et al. 2002) Shown to be reliable and valid in other populations.(Boyle, Furlong et al. 1995; Gemke and Bonsel 1996; Gold, Franks et al. 1996) the HUI3 has been used in several ongoing studies of interventions for individuals with sudden cardiac arrest.(Stiell, Wells et al. 1998; Nichol, Stiell et al. 1999) This health-related quality of life index is consistent with current standards for economic evaluation of health technologies.(Gold, Siegel et al. 1996)

Neurological status will be measured at one, three and six months after discharge by using the Adult Lifestyle and Function (ALFI) version of the Mini-Mental Status Exam (MMSE)(Folstein, Folstein et al. 1975; Roccaforte, Burke et al. 1992) The ALFI-MMSE has 23 items. Our experience using it in the PAD trial suggests that it requires approximately five minutes to administer. It is scored from 0 to 22, with a cutoff of 16/17 used to determine cognitive impairment. ALFI-MMSE correlates strongly (Pearson's r 0.73 to 0.85) with face-to-face MMSE across all patients or when grouped by Clinical Dementia Rating Scale class.(Roccaforte, Burke et al. 1992) Five items were discrepant ($p \leq 0.05$) between phone and face-to-face versions: day of the week, county, name of place, phrase repetition, and registration of the term "penny." Respondents were more likely to give incorrect answers face-to-face to the first three of these items, while repetition and registration of the item "penny" were significantly less accurate over the phone. Compared to the brief neuropsychiatric screening test, which is a weighted score of the Trailmaking A,(Armitage 1946) Word Fluency,(Thurston and Thurston 1949) Weschler Memory Scale-Mental Control and Logical Memory,(Weschler and Stone

1983) ALFI-MMSE had a sensitivity of 68% and specificity of 100% for mild cognitive impairment. The corresponding MMSE values were 67% and 100%.

Finally, depression will be assessed three and six months after discharge by using the Geriatric Depression Scale administered by telephone (T-GDS)(Burke, Roccaforte et al. 1995) since depression is observed in those with cardiovascular disease(Powell, Catellier et al. 2005) or who have survived cardiac arrest,(Roine, Kajaste et al. 1993) and can be difficult to differentiate from cognitive impairment. This instrument has 30 items that are answered either 'yes' or 'no.' It is scored from 0 to 30, with a cutoff of 10/11 used to determine cognitive impairment.(McDowell, Kristjansson et al. 1996) T-GDS has moderate test-retest reliability during a one-week period (Kappa 0.35 to 0.7, mean 0.52) Using a cutoff of 10/11T-GDS has a sensitivity of 86% and specificity of 70% for detecting depression compared to a comprehensive assessment by a geriatric psychiatrist. Although initially designed to measure depression in older adults, it is also internally consistent and valid in younger adults.(Rule, Harvey et al. 1990)

Withdrawal of Care

For subjects who die prior to hospital discharge, the hospital record will be examined to assess whether support was withdrawn because of poor neurological status or other reasons. Participating hospitals are encouraged to make explicit notation of this decision-making as part of the Clinical Guidelines for the Consortium.

Table 1: Cerebral Performance Category (CPC)

1. **Good Cerebral Performance [*Normal Life*]:**
   Conscious, alert able to work and lead a normal life. May have minor psychologic or neurologic deficits (mild dysphasia, nonincapacitating hemiparesis, or minor cranial nerve abnormalities).

2. **Moderate Cerebral Disability [*Disabled but Independent*]:**
   Conscious. Sufficient cerebral function for part-time work in sheltered environment or independent activities of daily life (dress, travel by public transportation, food preparation). May have hemiplegia, seizures, ataxia, dysarthria, dysphasia or permanent memory or mental changes.

3. **Severe Cerebral Disability [*Conscious but Disabled and Dependent*]:**
   Conscious; dependent on others for daily support (in an institution or at home with exceptional family effort). Has at least limited cognition. This category includes a wide range of cerebral abnormalities, from patients who are ambulatory but have severe memory disturbances or dementia precluding independent existence, to those who are paralysed and can communicate only with their eyes, as in the locked-in syndrome.

4. **Coma/Vegetative State [*Unconscious*]:**
   Unconscious, unaware of surroundings, no cognition. No verbal and/or psychologic interaction with environment.

5. **Brain Death *[Certified brain dead or dead by traditional criteria.]:***
   Certified brain dead or dead by traditional criteria.

Table 2. Modified Rankin Scale

The subject is assigned to a level according to their functional status.

0	No symptoms at all
1	No significant disability despite symptoms: *Able to carry out all usual activities.*
2	Slight disability.
3	Moderate disability: *Requiring some help but able to walk without assistance.*
4	Moderate to severe disability: *Unable to walk without assistance and unable to attend to own bodily needs without assistance.*
5	Severe disability: *Bedridden, incontinent and requiring constant nursing care and attention.*
6	Death.

Table 3. Health Utilities Index III

The scale assigns points in each of 8 domains (vision, hearing, speech, ambulation, dexterity, emotion, cognition and pain) that can be considered separately, or added together (with weighting) to provide a single summary score.

(http://www.fhs.mcmaster.ca/hug)

Attribute	Description
VISION	
1	Able to see well enough to read ordinary newsprint and recognize a friend on the other side of the street, without glasses or contact lenses.
2	Able to see well enough to read ordinary newsprint and recognize a friend on the other side of the street, but with glasses.
3	Able to read ordinary newsprint with or without glasses but unable to recognize a friend on the other side of the street, even with glasses.
4	Able to recognize a friend on the other side of the street with or without glasses but unable to read ordinary newsprint, even with glasses.
5	Unable to read ordinary newsprint and unable to recognize a friend on the other side of the street, even with glasses.
6	Unable to see at all.
HEARING	
1	Able to hear what is said in a group conversation with at least three other people, without a hearing aid.
2	Able to hear what is said in a conversation with one other person in a quiet room without a hearing aid, but requires a hearing aid to hear what is said in a group conversation with at least three other people.
3	Able to hear what is said in a conversation with one other person in a quiet room with a hearing aid, and able to hear what is said in a group conversation with at least three other people, with a hearing aid.
4	Able to hear what is said in a conversation with one other person in a quiet room, without a hearing aid, but unable to hear what is said in a group conversation with at least three other people even with a hearing aid.
5	Able to hear what is said in a conversation with one other person in a quiet room with a hearing aid, but unable to hear what is said in a group conversation with at least three other people even with a hearing aid.
6	Unable to hear at all.
SPEECH	
1	Able to be understood completely when speaking with strangers or friends.
2	Able to be understood partially when speaking with strangers but able to be understood completely when speaking with people who know me well.

3 Able to be understood partially when speaking with strangers or people who know me well.
4 Unable to be understood when speaking with strangers but able to be understood partially by people who know me well.
5 Unable to be understood when speaking to other people (or unable to speak at all).

AMBULATION

1 Able to walk around the neighborhood without difficulty, and without walking equipment.
2 Able to walk around the neighborhood with difficulty; but does not require walking equipment or the help of another person.
3 Able to walk around the neighborhood with walking equipment, but without the help of another person.
4 Able to walk only short distances with walking equipment, and requires a wheelchair to get around the neighborhood.
5 Unable to walk alone, even with walking equipment. Able to walk short distances with the help of another person, and requires a wheelchair to get around the neighborhood.
6 Cannot walk at all.

DEXTERITY

1 Full use of two hands and ten fingers.
2 Limitations in the use of hands or fingers, but does not require special tools or help of another person.
3 Limitations in the use of hands or fingers, is independent with use of special tools (does not require the help of another person).
4 Limitations in the use of hands or fingers, requires the help of another person for some tasks (not independent even with use of special tools).
5 Limitations in use of hands or fingers, requires the help of another person for most tasks (not independent even with use of special tools).
6 Limitations in use of hands or fingers, requires the help of another person for all tasks (not independent even with use of special tools).

EMOTION

1 Happy and interested in life.
2 Somewhat happy.
3 Somewhat unhappy.
4 Very unhappy.
5 So unhappy that life is not worthwhile.

COGNITION

1 Able to remember most things, think clearly and solve day to day problems.
2 Able to remember most things, but have a little difficulty when trying to think and solve day to day problems.
3 Somewhat forgetful, but able to think clearly and solve day to day problems.

4 Somewhat forgetful, and have a little difficulty when trying to think or solve day to day problems.
5 Very forgetful, and have great difficulty when trying to think or solve day to day problems.
6 Unable to remember anything at all, and unable to think or solve day to day problems.

PAIN 1 Free of pain and discomfort.
2 Mild to moderate pain that prevents no activities.
3 Moderate pain that prevents a few activities.
4 Moderate to severe pain that prevents some activities.
5 Severe pain that prevents most activities.

CEREBRAL PERFORMANCE CATEGORY SCALE TELEPHONE AND CHART REVIEW TOOL

Introduction

The research assistant will ask/review the following questions in order to categorize the patient as Cerebral Performance Category (CPC) scale 1-4, based upon current status. Telephone questions may be asked of a caregiver, if necessary.

Structured Chart Review Tool for Assessment of Cerebral Performance Category

Chart Review Questions

1. Is the patient able to follow any simple commands or say any words?
NO → CPC 4
YES → Go on

2. Is the assistance of someone essential for all or part of the day for activities of daily living (dressing, preparing meals, local travel, shopping)?
YES → CPC 3
NO → Go on

3. Is the patient able to return to work or social activities in any capacity (even limited)?
NO → CPC3
YES → Go on

4. Does the patient have any problems that are more than mild i.e. problems that prevent him/her from doing things that he/she would like to do or have to do (dysphasia, hemiplegia, ataxia, dysarthria, memory, cognition, personality)?
YES → CPC 2
NO → CPC 1

Structured Interviews for Assessment of Cerebral Performance Category

a) Telephone Interview of Caregiver

1. Is the patient able to follow simple commands and say a few words (i.e. conscious)?
   NO → CPC 4
   YES → Go on

2. Is the patient able to do normal daily activities without assistance (dressing, preparing meals, local travel, shopping)?
   NO → CPC 3
   YES → Go on

3. Does the patient have any problems that are more than mild, i.e. problems that prevent him/her from doing things that he/she would like to do or have to do (difficulty speaking, moving an arm, or walking; poor memory; getting along with others)?
   YES → CPC 2
   NO → Go on

4. Has the patient returned to a normal life (work, leisure, family activities)
   NO → CPC 2
   YES → CPC 1

b) Telephone Interview of Patient

1. Are you able to do your normal daily activities without assistance (dressing, preparing meals, local travel, shopping)?
   NO → CPC 3
   YES → Go on

2. Do you have any problems that are more than mild, i.e. problems that prevent you from doing things that you would like to do or have to do (difficulty speaking, moving an arm, or walking; poor memory; getting along with others)?
   YES → CPC 2
   NO → Go on

3. Have you returned to a normal life (work, leisure, family activities)?
   NO → CPC 2
   YES → CPC 1

Structured Interview for Assessment of Modified Rankin Scale

Notes

1. CONSTANT CARE

Patients are usually bedridden: patients may not actually remain in bed all the time, but moving them from the bed to sitting will require major assistance. Patients will also need assistance with other activities.

SECTIONS 2 AND 3: ASSISTANCE FOR ACTIVITIES OF DAILY LIVING Assistance may be considered essential when there is the need for physical help (by another person) with an activity or there is a need for supervision, or the person needs prompting or reminding to do a task.

Mark responses based on the ability of the patient to perform the activity and not whether the patient actually performs the activity currently. Please probe using the specific questions given in the sections below. Please use your judgment to decide whether the person can actually do something before recording a response. The need for supervision for safety reasons should be due to objective danger that is posed, rather than 'just in case'. People may feel that a person who has had cardiac arrest should not be left on their own, but that does not make the person with cardiac arrest dependent. A general need for companionship, care, or protection should not be considered assistance.

2. ASSISTANCE TO ATTEND TO BODILY NEEDS/ FOR WALKING

2.1. Assistance for eating

Patient may eat a modified diet on their own. This should not be considered assistance.

2.2. Assistance for using the toilet

Using toilet without assistance include, reaching the toilet/commode; undress sufficiently; clean self; dress and leave.

2.3. Assistance for routine daily hygiene

Daily Hygiene includes just the three activities indicated (washing face, doing hair, cleaning teeth/ fitting false teeth). It does not include bathing and showering, or shaving, which are more complex activities for which the person may require assistance. The ability to bath, shower or shave is not relevant for this section.

2.4. Assistance for walking

Specific question to ask: "If absolutely necessary could you walk across the room, even if your caregiver was not present?"

3. ASSISTANCE TO LOOK AFTER OWN AFFAIRS

3.1 Preparing a simple meal. Specific questions to ask: "If the person were on their own: Would they go hungry? Might they be at risk of burning the house down if they tried to cook?"

3.2 Performing basic household chores. Specific questions to ask: "Are they *able to do* chores, if necessary, even if they do not normally do them." Men may, report that they need assistance more often than women. Please clarify by probing about the person's *ability* to perform the chores.

3.3 Looking after household expenses. Specific questions to ask: "Do you look after your own pension/income? Do you arrange to pay bills?" Look for a change from previous level of responsibility. Note: the person may be reluctant to admit a problem. The question is NOT about financial needs (e.g. assistance from benefit agencies). It refers to whether or not patients are able to take responsibility for the money that they have.

3.4 Local travel. Specific questions to ask: “If you need to get somewhere can you manage to call a taxi?” The patient should be able to at least order and take a taxi alone. This question is NOT about being able to afford a taxi, but about the tasks involved. The question refers to whether or not the patients can get around locally by themselves.

On the ‘shopping’ and ‘local travel’ questions (independence outside the home) there is quite often some restriction before cardiac arrest. Please ask about this and record the response in the ‘Before Cardiac arrest’ column

3.5 Local shopping. Specific Questions to ask: “If your life depended on it – could you get out and buy even single items?” “Can the person go to a local shop to buy milk or a loaf of bread?” Could also include going to the pub/bar, ordering and paying for a drink by themselves

Interview

Please mark (X) in the appropriate box. Please record responses to all questions (unless otherwise indicated in the text), including those concerning status before cardiac arrest. See guidelines on the facing page for further information.

1 CONSTANT CARE		
Constant care means that someone needs to be available at all times. Care may be provided by either a trained or an untrained caregiver. The patient will usually be bedridden and may be incontinent. **1.1 Does the person require constant care?**	**Now**	**Before cardiac arrest**
	☐ Yes (5) ☐No	☐Yes ☐No

2 **ASSISTANCE TO ATTEND TO BODILY NEEDS/ FOR WALKING**		
Assistance includes physical assistance, verbal instruction, or supervision by another person.	**Now**	**Before cardiac arrest**
2.1 **Is assistance essential for eating?** (Eating without assistance: food and implements may be provided by others).	☐ Yes (4) ☐ No	☐ Yes ☐ No
2.2 **Is assistance essential for using the toilet?** (Using toilet without assistance: reach toilet/commode; undress sufficiently; clean self; dress and leave).	☐ Yes (4) ☐ No	☐ Yes ☐ No
2.3 **Is assistance essential for routine daily hygiene?** (Routine hygiene: washing face, doing hair, cleaning teeth/fitting false teeth. Implements may be provided by others and this should not be considered assistance).	☐ Yes (4) ☐ No	☐ Yes ☐No
2.4 **Is assistance essential for walking?** (Walking without assistance: Able to walk indoors around house or ward, may use any aid (e.g. stick/cane, walking frame/walker), however not requiring physical help or verbal instruction or supervision from another person).	☐ Yes (4) ☐ No	☐ Yes ☐No

3 ASSISTANCE TO LOOK AFTER OWN AFFAIRS		
Assistance includes physical assistance, or verbal instruction, or supervision by another person.	**Now**	**Before cardiac arrest**
3.1 Is assistance essential for preparing a simple meal? (For example, able to prepare breakfast or a snack)	☐Yes(3) ☐No	☐Yes ☐No
3.2 Is assistance essential for basic household chores? (For example, finding and putting away clothes, clearing up after a meal. Exclude chores that do not need to be done every day, such as using a vacuum cleaner.)	☐Yes(3) ☐No	☐Yes ☐No
3.3 Is assistance essential for looking after household expenses?	☐Yes(3) ☐No	☐Yes ☐No

3.4 Is assistance essential for local travel? (Patients may drive or use public transport to get around. Ability to use a taxi is sufficient, provided the person can phone for it themselves and instruct the driver.)	☐Yes(3) ☐No	☐Yes ☐No
3.5 Is assistance essential for local shopping? (Local shopping: at least able to buy a single item)	☐Yes(3) ☐No	☐Yes ☐No

Notes

4. USUAL DUTIES AND ACTIVITIES

The set of questions in Section 4 are about how the patient usually spends his/her day. In this section, questions concerning status before cardiac arrest are asked first, to establish which areas are relevant. If an activity is not relevant (e.g. the person was not working before cardiac arrest), then it is assumed that there is no change, and the interviewer proceeds to ask about the next area.
Concentrate on key areas relevant to the particular person. Not all will apply, but almost everyone will have some regular pre-cardiac arrest social & leisure activities.

It is change that is important. The section concerns fulfillment of major social roles, relative to the previous roles that the person had.

Change should come from impairment (not social circumstances). For example, change in financial circumstances may produce a change in social activities but this is not relevant.

Possible improvement in the future is not relevant (e.g. “I plan to go back to work next month”). The relevant time period is within the previous week or so.

4.1 Work 4.1.1 Work refers to paid employment, and does not include voluntary work (which can be included under ‘social and leisure activities’). Many elderly patients will have retired and this section will not be relevant. 4.1.2 Change in ability to work or study includes loss of employment or reduction in level of responsibility; change in education, or problems with study. Special arrangements which allow someone to return to work even though they would not normally be able to work should be considered as ‘reduced level of work’.
4.2 Family responsibilities Refers to the patient’s ability to look after others. Probe using specific examples such as “babysitting, looking after your partner, your parents, your grandchildren or dependent others”.

4.3 Social & leisure activities This refers to any specific free-time activities which the person did for pleasure. It is useful to first establish the person's main activities before cardiac arrest, and then ask about change in participation since the cardiac arrest. Probe with specific questions: "How did you spend your day before the cardiac arrest? How often did you get out? What activities did you do in your free time at home? Do you think your level of activity has changed?"

Interview

4. USUAL DUTIES AND ACTIVITIES. The next sets of questions are about how the patient usually spends his/her day.

4.1 Work

4.1.1	**Before the cardiac arrest, was the person working or seeking work (or studying as a student)?** (If the person was not employed or seeking work before the cardiac arrest, or the person was retired then indicate 'No' and go to 4.2)	☐ Yes	☐ No
4.1.2	**Since the cardiac arrest has there been a change in the person's ability to work or study?** (Change in ability to work or study includes loss of employment or reduction in level of responsibility; change in education or problems with study).	☐ Yes	☐ No
	If 'Yes', how restricted are they? Reduced level of work e.g. change from full-time to part-time or change in level of responsibility**.** ☐ (2) Currently unable to work. ☐ (2)		

4.2 Family responsibilities

4.2.1	**Before the cardiac arrest was the person looking after family at home?** (If this was not a major role before the cardiac arrest, indicate 'No' and go to 4.3)	☐ Yes	☐ No
4.2.2	**Since the cardiac arrest has there been a change in their ability to look after family at home?**	☐ Yes	☐ No
	If 'Yes', how restricted are they? (a) Reduced responsibility for looking after family. ☐ (2) (b) Currently unable to look after family. ☐ (2)		

4.3 Social & leisure activities

(Social and leisure activities include hobbies and interests. Includes activities outside the home or at home. Activities outside the home: going to the pub/bar, restaurant, club, church, cinema, visiting friends, going for walks. Activities at home: involving "active" participation including knitting, sewing, painting, games, reading books, home improvements).

4.3.1	**Before the cardiac arrest did the person have regular free-time activities?** (If the person had very restricted social & leisure activities before the cardiac arrest then indicate 'No' and go to 4.4).	☐Yes	☐No
4.3.2	**Since the cardiac arrest has there been a change in their ability to participate in these activities?**	☐Yes	☐No

	If 'Yes', how restricted are they? (a) Participate a bit less: at least half as often as before the cardiac arrest.	☐
	(b) Participate much less: less than half as often.	☐ (2)
	(c) Unable to participate: rarely, if ever, take part.	☐ (2)

Notes

4. <u>USUAL DUTIES AND ACTIVITIES</u>. …..Contd.

4.4 Family & friendships

It is useful to go through the problems listed, particularly change in mood. This includes the patient who has become isolated and / or withdrawn since suffering their cardiac arrest. In this case it is more relevant to consider how tolerable this for others rather than the frequency of the problem.

Patients can experience personality changes and may be more insensitive to their partners than before, and this may result in relationship problems. Patients may report that they are now more 'mellow' than before and can longer be bothered joining in conversations about trivia. This behavior may also result in reduced social interaction and could lead to increased isolation.

It is useful to obtain the views of a caregiver on relationship problems.

5. SYMPTOMS AS A RESULT OF THE CARDIAC ARREST

5.1 This question is used to establish a spontaneous report of symptoms due to the cardiac arrest, before going through the checklist

5.2 SYMPTOM CHECKLIST

These can be any symptoms or problems reported by the patient or found on neurological examination. It is important to exclude common problems and complaints not due to the cardiac arrest. If you are not sure that a symptom resulted from the cardiac arrest indicate that it was present ‘before cardiac arrest’ by marking the ‘yes’ box in the before cardiac arrest column. The responses that are considered for scoring are those that are present now, but not present before the cardiac arrest, implying that the symptoms are due to the cardiac arrest.

4. USUAL DUTIES AND ACTIVITIES. …..Contd.

4.4 Family & Friendships

(Problems with relationships include difficulties in relationships with people at home, loss of friendships or increase in isolation. Changes in the person may include: communication problems, quick temper, irritability, anxiety, insensitivity to others, mood swings, depression, and unreasonable behavior).

4.4.1	**Since the cardiac arrest has the person had problems with relationships or become isolated?** *If 'Yes', what is the extent of disruption/strain?* Occasional- less than weekly ☐ Frequent- once a week or more, but tolerable ☐ (2) Constant- daily & intolerable ☐ (2)	☐ Yes	☐ No
4.4.2	**Before the cardiac arrest were any similar problems present?**	☐ Yes	☐ No

5. SYMPTOMS AS A RESULT OF THE CARDIAC ARREST

(Can be any symptoms or problems reported by the patient or found on neurological examination).

5.1	**"Does the patient have any symptoms resulting from the cardiac arrest?"** (Record spontaneous answer to the question from respondent)	☐Yes(1)	☐ No

5.2.	**SYMPTOM CHECKLIST**	**Now**		**Before cardiac arrest**
5.2.1	**Does the person have difficulty reading or writing?**	☐Yes(1)	☐ No	☐ Yes ☐ No
5.2.2	**Does the person have difficulty speaking or finding the right word?**	☐Yes(1)	☐ No	☐ Yes ☐ No
5.2.3	**Does the person have problems with balance or coordination?**	☐Yes(1)	☐ No	☐ Yes ☐ No
5.2.4	**Does the person have visual problems?**	☐Yes(1)	☐ No	☐ Yes ☐ No
5.2.5	**Does the person have numbness (face, arms, legs, hands, feet)?**	☐Yes(1)	☐ No	☐ Yes ☐ No
5.2.6	**Has the person experienced loss of movement (face, arms, legs, hands, feet)?**	☐Yes(1)	☐ No	☐ Yes ☐ No
5.2.7	**Does the person have difficulty with swallowing?**	☐Yes(1)	☐ No	☐ Yes ☐ No
5.2.8	**Any other symptoms?** (Please record: …… ……)	☐Yes(1)	☐ No	☐ Yes ☐ No

Adult Lifestyle and Function version of Mini-Mental Status Exam

ALFI Mini-Mental State Examination

Date of Interview: ☐☐/☐☐/☐☐☐☐ (month) (day) (year)

Patient ID#: ☐☐–☐☐☐–☐ ☐☐☐☐

1. What is the year? ☐☐☐☐ (yyyy) { ○ Cannot answer ○ Other refusal }

2. What is the season?

○ Spring
○ Summer
○ Autumn
○ Winter
{ ○ Cannot answer ○ Other refusal }

3. What is the date? ☐☐ { ○ Cannot answer ○ Other refusal }

4. What is the day of the week?

○ Monday
○ Tuesday
○ Wednesday
○ Thursday
○ Friday
○ Saturday
○ Sunday
{ ○ Cannot answer ○ Other refusal }

5. What is the month?

○ January
○ February
○ March
○ April
○ May
○ June
○ July
○ August
○ September
○ October
○ November
○ December
{ ○ Cannot answer ○ Other refusal }

6. Can you tell me where you are right now? For instance, what state are you in?

○ Correct ○ Incorrect ○ Cannot answer ○ Other refusal

7. What country are you in?

○ Correct ○ Incorrect ○ Cannot answer ○ Other refusal

8. What town are you in?

○ Correct ○ Incorrect ○ Cannot answer ○ Other refusal

9. What is the name of the place that you are in?

○ Correct ○ Incorrect ○ Cannot answer ○ Other refusal

↳ { • "home" • "house" • address • other correct name of a facility or other person's house }

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ALFI Mini-Mental State Examination

Date of Interview: ☐☐/☐☐/☐☐☐☐ (month) (day) (year)

Patient ID#: ☐☐–☐☐☐–☐ ☐☐☐☐

10. I shall say three words for you to remember. Repeat them after I have said all three words.

(check each bubble if the word was repeated correctly):

- O Shirt
- O Brown
- O Honesty

11. Please subtract 7 from 100. *(Do this 5 times - may coach patient if needed)*:

(Count only 1 error if subject makes subtraction error, but subsequent answers are 7 less than the error):

Number Correct: O 5 O 4 O 3 O 2 O 1 O 0

12. What are the three words that I asked you to remember?

Shirt	Brown	Honesty
O Spontaneous recall	O Spontaneous recall	O Spontaneous recall
O Cue: **something to wear**	O Cue: **a color**	O Cue: **a good personal quality**
O Multiple: **shoes, shirt, socks**	O Multiple: **blue, black, brown**	O Multiple: **charity, honesty, modesty**
O Unable to recall	O Unable to recall	O Unable to recall

13. Repeat what I say: "No ifs, ands, or buts"

- O Correct
- O 2 out of 3 words in the phrase correct
- O 1 out of 3 words in the phrase correct
- O Unable to repeat, or misses the 's'

14. What is the name of the thing that we are using to talk now? *(Do not wait for the patient to name it)*

O Telephone, receiver, mouthpiece, etc O Inaccurate O Cannot answer O Other refusal

15. Now I'm going to give you some instructions to follow. I want you to do a 3 step task.

First, say "hello," then tap the telephone receiver 3 times with your finger, then say "I'm back" into the phone.

O Hello O Tap O I'm back O Cannot answer O Other refusal

Signature of person filling out this form

Code Number ☐☐☐☐

Geriatric Depression Scale

Choose the best answer for how you have felt over the past week:

1. Are you basically satisfied with your life? YES / NO

2. Have you dropped many of your activities and interests? YES / NO

3. Do you feel that your life is empty? YES / NO

4. Do you often get bored? YES / NO

5. Are you in good spirits most of the time? YES / NO

6. Are you afraid that something bad is going to happen to you? YES / NO

7. Do you feel happy most of the time? YES / NO

8. Do you often feel helpless? YES / NO

9. Do you prefer to stay at home, rather than going out and doing new things? YES / NO

10. Do you feel you have more problems with memory than most? YES / NO

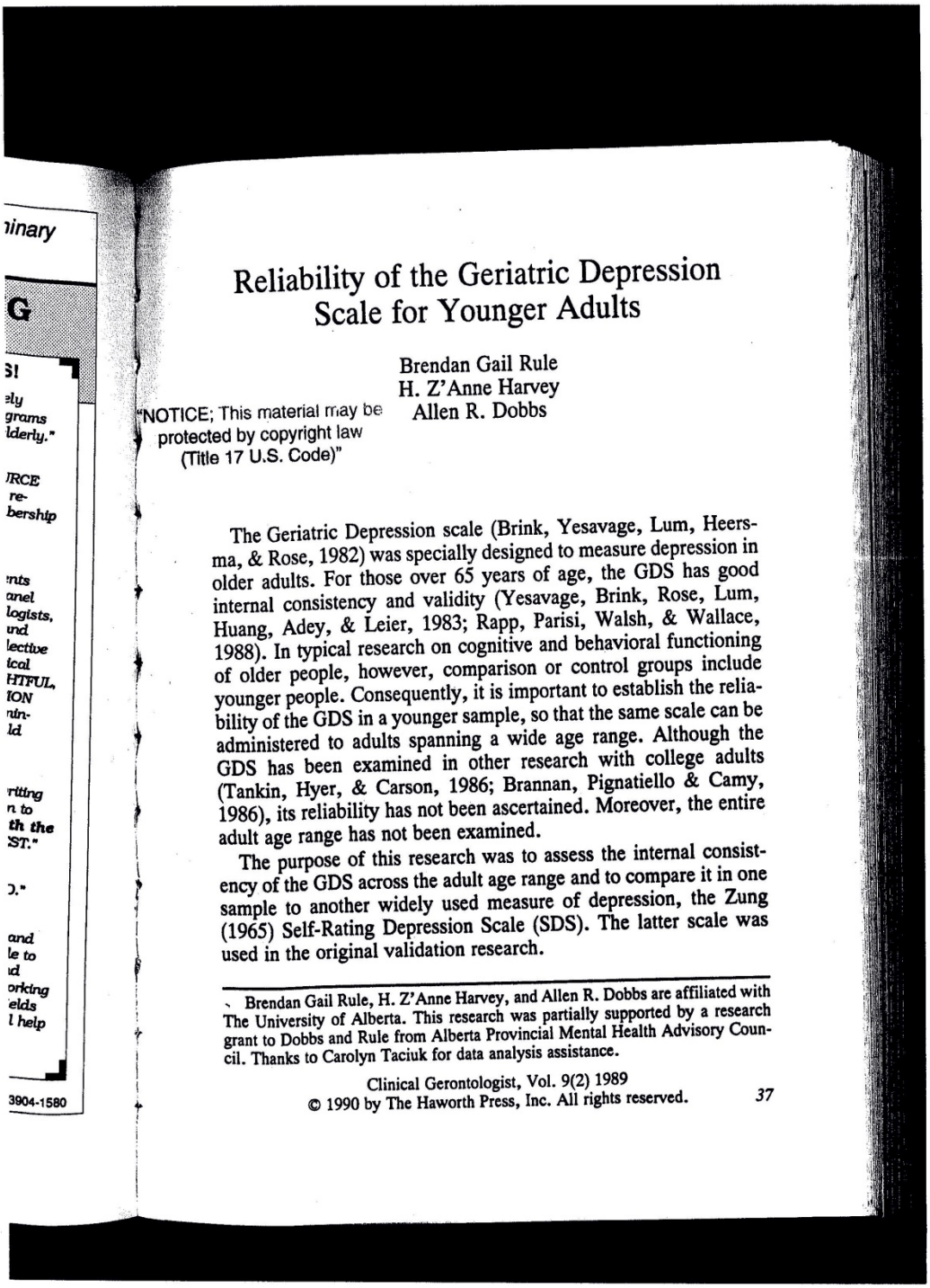
11. Do you think it is wonderful to be alive now? YES / NO

12. Do you feel pretty worthless the way you are now? YES / NO

13. Do you feel full of energy? YES / NO

14. Do you feel that your situation is hopeless? YES / NO

15. Do you think that most people are better off than you are? YES / NO



Reliability of the Geriatric Depression Scale for Younger Adults

Brendan Gail Rule
H. Z'Anne Harvey
Allen R. Dobbs

The Geriatric Depression scale (Brink, Yesavage, Lum, Heersma, & Rose, 1982) was specially designed to measure depression in older adults. For those over 65 years of age, the GDS has good internal consistency and validity (Yesavage, Brink, Rose, Lum, Huang, Adey, & Leier, 1983; Rapp, Parisi, Walsh, & Wallace, 1988). In typical research on cognitive and behavioral functioning of older people, however, comparison or control groups include younger people. Consequently, it is important to establish the reliability of the GDS in a younger sample, so that the same scale can be administered to adults spanning a wide age range. Although the GDS has been examined in other research with college adults (Tankin, Hyer, & Carson, 1986; Brannan, Pignatiello & Camy, 1986), its reliability has not been ascertained. Moreover, the entire adult age range has not been examined.

The purpose of this research was to assess the internal consistency of the GDS across the adult age range and to compare it in one sample to another widely used measure of depression, the Zung (1965) Self-Rating Depression Scale (SDS). The latter scale was used in the original validation research.

Brendan Gail Rule, H. Z'Anne Harvey, and Allen R. Dobbs are affiliated with The University of Alberta. This research was partially supported by a research grant to Dobbs and Rule from Alberta Provincial Mental Health Advisory Council. Thanks to Carolyn Taciuk for data analysis assistance.

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METHOD

Study I

Subjects: 196 students volunteered to participate in partial fulfillment of course requirements. The native language of the students was English and their ages ranged from 17 to 55 years. They were tested in classroom settings, using the 30-item GDS and 20-item Zung Self Rating Depression Scales. Subjects were debriefed and thanked.

RESULTS AND DISCUSSION

The mean scores and standard deviations for the younger adults on the GDS were 5.83 and 4.52 and on the Zung scale were 32.47 and 7.74. These are similar to those obtained by Yesavage et al. for their normal sample of people over 65 years of age: (M = 5.75, SD = 4.34 on the GDS and M = 34.31, SD = 6.66 on the Zung scale).

Four measures of internal consistency were completed for each depression scale: (1) the median correlation between the individual items and the corrected item total score (total score minus score on the particular item involved), (2) the average intercorrelation among the individual items, (3) Cronbach's (1951) alpha coefficient, and (4) split half reliability. Because subjects sometimes omitted items, the resulting n was 193 for GDS and 178 for the SDS. Table 1 presents the results comparing our younger sample with the older sample reported by Yesavage. The correlation between scores on the GDS and the Zung scale was .67 for our younger sample and .84 for the older sample tested by Yesavage et al.

The results show that the Geriatric Depression Scale is internally consistent and has convergent validity with the Zung scale in a sample ranging in age from 17 to 55 years old. Although the correlations are somewhat lower than those from an over 55-year-old sample, they are sufficiently high for research purposes (Nunnally, 1967).

Table 1

Table 1

Computed Correlations of Internal Consistency for the GDS and Zung Scale

	Younger Adults		Older Adults*	
	17 - 55 years		Over 65	
	GDS	Zung	GDS	Zung
Median correlation with total score	.38	.42	.56	.44
Mean interitem correlation	.15	.18	.36	.25
Alpha coefficient	.82	.81	.94	.87
Split-half reliability	.80	.78	.94	.81
	(p<0.05)		(p<0.05)	
	(N = 193)		(N = 178)	

*Based on data reported by Yesavage et al (1983)

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Study II

Subjects: Subjects were 389 community-dwelling residents, aged 29-99 years. They participated as part of a larger project concerned with the cognitive changes in aging.

METHOD

The GDS was administered during a structured interview in the first session of the study by a woman research assistant. Confidentiality was assured.

RESULTS AND DISCUSSION

The mean scores in the community sample for the 30, 40, 50, 60 and 70-year-olds were 4.03 (SD = 3.81), 4.15 (SD = 4.20), 5.14 (SD = 4.81), 4.64 (SD = 4.72), and 5.52 (SD = 4.87) respectively; and in the University sample for the teen, 20, 30, and over-40-year-olds were 5.76 (SD = 4.56), 4.42 (SD = 3.05), 4.55 (SD = 4.18) respectively.

The same four correlational tests (as well as a Guttman's split-half reliability), were calculated as in Study I. Table 2 displays these values for the community sample categorized into decades. The data from the University students were analyzed into decade categories for comparison purposes and are presented in Table 3. The reliability values are acceptably high for both samples. Chronbach's alpha, which is the standard for reliability estimates, ranges from .80 to .85 in the community sample. Similarly, the correlations are generally high in the University sample with the single exception of that for the 30-year-olds.

Our data suggest that the GDS is sufficiently reliable to use in research where a population of younger and older people is studied. Moreover, these data are important because of the younger age of the onset of presenile dementia and the relevance of identifying pseudodementia. Given the reliability of the GDS for people under 65 years of age, it may be useful for the latter purpose. The GDS is now widely used by clinicians to assist in making diagnostic decisions and our data provide further evidence of good psychometric

Table 2

Geriatric Depression Scale Reliability: Community Sample

Age Range	Cronbach's Alpha	Mean Inter-Item Correlation	Split-Half Spearman Brown	Guttman Split-Half	Median Correlation	N for Age Range
30-39	0.80	0.14	0.80	0.80	0.50	87
40-49	0.84	0.18	0.79	0.78	0.50	103
50-59	0.86	0.18	0.85	0.85	0.50	130
60-69	0.87	0.20	0.84	0.84	0.53	118
70+	0.85	0.18	0.79	0.79	0.52	84
30-65	0.85	0.18	0.84	0.84	0.48	389

Table 3

Geriatric Depression Scale Reliability: University Sample

Age Range	Cronbach's Alpha	Mean Inter-Item Correlation	Split-Half Spearman Brown	Guttman Split-Half	Median Correlation	N for Age Range
17-19	0.83	0.16	0.86	0.86	0.39	49
20-29	0.83	0.15	0.81	0.80	0.40	95
30-39	0.66	0.08	0.62	0.62	0.23	36
40-49	0.81	0.15	0.93	0.88	0.42	11
30-55	0.70	0.09	0.68	0.66	0.30	49

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properties. To verify the psychometric adequacy of the scale, especially for clinical purposes, subsequent research should examine its validity for classifying depressed people in a younger sample.

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Appendix 5: Effect of Cluster Size and Crossover

Clusters Without Crossover

The effective sample size of a cluster without crossover is given by

$$\frac{N}{1+(n_c-1)\rho}$$

where the intracluster correlation (ICC),

$$\rho = \frac{\sigma_B^2}{\sigma_B^2 + \sigma_W^2},$$

σ_B^2 is the variance in survival rates between clusters, σ_W^2 is the variance in survival rates within clusters, N is the total sample size, and n_c is the size of each cluster.(Hsieh, Lavori et al. 2003) The denominator, $1+(n_c-1)\rho$, also referred as the design effect, depicts the loss of efficiency by using cluster sampling.

For a mean cluster survival rate, r, between 0 and 10%, $\sigma_W^2 \approx r$. We have no prior knowledge of what σ_B^2 is, although a registry would make it possible to know that. It seems reasonable to consider sites as fixed effects, so we can consider σ_B^2 within a site. It also seems plausible that the survival rates across clusters at a site would follow a normal distribution with mean equal to the overall site survival rate and standard deviation somewhere between 1.5% and 2.5%. This would suggest $\sigma_B^2 = .015^2 = .000225 \text{ to } .025^2 = .000625$. If the overall site survival rate is 5%, this yields $\rho \approx .0045 \text{ to } .0125$. At such a site, the effective sample size given N = 1000 cardiac arrests with an average cluster size n_c would be

Number of Clusters	Cluster Size (n_c)	Effective Size ($\sigma_B^2 = .015^2$)	Effective Size ($\sigma_B^2 = .025^2$)
1000	1	1000	1000

100	10	960	900
20	50	820	623
10	100	693	450
2	500	309	140

Thus, if we use clusters without crossover, cluster size should be kept below about 50 so that loss of effective sample size is kept to a minimal.

Clusters with Crossover

The effective sample size of a cluster with crossover is

$$N\left(\frac{\sigma_B^2+\sigma_W^2}{\sigma_B^2}\right).$$

This was calculated by assuming that there are an equal number of individuals per cluster. Calculations for the variance of the difference between means of interventions are shown at the end of this appendix for all randomization methods. Based on these calculations, the effective sample size is actually increased by using a crossover design. However, these calculations assume independence between clusters and a similar correlation between observations within a cluster. Since these assumptions may not apply, it would be best to have independent randomization, but cluster with crossover randomization greatly improves the power compared to cluster without crossover randomization.

General Comments

All of the above are based on the assumption that there are enough similar clusters for the central limit process (that the mean is normally distributed) to apply. This is likely to be the case if there are 30 degrees of freedom left after adjusting for effects such as site, rhythm, response time, ITD or sham, etc., and if the clusters are reasonably similar. Because we have 10 sites, 10 reasonably similar clusters per site are adequate. Unfortunately, to use Generalized Estimating Equations methods (which allow us to adjust for episode specific factors) we need about 20 clusters to estimate the variance,

since the CLT has to apply to each site. Twenty or more clusters per site will also help insure balance since we will always have half of them doing each treatment at all times.

The primary role of the randomization is to ensure freedom from bias and balance between treatment arms. What randomizing individuals provides best is balance among important covariables. For the same reason, more clusters (hence smaller size clusters) and similar clusters will enhance balance among important covariables.(Kerry and Bland 2001; Raab and Butcher 2001)

Variance Calculations Dependent on Randomization Mechanism

Consider a binary outcome, Y_{ij}, to indicate 1 if subject j in cluster i dies due to cardiac arrest and 0 otherwise and a covariate X_{ij} to indicate 0 if they have intervention B and 1 if they have intervention A ($i = 1, \ldots, N_c$ and $j = 1, \ldots, n_i$). N_c denotes the number of clusters, while n_i denotes the number of subjects in cluster i. One of the studies primary objectives is to test if there is a difference between interventions A and B. Therefore the following test statistic is of interest is

$$\begin{aligned}
\bar{Y}_A - \bar{Y}_B &= \frac{\sum_{i=1}^{N_c}\sum_{j=1}^{n_i} Y_{ij}X_{ij}}{\sum_{i=1}^{N_s}\sum_{j=1}^{n_c} X_{ij}} - \frac{\sum_{i=1}^{N_c}\sum_{j=1}^{n_i} Y_{ij}(1-X_{ij})}{\sum_{i=1}^{N_s}\sum_{j=1}^{n_c}(1-X_{ij})} \\
&= \frac{\sum_{i-1}^{N_c}\sum_{j-1}^{n_i} Y_{ij}X_{ij}}{N_A} - \frac{\sum_{i-1}^{N_c}\sum_{j-1}^{n_i} Y_{ij}(1-X_{ij})}{N_B} \\
&= \frac{1}{N_A N_B}\sum_{i=1}^{N_c}\sum_{j=1}^{n_i} Y_{ij}((N_A+N_B)X_{ij} - N_A),
\end{aligned}$$

where N_A and N_B is the number study participants in interventions A and B, respectively.

There are three different randomization mechanisms being considered: independent episode randomization, cluster without crossover randomization, and cluster with crossover randomization. For each randomization mechanism the variance of the test statistic will be calculated. The design effect is then calculated as the ratio of variances for the test statistic under two different randomization methods.

Independent Randomization

If individual episodes are randomized independently to intervention then it is assumed that $Var(Y_{ij}) = \sigma_W^2 + \sigma_B^2$, $Cov(Y_{ij}, Y_{ij'}) = 0$, and $Cov(Y_{ij}, Y_{i'j'}) = 0$, where σ_W^2 is the within cluster variation and σ_B^2 is the between cluster variation. Therefore the variance of the test statistic is derived as,

$$\begin{aligned}
Var\left(\bar{Y}_A - \bar{Y}_B\right) &= Var\left(\frac{1}{N_A N_B}\sum_{i=1}^{N_c}\sum_{j=1}^{n_i} Y_{ij}((N_A+N_B)X_{ij} - N_A)\right) \\
&= \frac{1}{[N_A N_B]^2}\sum_{i=1}^{N_c}\sum_{j=1}^{n_i} Var(Y_{ij})\left[(N_A+N_B)X_{ij} - N_A\right]^2 \\
&= \frac{N_A+N_B}{N_A N_B}\left(\sigma_W^2 + \sigma_B^2\right).
\end{aligned}$$

Cluster without Crossover Randomization

Now assume that randomization is based on cluster. Therefore all individuals within the same cluster have the same randomized intervention and the clusters intervention does not change during the study. In this case then it is assumed that $Var(Y_{ij}) = \sigma_W^2 + \sigma_B^2$, $Cov(Y_{ij}, Y_{ij'}) = \sigma_B^2$, and $Cov(Y_{ij}, Y_{i'j'}) = 0$. Therefore the variance of the test statistic is derived as,

$$
\begin{aligned}
Var\left(\bar{Y}_A - \bar{Y}_B\right) &= Var\left(\tfrac{1}{N_A N_B}\sum_{i=1}^{N_c}\sum_{j=1}^{n_i} Y_{ij}((N_A+N_B)X_{ij} - N_A)\right) \\
&= \tfrac{1}{(N_A N_B)^2}\sum_{i=1}^{N_c}\left[\sum_{j=1}^{n_i} Var(Y_{ij})\left[(N_A+N_B)X_i - N_A\right]^2\right. \\
&\qquad \left. + 2\sum_{j=k+1}^{n_i}\sum_{k=1}^{n_i-1} Cov(Y_{ij},Y_{ik})\left[(N_A+N_B)X_i - N_A\right]^2\right] \\
&= \tfrac{N_A+N_B}{N_A N_B}\left(\sigma_W^2 - \sigma_B^2\right) + \tfrac{\sigma_B^2}{(N_A N_B)^2}\sum_{i=1}^{N_c} n_i(n_i-1)(N_B^2 X_i + N_A^2(1-X_i)).
\end{aligned}
$$

If we further assume that $n_i = n_c$, i.e. that there are equal number of study participants per cluster then,

$$
Var\left(\bar{Y}_A - \bar{Y}_B\right) = \frac{N_A+N_B}{N_A N_B}\left(\sigma_W^2 + n_c\sigma_B^2\right).
$$

Cluster with Crossover Randomization

The final randomization method is to randomize intervention by cluster, but then to crossover each cluster to the alternate intervention partway through the study. Since all individuals are still randomized by cluster the assumed $Var(Y_{ij}) = \sigma_W^2 + \sigma_B^2$, $Cov(Y_{ij}, Y_{ij'}) = \sigma_B^2$, and $Cov(Y_{ij}, Y_{i'j'}) = 0$ as in the case of cluster without crossover randomization. The variance of the test statistic is derived as,

$$
\begin{aligned}
Var\left(\bar{Y}_A - \bar{Y}_B\right) &= Var\left(\tfrac{1}{N_A N_B}\sum_{i=1}^{N_c}\sum_{j=1}^{n_i} Y_{ij}((N_A+N_B)X_{ij} - N_A)\right) \\
&= \tfrac{1}{(N_A N_B)^2}\sum_{i=1}^{N_c}\left[\sum_{j=1}^{n_i} Var(Y_{ij})\left[(N_A+N_B)X_{ij} - N_A\right]^2\right. \\
&\qquad \left. + 2\sum_{j=k+1}^{n_i}\sum_{k=1}^{n_i-1} Cov(Y_{ij},Y_{ik})\left[(N_A-N_B)X_{ij} - N_A\right]\left[(N_A+N_B)X_{ik} - N_A\right]\right] \\
&= \tfrac{N_A+N_B}{N_A N_B}\left(\sigma_W^2 + \sigma_B^2\right) \\
&+ \tfrac{\sigma_B^2}{(N_A N_B)^2}\sum_{i=1}^{N_c}\left[N_B^2 N_{Ai}(N_{Ai}-1) - 2N_A N_B N_{Ai} N_{Bi} + N_A^2 N_{Bi}(N_{Bi}-1)\right] \\
&= \tfrac{N_A+N_B}{N_A N_B}\sigma_W^2 + \tfrac{\sigma_B^2}{(N_A N_B)^2}\sum_{i=1}^{N_s}\left(N_B N_{Ai} - N_A N_{Bi}\right)^2,
\end{aligned}
$$

where $N_{Ai} = \sum_{j=1}^{n_i} X_{ij}$ and $N_{Bi} = \sum_{j=1}^{n_i}(1 - X_{ij})$.

Now to simplify assume that each cluster has the same number of treatment A and treatment B which implies that $N_{Ai} = N_A/N_c$ and $N_{Bi} = N_B/N_c$ yielding the

$$
Var\left(\bar{Y}_A - \bar{Y}_B\right) = \frac{N_A+N_B}{N_A N_B}\sigma_W^2.
$$

Design Effect

Given the variance calculations for the test statistic we can then calculate the design effect of crossover randomization designs compared to independent randomization by calculating the ratio of variances. The design effect for cluster without crossover randomization compared to independent randomization is,

$$\frac{\sigma_W^2 + n_c\sigma_B^2}{\sigma_W^2 + \sigma_B^2} = 1 + (n_c - 1)\left(\frac{\sigma_B^2}{\sigma_W^2 + \sigma_B^2}\right),$$

where n_c is the number of individual episodes per cluster.

The design effect for cluster with crossover randomization compared to independent randomization is,

$$\frac{\sigma_W^2}{\sigma_W^2 + \sigma_B^2} = 1 - \left(\frac{\sigma_B^2}{\sigma_W^2 + \sigma_B^2}\right).$$

Therefore the cluster with crossover randomization has the most power to detect differences between interventions.

Appendix 6: Data Collection Forms

Complete this form:
- any episode where EMS performed CPR (any compressions)
- for any episode where the ITD was removed from its sealed packaged (even if not used).

Main data source: PCR
Other data resource: Dispatch

ROC CARDIAC BLOOD FLOW TRIAL

Patient Enrollment

Date *(mm/dd/yyyy)* ___ / ___ / ___

Time call received at dispatch *(24hr clock)* ___ : ___ : ___ *(hh:mm:ss)*
○ **From PCR/other** ○ **From dispatch**

Incident Number *(optional)*

Factorial ID: ___ - ___ - ___

Site Linking ID *(optional)*

1. EMS response:

	Arriving vehicle	Agency name	Vehicle name	# of personnel	Time of arrival *24 hours (hh:mm:ss)*	Service level *BLS/BLS-D/ BLS+/ALS*	ITD Opened *Yes No*	ITD Used *Yes No*	ITD #
1:	_____				: :	_____	○ ○	○ ○	
2:	_____				: :	_____	○ ○	○ ○	
3:	_____				: :	_____	○ ○	○ ○	
4:	_____				: :	_____	○ ○	○ ○	

2. Exclusion Criteria:

a. Both protocols specific

Yes	No	
○	○	Age < age of consent
○	○	Pre-existing "Do Not Resuscitate" orders
○	○	Second enrollment for patient
○	○	Arrest due to traumatic cause
○	○	Drowning, strangulation, electrocution
○	○	Arrest due to exsanguination
○	○	Mechanical CPR device used
○	○	Known prisoner
○	○	Known pregnancy

b. ITD specific:

Yes	No	
○	○	Tracheostomy present
○	○	Sustained ROSC prior to ITD on scene

c. Analyze later vs. early specific:

Yes	No	
○	○	PAD/medical facility rhythm analysis
○	○	Non ROC EMS agency rhythm analysis
○	○	EMS witnessed arrest

3. What was the CPR therapy assignment for this arrest *(of the first arriving vehicle)*?

○ Analyze early
○ Analyze late
} Was assignment followed? ○ Yes ○ No → Complete **CTC Alert**

○ N/A- exclusion noted above in **Item 3c**

Person responsible for data on this form

Name:

enroll
draft version
Date: 02/10/06

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Complete this form:
- for any episode where CPR was performed (any amount of compressions) or ITD opened.
Main data resource: PCR
Other data resources: Dispatch, family members, witnesses

CARDIAC BLOOD FLOW TRIAL

Pre-hospital Time Record

Date *(mm/dd/yyyy)* ___ / ___ / ___

Time call received at dispatch *(24hr clock)* ___ : ___ : ___ *(hh:mm:ss)*
○ **From PCR/other** ○ **From dispatch**

Incident Number *(optional)*

Factorial ID: ___ - ___ - ___

Site Linking ID *(optional)*

Time Record:

1. The event ***"911 call received at primary PSAP"*** **is optional *** .
2. All events having an **"Event Order"** > 0 should have a **"Time of Event"** before you can sort them using the **"Calculate Time Intervals"** button.
3. If an event doesn't have an order, please enter 0. You cannot sort if an **"Event Order"** is blank.
4. Remember to sort the items by clicking the **"Calculate Time Intervals"** button (which will automatically calculate and prefill the time interval and cumulative time intervals) before saving the form.
5. The **"Original Order"** button when clicked restores the orginal paper order for the events. The **"Event Order"** and **"Time of Event"** are preserved but the **"Time Intervals"** will be erased.
6. The **"Reset Form"** button when clicked erases everything on the form.

Item	Event Order	Time of Event	Source (check one)				Time Interval	Interval Plausible
	1-20 0=NA	hh mm ss	Dispatch Log	PCR	Defib	Estimated	Computer to generate hh mm ss	↓
911 call received at PSAP*	☐	☐ : ☐ : ☐	○	○	○	○	☐ : ☐ : ☐	☐
911 call received at EMS dispatch	☐	☐ : ☐ : ☐	○	○	○	○	☐ : ☐ : ☐	☐
1st vehicle dispatch time	☐	☐ : ☐ : ☐	○	○	○	○	☐ : ☐ : ☐	☐
1st byst/dispatch CPR	☐	☐ : ☐ : ☐	○	○	○	○	☐ : ☐ : ☐	☐
1st non-EMS shock	☐	☐ : ☐ : ☐	○	○	○	○	☐ : ☐ : ☐	☐
1st vehicle arrival at scene	☐	☐ : ☐ : ☐	○	○	○	○	☐ : ☐ : ☐	☐
1st ITD vehicle arrival at scene	☐	☐ : ☐ : ☐	○	○	○	○	☐ : ☐ : ☐	☐
1st ALS arrival at scene	☐	☐ : ☐ : ☐	○	○	○	○	☐ : ☐ : ☐	☐
1st EMS rhythm after arrest	☐	☐ : ☐ : ☐	○	○	○	○	☐ : ☐ : ☐	☐
1st EMS CPR	☐	☐ : ☐ : ☐	○	○	○	○	☐ : ☐ : ☐	☐
1st ITD CPR	☐	☐ : ☐ : ☐	○	○	○	○	☐ : ☐ : ☐	☐
1st EMS shock assessment	☐	☐ : ☐ : ☐	○	○	○	○	☐ : ☐ : ☐	☐
1st EMS shock	☐	☐ : ☐ : ☐	○	○	○	○	☐ : ☐ : ☐	☐
Advanced airway established	☐	☐ : ☐ : ☐	○	○	○	○	☐ : ☐ : ☐	☐
1st ROSC	☐	☐ : ☐ : ☐	○	○	○	○	☐ : ☐ : ☐	☐
First time ITD removed	☐	☐ : ☐ : ☐	○	○	○	○	☐ : ☐ : ☐	☐
Sustained ROSC	☐	☐ : ☐ : ☐	○	○	○	○	☐ : ☐ : ☐	☐
Resuscitation stopped due to death	☐	☐ : ☐ : ☐	○	○	○	○	☐ : ☐ : ☐	☐
Patient transported from scene	☐	☐ : ☐ : ☐	○	○	○	○	☐ : ☐ : ☐	☐
ED arrival	☐	☐ : ☐ : ☐	○	○	○	○	☐ : ☐ : ☐	☐

Person responsible for data on this form

Name:

timerec
draft version
Date: 02/10/06

2

Complete this form:
- for any episode where CPR was performed (any amount of compressions)
Main data resource: PCR
Other data resources: Dispatch, family members, witnesses

ROC CARDIAC BLOOD FLOW TRIAL

Pre-hospital Data
Page 1 of 6

Date *(mm/dd/yyyy)* ___ / ___ / ___

Time call received at dispatch *(24hr clock)* ___ : ___ : ___ *(hh:mm:ss)*
○ **From PCR/other** ○ **From dispatch**

Incident Number *(optional)*

Factorial ID: ___ - ___ - ___

Site Linking ID *(optional)*

1. Location of Episode:
Census tract : ___
US: http://www.ffiec.gov/geocode/default.htm
Canada: http://geodepot.statcan.ca/Diss/maps/referencemaps/ct_e.cfm

○ Public *(check one only)*
- ○ Street/highway
- ○ Public building (schools, government office)
- ○ Place of recreation (park, stadium, lake)
- ○ Industrial place (factory, warehouse, construction site)
- ○ Other public property (sidewalk, store, church, restaurant, bar, hotel)

○ Non public *(check one only)*
- ○ Home residence (inside or immediately surrounding)
- ○ Farm/ranch
- ○ Healthcare facility
- ○ Residential institution (assisted living, nursing home)
- ○ Other private

2. Demographics:

a. Age: ___ ○ **years** ○ **months** ○ **days**

- ○ Calculated from DOB
- ○ Estimated by EMS

If no age available use categories:
- ○ Infant *(If < 1 year)*
- ○ Child *(1 - 11 years)*
- ○ Adolescent *(12 - 19 years)*
- ○ Adult *(20 - 39 years)*
- ○ Middle age *(40 - 60 years)*
- ○ Older *(61 - 75 years)*
- ○ Elderly *(> 75 years)*

b. Gender:
- ○ Male
- ○ Female

c. Race/Ethnicity: *(check all that apply)*
- ☐ Hispanic or Latino
- ☐ White
- ☐ African-American/Black
- ☐ American-Indian/Alaska Native
- ☐ Asian
- ☐ Native Hawaiian/Pacific Islander
- ☐ Other
- ☐ Unknown/not noted

continue to page 2

3

ROC CARDIAC BLOOD FLOW TRIAL

Pre-hospital Data

Date *(mm/dd/yyyy)* ___ / ___ / ___

Time call received at dispatch *(24hr clock)* ___ : ___ : ___ *(hh:mm:ss)*
○ **Estimated** ○ **From dispatch**

Incident Number *(optional)* ___

Factorial ID: ___ - ___ - ___

Site Linking ID *(optional)* ___

3. Witnessed collapse: *(check one only)*

- ○ Not witnessed (seen or heard)
- ○ Witnessed (seen or heard) by someone other than EMS responder
- ○ Witnessed (seen or heard) by EMS responder
- ○ Unknown/not noted

4. Was resuscitation attempted by bystanders?

- ○ Unknown
- ○ No
- ○ Yes → Was CPR attempted? ○ Yes ○ No
  - → Was AED applied?
    - ○ No
    - ○ Yes → Were shocks delivered? ○ No ○ Unknown ○ Yes → Number of shocks: ___
      - → AED applied by: ○ Lay person ○ Police ○ Healthcare ○ Other ○ Unknown

5. Were any shocks delivered by EMS responders?

- ○ No
- ○ Yes → Number of shocks: ___
  - → Energy level (1st EMS shock): ___ joules → ○ Biphasic ○ Monophasic

6. Type of EMS CPR: *(check all)*

- ○ Manual only-No ITD
- ○ Manual with ITD
- ○ Unknown

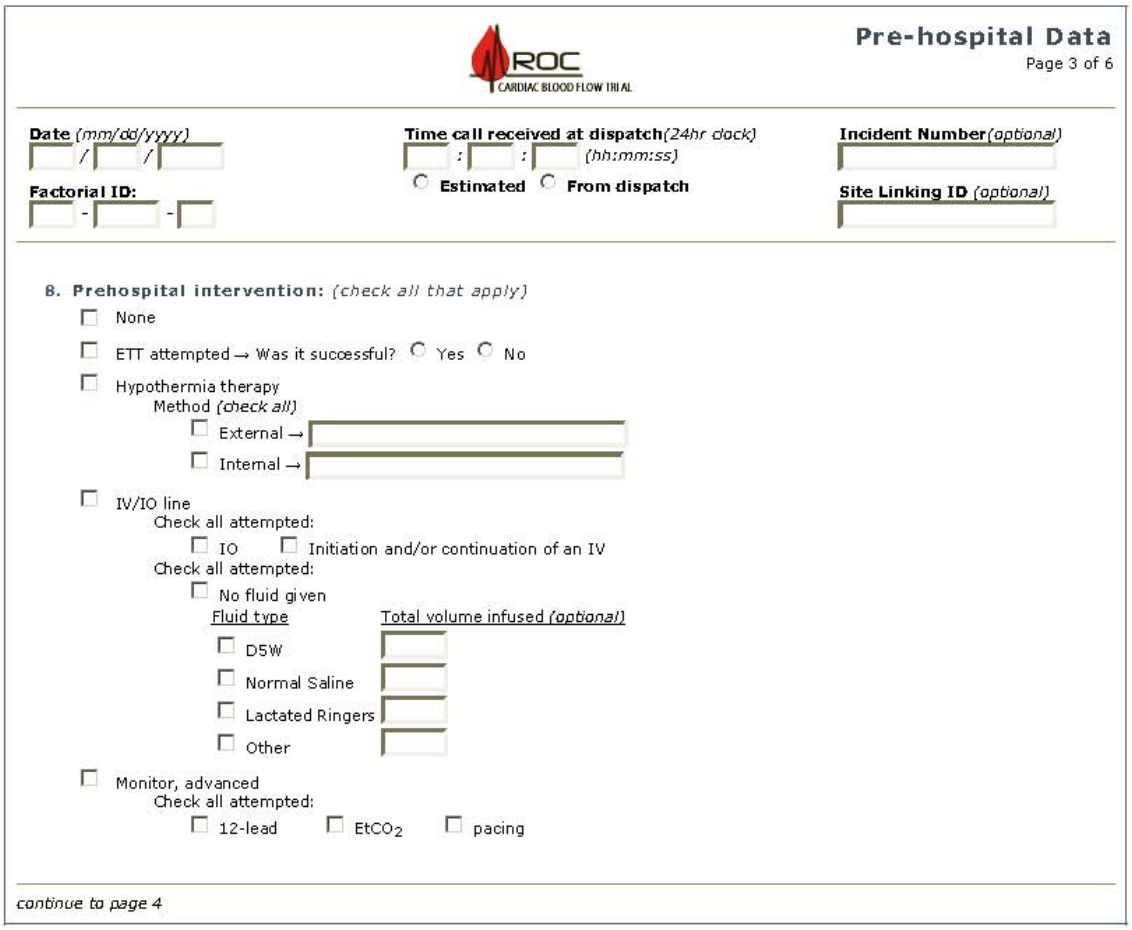
7. ITD information:

Vomit noted prior to/after ITD
- ○ Yes
- ○ No

Vomit noted during ITD
- ○ Yes
- ○ No

b. ITD attached to: *(check all)*
- ☐ Mask
- ☐ ETT
- ☐ Other advanced airway: ○ LMA ○ Combitube ○ King LT ○ PLA ○ Other: ___ *(20)*

continue to page 3



ROC CARDIAC BLOOD FLOW TRIAL

Pre-hospital Data

Page 3 of 6

Date *(mm/dd/yyyy)* ___ / ___ / ___

Time call received at dispatch *(24hr clock)* ___ : ___ : ___ *(hh:mm:ss)*

○ **Estimated** ○ **From dispatch**

Incident Number *(optional)*

Factorial ID: ___ - ___ - ___

Site Linking ID *(optional)*

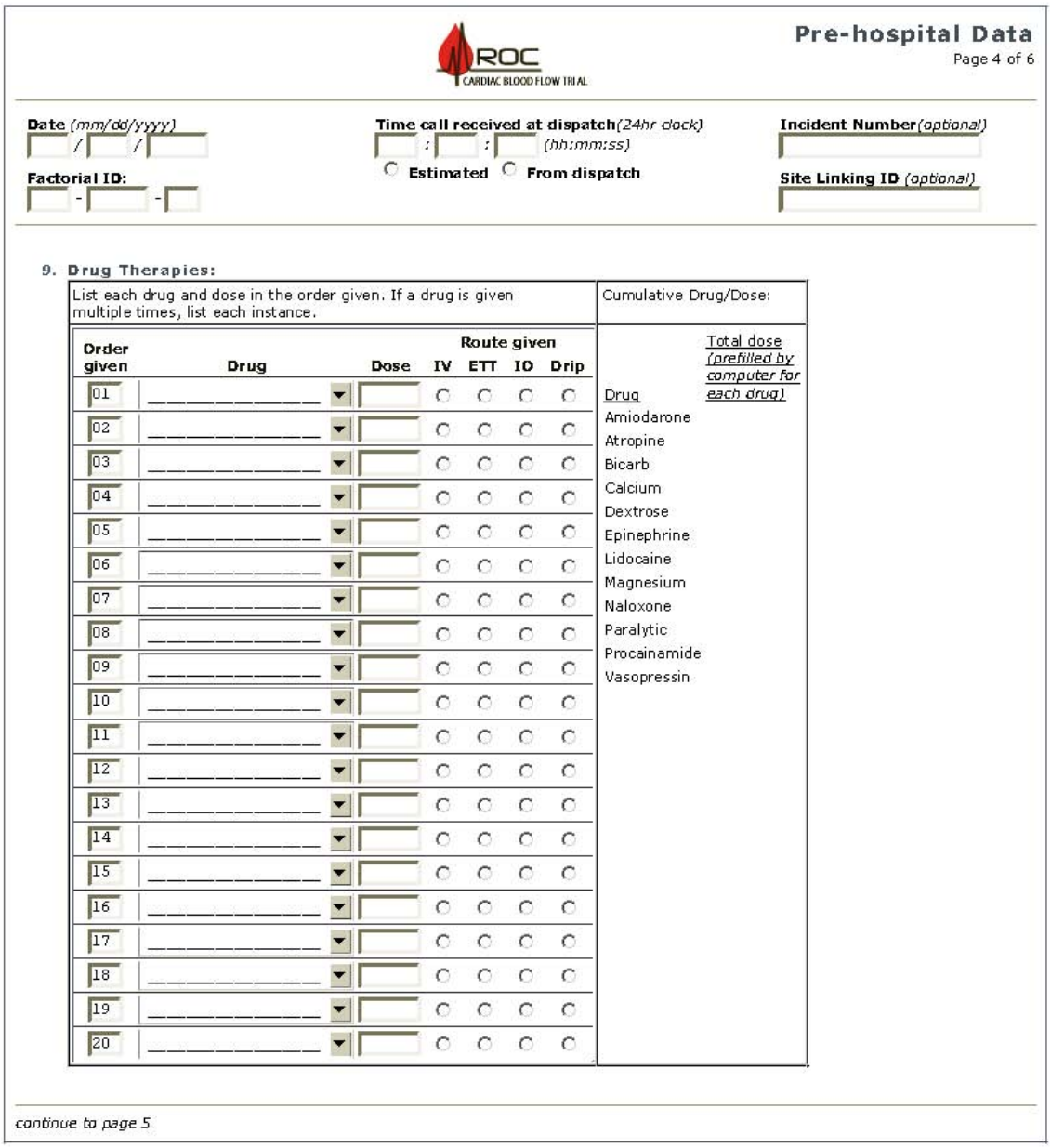
8. Prehospital intervention: *(check all that apply)*

- ☐ None
- ☐ ETT attempted → Was it successful? ○ Yes ○ No
- ☐ Hypothermia therapy
  - Method *(check all)*
    - ☐ External →
    - ☐ Internal →
- ☐ IV/IO line
  - Check all attempted:
    - ☐ IO ☐ Initiation and/or continuation of an IV
  - Check all attempted:
    - ☐ No fluid given

Fluid type	Total volume infused *(optional)*
☐ D5W	
☐ Normal Saline	
☐ Lactated Ringers	
☐ Other	

- ☐ Monitor, advanced
  - Check all attempted:
    - ☐ 12-lead ☐ $EtCO_2$ ☐ pacing

continue to page 4



ROC CARDIAC BLOOD FLOW TRIAL

Pre-hospital Data

Date *(mm/dd/yyyy)* ___ / ___ / ___

Time call received at dispatch *(24hr clock)* ___ : ___ : ___ *(hh:mm:ss)*

○ **Estimated** ○ **From dispatch**

Incident Number *(optional)*

Factorial ID: ___ - ___ - ___

Site Linking ID *(optional)*

9. Drug Therapies:

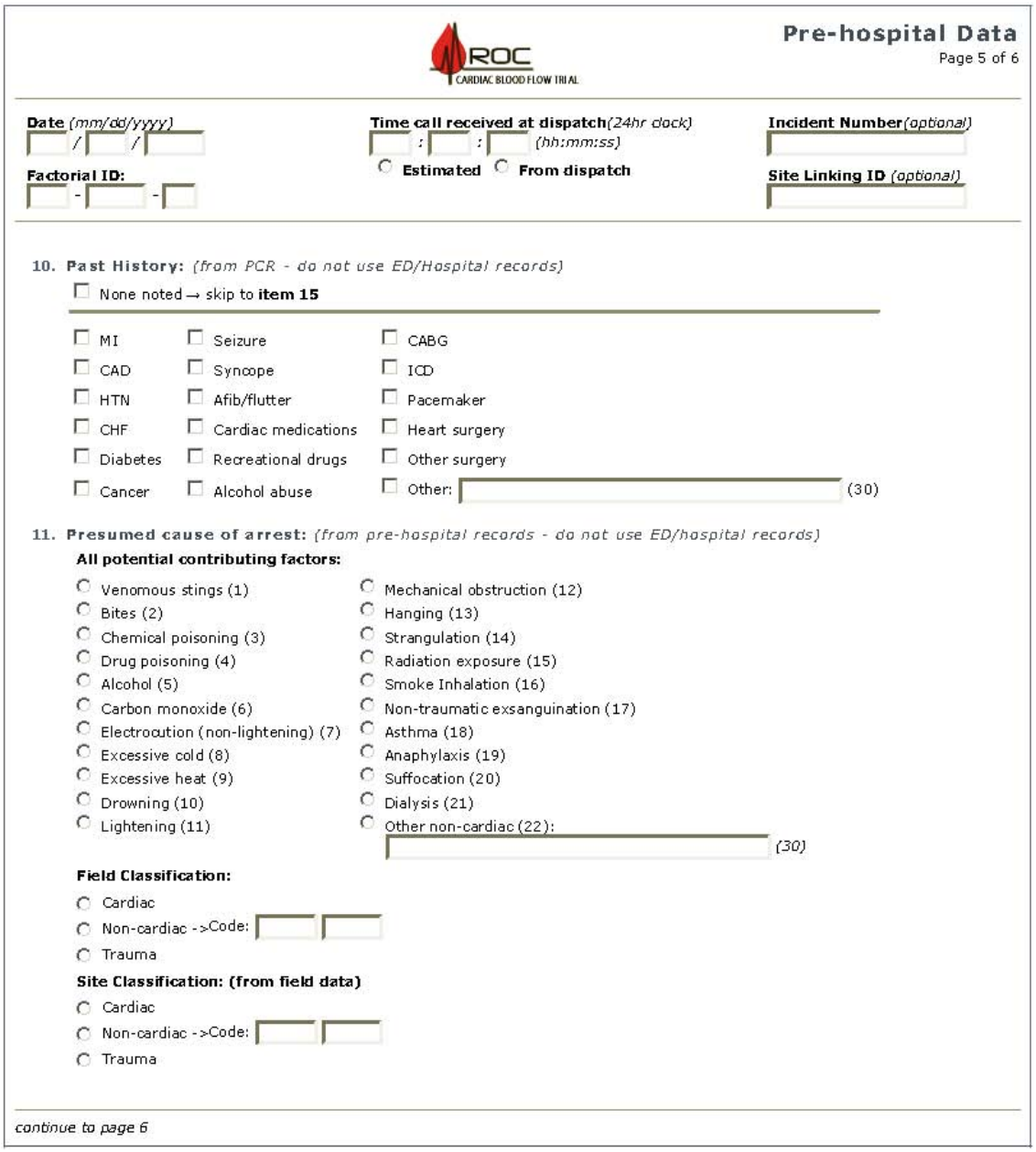
List each drug and dose in the order given. If a drug is given multiple times, list each instance.

Order given	Drug	Dose	Route given: IV	ETT	IO	Drip
01			○	○	○	○
02			○	○	○	○
03			○	○	○	○
04			○	○	○	○
05			○	○	○	○
06			○	○	○	○
07			○	○	○	○
08			○	○	○	○
09			○	○	○	○
10			○	○	○	○
11			○	○	○	○
12			○	○	○	○
13			○	○	○	○
14			○	○	○	○
15			○	○	○	○
16			○	○	○	○
17			○	○	○	○
18			○	○	○	○
19			○	○	○	○
20			○	○	○	○

Cumulative Drug/Dose:

Drug	Total dose *(prefilled by computer for each drug)*
Amiodarone	
Atropine	
Bicarb	
Calcium	
Dextrose	
Epinephrine	
Lidocaine	
Magnesium	
Naloxone	
Paralytic	
Procainamide	
Vasopressin	

continue to page 5



ROC CARDIAC BLOOD FLOW TRIAL

Pre-hospital Data
Page 5 of 6

Date *(mm/dd/yyyy)* ___ / ___ / ___

Time call received at dispatch *(24hr clock)* ___ : ___ : ___ *(hh:mm:ss)*
○ **Estimated** ○ **From dispatch**

Incident Number *(optional)*

Factorial ID: ___ - ___ - ___

Site Linking ID *(optional)*

10. Past History: *(from PCR - do not use ED/Hospital records)*

☐ None noted → skip to **item 15**

☐ MI	☐ Seizure	☐ CABG
☐ CAD	☐ Syncope	☐ ICD
☐ HTN	☐ Afib/flutter	☐ Pacemaker
☐ CHF	☐ Cardiac medications	☐ Heart surgery
☐ Diabetes	☐ Recreational drugs	☐ Other surgery
☐ Cancer	☐ Alcohol abuse	☐ Other: ___ (30)

11. Presumed cause of arrest: *(from pre-hospital records - do not use ED/hospital records)*

All potential contributing factors:

○ Venomous stings (1)	○ Mechanical obstruction (12)
○ Bites (2)	○ Hanging (13)
○ Chemical poisoning (3)	○ Strangulation (14)
○ Drug poisoning (4)	○ Radiation exposure (15)
○ Alcohol (5)	○ Smoke Inhalation (16)
○ Carbon monoxide (6)	○ Non-traumatic exsanguination (17)
○ Electrocution (non-lightening) (7)	○ Asthma (18)
○ Excessive cold (8)	○ Anaphylaxis (19)
○ Excessive heat (9)	○ Suffocation (20)
○ Drowning (10)	○ Dialysis (21)
○ Lightening (11)	○ Other non-cardiac (22): ___ *(30)*

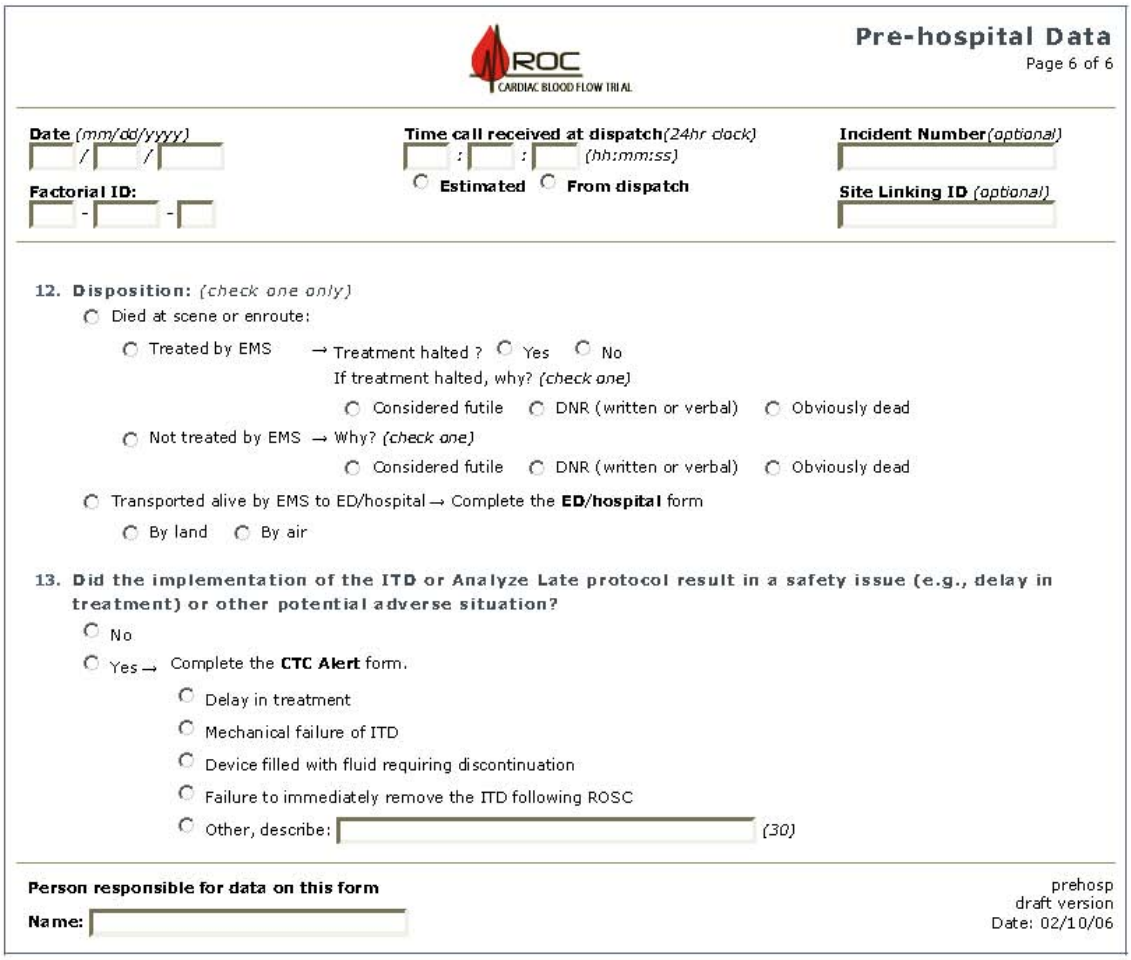
Field Classification:

○ Cardiac
○ Non-cardiac ->Code: ___ ___
○ Trauma

Site Classification: (from field data)

○ Cardiac
○ Non-cardiac ->Code: ___ ___
○ Trauma

continue to page 6



ROC CARDIAC BLOOD FLOW TRIAL

Pre-hospital Data

Page 6 of 6

Date *(mm/dd/yyyy)* ___ / ___ / ___

Time call received at dispatch *(24hr clock)* ___ : ___ : ___ *(hh:mm:ss)*

○ **Estimated** ○ **From dispatch**

Incident Number *(optional)*

Factorial ID: ___ - ___ - ___

Site Linking ID *(optional)*

12. Disposition: *(check one only)*

- ○ Died at scene or enroute:
  - ○ Treated by EMS → Treatment halted ? ○ Yes ○ No
    If treatment halted, why? *(check one)*
    ○ Considered futile ○ DNR (written or verbal) ○ Obviously dead
  - ○ Not treated by EMS → Why? *(check one)*
    ○ Considered futile ○ DNR (written or verbal) ○ Obviously dead
- ○ Transported alive by EMS to ED/hospital → Complete the **ED/hospital** form
  - ○ By land ○ By air

13. Did the implementation of the ITD or Analyze Late protocol result in a safety issue (e.g., delay in treatment) or other potential adverse situation?

- ○ No
- ○ Yes → Complete the **CTC Alert** form.
  - ○ Delay in treatment
  - ○ Mechanical failure of ITD
  - ○ Device filled with fluid requiring discontinuation
  - ○ Failure to immediately remove the ITD following ROSC
  - ○ Other, describe: ___ *(30)*

Person responsible for data on this form

Name: ___

prehosp
draft version
Date: 02/10/06

8

Complete this form for:
- episode qualifying for the Pre-hospital Form and the patient was admitted to an ED
Main data resouce: ED records

ROC CARDIAC BLOOD FLOW TRIAL

ED Admit

Date *(mm/dd/yyyy)* ___ / ___ / ___

Time call received at dispatch *(24hr clock)* ___ : ___ : ___ *(hh:mm:ss)*
○ From PCR/other ○ From dispatch

Incident Number *(optional)* ___

Factorial ID: ___ - ___ - ___

Site Linking ID *(optional)* ___

1. ED admit information:

ED name: _____

ED City: _____

2. Date/time of ED arrival:

Date: ___ / ___ / ___ *(mm/dd/yyyy)*

Time: ___ : ___ *24hr clock (hh:mm)*

3. Birth year: ___ *(yyyy)*

4. Major procedures while in the ED : *(check all)*

☐ CPR, Manual
☐ CPR, Mechanical
} Duration: ___ *(minutes)*

☐ Chest X-ray → Was pulmonary edema present?
- ○ No
- ○ Yes, check all:
  - ☐ Alveolar pulmonary edema
  - ☐ Interstitial pulmonary edema
  - ☐ Bilateral pleural effusion
  - ☐ Cardiomegaly
  - ☐ Pulmonary venous congestion

☐ Fibrinolytics

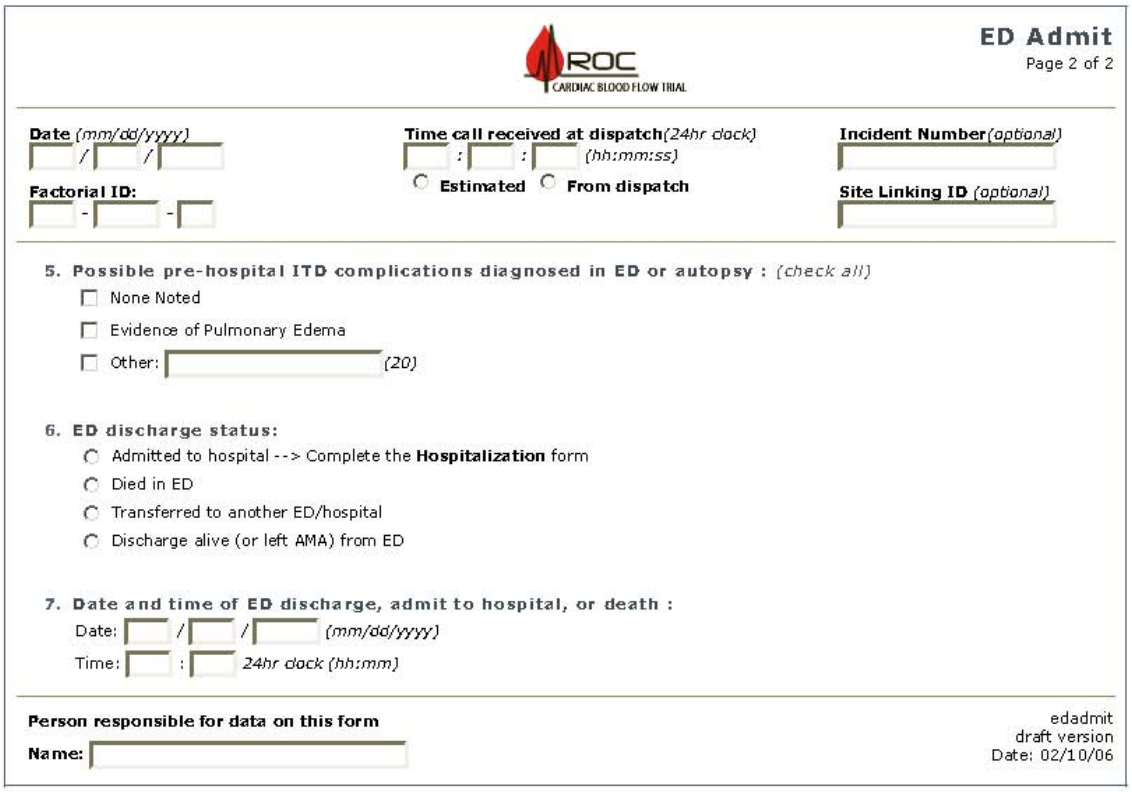
☐ Hypothermia therapy:
- a) Time started ___ : ___ *(hh:mm, 24 hr clock)*
- b) Duration ___ *(hours)*
- c) Method *(check all)*
  - ☐ External → ___
  - ☐ Internal → ___
- d) Lowest temperature ___ degrees → ○ Centigrade ○ Farenheit

☐ Open chest massage

☐ Other major cardiac procedure: ___ *(30)*

☐ None of the above

continue to page 2



ROC
CARDIAC BLOOD FLOW TRIAL

ED Admit
Page 2 of 2

Date *(mm/dd/yyyy)* ___ / ___ / ___

Time call received at dispatch *(24hr clock)* ___ : ___ : ___ *(hh:mm:ss)*
○ **Estimated** ○ **From dispatch**

Incident Number *(optional)* ___

Factorial ID: ___ - ___ - ___

Site Linking ID *(optional)* ___

5. Possible pre-hospital ITD complications diagnosed in ED or autopsy : *(check all)*

- ☐ None Noted
- ☐ Evidence of Pulmonary Edema
- ☐ Other: ___ *(20)*

6. ED discharge status:

- ○ Admitted to hospital --> Complete the **Hospitalization** form
- ○ Died in ED
- ○ Transferred to another ED/hospital
- ○ Discharge alive (or left AMA) from ED

7. Date and time of ED discharge, admit to hospital, or death :

Date: ___ / ___ / ___ *(mm/dd/yyyy)*

Time: ___ : ___ *24hr clock (hh:mm)*

Person responsible for data on this form

Name: ___

edadmit
draft version
Date: 02/10/06

10

Complete this form for:
- episode qualifying for the Pre-hospital Form and the patient was admitted to a hospital
Main data resource: Hospital records

ROC CARDIAC BLOOD FLOW TRIAL

Hospital Admit

Date *(mm/dd/yyyy)* ___ / ___ / ___

Time call received at dispatch *(24hr clock)* ___ : ___ : ___ *(hh:mm:ss)*
○ From PCR/other ○ From dispatch

Incident Number *(optional)* ___

Factorial ID: ___ - ___ - ___

Site Linking ID *(optional)* ___

1. Hospital admit information (1st hospital):

Hospital admittance date: ___ / ___ / ___ *(mm/dd/yyyy)*

Hospital name: _____

Hospital City: _____

2. Was the patient transfered to another hospital before discharge?

○ Yes → Name of last hospital pt. admitted to: ___
→ Total number of hospital pt. admitted to: ___

○ No

3. Birth year: ___ *(yyyy)*

4. Cause of arrest (based on hospital records/notes):

All potential contributing factors:

- ○ Venomous stings (1)
- ○ Bites (2)
- ○ Chemical poisoning (3)
- ○ Drug poisoning (4)
- ○ Alcohol (5)
- ○ Carbon monoxide (6)
- ○ Electrocution (non-lightening) (7)
- ○ Excessive cold (8)
- ○ Excessive heat (9)
- ○ Drowning (10)
- ○ Lightening (11)
- ○ Mechanical obstruction (12)
- ○ Hanging (13)
- ○ Strangulation (14)
- ○ Radiation exposure (15)
- ○ Smoke inhalation (16)
- ○ Non-traumatic exsanguination (17)
- ○ Asthma (18)
- ○ Anaphylaxis (19)
- ○ Suffocation (20)
- ○ Dialysis (21)
- ○ Other non-cardiac (22): ___ *(30)*

Site Classification: (from hospital data only)

- ○ Cardiac
- ○ Non-cardiac ->Codes from above: ___ ___
- ○ Trauma

continue to page 2

ROC
CARDIAC BLOOD FLOW TRIAL

Hospital Admit
Page 2 of 5

Date *(mm/dd/yyyy)* ___ / ___ / ___

Time call received at dispatch *(24hr clock)* ___ : ___ : ___ *(hh:mm:ss)*
○ **Estimated** ○ **From dispatch**

Incident Number *(optional)* ___

Factorial ID: ___ - ___ - ___

Site Linking ID *(optional)* ___

5. Major procedures while in the hospital: *(check all)*

- ☐ CPR
- ☐ Chest X-ray → Date: ___ / ___ / ___ *(mm/dd/yyyy)*
  If within 48 hours of admit, was pulmonary edema present?
  - ○ No
  - ○ Yes, check all:
    - ☐ Alveolar pulmonary
    - ☐ Interstitial pulmonary edema
    - ☐ Bilateral pleural effusion
    - ☐ Cardiomegaly
    - ☐ Pulmonary venous congestion
- ☐ Fibrinolytics
- ☐ Hypothermia therapy:
  a) Time started ___ : ___ *(hh:mm, 24 hr clock)*
  b) Duration ___ *(hours)*
  c) Method *(check all)*
  - ☐ External → ___
  - ☐ Internal → ___

  d) Lowest temperature ___ degrees → ○ Centigrade ○ Farenheit
  e) Number of hours to reach lowest temperature ___
- ☐ Cath, dianostic
- ☐ PCI
- ☐ CABG
- ☐ Pacemaker implant
- ☐ ICD implant
- ☐ Other major cardiac procedure: ___ *(30)*
- ☐ None of the above

6. Possible pre-hospital ITD complications diagnosed in hospital or autopsy: *(check all)*

- ☐ None
- ☐ Pulmonary edema
- ☐ Other, describe: ___

7. Census tract of residence prior to arrest: ___

US: http://www.ffiec.gov/geocode/default.htm
Canada: http://geodepot.statcan.ca/Diss/maps/referencemaps/ct_e.cfm

continue to page 3

ROC
CARDIAC BLOOD FLOW TRIAL

Hospital Admit
Page 3 of 5

Date *(mm/dd/yyyy)* / / **Time call received at dispatch** *(24hr clock)* : : *(hh:mm:ss)* **Estimated** **From dispatch** **Incident Number** *(optional)*

Factorial ID: - - **Site Linking ID** *(optional)*

8. Residential status prior to arrest:

- Home → Independent With assistance
- Rehabilitation
- Assisted living
- Nursing home
- Unknown

9. Disposition at discharge:

- Home → Independent With assistance
- Rehabilitation
- Assisted living
- Nursing home
- Remain in acute care hospital, reclassified as non-acute patient awaiting placement or chronic care
- Dead at discharge

10. Cerebral Performance Category at hospital discharge: *(based on medical record review)*

- CPC1 - Conscious, alert, able to work and lead a normal life. May have minor psychologic or neurologic deficits (mild dysphasia, non-incapacitating hemiparesis, or minor cranial nerve abnormalities).
- CPC2 - Conscious. Sufficient cerebral function for part-time work in a sheltered environment or independent activities of daily life (dress, travel by public transportation, food preparation). May have hemiplegia, seizures, ataxia, dysarthria, or permanent memory or mental changes.
- CPC3 - Conscious. Dependent on others for daily support (in an institution or at home with exceptional family effort). Has at least limited cognition. This category includes a wide range of cerebral abnormalities, from patiens who are ambulatory but have severe memory disturbances or dementia precluding independent existence, to those who are paralyzed and can communicate only with their eyes, as in the "locked-in" syndrome.
- CPC4 - Unconscious. Unaware of surroundings, no cognition. No verbal and/or psychologic interaction with environment.
- CPC5 - Brain dead, circulation preserved.
- Death at discharge.

Modified Rankin Scale at hospital discharge (based on medical records review):

- MRS0 - No symptoms at all.
- MRS1 - No significant disability: despite symptoms, able to carry out all usual duties and activities.
- MRS2 - Slight disability: unable to carry out all previous activities but able to look after own affairs without assistance.
- MRS3 - Moderate disability: requiring some help, but able to walk without assistance.
- MRS4 - Moderately severe disability: unable to walk without assistance, and unable to attend to own bodily needs without assistance.
- MRS5 - Severe disability: bedridden, incontinent and requiring constant nursing care and attention.
- Death at discharge.

continue to page 4

13

Date *(mm/dd/yyyy)* ___ / ___ / ___

Time call received at dispatch *(24hr clock)* ___ : ___ : ___ *(hh:mm:ss)*
○ **Estimated** ○ **From dispatch**

Incident Number *(optional)* ___

Factorial ID: ___ - ___ - ___

Site Linking ID *(optional)* ___

12. Date and time of awakening: *(based on nursing/medical records)*

Awakening is defined as the patients' ability to follow commands or to speak coherently

☐ No awakening → skip to **item 12**

Date of awakening: ___ / ___ / ___ *(mm/dd/yyyy)*
Time of awakening: ___ : ___ *24hr clock (hh:mm)*

13. Date and time of hospital discharge or death:

Date of discharge or death: ___ / ___ / ___ *(mm/dd/yyyy)*
Time of discharge or death: ___ : ___ *24hr clock (hh:mm)*
Was patient made DNR or care limited/withdrawn during hospitalization?
○ Yes → Date: ___ / ___ / ___ *(mm/dd/yyyy)*
○ No

If patient died, interval from 911 call received: ___ : ___ *(hh:mm)* or ☐ > 24 hrs
(auto fill during web entry, coordinator will verify accuracy)

14. Total days in hospital and ICU/CCU:

Total days in ICU/CCU: ___
Total days in hospital: ___ *(pt is considered d/'cd if discharged to rehab unit or equivalent)*

15. If death occured, check one main category and one subcategory:

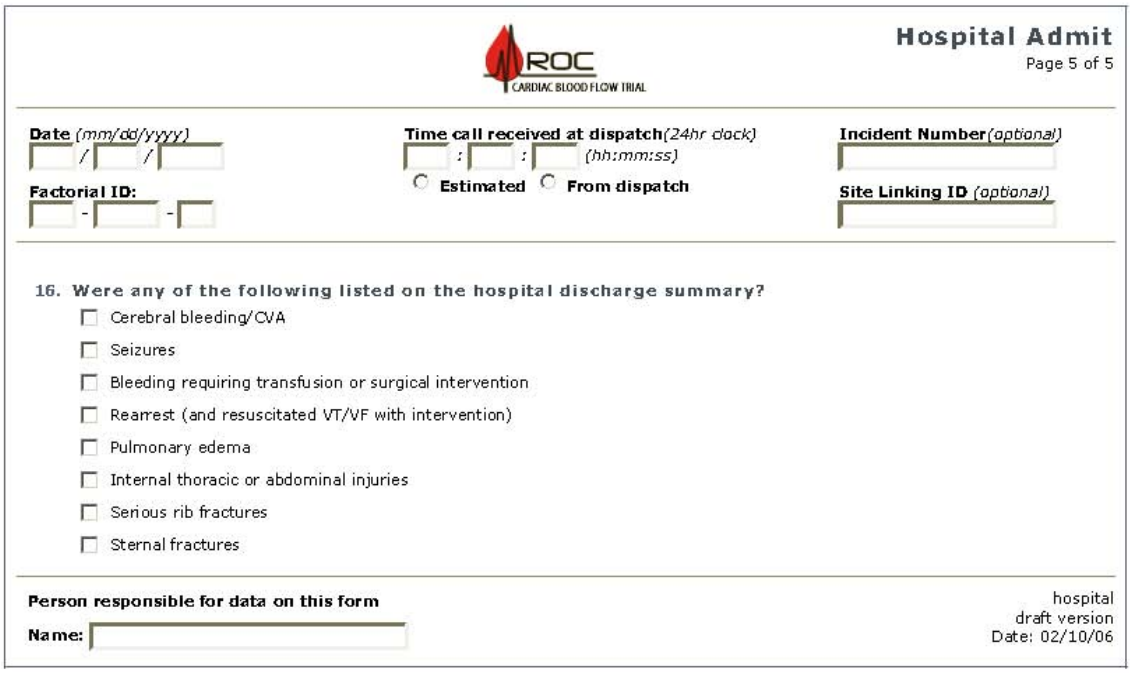
○ Subject is physiologically unstable, and continued life support is impossible or futile
Date of decision: ___ / ___ / ___ *(mm/dd/yyyy)*
- ○ Multi-system organ failure
- ○ Second cardiac arrest with unsuccessful resuscitation
- ○ Intractable shock

○ Subject has brain-death criteria, resulting in withdrawal of care and cardiovascular death
Date of decision: ___ / ___ / ___ *(mm/dd/yyyy)*

○ Subject is physiologically stable or continued life-support is possible. Because of other non-neurological considerations, care is withdrawn or limited resulting in death
Date of decision: ___ / ___ / ___ *(mm/dd/yyyy)*
- ○ Underlying terminal illness (metastic cancer, for example)
- ○ Pre-existing advanced directives or living will
- ○ Family or surrogate representation of subject's wishes

○ Subject is deemed to have poor neurological prognosis, and care is withdrawn or limited resulting in death
Date of decision: ___ / ___ / ___ *(mm/dd/yyyy)*

continue to page 5


ROC
CARDIAC BLOOD FLOW TRIAL
Hospital Admit
Page 5 of 5
Date (mm/dd/yyyy)
/ /
Time call received at dispatch(24hr clock)
: : (hh:mm:ss)
Estimated From dispatch
Incident Number(optional)
Factorial ID:
- -
Site Linking ID (optional)
16. Were any of the following listed on the hospital discharge summary?
Cerebral bleeding/CVA
Seizures
Bleeding requiring transfusion or surgical intervention
Rearrest (and resuscitated VT/VF with intervention)
Pulmonary edema
Internal thoracic or abdominal injuries
Serious rib fractures
Sternal fractures
Person responsible for data on this form
Name:
hospital
draft version
Date: 02/10/06

15

Complete this form:
- For each potential Adverse Situation where implementation of study protocol resulted in a potential safety issue to the patient, EMS staff, or bystander
- For public objection to either study
- For protocol violations/deviations/unsual circumstances

Report this information to the CTC within 1 business day of discovery

ROC CARDIAC BLOOD FLOW TRIAL

Alert CTC

Page 1 of 1

Date *(mm/dd/yyyy)* ___ / ___ / ___

Time call received at dispatch *(24hr clock)* ___ : ___ : ___ *(hh:mm:ss)*
○ **From PCR/other** ○ **From dispatch**

Incident Number *(optional)*

Factorial ID: ___ - ___ - ___

Site Linking ID *(optional)*

☐ Not associated with an episode → Date of Situation: ___ / ___ / ___ *(mm/dd/yyyy)*

1. **Date reported to CTC (today's date):** ___ / ___ / ___ *(mm/dd/yyyy)*

2. **Type of situation:** *(check all that apply)*

Potential Safety Issues Related to Study Protocol or ITD use

☐ ITD protocol caused delay/interruption of treatment → Estimated delay ___ minutes
☐ Analyze Late protocol caused delay/interupt in treatment
☐ Public formal objection to ITD Trial
☐ Other potential safety issue
☐ Pulmonary edema found on CXR within 48 hours of arrest
☐ ITD filled with fluid: ○ once ○ more than once
☐ Suspected mechanical failure of ITD → ITD # ___

Potential Protocol Violations/Deviations

☐ Age < age of consent (known prior to ITD use)
☐ Traumatic arrest/burns and ITD used
☐ ITD used after ROSC obtained
☐ Non-compliance with assigned therapy *(e.g. failure to transfer ITD from one airway to another, using more than one ITD)*
☐ Non-compliance with length of CPR
☐ Other potential protocol violation/protocol deviation
☐ Known prisoner
☐ Known pregnancy
☐ ITD opened, but not used

Other Unusual Circumstances

☐ Other unusual circumstances (e.g., missing ITD during inventory)

3. **Explain circumstances:**

___ *(60)*
___ *(60)*
___ *(60)*

Person responsible for data on this form
Name: ___

alertctc
draft version
Date: 02/10/06

Note: ***Principal Investigator will be asked to sign the confirmation sheet after this submission.***

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Complete this form:
- for all patients who were enrolled.

ROC CARDIAC BLOOD FLOW TRIAL

Patient/Family Consent

Date *(mm/dd/yyyy)* ___ / ___ / ___

Time call received at dispatch *(24hr clock)* ___ : ___ : ___ *(hh:mm:ss)*
○ From PCR/other ○ From dispatch

Incident Number *(optional)* ___

Factorial ID: ___ - ___ - ___

Site Linking ID *(optional)* ___

1. Was patient and/or family and/or LAR notified that patient was in study?

○ Yes → Who was notified? *(check all)*

- ☐ Family → Date: ___ / ___ / ___ (mm/dd/yyyy) → Relationship: ___ (20)
- ☐ Patient → Date: ___ / ___ / ___ (mm/dd/yyyy)
- ☐ LAR → Date: ___ / ___ / ___ (mm/dd/yyyy)

○ No*

2. Did patient and/or family and/or LAR consent to continuation in study?

○ Yes → Who gave consent? *(check all)*

- ☐ Family → Date: ___ / ___ / ___ (mm/dd/yyyy) → Relationship: ___ (20)
- ☐ Patient → Date: ___ / ___ / ___ (mm/dd/yyyy)
- ☐ LAR → Date: ___ / ___ / ___ (mm/dd/yyyy)

○ No* → Why not? *(check all)*

- ☐ Patient/family LAR refused consent
- ☐ Not applicable/expired
- ☐ Other*

3. Did patient and/or family and/or LAR consent to follow-up calls?

○ Yes → Who gave consent? *(check all)*

- ☐ Family → Date: ___ / ___ / ___ (mm/dd/yyyy) → Relationship: ___ (20)
- ☐ Patient → Date: ___ / ___ / ___ (mm/dd/yyyy)
- ☐ LAR → Date: ___ / ___ / ___ (mm/dd/yyyy)

○ No* → Why not? *(check all)*

- ☐ Patient/family/LAR refused consent
- ☐ Not applicable/expired
- ☐ Other*

4. If any of the starred bubbles are checked above (and greater than 1 month since the episode), explain the attempts made:

___ (60)
___ (60)
___ (60)

Person responsible for data on this form

Name: ___

consent
draft version
Date: 02/10/06

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Complete this form:
- For all patients that were discharged alive from the hospital and consented to 3 month follow-up

ROC CARDIAC BLOOD FLOW TRIAL

Follow-up (3 month)

Date *(mm/dd/yyyy)* ___ / ___ / ___

Time call received at dispatch *(24hr clock)* ___ : ___ : ___ *(hh:mm:ss)*
○ From PCR/other ○ From dispatch

Incident Number *(optional)* ___

Factorial ID: ___ - ___ - ___

Site Linking ID *(optional)* ___

1. Was the patient (or patient representative) successfully contacted?

○ Yes → Date of contact: ___ / ___ / ___ *(mm/dd/yyyy)*

○ No → Why not? ___ (30) --> Complete the **Contact Patient** form

2. Follow-up conducted with whom?

○ Patient
○ Family
○ Other → Relationship to patient: ___ (30)

3. Vital status:

○ Alive
○ Dead → Date of death: ___ / ___ / ___ *(mm/dd/yyyy)*
(skip the remaining questions and sign the form)

4. What QOL measures were done? *(check all)*

☐ CPC
☐ ALFI-MMSE
☐ HUI
☐ MRS
☐ GDS

5. If any of the measures in item 4 were not completed, why not?

___ *(60)*
___ *(60)*
___ *(60)*
___ *(60)*
___ *(60)*
___ *(60)*

Person responsible for data on this form

Name: ___

followup-3month
draft version
Date: 02/10/06

Complete this form: - for each cardiac arrest episode that was treated *Main Data Source:* ECG Strip *Other Data Source:* PCR	ROC CARDIAC BLOOD FLOW TRIAL	**CPR Process** Page 1 of 2 Version: 1 Date: 12-01-2005

Episode Information:

Date *(mm/dd/yyyy)* ___ / ___ / ___

Time call received at dispatch *(24hr clock)* ___ : ___ : ___ *(hh:mm:ss)*
○ **From PCR/other** ○ **From dispatch**

Incident Number *(optional)* ___

CTC Episode ID: ___ - ___ - ___

Site Linking ID *(optional)* ___

1) Initial cardiac arrest rhythm determined from: *(check one only)*

- ○ ECG continuous electronic recording
- ○ ECG "snap shot" or paper strip
- ○ PCR only

2) Time of initial rhythm determined from ECG recording:

___ : ___ : ___ *(hh:mm:ss, 24 hr clock)* OR ☐ Not applicable

3) Initial cardiac arrest rhythm: *(check one only)*

- ○ VF
- ○ Pulseless VT
- ○ PEA (organized pulseless) → rate: ___
- ○ Asystole
- ○ AED-shock (no strip)
- ○ AED-no shock (no strip)
- ○ Cannot determine
- ○ Missing (no documentation)

4) Device used: *(check all that apply)*

- ☐ Phillips → Feedback: ○ On ○ Off
- ☐ Zoll
- ☐ Medtronic
- ☐ Other, specify: ___ *(30)*

5) Does a continuous recording of ECG exist for the first 5 minutes of the EMS resuscitative effort?

- ○ Yes → How many recordings make up the first 5 minutes? ___
- ○ No → Why not?
  - ○ Stored ECG overwritten
  - ○ Other defibrillator 1st on scene
  - ○ CPR-process monitoring - capable defibrillator not brought to patient side
  - ○ CPR-process monitoring - capable defibrillator not available on rig
  - ○ Other, specify: ___ *(60)*
  - ○ Not known

Continue to page 2

Episode Information:

Date *(mm/dd/yyyy)* ___ / ___ / ___

Time call received at dispatch *(24hr clock)* ___ : ___ : ___ *(hh:mm:ss)*

○ **From PCR/other** ○ **From dispatch**

Incident Number *(optional)* ___

CTC Episode ID: ___ - ___ - ___

Site Linking ID *(optional)* ___

6) ECG Analysis:

(hh:mm:ss, 24 hr clock)

Time machine turned on: ___ : ___ : ___

Time pads placed: ___ : ___ : ___

Time resuscitation terminated: ___ : ___ : ___ OR ☐ Not applicable

Time ED arrival: ___ : ___ : ___ OR ☐ Not applicable

Min	Start time *(Auto fill)*	# Seconds without comp	# Vent	# Comp	Comp rate	CPR fraction	# Unanalyzable seconds	Comp depth *(optional)*	Comp release *(optional)*	ET CO_2 *(optional)*
1	: :									
2	: :									
3	: :									
4	: :									
5	: :									
6	: :									
7	: :									
8	: :									
9	: :									
10	: :									
11	: :									
12	: :									
13	: :									

Person responsible for data on this form
Name: ___

Appendix 7: Training Proficiency Goals

Providers will be given the opportunity to practice to proficiency each component of the protocol. The number of providers used during these rehearsals should simulate actual clinical practice whenever possible. The use of an AED or ALS defibrillator in manual mode should also be dictated by clinical practice, using the identical brand and technology that will be available during the trial. Various permutations of the study protocol should be presented, including each of the study arms. Specific assessment goals may include:

- Identification of appropriate study candidates (including inclusion/exclusion criteria)
- Proper enrollment procedure
- Appropriate role assignment ("compressor", AED/monitor, and ITD/ventilations)
- Correct number of chest compressions based on visual reminders
- Placement of AED/monitor and ITD application with initial airway management
- Use of ITD whenever chest compressions are performed throughout resuscitative efforts
- Open and apply a single ITD to each patient
- Use the first ITD available If multiple agencies respond to the same episode
- Analysis with defibrillation attempts if shock indicated
- Analysis without defibrillation if no shock indicated
- Resumption of chest compressions when appropriate after analysis +/- shock
- Maintenance of continuous tight facemask seal during chest compressions and ventilations using "E-C" hand technique (one airway rescuer) or two-handed technique (two airway rescuers)
- Transfer of ITD to invasive airway and activation of ventilation assist timing lights
- Clearance of ITD when filled with fluid followed by suctioning and ITD re-application
- Discontinuing use of the ITD if refills with fluid
- Proper handoff to ED personnel and retrieval of ITD
- Performance of optimal CPR (ventilation rate, chest compression rate and depth, complete chest wall recoil after each compression, and minimal "hands-off" time)
- Continue resuscitation efforts for at least 30 minutes when appropriate.

Appendix 8: Interim Monitoring Plan

Impedance Threshold Device Factor

In making the decision to recommend termination of the study, the Data Safety Monitoring Board shall be guided by a formal stopping rule based on the primary endpoint of the difference between treatment arms in the proportion of patients with neurologically intact (MRS $\leq$ 3) survival to hospital discharge. The test statistic shall be Pearson's chi-squared statistic, with additional secondary analyses adjusting for covariates performed using generalized linear regression models.

The clinical trial may be stopped early either for reasons of demonstrated efficacy (the ITD treatment arm has significantly higher rates of neurologically intact survival to hospital discharge than the sham device arm) or for reasons of futility (the proportion of patients with neurologically intact survival to hospital discharge is not sufficiently lower than that on the sham device arm to warrant continuation of the trial).

The formal stopping boundaries will be determined by an asymmetric one-sided design (Pampallona and Tsiatis 1994), a family also included in the unified family of group sequential stopping rules.(Kittelson and Emerson 1999) In the notation of the latter paper, the stopping rule will be based on a one-sided group sequential design testing an upper alternative hypothesis at a level of significance α =.025 with β=.900, an upper (efficacy) stopping boundary relationship specified by P_d = 0.8 (a boundary relationship that is intermediate to the O'Brien-Fleming type boundary(O'Brien and Fleming 1979) and the Pocock type boundary(Pocock 1977)), and a lower (futility) stopping boundary relationship specified by P_a =1.2 (a boundary that is more conservative with respect to early stopping than an O'Brien-Fleming). It is envisioned that three equally spaced formal interim analyses will be performed during the monitoring of the study. The following S+SeqTrial code can be used to generate the stopping rule:

```
itdDesign <- seqDesign(
    prob.model = "proportions",
    arms = 2,
    test.type = "greater",
    nbr.analyses = 3,
    alpha = c(0.1, 0.025), beta = c(0.975, 0.9),
    P = c(1.2, 0.8), R= c(0,0), A= c(0,0),
    null.hypothesis = 0.0533, alt.hypothesis = 0.0669,
    variance = "alternative",
    sample.size=14154,
    power= "calculate")
```

Under such a monitoring schedule and assuming a baseline neurologically intact survival rate of 5.33% on the sham device arm, a sample size of 14,154 evaluable patients (7,077 patients on each of the sham device and ITD treatment arms) will provide approximately 90% power to detect an improvement to a 6.69% rate of neurologically intact survival on the active ITD treatment arm (corresponding to a relative improvement of 25.5% in neurologically intact survival to discharge). Table 1 provides a more detailed

description of the power provided by such a sample size for a range of favorable event rates.

Table 1: Alternatives for which a sample size of 14,154 subjects provides the specified power as a function of sham device arm rates of neurologically intact (MRS ≤ 3) survival to hospital discharge

Power	0.0467 Sham Neuro Intact Surv to Hosp Discharge			0.0533 Sham Neuro Intact Surv to Hosp Discharge			0.0597 Sham Neuro Intact Surv to Hosp Discharge		
	ITD Neur Intact Surv to Hosp D/C	**Abs Diff**	**Rel Diff**	**ITD Neur Intact Surv to Hosp D/C**	**Abs Diff**	**Rel Diff**	**ITD Neur Intact Surv to Hosp D/C**	**Abs Diff**	**Rel Diff**
50%	.0542	.0075	16.0%	.0611	.0079	14.9%	.0680	.0083	14.0%
80%	.0575	.0108	23.2%	.0647	.0115	21.5%	.0718	.0121	20.2%
90%	.0593	.0126	27.0%	.0665	.0133	25.1%	.0737	.0140	23.5%
95%	.0608	.0141	30.2%	.0681	.0149	28.1%	.0754	.0157	26.3%
97.5%	.0621	.0154	33.1%	.0695	.0163	30.7%	.0769	.0172	28.8%

Under the planned schedule of three equally spaced analyses and assuming a baseline rate of 5.33% neurologically intact survival to hospital discharge with the sham device, Table 2 presents projected estimates of the stopping boundaries at each analysis for the specified stopping rule expressed as the absolute difference in neurologically intact survival rates (ITD – sham device). Also presented are the Z statistics and fixed sample lower one-sided P values which correspond to those stopping boundaries.

Table 2: Stopping boundaries for a level α=.025 one-sided group sequential design in the unified family (Kittelson and Emerson 1999) with power β=0.90 to detect a greater alternative, boundary shape parameters Pa = 1.2 for the futility boundary and Pd = 0.8 for the efficacy boundary, three equally spaced analyses, a maximal sample size of 14,154 subjects, and a rate of neurologically intact survival to hospital discharge of approximately 0.0601 on both treatment arms combined (e.g., 0.0533 on the sham device arm and 0.0669 on the active ITD arm)

Analysis	**Sample Size**	**Prop of Max Stat Info**	**Futility (lower) stopping boundary**			**Efficacy (upper) stopping boundary**		
			Abs Diff	**Z statistic**	**Fixed P (lower)**	**Abs Diff**	**Z statistic**	**Fixed P (lower)**
1	4718	0.33	-.0061	-0.889	.8131	.0196	2.837	.0023
2	9436	0.67	.0049	0.996	.1595	.0113	2.304	.0106
3	14154	1.00	.0081	2.040	.0207	.0081	2.040	.0207

Thus, according to the above table, if the rate of neurologically intact survival to hospital discharge on the combined treatment arms is 6.00%, an absolute difference of 1.96% or more (e.g., 5.02% on the sham device arm and 6.98% on the ITD arm) when 4,718 evaluable subjects have been accrued to the study (2,369 subjects on each arm), the stopping rule would suggest that the study be terminated early with a decision that treatment with the ITD results in a statistically significant improvement in neurologically intact survival to hospital discharge. On the other hand, if at that first analysis there were an absolute difference of 0.61% or less (e.g., 6.31% on the sham device arm and 5.70% on the ITD arm), the stopping rule would suggest that the study be terminated early with

a decision that it was futile to continue the trial because there was not sufficient evidence that any beneficial effect of ITD was clinically important.

As with the power properties of the study, the observed absolute difference in rates which correspond to the stopping boundaries is affected by the baseline rate of neurologically intact survival to hospital discharge on the sham device arm as well as any effect of the ITD on the rates of those favorable outcomes. Due to the need to estimate the baseline favorable event rates when performing the statistical test, the expression of the stopping boundaries as an absolute difference in rates thus depends on the overall favorable outcome rates on both arms combined. Note that the stopping boundary expressed as a Z statistic or a lower fixed sample P value statistic is unaffected by the observed favorable event rates, and thus the criteria used to compare observed interim results to the stopping boundary will be based on the value of the fixed sample P value.

Table 3 presents for the setting presented in Table 2 (i.e., a combined favorable outcome rate of 6.03%) the statistical inference that would be reported if the study were to result in observed treatment effects corresponding to the stopping boundaries. The estimates, P values, and confidence intervals reported in Table 3 have been adjusted for the stopping rule using the bias adjusted point estimate(Whitehead 1986) and confidence intervals and P values calculated from the ordering of the outcome space based on the maximum likelihood estimate.(Emerson and Fleming 1990) (Note that the fixed sample P value presented in Table 2 is not appropriate for statistical inference. Instead it is presented to facilitate the use of standard statistical software when computing the test statistic: Upper one-sided P values calculated by standard statistical software (i.e., as would be appropriate for nonsequential fixed sample studies) can be compared to the critical values for that statistic as presented in Table 2 in order to obtain a level .025 sequential hypothesis test.)

Table 3: Statistical inference regarding the effect of ITD on rates of neurologically intact survival to hospital discharge (measured as the absolute difference in favorable outcome rates between the ITD and sham device arms) which would be reported if observed results corresponded exactly to the stopping boundaries for a level .025 one-sided group sequential design as presented in Table 2

		Futility (lower) stopping boundary			Efficacy (upper) stopping boundary		
Analysis	Sample Size	Adjusted estimate	Exact 95% conf intvl	Adjusted P value	Adjusted estimate	Exact 95% conf intvl	Adjusted P value
1	4718	-0.47%	(-1.48%,0.75%)	0.779	1.80%	(0.59%,2.82%)	0.002
2	9436	0.54%	(-0.23%,1.47%)	0.081	1.05%	(0.13%,1.84%)	0.013
3	14154	0.80%	(0.00%,1.62%)	0.025	0.80%	(0.00%,1.62%)	0.025

As noted above, the exact stopping boundaries that are appropriate for the group sequential design will depend upon the exact schedule of interim analyses and the best estimate of the variability of the test statistic as computed from the observed favorable event rates. The intended schedule of interim analyses is three equally spaced analyses subject to minor variations due to the availability of the DSMB. In any case, the number and timing of interim analyses of the data for this trial will not be determined by the interim results of this study for the primary endpoint.

Modifications of the stopping rule to account for changes in the schedule of interim analyses and estimates of baseline favorable event rates will be made by using the

parametric form of the stopping rule as specified above, with constraints imposed on the fixed sample P value scale for analyses previously performed. Boundaries will be constrained on the scale of the maximum likelihood estimate of the treatment effect, with the current best estimate of the test statistic's variance used at each analysis.(Burington and Emerson 2003) In making such adjustments, the one-sided type I error will be maintained at .025, and the maximal sample size will be constrained at 14,154 evaluable subjects. Modifications of the stopping rule will be computed using S+SeqTrial (*S+SEQTRIAL User's Manual*, Insightful, Inc., Seattle WA, 2000).

At each formal interim analysis, the DSMB will use the stopping rule computed in the above manner as a guideline in evaluating the trial results with respect to rates of neurologically intact survival to hospital discharge. In making a recommendation to terminate the study, the DSMB will of course also consider information on safety endpoints, as well as consistency of outcomes for secondary endpoints and consistency of outcomes within important subgroups as described in the protocol.

At the conclusion of the clinical trial, reported point estimates, 95% confidence intervals, and P values for the primary endpoint will be adjusted for the true sampling distribution. Point estimates will be based on the bias adjusted point estimate (Whitehead 1986) and confidence intervals and P values calculated from the ordering of the outcome space based on the maximum likelihood estimate.(Emerson and Fleming 1990)

Analyze Early versus Analyze Late Factor

In making the decision to recommend termination of the study, the Data Safety Monitoring Board shall be guided by a formal stopping rule based on the primary endpoint of the difference between treatment arms in the proportion of patients with neurologically intact (MRS $\leq$ 3) survival to hospital discharge. The data will be analyzed in the context of a generalized linear mixed effects model which includes a fixed effect for treatment arm and random effects for each randomization cluster. The test statistic comparing treatment arms will be the Wald statistic computed as the regression parameter estimate for the treatment indicator divided by its estimated standard error.

The clinical trial may be stopped early either for reasons of demonstrated superiority of AL (the Analyze Late treatment arm has significantly higher rates of neurologically intact survival to hospital discharge than the Analyze Early arm) or for reasons of inferiority of AL (the Analyze Late treatment arm has significantly lower rates of neurologically intact survival to hospital discharge than the Analyze Early arm). At the final analysis, decisions can be made for the superiority, inferiority, or approximate equivalence of the AL arm relative to the AE arm with respect to the favorable event rates.

The formal stopping boundaries will be determined by a two-sided design,(O'Brien and Fleming 1979) a family also included in the unified family of group sequential stopping rules.(Kittelson and Emerson 1999) In the notation of the latter paper, the stopping rule will be based on a two-sided group sequential design testing a two-sided alternative hypothesis at a level of significance α =.05, an upper (superiority of Analyze Late) stopping boundary relationship specified by P_d = 1.0 (an O'Brien-Fleming type boundary relationship), and a lower (inferiority of Analyze Late) stopping boundary relationship specified by P_a =1.0 (an O'Brien-Fleming type boundary relationship). No early stopping

is possible with a decision for approximate equivalence between the two treatments. It is envisioned that up to three analyses (two formal interim analyses and the final analysis) will be performed during the monitoring of the study after accruing approximately 33%, 67%, and 100% of the maximal sample size. Due to the clustered randomization with crossover, it is estimated that the statistical information at each analysis will not be directly proportional to the sample size. When actually conducting the study, the proportion of statistical information available at each interim analysis will be estimated based on the actual cluster randomization and cross-over status, along with the favorable outcome event rates in the observed data. For purposes of evaluating the operating characteristics of the stopping rule, it is estimated that because little cross-over will have occurred at the time of the first interim analysis, only one-sixth of the planned maximal statistical information will be available. Similarly, it is estimated that only one-half the planned maximal statistical information will be available at the second interim analysis. Hence, for the purposes of description of its operating statistics, the following S+SeqTrial code (which incorporates a presumed 5% loss of efficiency due to the cluster randomization with cross-over) was used to generate the stopping rule:

```
alveDesign <- seqDesign(
    prob.model = "proportions",
    arms = 2,
    test.type = "two.sided", early.stopping=”alternative”,
    nbr.analyses = 3,
    size = 0.05,
    P = 1, R= 0, A= 0,
    null.hypothesis = 0.0541,    alt.hypothesis = 0.0745,
    variance = “alternative”,
    sample.size= c(1,3,6)/6*13239*0.95,
    power= “calculate”)
```

Under such a monitoring schedule and assuming a baseline neurologically intact survival rate of 5.41% on the Analyze Early arm, a sample size of 13,239 evaluable patients (6,620 patients on each of the Analyze Late and Analyze Early treatment arms) will provide approximately 99.6% power to detect an improvement to a 7.45% rate of neurologically intact survival on the Analyze Late treatment arm (corresponding to a relative improvement of 37.7% in neurologically intact survival to discharge). A more detailed description of the power provided by such a sample size for a range of favorable event rates (Table 4).

Table 4: Alternatives for which a sample size of 13,239 subjects provides the specified power as a function of Analyze Early arm rates of neurologically intact (MRS ≤ 3) survival to hospital discharge

Power	0.0475 AE Neuro Intact Surv to Hosp Discharge			0.0541 AE Neuro Intact Surv to Hosp Discharge			0.0606 AE Neuro Intact Surv to Hosp Discharge		
	AL Neur Intact Surv to Hosp D/C	Abs Diff	Rel Diff	AL Neuro Intact Surv to Hosp D/C	Abs Diff	Rel Diff	AL Neuro Intact Surv to Hosp D/C	Abs Diff	Rel Diff
80%	.0584	.0109	22.9%	.0656	.0115	21.3%	.0727	.0121	20.0%
90%	.0602	.0127	26.7%	.0675	.0134	24.9%	.0747	.0141	23.3%
95%	.0617	.0142	29.9%	.0691	.0150	27.8%	.0764	.0158	26.1%

97.5%	.0631	.0156	32.7%	.0706	.0165	30.4%	.0779	.0173	28.5%
99%	.0646	.0171	36.1%	.0722	.0181	33.5%	.0796	.0190	31.4%

Under the planned schedule of three equally spaced analyses and assuming a baseline Analyze Early rate of 5.41% neurologically intact survival to hospital discharge, Table 5 presents projected estimates of the stopping boundaries at each analysis for the specified stopping rule expressed as the absolute difference in neurologically intact survival rates (Analyze Late – Analyze Early). Also presented are the Z statistics and fixed sample lower one-sided P values which correspond to those stopping boundaries.

Table 5: Stopping boundaries for a level α=.05 two-sided group sequential design in the unified family (Kittelson and Emerson 1999) to detect a two-sided alternative, early stopping only to declare superiority or inferiority of the AL strategy, boundary shape parameters corresponding to O'Brien-Fleming boundaries, three analyses after accrual of 33%, 67%, and 100% of the maximal sample size of 13,239 evaluable subjects, and a rate of neurologically intact survival to hospital discharge of approximately 0.0643 on both treatment arms combined (e.g., 0.0541 on the Analyze Early arm and 0.0745 on the Analyze Late arm)

Analysis	Sample Size	Prop of Max Stat Info	Inferiority (lower) stopping boundary			Superiority (upper) stopping boundary		
			Abs Diff	Z statistic	Fixed P (lower)	Abs Diff	Z statistic	Fixed P (lower)
1	4413	0.17	-.0519	-4.844	1.0000	.0519	4.844	.0000
2	8826	0.50	-.0173	-2.797	.9974	.0173	2.797	.0026
3	13236	1.00	-.0086	-1.977	.9760	.0086	1.977	.0240

Thus, according to the above table, if the rate of neurologically intact survival to hospital discharge on the combined treatment arms is 6.43%, an absolute difference of 5.19% or more (e.g., 3.84% on the AE arm and 9.03% on the AL arm) when 4,413 evaluable subjects have been accrued to the study (2,206 subjects on each arm), the stopping rule would suggest that the study be terminated early with a decision that treatment with the Analyze Late strategy results in a statistically significant improvement in neurologically intact survival to hospital discharge. On the other hand, if at that first analysis the results were reversed (e.g., 9.03% on the AE arm and 3.84% on the AL arm), the stopping rule would suggest that the study be terminated early with a decision that the Analyze Late strategy results in a statistically significant decrease in the probability of neurologically intact discharge from the hospital.

As with the power properties of the study, the observed absolute difference in rates which correspond to the stopping boundaries is affected by the baseline rate of neurologically intact survival to hospital discharge on the AE arm as well as any effect of the AL strategy on the rates of those favorable outcomes. Due to the need to estimate the baseline favorable event rates when performing the statistical test, and the need to account for the pattern of cluster randomization and cross-over, the expression of the stopping boundaries will likely vary from those given in the above table. At each interim analysis, the actual proportion of statistical information available for analysis will be estimated according to the observed favorable event rates on the combined treatment arms and according to the exact patterns of accrual within clusters, the variability of the random effects across clusters, and the degree of cross-over implemented at the time of the analysis. The stopping boundaries appropriate to that proportion of statistical

information will then be computed, and the observed interim results will be compared to the stopping boundary expressed as the value of the fixed sample upper one-sided P value.

Table 6 presents for the setting presented in Table 5 (i.e., a combined favorable outcome rate of 6.36%) the statistical inference that would be reported if the study were to result in observed treatment effects corresponding to the stopping boundaries. The estimates, P values, and confidence intervals reported in Table 6 have been adjusted for the stopping rule using the bias adjusted point estimate (Whitehead 1986) and confidence intervals and P values calculated from the ordering of the outcome space based on the maximum likelihood estimate.(Emerson and Fleming 1990) (Note that the fixed sample P value presented in Table 2 is not appropriate for statistical inference. Instead it is presented to facilitate the use of standard statistical software when computing the test statistic: Upper one-sided P values calculated by standard statistical software (i.e., as would be appropriate for nonsequential fixed sample studies) can be compared to the critical values for that statistic as presented in Table 5 in order to obtain a level 0.05 sequential hypothesis test.)

Table 6: Statistical inference regarding the effect of the Analyze Late strategy on rates of neurologically intact survival to hospital discharge (measured as the absolute difference in favorable outcome rates between the AL and AE arms) which would be reported if observed results corresponded exactly to the stopping boundaries for a level 0.05 two-sided group sequential design as presented in Table 5

Analysis	Proportion of Maximal Statistical Information	AL Inferiority (lower) stopping boundary			AL Superiority (upper) stopping boundary		
		Adjusted estimate	Exact 95% conf intvl	Adjusted Two-sided P value	Adjusted estimate	Exact 95% conf intvl	Adjusted Two-sided P value
1	0.17	-4.91%	(-6.26%,-3.08%)	0.000	4.91%	(3.08%,6.26%)	0.000
2	0.50	-1.61%	(-2.50%,-0.51%)	0.003	1.61%	(0.51%,2.50%)	0.003
3	1.00	-0.82%	(-1.72%,0.00%)	0.025	0.82%	(0.00%,1.72%)	0.025

As noted above, the exact stopping boundaries that are appropriate for the group sequential design will depend upon the exact schedule of interim analyses and the best estimate of the variability of the test statistic as computed from the observed favorable event rates. The intended schedule of interim analyses is three analyses performed when 33%, 67%, and 100% of the planned maximal sample size has been accrued, but subject to minor variations due to the availability of the DSMB. In any case, the number and timing of interim analyses of the data for this trial will not be determined by the interim results of this study for the primary endpoint.

Modifications of the stopping rule to account for changes in the schedule of interim analyses and estimates of available statistical information will be made by using the parametric form of the stopping rule as specified above, with constraints imposed on the fixed sample P value scale for analyses previously performed. Boundaries will be constrained on the scale of the maximum likelihood estimate of the treatment effect, with the current best estimate of the test statistic's variance used at each analysis.(Burington and Emerson 2003) In making such adjustments, the two-sided type I error will be maintained at 0.05, and the maximal sample size will be constrained at 14,448 subjects. Modifications of the stopping rule will be computed using S+SeqTrial (*S+SEQTRIAL User's Manual*, Insightful, Inc., Seattle WA, 2000).

At each formal interim analysis, the DSMB will use the stopping rule computed in the above manner as a guideline in evaluating the trial results with respect to rates of neurologically intact survival to hospital discharge. In making a recommendation to terminate the study, the DSMB will of course also consider information on safety endpoints, as well as consistency of outcomes for secondary endpoints and consistency of outcomes within important subgroups as described in the protocol.

At the conclusion of the clinical trial, reported point estimates, 95% confidence intervals, and P values for the primary endpoint will be adjusted for the true sampling distribution. Point estimates will be based on the bias adjusted point estimate (Whitehead 1986) and confidence intervals and P values calculated from the ordering of the outcome space based on the maximum likelihood estimate.(Emerson and Fleming 1990)

Appendix 9: Interaction and Extension Monitoring Plan

This protocol describes the investigation of two interventions (ITD vs sham device and Analyze Late vs Analyze Early) in a partial factorial design. Based on the assumptions described in the power and sample size calculations for the individual interventions, it is estimated that over a 16-18 month period of patient accrual, approximately 15,436 EMS treated OOHCA patients at the 11 participating ROC sites will lead to the accrual of 14,154 evaluable patients for the comparison of the ITD to the sham device and 13,239 evaluable patients for the comparison of the Analyze Late to the Analyze Early strategy. The following table details regarding the distribution of those 15,436 patients according to presenting rhythm and randomized treatment group.

Table 1: Estimated distribution of 15,436 potentially eligible EMS treated OOHCA patients by presenting rhythm and randomization group.

Initial Rhythm	EMS Witnessed CA (AL vs AE Ineligible)			Analyze Early			Analyze Late	
	No Device	Sham	ITD	No Device	Sham	ITD	Sham	ITD
Asystole	0	277	277	0	1789	1789	1789	1789
PEA	0	254	254	0	837	837	837	837
VT/VF	231	310	310	451	526	526	751	751
TOTAL	231	842	842	451	3152	3152	3377	3377

Of the above patients, it is estimated that approximately 2% in each group would be judged nonevaluable for both the ITD/sham device comparison or the Analyze Late vs Analyze Early comparison due to OOHCA of presumed noncardiac origin (drowning, electrocution, strangulation) and an additional 2% would be judged nonevaluable for the ITD/sham device comparison due to a response time greater than 15 minutes or due to an opened device not being applied.

The ROC investigators do not anticipate a qualitative interaction between the ITD and the Analyze Late treatment strategies. The following table presents the estimated probabilities of neurologically intact survival to hospital discharge according to initial rhythm for the Analyze Early/sham device treatment arm, along with the estimated relative improvement for the other treatment combinations when compared to that arm.

Table 2: Estimated probabilities of survival to discharge for each combination of treatments under the alternative hypothesis used for power and sample size calculations for each intervention.

Presenting Rhythm	Stratum Weight	AE/sham	AL/sham		AE/ITD		AL/ITD	
		Prob Surv to Hosp D/C	Effect Rel to AE/sham	Prob Surv to Hosp D/C	Effect Rel to AE/sham	Prob Surv to Hosp D/C	Effect Rel to AE/sham	Prob Surv to Hosp D/C
Asystole	0.5481	0.0105	1.03	0.0108	1.40	0.0147	1.442	0.0151
PEA	0.2563	0.0420	1.03	0.0433	1.40	0.0588	1.442	0.0606
VT/VF	0.1956	0.2020	1.50	0.3030	1.20	0.2424	1.800	0.3636
TOTAL		0.0560		0.0763		0.0705		0.0949

Survival to Hosp D/C								

Owing to the interest in answering each question separately, the primary analyses for this trial were based on answering each main effect separately in a factorial analysis, rather than trying to detect the best outcome among four treatment arms. In the power and sample size calculations for the ITD/sham device comparison, the computations presumed no treatment difference between the Analyze Late and Analyze Early arms. Similarly, the power and sample size calculations for the Analyze Late vs Analyze Early comparison, the computations presumed no treatment difference between the ITD and sham device arms. This approach is the conservative one, as the study has substantially greater power to answer either question when power calculations presume both alternatives.

Despite the clinical interest in answering each question separately, the ethical imperatives inherent in clinical trials do demand that the following scenarios be considered during the monitoring of the study:

- *That the ITD might be beneficial in all patients, but that the Analyze Early strategy precludes placement of the ITD in a timely manner thus attenuating its effect.* In this scenario, there might be evidence of an interaction in which the ITD effect in the AL stratum was markedly better than that observed in the AE stratum. This would have the greatest safety implications if the Analyze Late strategy were superior to or equivalent to the Analyze Early strategy. Observation of such a substantial interaction at an interim monitoring could alter study intervention or call for an increased sample (e.g. extension of the study).
- *That the effect due to either the ITD or the Analyze Early strategy were so great as to successfully treat all patients who might reasonably be expected to respond to either treatment.* In this scenario, for instance, the survival of patients presenting in VT/VF (the group thought to have the biggest absolute effect) achieve some threshold reflecting the proportion of patients who could survive to hospital discharge with current prehospital and in hospital therapies following OOHCA. This would tend to result in evidence of an interaction in which the ITD effect in the AE stratum was markedly better than that observed in the AL stratum, if both the ITD and AL strategy were superior.
- *That any delay in initiating analysis for defibrillation (as might be caused by application of the ITD/sham device on the AE arm or by randomization to the AL arm) might prove deleterious in those patients who are likely to respond best to early defibrillations (i.e, the VT/VF 1st D Responders)*. In this scenario, we might see better survival in those patients responding to defibrillation on the Analyze Early arm before a device could be placed than would be observed for comparable patients randomized to the AL
- *That each treatment (ITD and the better of AL or AE) were so superior that the group receiving both superior treatments had a markedly better survival rate than did any of the other three arms.* This scenario can obtain whether the two interventions' effects are additive (no interaction), superadditive, or subadditive, so this is not really a question of interaction. Instead it relies on comparisons among the four treatment combinations.

In order to address the ethical and patient safety issues that might arise in the above scenarios, the DSMB will be presented with the following safety analyses directed

toward assessing interactions between the treatments, as well as toward pairwise comparisons among the four treatment arms. None of these analyses are regarded as primary, and all have severely limited power to detect differences between groups. As these are strictly safety endpoints and rather exploratory, no formal stopping rules are proposed. Repeated confidence intervals (Jennison and Turnbull, *Controlled Clinical Trials,* 1984) using an O'Brien-Fleming boundary shape function will be computed as necessary to provide the DSMB with some guidance regarding the precision of such interim analysis results in the context of sequential monitoring. All analyses of the treatment combinations will use only subjects who are judged evaluable by the criteria for the ITD/sham device comparison. The following table provides the estimated maximal sample sizes available for these analyses.

Table 3: Estimated maximal sample size of 12,970 evaluable patients available for safety analyses related to treatment combinations.

Initial Rhythm	Analyze Early			Analyze Late	
	No Device	Sham	ITD	Sham	ITD
Asystole	0	1718	1718	1718	1718
PEA	0	803	803	803	803
VT/VF	433	505	505	721	721
TOTAL	433	3026	3026	3243	3243

Pairwise Comparison of Treatment Combinations

The proportion of patients in the efficacy population with neurologically intact (MRS $\leq$ 3) survival to hospital discharge will be analyzed in the context of a generalized linear mixed effects model which includes the intercept, a fixed effect indicating patients treated with both the sham device and the Analyze Late strategy, a fixed effect indicating patients treated with both the ITD and the Analyze Early strategy, a fixed effect indicating patients treated with both ITD and Analyze Late strategy, and random effects for each randomization cluster in the AL/AE intervention. In this parameterization, comparisons between the Analyze Early and sham device treatment arm and each of the other treatment combinations can be based on the Wald statistic computed as the regression parameter estimate for the treatment combination indicator divided by its estimated standard error. Other contrasts can similarly be obtained from the regression parameter estimates. When requested by the DSMB, guidance about the precision of the interim analysis results will be provided using repeated confidence intervals with O'Brien-Fleming boundary shape parameters and an experimentwise 95% confidence level. Because cluster randomization with cross-over is used for the AL vs AE intervention, the statistical information for this interaction analysis would not be expected to be directly proportional to the sample size at each analysis. Estimating that approximately 25%, 50%, and 100% of the maximal statistical information will be available at the three analyses, the estimated precision of the repeated confidence intervals for the difference in the proportion with favorable response between any two treatment combinations will be approximately $\pm$0.047, $\pm$0.024, and $\pm$0.012. Issues related to the multiple comparisons inherent in testing pairwise combinations will also be considered using the covariance of the parameter estimates.

Detection of an Interaction

The proportion of patients in the efficacy population with neurologically intact (MRS $\leq$ 3) survival to hospital discharge will be analyzed in the context of a generalized linear mixed effects model which includes a fixed effect for ITD/sham device treatment arm, a fixed effect for AL/AE treatment arm, an interaction fixed effect indicating patients treated with both ITD and Analyze Late strategy, and random effects for each randomization cluster in the AL/AE intervention. The test statistic comparing treatment arms will be the Wald statistic computed as the regression parameter estimate for the treatment indicator divided by its estimated standard error. When requested by the DSMB, guidance about the precision of the interim analysis results will be provided using repeated confidence intervals with O'Brien-Fleming boundary shape parameters and an experimentwise 95% confidence level. Because cluster randomization with cross-over is used for the AL vs AE intervention, the statistical information for this interaction analysis would not be expected to be directly proportional to the sample size at each analysis. Estimating that approximately 25%, 50%, and 100% of the maximal statistical information will be available at the three analyses, the estimated precision of the repeated confidence intervals for the difference in the ITD treatment effect in the Analyze Late stratum and the ITD treatment effect in the Analyze Early stratum will be approximately $\pm$0.067, $\pm$0.034, and $\pm$0.017.

Propensity Score Analysis of Analyze Early with no Device

It is anticipated that some patients randomized to the Analyze Early intervention will experience ROSC after the first defibrillation and not need further CPR. As much as half of such patients may not have an ITD or sham device placed prior to their successful resuscitation. On the other hand, comparable patients randomized to the Analyze Late intervention will likely have an ITD or sham device placed prior to their first shock. Because the ITD/sham device treatment is blinded, this situation does not introduce bias into the analysis of the effect of the ITD on neurologically intact survival to hospital discharge. On the other hand, this causes an inability to ensure that the Analyze Early and Analyze Late treatment arms are balanced with respect to the use of the ITD across presenting rhythms. As the subset of patients who respond to early defibrillation are generally thought to have a higher probability of survival to hospital discharge, this means that there may be some slight confounding of the Analyze Late vs Analyze Early comparison by a beneficial effect of the ITD. If the ITD provides benefit in such patients, this confounding could also affect our ability to evaluate whether delaying analysis and defibrillation might be associated with worsened survival in the patients who would have responded to early defibrillation. There is no way *a priori* to identify these patients. However, we will be able to identify patients on the Analyze Early arm who did not have a device placed. We will then use a propensity score analysis in which we estimate the propensity for an Analyze Early patient to not have a device applied. The propensity score will be calculated in a logistic regression model of the log odds of having a device placed on the Analyze Early arm as a function of site (categorical), age, sex, indicator of witnessed arrest, indicator of bystander CPR, response time (call to 911 to arrival of EMS responders), indicator of public location, and initial rhythm (categorical). Comparisons of patients treated on Analyze Early without a device to patients treated on Analyze Late with or without a device will then be stratified on the propensity scores. We note that with approximately 445 patients (and an estimated 120 patients surviving to hospital discharge) in the group treated on Analyze Early without a device, our ability to definitively rule out safety issues is somewhat limited. Nevertheless, the experience of

these patients with respect to favorable outcomes and adverse events will be compared to patients on the Analyze Late arm who had similar propensity to have not been treated with an ITD or sham device had they been randomized to the Analyze Early arm. Analysis methods will otherwise follow the general approach described for the primary, secondary, and safety endpoints, though the sample sizes may demand coarser adjustment for randomization clusters.

Appendix 10: Sample Exception to Informed Consent Plan

Community consultation will occur prior to study commencement. The consultation will occur at a central location during an approximately 2-hour open meeting involving both invited participants and participants who attend because of public announcements. Invited participants will include: a) community leaders, b) representatives of community organizations, and c) the general public. A variety of community organizations and individuals will be invited to the community consultation meeting. A letter will be sent to invitees. The letter will seek suggestions for additional agencies or individuals to invite. Each invitation will be followed up with a phone call to assure that the invitation was received.

Organizations will be selected to match, as closely as possible, cardiac arrest subject demographics in each city, including race, age and gender. Individuals participating in the community consultation will ideally consist of a wide range of experts and laypersons within the research community. They will represent stakeholders in the issue of cardiac arrest and will have substantially different backgrounds and interests in this issue.

The community consultation meeting agenda will be developed in conjunction with the IRB and the research team. There will be a presentation by the PIs or their designate followed by a discussion and question and answer period. Material presented will include: a) background information on cardiac arrest, b) current lack of effective treatment for cardiac arrest, c) profile of typical cardiac arrest subjects, d) protocol description, e) experimental intervention rationale, f) randomization definition, g) potential study risks, h) potential study benefits, i) differences between research and treatment, j) rationale for exception to informed consent, and k) the ethical constructs of exception to informed consent. The PI will be present to answer questions and hear concerns regarding the project following the presentation. Minutes of the meeting will be transcribed. Members of the local IRBs who attend the community consultation meetings will determine if acceptable consultation has occurred for their community. If not, another community consultation meeting will be scheduled.

The requirements of 21 CFR 50.24 include informing the community that a research project will be done which may impact members of the local population. This notification will be made prior to the initiation of the project and after the project is completed. The content of the public disclosure messages will be derived in conjunction with the local IRBs and implemented following IRBs' approval of the public disclosure plan.

Investigator's Initial Community Notification Strategy:

- Ensure that all FDA communication requirements are met.
- Use television, newspapers, newsletters, and web site to notify public.
- Pursue all opportunities to get as much visibility as possible.
- Target the general population to reach all ethnic groups.
- Target populations at risk for developing cardiac arrest.
- Provide members of the community with various methods to contact investigators to acquire further information on the study or provide feedback possibly including telephone, mail, email, and website.
- Provide methods for investigators to capture and document feedback from the community and report those results to the IRC.

Content of Initial Community Notification:

It is impossible for a single public announcement to include all information that is found in the informed consent documents, the investigator's brochure, and the research protocol. We propose that the following are the most important issues for community understanding: a) the nature of the trial and that it involves victims of cardiac arrest; b) the trial involves exception to informed consent under emergency circumstances; c) the trial involves specific risks and benefits; and d) contact information on where to receive answers to concerns or questions as well as further information. The types of public disclosure and their content will be determined by the PI's at each site and local IRBs.

Types of Public Notification:

News Release

A news release will be distributed. The content will be approved by the IRB prior to distribution to any media. Public Relations and the PI will work with individual reporters to do follow-up stories.

Newspaper Announcement

An announcement will appear in the major metropolitan newspapers before and after the study. Additional newspapers or newsletters targeting specific minority populations will be considered as well.

Media Plan

The media plan includes use of television broadcasters in the respective sites for public announcements of the study elements.

Documentation and IRB Reporting

Investigators will document all inquiries from the public or interested parties on an Initial Public Notification Feedback Form. E-mail questions, comments, and feedback will also be documented. Investigators will collate and report results to the IRC before the start date of the study. Following public disclosure, the PI will obtain from the IRC all information concerning the public disclosure and will submit that to the FDA as required in 21 CFR 812.47(a).

According to the FDA's Final Rule, the investigator must attempt to notify all subjects that they have been enrolled in a study. If the subject is unable to comprehend this or dies, the investigator must attempt to inform the family members or legally authorized representatives. Since survival to hospital discharge following cardiac arrest is <20%, investigators anticipate the majority of their efforts will be attempting to contact family members.

We propose to follow the same process by which Notification and Informed Consent will be pursued as used by the Milwaukee RCC during the feasibility study with the ITD.(26) The process satisfied both local IRC and FDA regulations and the interpretations of those regulations as they related to 21 CFR 50.24. For all subjects who die in the field or the emergency department of the hospital, investigators will attempt to notify a legally authorized representative of the subject. If such representative is not reasonably available, a family member will be notified of the subject's inclusion, the details and other pertinent information regarding the study. Notification will occur either by attempting up to two phone calls to the subject's family or sending two letters to the subject's address (as listed on the EMS run report form, hospital chart information or telephone directory). Research team members will document all efforts to contact patients and their family members and maintain records according to the same process followed for all other record keeping during the study.

Telephone discussions and letters will fully inform the subject's representatives of the nature of the research project, the goals and objectives, the study protocols, the details of the FDA's Final Rule, and the information on community consultation and public notification that occurred. This communication will also elicit questions or concerns. Subject notification in each case will be documented and will become a permanent part of the study record.

For subjects who appear to have no relatives or person responsible (e.g., homeless), investigators will make every reasonable effort, including working with the County Medical Examiner, law enforcement and hospital personnel to help identify a next-of-kin for unidentified deceased subjects so that they may be notified.

Appendix 11: Minutes of ROC Data Safety Monitoring Board Meeting

Resuscitation Outcomes Consortium (ROC)
Data and Safety Monitoring Board Meeting
October 24, 2005 Summary Minutes

DSMB Members

Present: Jay Mason, M.D. (Chair), Ralph D'Agostino, Ph.D., Lance Becker, M.D. (by teleconference), Bishop Jane Holmes Dixon, Karl Kern, M.D., Laurence McCollough, Ph.D., Claudia Robertson, M.D., Robert Zalenski, M.D.
Absent: Peter Rhee, M.D., Herbert Wiedemann, M.D.

Investigators Present:

Alfred Hallstrom, Ph.D., Thomas Aufderheide, M.D., Eileen Bulger, M.D. (by teleconference), Clif Callaway, M.D. (by teleconference, for presentation of Functional Outcomes Study), Andrea Cook, Ph.D., Laurie Morrison, M.D. (by teleconference, for presentation of Registry), Graham Nichol, M.D., Judy Powell, B.S.N., Ian Stiell, M.D.

NIH Staff Present:

David Gordon, M.D., Ph.D. (Executive Secretary), Tracey Hoke, M.D., Sc.M. (Project Officer), Patrice Desvigne-Nickens, M.D., Alice Mascette, M.D., Marissa Miller, D.V.M., Susan Old, Ph.D.

The ROC DSMB convened on Monday, October 24, 2005. The agenda included a progress report on the already-approved Hypertonic Saline Following Traumatic Injury trial, review of a new protocol for the ITD X Analyze Later trial (already-approved by PRC), and review of the planned Registry and Functional Outcomes Pilot Study. After a round of introductions, the minutes from the June 24, 2005 DSMB teleconference were approved. Each of the protocols was then presented and discussed in open session. Finally, the DSMB met in Executive Session to develop the recommendations listed at the end of the section for each protocol.

Hypertonic Saline Dextran (HSD) Trial: Dr. Bulger reported on changes in the protocol that were prompted by the termination of her similar small R01 trial of HSD infusion in traumatic shock for futility after 200 (out of a planned 400) patients had been enrolled. The SBP < 90 mmHg entry criterion for the smaller trial permitted the enrollment of a substantial number of patients who ultimately needed little or no blood transfusion and thus, with the benefit of hindsight, were not truly in hypovolemic shock. HSD may have decreased survival in such patients, while increasing survival in patients who required 10 or more units of packed red blood cells (RBCs), though neither trend was statistically significant. Dr. Bulger and the ROC DCC analyzed these data to revise entry criteria for the ROC HSD trial to more effectively exclude patients who are not truly in shock, and who therefore might be harmed by HSD infusion. They found that excluding patients in the R01 trial with SBP between 70 and 90 mmHg who did not have reactive tachycardia (i.e., whose pulse rate did not exceed 108 beats per minute) would have increased the proportion of patients requiring 10 or more units of RBC from 56 to 63%, while excluding 25% of the enrolled patients. The ROC investigators propose to modify the entry criteria

for the ROC SHOCK cohort accordingly. They anticipate that this revision will extend the time required to complete enrollment to 3.5 years. The modified protocol also calls for increased sample sizes of 3726 for the SHOCK cohort and 2122 for the Traumatic Brain Injury (TBI) cohort, based on the more conservative estimated effect size suggested by the small trial. An *a priori* subgroup analysis has also been added for patients requiring transfusion of 0, 1-9, or ≥10 units of RBC. While the DSMB wondered whether the modest increase in the proportion of true traumatic shock patients was worth the loss of 25% of potentially eligible subjects, they acknowledged that this was probably the best one could do, and a good attempt to not enroll those who might be harmed by HSD. These changes must still be approved by the PRC and local IRBs.

The monitoring plan has been revised to take into account the extension and expansion of the study. The DSMB is comfortable with the revised plan, but remains concerned about the practicality of stopping the study in one of the two cohorts while continuing it in the other, if the results differ at some point in the study. It was noted that since HS and HSD are unavailable outside of the ROC study, stopping the study in one cohort for efficacy would actually serve to deny the more effective treatment to future patients who might otherwise get it if the study continued, rather than to make it available to patients who might otherwise receive the inferior standard infusion fluid. Thus, the ethics of continuing to randomize after a monitoring boundary is crossed in one cohort are complex. The DSMB reiterated that they will consider statistical stopping rules as informative rather than determinative.

Finally, Dr. Bulger reported that a decision on an IND for the use of HSD in the ROC protocol is still pending while the FDA considers the implications of the termination of the small HSD trial.

Recommendations (Executive Session):

- The protocol revisions were unanimously approved.
- The DSMB will closely monitor outcomes among patients who did not require extensive transfusions for evidence of harm.

ITD X Analyze Later Trial:

Dr. Stiell presented this protocol, which was recently approved by the ROC PRC. This protocol was originally presented as a randomized comparison of resuscitation with a real or sham impedance threshold device (ITD) after cardiac arrest. The primary end point was survival to discharge. Two major modifications have been made:

1. The study has been combined with a study (Analyze Later) comparing defibrillation after 50 versus 300 chest compressions in a 2x2 factorial design.
2. The primary end point has been modified to incorporate functional status as well as survival to hospital discharge.

Randomization into the Analyze Early (after 50 compressions) versus Analyze Later (after 300 compressions) groups will precede randomization into the real versus sham ITD groups. Patients who begin to breathe spontaneously before or immediately after defibrillation will not be randomized to the ITD trial. However, once the bag containing the real or sham ITD has been opened, the patient is considered as enrolled, even if the device is never used.

The redefinition of the primary end point to include functional outcomes (which was mandated by the FDA as a pre-condition for obtaining an IDE for the ITD) poses a significant complication in the consent process. Enrollment under the community waiver of informed consent permits the outcome (survival or death) to be determined from the hospital record without the explicit consent of the patient or his/her family. However, administering a questionnaire to a surviving patient to assess neurologic function requires informed consent, which will not be forthcoming in a proportion of patients. Since obtaining this consent is unlikely to be a random process, significant bias may be introduced in the primary end point. The investigators have proposed to avoid this bias by choosing a functional assessment (the Rankin Score) that can be assessed from the patient's chart without requiring informed consent to administer a questionnaire. They argue that the ascertainment of outcome from medical records is implicit in the community consent and that the addition of functional outcome to survival poses minimal additional risk to participants, given that appropriate measures to protect their privacy are in place. The DSMB concurred. A more detailed justification, provided by the DSMB ethicist, Dr. McCollough, is provided as an appendix.

The disposition by the FDA of the study's IDE application is still pending. Since the IDE would involve only the ITD trial, the fallback position in the event of further FDA reservations would be to implement the Analyze Later protocol (which does not require on IDE) while waiting for an FDA decision on the ITD trial.

The DSMB discussed the statistical implications of the trial's factorial design in which sites rather than patients are randomized to the Analyze Early versus Analyze Later strategy. The cluster randomization results in a 5% loss of efficiency; thus, the duration of follow-up will increase from 12 to 12.1 months. The sites will cross over halfway through the follow-up period; i.e., the sites initially randomized to Analyze Later will cross over to Analyze Early, and vice versa. Compliance will be closely monitored during the initial two weeks and during the two weeks following crossover. The DSMB expressed concern over the possibility of an interaction between the Analyze Later and ITD trials, particularly in view of the fact that patients in the Analyze Early arm are likely to receive the IDT (real or sham) earlier than those randomized to the Analyze Later arm. The investigators noted that the protocol provides for up to a doubling of the sample size if there is a large interaction and that if there were a large effect, the Analyze Later trial would probably be stopped early, at which point the interaction would cease. The investigators also pointed out that the factorial design controls for confounding by assuring that the early and late defibrillation strategies are evenly balanced between the real and sham ITD arms.

Dr. McCollough called the Board's attention to a new OHRP circular on adverse events. NHLBI policy requires early notification only of unexpected serious adverse events, though the DSMB may choose to cast a broader net. Dr. Hoke promised to distribute the web link to the new OHRP circular to the rest of the Board (this was done on October 25, 2005).

Recommendations (Executive Session):

- The DSMB unanimously approved the protocol and the contingency implementation plan.

Registry:

Dr. Morrison joined the meeting by teleconference to present plans for a registry of an estimated 17,500 cardiac arrest patients and 13,000 traumatic shock patients. The registry's goals are:

- To provide a context for generalizing the ROC results
- To accurately describe incidence in the population
- To identify and quantify prognostic factors for outcome
- To quantify seasonal and other variation in incidence.

Since the registry will pose minimal risk to patients, will not involve patient contact, and will not collect identifying information, informed consent is not required. The registry will include patients who are found dead at arrival. It is estimated that the registry will have power to detect a 2.5% difference in survival in terms of local practice patterns and standards of care.

Although the DSMB had some concerns about data quality (at least initially) and how representative the ROC sites were of the broader population, they strongly support this registry as a golden opportunity to collect data that are not currently available. They cautioned the investigators to be wary of the possible political implications of making EMS services look worse in some communities and better in others, but felt that communities had a right to know about their EMS performance stacked up against other communities. They inquired about what safeguards were in place to prevent selective reporting of cases with favorable outcomes. The fact that EMS runs are billable will help assure full reporting. The DSMB asked for a full plan to monitor completeness of reporting.

Recommendations (Executive Session):

- The DSMB unanimously approved and recommended proceeding with the ROC registry.

Functional Outcomes Pilot Study:

Dr. Callaway joined the meeting by teleconference to present the Functional Outcomes Pilot Study. The purpose of this study, which will involve the ROC sites at Pittsburgh, Oregon, and perhaps Alabama, is to compare and validate alternative instruments for assessing functional outcomes in the setting of recent cardiac arrest. Patients who were successfully resuscitated after cardiac arrest within the past year will be eligible. Patients will be recruited retrospectively from databases of recent cardiac arrest patients, as well as prospectively. In addition to comparing instruments, the study will address how well each outcome measure tracks over time. The data will be useful in addressing the precision and validity of the modified Rankin score as it is used to assess functional outcome in the ITD trial, although they are unlikely to be available in time to modify the choice of functional outcome measure in that trial.

The study will rely heavily on telephone mail and chart review to identify eligible patients and obtain data. The Pittsburgh IRB has approved the protocol, but it has not yet been presented to other IRBs. Dr. Callaway estimates that the University of Pittsburgh hospitals can provide up to 3-4 new patients per week, in addition to the estimated 100 patients with recent cardiac arrests in their database. Since the largest previous comparable studies are very small (20-40 patients) enrolling even 100 patients in this trial would be very useful. The DSMB strongly supported this study and urged the investigators to expedite the recruitment of Oregon, Alabama, and other interested ROC sites in this study, so that the data may be available in time to inform the outcome assessment in the ITD protocol. The DSMB also recommended retrospective ascertainment of subjects for the analysis.

Recommendations (Executive Session):

- The DSMB unanimously approved and recommended proceeding with the Functional Outcomes Pilot Study.
- They encouraged the incorporation of other ROC sites in addition to Pittsburgh to accelerate the accumulation of data that can help to guide the selection of functional end points in the ICD and other ROC protocols.

Next Meeting: The Board agreed to convene next by teleconference during the last week of May. May 24 and 26 were identified as potentially good dates. Calendars will be circulated by the Data Coordinating Center.

Appendix: After the meeting, DSMB ethicist Lawrence McCollough submitted the following paragraphs describing the ethical issues raised by using medical records to obtain functional outcomes in ROC patients who have consented to participate in the intervention according to federal exception from informed consent rules and IRB-mandated local community consent processes, but who have not consented for subsequent chart review and collection of follow-up data regarding both outcomes and adverse events.

> Informed consent is a reasoned decision-making process through which a research subject authorizes participation in a clinical trial. This process has two main functions. The first is to protect subjects from they regard as unacceptable risk. In these trials, the risk of continued participation (after initial waiver) involves loss of privacy/confidentiality. The study designs have minimized, if not eliminated this risk. The second is a Kantian concern that research subjects not be treated as means merely, i.e., used as a research subject without their consent. In the context of the history of human subjects research and research ethics, the use of subjects for badly designed trials that might be harmful is of paramount concern Inability to obtain data through discharge (because a subject refuses access to clinical records) will introduce bias and also add risk of undetected adverse events, especially unanticipated adverse events. Ironically, requiring informed consent would jeopardize study design and implementation and therefore could add, and not protect subjects from, risk. Requiring informed

consent for continued participation during hospitalization therefore lacks ethical justification in research ethics.

One could object on pure Kantian grounds that consent is required to prevent subjects from being used as means merely. The objection is deontological (i.e., based on moral considerations independent of consequences, e.g., respect for subjects as persons) and thus independent of concerns generated by history of human subjects research and research ethics. The usual way to accommodate this objection would be to plan a longer time to achieve study enrollment based on projected refusal rate. However, this option also introduces the risk of bias, especially if refusals of further participation were not random. Suppose for example that nearly all survivors with good functional outcomes consent to follow-up but that a substantial proportion of survivors with poor functional outcomes (or their families) refuse consent. Suppose further that the proportion of survivors with poor functional outcomes who refuse consent is higher among patients who received the sham ITD than the real ITD. Then the comparison of treatments could falsely show that the ITD is detrimental to functional outcome, and enrolling more subjects would only increase the precision of this biased estimate of the treatment effect. It is easy to construct a scenario with a bias favoring the real ITD. Thus, the pure Kantian objection can be accommodated only by placing subjects at risk of being used in research that could well have little or no scientific value, which violates the core ethical requirement of human subjects research. The pure Kantian objection therefore lacks ethical justification in research ethics and can be set aside.

Jay Mason, M.D.
Chairman

David J. Gordon, M.D., Ph.D.
Program Administrator

cc: Drs. Hoke, Lathrop, Mascette, Old, Sopko

Appendix 12: Justification for Waiver of Documented Written Consent.

Request for Waiver of Written Consent for ROC Cardiac Factorial Trial

In an emergency, there is not sufficient time to obtain informed consent from the patient or their legally-authorized representative. Thus, cardiopulmonary arrest research must operate under exemption from consent, either because of no or minimal risk, or through community waiver/exception of consent regulations as outlined by the Office for Human Research Protections (OHRP) and the FDA(US Department of Health and Human Services 1996), including local community consultation and public disclosure and patient or family notification and consent after the experimental intervention has been applied. Therefore we propose to conduct these trials under community consultation and exception from consent. Enrolled subjects or their legally-authorized representatives will be notified after the index event that they participated in a research study.

After administration of the experimental intervention under community waiver/exception of consent regulations, patients will be transferred to an acute hospital for ongoing resuscitation and post-resuscitation care. No study intervention will be administered to enrolled patients during the hospitalization period. Patients who consent to participate after discharge will be interviewed to assess their functional status, health-related quality of life, and degree of depression.

Review of the clinical record is necessary to ascertain whether individuals who received an experimental intervention under an Investigational Device Exemption were harmed by it. If consent is required for this review but not granted, then assessment of potential adverse effects will be incomplete. Such incomplete assessment of adverse effects is undesirable as it exposes study patients to undue risk.

Review of the clinical record is also necessary to determine important outcomes such as survival to discharge. If consent is required for this review but not granted, then these data are missing during analysis. If missing data are different from complete data, then the analysis is susceptible to bias, and the conclusions could be misleading. The only risk to patients associated with review of the clinical record after the intervention is loss of privacy and confidentiality. Therefore we seek approval to review the clinical record without documented consent under minimal risk criteria. The rationale for this approach is described in the preamble to the final rule for 21 CFR 50:

> "The agency thinks that it may not always be possible to develop a meaningful informed consent document for continued participation in the research, because the relevant information may vary significantly depending upon when it becomes feasible to provide the information to the subject or legally authorized representative. The agency is therefore, not requiring that such a form be developed. The agency notes however that Sec. 50.24 (a)(6) places the responsibility on the IRB to review and approve 'informed consent procedures and an informed consent document' for use with subjects or their legal representatives, and procedures and information to be used in consultations with family members, in situations where use of such procedures is feasible." [Page 51520]

During the comment period for these regulations, the agency received feedback that the subject should be able to choose to continue to participate fully in a study, to continue the intervention but not have their data included in the research database or results, or to discontinue the intervention and use of the subject's data. This was rejected on the following grounds:

'FDA regulations… require investigators to prepare and maintain adequate case histories recording all observations and other data pertinent to the investigation on each individual treated with the drug or exposed to the device. The agency needs all such data in order to be able to determine the safety and effectiveness of the device. The fact of having been in an investigator cannot be taken back. Also if a subject were able to control the use (inclusion and exclusion) of his or her data, and particularly if the clinical investigation were not blinded, the bias potential would be immense.'
[Page 51520]

The rationale for this approach to consent in this trial is also described in an attached manuscript accompanying this protocol. Collectively, the information above and the accompanying manuscript confirm that our proposed notification and consent process is necessary and sufficient to protect human subjects. Nonetheless, we describe below how our proposed approach is consistent with criteria for waiver of written informed consent.

a) The use or disclosure involves no more than minimal risk to the privacy of the research subject.

The study will collate coded patient data without individual identifiers. Such data includes:

i. Names;
ii. Postal address information, other than town or city, State, and zip code;
iii. Telephone numbers;
iv. Fax numbers;
v. Electronic mail addresses;
vi. Social security numbers;
vii. Medical record numbers;
viii. Health plan beneficiary numbers;
ix. Account numbers;
x. Certificate/license numbers;
xi. Vehicle identifiers and serial numbers, including license plate numbers;
xii. Device identifiers and serial numbers;
xiii. Web Universal Resource Locators (URLs);
xiv. Internet Protocol (IP) address numbers;
xv. Biometric identifiers, including finger and voice prints; and
xvi. Full face photographic images and any comparable images.

None of the above data will be sent to the data coordinating center during the conduct of this study.

All study personnel involved in data collection and analysis will be required to sign a confidentiality agreement. In addition, subjects will be identified in the database by a study identifier that is defined without reference to PHI. Links to these study identifiers will be kept in a separate secure location at each site, and not provided to the coordinating center. Database files will be maintained on a password protected computer in a secure location. After data collection the information will be destroyed.

b) The waiver of authorization will not have an adverse effect on the rights and welfare of the subject.

There will be no patient contact. There will be no intervention administered to patients during their hospitalization. No PHI will be transmitted to the coordinating center.

c) The researcher has an adequate plan to protect PHI from improper use or disclosure.

The researcher will not collect PHI, and therefore cannot use it or disclose it. Research staff at participating sites will collect PHI and link it to study identifiers. But this links will be maintained locally at each site, separately from the study database, and not transmitted to the coordinating center.

d) The researcher has an adequate plan to destroy identifiers at earliest opportunity.

Not applicable.

e) The researcher will not inappropriately re-use or disclose PHI in publications.

Not applicable.

f) The research could not practicably be conducted without access to and use of PHI.

Not applicable.

g) The research could not practicably be conducted without the waiver.

The majority of patients who experience out-of-hospital cardiac arrest die, and are therefore unable to provide informed consent. This research could not practicably be conducted without the waiver as study personnel could not determine the adverse effects occurring in hospital or vital status at discharge. Others have demonstrated that requirements for informed consent to participate in a research study are associated with bias in the type of patients sampled.(Tu, Willison et al. 2004) If sicker patients are less likely to consent, then sampling of consented patients will yield biased results.

h) The benefits of the proposed research outweigh the risks to the subjects.

The only risk to subjects is the potential for loss of privacy and confidentiality. Appropriate safeguards will be taken to safeguard against this. The potential benefits to enrolled patients are unbiased assessment of whether they have experienced an adverse effect associated with an experimental intervention. The potential benefits to society are determination of unbiased estimates of the short-term and long-term effect of the impedance threshold device upon outcomes after out-of-hospital cardiac arrest. Since cardiac arrest is common, lethal and debilitating, and outcomes after its treatment have not significantly improved for thirty years,(Cobb, Fahrenbruch et al. 1999; Herlitz, Bang et al. 2003; Rea, Eisenberg et al. 2003) it is important to evaluate objectively promising interventions for this disorder.

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List of Abbreviations

4.1 Abbreviations

AED	Automated External Defibrillator
ALFI	Adult Lifestyle and Function Interview
ALFI-MMSE	Adult Lifestyle and Function Interview Mini-Mental Status Exam
ALS	Advanced Life Support
ALvAE	Analyze Later vs Analyze Early
BLS	Basic Life Support
CA	Cardiac Arrest
CABG	Coronary Artery Bypass Graft
CAD	Coronary Artery Disease
CATH	Cardiac Catheritization
CPC	Cerebral Performance Category
CPR	Cardiopulmonary Resuscitation
CTC	Clinical Trial Center
D/C	Discharge
DNAR	Do Not Attempt Resuscitation (order)
DOA	Dead On Arrival
DSMB	Data Safety Monitoring Board
ED	Emergency Department
EMS	Emergency Medical Services
EtCO2	End Tidal Carbon Dioxide Measurement
ETT	Endotrachial Tube
FTE	Full-Time Equivalent
F/U	Follow-Up
FVS	Final vital status
GDS	Geriatric Depression Scale
HUI	Health Utilities Index
ICD	Implantable Cardioverter Defibrillator
ICU/CCU	Intensive Care Unit, Coronary Care Unit
ITD	Impedance Threshold Device
ITT	Intent to Treat
IV/IO	Intravenous, Intraosseous
LOS	Length of Stay
MDN	Median
mITT	Modified Intent to Treat
MRS	Modified Rankin Scale
NIH	National Institute of Health
OD	Overdose
OOH CA	Out-of-Hospital Cardiac Arrest
OPRR	Office for Protection from Research Risks
PAD	Public Access Defibrillation
PEA	Pulseless Electrical Activity
QOL	Quality of Life
REB	Research Ethics Board
ROSC	Return of Spontaneous Circulation
SD	Standard deviation
SOB	Shortness of Breath
SPA	Single Project Assurance
VT	Ventricular Tachycardia
VF	Ventricular Fibrillation

4.2 ROC PRIMED Comparison Populations

The PRIMED trial has several primary comparison populations, distinct between the ITD and ALvAE interventions.

ITD:

Intent to Treat (ITT) All episodes for which an ITD bag was opened by any responding agency, regardless of adherence to inclusion/exclusion or treatment received

Modified ITT (mITT) ITT minus any episodes with the following exclusion criteria:
- General study exclusions (child, pregnant, prisoner, DNR, arrest due to trauma, exsanguination or no EMS CPR or Defib.)
- ITD specific exclusions (tracheostomy, mechanical CPR, non-ROC vehicle applied pad and began CPR and dispatch time cannot be reliably obtained)
- ITD bag was opened but not used
- Cardiac arrest was due to drowning, strangulation, or electrocution
- EMS arrival time >15 minutes from time of dispatch

Safety All episodes for which a device was used

ALvAE:

Intent to Treat (ITT) All episodes minus any with the following exclusion criteria:
- General study exclusions (child, pregnant, prisoner, DNR, arrest due to trauma, exsanguination or no EMS CPR or defib)
- ALvAE specific exclusion (non-fire/EMS rhythm analysis, non-ROC agency on scene and began CPR)
- EMS witnessed episodes

Modified ITT (mITT) ITT minus any episodes that meet the following criteria:
- Cardiac arrest was due to drowning, strangulation or electrocution

Safety Same as ITT

The primary effectiveness analyses will be based on the mITT population, which excludes a group of patients who are conjectured to not benefit from the treatments, but for whom there is also no presumed contraindication of the treatment.

Schedule of Case Report Forms

5.1 ROC PRIMED Schedule of Episode Forms Collection

Name of Form	Any Treated CA*	Treated CA with no exclusions or ITD opened	ED Admission	Hospital Admission	AE Protocol deviation/violation, unusual circumstance	All Patients Eligible for Enrollment	All Patients Discharged Alive from Hospital
Patient Enrollment	X						
Pre-hospital Time Record		X					
Pre-hospital Data		X					
CPR Process		X					
ED Admit			X				
Hospital Admit				X			
ALERT CTC					X		
Patient/Family Consent		X					X
Month 1							X**
Month 3							X**
Month 6							X**

* A treated OOH-CA includes any CA where the patient was shocked for VF/VT by ROC EMS provider or a ROC EMS provider gave compressions during CPR.
**When ROC PRIMED forms are required for patients who are witnessed arrests or the ITD was opened but they do not meet the inclusion criteria for the study, the Follow-Up forms do not need to be completed.

Patient care reports (run reports), EMS CA documentation and continuous electronic ECGs will need to be submitted to the CTC for quality assurance review on randomly selected episodes. When chosen for review, the required data should be sent to the CTC within 2 weeks of the request. ED and hospital records will be reviewed on a random sample of patients during CTC site visits.

J:\ROC\PRIMED\Admin\Study-materials\MOO\ROC PRIMED Schedule of Episode Forms Collection.doc November 20, 2006 (updated 2008-5).

5.2 Timeline for ROC PRIMED Data Entry:

Within 3 days of episode date:

- **Enrollment form**

Within 2 weeks of episode date:

- **Pre-hospital Time record**
- **Pre-hospital form**

Within 3 weeks of hospital discharge or Day 28 (whichever comes first). Sites will be required to get this information in 2 weeks at the time of DSMB data cutoffs:

- **ED form**
- **Hospital form**
- **Pt/family Notification**

Within 4 weeks of episode date (sites need to look to determine if the EMS performed the correct randomization assignment within 2 weeks):

- **CPR Process form**

Review of the ECG and completion of the CPR Process form is necessary to help determine if the cluster assignment for Analyze Late vs. Early is accurate. The CTC will sample ECGs/CPR Process forms for adherence to the cluster arm. Timeliness of submission of the CPR process form will be especially important right after a changeover occurs in the cluster arm. Sites agreed to review the electronic ECG for the first 3-4 minutes to be able to determine whether the cluster assignment was followed in order to note this on the enrollment form within 2 weeks and the timeframe for completion of the CPR Process form will be extended to 4 weeks.

Within one month of follow-up period (1 month, 3 months, 6 months post hospital discharge):

- **Follow-up form**
- **QOL/Neuro Outcome forms**

- **ALERT CTC** Form (for potential adverse events) will be submitted within the time period specified by the FDA for adverse events. This time period starts at the time the site becomes aware of the event.

  Serious and life-threatening AEs (expected or unexpected): the CTC notifies the FDA, UW IRB and DSMB chairperson by phone within 72 hours and the site needs to notify their IRB/REB, and in writing to these agencies within 7 days. Therefore the sites need to notify the CTC ASAP and no later than 24 hours after becoming aware of the SAE in order to comply with the regulations.

Non-life-threatening, unexpected, serious AEs: the CTC notifies the FDA, IRB and DSMB chairperson in writing within 15 days and the site notifies their IRB/REB. Although more time is allowed when it is non-life-threatening, it is still important for the site to notify the CTC in a timely manner.

Data Collection Forms

Table of Contents

Episode Packet Forms:	
Form Name	**Version/Date**
Patient Enrollment	1.04.02 05/26/2009
Pre-Hospital Time Record	1.00.01 08/14/2007
Pre-Hospital Data	1.04.00 10/07/2008
CPR Process	1.02.00 10/06/2009
ED Admit	1.01.01 02/24/2009
Hospital Admit	1.06.01 08/25/2009
Alert CTC	1.08.01 10/13/2009
Patient/Family Consent	1.01.00 08/11/2009
Follow-up	1.04.00 08/25/2009
ALFI-MMSE	----------
Modified Rankin Scale	----------
Cerebral Performance Scale	----------
Health Utilities Index	----------
Geriatric Depression Scale	----------

Introduction

The ROC PRIMED forms packet is similar to the Epistry and the Hypertonic Saline forms packet, in that each form will have a date and the time call received at dispatch, along with the study ID, incident number, and site linking ID at the top of each page.

Cases Entered into ROC PRIMED and/or Epistry

For ROC PRIMED participating agencies, a ROC PRIMED Patient Enrollment form is completed for all **non-traumatic** cardiac arrest cases treated by ROC EMS (defined in ROC PRIMED as being EMS chest compressions or EMS defibrillation performed in the presence of ROC EMS). Separate Epistry data entry is not required for cardiac arrest cases treated by EMS and for which ROC PRIMED requires that *further* forms (beyond just the Patient Enrollment form) be completed. See the below table. Data for an episode that qualifies for both ROC PRIMED and Epistry will be entered only into the ROC PRIMED data set. The CTC will coordinate population of ROC PRIMED data into the Epistry data set (though no associated Case ID's or data forms will reside on the Epistry Episode List). Data is entered separately and only in Epistry up until the time an agency begins enrollment in the ROC PRIMED study.

Note, that all non-traumatic cardiac arrest cases that are 'not treated by EMS' are entered only into Epistry.

Cardiac Arrest	All ROC PRIMED forms	ROC PRIMED Patient Enrollment form	All Epistry forms
ALL ROC AGENCIES, BYSTANDER ONLY TREATMENT Treated with external defibrillation by lay responders/bystanders, but no EMS or fire chest compressions or defibrillation provided (includes patient with ROSC at time of EMS arrival).			X
ALL ROC AGENCIES, NOT TREATED Not treated by EMS-are pulseless and do not receive attempts to defibrillate or CPR by EMS or fire personnel. Includes those with DNR.			X Limited data set restricted to Patient Enrollment form
NO PARTICIPATING ROC PRIMED AGENCY PRESENT DURING CARDIAC ARREST Treated by EMS (received EMS chest compressions or EMS defibrillation when ROC EMS was *not* present, but was a part of the organized response) and meets inclusion criteria for Epistry cardiac arrest.			X

Cardiac Arrest	All ROC PRIMED forms	ROC PRIMED Patient Enrollment form	All Epistry forms
PARTICIPATING ROC PRIMED AGENCY PRESENT DURING CARDIAC ARREST, MEETS INCLUSION Treated by EMS (received EMS chest compressions or EMS defibrillation in the presence of ROC EMS) and the completed ROC PRIMED Patient Enrollment form indicates either a) the ITD was opened (item 1) and/or b) the arrest was witnessed by ROC EMS (item 2c, exclusion criteria for this line item is marked 'yes), or The ROC web will indicate an episode meets inclusion criteria and will indicate (on the Episode List and Episode Summary) that further ROC PRIMED forms beyond Patient Enrollment are required ('R). Where either a) or b) above occur, all ROC PRIMED forms through hospital discharge must be completed regardless of whether the ITD was applied.	X		
PARTICIPATING ROC PRIMED AGENCY PRESENT DURING CARDIAC ARREST, MEETS EXCLUSION Treated by EMS (received EMS chest compressions or EMS defibrillation in the presence of ROC PRIMED EMS participating agency) and the ROC PRIMED web indicates that NO further forms beyond Patient Enrollment are required (due to study exclusion criteria). This group of cases may include 'vulnerable patients' such as known prisoners, pregnant women, and children. Complete all Epistry forms when the ROC PRIMED web indicates (on the Episode List and Episode Summary) that NO further interventional trial forms ('- -') are required beyond Patient Enrollment.		X	X

6.1.1 Patient Enrollment Form

A ROC PRIMED Patient Enrollment form must be completed for all non-traumatic cardiac arrest patients that receive EMS chest compressions or EMS defibrillation by, or in the presence of, ROC EMS, whether or not there are suspected or known protocol exclusions. The purpose of the Patient Enrollment form is to capture all EMS treated, non-traumatic cardiac arrests which are a) potentially eligible for enrollment into ROC PRIMED, b) are ineligible but for whom an ITD package was opened, or c) are ineligible for enrollment (with the reason for ineligibility). Patient data in the ROC PRIMED Trial will be eligible for Epistry Trial analysis, though not every Epistry patient will be eligible for ROC PRIMED. After completing the Patient Enrollment form, the web-data entry system will determine if additional ROC PRIMED forms are required, or if the patient must be also entered into Epistry (where only the ROC PRIMED Patient Enrollment form was required).

A patient is eligible for ROC PRIMED if he/she receives a shock or at least one compression from, or in the presence of, a ROC EMS provider. It is extremely important to submit a Patient Enrollment form for every patient for whom the ITD package was opened, even if the patient was not deemed to be in cardiac arrest (no shock or EMS compressions given) or was not eligible for the trial. It is required that all ITD packages be tracked. For the ITD arm of the study, opening of the package is considered randomizing the patient. If the ITD package is opened at the scene, all the data forms through hospital discharge will be required for completion. This is required because it may not be clear when the ITD was opened whether or not it was placed. For safety purposes (the study is being conducted under an FDA IDE), the patient data must be tracked.

The source of the date and time of the episode must be entered, i.e., from the PCR/Other or from dispatch. The Patient Enrollment form also contains a bubble for “Unable to obtain (non-ROC agency first arrival and no agreement in place to get data, patient is excluded from Trial).” The reason for the “Unable to obtain” bubble is to indicate any episode in which a non-ROC agency arrived on the scene first, and the site did not have a previous agreement with the non-ROC agency to obtain the time call received at first dispatch center. There should be very few of these cases entered on the Patient Enrollment form, but if this occurred and an ITD was opened, the data forms through hospital discharge would need to be completed. Data for the Patient Enrollment form will come from the pre-hospital Patient Care Record (run report, acute care record, ambulance call report [ACR]), any EMS cardiac arrest supplemental form, and from dispatch.

IF THE SITE DOES NOT HAVE A PRIOR AGREEMENT TO OBTAIN THE TIME CALL FIRST RECEIVED AT DISPATCH FOR THE NON-ROC AGENCY THAT ARRIVES FIRST, THE PATIENT IS EXCLUDED FROM THE TRIAL AND NO FURTHER ROC PRIMED DATA FORMS BEYOND THE PATIENT ENROLLMENT FORM WILL BE COLLECTED AS LONG AS NO ITD PACKAGE WAS OPENED. IF THE ITD WAS OPENED, DATA MUST BE COLLECTED THROUGH HOSPITAL DISCHARGE FOR SAFETY, REGARDLESS OF WHICH AGENCY ARRIVED FIRST.

Beginning a case—In order to start entering a case into the ROC PRIMED database, you must have the date of the arrest and the time the call was received at the dispatch center for the first arriving agency (or mark ‘unable to obtain’ as above discussed). The gold standard is to obtain the time directly from the dispatch center because this is the most accurate. Other times (as

might be discerned in the pre-hospital written record) can serve as a place holder until the dispatch time can be obtained (be certain to mark 'from PCR/other' when entering a 'placeholder' time).

Timeliness—The Patient Enrollment form must be started within 3 days of the event (this is considered 'timely' notification to the CTC) and completed within 2 weeks of the date-of-episode.

Date of episode:

US sites enter date as mm/dd/yyyy and Canadian sites enter date as dd/mm/yyyy.

Time call received at dispatch:

The time call received at dispatch is the time of the earliest call received at the emergency communication center (or public safety answering point—PSAP) responsible for dispatching a vehicle as part of the EMS organized response (and includes all organized EMS respondents, i.e. fire and paramedics). For some sites, the time of the earliest call received at dispatch will be different from the time a call was received at the 911 call center. EMS and fire response may be dispatched from the same center or from different dispatch centers. A dispatch center downstream from the 911 call center is often referred to as a secondary PSAP. Indicate the time that the earliest call was recorded at the dispatch center whether it serves as a primary or secondary public safety answering point. The time a call is received at dispatch is defined in the ROC EMS structures database and indicates if a call time is recorded at 1st ring, call answered, 1st key stroke, or other. The time of call data should be obtained from dispatch records and not from EMS records unless they are automatically downloaded from dispatch. Handwritten dispatch time information should only be used as a last resort.

Time call received at dispatch is anticipated to be provided as hh:mm:ss (24 hour clock). Where a provided time is expressed as only as hh:mm leave the 'seconds' field blank (do not enter '0' or '00'). It is expected that most times provided *from dispatch* will have seconds. The *time call received at dispatch* will be considered "time zero" in many later analyses and precision of time, where available, is highly desirable. Sites are encouraged to establish relationships with *non-ROC* agencies that are commonly first on scene and harbor dispatch data.

Incident Number:

The *incident number* is an **optional** field defined by the site and intended as an aid to link records to the Site Linking ID or to the CTC Episode ID. If an *incident number* is provided on data forms, it will appear on the first printed Patient Enrollment form but will not be stored in the CTC database. Typically, this data field will contain the Incident Number that is an alphanumeric combination generated by the 911 dispatch system within each RCC. It can be used to identify an EMS call for which an EMS vehicle was dispatched and an EMS responder made patient contact. The incident number can be used to track a specific EMS run and EMS patient care record. In cases where multiple patients were evaluated at the same scene, this number may be applied to more than one patient included in the Epistry (i.e., the 911 dispatch Incident Number may not a unique patient identifier).

Site Linking ID:

The Site Linking ID number is an alphanumeric value assigned by the sites and is a specific identifier for each episode reported in the Epistry. The Site Linking ID must be unique across all of the site's patient records, but must not contain unique patient identifiers (e.g. name, date of birth, social security number). The Site Linking ID for a patient episode may be used across all ROC protocols for which the data is applicable (i.e. Epistry and HS, or Epistry and ROC PRIMED) to facilitate record keeping and data retrieval.
It is the responsibility of each RCC to maintain the link between the *Site Linking ID* (unique identifier) and patient identifiable data including patient care records. The CTC can provide algorithms or a set of pre-generated numbers upon request. Where transmitted to the CTC, the *Site Linking ID* is stored in the CTC main database. This ID will be included along with the CTC Episode ID in all CTC to RCC communications, site reports, and data exports. Reports to outside agencies and other consortium members will not include the *Site Linking ID.*

Item 1 –EMS response: (List agencies/vehicles in the order that they arrived at the scene)

Agency name: Provide the name of the agency for each of the first four responding EMS units (vehicles). Select the responding agency from the pull down menu. The pull down menu lists all agency names entered into the EMS Structures database. The pull down menu also lists "Non-ROC agency", "Not on List", "Unknown", and 'No additional responders". An entry must be selected for each of the four fields provided for 'Agency name."

"Non-ROC agency" is selected when an agency that is part of the organized EMS response is not a participant in ROC. While Non-ROC agencies may attend the episode, at least one ROC agency must be identified as one of the responding vehicles in order to save the form without errors. Where a responding ROC agency name is not listed in the pull down menu, select "Not on list" and save the form with errors. Return to the EMS Structures database and update its information to include the newly identified ROC agency – this will update the pull down menus. Resume data entry. "Unknown" agency may be selected as a placeholder when sorting out the response scenario. Selection of "Unknown" agency will allow the form to only be saved with errors.

"No additional responders" is selected to indicate that all responding agencies have been entered. If one, two or three vehicles responded to the cardiac arrest, enter that data, then indicate "No additional responders" for remaining Agency name fields, (after the last agency name entered) . If 4 vehicles responded to the cardiac arrest, it is not necessary to enter "No additional responders". This will enable the CTC to know that no further vehicles are expected for this episode. ENTER "NO ADDITIONAL RESPONDERS" ONLY AFTER YOU HAVE ENTERED ALL OF THE VEHICLES THAT ARRIVED AT THE SCENE. IF YOU ARE WAITING FOR MORE VEHICLE INFORMATION, WAIT UNTIL YOU HAVE ENTERED ALL AGENCY & VEHICLE DATA PRIOR TO ADDING "NO ADDITIONAL RESPONDERS".

If more than 4 vehicles arrive at the scene, the site should prioritize based on those agencies/vehicles with EMS providers who actively treated the patient. For example, if the fourth vehicle to arrive is the fire chief, and he observes the cardiac arrest but does not treat the patient, and ALS providers arrive as the fifth vehicle on scene and treat the patient, the fire chief vehicle should not be listed, but the ALS vehicle (fifth to arrive) should be listed.

Table 1: Summary of *Agency* and *Vehicle Name* response options and conditions for saving the Patient Enrollment form with and without errors.

Agency pull-down menu (error condition)	Vehicle pull-down menu (error condition)	
ROC agency picklist (OK)	ROC vehicle name picklist	(OK)
	Non-ROC	(OK)
	No Vehicle	(OK)
	Not in List	(save with errors)
	Unknown	(save w/o errors)
Non ROC agency (OK)	Non-ROC	(OK)
Not on List (save with errors)	Not on List	(no error message)
Unknown (save with errors)	Unknown	(no error message)
No additional responders (save without errors)	Unnecessary. Once this is selected no other information is required.	

To save a Patient Enrollment form without errors, at least one of the following agency/vehicle combinations MUST be provided: ROC agency/ROC vehicle or ROC agency/unknown vehicle.

Vehicle name:

Indicate the agency-specific vehicle name/identification numbers for each of the first four responding units (vehicles). See previous page on how to prioritize if there are more than four vehicles. Select the vehicle identifiers from the pull-down menu. The pull down menu lists all vehicle identifiers entered into the EMS Structures database that are associated with the previously selected Agency Name. Where a “ROC Agency” has been previously selected, the pull down menu also allows for selection of “Non-ROC vehicle”, “No vehicle”, “Not in List”, “Unknown” and “No additional responders“ . The “Non-ROC” option allows for the situation where not all tiers or portions of the selected agency are participating in the ROC. “No Vehicle” is reserved for those situations where an EMS provider is not assigned a vehicle, but is either stationed at an event or arena (such as a marathon or a football game) or whose means of transportation is not assigned an identification number (such as a bicycle). **“**Not in List” is reserved for those vehicles associated with ROC, but not yet entered in the EMS Structures database – when selected, the form can only be saved with errors, until EMS Structures is updated and the vehicle is re-identified on this form as a ROC listed vehicle. “Unknown” is reserved for those vehicles that the site has no means of otherwise identifying – when selected, the form can be saved with errors. “No additional responders” is an option for the vehicle data field when ‘No additional responders’ has been selected for the associated ‘Agency’ data field (see above Agency definitions).

Where a “Non-ROC” agency has been previously selected, the pull down menu only provides for a “Non-ROC vehicle – when selected, the form can be saved without errors.

Where a “Not on List” agency has been previously selected, the pull down menu only provides for a “Not on List” vehicle – when selected, the form can only be saved with

errors, until the EMS Structures database is updated and the Agency is re-identified as a ROC or Non-ROC agency and the associated vehicle identified.

Where “No Additional Responders” has been selected under agency, no additional information is required.

Where “Unknown” Agency has been previously selected, the pull down menu only provides for “Unknown” vehicle – when selected, the form can only be saved with errors, until the Agency is re-identified as a ROC or Non-ROC agency and the associated vehicle identified.

To save the Patient Enrollment form without errors, at least one of the first four EMS responding agencies and vehicles MUST provide one of these combinations: ROC agency/ROC vehicle or ROC agency/unknown vehicle.

Number of Personnel:
Indicate the number of crew members for each of the first four responding EMS units (vehicle). The field is auto-filled with data previously entered into the EMS Structures database.. Auto-filled values can and should be edited when pre-hospital documentation indicates the number of personnel is different. Where Vehicle Name is "No Vehicle", the Number of Personnel is two (2). Where a "Non-ROC" agency/vehicle name has been indicated and no documentation is available, leave the field blank (sites are encouraged to provide Non-ROC responder data where available).

Service Level:
Indicate the highest level of service provided by each of the first four responding EMS units (vehicles). Where Vehicle Name is "No Vehicle", indicate the level of service for the individual EMS provider that was present or responded to the episode. Where a "Non-ROC" agency/vehicle has been indicated and no documentation is available, leave the field blank (sites are encouraged to provide Non-ROC responder data where available).

BLS: Non-invasive emergency lifesaving care that is used to treat airway obstruction, respiratory arrest, or cardiac arrest. For example, cardiopulmonary resuscitation, but no AED capability.

BLS-D: In addition to cardiopulmonary resuscitation, includes defibrillation using an AED. Fire in Canada may be categorized as BLS-D if the responding unit is equipped with an AED.

BLS-+: In addition to BLS, and BLS-D, can administer symptom relief medication or start an IV or maintain or perform advanced airways, such as combitubes, laryngeal mask airways (LMA), or esophageal obturator airway (EOA).

ALS: Advanced lifesaving procedures, such as cardiac monitoring, administration of IV fluids and medications, and use of advanced airway adjuncts, such as oral or nasal endotracheal intubation, cricothyrotomy, ventilator, and continuous positive airway pressure (CPAP).

Time of Arrival:
Indicate what time each vehicle arrived (meaning wheels stopped moving). Where a "Non-ROC" agency/vehicle has been indicated and no documentation is available, leave the field blank

(sites are strongly encouraged to collect and provide non-ROC responder data where available). *Time of Arrival* should be provided hh:mm:ss when available. Where only hh:mm is available, leave the second's field blank (do not enter '0'; or '00').

Source:
For the Time of Arrival, indicate if the provided time is from the "Watch" (as written on the patient care record by an EMS responder), "Dispatch" (as provided by a dispatch log; where directly provided by dispatch records to an electronic PCR; or where local protocol is for EMS provider to call dispatch to obtain official time to be documented on the PCR), or "No Time" (to indicate the absence of a documented time of arrival for the responding agencies/vehicles). "No Time" should be reserved for "Non-ROC" agencies or "Non-ROC" vehicles. The gold standard is dispatch as the source for times. PCR times will be used for administration of treatments.

ITD opened, ITD used ITD number: For each ROC vehicle listed in Item 1, indicate if an ITD was opened in the presence of the patient. If it was opened, note whether the ITD was used, and enter the ITD number. If any ITD was opened and not used, or more than one ITD was opened by any of the providers at the scene for this episode, complete an Alert CTC form, and note the details surrounding this protocol violation.

Item 2 — Exclusion Criteria

a. *Both protocols specific:* Check the bubble "Yes" or "No" as to whether any exclusions existed for both protocols. If 'yes' and an ITD was opened in the presence of the patient, you must complete all forms through hospital discharge. After completing the Patient Enrollment form, the web-data entry system will indicate if further ROC PRIMED forms are required.
   - Age less than age of consent — This is less than the age of 18 years at most sites, but each site must follow their local regulations.
   - Pre-existing "Do Not Resuscitate" orders — If written Do Not Resuscitate (DNR) orders are given to the EMS providers after they have begun resuscitative efforts or a DNR order is substantiated by the patient's physician during the resuscitative effort, the bubble should be checked.

   - Arrest due to traumatic cause (blunt, penetrating, burns) — If the patient experiences a cardiac arrest due to a traumatic cause such as blunt or penetrating trauma or burns, the patient is excluded. The traumatic cardiac arrests should not be entered on the ROC PRIMED Patient Enrollment form unless the ITD was opened in the presence of the patient.

   - Arrest due to exsanguination — If a patient arrests due to exsanguination by medical cause, a Patient Enrollment form is completed, but the patient is excluded from the study. Very few patients are expected to arrest due to this cause, and it may be difficult to determine at the time of the resuscitation. If a patient has a small amount of fresh blood around the mouth or vomits old blood, this cannot be considered an arrest due to exsanguination.
   - Known prisoner — EMS providers have been instructed to exclude known prisoners for enrollment in the ROC PRIMED study, though resuscitative efforts using an ITD may occur prior to EMS being aware the patient is a prisoner. If a

known prisoner, no ITD was opened, and it was not a witnessed arrest, only the Patient Enrollment form is completed.

- If an ITD is opened, enter the ITD number on the Enrollment form or complete an Alert form with an explanation of the circumstances.
- Known pregnancy — ROC EMS providers have been instructed to not enroll a patient in the ROC PRIMED Trial if the patient is obviously pregnant, though pregnancy may not be known at the time of enrollment. If known pregnant and an ITD was not opened, complete the Patient Enrollment form. If an ITD was opened, it is required to complete all forms through hospital discharge. If it later becomes known that the patient was pregnant at the time of the resuscitation, it is not considered a protocol violation.
- No EMS CPR or EMS defibrillation-All ROC PRIMED patients are expected to receive either EMS compressions or EMS defibrillation by, or in the presence of, ROC EMS. If neither of these occurs but an ITD is opened, this exclusion should be checked and the forms completed through hospital discharge.

b. ITD specific: Check the bubble "Yes" or "No" as to whether any of the listed exclusions existed. If 'yes' and an ITD was opened in the presence of the patient, you must complete all forms through hospital discharge. After completing the Patient Enrollment form, the web-data entry system will indicate if further ROC PRIMED forms are required.
   - Tracheostomy present — Patients with a tracheostomy are excluded from enrollment in the ITD arm of the ROC PRIMED Trial. These patients may still be enrolled in the Analyze Late vs. Early arm of the Trial.
   - Mechanical CPR/ventilator device used — The use of mechanical CPR devices such as the AutoPulse, Lucas device, or the Thumper, or any other mechanical CPR devices are not allowed for use with the ITD. Mechanical ventilation is not allowed for use with the ITD.
   - Non-ROC vehicle applied pads or began CPR (and no agreement in place to obtain time first call received data) — The time of the first call received at dispatch is crucial in analysis for the ROC PRIMED Trial. If an agency and the site do not have an agreement to obtain this data prior to beginning the ROC Trial, the patient is excluded from the Trial.

   If the patient is excluded from the ITD study arm, the patient may still be eligible for the Analyze Late vs. Analyze Early arm if the site has an agreement in place to obtain the first call received at dispatch time from the non-ROC agency, or if the first arriving agency is a ROC agency.

c. Analyze Late vs. Analyze Early specific: Check the bubble "Yes" or "No" as to whether any of the listed exclusions existed. If 'yes' and an ITD was opened in the presence of the patient, you must complete all forms through hospital discharge. After completing the Patient Enrollment form, the web-data entry system will indicate if further ROC PRIMED forms are required.
   - Non-fire/EMS rhythm (that is non-fire and non-EMS) analysis (e.g. AED/defib. use by lay person) — Any patient with a non-fire or non-EMS rhythm analysis which is done with an AED or defibrillator by a bystander, lay person, health care

provider in a clinic, dialysis center, nursing home, or rehab facility that is outside of a hospital, or with a police AED will not be entered into the Analyze Late vs. Early arm.

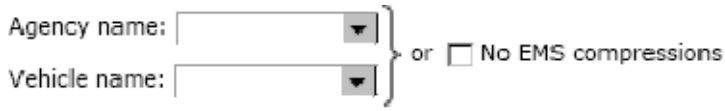
- Non-ROC EMS agency on scene and placed pads or began CPR or EMS directed bystander to continue CPR.— If a non-ROC EMS agency arrives on the scene prior to the ROC EMS and places the AED or defibrillator pads or begins CPR, the patient is excluded from the Analyze Late vs. Early arm of the Trial. The participating ROC EMS providers need to be made aware of the potential non-ROC agencies which operate in their area. "EMS directed bystander to continue CPR" was added for the rare case in which one EMS vehicle arrived at the scene with only 2 providers and the ROC EMS asked the bystanders to continue CPR while the EMS instituted other resuscitative measures. This item should not be checked for a situation in which the EMS asked them to continue CPR as they arrived at patient's side and opened the AED, but rather a situation documented by EMS in which the bystander was asked to continue CPR for a longer period of time while the EMS performed other resuscitative measures and this circumstance was documented by EMS. Police, off-duty EMS, nurses or doctors at dialysis centers, nursing homes and other health care clinics are considered bystanders.
- ROC EMS witnessed arrest — Because the standard protocol for EMS witnessed cardiac arrest is to analyze immediately, any episode which is initially witnessed by ROC EMS is excluded from the analysis of Analyze Late vs. Early arm. Because of the potential safety issues with delayed shock (due to study process), all ROC EMS witnessed arrests will be followed through hospital discharge, but follow-up forms are not required.
- If the patient is excluded from the Analyze Late vs. Early arm, the patient may still be eligible for the ITD arm if the site has an agreement in place to obtain the first call received at dispatch from the non-ROC agency, or if the first arriving agency is a ROC agency.

Item 3 — If all exclusion criteria answered "No" in Item 2a & 2b AND "No" ITD opened in Item 1, why was ITD not opened?

If an ITD was not opened and a patient had all exclusions marked 'no' in Items 2a and 2b, indicate the reason for this. Possible reasons are: the patient had sustained ROSC prior to opening of the ITD, the providers forgot (such as. forgot to bring it with them from the station or rig; forgot it was in their pocket; forgot to open it early in the resuscitative effort; or 'other' reasons which prevented them from opening the ITD (such as provider does not participate in research; packaged ITD was run over by the rig, etc). If 'other' marked, specify the reason for no ITD being opened.

Item 4 — CPR Assignment:

a. *What agency and vehicle (either ROC or non-ROC) was FIRST to direct the initial chest compressions?*

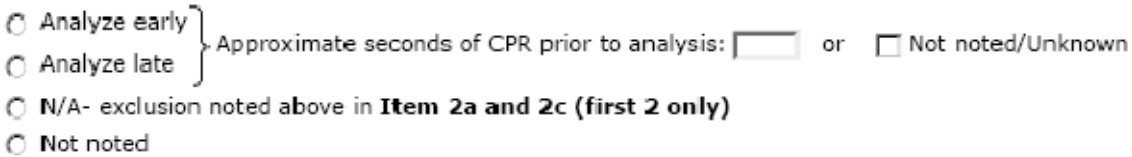


Using the pull-down menu, indicate which agency and vehicle directed the first EMS chest compressions as indicated on the PCR or cardiac arrest research form. This agency/vehicle should be listed in Item 1 of the Patient Enrollment form as one of the first four arriving vehicles. If a 'non-ROC vehicle' was the first to provide chest compressions, use the pull-down menu to indicate it was non-ROC. **"**Not in List" is reserved for those vehicles associated with ROC, but not yet entered in the EMS Structures database – when selected, the form can only be saved with errors, until EMS Structures is updated and the vehicle is re-identified on this form as a ROC listed vehicle. "Unknown" is reserved for those vehicles that the site has no means of otherwise identifying – when selected, the form can be saved without errors after providing an override reason. If no EMS compressions were done because the patient was defibrillated prior to chest compressions or the patient was not in cardiac arrest, check "No EMS Compressions"

b. *If randomized by defibrillator, note the AED/defibrillator study number:*

This is the number assigned by the CTC for the defibrillator if the agency cluster was determined by defibrillator rather than by agency, station, or rig.

c. *Intended EMS CPR assignment: (of the first arriving ROC vehicle)*



Indicate the CPR assignment that the first arriving ROC vehicle who directed the initial chest compression thought they were randomized as indicated by the PCR or cardiac arrest research form. If the cardiac arrest was a witnessed by EMS, check "Analyze Early" as all ROC EMS witnessed arrests should be in the Analyze Early arm. Then, indicate the number of seconds of CPR that was done prior to the first shock assessment, or mark 'not noted/unknown' if there is no associated documentation. If an exclusion was marked 'yes' in Item 2a or 2c (first 2 only; 'Non-fire/EMS rhythm analysis' or 'Non ROC EMS agency on scene…')) check 'N/A-exclusion noted above'. If there is no indication on the PCR or cardiac arrest research record as to the intended CPR assignment, thus no indication of the number of seconds of CPR prior to shock assessment, check "Not noted".

Item 5 -Any indication that the patient was enrolled in another clinical trial?

Indicate whether the patient was or was not enrolled in another non-ROC clinical trial, either pre-hospital or in-hospital. If yes, enter the name of the study and briefly describe the type of clinical trial.

NOTES:
1. Known prisoner cases do not require forms beyond **Patient Enrollment**. If an ITD was opened, then the **Patient/Family Consent** and **Alert CTC** forms are also required.
2. Except prisoners, if an ITD was opened or ROC EMS witnessed arrest, then all applicable forms through hospital discharge must be completed, regardless of exclusions.
3. Excepting the above two notes, no further forms are required if a case is excluded from both study arms.

** REMINDER: If EMS gives CPR or defibrillates a patient prior to receiving the DNR order, no ITD was opened, and it was not a ROC EMS witnessed arrest, then complete only the **Patient Enrollment** form (and any applicable **Alert CTC** forms).

Name of person responsible for data on this form:

Name of the individual that logged into the electronic data transmission system for clinical study forms. This individual will have registered as a CTC for the purpose of participating as a coordinator or investigator in a ROC clinical trial and has designated a user name and password as their "Electronic Signature." The individual has agreed to consider their electronic signature as equivalent to their handwritten signature, to maintain the confidentiality of their user name and password, and to not let others use it. Refer to the "Electronic Signature Agreement" (accessed after logging on to the ROC website) posted at https://roc.uwctc.org/tiki/roc-data-entry.

After verifying the entered data and electronic signature are correct, print the web-forms for your files, or convert the web-forms to PDF format and store electronically. Edits made later to the original web-entered forms are associated with the electronic signature of the individual making the changes and are documented in the file's edit history.

Complete this form:
- for any episode where ROC EMS CPR *(any compressions)*/defibrillation was performed or ITD opened *(even if not used)*

Main data resource: PCR
Other data resources: Dispatch

Patient Enrollment

Version 1.04.02
Date: 05/26/2009

Episode Information:

Date *(mm/dd/yyyy)* ___/___/___

Time call received at dispatch *(hh:mm:ss; 24hr clock)* ___:___:___

○ From PCR/other ○ From dispatch

○ Unable to obtain *(Non-ROC agency first arrival & no agreement in place to get data, patient is excluded from Trial)*

ROC PRIMED ID: ___-___-___

Incident Number *(optional)* _____

Site Linking ID *(optional)* _____

1. EMS response: *(List vehicles in the order that they arrived at the scene)*

	Agency name	Vehicle name	# of personnel	Service level: BLS	BLS-D	BLS+	ALS	Time of arrival *(24 hours) hh:mm:ss*	Source: Watch	Dispatch	No Time	ITD Opened* Yes No	ITD Used Yes No	ITD # *nn-nnn-n*
1:				○	○	○	○	___:___:___	○	○	○	○ ○	○ ○	___-___-___
2:				○	○	○	○	___:___:___	○	○	○	○ ○	○ ○	___-___-___
3:				○	○	○	○	___:___:___	○	○	○	○ ○	○ ○	___-___-___
4:				○	○	○	○	___:___:___	○	○	○	○ ○	○ ○	___-___-___

* If more than one ITD opened or any ITD opened and not used, complete **Alert CTC** form.

2. Exclusion Criteria:

Except for prisoners, if an ITD was opened or ROC EMS witnessed arrest, then all applicable forms through hospital discharge still must be completed **regardless** of exclusions.

a. Both protocols specific:

Yes	No	
○	○	Age < age of consent
○	○	Pre-existing "Do Not Resuscitate" orders **
○	○	Arrest due to traumatic cause *(blunt, penetrating, burns)*
○	○	Arrest due to exsanguination
○	○	Known prisoner → Complete only the **Patient Enrollment** form. If an ITD was opened, then also complete the **Patient/Family Consent** and **Alert CTC** forms.
○	○	Known pregnancy
○	○	No EMS CPR or EMS defibrillation

b. ITD specific:

Yes	No	
○	○	Tracheostomy present
○	○	Mechanical CPR/ventilator device used
○	○	Non-ROC vehicle applied pads or began CPR *(and no agreement in place to get time call received data)*

c. Analyze Late vs. Early specific:

Yes	No	
○	○	Non-fire/EMS rhythm analysis (e.g. AED/defib. use by lay person)
○	○	Non ROC EMS agency on scene and placed pads or began CPR
○	○	ROC EMS witnessed arrest → Complete all applicable forms through hospital discharge (regardless of exclusions).

3. If all exclusion criteria answered "No" in Item 2a & 2b AND "No" ITD Opened in Item 1, why not?

○ Sustained ROSC prior to ITD

○ Forgot

○ Other _____ *(60)*

continue to next page

Episode Information:

Date *(mm/dd/yyyy)* ___/___/___

Time call received at dispatch *(hh:mm:ss; 24hr clock)* ___:___:___

○ From PCR/other ○ From dispatch

○ Unable to obtain *(Non-ROC agency first arrival & no agreement in place to get data, patient is excluded from Trial)*

ROC PRIMED ID: ___-___-___

Incident Number *(optional)* _____

Site Linking ID *(optional)* _____

4. CPR Assignment:

a. What agency and vehicle (either ROC or non-ROC) was FIRST to direct the initial chest compressions?

Agency name: _____
Vehicle name: _____
} or ☐ No EMS compressions

b. If randomized by defibrillator, note the AED/defibrillator study number:

_____ - ___

c. Intended ROC EMS CPR assignment: *(of the first arriving ROC vehicle who directed the initial chest compressions)*

○ Analyze early
○ Analyze late
} Approximate seconds of CPR prior to analysis: ___ or ☐ Not noted/Unknown

○ N/A- exclusion noted above in **Item 2a and 2c (first 2 only)**

○ Not noted

5. Any indication that the patient was enrolled in another clinical trial?

○ No

○ Yes, non-ROC clinical trial → Specify: _____

NOTES:

1. Known prisoner cases do not require forms beyond **Patient Enrollment**. If an ITD was opened, then the **Patient/Family Consent** and **Alert CTC** forms are also required.
2. Except prisoners, if an ITD was opened or ROC EMS witnessed arrest, then all applicable forms through hospital discharge must be completed, regardless of exclusions.
3. Excepting the above two notes, no further forms are required if a case is excluded from both study arms.

** REMINDER: If EMS gives CPR or defibrillates a patient prior to receiving the DNR order, no ITD was opened, and it was not a ROC EMS witnessed arrest, then complete only the **Patient Enrollment** form (and any applicable **Alert CTC** forms).

Person responsible for data on this form: _____

6.2.1 Pre-hospital Time Record Form

The purpose of the Pre-Hospital Time Record is to determine the correct times and sequence of events. The items listed in the Time Record are the typical events that would occur during a cardiac arrest. Complete this form for all patients who met the ROC PRIMED enrollment or safety follow-up criteria for episodes in which the ITD was opened.

Event Order: For each listed event that occurred during the course of prehospital care, provide the event order (1-19), the Watch (PCR) time and/or the Dispatch/Defib time (on 24 hour clock, hh:mm:ss). If an event did not occur during the course of prehospital care, enter '0' for that event order (e.g. If the patient survived to ED, then 'Resus. Stopped due to death" should have an event order of '0'). Enter the event order as '0' for '911 call received at primary PSAP' if no documented time exists. If more than one event is documented as having occurred at the same time, provide the same event order for the two or more events. Where local practice is to provide identical times for known serial events, distinguish those with true identical times and provide data; for the remaining events provide plausible event orders based on recorded narrative, leave related time fields blank, and mark 'no doc time.' Where an event order is determined to be the same for two or more events *and* the watch times for each is different (such as might occur if more than one wristwatch were used on the scene), you are asked to confirm this condition and override the error message. Where an event order is determined to be the same for two or more events and provided times are sourced from the same dispatch/defib, it is expected that the provided times will be the same. The order of events can be re-sorted to the chronological order entered by pressing the 'Sort Event Order' or 'Align Times' buttons.

If you left out an item in the event order, it is not necessary to reorder all the affected lines—instead give the overlooked event a decimal number to place it between two existing numbers (such as 2.5 to place the event between the previously entered event 2 and 3). When the 'Sort Event Order' or 'Align Times' button is clicked, all events will be resorted and numbered to accommodate the decimal entry. NOTE: where the event orders have been changed, all previously 'aligned' times and intervals will be removed. Click the 'Align Times' button for recalculation of the aligned times and intervals.

Time of Event: Watch time is that time documented on the patient care record by the EMS provider, likely having been sourced from a wristwatch or clock. Dispatch/Defib time is that provided by the dispatch log and is the gold standard; a time annotated on the defibrillator/AED record, or where site/agency protocol requires EMS to routinely contact Dispatch to acquire the time(s) documented on the PCR. For each event with an event order of 1-19, provide either the Watch or Dispatch/Defib times when available. Where a time has been documented in the patient record as hh:mm, leave the seconds ('ss') field blank, do not enter '00.' If no documented time exists (from either the PCR or dispatch) for a specific event (with event order 1-19), check the 'No Doc Time' box and leave the associated time fields blank. For events with a '0' sort order, leave the Watch and Dispatch/Defib time columns blank and do not check 'no doc time.'

Dispatch/Defib times are generally documented as hh:mm:ss. Sites are encouraged to work with their Dispatch services to acquire 911 call times with seconds. Where no seconds are provided, leave the seconds ('ss') field blank, do not enter '00.' If a dispatch center does not synchronize their times to the atomic clock, the site should strongly encourage them to do so and provide them with a link to an atomic clock website.

For event times that appear to be affected by the crossing of a time zone or daylight savings time, enter the time documented in the PCR, dispatch log, or AED/defibrillator record. Do not adjust the times entered for the 'Time of Event.' Adjustment of times is reserved for the 'Aligned Time' column when assessing time intervals and cumulative times.

Source Disp/Defib: For each Dispatch/Defib time provided, indicate the source of that time by completing the 'Source Disp/Defib' column. If the time is from Dispatch, enter '0.' Enter '1', '2', etc for each of the series of defibrillators/AEDs that provided time of events during the course of care (i.e., '1' is the first defibrillator used, '2' is the second defibrillator used and so on).

Defib Appears Synched to Atomic Clock: Complete this column where a Dispatch/Defib time is marked as '1', '2', etc (indicating a defibrillator/AED source for time). Mark the corresponding box when documented times and your knowledge of EMS agency synchronizing protocols appear to be, in your judgment, synchronized with the atomic clock. For example: a defibrillator may provide a time that is 1 hour different than other associated times; you know the EMS agency synchronizes monthly; you know that daylight savings time just took effect; therefore you conclude that the defibrillator does NOT appear synchronized (at the time of this event) and you do NOT mark the corresponding box for 'Defib Appears Synched to atomic Clock.' Another example: a defibrillator provides a time that is 5 minutes different than a Watch time documented for the same ordered event; you know the EMS agency synchronizes monthly; you understand that wristwatch and clock times are often subject to drift and sloppy setting; therefore you conclude that the defibrillator DOES appear synchronized and you DO mark the corresponding box for 'Defib Appears Synched.....' For defibrillators which are downloaded to a computer, the computer to which an agency or site downloads the ECG should be synchronized to the atomic clock.

Aligned Time and Adj: The Aligned Time column is filled automatically when the 'Align times' button is pressed. A computer algorithm assesses times entered for 'Time of Event.' The algorithm moves Dispatch times (Source marked as '0') and Defibrillator times (when marked as 'appears synched to atomic clock') over to the 'Aligned time" column. Events with watch time only are aligned (adjusted) by the computer where adjacent events provide both a watch time and a dispatch or synchronized defibrillator time for comparisons (much like a Rosetta stone). A '?' to the right of the 'Adj' column indicates those times that have been adjusted (aligned) by the computer algorithm. Click on the '?' to learn which event(s) the 'Aligned time' is based upon. You may manually adjust the 'Aligned time' where knowledge of the EMS system or judgment of EMS documentation suggest an aligned time other than that provided by the computer algorithm. Aligned times are not filled or calculated for events where neither a Watch or Dispatch/Defib time is provided--aligned time fields are left blank. The site is encouraged, where reasonable surrogate information allows, to provide aligned times for blank fields (such as when EMS did not document their arrival at the ED, but the site knows what time the patient was admitted to the ED/hospital).

The 'Adjusted Time' box is automatically checked when you replace an aligned time (that was automatically filled) with a time judged to better represent the episode course of prehospital care.

Use the 'Adj' column to adjust for times that appear to be affected by the crossing of a time zone or daylight savings time—calculate the time difference imposed (such as +1 hour, -1 hour) on any of the 'Time of Event' times and adjust the time to reflect the 'true' time in the 'adj' column.

Time Interval and Cumulative time: Time intervals (the elapsed time between two adjacent events) and cumulative times (the sum of elapsed times) are calculated and filled automatically when the 'Align time' button is pressed. Review the calculated intervals to assess if they "make sense." Where calculated intervals are either negative (-) or excessively short or long, review and verify the values entered for 'Time of Event' (Watch and Dispatch times). Where entered times are transcribed accurately and calculated intervals do not make sense, the site can readjust the 'aligned' times using local knowledge of the various time sources.

Question '?' and exclamation '!' marks: A question mark '?' appears between the 'Adj' and 'time interval' columns for each aligned time that has been either adjusted or calculated by the computer algorithm. Click on the '?' to learn which event(s) were used for the computer algorithm. An exclamation '!' mark appears on a line if something obvious is missing (such as 'no 'doc time' not checked for an event with an order 1-19 and no times entered).

Buttons at the bottom of the form:

- "Sort Event Order" - Sorts events into numerical order (1-19, with 0's at end of list), but does not calculate or automatically fill aligned times.
- "Align times" - sorts events into numerical order (1-19, 0's at end of list) and moves watch time, dispatch time or a computer aligned time into the "Aligned Time" column. Pressing "Align Times" will also calculate the time intervals and cumulative time. Events with watch time only will be aligned via computer algorithm if adjacent event(s) have both a watch time and a dispatch time. When the 'Aligned Times" button is pressed, aligned times and intervals will be recalculated every time a time is modified. If this is annoying, press the 'Turn Align Off' button—this will erase any previous computer aligned times and computer calculated intervals. To recalculate aligned times and intervals, again press 'Align Times.' A question mark ('?') between the "Adj" column and the "time interval" indicates that the time is computer aligned. Clicking on the question mark tells you which event(s) the canceled aligned time is based on.
- "Turn Align Off" – Erases any previous computer aligned times and computer calculated intervals. Intended to be used where multiple times are being modified and triggering the recalculation of aligned times and calculated intervals. This button does not erase times adjusted ('adj') by the site. To re-establish computer aligned times and computer calculated intervals (as is required to save the form without errors), again press 'Aligned Times."
- ‘‘Original Order" – this returns the rows for 'Event' and 'Event order' to the original list as displayed when the form is first opened (and on the form worksheets) and erases any computer aligned time and calculated intervals. The most recently entered 'Event order' number(s) (0, 1-19) are not erased.
- ‘‘Reset form" – Pressing this button erases/blanks out all previously entered data on the time form so that you can start over.

Item 1 – 911 call received at primary PSAP (optional):

Time of the earliest call received at the initial public safety answering point (PSAP). This initial answering center is sometimes referred to as a primary PSAP. This center may be

responsible for dispatching the EMS organized response (includes all organized EMS respondents, i.e., fire and paramedics), or it may transfer 911 calls to a different (downstream) EMS or fire Dispatch location. A downstream dispatch center is often referred to as a secondary PSAP. Record the time of the earliest call received at the first public safety answering point. If no documented time is available, enter '0' for the event order, leaving time fields and 'No Doc Time' box blank.

Item 2 – 1st 911 call received at dispatch:

Time of the earliest call received at the emergency communication center responsible for dispatching a vehicle as part of the EMS organized response (includes all organized EMS respondents, i.e., fire and paramedics). This time should almost always come from dispatch logs or record. It may come from the PCR if the times on the PCR are automatically downloaded from dispatch (the 'source' for such a downloaded time would be marked as 'dispatch'). Do not confuse electronically downloaded dispatch times to the PCR with electronically charted times—working knowledge of the agency practices is necessary to differentiate these two. **If the '911 call received at dispatch' from the 'dispatch source' is different than the 'time call received at dispatch' entered on the Patient Enrollment form because that time came 'from the PCR/other', the Patient Enrollment form should be changed to reflect the time obtained 'from dispatch'.**

For some sites, the time of earliest call received at dispatch will be different from the time the call was received at the 911 call center or primary public safety answering point (PSAP). In these cases, dispatch for EMS and fire response are downstream from the 911 call center. EMS and fire response may be dispatched from the same center or from different dispatch centers. A downstream dispatch center is often referred to as a secondary PSAP. Indicate the time the earliest call was recorded at the first dispatching center, whether a primary or secondary public safety answering point.

The time a call is received at dispatch is defined in the ROC EMS Structures database and indicates if calls are recorded at 1st ring, when answered, 1st key stroke, or other. It is preferred that this time of call data be the first ring and be obtained from dispatch records and not from EMS records unless they are automatically downloaded from dispatch. Handwritten or electronically charted dispatch time information should only be used as a last resort!

The time a call is received at dispatch will serve as "time zero" where no time is provided for the optional field titled "911 call received at primary PSAP." Over time, "time zero" should be defined as first ring at the 911 call center.

Item 3 – 1st vehicle dispatch time:

The time recorded for when the crew of the first dispatched responding vehicle was notified (include fire responders). The '1st vehicle dispatch time' may or may not be associated with the vehicle that is '1st arrival at scene.' It is preferred that the requested time come from dispatch rather than handwritten or electronically charted EMS notes.

Item 4 – 1st non-EMS shock:

Time when the first non-EMS shock is delivered to the patient. A non-EMS shock refers to a shock from an AED or manual defibrillator which was operated by a bystander before the EMS or fire providers arrive at the scene. A bystander is defined as any person who responds and is NOT on duty with an EMS agency at the time of the arrest. Bystanders include laypersons, nurses or physicians in a health clinic, dialysis center, nursing home or a cardiac rehabilitation center; an off-duty fire-fighter or paramedic; or a police officer. Non-EMS AED/defibrillators also include public access AEDs (shopping malls, airports, etc) and defibrillators at satellite healthcare facilities such as day surgery, dialysis centers, nursing homes, assisted living and cruise ships.

The site Coordinator should attempt to get an electronic or paper copy of the ECG in order to obtain the time of the 1st non-EMS shock and the initial non-EMS cardiac arrest rhythm.

Item 5 – 1st vehicle arrival at scene:

Time the first responding vehicle arrives on the scene, wheels stopped. This time should come from dispatch rather than handwritten or electronic EMS notes. Where the cardiac arrest is witnessed by EMS *and* the EMS provider is indicated as having 'no vehicle' (on the Patient Enrollment Form, as when an EMS provider may be stationed at the scene such as at a stadium, race, or aid station), then consider their 'arrival' as being that for the '1st vehicle arrival at scene.' The next arriving EMS responder/vehicle is handled as the 2nd arriving vehicle or the 1st ALS arrival at scene, depending on the nature of the tiered response. 1st vehicle arrival at scene may be associated with a ROC or non-ROC vehicle or 'no vehicle.'

Autofill at web-entry: 'Time of Event' 1st vehicle arrival at scene' is filled and 'Source Disp/Defib' entered as '0' automatically IF the Patient Enrollment form has been previously completed and saved (with or without errors) with 'Time of arrival' for the 1st arriving EMS agency and the source of that time marked as 'From dispatch.' Autofilled values can be edited.

Item 6 – 1st EMS AED/defib turned on:

The time that the EMS responder powers on the automatic external defibrillator (AED) or monitor/defibrillator. It will be used as a surrogate for arrival of the EMS responder at patient side in a cardiac arrest not witnessed by the EMS responder.

Autofill at web-entry: Dispatch/defib time for '1st EMS AED/defib turned on" is auto-filled IF the CPR Process form (either saved with or without errors) contains a time entered for "Time machine turned on.' Autofilled values can be edited.

Item 7 – 1st ALS arrival at scene:

Time first advanced life support (ALS) designated EMS responder arrived on scene. If arriving by vehicle, time of arrival is when the wheels stopped moving. The 1st ALS arrival at scene may be associated with a ROC or non-ROC EMS response. First ALS arrival includes those situations where ALS EMS personnel arrive by non-conventional transportation (e.g. bicycle, dog sled, golf cart) or where ALS EMS personnel are stationed/staffing a public

event (e.g., marathon, football game). This time should come from dispatch rather than handwritten or electronic charted EMS notes.

Autofill at web-entry: 'Time of Event' 1st ALS arrival at scene' is filled and 'Source Disp/Defib' entered as '0' automatically IF the Patient Enrollment form has been previously completed and saved (with or without errors) with 'Time of arrival' for the 1st arriving EMS agency with a 'Service level' marked ALS, and the source of that time marked as 'From dispatch.' Autofilled values can be edited.

Item 8 – Time of arrest if EMS witnessed:

Time of initial cardiac arrest where the organized EMS response (includes fire) has arrived on scene prior to the onset of the cardiac arrest. This might occur where EMS or fire has been called for 'chest pain' or where EMS or fire is stationed at a public event such as a marathon or football game. If a bystander began CPR prior to EMS arrival but the patient had a pulse when EMS arrived, and later arrested in front of EMS, it would be called an EMS witnessed arrest. If the patient was defibrillated by an AED/defibrillator used by a lay person, health care provider, police or off-duty paramedic prior to EMS arrival, the CA would not be considered EMS witnessed.

The preferred source for this data element is voice recording (where available). The second and third preferred sources for this data element are respectively, the time synched continuous electronic ECG and the PCR. Time AED/defib is turned on is NOT considered a surrogate for 'time of arrest if EMS witnessed.

For cases monitored with pads or electrodes: Time of arrest is the onset of ventricular fibrillation (VF) or asystole. If the potential 'arrest' rhythm is ventricular tachycardia (VT) or PEA, then, the onset of VT or PEA must be temporally associated (so as to discern a perfusing from a non-perfusing rhythm) with either voice annotation, or with chest compression or shock artifact. If VT or PEA is associated with CPR, the time of arrest is when compressions are started. If VT is associated with a shock, the time of arrest is when analysis is started.

For cases not monitored (no pads or electrodes are on patient at time of arrest; or continuous electronic recording is not available): the time of arrest is determined from the PCR (if documented time is plausible).

Item 9 – 1st CA EMS rhythm:

Time of the FIRST interpretable cardiac arrest rhythm after confirmation of cardiac arrest and captured by an EMS responder, either ROC or non-ROC. Look for the '1st CA EMS rhythm' for up to 5 minutes after pad or electrode placement and prior to documentation of drugs given or a shock delivered by EMS or fire. EMS responder is defined as a person on duty for an organized EMS or fire agency at the time of the response. If the rhythm cannot be determined during this period, then mark 'cannot determine.' This rhythm is not one obtained by bystanders (doctors, nurses, police, off duty paramedics, off duty fire providers, and laypersons). The '1st CA EMS rhythm' cannot be a perfusing rhythm.

If the first vehicle was non-ROC EMS and you don't have access to the information, record an event order and check "no documented time".

Source of rhythm: The preferred source for capturing both the time of this event and the rhythm type is the time synched continuous electronic ECG, but ONLY IF THIS IS THE ECG FROM THE FIRST EMS AED/DEFIB APPLIED following the cardiac arrest. The primary goal is to get the first rhythm after the arrest. The '1st CA EMS rhythm' is not necessarily obtained from the first available electronic ECG (such as when only the 2nd arriving EMS recording is available). The second preferred source is a rhythm strip recording. The third preferred source is the rhythm documented in the PCR. Use the PCR only as a last resort (such as when the first electronic download is not available). Do not use information obtained from the compression channel generated by use of a 'puck' (Philips) or from compression annotations generated by use of CPR-D pads (ZOLL, Magnified ECG or CPR Quality Calculations tabs) to determine the '1st CA EMS rhythm.

Timing of the rhythm: Look for the EARLIEST rhythm from the time the pads were placed (from the FIRST EMS defibrillator placed), within the first 10 seconds if possible. For an EMS witnessed arrest (occurring after the arrival of EMS), look for the earliest rhythm following the onset of cardiac arrest, within the first 10 seconds if possible. If the ECG during the first 10 seconds is obscured then look either during a ventilatory pause, possibly during compressions if there are QRS complexes, or at the earliest pause in CPR for rhythm analysis, then look for the '1st CA EMS rhythm' for up to 5 minutes after pad placement and prior to documentation of drugs given or a shock delivered by EMS or fire.

Length of rhythm: There is no required length of time that a rhythm must be evident (such as transitional rhythms) to be considered the '1st cardiac arrest rhythm'. Use your best judgment in determining the rhythm during even a few seconds of interpretable ECG. The objective is to capture the earliest cardiac arrest rhythm, not necessarily the rhythm that is the easiest or clearest to discern. This is recognized to be a tradeoff. Where the reviewer observes a rhythm different than that indicated by the AED analysis (shock or no-shock) or the PCR, defer to the reviewer's finding as long as careful consideration is given to which source contains the information from the first EMS or fire defibrillator placed.

EMS witnessed arrest: If pads were placed prior to the EMS witnessed arrest, determine the 1st cardiac arrest rhythm within 5 minutes (if possible, within 10 seconds) immediately following arrest and prior to documentation of drugs given or a shock delivered by EMS or fire. If pads are placed after the onset of EMS witnessed arrest, then determine the '1st CA EMS rhythm' within the 5 minutes immediately following placement of the pads or electrodes and prior to documentation of drugs given or a shock delivered.

Autofill at web-entry: Dispatch/Defib time for '1st EMS rhythm after arrest' is auto-filled IF the CPR Process form (either saved with or without errors) contains a time entered for "EMS 1st CA rhythm *and* the source is marked as being continuous. Autofilled values can be edited.

Item 10 –1st EMS CPR:

This data element is intended to capture the time when the first chest compression was applied by a responding EMS or fire provider either non-ROC or ROC. If a bystander AED/defibrillator successfully converted the patient to ROSC prior to EMS arrival and the

patient did not re-arrest requiring ROC EMS CPR or defibrillation, the ITD was not opened and no safety concerns were present, the CA does not qualify for enrollment in PRIMED.

If a non-ROC vehicle is the first EMS or fire provider and initiates CPR, but the continuous ECG recording or PCR is not available, provide the sort order for the event and indicated 'no doc time' (do not use the ROC EMS documented time for their later provided continuation of CPR efforts). The sort-order of the event is important even in the absence of a documented time ('watch' or 'defib/dispatch') or an inferred time ('aligned').

It is recognized that this data element is a challenge to acquire. Where possible, sites are encouraged to work with EMS agencies to standardize practices that provide accurate time documentation or surrogates for time of '1st EMS CPR'—such as employing digital timers for CPR or training them to power on the AED/defibrillator when they arrive at patient side.

Source: The preferred source for this data element is voice recording (where available, such as when the provider says "CPR was started X seconds before the machine was turned on."). The second preferred source is the continuous electronic ECG or compression channel (such as when the arrest is EMS witnessed). The third and fourth preferred sources are the PCR and inferred times (such as time '1st AED/defib turned on' plus X seconds). Provide <u>all</u> documented times and/or inferred times routinely incorporated into local practices. Enter the time in time column appropriate to its source:

<u>Watch times:</u> those written in the patient care record.

<u>Defib/dispatch times:</u> those sourced from a device time-stamped snapshot or continuous ECG. Includes times calculated from time-stamped continuous ECG with voice recording commentary—for such defib/dispatch times, enter the value with seconds left blank, with no ':00'. Defib/dispatch includes times calculated from a time-stamped compression channel (Philips) where the 'puck' is on and recording prior to onset of CPR and placement of the pads.

<u>Aligned times:</u> those derived or inferred through knowledge or assumptions made of local practice, such as presuming that CPR is started when, or 30 seconds after, the AED/defib is turned on or pads are placed.

Public Access Defibrillation: Indicate a sort order of '0' for cases where non-ROC, or ROC EMS or fire, did not initiate chest compressions (such as where a bystander AED/defibrillator successfully converted the patient to ROSC prior to EMS or fire arrival and the patient did not re-arrest requiring CPR).

EMS witnessed: For cases where the arrest is considered 'EMS witnessed' (by responding EMS or fire providers), a sort order and time (or 'no doc time') for '1st EMS CPR' is required.

Item 11 –1st ITD CPR:

Time of first EMS compressions once the ITD was attached to the patient's face mask or advanced airway. In most cases, this is expected to occur within a couple of minutes of '1st EMS CPR' if the first arriving vehicle is a ROC vehicle carrying the ITD.

Item 12 –1st EMS shock assessment:

The time when EMS or fire providers, either ROC or non-ROC, initially analyze or assess the rhythm to determine whether or not a shock is indicated. This applies even if the assessed rhythm is not VF/VT and no shock is given. For the ROC PRIMED study, it is the intent of this data variable to determine compliance with randomization to 'analyze early' or 'analyze late' CPR assignments.

For AED continuous ECG: The time associated with the start of the first AED analysis event, free of significant artifact and CPR. Some devices are programmed to analyze automatically (such as when the device is powered on or pads placed) and/or initiate a shock—if the analysis is aborted (stopped) by EMS, do not consider that analysis for '1st EMS shock assessment.'

ZOLL AED Pro and E-Series in Auto Defib mode: this is the time of the first "Analysis Started" event. The AED marks when analysis starts and when the device instructs the provider as to whether a shock is needed. Use the former mark.
Medtronic AED (Lifepak 500 or 1000, and Lifepak 12 in AED mode): use 'Analysis 1' which indicates the initiation of analysis (button pushed).
Philips MRX: When in AED mode, the annotation log states "analyzing" to indicate the beginning of analysis for a shock. Use the first such notation (except where aborted by EMS) as '1st EMS shock assessment'. Where 'analyzing' is indicated (and analysis was not aborted), but the compression channel (generated by the 'puck' indicates that CPR is stopped at a later time, document the later time).

Manual defibrillator continuous ECG: The time associated with the intention of pausing CPR for the assessment of the rhythm for a determination to shock or not shock. The reviewer will have to make a judgment as to when the EMS or fire provider paused for assessment of the rhythm. This may include:

a) interruption of CPR with the intent to assess the rhythm to determine if a shock is needed (this might be a pause in the impedance tracing noting chest compressions, use of voice recordings to confirm intent, etc) or
b) Identifying the first pause in compressions > 4 or < 10 seconds in duration with no movement artifact (a pause in compressions of 4-10 seconds is "presumed ventilation pause" per the ROC PRIMED protocol), or
c) If the intent is not apparent, use a combination of the information on the PCR, EMS questionnaire, or other resource to try to determine when the first rhythm assessment occurred to assess whether or not a shock was indicated. If no times are available, determine and provide at least the order of events.

Timing of event: The time of '1st EMS shock assessment' associated with different events depending on the response scenario. The time of '1st EMS shock assessment' may:

a) be same time as the '1st CA EMS rhythm' when the initial EMS shock assessment is conducted close to the time of EMS AED pad or manual defibrillator electrode/pads placement, OR when ALS arrives first on scene with a manual defibrillator (such as a Lifepak 10 or 12).
b) occur shortly (about 30 seconds) after CPR is started (such as 'analyze early' in the ROC PRIMED trial) or immediately after an arrest when witnessed by EMS (if pads or electrodes were placed prior to the arrest).

Complete this form:
-for any episode where patient met enrollment or safety criteria or ITD opened
Main data resource: PCR
Other data resources: Dispatch

Pre-hospital Time Record

Version 1.00.01
Date: 08/14/2007

Episode Information:

Date *(mm/dd/yyyy)* ___ / ___ / ___

Time call received at dispatch *(hh:mm:ss; 24hr clock)* ___ : ___ : ___

○ From PCR/other ○ From dispatch
○ Unable to obtain *(Non-ROC agency first arrival & no agreement in place to get data, patient is excluded from Trial)*

ROC PRIMED ID: ___ - ___ - ___

Incident Number *(optional)* ___

Site Linking ID *(optional)* ___

Time Record:

-Fill in Event Order, Watch time, and/or Dispatch/Defib time for all events that occurred. If an event did not occur, enter "0" for Event Order.
-If the time of event in "Dispatch/Defib" is from Dispatch, enter "0" in the "Source Disp/Defib" box; otherwise enter "1","2", ... where "1" is the 1st defibrillator used, "2" is the second defibrillator used and so on.
-If the time of event in "Dispatch/Defib" is from a defibrillator and if that defibrillator appeared to be synched to the atomic clock, check the "Synched to Atomic Clock" box. If the defibrillator was *not* synched to the atomic clock (e.g. time seems off), enter the probable time in the "Aligned Time" field.
-If no documented time exists (from Watch, Dispatch, or defib) for an event that occurred, fill in event order, leave the time fields blank and check the "No Doc Time" box. The exception is "911 call received at primary PSAP" (enter the event order as "0" if you do not know the time).
-**Additional Instructions/Documentation**

Event	Event Order	Time of Event		Source Disp Defib	Defib Appears Synched to Atomic Clock	No Doc Time	*Computer to generate (you may adjust)*	
		Watch	Dispatch/Defib				Aligned Time	Adj
	1-19 0=NA	*hh:mm:ss*	*hh:mm:ss*				*hh:mm:ss*	↓
911 call received at primary PSAP		: :	: :		☐	☐	: :	☐
1st 911 call received at dispatch		: :	: :		☐	☐	: :	☐
1st vehicle dispatch time		: :	: :		☐	☐	: :	☐
1st non-EMS shock		: :	: :		☐	☐	: :	☐
1st vehicle arrival at scene		: :	: :		☐	☐	: :	☐
1st EMS AED/defib turned on		: :	: :		☐	☐	: :	☐
1st ALS arrival at scene		: :	: :		☐	☐	: :	☐
Time of arrest if EMS witnessed		: :	: :		☐	☐	: :	☐
1st CA EMS rhythm		: :	: :		☐	☐	: :	☐
1st EMS CPR		: :	: :		☐	☐	: :	☐
1st ITD CPR		: :	: :		☐	☐	: :	☐
1st EMS shock assessment		: :	: :		☐	☐	: :	☐
1st EMS shock		: :	: :		☐	☐	: :	☐
Advanced airway established		: :	: :		☐	☐	: :	☐
1st ROSC		: :	: :		☐	☐	: :	☐
First time ITD removed		: :	: :		☐	☐	: :	☐
Resus. stopped due to death		: :	: :		☐	☐	: :	☐
Patient transported from scene		: :	: :		☐	☐	: :	☐
ED or EMS destination arrival		: :	: :		☐	☐	: :	☐

Sort Event Order | Align Times | Turn Align Off | Original Order | Reset Form

Note: Time Intervals will be computed at data entry time.

Person responsible for data on this form: ___

6.3.1 Pre-hospital Data Form

The purpose of the Pre-hospital Data form is to collect information from the time the 911 call was received at dispatch through the time that the patient either died in the field or was admitted to the emergency department. The information for this form will come from the pre-hospital PCR (ACR), dispatch, electrocardiogram (ECG), and any cardiac arrest supplemental forms completed by the EMS providers. The episode date, time, and episode ID will be pre-filled by the web data entry program, and it will be consistent with the date and time recorded on the Patient Enrollment form. Pre-filled data should be reviewed for accuracy. If the time entered on the Time Record is different from the time on the Patient Enrollment form, the incorrect time should be changed so both forms note the correct time. This may pertain especially to the time the call was received at dispatch. This time should come from dispatch and not the PCR.

Item 1– Location of Episode

a. Location: Identify location of the episode using census tract, latitude/longitude (lat/long), or Universal Transverse Mercator (UTM) location types. Select one location type for an episode and provide the related coordinates. A site may use different location types for different episodes. Mark unknown/not noted when no location of episode can be identified, despite concerted efforts. It is the responsibility of each ROC site to comply with local and governing privacy requirements and to report location of episode only to the limit allowed.

Census tract: For the United States, go to http://www.ffiec.gov/geocode/default.htm. Select 'year' as 2006. For each episode enter the street address along with the city and state or the zip code. If the episode occurred at an intersection and you do not have the exact address, enter the name of the intersection (N.E. 45th and 11th Ave. N.E.) where it asks for the street address on the 'ffiec geocoding system web-page.' Once the information has been entered, click the 'Search' button. This connects to the 'Geocode Search Result' page where state code, county code, and tract code numbers are identified in red. The web-site provided MSA/MD code is not entered into Epistry. For state code, enter 2 digits (01-99). For county code, enter 3 digits (001-999, including leading and trailing zeros). For tract code, enter 6 digit number including decimal (1234.56, including leading and trailing zeros). Mark unknown/not noted if state-county-tract codes are not found despite efforts to provide complete address or intersection information and alternate location of episode location types (lat/long, UTM) are not available.

For Toronto: CTName/CTUID: CTName and CTUID are each an expression of census tract location in Canada and can be derived by conversion of local postal codes using specialized software. 'CTName' data format is restricted for location of episodes that occur within metropolitan Toronto. 'CTUID' data format can be used for any location within Canada, including metropolitan Toronto.

CTName—use of this number format is restricted to metropolitan Toronto. Just as a telephone number is unique only when preceded by an area code, CTName is a unique locator only when preceded by a Census Metropolitan Area/Census Agglomeration (CMA/CA) number. Thus, the CTName data format is *restricted* to use for a known area (that of metropolitan Toronto) because of the absence of a preceding CMA/CA number

(see below CTUID description). For metropolitan Toronto CTName, enter 6 digits (1234.56) including decimal point and all leading and trailing zeros. Note: Toronto CTName is provided at local request, and is not intended to limit Toronto from using other formats for providing location of episode (CTUID, lat/long, or UTM location).

CTUID—This is a unique combination of CMA/CA and CTName numbers and is available when converting a Canadian postal code to census tract format. For CTUID, enter 9 digits (1234567.89) including decimal point and all leading and trailing zeros. The first 3 digits of the CTUID indicate the unique CMA/CA location—for example, Toronto CMA/CA is 535, Hamilton CMA/CA is 537. So, a Hamilton CTUID would be formatted as 537XXXX.XX

Lat/long (latitude/longitude): Latitude/longitude is a coordinate system to locate a position on the earth, expressed in degrees (relative to a full circle). Latitude runs north/south. Longitude runs east/west. Select which of three (3) data formats the lat/long coordinates are being provided: decimal degrees (DD), DM (degrees:minutes), or DMS (degrees:minutes:seconds or 12:12:12). The most common format is decimal degrees (example: 123.1234) and is recommended for ROC data entry. The latitude and longitude for an episode must be reported in the same format. No directional designate (north, south, east, west, or '-' sign) is required as all ROC sites are within North America.

Decimal degrees—the most common format for lat/long. In its most precise form, decimal degrees is expressed as 123.123456. For privacy purposes, decimal degrees are rounded (up or down) and reported for ROC to a maximum of four decimals (123.1 to 123.1234, including all leading zeros). No directional designate or '-' sign are to be included. Where local rules to protect privacy restrict lat/long to be reported to less than 4 decimals (as in British Columbia).

DM or Degrees:minutes—for latitude, enter 5 characters including colon and no spaces (such as 49:30 or 49:03, designating 30 minutes and 3 minutes respectively). Do not provide decimal place values (such as 49:30.24 is reported as 49:30). For longitude, enter 5-6 characters including colon and no spaces (such as 122:20, 79:24, 114:01 or 96:46 designating 20, 24, 1, and 46 minutes respectively).

DMS or Degrees:minutes:seconds—it is rare that this lat/long format would be used. Contact the CTC to discuss if this report format is contemplated or preferred over the decimal degrees format.

Datum (or map datum)--this is the topographic map standard to which the lat/long coordinates are applied. There are three map datums used in the western hemisphere: NAD27 (North American Datum 1927), NAD83 (North American Datum 1983), and WGS84 (World Geodetic System 1984, based on satellite measurements). There is a measurable difference between the map datums, and thus important to know the source for measurements for later geographic analyses.

UTM (Universal Transverse Mercator): The UTM coordinate system is a grid-based method to identify a location on the earth. Unlike lat/long coordinates, the UTM coordinate system divides the surface of the earth into zones, or uniform grid squares, each identified by a number (North America is assigned numbers 7 through 21) and a letter. The location of a position within a zone is expressed by using both 'easting' and 'northing' values, and are expressed in either meters or kilometers units of measure.

Easting—this is the projected distance within the zone. Provide the first 3 (kilometers) or 6 (meters) digits of the 'easting' coordinate. Do not round. Instead, truncate the number to the required field length (e.g. 821.8 km is entered as 821, not 822). Indicate the units of measure. Where local privacy guidance restricts coordinates to less than 3 (kilometers) or 6 (meters) digits, truncate the number and replace with '0's' (e.g. 828 km is entered as 820 or 800).

Northing—this is the projected distance from the equator and can be expressed in meters or kilometers (most common) units of measure. Provide the first 4 (kilometers) or 7 (meters) digits of the 'northing' coordinate. Do not round. Instead, truncate the number to the required field length (e.g. 8218.68 km is entered as 8218, not 8219). Indicate the units of measure. Where local privacy guidance restricts coordinates to less than 4(kilometers) or 7 (meters) digits, truncate the number and replace with '0's' (e.g. 8218 km is entered as 8210 or 8200).

Zone—the UTM designated grid area associated with the provided 'easting' value. Provide the one or two digit zone number (it is anticipated that ROC sites would provide a number ranging 10 to 18) without the associated letter (e.g. Zone 17N is entered as 17; the 'N' is not required for the ROC footprint).

b. Public or non-public: Indicate whether or not the location of the episode occurred in a public or non public setting. For either public or non-public, select one description from the lists provided that best describes the location of the episode.

Public (check one only)

Street/highway: includes highway, alley, road, public thoroughfare, and NEMSIS 1160.

Public building: includes schools and their playground/athletic fields, government offices, and NEMSIS 1165.

Place of recreation: includes park, stadium, lake and place of recreation or sport. Includes NEMSIS 1155 place of recreation or sport.

Industrial place: includes factory, warehouse, construction site, and industrial place and premises, mine and quarry Includes NEMSIS 1150 industrial place and premises, and NEMSIS 1145 mine and quarry.

Other public property: includes sidewalk, store, church, restaurant, bar, hotel, and trade or service. Also includes train tracks. Includes NEMSIS 1170 trade or service.

Non public (check one only)

Home residence: includes inside or immediately surrounding the apartment, home/mobile home/farmhouse, garage, yard, and garden. Also includes adult family home and shelters for the homeless. Includes NEMSIS 1135 home/residence.

Farm/ranch: includes farm land, pasture, barn or other outbuilding. Includes NEMSIS 1140.

Healthcare facility: Includes dialysis center or outpatient clinic, and NEMSIS 1175. Does not included nursing home (note that NEMSIS includes this in both 1175 and 1180).

Residential institution: includes assisted living, nursing home, jail, or residential institution. Includes NEMSIS 1180.

Other private: those private locations not included above.

Item 2 – *Demographics*

a. Age: Enter the patient's age as noted on the PCR. Indicate whether the age was calculated from date of birth or estimated by EMS.

If no age is written on the PCR, indicate the age group that is noted on the PCR by marking child, adolescent, adult, middle age, older, or elderly. This is a judgment based on a description of the patient on the PCR. If no notation is made to indicate a possible age on the PCR, contact the EMS provider and document your conversation in this episode file. We must know the approximate age, as this is an exclusion criterion for the study.

b. Gender: Indicate if the patient is male or female. If the patient's gender is not noted on the EMS provider's PCR, contact one of the EMS providers who participated in the cardiac arrest resuscitation to obtain this information

c. Race/Ethnicity (check all that apply): Check all that apply from the list provided. Where self-identification is not feasible or appropriate, attempt to determine ethnicity and race or multiple races.

Definitions for race/ethnicity:
Hispanic or Latino: A person of Cuban, Mexican, Puerto Rican, South or Central American, or other Spanish culture or origin. The term, "Spanish origin," can be used in addition to "Hispanic or Latino." Includes NEMSIS 690.

White: A person having origins in any of the original peoples of Europe, the Middle East, or North Africa. Includes NEMSIS 680.

African-American/Black: A person having origins in any of the black racial groups of Africa. Terms such as "Haitian" or "Negro" can be used in addition to "Black or African American." American-Indian/Alaska Native: A person having origins in any of the original peoples of North and South America (including Central America), and who maintains tribal affiliation or community attachment. Includes NEMSIS 660.

Asian: A person having origins in any of the original peoples of the Far East, Southeast Asia, or the Indian subcontinent including, for example, Cambodia, China, India, Japan, Korea, Malaysia, Pakistan, the Philippine Islands, Thailand, and Vietnam. Includes NEMSIS 665.

Native Hawaiian/Pacific Islander: A person having origins in any of the original peoples of Hawaii, Guam, Samoa, or other Pacific Islands. Includes NEMSIS 675.

Other: Identifiable race/ethnicity not described above. Includes NEMSIS 685.

Unknown/Nothing noted: EMS provider is not able to determine the patient's race and ethnicity and notes it in the patient care record, or information has not been recorded. Includes NEMSIS -10, -5, 015.

Item 3 – *Cardiac arrest occurred:*

Indicate if the cardiac arrest occurred before or after the EMS (includes fire) providers arrived on the scene, or if the patient did not have a cardiac arrest (as might apply when an ITD in error).

After EMS (includes fire) arrival/witnessed by EMS—If the CA was witnessed by either ROC or non-ROC EMS providers, check this bubble and skip to Item 4. Includes NEMSIS 2245, cardiac arrest after EMS arrival. Does not include police.

Before EMS arrival—If the cardiac arrest occurred before EMS arrival, check the corresponding bubble and indicate whether or not the arrest was witnessed by a lay person.

Witnessed (seen or heard) by someone other than EMS – includes those instances where a cardiac arrest or collapse is witnessed by a lay person, a healthcare provider or an off-duty EMS or fire provider who witness the event but are not part of the organized EMS response to this episode. Includes NEMSIS 2310, NEMSIS 2315, and NEMSIS 2240.

Not witnessed –not witnessed prior to EMS arrival. Includes NEMSIS 2320.

Unknown/not noted—includes cases where this information has not been documented by EMS. Includes NEMSIS -10.

Patient did not have a cardiac arrest-If the patient did not have a cardiac arrest as noted on the Patient Enrollment form, Item 2a, this 'patient did not have a cardiac arrest' bubble should here be checked. This situation may occur if the EMS providers opened the ITD package because they thought the patient was going into CA but it did not happen. Data forms through hospital discharge are required even if there was no indication that the ITD was attached to the BVM or advanced airway.

Item 4 – *Was resuscitation attempted by bystanders?(check one)*

Indicate whether or not resuscitation attempts were made by bystanders or whether this was unknown. If 'yes', resuscitation attempts were made by bystanders, indicate whether CPR (chest compressions and/or ventilations) was attempted and whether the AED/defibrillator was applied. If the AED/defibrillator was applied, indicate whether shocks were delivered and, if so, the number of shocks, if known. Indicate whether the AED/defibrillator was applied by a layperson, police, health care, other, or if it is unknown/not noted. A bystander is defined as any person who responds and is NOT on duty with an EMS agency at the time of the arrest. Bystanders include doctors, nurses, police, off duty paramedics, off duty fire providers, and laypersons. This also includes healthcare providers at satellite healthcare facilities such as day surgery, dialysis centers, nursing homes, assisted living and cruise ships.

Item 5 – ***EMS chest compressions*** *(check all that apply)*

Indicate whether manual chest compressions mechanical compressions (such as Thumper, AutoPulse), or no chest compressions were administered by non-ROC or ROC EMS during CPR. There may be occasional times when a mechanical compression device is used by a non-ROC EMS agency or a ROC agency which is not participating in the ITD portion of the study. It is a protocol violation to use the ITD along with a mechanical compression device or mechanical ventilator, and if this occurs, complete an Alert CTC form. There may be an occasional time when no EMS chest compressions are administered because the patient was resuscitated by a shock prior to receiving compressions or the patient was not in cardiac arrest.

Item 6 – ***ITD information***

If no ITD was used during the course of resuscitation efforts, check this box and skip to Item 7. 'Use' is defined as attachment of the ITD to a patient's mask or advanced airway for any length of time.

a. Emesis noted—Note 'yes' or 'no' whether emesis was recorded on the EMS provider record, both prior to placement of the ITD or during its use. If emesis was not noted on the record, check "No."

b. ITD attached to: (check all)—Indicate what the ITD was attached to at any time during the resuscitation effort, either mask, ETT (oral or nasal endotracheal tube), or other advanced airway, such as LMA (laryngeal mask airway), Combitube, King LT, PLA (perilaryngeal airway), or other. If "Other," indicate what advanced airway was used—this includes other supraglottic airways (specify) and EOA (esophageal obturator airway).

c. Filter used?—Indicate whether a filter was used on the airway by the EMS provider when the ITD was used, and if "Yes," the type or types of filter used. If an EMS agency always uses a filter during the resuscitative effort and it is one particular type of filter, but it is not routinely documented as such because it is part of the protocol, indicate the type.

d. Timing light failed?—Indicate 'yes' or 'no' whether the timing light on the ITD was NOT functioning once turned on; or if the timing light was NOT used (such as when not turned 'on'; might occur when a 30:2 or other compression to ventilation ratio is performed). When turned 'on' the ITD is programmed to flash at a rate of 10:1.

e. Mask & ITD: Any indication that there were problems maintaining a tight seal (e.g. facial hair, height of equipment, etc.)?—Indicate if there were difficulties noted in maintaining a tight seal with the mask and the ITD. If 'yes' specify the possible reason for this. Possible reasons might include a large amount of facial hair, the height stack of the equipment, if an end tidal CO2 detector is used, missing teeth or dentures, or not enough EMS providers were available to help maintain the seal.

f. Was there any indication that a tight seal was not maintained during COMPRESSIONS and ventilations?-Indicate if the EMS providers reported that a tight seal was not maintained

during COMPRESSIONS and ventilations. It is extremely important that a tight seal is maintained during COMPRESSIONS as this is necessary to receive the potential benefit of the ITD.

Item 7 – *Pre-hospital intervention: (check all that apply)*

Mark 'No EMS prehospital interventions from the list below were recorded' where no one item in the provided list has been documented or interpreted as having occurred as part of the non-roc or ROC EMS response protocol. Mark this option only when full documentation for the organized EMS response is available to the ROC coordinator (such as both the BLS and ALS record; or a non-ROC agency or vehicle was part of the response team).

For each listed intervention, mark 'done' if the procedure was 'attempted' (performed) by EMS responders during the pre-hospital course of care. Indicate 'NA/NR' (not available or not recorded) if the procedure was not recorded in the patient care record or was not part of the EMS response protocol.

Where only partial documentation is available to the ROC coordinator (as where a non-ROC BLS or ALS was first on scene or where the ALS or the BLS record is missing), the Coordinator should contact the provider to obtain the information. Mark those prehospital interventions that available documentation indicates were 'done.' Mark 'NA/NR' for interventions that available and skill-related documentation (e.g. BLS record missing, but ALS record available and indicates no IV/IO line was started) is available. Leave both 'NA/NR' and 'done' blank for a prehospital intervention for which the skill-related documentation (e.g. BLS record is available, but ALS record is missing so 'IV/IO line' and 'airway, advanced' might be left blank)–then, override the error message and indicate which documentation is missing. Where only partial documentation is available, do not mark 'no prehospital interventions recorded.'

If documents are missing, the Coordinator needs to contact the EMS agency and attempt to obtain the data and document the attempt on the patient record.

Definitions for pre-hospital interventions:

Airway, bag-mask: patient ventilation is assisted with a face mask and anesthesia bag (with or without oxygen)

Continuation of non-EMS advanced airway: A patient may arrest in a clinic, dialysis center or cardiac rehabilitation center, and the medical provider places an advanced airway prior to arrival of the EMS.

EMS Airway, advanced: Mark 'done' if the non-ROC or ROC EMS responders (includes fire) attempted the placement of an advanced airway. If 'done', check all methods that were attempted or successful.

Oral ET: if noted in the chart, indicate the number of attempts at establishing a patent oral endotracheal airway. Mark 'not noted' if EMS or fire notes do not indicate the number of attempts. Indicate 'yes' or 'no' if oral intubation was successful. Includes NEMSIS 96.040.

Combitube, LMA, etc: Includes King LT, PLA (perilaryngeal airway), EOA (esophageal obturator airway), or other supraglottal airway. Mark 'not noted' if EMS or fire notes do not indicate the number of attempts. Indicate 'yes' or 'no' if placement of a supraglottal airway was successful. Includes NEMSIS 96.052, NEMSIS 96.030.

Nasal ET if noted in the chart, indicate the number of attempts at establishing a patent nasal endotracheal airway. Mark 'not noted' if EMS or fire notes do not indicate the number of attempts. Indicate 'yes' or 'no' if nasal intubation was successful. Includes NEMSIS 96.041.

RSI: rapid sequence intubation. RSI is indicated if the PCR states 'RSI' or includes charted evidence of step-wise series of three drugs (sedative, analgesic, and paralytic) coupled with an attempt to intubate.

Cricothyrotomy: includes needle cricothyrotomy and surgical cricothyrotomy. Includes NEMSIS 31.120.

CPAP: continuous positive airway pressure. Includes NEMSIS 93.900.

Ventilator: airway ventilator. Ventilators are excluded when using the ITD. If this protocol violation occurred, complete an Alert CTC form. Includes NEMSIS 96.700.

CPR—EMS providers attempted cardiopulmonary resuscitation. Rescue breathing only does not constitute CPR. Includes NEMSIS 99.600.

Hypothermia—Mark if hypothermia therapy was used at the scene or enroute prior to arrival at the ED. This includes cold intravenous saline, ice packs, or other hypothermia therapies.

IV/IO line – Check all attempted—indicate if intravenous (IV) or intraosseous (IO) line placement was attempted. If attempted (or was a continuation of an IV), indicate if it was successful. The continuation of an IV would be checked if the IV was initiated by a nurse or physician prior to arrival of the EMS providers, such as at a clinic or dialysis center. Indicate whether fluids were given TKO (a slow drip rate 'to keep open'), a measurable volume was infused, or whether it is unknown whether fluids were given. If fluid was given, indicate the type, either D5W, normal saline, lactated Ringers, other, or if the fluid type is unknown/not noted. Entry of the volume infused is optional. IV/IO NEMSIS codes include 41.920, 41.921, 38.991, 38.992, 39.995, 39.996, 38.993, 38.994, and 89.620.

Monitor, advanced Check all attempted—Mark when one or more of the listed advanced monitoring procedures is attempted by non-ROC or ROC EMS (includes fire): 12-lead ECG, EtCO2, or Pacing. If the patient arrested at a clinic, and the clinic nurse or physician did a 12-lead ECG but the EMS provider did not do one, check "No."

Item 8 – Drug therapies noted: (check all that apply)

Indicate which of the listed drugs were administered at any time during the pre-hospital EMS course of care. Suspected extravasation of a drug is considered to have been administered. Check all listed drugs that apply. Where only partial EMS documentation is available to the ROC coordinator (as where the ALS or BLS or non-ROC record is missing), mark 'yes' or 'NA/NR'

(not available/not recorded) for those drug therapies for which skill-related (such as the ALS patient care record) documentation is available. Leave 'NA/NR' and 'yes' blank for a prehospital drug therapy for which the skill-related documentation is missing—then override the error message and indicate which documentation is missing. It is not intended that medications administered prior to arrival of the organized EMS response be listed (e.g. Where a cardiac arrest occurs at a dialysis center or at a health clinic, attending medical staff might administer epinephrine prior to arrival of the organized EMS response—this epinephrine would not be listed as EMS pre-hospital data; epinephrine later administered by EMS would be listed).

For each drug given (note required or optional data elements) provide the total dose administered and all routes used.

Definitions for drug therapies:

Total Dose is the sum of all doses of a drug administered during the course of EMS pre-hospital care, regardless or the route of administration. Doses are expressed in milligrams (mg) for epinephrine, amiodarone, atropine, lidocaine, naloxone, calcium, magnesium, and procainamide; milliequivalents (mEq) for sodium bicarbonate; grams (g) for dextrose; and international units (IU) for vasopressin.

Route of administration: Check all that apply for a given drug-- intravenous (IV); endotracheal tube (ETT); intra-osseous (IO), or drip (as for a titration)

Reporting requirements for Drug therapies are divided into four categories:

I. *Drug/dose/route required*: Indicate if Epinephrine was administered at any time during course of pre-hospital care. If so, provide the total dose administered (mg) and the route(s) it was given.

II. *Drug required and dose/route optional:* Amiodarone, Atropine, Sodium bicarbonate, Lidocaine.

III. *Drug/dose/route optional:* Calcium, Dextrose, Magnesium, Naloxone, Procainamide, Vasopressin.

IV. *Drug class optional:* Inotropes (includes dopamine, dobutamine, isoproterenol), paralytics (includes succinylcholine, pancuronium, vecuronium).

Item 9 – *Past History: (from PCR – do not use ED/Hospital records)*:

This section is intended to capture the past medical history noted in the non-ROC or ROC EMS (includes fire) prehospital record. This documentation may be in the form of checked boxes in a dedicated history portion of the patient record, or it may be found in the narrative. The 'Past History' question is intended to capture prior medical history that may or may not have been related to this cardiac arrest. No causation or threshold of evidence is required to here indicate a 'past history'. If no past history is noted on the PCR or cardiac arrest provider form, mark 'None noted' and skip to Item 10.

– MI—myocardial infarction

- CAD—coronary artery disease; this includes history of angina/chest pain.
- HTN—hypertension
- CHF—congestive heart failure
- Diabetes
- Cancer
- Seizure—either petit or grand mal
- Syncope
- Afib/flutter
- Cardiac medications (e.g., digoxin, beta-blockers, antiarrhythmics, nitrates, etc.)
- Recreational drugs
- Alcohol abuse
- CABG—coronary artery bypass graph
- ICD—implantable cardioverter-defibrillator
- Pacemaker
- Heart surgery (other than CABG which is noted above, includes valve surgery, PTCA/percutaneous transluminal angioplasty, stents).
- Other surgery—need not be cardiac in nature
- Other: (fill in)—Indicate any other significant medical history noted (such as kidney failure/chronic dialysis, asthma, emphysema,

Item 10 – *Etiology of arrest: Field and site classifications; obvious cause*

a. Field Classification *(from field data) (required)*
Where EMS responders are provided a dedicated location on the PCR to record their impression of the etiology of arrest, indicate their recording as either 'no obvious cause' (includes presumed cardiac) or 'obvious cause.' If a cause of arrest is recorded by EMS in the PCR's dedicated location (not in the narrative) as presumed to be other than cardiac etiology, go to column A ('Field classification') and select the one recorded 'obvious cause' of arrest. It is intended that the EMS designation for etiology of arrest be taken at face value and is not to be translated by the obvious cause definitions provided for later site classification of etiology of arrest. If the EMS recorded cause of arrest is not listed in Column A, mark 'other obvious cause' and specify (60 characters). It is not intended that past medical history, or contributing factors or circumstances be recorded here.

Where the PCR does not provide a dedicated location to record the field EMS impression of the etiology of arrest, mark 'No field classification, do not complete column A ('Field classification') and move to question 10b, 'Etiology of arrest: Site classification.'

b. Site Classification *(from field data) (required)*

Indicate the apparent cause of arrest, either 'obvious' or 'no obvious', based only on information documented in the pre-hospital care record and any EMS supplemental CA forms. It is anticipated that the majority of arrests will fall into the 'no obvious cause' category and will include those cases that are presumed cardiac or do not clearly fit in any of the 'obvious cause' categories listed in column B (site classification) and defined below. The selected ‘site classification’ for etiology of arrest may differ from that documented for the 'field classification.' The ‘field classification’ will have been documented based upon local provider protocol, definitions, and/or habit. The ‘site classification’ will be based upon the site Coordinator’s interpretation of the complete pre-hospital record and conformance to the below definitions. Mark 'obvious cause' only when the cause of out of hospital cardiac arrest clearly meets the defined criteria. Arrest patients with an 'obvious cause' become a unique subgroup that may have different treatments and outcomes.

Definitions for ‘site classification’ of obvious cause of arrest:

Anaphylaxis: Cases of sudden collapse with other clear signs of anaphylaxis including urticaria, facial and tongue swelling, respiratory distress, and clear exposure to an allergen (e.g., bee sting or ingested food with known allergy) that triggered the event. In addition to these physical and historical findings, an Epipen (intramuscular injectable source of epinephrine) may have been used. However, a used Epipen without physical signs of anaphylaxis (or witnessed by bystanders) is not diagnostic for this etiology option.

Chemical poisoning (intentional or unintentional, includes carbon monoxide, toxic gases): This category does NOT include prescribed medications, recreational drugs, or ethanol (see “Drug Poisoning”). However, isopropyl alcohol, ethylene glycol and methanol are included as “chemical poisoning”. This category will include all cases where there is high likelihood that the cardiac arrest would not have occurred in the absence of a poison. Chemical poisons are considered substances that would not normally be ingested, inhaled or consumed and may be environmental or industrial, including such items as insecticides, herbicides, industrial gases, cleaning solutions, carbon monoxide sources (e.g., automobile exhaust or space heaters), or similar compounds. The cardiac arrest timing and clinical scenario should be consistent with the presumed chemical poisoning. This etiology includes both intentional chemical poisoning (i.e., cases where ingestion, inhalation or contact with a chemical poison for the purposes of suicide is clear - suicide note, witnesses confirm discussion of suicidal intent or witnessed clear impulsive intentional ingestion temporarily related to the collapse), and unintentional chemical poisoning (cases where witnessed chemical exposure precedes the collapse by 3-5 minutes). This category would include cases where witnesses confirm contact with a chemical poison just prior to collapse.

Drowning: victim is found by provider or bystanders submersed in water without an alternative causation.

Examples of cases that fit this definition include; young and presumably healthy person found floating in the water with no evidence of overdose or drug ingestion; in the absence of other contributing factors, any patient who was witnessed to be choking or coughing before going under water.

Examples of cases that do NOT fit this definition include; patients who suffer trauma immediately prior to falling in the water (the case should be entered in the trauma, not the cardiac, patient cohort; for patients presumed to be older than 39 years of age one cannot be certain whether the submersion or some medical event was the cause of death so 'no obvious cause' would generally be selected; person who was inebriated or toxic on a drug who then drowned (the case should be classified as 'no obvious cause').

References: *S*alomez F, Vincent JL. Drowning: a review of epidemiology, pathophysiology, treatment and prevention. *Resuscitation.* 2004 Dec;63(3):261-8.

Idris AH, Berg J, Bierens L, et al. Recommended guidelines for uniform reporting of data from drowning: the 'Utstein style.' *Circulation.* 2003 Sept; 108:2565-2574.

Drug poisoning (intentional or unintentional, includes ethanol): This category includes prescribed medications, recreational drugs, and ethanol. Intentional drug overdose may include cases where ingestion of a drug (i.e., prescribed or over the counter medication, recreational drugs including alcohol) for the purposes of suicide is clear (suicide note, witnesses confirm discussion of suicidal intent or witnessed clear impulsive intentional ingestion temporarily related to the collapse). Unintentional drug overdose may include cases where witnessed inhaled or intravenous or oral recreational drug use immediately precedes the collapse. The Drug Poisoning category includes cases where witnesses confirm the situation, for example an injection of heroin just prior to collapse or where the evidence strongly suggests immediate use prior to arrest (e.g., tourniquet on arm and empty syringe at side).

Examples of cases that fit this definition; a victim collapses and there are empty pill bottles or ethanol containers at the scene without clear evidence of suicidal intent.

Examples of cases that DO NOT fit this definition; patient with a history of recreational drug use within 24 hours of the event (e.g., adolescent found collapsed at a party or the known alcoholic found dead the morning after heavily imbibing); classify these types of cases as 'no obvious cause' (presumed cardiac).

Electrocution (non-lightning): This category includes all cases where the patient has an electrical cutaneous burn in the setting of contact with a high voltage source. Electrocution would be also the obvious choice if the victim was found attached or nearly so, to a high-tension source of current. This category also includes all cases where the patient has been removed from the source of high tension current but the event was witnessed.

Excessive cold: Low ambient temperature (below 32F or 0C) where an obviously healthy individual is inappropriately clothed for the ambient temperature.

Excessive heat: Situations in which an obviously healthy person experiences a cardiac arrest and the most significant contributing factor is increased ambient temperature i.e., exercise on a hot day or confined in a locked car or lost hiking in the desert.

Examples of cases that fit this definition; the inebriated patient found outside for a prolonged period of time exposed to extreme heat or cold.

Foreign body obstruction: Cases of sudden airway obstruction leading to cardiac arrest due to ingestion of a foreign body identified by history or by direct visualization within the airway. Some of these cases may be preceded by choking.

Examples of cases that fit this definition include; small child (age 4 or less) choking after a balloon popped in front of their face or after eating a hot dog and succumbs to cardiac arrest; or man observed to be eating and suddenly begins to choke and hold his throat prior to collapsing; or on intubation a foreign body is visualized +/- removed.

Examples of cases that DO NOT fit this definition include: paramedics report inability to ventilate the patient and presume airway obstruction without finding the source of the obstruction;

Hanging: Cases of sudden airway obstruction leading to cardiac arrest secondary to hanging. Requires either the presence of ligature present around the neck, found hanging, or marks on the neck compatible with a previous ligature in the setting that suggests this was the obvious cause of death.

Examples of cases that fit this definition; case in which the victim is found with a rope around the neck after fire or police have cut them down from a gallows equivalent

Examples of cases that would NOT fit this definition: victim has a ligature around the neck without any evidence at the scene of any attempt to hang himself; a victim who has been strangled by an assailant's hands during an altercation (this case would be classified as 'obvious cause' Strangulation).

Lightning: cases of cardiac arrest where the event was directly attributed to lightning strike or blast effect from lightning temporally related to the event i.e., immediately following the strike, burn marks on the ground or nearby objects, melting of metal objects, or documented classic signs of electrocution by lightning.

Examples of cases that fit this definition: witnessed lightning strike on golf course where members of a foursome documented direct hit to one of their group and called 911; or unwitnessed cases where there are visible signs of lightning strike including cutaneous burns described as Lichtenburg figures, flash burns, punctuate burns, contact burns, or linear burns in the skin folds.

Example of a case that does NOT fit this definition: man found outside in the rain without witnesses to verify direct strike or blast effect or any signs or symptoms of lightning related electrocution.

Mechanical suffocation: Mechanical suffocation causing arrest is distinct from hanging, strangulation, choking, respiratory, anaphylaxis, or SIDS etiologies. This category will

rarely be coded. It is included for a unique and very specific group of patients who arrest because of suffocation due to an external physical barrier.

Examples of cases that fit this definition: someone with the plastic bag over the head; a pillow or another object was used to suffocate the patient; or a child or adult with tracheostomy site who develops an obstruction.

Non-traumatic exsanguination: This category includes the rare situation where it is highly likely that the patient “bled to death” in a short period of time and there is strong evidence that acute and catastrophic loss of blood was the direct cause of the arrest.

Examples of cases that fit this definition: hemodialysis line disconnected with obvious large loss of blood; vomiting of blood with EMS witnessed and documented large loss of blood; blood in stool (lower GI bleed) with EMS witnessed and documented large loss of blood.

Examples of cases that DO NOT fit this definition: vomiting blood with unknown amount or small amount on face or clothes; possible or suspected ruptured aortic aneurysm (this can never be proven without autopsy or diagnostic imaging); epistaxis; hemoptysis

Radiation: This etiology will be rarely coded. Cardiac arrest due to radiation requires an acute and massive radiation exposure that temporally (typically within seconds to minutes) produces a cardiac arrest.

Examples of cases that fit this definition: industrial exposure or terrorist event with presumed high radiation levels.

Respiratory: Adult cardiac arrest due to primary respiratory cause requires that the patient have 1) an established medical history of asthma and 2) a witnessed reported clinical course prior to arrest implicating asthma. Although there are no absolutes, death due to asthma (as a respiratory 'obvious cause') would generally be expected to evolve over hours or even days with progressive shortness of breath as the principal symptom rules. Pediatric (patients < 16 years) cardiac arrest due to primary respiratory cause requires that the patient have 1) an established history of an underlying disease that places the patient at higher risk for respiratory disease (see below examples) and 2) a witnessed reported clinical course of an acute respiratory problem prior to the arrest.

Examples of adult cases that fit this definition: a) 54 yo male with history of asthma, hospitalized previously, who experienced progressive shortness of breath over the past day following URI for past week. He has been using inhalers around the clock since yesterday and took an extra dose of prednisone this morning. His spouse called 9-1-1 when his respiratory symptoms made him unable to talk or answer questions. No chest pain or prior heart history. EMS arrives to find the patient unresponsive without pulse or respirations. Rationale: Several circumstances suggest a primary respiratory arrest: 1) the history suggests that he has fairly significant asthma, the clinical circumstances are highly consistent with an asthma exacerbation with similar past events, and there is information indicating that he did

not have clinical heart disease. Hence the level of information sufficiently implicates a respiratory mechanism as the primary cause; b) 16 year old woman with a history of asthma witnessed by bystander or responder to have inspiratory and expiratory wheezing prior to in cardiac arrest.

Examples of pediatric cases (patients < 16 years of age) that fit this definition: a) Child receiving chronic oxygen therapy or respiratory assistance, such as a premature infant at home on oxygen with an increase in oxygen requirement over the previous hours or days; b) Child with acute febrile respiratory illness in the days or hours prior to arrest, such as an otherwise healthy child with a presumed respiratory infections disease preceding the event; c) child with history of asthma and progressive acute respiratory distress (“asthma attack”) whereby witnessed respiratory distress progresses over hours until he/she cannot talk, then turns blue, and collapses.

Examples of cases that do NOT fit this definition include: a) 65 yo male with history of COPD (home oxygen dependent) and heart disease (prior bypass) was last seen at breakfast by his wife. He had no complaints at that time. When she returned home later that morning she found him unresponsive on the couch with his home nebulizer running. She called 9-1-1 and the EMS arrived to find him without pulse or respiration. Rationale: Although the patient had fairly severe chronic lung disease, he did not have clear prodromal symptoms or signs indicating progressive respiratory decline. The scene was suggestive that he experienced some symptoms prior to death since the nebulizer machine was running but this could have been due to a variety of cardiopulmonary symptoms. This patient should be classified as no obvious cause (presumed cardiac); b) 75 yo female nursing home resident develops cough for at least 1 day and then increasing shortness of breath this morning. The nursing home staff had provided oxygen and an albuterol but without relief. At the time of the 9-1-1 call she was awake but unable to speak due to extreme respiratory distress. When EMS arrives she is unresponsive without pulse or blood pressure and nursing staff have initiated CPR. Her history is notable for history of asthma for which she uses 2 different inhalers. Rationale: The patient did have some history of lung disease and some symptoms of progressive dyspnea. However the severity of lung disease is not clear and the symptoms could be consistent with other etiologies of arrest. For example, this patient could be manifesting congestive heart failure or pulmonary embolism. Although a judgment, the level of information leaves some question as to whether respiratory disease was the primary etiology. The best etiology classification for this patient would be 'no obvious cause' (presumed cardiac).

Examples of pediatric cases (patients <16 years of age) that do NOT fit this definition: a) Developmentally disabled child without a supported airway found pulseless and apneic, such as 6 year old child with cerebral palsy and limited ambulation found pulseless and apneic in bed (this case would be coded as 'no obvious cause'); b)child with a supported airway (i.e., Tracheostomy) and found pulseless and apneic (this case would be coded as 'obvious cause' mechanical suffocation); c) prior history of congenital heart disease and no other 'obvious cause' identified—congenital heart disease is not an etiologic classification, but should be included as a 'contributing factor.' This case would be coded as 'no obvious cause' (presumed cardiac).

SIDS (sudden infant death syndrome, less than 12 months of age): Cases of death where an infant, ages 1 month to 12 months is found in their crib/bed and death was unwitnessed. All three criteria—age, crib/bed location, and unwitnessed death—must be present to be categorized as SIDS. Background of sudden infant death syndrome: The American Academy of Pediatrics—SIDS, also called crib or cot death, is the sudden death of an infant under 1 year of age that remains unexplained after thorough case investigation, including performance of a complete autopsy, examination of the death scene, and a review of the clinical history. [NOTE: Site classification of etiology of arrest for classification of SIDS as an obvious cause is to be determined solely from the prehospital patient care record. SIDS is the most common cause of death between 1 and 6 months of age. The incidence of SIDS peaks between 2 and 4 months of age. Approximately 90% of SIDS deaths occur before the age of 6 months.]

SIDS is suspected when a previously healthy infant, usually younger than 6 months, is found dead in bed, prompting an urgent call for emergency assistance. Often, the baby is fed normally just before being placed in bed to sleep, no outcry is heard, and the baby is found in the position in which he or she had been placed at bedtime or naptime. In some cases, cardiorespiratory resuscitation initiated at the scene by emergency personnel is continued without apparent beneficial effect en route to the hospital, where the baby is finally declared dead. Evidence of terminal motor activity, such as clenched fists, may be seen. There may be serosanguineous, watery, frothy, or mucoid discharge coming from the nose or mouth. Skin mottling and postmortem lividity in dependent portions of the infant's body are commonly found. Review of the medical history, scene investigation, radiographs, and autopsy are unrevealing.

The Canadian Pediatric Society refers to SIDS as the sudden and unexpected death of an apparently healthy infant usually less than one year of age, which remains unexplained even after a full investigation. On average, 3 infants a week are reported to die of SIDS in Canada. Although in Canada there has been a decrease in the number of infant deaths reported as SIDS, it still remains a significant public health concern. Aboriginal infants have a risk of SIDS that is higher than the risk to non-Aboriginal infants.

Example of pediatric case (less than 12 months of age) that are included: Although there is some controversy and a few documented cases of long QT causing what appears to be SIDS, the evidence supports that most are related to respiratory issues. A case can be made that this is mechanical suffocation, but that can not reliably be done in the absence of a thorough review of the history and even location of the death. We need to be consistent with this as we will have many cases of this and CPR will be delivered.

Smoke inhalation: Cases of collapse in a fire setting with significant smoke exposure. This is defined as the patient who was exposed to fire in a closed space (Ryan et al N Engl J Med, 1998).

Strangulation: The impression of EMS responders is that the patient’s most significant condition that led to cardiopulmonary arrest is strangulation. Strangulation is a form of asphyxia (though not categorized as 'obvious cause' asphyxia) characterized by closure of the blood vessels or air passages of the neck as a result of external pressure on the

neck (McClane et al J Emerg Med 2001) The paramedic usually describes crush marks around the neck.

Examples of cases that fit this definition: victim becomes non-responsive during a witnessed altercation where the assailants hands were around the neck.

Examples of cases that would NOT fit this definition: a) where the individual was involved in an altercation and becomes unresponsive without witnesses documenting strangulation just prior to collapse; b) victim has bruising around the neck without documented history of strangulation related to the collapse;

Terminal illness (includes end-stage diseases such as cancer): Death due to “terminal” condition is one in which death is expected and for which there is evidence of poor function or functional decline prior to death. Both conditions need to be met. Terminal condition will most often be considered in patients with advanced cancer. An individual whose function is declining and for whom death is expected should be classified as terminal illness (see below examples).

Examples of cases that fit this definition: a) 45 year old woman is found unresponsive and not breathing. She has advanced pancreatic cancer and is enrolled in an experimental treatment protocol. She has been sleeping mostly during the last week because of weakness and malaise and has declined to return to the hospital. She was quite difficult to arouse earlier in the day; b) 88 yo male with liver cancer who has been mostly bedridden the past month. He has been progressively more confused over the last two days to the point where his caretaker could not wake him.

Examples of cases that do NOT fit this definition: a) Patient with advanced cancer who is reasonably functional – carrying out ADLs, living independently, and collapses would be classified as “no obvious cause” (presumed cardiac); b) 68 yo male with metastatic colon cancer (“his cancer had spread to his lung and liver” per bystander son) who collapsed while walking in the park. “He had gotten a bit weaker over the past year but seemed fine today”. The son is not aware of other conditions or medications. Classify this case as 'no obvious cause' (presumed cardiac); c) 71 yo female found unresponsive by her husband. She has lung cancer that has spread to her bones and a past history of a “heart attack” 2 years ago. Her husband reports that “she has been receiving radiation treatment for the cancer and the doctors weren’t sure how long she had.” This morning she had no complaints and they were leaving the house to go shopping when she collapsed. Classify this case as 'no obvious cause' (presumed cardiac).

Trauma (includes blunt, penetrating or burns): Patients who have experienced a cardiac arrest directly caused by blunt, penetrating or burn injury should be enrolled in the Trauma Epistry cohort, not the cardiac arrest cohort.

Examples of cases that do NOT fit this definition: a patient scenario where it is clear from the bystander history that the patient collapsed due to some medical condition prior to experiencing the trauma (such as an elderly male that was clutching his chest, was short of breath, and fell). This patient would be entered in the cardiac

arrest cohort and if the etiology of the arrest is unclear, would be marked 'no obvious cause' (presumed cardiac).

Venomous stings and venomous bites: This category will include all cases where there is visual evidence or witnessed attack of a venomous organism (e.g., animal, reptile, insect) that immediately preceded and presumably precipitated the cardiac arrest. Evidence for the sting must include visible localized skin findings (e.g., local erythema or edema at site) and/or witnessed report by bystanders of history that supports this etiology. If a venomous sting precipitated anaphylaxis, the obvious cause “Anaphylaxis” should be marked.

c. Were there contributing factors directly related to this cardiac arrest? *(from field data; site abstracts information) (required)*

This section is intended to capture the variety of factors that were observed by, or reported to, the EMS responders during the course of prehospital care. The site coordinator will mark all applicable conditions that are documented in the PCR (whether narrative or check item format) or EMS supplemental CA forms that may have been related to the cardiac arrest. It is not necessary for a 'contributing factor' to meet the same burden of proof as does 'obvious cause' for Etiology of Arrest: Site Classification. Check all contributing factors that appear to be directly related to this cardiac arrest. If a factor has been marked in column B as a Site Classification ‘obvious cause’, do not mark it again in column C as a contributing factor.

Definitions for contributing factors:

Anaphylaxis: Signs of anaphylaxis including urticaria, facial and tongue swelling, respiratory distress, and clear exposure to an allergen (e.g. bee sting or ingested food with known allergy) that triggered the event. An Epipen (intramuscular injectable source of epinephrine) may have been used.

Chemical poisoning (intentional or unintentional, includes carbon monoxide, toxic gases): This category does NOT include prescribed medications, recreational drugs, or ethanol (see “Drug Poisoning”). However, isopropyl alcohol, ethylene glycol and methanol are included as “chemical poisoning”. Chemical poisons are considered substances that would not normally be ingested, inhaled or consumed and may be environmental or industrial, including such items as insecticides, herbicides, industrial gases, cleaning solutions, carbon monoxide sources (e.g. automobile exhaust or space heaters), or similar compounds.

Dialysis: The patient was undergoing or very recently underwent dialysis treatment (peritoneal or hemodialysis). This does not include exsanguination secondary to disconnection of dialysis shunts—see 'non-traumatic exsanguination.’

Drowning: victim is found by provider or bystanders submersed in water or witnessed to be choking or coughing before going under water.

Drug poisoning (intentional or unintentional, includes ethanol): Includes prescribed or over the counter medications, recreational drugs, and ethanol (alcohol).

Electrocution (non-lightning): This category includes all cases where the patient has an electrical cutaneous burn in the setting of contact with a high voltage source. Electrocution would be also the obvious choice if the victim was found attached or nearly so, to a high-tension source of current. This category also includes all cases where the patient has been removed from the source of high tension current but the event was witnessed.

Excessive cold: Low ambient temperature (below 32F or 0C) where an obviously healthy individual is inappropriately clothed for the ambient temperature.

Excessive heat: High ambient temperature i.e., exercise on a hot day or confined in a locked car or lost hiking in the desert.

*Foreign body obstruction: S*udden airway obstruction due to ingestion of a foreign body identified by history or by direct visualization within the airway. Some of these cases may be preceded by choking.

Hanging: Cases of sudden airway obstruction secondary to hanging. Patient may have a ligature present around the neck, be found hanging, or have marks on the neck compatible with a previous ligature. It would be unusual for hanging to be a contributing factor rather than an 'obvious cause' of arrest.

Lightning: cases of cardiac arrest where a lightning strike or blast effect from lightning temporally related to the event i.e., immediately following the strike, burn marks on the ground or nearby objects, melting of metal objects, or documented classic signs of electrocution by lightning.

Mechanical suffocation: Mechanical suffocation is distinct from hanging, strangulation, choking, respiratory, anaphylaxis, or SIDS etiologies. It includes suffocation due to an external physical barrier. May include someone with a plastic bag over the head; pillow or another object used to suffocate the patient; or a child or adult with a tracheostomy site who develops an obstruction.

Non-traumatic exsanguination: There is evidence that acute and catastrophic loss of blood occurred in a short period of time. May include disconnection of a hemodialysis line; vomiting of blood; blood in stool.

Radiation: Radiation requires an acute and massive radiation exposure that temporally (typically within seconds to minutes) produces a cardiac arrest. May include industrial exposure or terrorist event with presumed high radiation levels.

Respiratory: Adult cardiac arrest due to a medical history of COPD or asthma or a witnessed reported clinical course prior to arrest implicating respiratory difficulties. May evolve over hours or even days with progressive shortness of breath as the principal symptom rules. May have been using inhalers with increased frequency or increased dose of prednisone. May have been at home with oxygen with an increase in oxygen requirement over the hours prior to arrest. Pediatric (patients < 16 years) cardiac arrest due to 1) an established history of an underlying disease that places the patient at higher risk for respiratory disease (see below examples) and 2) a witnessed reported clinical course of an acute respiratory problem prior to the arrest. This does not include a child

with a supported airway (i.e., Tracheostomy) found pulseless and apneic--this would be 'mechanical suffocation.'

SIDS (sudden infant death syndrome, less than 12 months of age): Cases of death where an infant, ages 1 month to 12 months is found in their crib/bed and death was unwitnessed. All three criteria—age, crib/bed location, and unwitnessed death—must be present to be categorized as SIDS. See Etiology of arrest 'Obvious cause' definitions for background on SIDS.

Smoke inhalation: Cases of collapse in a fire setting with significant smoke exposure. This is defined as the patient who was exposed to fire in a closed space (Ryan et al N Engl J Med, 1998).

Strangulation: Strangulation is a form of asphyxia (though not categorized as 'contributing factor' asphyxia) characterized by closure of the blood vessels or air passages of the neck as a result of external pressure on the neck (McClane et al J Emerg Med 2001) The paramedic usually describes crush marks or bruising around the neck.

Terminal illness (includes end-stage diseases such as cancer): "Terminal" illness is one in which death is expected and for which there is evidence of poor function or functional decline prior to death.

Trauma (includes blunt, penetrating or burns): Patients who have experienced a cardiac arrest directly caused by blunt, penetrating or burn injury should not be enrolled in ROC PRIMED unless the ITD was opened.

Venomous stings and venomous bites: This category will include cases where there is evidence or witnessed attack of a venomous organism (e.g., animal, reptile, insect) that immediately preceded and presumably precipitated the cardiac arrest. Evidence may include visible localized skin findings (e.g., local erythema or edema at site) and/or witnessed report by bystanders of history that supports this etiology. If a venomous sting precipitated anaphylaxis, the contributing factor "Anaphylaxis" should be marked.

Item 11 – *Disposition*

Indicate the patient's status at the conclusion of the pre-hospital course of care, whether died at scene or en route, or was transported by EMS to an ED/hospital with ROSC or ongoing resuscitation. If the patient died at the scene or en route, indicate if the treatment was halted because it was considered futile, DNR orders, either written or verbal, were presented, or the patient was obviously dead (such as when a first responder initiates CPR, and ALS arrives at the scene and halts the resuscitation due to the patient being obviously dead). If the patient was transported, indicate the transportation method, either land or air. All cardiac arrests in the PRIMED study are expected to be transported by land rather than by air. Indicate the patient's status at arrival of the first ED, whether ROSC was present, or CPR was being performed at ED arrival. If there was ongoing resuscitation on ED arrival and the patient was declared dead by the ED staff, complete the ED Admit form, the same as if the patient had ROSC at ED arrival. If the patient was transported by EMS after the resuscitation was stopped in the field (e.g., in public location and the body is to be transported) mark 'Disposition' as 'died at scene or enroute.'

Item 12 – ***Did the implementation of the ITD or Analyze Late vs. Early protocol result in a safety issue (e.g., delay in treatment) or other potential adverse situation?***

Indicate 'yes' or 'no' whether the ITD or the Analyze Late vs. Early protocol resulted in a patient safety issue or any other potential safety issue or adverse situation occurred. If 'yes', indicate all conditions that occurred. Complete the Alert CTC form.

- Delay in treatment—This should be marked if there was a delay in treatment of the patient that would not have otherwise occurred during the course of EMS treatment, such as due to an attempt to decide whether the patient was in the Analyze Late vs. Early protocol, due to attempts to open the ITD or place the ITD on the patient. In addition, patients who have EMS witnessed arrests should be defibrillated immediately.

- Suspected mechanical failure of ITD—This should be checked if the ITD appeared to have failed, such as when the airway equipment was attached and the EMS provider was unable to ventilate the patient through the ITD, or the ITD was visibly cracked or broken. If the ITD timing lights failed to flash, this is not considered a mechanical failure of the ITD, and this bubble should not be checked, but Item 6d should be checked.

- Airway bleeding—Mark this if prehospital records (or EMS intake interview) indicates, that upon arrival or during the EMS course of care, bleeding was observed in the oro- or naso-pharynx region, or the advanced airway. It is not the intention of this potential adverse situation to capture conditions where *only* pink frothy sputum or blood-tinged fluid was observed. If fire/EMS charting indicates airway bleeding, but does not provide enough detail for you to discern only pink frothy sputum or blood-tinged fluids from other presentations of airway bleeding, do mark this item and trigger an Alert CTC form. Then, after discussions with the EMS, complete the details of the Alert CTC form. Where discussions with EMS clarify that *only* pink-tinged or blood-tinged fluid was present, complete the triggered Alert CTC form and indicate this (the CTC will adjudicate such reports as non-reportable events). Document your discussions with EMS providers (that further characterize written pre-hospital records) in the patient's ROC PRIMED record.

- ITD filled with fluid—If the ITD fills with fluid, even once, note this here. If EMS providers were able to clear and reuse the ITD, note this on Alert CTC form.

- Failure to immediately remove the ITD following ROSC—Indicate whether the EMS providers failed to remove the ITD once ROSC was achieved. This information should be obtained either when the EMS provider contacts the site Coordinator post-arrest for notification of the arrest or it is noted on the cardiac arrest information sheet.

- Other—If a potential safety or adverse condition occurred that is not above described, mark 'other' and briefly specify the situation that was of concern. EMS

providers should be encouraged to report all possible adverse situations or unusual situations to the Coordinator so that they can be reviewed accordingly.

Person responsible for data on this form

Name of the individual that logged into the electronic data transmission system for clinical study forms. This individual will have registered as a member with the CTC for the purpose of participating as a coordinator or investigator in a ROC clinical trial and has designated a user name and password as their "Electronic Signature." The individual has agreed to consider their electronic signature as equivalent to their handwritten signature, to maintain the confidentiality of their user name and password, and to not let others use it. Refer to the "Electronic Signature Agreement" (accessed after logging on to the ROC website) posted at https://roc.uwctc.org/tiki/roc-data-entry.

After verifying the entered data and electronic signature are correct, print the web-forms for your files, or convert the web-forms to PDF format and store electronically. Edits made later to the original web-entered forms are associated with the electronic signature of the individual making the changes and are documented in the file's edit history.

Complete this form:
-for any episode where patient met enrollment or safety criteria or ITD opened
Main data resource: PCR
Other data resources: Dispatch

Pre-hospital Data

Version 1.04.00
Date: 10/07/2008

Episode Information:

Date *(mm/dd/yyyy)* ___/___/___

Time call received at dispatch *(hh:mm:ss; 24hr clock)* ___:___:___

○ From PCR/other ○ From dispatch
○ Unable to obtain *(Non-ROC agency first arrival & no agreement in place to get data, patient is excluded from Trial)*

ROC PRIMED ID: ___-___-___

Incident Number *(optional)* _____

Site Linking ID *(optional)* _____

1. Location of Episode:

a. Location *(check one only)*

○ Census tract:
US: State ___ County ___ Tract _____ Link **http://www.ffiec.gov/Geocode/default.aspx**
Toronto: CTName/CTUID _____ *(nnnn.nn/nnnnnnn.nn)*

○ Lat/long:
Latitude _____ → ○ Decimal degrees ○ DMS ○ DM
Longitude _____ → ○ Decimal degrees ○ DMS ○ DM
Datum → ○ NAD83 ○ NAD27 ○ WGS84

○ UTM:
Easting _____ → ○ Meters ○ Kilometers
Northing _____ → ○ Meters ○ Kilometers
Zone ___

○ Unknown/not noted

b. Public or non public?

○ Public *(check one only)*
- ○ Street/highway
- ○ Public building *(schools, government office)*
- ○ Place of recreation *(park, stadium, lake)*
- ○ Industrial place *(factory, warehouse, construction site)*
- ○ Other public property *(sidewalk, store, church, restaurant, bar, hotel)*

○ Non public *(check one only)*
- ○ Home residence (inside or immediately surrounding)
- ○ Farm/ranch
- ○ Healthcare facility
- ○ Residential institution (assisted living, nursing home)
- ○ Other private

2. Demographics:

a. Age: ___ *(years)*

○ Calculated from DOB
○ Estimated by EMS

If no age available use categories below:
- ○ Child *(1 - 11 years)*
- ○ Adolescent *(12 - 19 years)*
- ○ Adult *(20 - 39 years)*
- ○ Middle age *(40 - 60 years)*
- ○ Older *(61 - 75 years)*
- ○ Elderly *(> 75 years)*

b. Gender:

○ Male ○ Female

c. Race/Ethnicity: *(check all that apply)*

☐ Hispanic or Latino
☐ White
☐ African-American/Black
☐ American-Indian/Alaska Native
☐ Asian
☐ Native Hawaiian/Pacific Islander
☐ Other
☐ Unknown/not noted

continue to next page

Episode Information:

Date *(mm/dd/yyyy)* ___/___/___
Time call received at dispatch *(hh:mm:ss; 24hr clock)* ___:___:___
○ From PCR/other ○ From dispatch
○ Unable to obtain *(Non-ROC agency first arrival & no agreement in place to get data, patient is excluded from Trial)*
ROC PRIMED ID: ___-___-___
Incident Number *(optional)* _____
Site Linking ID *(optional)* _____

3. Cardiac arrest occurred:

- ○ After EMS (includes fire) arrival/witnessed by EMS → skip **Item 4**
- ○ Before EMS arrival
  - ○ Witnessed (seen or heard) by someone (other than EMS personnel)
  - ○ Not witnessed (seen or heard)
  - ○ Unknown/not noted
- ○ Patient did not have a cardiac arrest

4. Was resuscitation attempted by bystanders?

- ○ Unknown/not noted
- ○ No
- ○ Yes→ Was CPR attempted? ○ Yes ○ No
  → Was AED/defib applied?
  - ○ No
  - ○ Yes→ Were shocks delivered? ○ No ○ Unknown/not noted ○ Yes → # of shocks: ___ Or ☐ Unknown
    → AED/defib applied by: ○ Lay person ○ Police ○ Healthcare ○ Other ○ Unknown/not noted

5. EMS Chest compressions:

- ☐ Manual
- ☐ Mechanical compression/ventilation
  → Was ITD used during mechanical compression/ventilation? ○ No ○ Yes → Complete **Alert CTC** form
- ☐ No EMS chest compressions

6. ITD information:

☐ No ITD used → skip to **Item 7**

a. Emesis noted-
Prior to ITD placement? ○ Yes ○ No
During ITD use? ○ Yes ○ No

b. ITD attached to: *(check all)*
- ☐ Mask
- ☐ ETT
- ☐ Other advanced airway: ○ LMA ○ Combitube ○ King LT ○ PLA ○ Other: _____ *(20)*

c. Filter used?
○ No ○ Yes → Types: 1) _____ 2) _____

d. Timing light failed?
○ No ○ Yes ○ Light not used

e. Mask & ITD: Any indication that there were problems maintaining a tight seal *(e.g. facial hair, height of equipment, etc.)***?**
- ○ No
- ○ Yes → Why: _____ *(30)*
- ○ Mask not used

f. Was there any indication that a tight seal was not maintained during COMPRESSIONS and ventilations?
- ○ Yes
- ○ No

continue to next page

Episode Information:

Date *(mm/dd/yyyy)* ___/___/___

Time call received at dispatch *(hh:mm:ss; 24hr clock)* ___:___:___

○ From PCR/other ○ From dispatch
○ Unable to obtain *(Non-ROC agency first arrival & no agreement in place to get data, patient is excluded from Trial)*

ROC PRIMED ID: ___-___-___

Incident Number *(optional)* _____

Site Linking ID *(optional)* _____

7. Pre-hospital intervention:

☐ No EMS Pre-hospital interventions from the list below were recorded

NA/NR Done

○ ○ Airway, bag-mask
○ ○ Continuation of non-EMS advanced airway
○ ○ EMS Airway, advanced - *Check all attempted/used:*
- ☐ Oral ET
  - # of attempts ___ OR ☐ Not noted
  - Was it successful? ○ No ○ Yes
- ☐ Combitube, LMA, etc.
  - # of attempts ___ OR ☐ Not noted
  - Was it successful? ○ No ○ Yes
- ☐ Nasal ET
  - # of attempts ___ OR ☐ Not noted
  - Was it successful? ○ No ○ Yes
- ☐ RSI
- ☐ Cricothyrotomy
- ☐ CPAP
- ☐ Ventilator

○ ○ CPR
○ ○ Hypothermia therapy
○ ○ IV/IO line -

Check all attempted:
- ☐ IO → Was it successful? ○ Yes ○ No
- ☐ Initiation and/or continuation of an IV → Was it successful? ○ Yes ○ No

Was fluid given?
- ○ No
- ○ Unknown/not noted
- ○ TKO *(To Keep Open)*
- ○ Yes *(Check all given)*

Fluid type	Total volume infused *(optional)*
☐ D5W	___ mls
☐ Normal Saline	___ mls
☐ Lactated Ringers	___ mls
☐ Other	___ mls
☐ Unknown/not noted	

○ ○ Monitor, advanced - *Check all attempted:*
- ☐ 12-lead
- ☐ $EtCO_2$
- ☐ Pacing

continue to next page

Episode Information:

Date *(mm/dd/yyyy)* ___/___/___
Time call received at dispatch *(hh:mm:ss; 24hr clock)* ___:___:___
○ From PCR/other ○ From dispatch
○ Unable to obtain *(Non-ROC agency first arrival & no agreement in place to get data, patient is excluded from Trial)*
ROC PRIMED ID: ___-___-___
Incident Number *(optional)*
Site Linking ID *(optional)*

8. Drug therapies noted:

Drug Given NA/NR Yes Name	Total Dose	Route *(check all attempted)* IV	ETT	IO	Drip
I. REQUIRED:					
○ ○ Epinephrine	___ mg	☐	☐	☐	☐
II. TOTAL DOSE/ROUTE ARE *OPTIONAL* FOR THE FOLLOWING:					
○ ○ Amiodarone	___ mg	☐	☐	☐	☐
○ ○ Atropine	___ mg	☐	☐	☐	☐
○ ○ Bicarb	___ mEq	☐	☐	☐	☐
○ ○ Lidocaine	___ mg	☐	☐	☐	☐
III. DRUG NAME/TOTAL DOSE/ROUTE ARE *OPTIONAL* FOR THE FOLLOWING:					
○ ○ Calcium	___ mg	☐	☐	☐	☐
○ ○ Dextrose	___ g	☐	☐	☐	☐
○ ○ Magnesium	___ mg	☐	☐	☐	☐
○ ○ Naloxone	___ mg	☐	☐	☐	☐
○ ○ Procainamide	___ mg	☐	☐	☐	☐
○ ○ Vasopressin	___ IU	☐	☐	☐	☐
DRUG CLASS GIVEN IS *OPTIONAL* FOR THE FOLLOWING:					
○ ○ Inotropes					
○ ○ Paralytics					

9. Past History: *(from PCR - do not use ED/Hospital records)*

☐ None noted → skip to **Item 10**

☐ MI
☐ CAD
☐ HTN
☐ CHF
☐ Diabetes
☐ Cancer
☐ Seizure
☐ Syncope
☐ Afib/flutter
☐ Cardiac medications
☐ Recreational drugs
☐ Alcohol abuse
☐ CABG
☐ ICD
☐ Pacemaker
☐ Heart surgery
☐ Other surgery
☐ Other: ___ *(30)*

10. Etiology of arrest:

a. Field Classification *(from field data) (required)*

○ No field classification
○ No obvious cause identified (includes NEMSIS 2250 presumed cardiac) } Do Not complete Column A below
○ Obvious cause → *(check one cause in Column A below)*

continue to next page

Episode Information:

Date *(mm/dd/yyyy)* ___/___/___
Time call received at dispatch *(hh:mm:ss; 24hr clock)* ___:___:___
○ From PCR/other ○ From dispatch
○ Unable to obtain *(Non-ROC agency first arrival & no agreement in place to get data, patient is excluded from Trial)*
ROC PRIMED ID: ___-___-___
Incident Number *(optional)*
Site Linking ID *(optional)*

*Continued from page 4 - **Item 10***

b. Site Classification *(from field data) (required)*

○ No obvious cause identified (includes NEMSIS 2250 presumed cardiac) → *Do Not complete Column B below*
○ Obvious cause → *(check one cause in Column B below)*

c. Were there contributing factors directly related to this cardiac arrest?*(from field data; site abstracts information) (required)*

— See Manual of Operations for expanded definitions
○ None noted → *Do Not complete Column C below*
○ Yes → *(check all that apply in Column C below)*

Obvious Cause	A Field Classification	B Site Classification	C Contributing Factors
Anaphylaxis	○	○	☐
Chemical poisoning *(intentional or unintentional, includes carbon monoxide, toxic gases)*	○	○	☐
Dialysis	-	-	☐
Drowning	○	○	☐
Drug poisoning *(intentional or unintentional, includes alcohol)*	○	○	☐
Electrocution *(non-lightning)*	○	○	☐
Excessive cold	○	○	☐
Excessive heat	○	○	☐
Foreign body obstruction	○	○	☐
Hanging	○	○	☐
Lightning	○	○	☐
Mechanical suffocation	○	○	☐
Non-traumatic exsanguination	○	○	☐
Radiation exposure	○	○	☐
Respiratory	○	○	☐
SIDS *(sudden infant death syndrome)*	○	○	☐
Smoke inhalation	○	○	☐
Strangulation	○	○	☐
Terminal illness *(includes end-stage diseases such as cancer)*	○	○	☐
Trauma *(includes blunt, penetrating or burns)*	○	○	☐
Venomous stings	○	○	☐
* Other obvious cause	○	○	☐

* Other cause (A - Field classification): (60)
* Other cause (B - Site classification): (60)
* Other cause (C - Contributing Factors): (60)

continue to next page

Episode Information:

Date *(mm/dd/yyyy)*
/ /

Time call received at dispatch *(hh:mm:ss; 24hr clock)*
: :

○ From PCR/other ○ From dispatch

○ Unable to obtain *(Non-ROC agency first arrival & no agreement in place to get data, patient is excluded from Trial)*

ROC PRIMED ID:
- -

Incident Number *(optional)*

Site Linking ID *(optional)*

11. Disposition:

○ Died at scene or en route
Why was treatment halted? *(check one)*
- ○ Considered futile
- ○ DNR (written or verbal)
- ○ Obviously dead

○ Transported by EMS to ED/hospital with ROSC or ongoing resuscitation → Complete the **ED Admit** form
Transported method:
- ○ By land
- ○ By air

Patient status at ED arrival:
- ○ ROSC present
- ○ Ongoing resuscitation

12. Did the implementation of the ITD or Analyze Late vs. Early protocol result in a safety issue (e.g., delay in treatment) or other potential adverse situation?

○ No

○ Yes → Complete **Alert CTC** form.
- ☐ Delay in treatment
- ☐ Suspected mechanical failure of ITD
- ☐ ITD filled with fluid
- ☐ Airway bleeding
- ☐ Failure to immediately remove the ITD following ROSC
- ☐ Other, describe: _____ *(30)*

Person responsible for data on this form:

6.4.1 CPR Process Form

The purpose of the CPR Process form is to document the elements of cardiopulmonary resuscitation and the electrocardiogram data. The CPR process measurements can be utilized for quality assurance purposes with the EMS providers. The information will include the initial (EMS and non-EMS) rhythm, rhythms post-shock, the device manufacturer(s) used in this resuscitation, minute-by-minute notations of the number of ventilations, compressions, the rate of compression, and CPR fraction (the ratio of compressions to lack of compressions). Optional data fields are provided for sites participating in the CPR Feedback substudy and/or the Ventilation substudy. This form also provides for the capability to attach the electronic ECG recordings (with or without the capnography channel) and upload them to the ROC database/library.

The episode date/time and episode ID will be pre-filled by the web data entry program and will be consistent with the date and time recorded on the Patient Enrollment form. It should be reviewed for accuracy.

Item 1 – *Does a continuous ECG recording exist for any of the EMS (includes fire) resuscitation?*

Indicate no or yes, whether a continuous (not a "snap shot") electronic ECG recording of the ROC EMS resuscitative effort (either in part or entire) was downloaded from EMS (includes fire) to the ROC site. This is not intended to include 12-lead ECG recordings or paper rhythm strips. This is also not intended to include electronic ECG recordings from lay or bystander use of AEDs (such as public access, police, health care clinic).

If yes, an electronic recording was downloaded from EMS, indicate whether the available recording(s) collectively represent the 'entire' or 'part' of the EMS resuscitative effort. Some EMS systems have tiered response by fire, BLS, and ALS so that more than 1 electronic ECG recording must be separately retrieved and downloaded. Indicate the number of EMS recordings that comprise the resuscitative effort, counting each separate electronic ECG recording available from fire, BLS, and/or ALS. If more than one ECG from the same manufacturer exists, they should be counted separately, but merged if possible and uploaded to the CTC as one file.

If the initial CA rhythm was obtained from a non-EMS ECG device (such as used by a bystander), the Coordinator should try to obtain the recording to review the initial rhythm and any shocks delivered for documentation on the ROC forms. The non-EMS ECG can be kept at the site, and it should not be sent to the CTC.

Item 2 –*Device used: (check all that apply)*

For up to the first three EMS defibrillation devices used (such as might occur in a tiered EMS response system where fire BLS places a device and ALS replaces it with their own upon arrival), indicate the brand (manufacturer)--either Medtronic, Philips, ZOLL, or other. If other, specify the manufacturer (30 characters maximum).

For each device used, indicate if the audio feedback function (related to CPR performance) was turned on or muted (this capability is only for the Philips device, so all other devices should be "No"), an electronic ECG recording exists, and whether the recording was reviewed by the ROC Coordinator. The Coordinator may choose to attach/upload the recording to the ROC-web prior to its review by the site and then at a later date, revisit the form for review and change the "No" to a "Yes," then replace the upload with the reviewed/annotated recording.

Use the 'attach recording' section to browse the site's local database to identify and attach the ECG file that corresponds to the device indicated (Medtronic: .pco; Philips: .zip; ZOLL: .zol). 'DEL' allows a selected file to be unattached.

Naming files for upload to ROC-website: An attached ECG file name ***must*** include the ***entire*** study identification number assigned by the CTC for the Epistry case. Examples of an 'entire' Epistry case ID; DAL-123456-1 or ARC-000456-3 or PGH-123450-2 (include site code, all dashes and leading and trailing zeros, and the check digit). It is recommended that you prepend the current name of the file with the ROC case ID and device order. This will allow you to see both the original file name and the ROC case ID in the file name making it easier to determine which of your original files was used to create a given ROC upload file. For example, if you have a file called 2007-12-31.ZOL that needs to be attached to the first device listed for case CTC-000000-0 you would rename the file. CTC-000000-0-dev1-2007-12-31.ZOL.
NOTE for ZOLL recordings: The ROC website currently accepts only files with '.ZOL'. The .ZOL file format is acquired by choosing *File->Rename* Sites. The ROC website does not currently accept .CRD or .FUL file formats (obtained by choosing *File->Export->Entire Defibrillator Record, Binary (.crd/.ful))* from the menu. The CTC is evaluating the upload option for the .CRD and .FUL formats.
Another NOTE for ZOLL recordings: The .ZOL files have to de-identified following the below outlined process:

1. Create a folder that is used for containing files to be uploaded to the ROC website. This step only needs to be done once and not for every case. This cannot be the same folder that holds the original .ZOL files that your site receives from the participating agencies. Do not use this folder for storing cases that have not been de-identified.
2. Open the desired case in the RNCR software. This can be done by double clicking on the file itself or by clicking the *Open* icon and browsing for the file.
3. Select *File -> Send to -> Folder* from the menu.
4. Answer "Yes" when asked "Remove personally identifying data?"
5. When the *Browse for Folder* window appears choose the roc upload folder. This will create a file in the folder with the exact same name as the .zol file that you are currently reading.
6. If this file does not have the ROC case id in the file name you need to rename the file.
    1. Close the file that is currently open by selecting *File -> Close* from the menu. Important: do not skip this step and go immediately to step 2 because the software messes up when you attempt to open another file when one is already open.
    2. Open the file that you created with the *Send to* command. Remember that
        1. Click the *Open* icon in the icon bar
        2. Browse to your ROC upload directory and select the file from those shown.
    3. Rename the file by selecting *File -> Rename* from the menu. It is recommended that you follow the renaming process as described above.

Only one recording is intended to be uploaded for each of the three listed devices. Where more than one recording exists for the same device (such as when a device was applied, then turned off, and later turned on) can recordings into one zip file and attach it (using the required file naming conventions, as above) for upload.

It is expected that for each device used for which a 'recording exists', a file will be attached for upload. Where multiple ECG files are merged to one (such as when the BLS and ALS device ECG files are merged to represent the entire EMS response), indicate that a recording exists for each of the devices used, leave the 'attach recording' file name field blank, and provide an explanation in the error-override message box that indicates the merge of recordings for devices x and y (specify).

Item 3 - *Were any shocks delivered by EMS responders?*

Indicate no or yes, if any defibrillation shocks were delivered by EMS responders (includes volunteer fire who are responding as part of an organized EMS system). If yes, indicate the number of shocks. Shocks are considered as "delivered" regardless of their apparent success. Do not consider defibrillation shocks that are delivered by a bystander, police, healthcare provider, or person that is not part of the organized EMS response to this episode. If shocks were delivered by EMS responders, indicate how many shocks.

Item 4 – *Sequence of events*

This section contains 12 potential items which may occur during this resuscitation effort. For each of the items listed under Rhythm/Shock Event, indicate NA, if it was not applicable, or indicate the time of rhythm/shock event. 'NA' is reserved for events that were not associated with the case; it is not intended to indicate 'not available' or 'cannot determine.' If you do not have a time for a rhythm or shock that is derived from an electronic ECG recording, leave the time blank and override the error. For each of the events in Item 4, indicate the rhythm and the source for these rhythms. Indicate the associated 'rhythm' for each event, regardless of the source or the ability to provide a time from an electronic ECG recording. For 'rhythm', the continuous ECG is the preferred source, with the ECG snapshot or strips next, and PCR documentation last.

Please see definitions of rhythms, N/A and Cannot Determine at end of CPR Process form instructions.

1) 1st CA rhythm with non-EMS AED/defib— A non EMS AED/defibrillator includes any use by bystanders before the EMS or fire providers arrive at the scene. Bystander is defined as any person who responds and is NOT on duty with an EMS agency at the time of the arrest including off duty paramedics, off duty fire providers, doctors, nurses, police and laypersons. Non EMS AED/defibrillators include public access AEDs (shopping malls, airports, etc) and defibrillators at satellite healthcare facilities such as day surgery, dialysis centers, nursing homes, assisted living and cruise ships). Fire is considered part of the EMS response.

Often the ECG is not available for review and instead the site must rely on the PCR for information. This is usually in the form of notation as to either administering shocks or having

had no shock advised. If a shock is administered, mark VT/VF (includes AED shock). If no shock was advised, mark AED-no shock, no strip. If no ECG download or paper copy exists and the PCR is being used to determine the first non-EMS rhythm, the PCR must clearly indicate that this was the **initial** non-EMS rhythm, mark 'cannot determine'. In most cases the time of the rhythm will be missing unless there is an electronic ECG. If the time is missing please leave blank and override the error.

2) EMS 1st CA rhythm within 10 secs of pad placement: Time of the FIRST interpretable cardiac arrest rhythm after confirmation of cardiac arrest that is captured by an EMS or fire provider, either ROC or non-ROC (EMS or fire provider is defined as a person on duty for an organized EMS agency at the time of the response, including fire). Police are considered bystanders. The 1st CA EMS rhythm cannot be a perusing rhythm. Police are considered bystanders. This rhythm cannot be a perusing rhythm.

This element is only interested in the FIRST 10 SECONDS after pad placement. If pads have been placed and there is no ECG, check 'cannot determine'. If you have an ECG but it is obscured during the first 10 seconds after pad placement mark "cannot determine" as you will have another chance to note the rhythm in the next question.

This data element does not include rhythms captured by non-EMS defibrillators. See Line 1 (1ST CA rhythm with non-EMS AED/defib) for a description of Non-EMS defibrillation.

Source of rhythm: The source for capturing both the time of this event and the rhythm type is the continuous electronic ECG, but ONLY IF THIS IS THE ECG FROM THE FIRST ARRIVING VEHICLE. The primary goal is to get the first rhythm after the first pad placement. If the ECG is not available, then check NA. Information from the early placement of a CPR compression 'puck' will not help in this determination.

Timing of the rhythm: Look for the EARLIEST rhythm from the time the pads were placed (from the FIRST EMS defibrillator placed), within the first 10 seconds. For an EMS witnessed arrest (occurring after the arrival of EMS), look for the earliest rhythm following the onset of cardiac arrest, within the first 10 seconds. If the ECG during the first 10 seconds is obscured, then check "cannot determine" and move to the next question.

Length of rhythm: There is no required length of time that a rhythm must be evident (such as transitional rhythms) to be considered the '1st cardiac arrest rhythm'. The objective is to capture the earliest rhythm, not necessarily the easiest or most clear to discern (this is recognized to be a tradeoff). Use your best judgment in determining the rhythm during even a few seconds of interpretable ECG. Where the reviewer observes a rhythm different than that indicated by the AED analysis (shock or no-shock) defer to the reviewer's finding as long as careful consideration as to which source contains the information from the FIRST EMS defibrillator placed.

EMS witnessed arrest: If an arrest is witnessed by EMS or fire providers and pads were placed *prior* to the arrest, then determine the 1st cardiac arrest rhythm within the 10 seconds immediately following arrest. If an arrest is witnessed by EMS or fire providers and pads are placed *after* the onset of arrest, then determine the 1st cardiac arrest rhythm within the 10 seconds immediately following placement of the pads.

Definitions of rhythms:
a). *VF/VT (includes AED shock)*: Ventricular fibrillation/ventricular tachycardia–irregular, disorganized ventricular electrical activity of variable amplitude exceeding 0.2mV, or; HR > 100 bum with QRS duration greater than 110 mess. with evidence of AV dissociation and absence of palpable pulse, or; cardiac arrest rhythm for which an AED advised a shock (need not have the ECG strip), or; cardiac arrest rhythm documented in the prehospital PCR.

b). Pulseless electrical activity (PEA): Electrical activity with R-waves of any width at an average rate of >10 beats per minute (e.g. organized ventricular electrical activity with R-waves of any width that occur more than once over a 6-second period). If PEA, indicate the rate in beats per minute or if 'unknown/not noted'. Occasionally, EMS will note in the PCR, "idioventricular rhythm with no pulse" and no heart rate is documented—in these cases, mark the rhythm as PEA.

c. Asystole or PEA: Background activity less than 0.2mV in amplitude with ≤ 10 beats per minute average rate (e.g. a 6 second strip without ventricular complexes).

1. Mark 'asystole' where low voltage baseline activity (< 0.2 mV) and no QRS complexes transpire for a minimum of 6 second window (this is intended to indicate a rate of ≤ 10 bpm). If less than a 6 second strip is available use your best judgment to determine asystole vs. PEA but determination of a rhythm is preferable to reporting "cannot determine".

2. Mark PEA if 1 or more complexes are evident within 6 second window (suggesting a rate of > 10 bpm). If less than a 6 second strip is available use your best judgment to determine asystole vs. PEA but determination of a rhythm is preferable to reporting "cannot determine".

d. AED-no shock (no strip): Notes from the patient record indicate that analysis was done and no shock was advised or delivered, but no ECG strip available.

e. Cannot determine: Select this if any EMS or fire provider placed pads but the ECG recording is missing, artifact or compressions obscure the rhythm or documentation is incomplete regarding the initial cardiac arrest rhythm. Includes rhythms for which the ECG documentation or indication of AED shock status is not available or missing from the PCR.

f. NA-(not applicable)-Use of this does not apply to situations where the ECG or rhythm is missing (see cannot determine). Not applicable means there was not an EMS or fire provider cardiac arrest rhythm as in the case where a bystander administered an AED shock but by the time the EMS arrived the rhythm was perfusing and the patient never re-arrests OR in the case where the EMS did not place any defib or AED pads and had no knowledge of the rhythm.

3) 1st CA EMS rhythm if the line 2 "rhythm = Cannot Determine"— If Line 2 is marked 'cannot determine' or NA, indicate the time when the FIRST interpretable cardiac arrest rhythm after confirming the ONSET of cardiac arrest is captured by the EMS or fire provider, either ROC or non-ROC. This includes responses by fire, but not police. Police are considered bystanders. If the first vehicle was non-ROC and you don't have access to the information, mark 'cannot determine,' . If a time for line 2 '1st CA EMS rhythm within 10 secs of pad

placement' was entered, then here mark ' NA'. If antiarrhythmic drugs were given prior to determining this rhythm, then mark N/A.

This data element does not include rhythms captured by Non --EMS or police provider defibrillators. See Line 1 (1ST CA rhythm with non-EMS AED/defib) for a description of Non-EMS defibrillation.

Source of rhythm: The preferred source for capturing both the time of this event and the rhythm type is the continuous electronic ECG BUT ONLY IF THIS IS THE ECG FROM THE FIRST EMS Defibrillator placed. The primary goal is to get the first rhythm rather than the electronic ECG rhythm. The second preferred source is a rhythm strip recording. The third preferred source is the rhythm documented in the PCR. Use the PCR only as a last resort. Information from the early placement of a CPR compression 'puck' will not help in this determination.

Timing of the rhythm: Look for the EARLIEST rhythm from the time the pads were placed (from the FIRST EMS or fire provider Defibrillator placed). For an EMS or fire provider witnessed arrest (occurring after the arrival of EMS), look for the earliest rhythm following the onset of cardiac arrest. If the ECG during the first 10 seconds is obscured then look either during a ventilatory pause, possibly during compressions if there are QRS complexes, or at the earliest pause in CPR for rhythm analysis. Look for the 1st CA EMS rhythm for up to 5 minutes after pad placement and prior to documentation of drugs given or a shock delivered by EMS or fire (whichever is earlier). If the rhythm cannot be determined within this period, then mark 'cannot determine.'

Length of rhythm: There is no required length of time that a rhythm must be evident (such as transitional rhythms) to be considered the '1st cardiac arrest rhythm'. The objective is to capture the earliest rhythm, not necessarily the easiest or most clear to discern (this is recognized to be a tradeoff). Use your best judgment in determining the rhythm during even a few seconds of interpretable ECG. Where the reviewer observes a rhythm different than that indicated by the AED analysis (shock or no-shock) or the PCR, defer to the reviewer's finding as long as careful consideration as to which source contains the information from the FIRST EMS Defibrillator placed.

EMS witnessed arrest: If pads were placed *prior* to the EMS or fire provider witnessed arrest, determine the 1st CA EMS rhythm within 5 minutes or prior to documentation of drugs given (which ever is earliest) immediately following arrest. If pads are placed *after* the onset of EMS witnessed arrest, then determine the 1st cardiac arrest rhythm within 5 minutes or prior to documentation of drugs given (which ever is earliest) immediately following placement of the pads.

Definitions of rhythms*:*

a). *VF/VT (includes AED shock):* Ventricular fibrillation/ventricular tachycardia–irregular, disorganized ventricular electrical activity of variable amplitude exceeding 0.2mV, or; HR > 100 bpm with QRS duration greater than 110 msec. with evidence of AV dissociation and absence of palpable pulse, or; cardiac arrest rhythm for which an AED advised a shock (need not have the ECG strip), or; cardiac arrest rhythm documented in the prehospital PCR

b). Pulseless electrical activity (PEA): Electrical activity with R-waves of any width at an average rate of >10 beats per minute (e.g. organized ventricular electrical activity with R-

waves of any width that occur more than once over a 6-second period). If PEA, indicate the rate in beats per minute or if 'unknown/not noted'. Occasionally, EMS will note in the PCR, “idioventricular rhythm with no pulse” and no heart rate is documented—in these cases, mark the rhythm as PEA.

c. Asystole or PEA: Background activity less than 0.2mV in amplitude with ≤ 10 beats per minute average rate (e.g. a 6 second strip without ventricular complexes).

1. Mark ‘asystole’ where low voltage baseline activity (< 0.2 mV) and no QRS complexes transpire for a minimum of 6 second window (this is intended to indicate a rate of ≤ 10 bpm). If less than a 6 second strip is available use your best judgment to determine asystole vs. PEA but determination of a rhythm is preferable to reporting “cannot determine”.

2. Mark PEA if 1 or more complexes are evident within 6 second window (suggesting a rate of > 10 bpm). If less than a 6 second strip is available use your best judgment to determine asystole vs. PEA but determination of a rhythm is preferable to reporting “cannot determine”.

d. AED-no shock (no strip): Notes from the patient record indicate that analysis was done and no shock was advised or delivered, but no ECG strip available.

e. *Cannot determine:* Select this if any EMS or fire provider placed pads but the ECG recording is missing, artifact or compressions obscure the rhythm or documentation is incomplete regarding the initial cardiac arrest rhythm. Includes rhythms for which the ECG documentation or indication of AED shock status is not available or missing from the PCR.

f. NA-(not applicable)-Use of this does not apply to situations where the ECG or rhythm is missing (see cannot determine). Not applicable means there was not an EMS cardiac arrest rhythm as in the case where a bystander administered an AED shock but by the time the EMS or fire provider arrived the rhythm was perfusing and the patient never re-arrests OR in the case where the EMS or fire provider did not place any defib or AED pads and had no knowledge of the rhythm.

NA might also be used in cases where the ITD was placed during protocol violations. For example, if the ITD was opened or placed on someone who was not in a cardiac arrest.

4) –1st EMS shock assessment: The time when EMS or fire providers, either ROC or non-ROC, initially analyze or assess the rhythm to determine whether or not a shock is indicated. This applies even if the assessed rhythm is not VF/VT and no shock is given. For the PRIMED study, it is the intent of this data variable to determine compliance with randomization to ‘analyze early’ or ‘analyze late’ CPR assignments.

For AED continuous ECG: The time associated with the start of the first AED analysis event, free of significant artifact and CPR. Some devices are programmed to analyze automatically (such as when the device is powered on or pads placed) and/or initiate a shock—if the analysis is aborted (stopped) by EMS, do not consider that analysis for ‘1st EMS shock assessment.’

a) For the ZOLL AED Pro and E-Series in Auto Defib mode: this is the time of the first "Analysis Started" event. The AED marks when analysis starts and when the device instructs the provider as to whether a shock is needed. Use the former mark.

b) For the Medtronic AED (Lifepak 500 or 1000, and Lifepak 12 in AED mode): use 'Analysis 1' which indicates the initiation of analysis (button pushed).

c) For the Philips MRX: When in AED mode, the annotation log states "analyzing" to indicate the beginning of analysis for a shock. Use the first such notation (except where aborted by EMS) as '1st EMS shock assessment'. Where 'analyzing' is indicated (and analysis was not aborted), but the compression channel (generated by the 'puck' indicates that CPR is stopped at a later time, document the later time).

Manual defibrillator continuous ECG: The time associated with the intention of pausing CPR for the assessment of the rhythm for a determination to shock or not shock. The reviewer will have to make a judgment as to when the EMS or fire provider paused for assessment of the rhythm. This may include:

a) Interruption of CPR with the intent to assess the rhythm to determine if a shock is needed (this might be a pause in the impedance tracing noting chest compressions, use of voice recordings to confirm intent, etc) or

b) Identifying the first pause in compressions > 4 or < 10 seconds in duration with no movement artifact (a pause in compressions of 4-10 seconds is "presumed ventilation pause" per the ROC PRIMED protocol), or

c) If the intent is not apparent, use a combination of the information on the PCR, EMS questionnaire, or other resource to try to determine when the first rhythm assessment occurred to assess whether or not a shock was indicated. If no times are available, determine and provide at least the order of events.

Timing of event: The time of '1st EMS shock assessment' may be associated with other rhythm/shock events depending on the response scenario. The time of '1st EMS shock assessment' may:

a) be same time as the '1st CA EMS rhythm' when the initial EMS shock assessment is conducted close to the time of EMS AED pad or manual defibrillator electrode/pads placement, OR when ALS arrives first on scene with a manual defibrillator (such as a Lifepak 10 or 12).

b) occur shortly (about 30 seconds) after CPR is started (such as 'analyze early' in the ROC PRIMED trial) or immediately after an arrest when witnessed by EMS (if pads or electrodes were placed prior to the arrest).

c) occur several minutes (about 3 minutes) after pads are placed when a ROC vehicle is first on scene, places the initial pads, and EMS CPR is prescribed for 3 minutes (such as 'analyze late' in the ROC PRIMED clinical trial).

Source of data: The preferred source for '1st EMS shock assessment' time is the AED event report or the continuous electronic ECG. The second preferred source is documentation in the PCR of a shock advised or not advised. If no continuous electronic ECG is available the

reviewer must carefully review the PCR, additional written EMS or fire provider worksheets, or even phone calls to EMS or fire (document such calls in the research file) to determine if the AED shocked or did not shock the FIRST RHYTHM during the FIRST ANALYSIS following arrival of the organized EMS response. If no times are available the site should determine and provide at least the order of events.

Cases where impedance is missing: For Medtronic and Philips manual devices the EMS or fire provider might switch to a monitoring mode (or Lead II) where impedance tracings are not collected which might make it difficult to determine when the shock assessment occurred. For Medtronic cases where the mode has been switched the reviewer cannot collect further CPR process information. For Philips the reviewer might be able to see the compression activity but there are no statistics reported so sites should just end the reporting of these measures rather trying to calculate by hand.

In sites with an all ALS response team the recommendation would be to continually educate the EMS regarding the need to have the machine in the mode necessary to capture CPR process data (Medtronic—'paddles mode', Philips—'defib mode').

5) EMS 1st Shock—If a patient receives no shocks by EMS or fire during resuscitation, Items 5 through 12 should be marked NA. If the patient was shocked, indicate the time of the shock, the rhythm the patient was being shocked for, and the source for the data. It is anticipated that the patient would be in VF/VT at the first shock, but it is possible that the patient was in asystole and the EMS providers opted to shock the patient, or an AED mis-detected the rhythm. Under Source, indicate the number of seconds for which no CPR occurred ("Pause") prior to the first shock, due to hands-off time for analysis and charging of the device. Indicate the number of seconds for which no CPR occurred ("Pause") post-shock prior to resumption of compressions. If the patient obtained ROSC, the resuscitative effort ended after the first shock, or if CPR was not resumed (as when the resuscitation is terminated), leave the post-pause time blank; then mark NA for items 7 through 12..

6) Rhythm post shock (90-150 seconds)- Indicate the rhythm observed at 2 minutes (120 seconds) post shock, +/- 30 seconds on either side (90-150 seconds). If you are unable to determine the rhythm right at the 2 minute mark, work backwards or forwards to the first rhythm observed nearest the 2 minute post-shock mark within 30 seconds before or after. If there is no discernable rhythm within the 2 minute post-shock mark +/- 30 second window, then check "cannot determine". No specified duration of an observed rhythm is required for determination of the rhythm type. The preferred source for this data element is the continuous electronic ECG. The second and third preferred sources are respectively, a rhythm strip or the PCR. If unable to determine the rhythm @90-150 sec., note the first evaluable rhythm at least 30 seconds after shock.

7) Rhythm at next analysis after first shock—Indicate the rhythm at the next analysis. This rhythm analysis may or may not be associated with a subsequent shock advised or delivered. Fire and BLS may pause for analysis when using an AED, but it may be difficult to determine when ALS is analyzing the rhythm for a shock. Where difficult to determine when ALS is analyzing after the first shock, it is to be determined at 2 minutes (90-120 seconds) after the

time for “Rhythm post-shock.” The “Rhythm post-shock and “Rhythm @ next analysis after next shock “may occur simultaneously.

If only one shock was delivered by EMS or fire, mark lines 8 through 12 as ‘NA.’

8) EMS 2nd shock—If a patient receives no 2nd EMS shock (includes fire) during resuscitation, Items 8 through 12 should be marked NA. If the patient was shocked, indicate the time of the shock, the rhythm the patient was being shocked for, and the source for the data. It is anticipated that the patient would be in VF/VT at the first shock, but it is possible that the patient was in asystole and the EMS providers opted to shock the patient, or an AED mis-detected the rhythm. Under Source, indicate the number of seconds for which no CPR occurred (“Pause”) prior to the 2nd shock, due to hands-off time for analysis and charging of the device. Indicate the number of seconds for which no CPR occurred (“Pause”) post-shock prior to resumption of compressions. If the patient obtained ROSC, the resuscitative effort ended after the 2nd shock, or if CPR was not resumed (as when the resuscitation is terminated), leave the post-pause time blank, complete line 9, and mark NA for items 10 through 12.

9) Rhythm post 2nd shock (90-150 secs*) Mark ‘NA’ if a 2nd EMS shock (includes fire) was not delivered. If delivered, indicate the rhythm observed at 2 minutes (120 seconds) post shock, +/- 30 seconds on either side (90-150 seconds). If you are unable to determine the rhythm right at the 2 minute mark, work backwards or forwards to the first rhythm observed nearest the 2 minute post-shock mark within 30 seconds before or after. If there is no discernable rhythm within the 2 minute post-shock mark +/- 30 second window, then check “cannot determine”. No specified duration of an observed rhythm is required for determination of the rhythm type. The preferred source for this data element is the continuous electronic ECG. The second and third preferred sources are respectively, a rhythm strip or the PCR. If unable to determine the rhythm @90-150 sec., note the first evaluable rhythm at least 30 seconds after shock.

10) Rhythm at next analysis after 2nd shock Indicate the rhythm at the next analysis after the 2nd shock. This rhythm analysis may or may not be associated with a subsequent shock advised or delivered. Fire and BLS may pause for analysis when using an AED, but it may be difficult to determine when ALS is analyzing the rhythm for a shock. Where difficult to determine when ALS is analyzing after the 2nd shock, it is to be determined at 2 minutes (90-120 seconds) after the time for “Rhythm post-shock” The “Rhythm post-shock and “Rhythm @ next analysis after next shock “ may occur simultaneously.

11) EMS 3rd shock: If a patient receives no 3rd EMS shock (includes fire) during resuscitation, Items 11 and 12 should be marked NA. If the patient was shocked, indicate the time of the 3rd shock, the rhythm the patient was being shocked for, and the source for the data. It is anticipated that the patient would be in VF/VT, but it is possible that the patient was in asystole and the EMS providers opted to shock the patient, or an AED mis-detected the rhythm. Under Source, indicate the number of seconds for which no CPR occurred (“Pause”) prior to the 3rd shock, due to hands-off time for analysis and charging of the device. Indicate the number of seconds for which no CPR occurred (“Pause”) post-shock prior to resumption of compressions. If the patient obtained ROSC, the resuscitative effort ended after the first shock, or if CPR was not resumed (as when the resuscitation is terminated), leave the post-pause time blank; then mark NA for items 11 and 12.

12*) Rhythm post 3rd shock (90-150 secs*)* Mark 'NA' if a 3rd EMS shock (includes fire) was not delivered. If delivered, indicate the rhythm observed at 2 minutes (120 seconds) post shock, +/- 30 seconds on either side (90-150 seconds). If you are unable to determine the rhythm right at the 2 minute mark, work backwards or forwards to the first rhythm observed nearest the 2 minute post-shock mark within 30 seconds before or after. If there is no discernable rhythm within the 2 minute post-shock mark +/- 30 second window, then check "cannot determine". No specified duration of an observed rhythm is required for determination of the rhythm type. The preferred source for this data element is the continuous electronic ECG. The second and third preferred sources are respectively, a rhythm strip or the PCR.

Note: Cases without CPR between shocks

For any series of shocks without CPR between them leave the post shock pause blank for the 1st in the stack. Leave the pre-shock pause blank for the last in the stack. And, leave the pre and post pauses blank for any other shocks in the series. You will receive error messages for each of these blank fields which must be overridden with the explanation that these shocks are part of a series of shocks without CPR between them. The post shock pause for the last shock in the series will be used for time interval calculations.

-No CPR between shocks-pre shock pause- this time interval will be the pre shock pause (as per above instructions for the first shock in a series of 2 or 3 (or more) shocks).

-No CPR between shocks-post shock pause- this time interval will be the time from shock 1 delivery to the resumption of CPR as noted by the resumption of a CPR waveform on the CPR process file. If the resumption of CPR occurs after the 2nd shock, please leave the post shock pause 1 and pre shock pause 2 blank and override the error message. Post shock pause 2 will be the time interval calculated.

If the resumption of CPR occurs after the 3rd shock, please leave post shock pause 1, pre shock pause 2, post shock pause 2 and pre shock pause 3 blank and override the error message. Post shock pause 3 will be the time interval calculated. Follow this same procedure if there are more than 3 shocks without CPR between the shocks.

Item 5 – *ECG Analysis*

Fill in the following time points. If data has been previously entered in the Pre-hospital time record and the CPR Process form is blank, three selected ECG analysis times ('time of arrest if EMS witnessed'; 'time resuscitation stopped due to death'; and 'time of ED arrival') will be autofilled at web-entry. These autofilled times may be edited—where edits are made to the autofilled times, the site is encouraged to review and edit the data entered on the Prehospital Time Record to reflect any changes. Enter times as hh:mm:ss on 24 hour clock—enter '00' for seconds only when source documents provide them, not as a placeholder:

Time first EMS AED/defibrillator turned on*:* Time the initial (first) EMS responder (includes fire) AED or manual defibrillator is powered on. This does not include bystander, police, or healthcare provider. Indicate if the time is 'not available'. If 'not available' and only 1 device was used during the course of EMS prehospital resuscitation, stop here (question 6 is not required).

Time first EMS pads placed*:* Indicate when pads (capable of defibrillation) of the FIRST ROC EMS or fire defibrillator/monitor of the FIRST EMS or fire provider AED or manual defibrillator were in contact with the skin, as evidenced by the commencement of ECG recording or impedance signal. If pads lose contact and there is more than one time to pad placement time, use the first time the pads were placed. It is expected that 'time first EMS pads placed' will be left blank if 'time first EMS AED/defibrillator turned on' is 'not available'. Do not use time ECG-only electrodes (sometimes called 'pads') are placed. The time the EMS pads are placed is auto filled as the 'start time' for the Item 6, CPR process measurements.

If the accelerometer (Philips device) or 'puck' is placed before the defibrillation pads, DO NOT use this time as '1st EMS pads placed.' DO NOT manually try to calculate the CPR fraction, # compressions, or compression rate prior to defibrillation pads placed. Starting from the time the initial pads were placed allows consistent comparison between devices.

If this time is unknown (as when a non-ROC agency is first on scene to place defibrillation pads and the electronic ECG recording is not available), leave it blank and override the resulting error message, providing the reason.

Time of arrest if EMS witnessed: Autofill at web-entry: 'Time of arrest if EMS witnessed' is filled automatically IF the Prehospital Time Record form has been previously completed and saved (with or without errors) Auto filled values can be edited.

Time of initial cardiac arrest is used when the responding EMS or fire provider (either ROC or non-ROC has arrived on scene prior to the onset of the cardiac arrest. For example, where EMS or fire has been called for 'chest pain' or where EMS or fire is stationed at a public even such as a marathon or football game. If a bystander began chest compressions prior to EMS or fire arrival, the patient had a pulse when EMS arrived, and the patient later arrested in front of EMS, the cardiac arrest would be considered as witnessed by EMS. If the patient was defibrillated by an AED/defibrillator used by a lay person, health care provider, police or off-duty paramedic prior to EMS arrival, the patient has ROSC upon EMS arrival, but later re-arrests in front of EMS, the cardiac arrest would not be considered EMS witnessed.

If not witnessed by EMS or fire provider, leave the time blank on the CPR process form. The preferred source for this data element is voice recording (where available). The second and third preferred sources for this data element are respectively, the continuous electronic ECG and the PCR. Time AED/defib is turned on is NOT considered a surrogate for 'time of arrest if EMS witnessed.

> For cases monitored with pads or electrodes: Time of arrest is the onset of ventricular fibrillation (VF) or asystole. If the potential 'arrest' rhythm is ventricular tachycardia (VT) or PEA, then, the onset of VT or PEA must be temporally associated (so as to discern a perfusing from a non-perfusing rhythm) with either voice annotation, or with chest compression or shock artifact. If VT or PEA is associated with CPR, the time of arrest is when compressions are started. If VT is associated with a shock, the time of arrest is when analysis is started.

For cases not monitored (no pads or electrodes are on patient at time of arrest; or continuous electronic recording is not available): the time of arrest is determined from the PCR (if documented time is plausible). When entering a time as documented in the PCR, enter hh:mm as written; do not add ':00' for seconds as a placeholder.

Time of advanced airway placement: Advanced airway includes intubation, LMA and other supraglottal airways. Indicate if either 'no advanced airway' was placed (such as when only bag mask valve have been used) or 'unable to determine' the time of placement.

Time resuscitation stopped due to death: Autofill at web-entry: 'Time resuscitation stopped due to death' is filled automatically IF the Prehospital Time Record form has been previously completed and saved (with or without errors). Auto filled values can be edited.

Indicate when EMS resuscitation stopped due to a decision to end rescue efforts. Indicate "Not applicable" if CPR was ongoing upon ED arrival/hospital admission.

Time ED arrival: Autofill at web-entry: 'Time of ED arrival' is filled automatically IF the Prehospital Time Record form has been previously completed and saved (with or without errors). Auto filled values can be edited.

Time when the patient transporting vehicle stops moving on arrival at the receiving hospital or ED. Indicate "Not applicable" if patient was not transported to the ED/hospital.

Item 6 – *Did the ECG provide CPR process measurements?:*

Indicate no or yes if the available ROC electronic ECG information provides or allows CPR process measurements. If no, stop here. If yes, provide a minimum of 5 minutes CPR process data for the resuscitative effort (5 minutes beginning with the first available ECG recordings). If the patient received an advanced airway, an additional 5 minutes of CPR process data should also be obtained starting from the time of placement of the advanced airway. If you are unable to determine when the patient was intubated or an advanced airway placed, enter 20 continuous minutes of CPR process data starting from the time the pads were placed. Where feasible, provide data for each minute of the resuscitative effort, up to 20 minutes. Optional data elements are provided for more extensive reporting and for the Ventilation Substudy.

Device order: More than one device may be used during the course of the resuscitative effort. '1' is auto filled for all rows IF 'Time first EMS pads placed' has been entered in the prior question (#5 ECG Analysis). When (during the course of prehospital care) CPR process data comes from a second device source, enter '2' for that row—all below rows will be autofilled with '2' (and so on for subsequent devices).

If 'Time first EMS pads placed' was not entered in the prior question, enter '1' for the first row and mark 'no ECG' (to indicate that there is no electronic ECG from which to determine CPR process measures for that device).

Where an EMS device has been used, but no CPR process measures are available for that period of time, enter 1, 2, or 3, etc to indicate the device order of use (and mark 'no ECG data'). No other data for that row is expected.

Enter '0' in the 'Device order' column immediately below the last row of CPR process data to be entered—this signifies the term of the data provided and releases error checks for subsequent rows.

Start time: The hh:mm:ss for the first and subsequent minutes are auto filled at web-entry, beginning with the 'time first EMS pads placed' entered in the prior question (#5 ECG Analysis). The autofilled time may be edited and subsequent minutes will adjust to 1 minute increments from the edited time. Where the change of devices causes a lapse in time, enter the new device number and enter the 'start time' of that device—all below rows will be autofilled with 1 minute increments from that edited 'start time'. If 'time first EMS pads placed' has been left blank (as the data was not available), leave the start time blank and mark 'no ECG'. Move to the next row and enter the next 'device order' and either mark 'no ECG' or enter the 'start time' for the recording (whichever is appropriate). Where the 'start time' for each subsequent 'device used' is entered, all below rows will be autofilled with 1 minute increments from that edited 'start time.' NOTE: each row of the 'Start time' column is numbered 1, 2, 3, etc, representing the number of rows, not necessarily the number of minutes for which CPR process measures are provided.

No ECG: check this box for a device used for which no electronic CPR process data is available. When checked, no other data for that row is required. It is intended that the device number be entered once and 'no ECG' marked. 'No ECG' is intended for use to indicate when an entire recording is missing, not minutes within a recording—see '#seconds with no measures."

#Ventilations: The number of ventilations counted for a minute, or for the portion of the minute for which the continuous-recorded signal could be analyzed. A separate approach is taken for each device used:

Medtronic—BLS device (Lifepak 500) does not have a bio-impedance channel filtered for ventilations. The ALS device (Lifepak 12, in manual or AED mode) has a composite bio-impedance channel requiring manual annotation of waveforms. Such composite waveforms are complex and are difficult to annotate for ventilations during chest compressions. However, during epochs or time intervals with no compressions, recent investigative work by Dr. Ahamed Idris suggests that ventilations can be observed both before and after intubation (either spontaneous or with positive pressure ventilations). Following are Idris guidelines for recognizing and counting ventilations on the Medtronic bioimpedance channel:

Device related

1. Review files with ventilation filter OFF and compression filter OFF to review 'raw file'. Use ventilation filter as needed to filter out high frequency interference (such as 60 Hz cycle, transient spikes).
2. Count ventilations in Medtronic PCO files during epochs that are free of chest of chest compressions.
3. A ventilation waveform at the end of an epoch which becomes intruded upon by compressions may be counted in order to complete the interval if the ventilation is clean.

4. Ventilations may be counted in epochs with chest compressions if the ventilations are absolutely uniform & rhythmic.

Waveform characteristic

1. Single broad/wide parabola
2. Duration of less than or equal to 2.5 seconds
3. Amplitude equal to at least 75% of the amplitude of the majority of waves, or equal to the amplitude of a "typical" waveform for that particular file
4. Keep a "questionable" ventilation if not filtered out by software—*they reviewed with ventilation filter on and off*

Reviewer ambiguity

1. Be liberal with eliminating entire epochs if guessing becomes excessive.

If unable to discern ventilations from compressions for a given full minute (60 seconds), leave the minute's filed for '# bens' blank. If continuous capnography (a separate device) was used during the course of care, the site is encouraged to provide values for that data element for the given minutes. Error checks will not be triggered for blank '#vents' for Medtronic devices. The approach to ventilations for Medtronic devices will be revised with evolution in understanding and technology.

Philips— look at recorded ventilation waveform, minute by minute. For each minute, assess if the ventilation signal is corrupted. If corrupted (such as 60 cycle interference or movement), leave that minute's '# vent' data field blank (do not enter '0') and override and give a reason for the related error message. Do not over-read or annotate (add or delete) ventilations, even if voice channel or continuous capnography available. For minutes with no corrupted signal (either pre-or post-intubation), enter '# vents' reported by QCPR Review. Though optional, it is strongly encouraged to enter values for 'capnography vents' for later comparison with the ventilation channel.

ZOLL—do not enter values for '# vent", leaving the field blank. Error checks will not be triggered for blank '#vents' for ZOLL devices. Ventilations will be revisited when ETCO2 is introduced by the manufacturer.

 # Compressions: The number of chest compressions actually delivered in a given minute. If part of a minute cannot be analyzed, record the number of seconds in the "number of seconds with no measures" column. A separate approach is taken for each device used:

Medtronic—Review and annotate the impedance recording to indicate compressions (adding or deleting counted compressions). Sites may use voice recording to assist with annotating the recording. Generate the report and enter values for '# comp'.

Philips—when the compression channel recording is available (as when the 'puck' and pads are placed and a waveform produced, and the device set to 'defibrillation mode'), generate the report and enter statistics values for '# compressions.' If only the force channel (as when only the 'puck' is placed) or the impedance channel (as when only the pads are placed or the device is switched to 'Monitor Mode') is available, hand count compressions for each minute.

ZOLL—Review the compression channel. The compression channel cannot be annotated by the reviewer. Instead the software uses criteria to judge whether a

compression was present or not. Generate the report statistics and enter reported values for '# compressions'. ZOLL reported values for 'Comp rate' is the same as ROC '# comp'.

Compression rate: The device-calculated median rate at which chest compressions were performed for a given minute. If part of a minute cannot be analyzed record the number of seconds in the "number of seconds with no measures" column. A separate approach is taken for each device used:

Medtronic—enter the reported CodeStat values.

Philips—For minutes where the compression channel (derived from the force and impedance channels) provide the values reported by QCPR Review. For any minute where compressions have been hand counted (when the QCPR Review software does not generate statistics) for 1-60 seconds calculate the Compression Rate for a given minute using a standard approach used by the PGH site/spreadsheet: ((#compressions/(60-unanalyzed seconds-seconds no compressions))*60. Contact PGH or the CTC for an Excel spreadsheet for automatic calculations.

ZOLL— For ROC, take the ZOLL reported '# compressions' and divide by the reported CPR fraction. Compression rate for ROC data entry is not to be confused with 'compression rate' reported by ZOLL RescueNet Code Review. Be certain that the complete resuscitative effort is included in the device statistics—that is, the start time corresponds to that time entered for 'Time 1st pads placed' or 'Time of arrest if EMS witnessed' and end of resuscitative effort corresponds with 'Time resus stopped due to death', time resus stopped due to persistent ROSC, or time of ED/hospital arrival (which ever start and stop time is relevant to the case).

CPR fraction*:* The portion of time during which chest compressions were administered, expressed as a fraction. Report the value calculated/documented by the manufacturer software.

Medtronic—divide 'compression ratio' by 100. The 'compression ratio' should not be confused with the 'CPR ratio". The 'compression ratio' should be used for ROC because it has a default setting of 3 seconds in calculating the pause from CPR. The CPR ratio has a default setting of 10 seconds in calculating the pause from CPR and should NOT be used for ROC. Agencies might want to use this for another purpose beyond ROC. The report shows both ratios unless the administrator goes into the settings and removes the CPR ratio. Please remove the CPR ratio from the minute by minute report to avoid confusion.

Philips—use the FR (flow ratio) column. The company has recently reorganized the statistical printout to align more with ROC data points. Where compressions have been hand counted (when the QCPR Review software does not generate statistics) for a 1-60 seconds, calculate the CPR Fraction for a given minute (using a standard approach used by the PGH site/spreadsheet): (60-unanalyzed seconds-seconds no compression)/(60-unanalyzed seconds). Round to 2 digits (for example 0,65) Contact PGH or the CTC for an Excel spreadsheet for automatic calculations.

ZOLL—this is calculated automatically and reported on the summary. Be certain that the complete resuscitative effort is included in the device statistics—that is, the start time corresponds to that time entered for 'Time 1st pads placed' or 'Time of arrest if EMS

witnessed' and end of resuscitative effort corresponds with 'Time resus stopped due to death', time resus stopped due to persistent ROSC, or time of ED/hospital arrival (which ever start and stop time is relevant to the case).

 # secs with no measures and why: The number of seconds in a minute (0-60) during which CPR measures cannot be determined. For 1-60 seconds with no measures, select the reason why from the pull down menu—reasons why are 'ROSC' (so no CPR performed) and 'unanalyzable' (such as when the patient is being moved, cable is disconnected temporarily). For Medtronic devices, the formula to derive '# seconds with no measures' is (100% minus Compr. Ratio)*0.6.

Compression depth (optional): for those machines capable of reporting compression depth. This data element is required for sites participating in the Philips Feedback Study. A separate approach is taken for each device used:

Medtronic—does not have this feature.

Philips—unit of measure expected to be millimeters (mm). This data element is the calculated average measured depth of compression for a minute, provided on the Detailed Statistics page. Enter data only for minutes where QCPR Review software based its calculation on a full minute of data (where both the puck and pads were placed, and the device in 'defibrillation mode' for the full 60 seconds). Where a portion of the compressions were hand counted (the QCPR Review software did not count compressions for the full 60 seconds), leave the data field blank (do not enter '00') for any minute affected.

ZOLL—units of measure expected to be centimeters (cm)--be certain that the units of measure is <u>not</u> set to inches.

Compression release (optional): for those machines capable of reporting the number of compressions with incomplete release (as assessed by the device) on the upswing of the compression. This data element is required for sites participating in the Philips Feedback Study. A separate approach is taken for each device used:

Medtronic—does not have this feature

Philips—the number of compressions in a given minute with incomplete release (as assessed by the device) on the upswing of the compression. This data element is referred to as “Compressions Leaning” in the QCPR Review report. Enter data only for minutes where QCPR Review software based its calculation on a full minute of data (where both the puck and pads were placed, the device in 'defibrillation mode' for the full 60 seconds, and all compressions were counted by the device). Where a portion of the compressions were hand counted (the QCPR Review software did not count compressions for the full 60 seconds), leave the data field blank (do not enter '00') for any minute affected.

ZOLL—does not have this feature

Peak ETCO2 (optional): for those sites that have continuous end tidal CO2 levels reported as part of the electronic download indicate the average CO2 level over 60 seconds.

Capnography ventilations and # seconds missing (optional)*:* for those sites that have continuous end tidal CO2 levels, record the ventilations per minute as reported by the analysis software. Indicate the number of seconds in a minute (0-60) for which capnography signal was interrupted. If # seconds missing is 60, then no data (do not put '0' as a place holder) should be entered for 'capnography ventilations.'

Complete this form:
for each cardiac arrest episode that was enrolled and/or the ITD was opened.
Main Data Source: ECG strip
Other Data Source: PCR

CPR Process

Date: 10-06-2009
Version: 1.02.00

Episode Information:

Date *(mm/dd/yyyy)* ___ / ___ / ___

ROC PRIMED ID ___

Time call received at dispatch *(hh:mm:ss; 24hr clock)*
___ : ___ : ___ ○ From PCR/other ○ From dispatch
○ Unable to obtain *(Non-ROC agency 1st arrival, patient excluded from trial)*

Incident Number *(optional)* ___

Site-linking ID *(optional)* ___

1. **Does a continuous ECG recording exist for the EMS (includes fire) resuscitation?**
   - ○ No
   - ○ Yes→ For the entire resuscitation or only part? ○ Entire ○ Part of the resuscitation
     → How many EMS recordings are there? ___

2. **Device used:**

Order ECG Placed	Manufacturer: Medtronic	Philips	Zoll	Other	If Other; specify	(Required) Feedback Turned on: Yes	No	Feedback Muted: Yes	No	Recording Exists: Yes	No	Reviewed by site: Yes	No	Attach Recording: File Name
1	○	○	○	○		○	○	○	○	○	○	○	○	Upload
2	○	○	○	○		○	○	○	○	○	○	○	○	Upload
3	○	○	○	○		○	○	○	○	○	○	○	○	Upload

3. **Were any shocks delivered by EMS responders?**
   - ○ No
   - ○ Yes → Number of shocks: ___

4. **Sequence of events:**

Rhythm/Shock Event	NA	Time of Rhythm/Shock *(hh:mm:ss)*	Is this adjusted aligned time? (See Time Record form)	Rhythm *(check one)*: VF/VT (includes AED shock)	PEA	Asystole	Perfusing	AED-No shock, No strip	Cannot Determine	Source *(check one)*: Continuous ECG	Snapshot ECG	PCR	Pause -Pre (time)	Pause -Post (time)
1) 1st CA rhythm with non-EMS AED/defib"	☐	: :	☐	○	○	○	-	○	○	○	○	○	-	-
2) 1st CA EMS rhythm within 10 secs of pad placement	☐	: :	☐	○	○	○	-	○	○	○	○	○	-	-
3) 1st CA EMS rhythm if the line 2 'rhythm = Cannot Determine'	☐	: :	☐	○	○	○	-	○	○	○	○	○	-	-
4) 1st EMS shock assessment	☐	: :	☐	○	○	○	○	○	○	○	○	○	-	-
5) EMS 1st shock" class="lab	☐	: :	☐	○	○	○	-	-	○	○	○	○		
6) Rhythm post shock (90-150 secs*)	☐	: :	☐	○	○	○	○	○	○	○	○	○	-	-
7) Rhythm at next analysis after 1st shock	☐	: :	☐	○	○	○	○	○	○	○	○	○	-	-
8) EMS 2nd shock	☐	: :	☐	○	○	○	-	-	○	○	○	○		
9) Rhythm post 2nd shock (90-150 secs*)	☐	: :	☐	○	○	○	○	○	○	○	○	○	-	-
10) Rhythm at next analysis after 2nd shock	☐	: :	☐	○	○	○	○	○	○	○	○	○	-	-
11) EMS 3rd shock	☐	: :	☐	○	○	○	-	-	○	○	○	○		
12) Rhythm post 3rd shock (90-150 secs*)	☐	: :	☐	○	○	○	○	○	○	○	○	○	-	-

*** If unable to determine @ 90 - 150 seconds, note first evaluable rhythm at least 30 seconds after shock**

Complete this form:
for each cardiac arrest episode that was enrolled and/or the ITD was opened.
Main Data Source: ECG strip
Other Data Source: PCR

CPR Process

Date: 10-06-2009
Version: 1.02.00

Episode Information:

Date *(mm/dd/yyyy)* ___ / ___ / ___

ROC PRIMED ID ___

Time call received at dispatch *(hh:mm:ss; 24hr clock)* ___ : ___ : ___ ○ From PCR/other ○ From dispatch

○ Unable to obtain *(Non-ROC agency 1st arrival, patient excluded from trial)*

Incident Number *(optional)* ___

Site-linking ID *(optional)* ___

5. ECG Analysis:

(hh:mm:ss)

Time first EMS machine turned on: ___ : ___ : ___ OR ☐ Not available → **STOP HERE IF ONLY 1 DEVICE USED**

Time first EMS pads placed: ___ : ___ : ___

Time of arrest if EMS witnessed: ___ : ___ : ___

Time of advanced airway placement: ___ : ___ : ___ OR ○ Unable to determine ○ No advanced airway

Time resuscitation stopped due to death: ___ : ___ : ___ OR ☐ Not applicable

Time of ED arrival: ___ : ___ : ___ OR ☐ Not applicable

6. Did the ECG provide CPR process measurements?

○ No → **STOP HERE**

○ Yes → Complete the following section for the resuscitative effort
(for optional Ventilation study, complete for entire resuscitation effort)

Options for # seconds with No measures
1 - ROSC 2 - Unanalyzable

Device order	Start time (Auto fill) hh:mm:ss	No ECG	# Vent	# Comp	Comp rate	CPR fraction	# secs with No measures → Why	--(Optional)-- Comp depth	Comp release	Peak ET CO_2	Capnography Vents	# secs missing	# audio vents
	1. : :	☐					→						
	2. : :	☐					→						
	3. : :	☐					→						
	4. : :	☐					→						
	5. : :	☐					→						
	6. : :	☐					→						
	7. : :	☐					→						
	8. : :	☐					→						
	9. : :	☐					→						
	10. : :	☐					→						
	11. : :	☐					→						
	12. : :	☐					→						
	13. : :	☐					→						
	14. : :	☐					→						
	15. : :	☐					→						
	16. : :	☐					→						

Person responsible for data on this form: ___

6.5.1 ED Admit Form

The purpose of the ED form is to document information occurring during the Emergency Department (ED) admission. A patient without ROSC who is transported to the ED in order to be pronounced dead should not have an ED form completed. If a patient bypasses the ED and goes directly to the cath lab, the cath lab is considered an admission to the hospital and only minimum information will be required on an ED form.

The ED Admit form should be completed for any patient who qualified for the Pre-hospital form and was transported to the ED with ongoing CPR or ROSC. This includes any episode in which the ITD package was opened, even if the patient was ineligible for ROC PRIMED. The information for the ED Admit form should come from the emergency department records.

The date of the cardiac arrest and the time the call was received at dispatch will be prefilled from the Enrollment form. The ROC PRIMED forms packet is similar to the Epistry and the Hypertonic Saline forms packet, in that each form will have a date and the time call received at dispatch, along with the study ID, incident number, and site linking ID at the top of each page. The information is prefilled by the web data entry program and should be reviewed for accuracy.

If patient bypassed ED and was admitted directly to hospital, complete Items 1 and 3 only, then complete the Hospital Admit form.

Item 1 – *ED admit information*

If the EMS providers bring the patient to the hospital but bypass the ED and take him directly to the ICU/CCU, check “Patient bypassed ED and admitted directly to hospital.” Complete Item 3 on the ED form.

If the patient is transported to the ED, use the pull-down menu to note the name of the emergency department to which the patient was admitted. If your site is large and has more than one hospital with the same name, be sure you select the correct hospital and city from the pull down menu.

Item 2 – *Date/time of ED arrival/admit*

Enter the date the patient arrived at the emergency department. This date may be different from the date on the Patient Enrollment form if the cardiac arrest occurred late in the evening and the patient was not admitted to the ED until early the following morning. Note: Enter the time on the 24-hour clock that the patient was admitted to the ED.

Item 3 – *Demographics (obtained from either ED or hospital information):*

a. Birth year—Enter the year the patient was born. If the year is not noted on the ED Admit but the patient is admitted to the hospital and the year is noted in the hospital records, use that year for the ED Admit form.

b. Race *(check all that apply)*— Check all that apply from the list provided, or if it is unknown/not noted. It is anticipated that race will be either self-reported or indicated by the patient's friends or family during the ED/hospital course of care.

American-Indian/Alaska Native: A person having origins in any of the original peoples of North and South America (including Central America), and who maintains tribal affiliation or community attachment.

Asian: A person having origins in any of the original peoples of the Far East, Southeast Asia, or the Indian subcontinent including, for example, Cambodia, China, India, Japan, Korea, Malaysia, Pakistan, the Philippine Islands, Thailand, and Vietnam.

Black/African-American: A person having origins in any of the black racial groups of Africa. Terms such as "Haitian" or "Negro" can be used in addition to "Black or African American."

Native Hawaiian/Pacific Islander: A person having origins in any of the original peoples of Hawaii, Guam, Samoa, or other Pacific Islands.

White: A person having origins in any of the original peoples of Europe, the Middle East, or North Africa.

Unknown/Not noted: Health care provider is not able to determine the patient's race and notes it in the patient care record, or information has not been recorded.

c. Ethnicity: (*Check one only)*—Check one only from the list provided.

Hispanic or Latino: A person of Cuban, Mexican, Puerto Rican, South or Central American, or other Spanish culture or origin. The term, "Spanish origin," can be used in addition to "Hispanic or Latino."

Non Hispanic or Latino: A person does not indicate their Hispanic or Latino ethnicity or they do not meet the definition for Hispanic or Latino.

Unknown/Not noted: Health care provider is not able to determine the patient's ethnicity and notes it in the patient care record, or information has not been recorded.

Item 4 – *Major procedures while in the ED*

If no major procedures were performed while the patient was in the ED and prior to death or admission to the hospital, check the “No major procedures” bubble. For the following procedures, check the bubble for “NA/NR” (not applicable/not recorded) or “Done.”

CPR, manual--Indicate if manual chest compressions were delivered in the ED.

Manual CPR—Indicate if Mechanical chest compressions were delivered (as with a Thumper if the ED notes indicate CPR was performed in the ED.

Chest X-ray results—Indicate 'done' if results are available for a chest x-ray taken during the ED course of care. If results for more than one chest x-ray taken during the ED stay, enter results of the first CXR only.

a. Specific notations: *(check all that apply)*—Chest X-rays are frequently done in the ED prior to admission to the hospital. If a chest X-ray was done, review the radiology report and note whether the following specific wording was used: alveolar pulmonary edema, bilateral pleural effusion, pulmonary venous congestion, interstitial pulmonary edema, or cardiomegaly were noted.

b. Was pulmonary edema noted?—Check "Yes" or "No" to indicate whether it was noted on the report. If the ROC PRIMED Coordinator has any question as to the meaning of the radiology report, the site PI or ROC PRIMED Investigator should be consulted in order to complete this data item.

Fibrinolytics--Indicate if fibrinolytics were given during the ED. Some examples of fibrinolytics are TNKase (tenecteplase); Retrovase (Reteplase); Streptase; kabikinase (streptokinase).

–

Hypothermia therapy—If hypothermia therapy was given in the ED, indicate the time it was started and the lowest temperature in either Centigrade or Fahrenheit which is noted in the ED record after the therapy was begun. If hypothermia was begun by the EMS in the prehospital setting and continued in the ED, enter the time of ED admit as the 'time started' for ED hypothermia therapy.

Other major cardiac procedure—If another major cardiac procedure was done in the emergency department, check that bubble and indicate what procedure or procedures were done. 'Other major' cardiac procedures might include open chest cardiac massage, pericardiocentisis tracheotomy, etc.

Item 5– *Possible pre-hospital complications diagnosed in ED or autopsy: (check all that apply)*

After reviewing the ED records and the autopsy report (if done), check whether any pre-hospital complications were noted, whether there was evidence of pulmonary edema by the first CXR within 48 hours of the cardiac arrest, airway bleeding (bloody fluid or frank blood observed in the oro- or naso-pharynx region or advanced airway) *not previously reported* on the Pre-Hospital form, or if there were other possible pre-hospital complications noted in the reports. It is not the intention of this report of possible pre-hospital complications to capture conditions where *only* pink frothy sputum or blood-tinged fluid was observed. It is the intent of this report of complications to capture those possibly related to the pre-hospital course of care; airway bleeding attributed to the pre-hospital timeframe would be expected to occur within 24 hours of the cardiac arrest. If "Other" is checked, enter and describe the complication or complications which were found.

Item 6– *ED discharge status (check one only)*

Choose the bubble to indicate the patient's status after arriving at the emergency department for which this ED Admit form has been initiated. If the patient was admitted to the hospital from this ED, complete the Hospitalization form. If the patient was transferred from this ED directly to another hospital (bypassing other EDs), from the present ED, check that bubble and complete the Hospital form. If the patient died in this ED prior to admission to the hospital, check the "Died in ED" bubble. If the patient was transferred to another ED, complete a separate ED Admit form for the emergency department which the patient was transferred to. If the patient was discharged alive (or left AMA. against medical advice) from the ED for which this ED Admit form has been initiated, check this bubble. We do not expect any true cardiac arrest patient to be discharged alive or leave AMA from the ED, so this button may never or rarely be checked. It is possible that an ITD package is opened, when in retrospect the patient never experienced a cardiac arrest, the EMS never shocked or gave the patient CPR, and the patient was discharged alive from the ED, but, again, this should be rare.

Item 7 – *Date and time of ED discharge, admit to hospital, or death*

Indicate the date and time that the patient is either discharged (rare), admitted to the hospital, transferred to another ED, or declared dead while in the ED for which this ED Admit form has been initiated. **If patient admitted to hospital or transferred to another ED, skip Item 8**, as the 'Etiology of Arrest' as classified by the site will be completed on the Hospital form or the ED Admit form associated with the final disposition ('died in ED' or 'discharged alive from ED.')

Item 8 – *Etiology of arrest*

This item is completed for the ED admission that is associated with the final vital status (either 'died in ED' or 'discharged alive from ED'. Skip this item if the patient was either admitted to the hospital or transferred to another ED at the conclusion of this visit.

a. Site Classification *(based on all available information including prehospital records, ED notes, lab results and/or public records)* If no obvious cause is found for the cardiac arrest from the obvious cause list below, check "No obvious cause identified" ('presumed cardiac') for this item. If the site Coordinator determines that the CA occurred due to a non-cardiac cause, check "Obvious cause" Mark 'obvious cause' only when the cause of out of hospital cardiac arrest clearly meets the below defined criteria. Indicate the 'obvious cause' in column A.

b. Were there contributing factors directly related to this cardiac arrest? *(based on all available information including ED notes and public records)* Check "None noted" if no factors were present. If contributing factors were present, check "Yes." This section is intended to capture the variety of factors that were observed by, or reported during the course of prehospital and ED care. The site coordinator will mark all applicable conditions that are documented in the patient record (whether narrative or check item format) that may have been related to the cardiac arrest. It is not necessary for a 'contributing factor' to meet the same burden of proof as does 'obvious cause' for Etiology of Arrest: Site Classification. Check all contributing factors that appear to be directly related to this cardiac arrest. See below defined criteria for Contributing Factor.

Definitions for ‘Obvious Cause’ of arrest:

Anaphylaxis: Cases of sudden collapse with other clear signs of anaphylaxis including urticaria, facial and tongue swelling, respiratory distress, and clear exposure to an allergen (e.g., bee sting or ingested food with known allergy) that triggered the event. In addition to these physical and historical findings, an Epipen (intramuscular injectable source of epinephrine) may have been used. However, a used Epipen without physical signs of anaphylaxis (or witnessed by bystanders) is not diagnostic for this etiology option.

Chemical poisoning (intentional or unintentional, includes carbon monoxide, toxic gases): This category does NOT include prescribed medications, recreational drugs, or ethanol (see “Drug Poisoning”). However, isopropyl alcohol, ethylene glycol and methanol are included as “chemical poisoning”. This category will include all cases where there is high likelihood that the cardiac arrest would not have occurred in the absence of a poison. Chemical poisons are considered substances that would not normally be ingested, inhaled or consumed and may be environmental or industrial, including such items as insecticides, herbicides, industrial gases, cleaning solutions, carbon monoxide sources (e.g., automobile exhaust or space heaters), or similar compounds. The cardiac arrest timing and clinical scenario should be consistent with the presumed chemical poisoning. This etiology includes both intentional chemical poisoning (i.e., cases where ingestion, inhalation or contact with a chemical poison for the purposes of suicide is clear - suicide note, witnesses confirm discussion of suicidal intent or witnessed clear impulsive intentional ingestion temporarily related to the collapse), and unintentional chemical poisoning (cases where witnessed chemical exposure precedes the collapse by 3-5 minutes). This category would include cases where witnesses confirm contact with a chemical poison just prior to collapse or hospital work-up later confirms.

Drowning: victim is found by provider or bystanders submersed in water without an alternative causation.

> Examples of cases that fit this definition include; young and presumably healthy person found floating in the water with no evidence of overdose or drug ingestion; in the absence of other contributing factors, any patient who was witnessed to be choking or coughing before going under water; water in lungs found at autopsy.
>
> Examples of cases that do NOT fit this definition include; patients who suffer trauma immediately prior to falling in the water (the case should be entered in the trauma, not the cardiac, patient cohort; for patients presumed to be older than 39 years of age one cannot be certain whether the submersion or some medical event was the cause of death so 'no obvious cause' would generally be selected; person who was inebriated or toxic on a drug who then drowned (the case should be classified as 'no obvious cause').
>
> References: *S*alomez F, Vincent JL. Drowning: a review of epidemiology, pathophysiology, treatment and prevention. *Resuscitation.* 2004 Dec;63(3):261-8.
>
> Idris AH, Berg J, Bierens L, et al. Recommended guidelines for uniform reporting of data from drowning: the 'Utstein style.’ *Circulation.* 2003 Sept; 108:2565-2574.

Drug poisoning (intentional or unintentional, includes ethanol): This category includes prescribed medications, recreational drugs, and ethanol. Intentional drug overdose may include cases where ingestion of a drug (i.e., prescribed or over the counter medication, recreational

drugs including alcohol) for the purposes of suicide is clear (suicide note, witnesses confirm discussion of suicidal intent or witnessed clear impulsive intentional ingestion temporarily related to the collapse). Unintentional drug overdose may include cases where witnessed inhaled or intravenous or oral recreational drug use immediately precedes the collapse. The Drug Poisoning category includes cases where witnesses confirm the situation, for example an injection of heroin just prior to collapse or where the evidence strongly suggests immediate use prior to arrest (e.g., tourniquet on arm and empty syringe at side).

> Examples of cases that fit this definition; a victim collapses and there are empty pill bottles or ethanol containers at the scene with clear evidence of suicidal intent.
>
> Examples of cases that DO NOT fit this definition; patient with a history of recreational drug use within 24 hours of the event (e.g., adolescent found collapsed at a party or the known alcoholic found dead the morning after heavily imbibing); classify these types of cases as 'no obvious cause' (presumed cardiac).

Electrocution (non-lightning): This category includes all cases where the patient has an electrical cutaneous burn in the setting of contact with a high voltage source. Electrocution would also be the obvious choice if the victim was found attached or nearly so, to a high-tension source of current. This category also includes all cases where the patient has been removed from the source of high tension current but the event was witnessed.

Excessive cold: Low ambient temperature (below 32F or 0C) where an obviously healthy individual is inappropriately clothed for the ambient temperature.

Excessive heat: Situations in which an obviously healthy person experiences a cardiac arrest and the most significant contributing factor is increased ambient temperature i.e., exercise on a hot day or confined in a locked car or lost hiking in the desert.

> Examples of cases that fit this definition; the inebriated patient found outside for a prolonged period of time exposed to extreme heat.

Foreign body obstruction: Cases of sudden airway obstruction leading to cardiac arrest due to ingestion of a foreign body identified by history or by direct visualization within the airway. Some of these cases may be preceded by choking.

> Examples of cases that fit this definition include; small child (age 4 or less) choking after a balloon popped in front of their face or after eating a hot dog and succumbs to cardiac arrest; or man observed to be eating and suddenly begins to choke and hold his throat prior to collapsing; or on intubation a foreign body is visualized +/- removed.
>
> Examples of cases that DO NOT fit this definition include: paramedics report inability to ventilate the patient and presume airway obstruction without finding the source of the obstruction;

Hanging: Cases of sudden airway obstruction leading to cardiac arrest secondary to hanging. Requires either the presence of ligature present around the neck, found hanging, or marks on the neck compatible with a previous ligature in the setting that suggests this was the obvious cause of death.

Examples of cases that fit this definition; case in which the victim is found with a rope around the neck after fire or police have cut them down from a gallows equivalent

Examples of cases that would NOT fit this definition: victim has a ligature around the neck without any evidence at the scene of any attempt to hang himself; a victim who has been strangled by an assailant's hands during an altercation (this case would be classified as 'obvious cause' Strangulation).

Lightning: cases of cardiac arrest where the event was directly attributed to lightning strike or blast effect from lightning temporally related to the event i.e., immediately following the strike, burn marks on the ground or nearby objects, melting of metal objects, or documented classic signs of electrocution by lightning.

Examples of cases that fit this definition: witnessed lightning strike on golf course where members of a foursome documented direct hit to one of their group and called 911; or unwitnessed cases where there are visible signs of lightning strike including cutaneous burns described as Lichtenburg figures, flash burns, punctuate burns, contact burns, or linear burns in the skin folds.

Example of a case that does NOT fit this definition: man found outside in the rain without witnesses to verify direct strike or blast effect or any signs or symptoms of lightning related electrocution.

Mechanical suffocation: Mechanical suffocation causing arrest is distinct from hanging, strangulation, choking, respiratory, anaphylaxis, or SIDS etiologies. This category will rarely be coded. It is included for a unique and very specific group of patients who arrest because of suffocation due to an external physical barrier.

Examples of cases that fit this definition: someone with the plastic bag over the head; a pillow or another object was used to suffocate the patient; or a child or adult with tracheostomy site who develops an obstruction.

Non-traumatic exsanguination: This category includes the rare situation where it is highly likely that the patient "bled to death" in a short period of time and there is strong evidence that acute and catastrophic loss of blood was the direct cause of the arrest.

Examples of cases that fit this definition: hemodialysis line disconnected with obvious large loss of blood; vomiting of blood with EMS witnessed and documented large loss of blood; blood in stool (lower GI bleed) with EMS witnessed and documented large loss of blood.

Examples of cases that DO NOT fit this definition: vomiting blood with unknown amount or small amount on face or clothes; possible or suspected ruptured aortic aneurysm (this can never be proven without autopsy or diagnostic imaging); epistaxis; hemoptysis

Radiation: This etiology will be rarely coded. Cardiac arrest due to radiation requires an acute and massive radiation exposure that temporally (typically within seconds to minutes) produces a cardiac arrest.

Examples of cases that fit this definition: industrial exposure or terrorist event with presumed high radiation levels.

Respiratory: Adult cardiac arrest due to primary respiratory cause requires that the patient have 1) an established medical history of asthma and 2) a witnessed reported clinical course prior to arrest implicating asthma. Although there are no absolutes, death due to asthma (as a respiratory 'obvious cause') would generally be expected to evolve over hours or even days with progressive shortness of breath as the principal symptom rules. Pediatric (patients < 16 years) cardiac arrest due to primary respiratory cause requires that the patient have 1) an established history of an underlying disease that places the patient at higher risk for respiratory disease (see below examples) and 2) a witnessed reported clinical course of an acute respiratory problem prior to the arrest.

Examples of adult cases that fit this definition: a) 54 yo male with history of asthma, hospitalized previously, who experienced progressive shortness of breath over the past day following URI for past week. He has been using inhalers around the clock since yesterday and took an extra dose of prednisone this morning. His spouse called 9-1-1 when his respiratory symptoms made him unable to talk or answer questions. No chest pain or prior heart history. EMS arrives to find the patient unresponsive without pulse or respirations. Rationale: Several circumstances suggest a primary respiratory arrest: 1) the history suggests that he has fairly significant asthma, the clinical circumstances are highly consistent with an asthma exacerbation with similar past events, and there is information indicating that he did not have clinical heart disease. Hence the level of information sufficiently implicates a respiratory mechanism as the primary cause; b) 16 year old woman with a history of asthma witnessed by bystander or responder to have inspiratory and expiratory wheezing prior to in cardiac arrest.

Examples of pediatric cases (patients < 16 years of age) that fit this definition: a) Child receiving chronic oxygen therapy or respiratory assistance, such as a premature infant at home on oxygen with an increase in oxygen requirement over the previous hours or days; b) Child with acute febrile respiratory illness in the days or hours prior to arrest, such as an otherwise healthy child with a presumed respiratory infections disease preceding the event; c) child with history of asthma and progressive acute respiratory distress (“asthma attack”) whereby witnessed respiratory distress progresses over hours until he/she cannot talk, then turns blue, and collapses.

Examples of cases that do NOT fit this definition include: a) 65 yo male with history of COPD (home oxygen dependent) and heart disease (prior bypass) was last seen at breakfast by his wife. He had no complaints at that time. When she returned home later that morning she found him unresponsive on the couch with his home nebulizer running. She called 9-1-1 and the EMS arrived to find him without pulse or respiration. Rationale: Although the patient had fairly severe chronic lung disease, he did not have clear prodromal symptoms or signs indicating progressive respiratory decline. The scene was suggestive that he experienced some symptoms prior to death since the nebulizer machine was running but this could have been due to a variety of cardiopulmonary symptoms. This patient should be classified as no obvious cause (presumed cardiac); b) 75 yo female nursing home resident develops cough for at least 1 day and then increasing shortness of breath this morning. The nursing home staff had provided oxygen and an albuterol but without relief. At the time of the 9-1-1 call she was awake but unable to speak due to extreme respiratory distress. When EMS arrives she is

unresponsive without pulse or blood pressure and nursing staff have initiated CPR. Her history is notable for history of asthma for which she uses 2 different inhalers. Rationale: The patient did have some history of lung disease and some symptoms of progressive dyspnea. However the severity of lung disease is not clear and the symptoms could be consistent with other etiologies of arrest. For example, this patient could be manifesting congestive heart failure or pulmonary embolism. Although a judgment, the level of information leaves some question as to whether respiratory disease was the primary etiology. The best etiology classification for this patient would be 'no obvious cause' (presumed cardiac).

Examples of pediatric cases (patients <16 years of age) that do NOT fit this definition: a) Developmentally disabled child without a supported airway found pulseless and apneic, such as 6 year old child with cerebral palsy and limited ambulation found pulseless and apneic in bed (this case would be coded as 'no obvious cause'); b)child with a supported airway (i.e., Tracheostomy) and found pulseless and apneic (this case would be coded as 'obvious cause' mechanical suffocation); c) prior history of congenital heart disease and no other 'obvious cause' identified—congenital heart disease is not an etiologic classification, but should be included as a 'contributing factor.' This case would be coded as 'no obvious cause' (presumed cardiac).

SIDS (sudden infant death syndrome, less than 12 months of age): Cases of death where an infant, ages 1 month to 12 months is found in their crib/bed and death was unwitnessed. All three criteria—age, crib/bed location, and unwitnessed death—must be present to be categorized as SIDS. Background of sudden infant death syndrome: The American Academy of Pediatrics—SIDS, also called crib or cot death, is the sudden death of an infant under 1 year of age that remains unexplained after thorough case investigation, including performance of a complete autopsy, examination of the death scene, and a review of the clinical history. [NOTE: Site classification of etiology of arrest for classification of SIDS as an obvious cause is to be determined solely from the prehospital patient care record. SIDS is the most common cause of death between 1 and 6 months of age. The incidence of SIDS peaks between 2 and 4 months of age. Approximately 90% of SIDS deaths occur before the age of 6 months.]

SIDS is suspected when a previously healthy infant, usually younger than 6 months, is found dead in bed, prompting an urgent call for emergency assistance. Often, the baby is fed normally just before being placed in bed to sleep, no outcry is heard, and the baby is found in the position in which he or she had been placed at bedtime or naptime. In some cases, cardiorespiratory resuscitation initiated at the scene by emergency personnel is continued without apparent beneficial effect en route to the hospital, where the baby is finally declared dead. Evidence of terminal motor activity, such as clenched fists, may be seen. There may be serosanguineous, watery, frothy, or mucoid discharge coming from the nose or mouth. Skin mottling and postmortem lividity in dependent portions of the infant's body are commonly found. Review of the medical history, scene investigation, radiographs, and autopsy are unrevealing.

The Canadian Pediatric Society refers to SIDS as the sudden and unexpected death of an apparently healthy infant usually less than one year of age, which remains unexplained even after a full investigation. On average, 3 infants a week are reported to die of SIDS in Canada. Although in Canada there has been a decrease in the number of infant deaths reported as SIDS, it still remains a significant public health concern.

Aboriginal infants have a risk of SIDS that is higher than the risk to non-Aboriginal infants.

Example of pediatric cases (less than 12 months of age) that are included: Although there is some controversy and a few documented cases of long QT causing what appears to be SIDS, the evidence supports that most are related to respiratory issues. A case can be made that this is mechanical suffocation, but that cannot reliably be done in the absence of a thorough review of the history and even location of the death. We need to be consistent with this as we will have many cases of this and CPR will be delivered.

Smoke inhalation: Cases of collapse in a fire setting with significant smoke exposure. This is defined as the patient who was exposed to fire in a closed space (Ryan et al N Engl J Med, 1998).

Strangulation: The impression of EMS responders is that the patient's most significant condition that led to cardiopulmonary arrest is strangulation. Strangulation is a form of asphyxia (though not categorized as 'obvious cause' asphyxia) characterized by closure of the blood vessels or air passages of the neck as a result of external pressure on the neck (McClane et al J Emerg Med 2001) The paramedic usually describes crush marks around the neck.

Examples of cases that fit this definition: victim becomes non-responsive during a witnessed altercation where the assailants hands were around the neck.

Examples of cases that would NOT fit this definition: a) where the individual was involved in an altercation and becomes unresponsive without witnesses documenting strangulation just prior to collapse; b) victim has bruising around the neck without documented history of strangulation related to the collapse;

Terminal illness (includes end-stage diseases such as cancer): Death due to "terminal" condition is one in which death is expected and for which there is evidence of poor function or functional decline prior to death. Both conditions need to be met. Terminal condition will most often be considered in patients with advanced cancer. An individual whose function is declining and for whom death is expected should be classified as terminal illness (see below examples).

Examples of cases that fit this definition: a) 45 year old woman is found unresponsive and not breathing. She has advanced pancreatic cancer and is enrolled in an experimental treatment protocol. She has been sleeping mostly during the last week because of weakness and malaise and has declined to return to the hospital. She was quite difficult to arouse earlier in the day; b) 88 yo male with liver cancer who has been mostly bedridden the past month. He has been progressively more confused over the last two days to the point where his caretaker could not wake him.

Examples of cases that do NOT fit this definition: a) Patient with advanced cancer who is reasonably functional – carrying out ADLs, living independently, and collapses would be classified as "no obvious cause" (presumed cardiac); b) 68 yo male with metastatic colon cancer ("his cancer had spread to his lung and liver" per bystander son) who collapsed while walking in the park. "He had gotten a bit weaker over the past year but seemed fine today". The son is not aware of other conditions or medications. Classify this case as 'no obvious cause' (presumed cardiac); c) 71 yo female found unresponsive by her husband. She has lung cancer that has spread to her bones and a past history of a

"heart attack" 2 years ago. Her husband reports that "she has been receiving radiation treatment for the cancer and the doctors weren't sure how long she had." This morning she had no complaints and they were leaving the house to go shopping when she collapsed. Classify this case as 'no obvious cause' (presumed cardiac).

Trauma (includes blunt, penetrating or burns): Patients who have experienced a cardiac arrest directly caused by blunt, penetrating or burn injury should be enrolled in ROC PRIMED only if the ITD was opened.

Examples of cases that do NOT fit this definition: a patient scenario where it is clear from the bystander history that the patient collapsed due to some medical condition prior to experiencing the trauma. This patient would be entered in the cardiac arrest cohort and if the etiology of the arrest is unclear, would be marked 'no obvious cause' (presumed cardiac).

Venomous stings and venomous bites: This category will include all cases where there is visual evidence or witnessed attack of a venomous organism (e.g., animal, reptile, insect) that immediately preceded and presumably precipitated the cardiac arrest. Evidence for the sting must include visible localized skin findings (e.g., local erythema or edema at site) and/or witnessed report by bystanders of history that supports this etiology. If a venomous sting precipitated anaphylaxis, the obvious cause "Anaphylaxis" should be marked.

Definitions for 'Contributing Factors'

Anaphylaxis: Signs of anaphylaxis including urticaria, facial and tongue swelling, respiratory distress, and clear exposure to an allergen (e.g. bee sting or ingested food with known allergy) that triggered the event. An Epipen (intramuscular injectable source of epinephrine) may have been used.

Chemical poisoning (intentional or unintentional, includes carbon monoxide, toxic gases): This category does NOT include prescribed medications, recreational drugs, or ethanol (see "Drug Poisoning"). However, isopropyl alcohol, ethylene glycol and methanol are included as "chemical poisoning". Chemical poisons are considered substances that would not normally be ingested, inhaled or consumed and may be environmental or industrial, including such items as insecticides, herbicides, industrial gases, cleaning solutions, carbon monoxide sources (e.g. automobile exhaust or space heaters), or similar compounds.

Dialysis: The patient was undergoing or very recently underwent dialysis treatment (peritoneal or hemodialysis). This does not include exsanguination secondary to disconnection of dialysis shunts—see 'non-traumatic exsanguination.'

Drowning: victim is found by provider or bystanders submersed in water or witnessed to be choking or coughing before going under water.

Drug poisoning (intentional or unintentional, includes ethanol): Includes prescribed or over the counter medications, recreational drugs, and ethanol (alcohol).

Electrocution (non-lightning): This category includes all cases where the patient has an electrical cutaneous burn in the setting of contact with a high voltage source. Electrocution would be also the obvious choice if the victim was found attached or nearly so, to a high-tension source of current. This category also includes all cases where the patient has been removed from the source of high tension current but the event was witnessed.

Excessive cold: Low ambient temperature (below 32F or 0C) where an obviously healthy individual is inappropriately clothed for the ambient temperature.

Excessive heat: High ambient temperature i.e., exercise on a hot day or confined in a locked car or lost hiking in the desert.

*Foreign body obstruction: S*udden airway obstruction due to ingestion of a foreign body identified by history or by direct visualization within the airway. Some of these cases may be preceded by choking.

Hanging: Cases of sudden airway obstruction secondary to hanging. Patient may have a ligature present around the neck, be found hanging, or have marks on the neck compatible with a previous ligature.

Lightning: cases of cardiac arrest where a lightning strike or blast effect from lightning temporally related to the event i.e., immediately following the strike, burn marks on the ground or nearby objects, melting of metal objects, or documented classic signs of electrocution by lightning.

Mechanical suffocation: Mechanical suffocation is distinct from hanging, strangulation, choking, respiratory, anaphylaxis, or SIDS etiologies. It includes suffocation due to an external physical barrier. May include someone with a plastic bag over the head; pillow or another object used to suffocate the patient; or a child or adult with a tracheostomy site who develops an obstruction.

Non-traumatic exsanguination: There is evidence that acute and catastrophic loss of blood occurred in a short period of time. May include disconnection of a hemodialysis line; vomiting of blood; blood in stool.

Radiation: Radiation requires an acute and massive radiation exposure that temporally (typically within seconds to minutes) produces a cardiac arrest. May include industrial exposure or terrorist event with presumed high radiation levels.

Respiratory: Adult cardiac arrest due to a medical history of COPD or asthma or a witnessed reported clinical course prior to arrest implicating respiratory difficulties. May evolve over hours or even days with progressive shortness of breath as the principal symptom rules. May have been using inhalers with increased frequency or increased dose of prednisone. May have been at home with oxygen with an increase in oxygen requirement over the hours prior to arrest. Pediatric (patients < 16 years) cardiac arrest due to 1) an established history of an underlying disease that places the patient at higher risk for respiratory disease (see below examples) and 2) a witnessed reported clinical course of an acute respiratory problem prior to the arrest. This does not include a child with a supported airway (i.e., Tracheostomy) found pulseless and apneic--this would be 'mechanical suffocation.'

SIDS (sudden infant death syndrome, less than 12 months of age): Cases of death where an infant, ages 1 month to 12 months is found in their crib/bed and death was unwitnessed. All three criteria—age, crib/bed location, and unwitnessed death—must be present to be categorized as SIDS. See Etiology of arrest 'Obvious cause' definitions for background on SIDS.

Smoke inhalation: Cases of collapse in a fire setting with significant smoke exposure. This is defined as the patient who was exposed to fire in a closed space (Ryan et al N Engl J Med, 1998).

Strangulation: Strangulation is a form of asphyxia (though not categorized as 'contributing factor' asphyxia) characterized by closure of the blood vessels or air passages of the neck as a result of external pressure on the neck (McClane et al J Emerg Med 2001) The paramedic usually describes crush marks or bruising around the neck.

Terminal illness (includes end-stage diseases such as cancer): "Terminal" illness is one in which death is expected and for which there is evidence of poor function or functional decline prior to death.

Trauma (includes blunt, penetrating or burns): Patients who have experienced a cardiac arrest directly caused by blunt, penetrating or burn injury are not intended to be enrolled in ROC PRIMED.

Venomous stings and venomous bites: This category will include cases where there is evidence or witnessed attack of a venomous organism (e.g., animal, reptile, insect) that immediately preceded and presumably precipitated the cardiac arrest. Evidence may include visible localized skin findings (e.g., local erythema or edema at site) and/or witnessed report by bystanders of history that supports this etiology. If a venomous sting precipitated anaphylaxis, the contributing factor "Anaphylaxis" should be marked.

Other obvious cause, specify: enter other causes that are obviously related to this arrest (60 characters maximum).

Person responsible for data on this form

Name of the individual that logged into the electronic data transmission system for clinical study forms. This individual will have registered as a member with the CTC for the purpose of participating as a coordinator or investigator in a ROC clinical trial and has designated a user name and password as their "Electronic Signature." The individual has agreed to consider their electronic signature as equivalent to their handwritten signature, to maintain the confidentiality of their user name and password, and to not let others use it. Refer to the "Electronic Signature Agreement" (accessed after logging on to the ROC website) posted at https://roc.uwctc.org/tiki/roc-data-entry.

After verifying the entered data and electronic signature are correct, print the web-forms for your files, or convert the web-forms to PDF format and store electronically. Edits made later to the original web-entered forms are associated with the electronic signature of the individual making the changes and are documented in the file's edit history.

Complete this form:
- episode qualifying for the Pre-hospital Form and the patient was admitted to the ED or the Hospital
- one for each ED patient admitted to

Main data resource: ED records

ED Admit

Version 1.01.01
Date: 02/24/2009

Episode Information:

Date *(mm/dd/yyyy)* ___/___/___

Time call received at dispatch *(hh:mm:ss; 24hr clock)* ___:___:___

○ From PCR/other ○ From dispatch

○ Unable to obtain *(Non-ROC agency first arrival & no agreement in place to get data, patient is excluded from Trial)*

ROC PRIMED ID: ___-___-___

Incident Number *(optional)*

Site Linking ID *(optional)*

1. ED admit information:

☐ Patient bypassed ED and admitted directly to hospital → Complete **Item 3** only, then complete **Hospital Admit** form.

ED name:

2. Date/time of ED arrival/admit:

Date: ___/___/___ *(mm/dd/yyyy)* Time: ___:___ *24 hr clock(hh:mm)*

3. Demographics (obtained from either ED or hospital information):

a. Birth year: ____ *(yyyy)*

b. Race *(check all that apply)*

☐ American-Indian/Alaska Native

☐ Asian

☐ Black/African-American

☐ Native Hawaiian/Pacific Islander

☐ White

☐ Unknown/not noted

c. Ethnicity: *(check one only)*

○ Hispanic or Latino

○ Not hispanic or Latino

○ Unknown/not noted

4. Major procedures while in the ED:

☐ No major procedures from the list below were noted

NA	NR	Done	
○	○	○	CPR, Manual
○	○	○	CPR, Mechanical
○	○	○	Chest X-ray results

a. Specific notations: *(check all that apply)*

☐ Alveolar pulmonary edema ☐ Bilateral pleural effusion ☐ Pulmonary venous congestion

☐ Interstitial pulmonary edema ☐ Cardiomegaly ☐ None of these noted

b. Was pulmonary edema noted?

○ Yes ○ No

○	○	○	Fibrinolytics
○	○	○	Hypothermia therapy:

Time started ___:___ *24 hr clock(hh:mm)*

Lowest temperature ____ degrees → ○ Centigrade ○ Fahrenheit

○	○	○	Other major cardiac procedure: *(30)*

continue to next page

Episode Information:

Date *(mm/dd/yyyy)* ___/___/___

Time call received at dispatch *(hh:mm:ss; 24hr clock)* ___:___:___

○ From PCR/other ○ From dispatch

○ Unable to obtain *(Non-ROC agency first arrival & no agreement in place to get data, patient is excluded from Trial)*

ROC PRIMED ID: ___-___-___

Incident Number *(optional)*

Site Linking ID *(optional)*

5. **Possible pre-hospital complications related to study protocol or ITD use diagnosed in ED or autopsy :** *(check all that apply)*

   ☐ None Noted

   ☐ Evidence of Pulmonary Edema found on CXR within 48 hours of arrest
   ☐ Airway bleeding not reported on the Pre-hosp form
   } Complete **Alert CTC** form

   ☐ Other, describe: *(30)*

6. **ED discharge status:** *(check one only)*

   ○ Admitted to hospital → Complete **Hospital Admit** form

   ○ Transferred directly to another hospital (bypassing other EDs) → Complete the **Hospital Admit** form.

   ○ Died in ED

   ○ Transferred to another ED

   ○ Discharged alive (or left AMA) from ED

7. **Date and time of ED discharge, admit to hospital, transfer to another ED, or death:**

   Date: ___/___/___ *(mm/dd/yyyy)* Time: ___:___ *24 hr clock(hh:mm)*

If patient admitted to hospital or transferred to another ED, skip Item 8.

continue to next page

Episode Information:

Date *(mm/dd/yyyy)* ___/___/___

Time call received at dispatch *(hh:mm:ss; 24hr clock)* ___:___:___

○ From PCR/other ○ From dispatch

○ Unable to obtain *(Non-ROC agency first arrival & no agreement in place to get data, patient is excluded from Trial)*

ROC PRIMED ID: ___-___-___

Incident Number *(optional)*

Site Linking ID *(optional)*

8. Etiology of Arrest:

a. Site Classification *(based on all available information including ED notes and public records)*

○ No obvious cause identified (Ut stein"presumed cardiac")

○ Obvious cause → *(check one cause in Column A below)*

b. Were there contributing factors directly related to this cardiac arrest?

(based on all available information including ED notes and public records)

— See Manual of Operations for expanded definitions

○ None noted → *Do Not complete Column B below*

○ Yes → *(check all that apply in Column B below)*

Obvious Cause	A Site Classification	B Contributing Factors
Anaphylaxis	○	☐
Chemical poisoning *(intentional or unintentional, includes carbon monoxide, toxic gases)*	○	☐
Dialysis	-	☐
Drowning	○	☐
Drug poisoning *(intentional or unintentional, includes alcohol)*	○	☐
Electrocution *(non-lightning)*	○	☐
Excessive cold	○	☐
Excessive heat	○	☐
Foreign body obstruction	○	☐
Hanging	○	☐
Lightning	○	☐
Mechanical suffocation	○	☐
Non-traumatic exsanguination	○	☐
Radiation exposure	○	☐
Respiratory	○	☐
SIDS *(sudden infant death syndrome)*	○	☐
Smoke inhalation	○	☐
Strangulation	○	☐
Terminal illness *(includes end-stage diseases such as cancer)*	○	☐
Trauma *(includes blunt, penetrating or burns)*	○	☐
Venomous stings	○	☐
* Other obvious cause	○	☐

* Other cause (A - Site classification): (60)

* Other cause (B - Contributing Factors): (60)

6.6.1 Hospital Admit Form

The purpose of the Hospital Admit form is to document the major procedures occurring during hospitalization, possible complications due to the study intervention treatment, determination of the cause of cardiac arrest (either no obvious cause or obvious cause), potential contributing factors to the cardiac arrest, the cerebral performance category, the Modified Rankin Scale at discharge, and the outcome of the patient. The source of data for this form is the hospital records.

Admittance to the hospital is defined as completion of hospital admission paperwork. Most patients will arrive in the emergency department and then be transferred to the hospital intensive care unit, though some patients may be admitted directly from the ambulance to the intensive-care unit. The episode date, time and episode ID will be prefilled by the web data entry program. It will be consistent with the date and time recorded on the Patient Enrollment form. It should be reviewed for accuracy.

Item 1 – *Hospital admit information (1st hospital)*

Enter the date the patient was admitted to the first hospital, the hospital name, and the hospital zip/postal code. This may or may not be the same location as the 1st ED. The hospital names and zip/postal codes are a pull-down menu from information entered by the site in the EMS structures database. If 'not in list' selected, the form must be saved with errors; then update EMS structures with the needed hospital information, if it is a ROC hospital with IRB or MOA allowing record review for ROC PRIMED. If 'unknown' selected, you must indicate why the hospital destination was unknown.

Item 2 – *Was the patient transferred to another hospital before discharge?*

Indicate whether or not the patient was admitted to more than one hospital during the course of treatment, and if yes, use the pull-down menu to document the name or names of subsequent hospitals the patient was admitted to in a chronological order. Enter the date of the transfer from one hospital to the next by noting the date of arrival to the right of the hospital listed. If the patient was admitted to more than one acute care hospital, ED and hospital records will need to be reviewed for all hospitals and all information entered on one hospital form. Hospital records are usually sent with the patient when he is transferred to another hospital, thus the potential for you to review the records at the final hospital.

Item 3 – *Major procedures while in the hospital*

If no major procedures from the list in Item 3 were done while the patient was hospitalized, check the applicable box. If one or more procedures 'done' , indicate "Not Applicable/Not Required" or "Done" for each of the listed procedures.

CPR—Indicate if CPR was done in the hospital. If the patient received CPR in the emergency department but did not receive CPR once admitted to the hospital, ICU or ward, indicate "NA/NR."

Chest X-ray within 48 hours of arrest—Complete this item only if no chest X-ray was done in the ED. If, on completing the ED Admit form chest X-ray question (Item 4), you were not aware of the chest X-ray being done and you did not document results on the ED form and subsequently become aware of the ED X-ray while the patient is hospitalized, that data should be entered into the ED Admit form. Indicate the date and time of the first chest X-ray which occurred during the first 48 hours. Chest X-ray results:

a. Specific notations: *(check all that apply)*—Check if the specific wording was used in the X-ray report, or if none of this vocabulary was used: alveolar pulmonary edema, bilateral pleural effusion, pulmonary venous congestion, interstitial pulmonary edema, or cardiomegaly.

b. Was pulmonary edema noted on the radiology report? 'While reviewing the hospital records, if you are uncertain by the meaning of terminology used in the report, document the data and consult with your PI or Co-Investigator prior to completing this question. Pulmonary edema is listed as a possible adverse event for the ROC PRIMED Trial, and it is critical that this information be entered correctly. If pulmonary edema is reported, an Alert CTC form should be completed.

Fibrinolytics—Indicate whether fibrinolytics were given during the hospital admission. Some examples of fibrinolytics are TNKase (tenecteplase); Retrovase (Reteplase); Streptase; kabikinase (streptokinase).

Hypothermia therapy—Indicate whether hypothermia therapy was given during the hospital stay, and note the time it began, or if it was in progress upon transfer from the emergency department, check the "Continued from ED" box. Note the date and time the hypothermia therapy was stopped in the hospital and the lowest temperature achieved while receiving the treatment after the patient was admitted to the hospital.

Catheterization—Indicate if a cardiac catheterization, whether diagnostic or interventional (as might be done to open narrowed valves or arteries or to deploy devices/stents to open or occlude vessels) was done. If done, indicate whether the procedure was done within 24 hours of arrival at the ED or after 24 hours or ED (not to be confused with Hospital) admission.

CABG—coronary artery bypass grafting, done either with minimally invasive or open chest surgery.

Pacemaker implant—placement of a permanent pacemaker. This does not include temporary pacing during the course of hospital stay (this might be reported in the 'other' major cardiac procedures). This does not include the placement of an implantable device with dual defibrillator/pacemaker function (mark 'ICD implant' if a combined device is implanted).

ICD implant--implantable cardioverter defibrillator. If implanted, indicate if it is BiV (biventricular) or mark 'other' for other configurations such as a single chamber device.

Other major cardiac procedures—indicate other major procedures performed during the hospital course of care. Do not include minor procedures such as ECGs, ultrasounds, MRI, etc. If the "Other" box is checked, indicate the procedure or procedures which were done.

Item 4 – *Possible pre-hospital complications diagnosed in hospital or autopsy*

If no pre-hospital complications were documented in the hospital or autopsy records, mark "None Noted." If pulmonary edema was diagnosed in the hospital as a possible pre-hospital complication on the first CXR report within 48 hours of arrest and no CXR was done in the ED, check "Evidence of Pulmonary Edema found on 1st CXR within 48 hours of arrest". Check the 'evidence of pulmonary edema' box only if no CXR was done in the ED. Check 'Airway bleeding not reported on Pre-hosp or ED Admit forms' if bloody fluids (more than pink or red tinged fluids/secretions) or frank blood were observed in the oro- or naso-pharynx region, or the advanced airway. Airway bleeding attributed to the pre-hospital timeframe would be expected to occur within 24 hours of the cardiac arrest. This is intended to capture reports first made after hospital admission and previously reported on either the pre-hospital or ED forms. If other possible pre-hospital complications were first reported during the hospitalization or on autopsy, check "Other" and describe the complication. Complete only one Alert CTC form for each possible complication or potential adverse situation. If you have previously reported this condition, do not fill out another Alert CTC form.

Item 5 – *Residential status prior to arrest*

The type/location of patient residence prior to Epistry enrollment for cardiac arrest. This item may or may not be the same location as that indicated for the location of episode. Definitions include:

> *Home:* Patient was living in his own home or a home like situation (maybe with a relative). Indicate whether they were *independent* or living at home *with assistance* (e.g. visiting nurse, chore services or outpatient physical therapy or occupational therapy).
>
> *Rehabilitation*: Defined as a facility with the purpose of providing temporary care that allows the patient to regain strength and function with the intent of returning home or to an assisted living facility.
>
> *Assisted living:* includes an environment with services such as physical therapy, occupational therapy; or a group home, adult day home or halfway house. Distinguished from 'home' in that 'assisted living' is generally a fee-based environment.
>
> *Nursing home:* includes a location where others are fully responsible for the care of the patient on a long-term basis or a location where the patient receives high level nursing care on a short-term basis.
>
> *Unknown/not noted:* type of residence prior to enrollment is not known or is not noted in the patient care record.

Item 6 – *Etiology of arrest*

This item is completed for the Hospital admission that is associated with the final disposition at discharge (Item 7 Hospital Admit form)

a. *Site Classification*— This data element is intended to be completed by the ROC PRIMED Coordinator. The ROC PRIMED Coordinator classification may differ from that documented for the 'field' or 'site' classifications for the case on the Pre-hospital Data form. This is anticipated and may be due to the broader set of records with which the Coordinator is allowed to use when classifying etiology of arrest for the Hospital Admit form.

   It is anticipated that the majority of arrests will fall into the 'no obvious cause' category and will include those cases that are presumed cardiac or do not clearly fit in any of the 'obvious cause' categories listed and defined below. Also mark 'no obvious cause' (presumed cardiac) where the hospital course of care confirms a cardiac cause of arrest (such as 12-lead ECG findings or enzyme lab results). Mark 'obvious cause' only when the cause of out of hospital arrest is clearly other than cardiac and meets the defined criteria.

The site classification column should be completed using information obtained from the hospital records and public records, such as a death certificate or an autopsy. If the Coordinator determines from the records that there is an obvious cause for the cardiac arrest other than cardiac, the bubble under Column A next to the identified obvious cause should be checked. Only one obvious cause should be marked. If an obvious cause is determined and that is not on the list,

b. *Were there contributing factors directly related to this cardiac arrest?* —Though there may not be sufficient information for the Coordinator to determine a specific obvious cause, there may be contributing factors related to the cardiac arrest, and these should be noted. In Column B, check all factors which may have contributed to the cardiac arrest, or, if another contributing factor not listed was present, mark that at the bottom of the list. If there were no contributing factors noted on review of the records, mark “None noted.” Use all available information including Hospital notes, lab results, and public records. It is not necessary for a 'contributing factor' to meet the same burden of proof as does 'obvious cause' for Etiology of Arrest:

<u>Definitions for obvious cause of arrest:</u>

Anaphylaxis: Cases of sudden collapse with other clear signs of anaphylaxis including urticaria, facial and tongue swelling, respiratory distress, and clear exposure to an allergen (e.g., bee sting or ingested food with known allergy) that triggered the event. In addition to these physical and historical findings, an Epipen (intramuscular injectable source of epinephrine) may have been used. However, a used Epipen without physical signs of anaphylaxis (or witnessed by bystanders) is not diagnostic for this etiology option.

Chemical poisoning (intentional or unintentional, includes carbon monoxide, toxic gases): This category does NOT include prescribed medications, recreational drugs, or ethanol (see “Drug Poisoning”). However, isopropyl alcohol, ethylene glycol and methanol are included as “chemical poisoning”. This category will include all cases where there is high likelihood that the cardiac arrest would not have occurred in the absence of a poison. Chemical poisons are considered substances that would not normally be ingested, inhaled or consumed and may be environmental or industrial, including such items as insecticides, herbicides, industrial gases, cleaning solutions, carbon monoxide sources (e.g., automobile exhaust or space heaters), or similar compounds. The cardiac arrest timing and clinical scenario should be consistent with the

presumed chemical poisoning. This etiology includes both intentional chemical poisoning (i.e., cases where ingestion, inhalation or contact with a chemical poison for the purposes of suicide is clear - suicide note, witnesses confirm discussion of suicidal intent or witnessed clear impulsive intentional ingestion temporarily related to the collapse), and unintentional chemical poisoning (cases where witnessed chemical exposure precedes the collapse by 3-5 minutes). This category would include cases where witnesses confirm contact with a chemical poison just prior to collapse or hospital work-up later confirms contact.

Drowning: victim is found by provider or bystanders submersed in water without an alternative causation.

> Examples of cases that fit this definition include; young and presumably healthy person found floating in the water with no evidence of overdose or drug ingestion; in the absence of other contributing factors, any patient who was witnessed to be choking or coughing before going under water; water in lungs found at autopsy.
>
> Examples of cases that do NOT fit this definition include; patients who suffer trauma immediately prior to falling in the water (the case should be entered in the trauma, not the cardiac, patient cohort); for patients presumed to be older than 39 years of age one cannot be certain whether the submersion or some medical event was the cause of death so 'no obvious cause' would generally be selected; person who was inebriated or toxic on a drug who then drowned (the case should be classified as 'no obvious cause').
>
> References: *S*alomez F, Vincent JL. Drowning: a review of epidemiology, pathophysiology, treatment and prevention. *Resuscitation.* 2004 Dec;63(3):261-8.
>
> Idris AH, Berg J, Bierens L, et al. Recommended guidelines for uniform reporting of data from drowning: the 'Utstein style.' *Circulation.* 2003 Sept; 108:2565-2574.

Drug poisoning (intentional or unintentional, includes ethanol): This category includes prescribed medications, recreational drugs, and ethanol. Intentional drug overdose may include cases where ingestion of a drug (i.e., prescribed or over the counter medication, recreational drugs including alcohol) for the purposes of suicide is clear (suicide note, witnesses confirm discussion of suicidal intent or witnessed clear impulsive intentional ingestion temporarily related to the collapse). Unintentional drug overdose may include cases where witnessed inhaled or intravenous or oral recreational drug use immediately precedes the collapse. The Drug Poisoning category includes cases where witnesses confirm the situation, for example an injection of heroin just prior to collapse or where the evidence strongly suggests immediate use prior to arrest (e.g., tourniquet on arm and empty syringe at side).

> Examples of cases that fit this definition; a victim collapses and there are empty pill bottles or ethanol containers at the scene with clear evidence of suicidal intent.
>
> Examples of cases that DO NOT fit this definition; patient with a history of recreational drug use within 24 hours of the event (e.g., adolescent found collapsed at a party or the known alcoholic found dead the morning after heavily imbibing); classify these types of cases as 'no obvious cause' (presumed cardiac).

Electrocution (non-lightning): This category includes all cases where the patient has an electrical cutaneous burn in the setting of contact with a high voltage source. Electrocution

would also be the obvious choice if the victim was found attached or nearly so, to a high-tension source of current. This category also includes all cases where the patient has been removed from the source of high tension current but the event was witnessed.

Excessive cold: Low ambient temperature (below 32F or 0C) where an obviously healthy individual is inappropriately clothed for the ambient temperature.

Excessive heat: Situations in which an obviously healthy person experiences a cardiac arrest and the most significant contributing factor is increased ambient temperature i.e., exercise on a hot day or confined in a locked car or lost hiking in the desert.

> Examples of cases that fit this definition; the inebriated patient found outside for a prolonged period of time exposed to extreme heat.

Foreign body obstruction: Cases of sudden airway obstruction leading to cardiac arrest due to ingestion of a foreign body identified by history or by direct visualization within the airway. Some of these cases may be preceded by choking.

> Examples of cases that fit this definition include; small child (age 4 or less) choking after a balloon popped in front of their face or after eating a hot dog and succumbs to cardiac arrest; or man observed to be eating and suddenly begins to choke and hold his throat prior to collapsing; or on intubation a foreign body is visualized +/- removed.
>
> Examples of cases that DO NOT fit this definition include: paramedics report inability to ventilate the patient and presume airway obstruction without finding the source of the obstruction;

Hanging: Cases of sudden airway obstruction leading to cardiac arrest secondary to hanging. Requires either the presence of ligature present around the neck, found hanging, or marks on the neck compatible with a previous ligature in the setting that suggests this was the obvious cause of death.

> Examples of cases that fit this definition; case in which the victim is found with a rope around the neck after fire or police have cut them down from a gallows equivalent.
>
> Examples of cases that would NOT fit this definition: victim has a ligature around the neck without any evidence at the scene of any attempt to hang himself; a victim who has been strangled by an assailant’s hands during an altercation (this case would be classified as 'obvious cause' Strangulation).

Lightning: cases of cardiac arrest where the event was directly attributed to lightning strike or blast effect from lightning temporally related to the event i.e., immediately following the strike, burn marks on the ground or nearby objects, melting of metal objects, or documented classic signs of electrocution by lightning.

> Examples of cases that fit this definition: witnessed lightning strike on golf course where members of a foursome documented direct hit to one of their group and called 911; or unwitnessed cases where there are visible signs of lightning strike including cutaneous burns described as Lichtenburg figures, flash burns, punctuate burns, contact burns, or linear burns in the skin folds.

Example of a case that does NOT fit this definition: man found outside in the rain without witnesses to verify direct strike or blast effect or any signs or symptoms of lightning related electrocution.

Mechanical suffocation: Mechanical suffocation causing arrest is distinct from hanging, strangulation, choking, respiratory, anaphylaxis, or SIDS etiologies. This category will rarely be coded. It is included for a unique and very specific group of patients who arrest because of suffocation due to an external physical barrier.

Examples of cases that fit this definition: someone with the plastic bag over the head; a pillow or another object was used to suffocate the patient; or a child or adult with tracheostomy site who develops an obstruction.

Non-traumatic exsanguination: This category includes the rare situation where it is highly likely that the patient "bled to death" in a short period of time and there is strong evidence that acute and catastrophic loss of blood was the direct cause of the arrest.

Examples of cases that fit this definition: hemodialysis line disconnected with obvious large loss of blood; vomiting of blood with EMS witnessed and documented large loss of blood; blood in stool (lower GI bleed) with EMS witnessed and documented large loss of blood.

Examples of cases that DO NOT fit this definition: vomiting blood with unknown amount or small amount on face or clothes; possible or suspected ruptured aortic aneurysm (this can never be proven without autopsy or diagnostic imaging); epistaxis; hemoptysis

Radiation: This etiology will be rarely coded. Cardiac arrest due to radiation requires an acute and massive radiation exposure that temporally (typically within seconds to minutes) produces a cardiac arrest.

Examples of cases that fit this definition: industrial exposure or terrorist event with presumed high radiation levels.

Respiratory: Adult cardiac arrest due to primary respiratory cause requires that the patient have 1) an established medical history of asthma and 2) a witnessed reported clinical course prior to arrest implicating asthma. Although there are no absolutes, death due to asthma (as a respiratory 'obvious cause') would generally be expected to evolve over hours or even days with progressive shortness of breath as the principal symptom rules. Pediatric (patients < 16 years) cardiac arrest due to primary respiratory cause requires that the patient have 1) an established history of an underlying disease that places the patient at higher risk for respiratory disease (see below examples) and 2) a witnessed reported clinical course of an acute respiratory problem prior to the arrest.

Examples of adult cases that fit this definition: a) 54 yo male with history of asthma, hospitalized previously, who experienced progressive shortness of breath over the past day following URI for past week. He has been using inhalers around the clock since yesterday and took an extra dose of prednisone this morning. His spouse called 9-1-1 when his respiratory symptoms made him unable to talk or answer questions. No chest pain or prior heart history. EMS arrives to find the patient unresponsive without pulse or respirations. Rationale: Several circumstances suggest a primary respiratory arrest: 1)

the history suggests that he has fairly significant asthma, the clinical circumstances are highly consistent with an asthma exacerbation with similar past events, and there is information indicating that he did not have clinical heart disease. Hence the level of information sufficiently implicates a respiratory mechanism as the primary cause; b) 16 year old woman with a history of asthma witnessed by bystander or responder to have inspiratory and expiratory wheezing prior to cardiac arrest.

Examples of pediatric cases (patients < 16 years of age) that fit this definition: a) Child receiving chronic oxygen therapy or respiratory assistance, such as a premature infant at home on oxygen with an increase in oxygen requirement over the previous hours or days; b) Child with acute febrile respiratory illness in the days or hours prior to arrest, such as an otherwise healthy child with a presumed respiratory infection preceding the event; c) child with history of asthma and progressive acute respiratory distress (“asthma attack”) whereby witnessed respiratory distress progresses over hours until he/she cannot talk, then turns blue, and collapses.

Examples of cases that do NOT fit this definition include: a) 65 yo male with history of COPD (home oxygen dependent) and heart disease (prior bypass) was last seen at breakfast by his wife. He had no complaints at that time. When she returned home later that morning she found him unresponsive on the couch with his home nebulizer running. She called 9-1-1 and the EMS arrived to find him without pulse or respiration. Rationale: Although the patient had fairly severe chronic lung disease, he did not have clear prodromal symptoms or signs indicating progressive respiratory decline. The scene was suggestive that he experienced some symptoms prior to death since the nebulizer machine was running but this could have been due to a variety of cardiopulmonary symptoms. This patient should be classified as no obvious cause (presumed cardiac); b) 75 yo female nursing home resident develops cough for at least 1 day and then increasing shortness of breath this morning. The nursing home staff had provided oxygen and an albuterol but without relief. At the time of the 9-1-1 call she was awake but unable to speak due to extreme respiratory distress. When EMS arrives she is unresponsive without pulse or blood pressure and nursing staff have initiated CPR. Her history is notable for history of asthma for which she uses 2 different inhalers. Rationale: The patient did have some history of lung disease and some symptoms of progressive dyspnea. However the severity of lung disease is not clear and the symptoms could be consistent with other etiologies of arrest. For example, this patient could be manifesting congestive heart failure or pulmonary embolism. Although a judgment, the level of information leaves some question as to whether respiratory disease was the primary etiology. The best etiology classification for this patient would be 'no obvious cause' (presumed cardiac).

Examples of pediatric cases (patients <16 years of age) that do NOT fit this definition: a) Developmentally disabled child without a supported airway found pulseless and apneic, such as 6 year old child with cerebral palsy and limited ambulation found pulseless and apneic in bed (this case would be coded as 'no obvious cause'); b)child with a supported airway (i.e., Tracheostomy) and found pulseless and apneic (this case would be coded as 'obvious cause' mechanical suffocation); c) prior history of congenital heart disease and no other 'obvious cause' identified—congenital heart disease is not an etiologic classification, but should be included as a 'contributing factor.' This case would be coded as 'no obvious cause' (presumed cardiac).

SIDS (sudden infant death syndrome, less than 12 months of age): Cases of death where an infant, ages 1 month to 12 months is found in their crib/bed and death was unwitnessed. All three criteria—age, crib/bed location, and unwitnessed death—must be present to be categorized as SIDS. Background of sudden infant death syndrome: The American Academy of Pediatrics—SIDS, also called crib or cot death, is the sudden death of an infant under 1 year of age that remains unexplained after thorough case investigation, including performance of a complete autopsy, examination of the death scene, and a review of the clinical history. [NOTE: Site classification of etiology of arrest for classification of SIDS as an obvious cause is to be determined solely from the prehospital patient care record. SIDS is the most common cause of death between 1 and 6 months of age. The incidence of SIDS peaks between 2 and 4 months of age. Approximately 90% of SIDS deaths occur before the age of 6 months.]

> SIDS is suspected when a previously healthy infant, usually younger than 6 months, is found dead in bed, prompting an urgent call for emergency assistance. Often, the baby is fed normally just before being placed in bed to sleep, no outcry is heard, and the baby is found in the position in which he or she had been placed at bedtime or naptime. In some cases, cardiorespiratory resuscitation initiated at the scene by emergency personnel is continued without apparent beneficial effect en route to the hospital, where the baby is finally declared dead. Evidence of terminal motor activity, such as clenched fists, may be seen. There may be serosanguineous, watery, frothy, or mucoid discharge coming from the nose or mouth. Skin mottling and postmortem lividity in dependent portions of the infant's body are commonly found. Review of the medical history, scene investigation, radiographs, and autopsy are unrevealing.
>
> The Canadian Pediatric Society refers to SIDS as the sudden and unexpected death of an apparently healthy infant usually less than one year of age, which remains unexplained even after a full investigation. On average, 3 infants a week are reported to die of SIDS in Canada. Although in Canada there has been a decrease in the number of infant deaths reported as SIDS, it still remains a significant public health concern. Aboriginal infants have a risk of SIDS that is higher than the risk to non-Aboriginal infants.
>
> Example of pediatric cases (less than 13 months of age) that are included: Although there is some controversy and a few documented cases of long QT causing what appears to be SIDS, the evidence supports that most are related to respiratory issues. A case can be made that this is mechanical suffocation, but that cannot reliably be done in the absence of a thorough review of the history and even location of the death. We need to be consistent with this as we will have many cases of this and CPR will be delivered.

Smoke inhalation: Cases of collapse in a fire setting with significant smoke exposure. This is defined as the patient who was exposed to fire in a closed space (Ryan et al N Engl J Med, 1998).

Strangulation: The impression of EMS responders is that the patient’s most significant condition that led to cardiopulmonary arrest is strangulation. Strangulation is a form of asphyxia (though not categorized as 'obvious cause' asphyxia) characterized by closure of the blood vessels or air passages of the neck as a result of external pressure on the neck (McClane et al J Emerg Med 2001) The paramedic usually describes crush marks around the neck.

Examples of cases that fit this definition: victim becomes non-responsive during a witnessed altercation where the assailants hands were around the neck.

Examples of cases that would NOT fit this definition: a) where the individual was involved in an altercation and becomes unresponsive without witnesses documenting strangulation just prior to collapse; b) victim has bruising around the neck without documented history of strangulation related to the collapse;

Terminal illness (includes end-stage diseases such as cancer): Death due to “terminal” condition is one in which death is expected and for which there is evidence of poor function or functional decline prior to death. Both conditions need to be met. Terminal condition will most often be considered in patients with advanced cancer. An individual whose function is declining and for whom death is expected should be classified as terminal illness (see below examples).

Examples of cases that fit this definition: a) 45 year old woman is found unresponsive and not breathing. She has advanced pancreatic cancer and is enrolled in an experimental treatment protocol. She has been sleeping mostly during the last week because of weakness and malaise and has declined to return to the hospital. She was quite difficult to arouse earlier in the day; b) 88 yo male with liver cancer who has been mostly bedridden the past month. He has been progressively more confused over the last two days to the point where his caretaker could not wake him.

Examples of cases that do NOT fit this definition: a) Patient with advanced cancer who is reasonably functional – carrying out ADLs, living independently, and collapses would be classified as “no obvious cause” (presumed cardiac); b) 68 yo male with metastatic colon cancer (“his cancer had spread to his lung and liver” per bystander son) who collapsed while walking in the park. “He had gotten a bit weaker over the past year but seemed fine today”. The son is not aware of other conditions or medications. Classify this case as 'no obvious cause' (presumed cardiac); c) 71 yo female found unresponsive by her husband. She has lung cancer that has spread to her bones and a past history of a “heart attack” 2 years ago. Her husband reports that “she has been receiving radiation treatment for the cancer and the doctors weren’t sure how long she had.” This morning she had no complaints and they were leaving the house to go shopping when she collapsed. Classify this case as 'no obvious cause' (presumed cardiac).

Trauma (includes blunt, penetrating or burns): Patients who have experienced a cardiac arrest directly caused by blunt, penetrating or burn injury should be enrolled in the Trauma Epistry cohort, not the cardiac arrest cohort.

Examples of cases that do NOT fit this definition: a patient scenario where it is clear from the bystander history that the patient collapsed due to some medical condition prior to experiencing the trauma. This patient would be entered in the cardiac arrest cohort and if the etiology of the arrest is unclear, would be marked 'no obvious cause' (presumed cardiac).

Venomous stings and venomous bites: This category will include all cases where there is visual evidence or witnessed attack of a venomous organism (e.g., animal, reptile, insect) that immediately preceded and presumably precipitated the cardiac arrest. Evidence for the sting must include visible localized skin findings (e.g., local erythema or edema at site) and/or

witnessed report by bystanders of history that supports this etiology. If a venomous sting precipitated anaphylaxis, the obvious cause “Anaphylaxis” should be marked.

Definitions for Contributing Factors:

Anaphylaxis: Signs of anaphylaxis including urticaria, facial and tongue swelling, respiratory distress, and clear exposure to an allergen (e.g. bee sting or ingested food with known allergy) that triggered the event. An Epipen (intramuscular injectable source of epinephrine) may have been used.

Chemical poisoning (intentional or unintentional, includes carbon monoxide, toxic gases): This category does NOT include prescribed medications, recreational drugs, or ethanol (see “Drug Poisoning”). However, isopropyl alcohol, ethylene glycol and methanol are included as “chemical poisoning”. Chemical poisons are considered substances that would not normally be ingested, inhaled or consumed and may be environmental or industrial, including such items as insecticides, herbicides, industrial gases, cleaning solutions, carbon monoxide sources (e.g. automobile exhaust or space heaters), or similar compounds.

Dialysis: The patient was undergoing or very recently underwent dialysis treatment (peritoneal or hemodialysis). This does not include exsanguination secondary to disconnection of dialysis shunts—see 'non-traumatic exsanguination.'

Drowning: victim is found by provider or bystanders submersed in water or witnessed to be choking or coughing before going under water.

Drug poisoning (intentional or unintentional, includes ethanol): Includes prescribed or over the counter medications, recreational drugs, and ethanol (alcohol).

Electrocution (non-lightning): This category includes all cases where the patient has an electrical cutaneous burn in the setting of contact with a high voltage source. Electrocution would also be the obvious choice if the victim was found attached or nearly so, to a high-tension source of current. This category also includes all cases where the patient has been removed from the source of high tension current but the event was witnessed.

Excessive cold: Low ambient temperature (below 32F or 0C) where an obviously healthy individual is inappropriately clothed for the ambient temperature.

Excessive heat: High ambient temperature i.e., exercise on a hot day or confined in a locked car or lost hiking in the desert.

*Foreign body obstruction: S*udden airway obstruction due to ingestion of a foreign body identified by history or by direct visualization within the airway. Some of these cases may be preceded by choking.

Hanging: Cases of sudden airway obstruction secondary to hanging. Patient may have a ligature present around the neck, be found hanging, or have marks on the neck compatible with a previous ligature.

Lightning: cases of cardiac arrest where a lightning strike or blast effect from lightning temporally related to the event i.e., immediately following the strike, burn marks on the ground or nearby objects, melting of metal objects, or documented classic signs of electrocution by lightning.

Mechanical suffocation: Mechanical suffocation is distinct from hanging, strangulation, choking, respiratory, anaphylaxis, or SIDS etiologies. It includes suffocation due to an external physical barrier. May include someone with a plastic bag over the head; pillow or another object used to suffocate the patient; or a child or adult with a tracheostomy site who develops an obstruction.

Non-traumatic exsanguination: There is evidence that acute and catastrophic loss of blood occurred in a short period of time. May include disconnection of a hemodialysis line; vomiting of blood; blood in stool.

Radiation: Radiation requires an acute and massive radiation exposure that temporally (typically within seconds to minutes) produces a cardiac arrest. May include industrial exposure or terrorist event with presumed high radiation levels.

Respiratory: Adult cardiac arrest due to a medical history of COPD or asthma or a witnessed reported clinical course prior to arrest implicating respiratory difficulties. May evolve over hours or even days with progressive shortness of breath as the principal symptom rules. May have been using inhalers with increased frequency or increased dose of prednisone. May have been at home with oxygen with an increase in oxygen requirement over the hours prior to arrest. Pediatric (patients < 16 years) cardiac arrest due to 1) an established history of an underlying disease that places the patient at higher risk for respiratory disease (see below examples) and 2) a witnessed reported clinical course of an acute respiratory problem prior to the arrest. This does not include a child with a supported airway (i.e., Tracheostomy) found pulseless and apneic--this would be 'mechanical suffocation.'

SIDS (sudden infant death syndrome, less than 12 months of age): Cases of death where an infant, ages 1 month to 12 months is found in their crib/bed and death was unwitnessed. All three criteria—age, crib/bed location, and unwitnessed death—must be present to be categorized as SIDS. See Etiology of arrest 'Obvious cause' definitions for background on SIDS.

Smoke inhalation: Cases of collapse in a fire setting with significant smoke exposure. This is defined as the patient who was exposed to fire in a closed space (Ryan et al N Engl J Med, 1998).

Strangulation: Strangulation is a form of asphyxia (though not categorized as 'contributing factor' asphyxia) characterized by closure of the blood vessels or air passages of the neck as a result of external pressure on the neck (McClane et al J Emerg Med 2001) The paramedic usually describes crush marks or bruising around the neck.

Terminal illness (includes end-stage diseases such as cancer): "Terminal" illness is one in which death is expected and for which there is evidence of poor function or functional decline prior to death.

Trauma (includes blunt, penetrating or burns): Patients who have experienced a cardiac arrest directly caused by blunt, penetrating or burn injury should be enrolled in the Trauma Epistry cohort, not the cardiac arrest cohort.

Venomous stings and venomous bites: This category will include cases where there is evidence or witnessed attack of a venomous organism (e.g., animal, reptile, insect) that immediately preceded and presumably precipitated the cardiac arrest. Evidence may include visible localized skin findings (e.g., local erythema or edema at site) and/or witnessed report by bystanders of history that supports this etiology. If a venomous sting precipitated anaphylaxis, the contributing factor "Anaphylaxis" should be marked.

Other obvious cause, specify: enter other causes that are obviously related to this arrest (60 characters maximum).

Item 7 – *Disposition at discharge:*

Indicate patient status when the course of acute care associated with this cardiac arrest was completed. Disposition at discharge is reported for the latest (last) acute care hospital that the patient was admitted or transferred to during the course of care.

o *Dead at discharge →skip to Item 10*
o *Alive →Complete disposition:*

Home—A relative term, meaning the patient was discharged to their own home or a home like situation (e.g., with a relative). Indicate whether they were independent or needed assistance in their home, such as from a friend, relative, chore services. If it is not clear whether the patient was independent or needed assistance upon discharge to home, check "Unknown/Not noted.

Rehabilitation—Rehabilitation is defined as being discharged from an acute care hospital to either an adjoining rehab facility or admitted to a separate rehab facility, with the purpose of providing temporary care which would allow the patient to regain strength and function with the intent of returning home or to an assisted living facility. A hospital may have a separate unit within the building which is their rehabilitation center to which a patient moves after the acute care treatment is completed. Typically, the patient is considered discharged from the acute care and readmitted to the rehab unit for purposes of billing. It is important to clarify this situation when the patient is moved to a rehab unit but not moved outside the hospital walls.

Assisted living—An assisted living facility would include a location where the patient assumes partial responsibility for their daily care on a long-term basis. This includes an environment with services such as physical therapy, occupational therapy; or a group home, adult day home or halfway house. Distinguished from 'home' in that 'assisted living' is generally a fee-based environment.

Nursing home—A nursing home includes a location where others are fully responsible for the care of the patient on a long-term basis or a location where the patient can receive high-end nursing care on a short-term basis.

Remain in acute care hospital, reclassified as non-acute patient awaiting placement or chronic care—There are occasional situations in which a patient has been cleared for discharge by his or her physician but there are no beds available in a nursing home facility

for the patient. If a patient is ready to be discharged but remains in the hospital only while awaiting a bed in a non-acute institution, check this bubble.

Item 8 – ***Structured Chart Review Tool for Assessment of Cerebral Performance Category at discharge:***

Cerebral Performance Category (CPC) indicates final neurological status at time of final hospital discharge or death. Use chart review to categorize the patient's condition. The responses below will be later mapped (in analysis) to traditional CPC codes. Consider each of the questions below separate from each other—they are not intended to be dependent responses.

a. *Is the patient able to follow any simple commands or say any words?* Indicate no or yes if these capabilities are indicated or implied in the ED/hospital patient care records as a patient condition at the time of discharge.

b. *Is the assistance of someone essential for all or part of the day for activities of daily living (dressing, preparing meals, local travel, shopping)?* Indicate no if, in your judgment after reviewing the hospital chart, it appears that assistance is not likely to be essential for activities of daily living after hospital discharge. Your judgment may be based upon in-hospital assessments made by occupational or physical therapy, nursing notes speaking to independence, stability, mobility, etc. Indicate yes if, in your judgment it appears that assistance is essential after discharge.

c. *Is the patient able to return to work or social activities in any capacity (even limited)?* Indicate no or yes whether, in your judgment after reviewing the hospital chart, it appears the patient is able to return to even a limited capacity of work or social activities. This does not require that the patient have plans or a desire to return to work, only if they are capable of doing so.

d. *Does the patient have any problems that are more than mild, i.e., problems that prevent him/her from doing things he/she would like or have to do (such as dysphasia, hemiplegia, ataxia, dysarthria, memory, cognition, personality)?* Indicate yes, if the patient is documented to exhibit/experience impairments that are, in the judgment of the reviewer, to be more than mild in nature at the time of discharge.

Definitions of selected terms:
Ataxia—an abnormality of coordination, as might cause an abnormal or staggered gait.
Cognition—the mental process of knowing, including aspects such as awareness, perception, reasoning, and judgment
Dysarthria—speech that is characteristically slurred, slow, and difficult to produce. May have Problems with the voice qualities of speech.
Dysphagia—difficulty in swallowing
Hemiplegia—paralysis of one side of the body

Item 9 – ***Modified Rankin Scale at hospital discharge*:**

The Modified Rankin Scale is a tool used to assess functional outcome. Generally used as an interview tool, the Modified Rankin Scale has been revised for ROC PRIMED to be used as a chart review tool. At the time of patient discharge, review the patient's records to select the one description that best describes the patient's functionality at the time of final hospital discharge. Physician, nurse, social worker and therapist records can be used to determine the MRS.

MRS0 –no symptoms at all.

MNRS1 –no significant disability: despite symptoms, able to carry out all usual duties and activities.

MRS2 –slight disability: unable to carry out all previous activities but able to look after own affairs without assistance.

MRS3 –moderate disability: requiring some help, but able to walk without assistance.

MRS4 –moderately severe disability: unable to walk without assistance, and unable to attend to own bodily needs without assistance.

MRS5 –severe disability: bedridden, incontinent and requiring constant nursing care and attention.

Death at discharge—modified Rankin Scale is not applicable as the patient was not alive at discharge

Item 10 – *Date and time of hospital discharge or death*:

Indicate the date and time the patient was either discharged from the acute care hospital or the date and time the patient died.

If the patient's status was changed to Do Not Resuscitate (DNR) or the care was limited or withdrawn per physician's orders during the hospitalization, indicate "Yes" and the date the patient's status changed. This date should come from the hospital record documentation.

Item 11 – *Total days in the ICU/CCU*

Indicate the total combined number of days the patient was in the intensive care unit (ICU) or coronary care unit (CCU). The total number of days the patient was hospitalized will be prefilled from the information entered in Items 1 and 2 of the Hospital Admit form. Confirm that this number is correct prior to entering the total days in the ICU/CCU. If the patient is transferred from the ICU/CCU to the ward but is readmitted to the ICU/CCU within 24 hours, count the day as an ICU/CCU day. If a patient is in the ICU/CCU for part of the day, then transferred to the ward and remains there, count it as an ICU/CCU day.

Item 12 – *If death occurred, check one main category and one subcategory (where applicable)*

There are four possible options for Item 12, and each requires a date of either the death or the date the decision was made to withdraw or limit care. It may be necessary to discuss some cases with your PI or ROC PRIMED Investigator.

Subject is unstable, and continued life support is impossible or futile—Check this bubble if the patient died from either multi-system organ failure, recurrent cardiac arrest with unsuccessful resuscitation, or intractable shock.

- Multi-system organ failure refers to the failure of more than one organ, such as cardiac, kidney, or liver, which resulted in death. This does not include the brain (see below selection options).

- Recurrent cardiac arrest with unsuccessful resuscitation refers to a patient who suffered another cardiac arrest while in hospital and attempts were made with CPR, defibrillation, or medications to revive the patient, either at one time or multiple times during the hospitalization, prior to the unsuccessful resuscitation.

- Intractable shock refers to shock in which, despite active treatment, the patient continued to deteriorate and then died.

Subject has brain-death criteria, resulting in withdrawal of care and cardiovascular death—This refers to a patient who, despite being physiologically stable, is determined as brain dead by the criteria of the hospital to which the patient is admitted. These criteria often include: serial EEGs showing little or no brain activity and evaluations by more than one neurologist. Indicate the date noted in the hospital records in which the brain death status was declared.

Subject is stable or continued life-support is possible. Because of other non-neurological considerations, care is withdrawn or limited resulting in death.

- Underlying terminal illness *(*metastatic cancer, for example*)*—Underlying terminal illness refers to a patient who may have a metastatic cancer or another disease, but due to the terminal nature of the disease, care is withdrawn or limited resulting in death during the hospitalization.

- Pre-existing advanced directives or living will—A patient may have been resuscitated and admitted to the hospital prior to the knowledge of a DNR, advanced directives, or a living will being available, and though the patient's physiological condition is stable, these directives are honored and care is either withdrawn or limited (such as stopping ventilator dependence, etc.), which results in death during the hospitalization.

- Family or surrogate representation of subject's wishes—This refers to a patient who may be physiologically stable and who did not sign an advanced directive prior to experiencing the cardiac arrest but may have expressed their wishes to family members or a surrogate representative, and these wishes are honored. The date this decision was made during the hospitalization should be recorded in the hospital records.

Subject is deemed to have poor neurological prognosis, and care is withdrawn or limited resulting in death—The neurological prognosis for a patient may be poor due to a cerebral vascular accident, a long downtime prior to CPR being initiated, or another medical condition, and thus a decision is made to either withdraw or limit care (such as antibiotics, pressors, etc.) resulting in death. Enter the date the decision was made to withdraw or limit treatment as per the hospital records.

Item 13 – *Were any of the following listed on the hospital discharge summary? (check all that apply)*

If there were no conditions listed below on the hospital discharge summary, check "None noted." Check all listed conditions that are noted (with identical or like meaning vocabulary) in the hospital discharge summary.

- o Cerebral bleeding/cerebrovascular accident (CVA) (such as 'stroke')
- o Seizures (such as epilepsy; focal, generalized)
- o Bleeding requiring transfusion or surgical intervention
- o Rearrest *(and resuscitated with intervention)*
- o Pulmonary edema (at any point during the hospital course of care; not restricted to the first 48 hours from ED admission)
- o Internal thoracic or abdominal injuries (e.g., liver laceration, pneumothorax).
- o Rib fractures
- o Sternal fractures
- o ARDS (acute respiratory distress syndrome; respiratory distress syndrome; not pneumonia)
- o Liver failure
- o Renal failure (not renal insufficiency)
- o Sepsis
- o Pneumonia
- o New myocardial infarction (MI) (associated with either the prehospital arrest or the course of ED/.hospital care)

Complete an Alert CTC form if pulmonary edema was noted on the first X-ray within 48 hours of the arrest (either on the ED chest X-ray or if no chest X-ray done until hospitalization). If rib fractures or sternal fractures noted, complete Alert CTC form. Include rib or sternal fractures that may have occurred due to pre-hospital or hospital CPR, as it may be difficult to distinguish between the two causes.

If a site is participating in the MI substudy, the following questions should be answered for all patients admitted to the hospital.

Item 14 – Was a troponin level obtained within 48 hours of ED/hospital arrival?

If Yes, note the highest concentration reported during the 1st 48 hours after arrival: (ng/ml). Indicate if the result was within the normal limits or outside the normal limits for the lab where the test was performed.

Item 15 – Did the patient have an ST elevation MI, defined as: ST elevation MI on the first ECG in the first 48 hours after arrival at the ED/hospital as defined by the ECG report/overreading MD?

If the initial ECG report (for an ECG acquired within the first 48 hours of ED arrival/hospital admission) specifically states ST elevation and an associated myocardial infarction (MI), then check "Yes." Otherwise, check 'no'.

Person responsible for data on this form

Name of the individual that logged into the electronic data transmission system for clinical study forms. This individual will have registered as a member with the CTC for the purpose of participating as a coordinator or investigator in a ROC clinical trial and has designated a user name and password as their "Electronic Signature." The individual has agreed to consider their electronic signature as equivalent to their handwritten signature, to maintain the confidentiality of their user name and password, and to not let others use it. Refer to the "Electronic Signature Agreement" (accessed after logging on to the ROC website) posted at https://roc.uwctc.org/tiki/roc-data-entry.

After verifying the entered data and electronic signature are correct, print the web-forms for your files, or convert the web-forms to PDF format and store electronically. Edits made later to the original web-entered forms are associated with the electronic signature of the individual making the changes and are documented in the file's edit history.

Complete this form:
for episode qualifying for the Pre-hospital Form
and the patient was admitted to a hospital
Main data resource: Hospital records

Hospital Admit

Date: 08-25-2009
Version: 1.07.00

Episode Information:

Date *(mm/dd/yyyy)* ___ / ___ / ___

ROC PRIMED ID ___

Time call received at dispatch *(hh:mm:ss; 24hr clock)*
___ : ___ : ___ ○ From PCR/other ○ From dispatch
○ Unable to obtain *(Non-ROC agency 1st arrival, patient excluded from trial)*

Incident Number *(optional)* ___

Site-linking ID *(optional)* ___

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1. **Hospital admit information** *(1st hospital)*:
   Hospital admittance date: ___ / ___ / ___ *(mm/dd/yyyy)*
   Hospital name: ___
2. **Was the patient transferred to another acute care hospital before discharge?**
   ○ No
   ○ Yes →

Name of next acute hospital	Date of transfer *(mm/dd/yyyy)*
	___ / ___ / ___
	___ / ___ / ___
	___ / ___ / ___
	___ / ___ / ___

3. **Major procedures while in the hospital:**
   ☐ No major procedures from the list below noted

NA/NR	Done	
○	○	CPR
○	○	Chest X-ray within 48 hours of arrest *(complete only if no CXR done in ED)* Date ___ / ___ / ___ *(mm/dd/yyyy)* Time ___ : ___ *(hh:mm)* Chest X-ray results a) Specific notations: *(check all that apply)* ☐ Alveolar pulmonary edema ☐ Bilateral pleural effusion ☐ Pulmonary venous congestion ☐ Interstitial pulmonary edema ☐ Cardiomegaly ☐ None of these noted b) Was pulmonary edema noted? ○ Yes ○ No
○	○	Fibrinolytics
○	○	Hypothermia therapy a) Time started ___ : ___ *24hr clock(hh:mm)* Or ☐ Continued from ED b) Date/Time hypothermia therapy was stopped in the hospital Date ___ / ___ / ___ *(mm/dd/yyyy)* Time ___ : ___ *24hr clock(hh:mm)* c) Lowest temperature ___ degrees → ○ Centigrade ○ Fahrenheit
○	○	Cath, diagnostic → ○ Within 24 hours of arrival at ED ○ After 24 hours of arrival at ED
○	○	Cath, interventional *(PCI, Stent, etc.)* → ○ Within 24 hours of arrival at ED ○ After 24 hours of arrival at ED
○	○	CABG
○	○	Pacemaker implant
○	○	ICD implant → ○ BiV ○ Other
○	○	Other major cardiac procedure: ___ *(30)*

Episode Information:

Date *(mm/dd/yyyy)* ___ / ___ / ___

ROC PRIMED ID ___

Time call received at dispatch *(hh:mm:ss; 24hr clock)*
___ : ___ : ___ ○ From PCR/other ○ From dispatch
○ Unable to obtain *(Non-ROC agency 1st arrival, patient excluded from trial)*

Incident Number *(optional)* ___

Site-linking ID *(optional)* ___

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4. Possible pre-hospital complications related to study protocol or ITD use diagnosed in hospital or autopsy: *(Check all that apply)*

- ☐ None Noted
- ☐ Evidence of Pulmonary Edema found on 1st CXR within 48 hours of arrest *(complete only if no CXR done in ED)*.
- ☐ Airway bleeding not reported on Pre-hosp or ED Admit forms
- ☐ Other, describe: ___ *(30)*

} Complete **Alert CTC** form

5. Residential status prior to arrest:

- ○ Home →
  - ○ Independent
  - ○ With assistance
  - ○ Unknown/not noted
- ○ Rehabilitation
- ○ Assisted living
- ○ Nursing home
- ○ Unknown

6. Etiology of Arrest:

a. Site Classification *(based on all available information including ED/hospital records/notes and public records)*

- ○ No obvious cause identified (Utstein "presumed cardiac")
- ○ Obvious cause → *(check one cause in Column A below)*

b. Were there contributing factors directly related to this cardiac arrest?
(based on all available information including ED/hospital records/notes and public records)
— See Manual of Operations for expanded definitions

- ○ None noted → *Do Not complete Column B below*
- ○ Yes → *(check all that apply in Column B below)*

Obvious Cause	A Site Classification	B Contributing Factors
Anaphylaxis	○	☐
Chemical poisoning *(intentional or unintentional, includes carbon monoxide, toxic gases)*	○	☐
Dialysis	-	☐
Drowning	○	☐
Drug poisoning *(intentional or unintentional, includes alcohol)*	○	☐
Electrocution *(non-lightning)*	○	☐
Excessive cold	○	☐

Episode Information:

Date *(mm/dd/yyyy)*
/ /

ROC PRIMED ID

Time call received at dispatch *(hh:mm:ss; 24hr clock)*
: : ○ From PCR/other ○ From dispatch
○ Unable to obtain *(Non-ROC agency 1st arrival, patient excluded from trial)*

Incident Number *(optional)*

Site-linking ID *(optional)*

Obvious Cause	A Site Classification	B Contributing Factors
Excessive heat	○	☐
Foreign body obstruction	○	☐
Hanging	○	☐
Lightning	○	☐
Mechanical suffocation	○	☐
Non-traumatic exsanguination	○	☐
Radiation exposure	○	☐
Respiratory	○	☐
SIDS *(sudden infant death syndrome)*	○	☐
Smoke inhalation	○	☐
Strangulation	○	☐
Terminal illness *(includes end-stage diseases such as cancer)*	○	☐
Trauma *(includes blunt, penetrating or burns)*	○	☐
Venomous stings	○	☐
* Other obvious cause	○	☐

* Other cause (A - Site classification): (60)
* Other cause (B - Contributing Factors): (60)

7. Vital Status at discharge:

- ○ Dead → skip to **Item 10**
- ○ Alive → complete disposition:
  - ○ Home → ○ Independent ○ With assistance ○ Unknown/not noted
  - ○ Rehabilitation
  - ○ Assisted living
  - ○ Nursing home
  - ○ Remain in acute care hospital, reclassified as non-acute patient awaiting placement or chronic care

Episode Information:

Date *(mm/dd/yyyy)* ___ / ___ / ___

ROC PRIMED ID ___

Time call received at dispatch *(hh:mm:ss; 24hr clock)*
___ : ___ : ___ ○ From PCR/other ○ From dispatch
○ Unable to obtain *(Non-ROC agency 1st arrival, patient excluded from trial)*

Incident Number *(optional)* ___

Site-linking ID *(optional)* ___

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8. **Structured Chart Review Tool for Assessment of Cerebral Performance Category at discharge:**
   a. **Is the patient able to follow any simple commands or say any words?**
      - ○ No → skip to **Item 9**
      - ○ Yes
   b. **Is the assistance of someone essential for all or part of the day for activities of daily living (dressing, preparing meals, local travel, shopping)?**
      - ○ No
      - ○ Yes →Could the patient carry out some activities of daily living for 24 hours or overnight?
        - ○ Yes
        - ○ No → Skip to **Item 9**
   c. **Is the patient able to return to work or social activities in any capacity (even limited)?**
      - ○ No → skip to **Item 9**
      - ○ Yes
   d. **Does the patient have any problems that are more than mild i.e. problems that prevent him/her from doing things that he/she would like to do or have to do (dysphasia, hemiplegia, ataxia, dysarthria, memory, cognition, personality)?**
      - ○ No
      - ○ Yes
9. **Modified Rankin Scale at hospital discharge:**
   - ○ MRS0 - No symptoms at all
   - ○ MRS1 - No significant disability despite symptoms: *able to carry out all usual duties and activities*
   - ○ MRS2 - Slight disability: *unable to carry out all previous activities but able to look after own affairs without assistance*
   - ○ MRS3 - Moderate disability: *requiring some help, but able to walk without assistance*
   - ○ MRS4 - Moderately severe disability: *unable to walk without assistance, and unable to attend to own bodily needs without assistance*
   - ○ MRS5 - Severe disability: *bedridden, incontinent and requiring constant nursing care and attention*
10. **Date and time of acute care hospital discharge, re-classification, or death:**
    Date: ___ / ___ / ___ *(mm/dd/yyyy)*
    Time: ___ : ___ *(hh:mm)*
    Was patient made DNR or care limited/withdrawn during hospitalization?
    - ○ No
    - ○ Yes → Date: ___ / ___ / ___ *(mm/dd/yyyy)*
11. **Total days in the ICU/CCU:** ___
    Number of days in hospital: ___ *(prefill)*

Episode Information:

Date *(mm/dd/yyyy)* ___ / ___ / ___

ROC PRIMED ID ___

Time call received at dispatch *(hh:mm:ss; 24hr clock)* ___ : ___ : ___ ○ From PCR/other ○ From dispatch

○ Unable to obtain *(Non-ROC agency 1st arrival, patient excluded from trial)*

Incident Number *(optional)* ___

Site-linking ID *(optional)* ___

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12. If death occurred, check one main category and one subcategory *(where applicable)*:

○ Subject is unstable, and continued life support is impossible or futile
Date of death: ___ / ___ / ___ *(mm/dd/yyyy)*
- ○ Multi-system organ failure
- ○ Recurrent cardiac arrest with unsuccessful resuscitation
- ○ Intractable shock

○ Subject has brain-death criteria, resulting in withdrawal of care and cardiovascular death
Date of decision: ___ / ___ / ___ *(mm/dd/yyyy)*

○ Subject is stable or continued life-support is possible. Because of other non-neurological considerations, care is withdrawn or limited resulting in death
Date of DNR decision: ___ / ___ / ___ *(mm/dd/yyyy)*
- ○ Underlying terminal illness *(metastatic cancer, for example)*
- ○ Pre-existing advanced directives or living will
- ○ Family or surrogate representation of subject's wishes

○ Subject is deemed to have poor neurological prognosis, and care is withdrawn or limited resulting in death
Date of DNR decision: ___ / ___ / ___ *(mm/dd/yyyy)*

13. Were any of the following listed on the hospital discharge summary? *(check all that apply)*

- ☐ None noted
- ☐ Cerebral bleeding/CVA
- ☐ Seizures
- ☐ Bleeding requiring transfusion or surgical intervention
- ☐ Rearrest *(and resuscitated with intervention)*
- ☐ Pulmonary edema
- ☐ Internal thoracic or abdominal injuries
- ☐ Rib fractures
- ☐ Sternal fractures
- ☐ ARDS
- ☐ Liver failure
- ☐ Renal failure
- ☐ Sepsis
- ☐ Pneumonia
- ☐ MI

Interim vital status: Complete this if patient still hospitalized at the time of hospital form completion or DSMB vital status sweep
Patient still hospitallized as of this date: ___ / ___ / ___ *(mm/dd/yyyy)*

14. Was a troponin level obtained within 48 hours of ED/hospital arrival?

○ No
○ Yes → What was the highest concentration during the 1st 48 hours after arrival: ___ (ng/ml)
- ○ Within normal limits ○ Out of normal limits

15. Did the patient have an ST elevation MI, defined as: ST elevation MI on the 1st ECG in the first 48 hours after arrival at the ED/hospital as defined by the ECG report/overreading MD?

○ No ○ Yes

Person responsible for data on this form: ___

6.7.1 Alert CTC Form

The purpose of the Alert CTC form is to notify the CTC regarding a potential adverse event, a protocol violation/deviation, or unusual circumstances related to the study. If any of the listed events occur, the CTC should be notified within one business day of discovery by completion of Alert CTC form on the data entry website. The list provided is an example of items which should be reported to the CTC, but there are many other possible items which may require completion of this form. Basically, if there is any doubt whether an event should be reported, it should, at the very least, warrant a phone call to the CTC in order to discuss the situation. All potential events will be reviewed by the CTC. It is important to emphasize to the EMS providers that they should notify the site's ROC PRIMED study Coordinator of any unusual events, even if they appear unrelated to the study therapy or insignificant to the provider. A single experience or observation at one site may not seem important, but if that event or circumstance occurred at multiple sites, it could be an indication of a problem which needs further investigation. The Alert CTC form should be completed for each potential adverse event where implementation of study protocol results in a potential safety issue either to the patient, EMS staff, or bystander, or there is public objection to the study.

Entering information on an ALERT CTC form associated with an episode:
The ALERT CTC column on the Episode List will show a green "R" for required form (based on data previously entered), a green "?" for entering additional ALERT CTC forms for independent experiences/observations that did not trigger an "R" on the Episode List, a black "C" for complete, and/or a red "E" for error indicating the status of one or more of the forms. On rare occasions, a black "P" will appear if the ALERT CTC form was already completed but no longer required based on data from other forms. Use the Request System to ask the CTC to delete forms in 'P' status.

When entering ROC PRIMED data, if a particular data item indicates a possible adverse event, an ALERT CTC form will be generated and a green "R" will appear in the ALERT column on the Episode List to indicate that an ALERT CTC form is required. When you click on the R, the Episode Summary information will appear with the ALERT CTC forms that are required. The form will have the reason for the ALERT CTC at the top of the page in red. For example: "The purpose of this Alert CTC Form is: ITD opened but not used. Please open the corresponding Alert CTC Form if you alert for a different reason."

If an ALERT CTC form is not generated by data entry but you become aware of an adverse event or an unusual circumstance that requires an ALERT CTC form, click on the green "?" and the Episode Summary page will appear. At the left-hand side of the page, below the Episode Summary Information, click on "Create New Alert CTC Form" and a blank ALERT CTC form with the episode ID will appear. Complete this form with the reason for the ALERT and a "C" for complete or an "E" showing incomplete/errors will appear on the Episode List. The Episode List page will always display a green "?" in the ALERT CTC column so you can add an ALERT CTC form if needed for this episode.

Indicate the date of the cardiac arrest and the time the call was received at dispatch. The ROC PRIMED forms packet is similar to the Epistry and the Hypertonic Saline forms packet, in that each form will have a date and the time call received at dispatch, along with the study ID, incident number, and site linking ID at the top of each page. The incident ID and the site linking ID are optional.

Alert CTC form not associated with a patient episode:
If an incident occurs requiring an ALERT CTC form that is not associated with a patient episode (such as public objection to the ITD or AEvsAL study) data can be entered by clicking on the ALERT CTC button on the ROC PRIMED Main Menu (right side of page). In the Episode Situation box at the top of the Alert CTC form page, check "Not associated with an episode" and enter the date the situation occurred. For example, this could be a missing or broken ITD or a public objection to the trial. In this case, an Alert CTC form can be completed by checking the "Not associated with an episode" button at the top of the form. The date of the situation is the date that it occurred or, if that date is unknown, indicate the date you became aware of the situation. The date of the situation may or may not be the same date of the episode.

List of Alert CTC forms:
To view all ALERT CTC forms, click on the tab at the top of the ROC PRIMED Main Menu labeled "List of ALERT CTC forms". The upper section lists all "Started Alert forms associated with a patient episode." The middle section lists "Empty alert forms associated with episodes.". The lower section lists the "Alert NOT associated with an episode."

Item 0-- *Is this issue associated with an episode:*

Indicate 'yes' or 'no' if the experience or observation to be reported on this Alert CTC form is associated with a specific patient episode. If 'no', indicate the date the situation occurred (not necessarily the date you became aware of the situation). If 'yes', enter the case episode ID (beginning with the site alpha letters, i.e. VAN or OTT) and at least 3 digits to activate the autocompletion feature). The format for the Episode ID to be entered is XXX-12345PR-6

Item 1 – *Date reported to CTC*

Enter the date that the Alert CTC form is initiated (whether or not completed on that date or left in 'E' status). This date may or may not be the same as either that for the date of the situation to be reported or the date of the episode.

Item 2 – *Type of situation:*

For issues marked as being potential safety issues, protocol violations or deviations, or other situations warranting reporting, also provide a description of the circumstances in Item 3, "Explain circumstances," (300 characters). It is intended that all reported conditions on one Alert CTC form are associated with the same 'issue'. Complete a separate Alert CTC for each separate issue. For example, reporting pulmonary edema found on a CXR within 48 hours of the arrest would be expected to be on a separate Alert CTC form than that used to report a public formal objection to the trial. Conversely (and depending on the circumstances) a single Alert CTC form might be used to report that the ITD filled with fluid more than once and there was an associated airway bleed, or delay/interruption of treatment due to the ITD.

Potential Safety Issues Related to Study Protocol or ITD use—indicate all conditions that are being reported as related to the potential adverse situation where implementation of the study protocol resulted in a potential safety issue to the patient, EMS staff, or bystander.

ITD protocol caused delay/interruption of treatment—It is possible that treatment such as compressions or defibrillation were delayed or interrupted for an unacceptable period of time due to providers looking for the ITD, attempting to place the ITD on the airway apparatus, or confusion over how to use the ITD. If a delay or interruption occurred, enter the estimated number of minutes (rounded to whole) of the delay in treatment.

Analyze late vs. early protocol caused delay/interrupt in treatment—There is a possibility of confusion as to whether the patient was in the Analyze Late vs. Early protocol, and if it is deemed that a delay or interruption of care occurred due to this protocol, enter the estimated number of minutes (rounded to whole) that treatment was delayed.

Public formal objection to Trial—An individual who may object to the trial may voice their concern, and this does not require an Alert CTC form to be completed. But, if a community (or their designated spokesperson) or a group of people objected to the trial, check this box.

Other potential safety issue—It is impossible to list all potential safety issues which could occur during a trial, so check this box if, in your judgment, a safety issue occurred and the item is not listed on this form. If 'other potential safety issue', describe the situation in Item 3, "Explain circumstances" (300 characters).

Pulmonary edema found on CXR within 48 hours of arrest—A protocol-listed potential adverse event is pulmonary edema. The majority of patients admitted to the ED or the hospital will have a chest X-ray within 48 hours of arrest. The radiology report should be reviewed for a diagnosis of pulmonary edema on the chest X-ray, and, if found, check this bubble. If the radiology report is unclear as to whether pulmonary edema occurred, the site PI or Co-Investigator should review the report. In the absence of a stated diagnosis, radiologist commentary of findings such as interstitial edema, pleural effusion, Kerley B lines, or diffuse lung opacities are NOT to be recorded as pulmonary edema.

Suspected mechanical failure of ITD—If the EMS provider suspects the ITD or flex tubing has malfunctioned or broken during the course of care, he or she should discontinue use of the device, report this and return the ITD or tubing to the study Coordinator for further evaluation. The ITD ID number should be documented on this alert form. The site Coordinator will need to return the ITD or tubing to the CTC for evaluation. Failure of the timing lights does not constitute a potential safety issue to be reported on a CTC Alert Form, but the EMS provider should report any timing light failures to the site Coordinator, as this information is to be documented on the Pre-hospital data form.

Failure to immediately remove the ITD after ROSC—If ROSC is obtained while the ITD is being used in the patient airway, the ITD should be immediately removed. If ROSC is

lost again, the ITD should be reattached to the airway set-up. The Coordinator should ask the EMS provider, during the post-cardiac arrest follow-up call or on the cardiac arrest study documentation form, whether the ITD was removed at times of transient or sustained ROSC. If not removed, enter the number of cumulative seconds that the ITD remained in the airway line during ROSC.

ITD filled with fluid—The ITD may fill with fluid either from emesis, patient secretions, or pulmonary edema, and can affect the functioning of the ITD. The EMS providers should indicate, either on the post-cardiac arrest call with a Coordinator or on their cardiac arrest study documentation form, whether the ITD filled with fluid at any point during the course of prehospital care. Most sites are planning on emptying the ITD once and continuing to use it, while other sites may discontinue use of the ITD when it first fills with fluid. Either way, indicate whether it filled with fluid once or more than once. If the ITD filled with fluid twice, its use should be discontinued, per protocol guidelines.

Airway bleeding, complete all items a, b and c—EMS or ED/hospital personnel may report finding frank blood, bloody fluid, pink frothy fluid, or blood-tinged fluids in the airway secretions, the oro- or naso-pharynx region, or the advanced airway. Only the finding of frank blood or bloody fluids in the described regions are here considered 'airway bleeding'. Blood-tinged or pink frothy fluids, are alone, not here considered as 'airway bleeding', but should be so characterized if an Alert CTC is otherwise triggered for reporting of frank blood or bloody fluids in the airway. Notation of airway bleeding upon EMS arrival, during the course of EMS or ED/hospital care, or after resuscitation efforts have ceased, is to be reported as a potential safety issue. Airway bleeding need be reported on only one Alert CTC form—triggered by the earliest recognition of airway bleeding, be it in the prehospital or ED/hospital setting (and attributed to the prehospital course of care). Airway bleeding noted in the ED/hospital and attributed to the pre-hospital timeframe would be expected to occur within 24 hours of the cardiac arrest. Prior to October 2008, reports of airway bleeding required a letter from the site Principal Investigator to the CTC within 5 business days of the site being notified of the adverse event. Beginning October 2008, the Alert CTC Form was adapted to capture the circumstances of the observed bleed, relevant patient history, and the site PI/investigator's determination of the severity of the bleed. It is intended that a letter-of-explanation by the PI will rarely be required, and will be then be requested by the DSMB for a given case. The site must separately comply with its local IRB requirements for their notification of adverse events. All sections of the Alert CTC Airway Bleeding section (a, b, and c) must be completed.

If an Alert CTC form is triggered when marking 'airway bleeding' on the Pre-hospital form (because the initial EMS intake interview or review of the PCR has evidence of 'airway bleeding') but subsequent follow-up, clarification, or additional documentation with the EMS provider indicates that bloody fluid or frank blood (other than pink frothy or bloody tinged fluids) was *not* observed, then complete the Alert CTC form in Airway Bleeding sections a-c and explain the circumstances in item #3—the CTC will adjudicate such situations as 'non-reportable events.'

a. Bleeding occurred?
Indicate if the observed bleeding occurred (or was first observed/recorded) before or after each of four situations: arrival of the first EMS (either ROC or non-ROC) response; placement of the ITD (either onto a facemask or advanced airway); attempts at, or placement of, an advanced airway by EMS (either ROC or non-ROC);

and arrival at the ED/hospital. Mark 'N/A' when the situation is not applicable to the clinical course of care, or the temporal relationship of the bleed and situation is unknown. The site is asked to establish the sequence of events to the observed airway bleeding. It is not the intent of the Alert CTC form to report only the evidence of blood-tinged or pink frothy fluids.

b. Patient history information:
For each of the four listed conditions (with which airway bleeding is known to be associated), indicate 'yes' or 'no/not noted' if prehospital or ED/hospital records cites their presence or suspicion. More than one listed condition may apply. If 'yes', provide description of disease or name of drug where indicated. Anticoagulants/antiplatelets—drugs prescribed to help prevent the clotting of blood; includes (but not limited to) aspirin, heparin, warfarin (Coumadin), clopidogrel (Plavix), ticlopidine (Ticlid), and dipyridamole (Persantine). Patient receiving cancer chemotherapy—may be on chronic at-home prescription or bystanders report recent infusion of therapy at an in-patient or out-patient setting. Known lung cancer—may be referred to as carcinoma, metastasis, black lung, or tumor. Known gastrointestinal disease—may be cancer or non-cancer related, including esophageal varices, liver disease, stomach ulcers, ulcerative colitis, or recent GI surgery. Describe the reported condition. Other relevant comorbidity—describe any other reported condition that might cause the presence of 'airway bleeding' as above described, including (but not limited to) recent hemodialysis or lung surgery, alcoholism, hemophilia, or bleeding disorder.

c. Site PI/Investigator determination of severity of bleed:
Fluid description--Describe the presentation(s) of the observed blood in the airway, marking 'yes' or 'no' for each of the listed descriptors. More than one description of the bloody fluid can be marked 'yes'; The exact phrase (such as 'pink frothy' or 'frank blood';) need not be specifically stated in the patient record. Rather, the data abstractor is to review the documented circumstances and mark the description that seems to best reflect the degree of airway bleeding. 'Blood tinged fluid' would be body secretions with spots or flecks of blood; 'Bloody fluid' would be body secretions with large parts blood; 'Frank blood' being little, if no, other body fluids/secretions. For each 'Bloody fluid' and 'frank blood' provide an estimate of the volume of fluid observed—'small' is on the order of a tablespoon, or the palm of a hand; 'large' is on the order of a unit of blood (approximately 300 cc) or more; 'medium' is everything in between. Indicate 'yes' or 'no' if the reported bleeding is determined by the PI/investigator to be the cause of death (not necessarily the cause of the cardiac arrest).

Life threatening?—Indicate if the PI/investigator determines the reported airway bleed to have been life threatening. Recognizing that the patient is in cardiac arrest when the airway bleed is observed, the PI/investigator is asked to discern if the reported airway bleed (considering its description and quantity), was by itself a life threatening condition, or one that negatively affected the patient's chances for survival.

Related to study intervention?—Indicate if the PI/investigator determines if the reported airway bleed is related to either or both the AEvAL and ITD arms of the ROC PRIMED study. That is, would the observed airway bleed have likely occurred

in this patient in the absence of the AEvAL assessment, or deployment of the ITD onto either the face mask or advanced airway.

Expected?—Indicate if the PI/investigator would have anticipated the airway bleed (as characterized in this Alert CTC form) given the circumstances of the patient presentation (considering on-scene response and patient history).

Additional information regarding the source of the blood in airway should be entered in Item #3-"Explain Circumstances", at the bottom of the Alert page. This information may include whether an injury was noted to the lip, teeth, mouth, tongue or a deeper oropharyngeal structure, and if bloody emesis or blood in the endotracheal tube was noted, or if the source is unknown.

Potential Protocol Violations/Deviations—indicate all conditions that are being reported as potential protocol violations or deviations. Provide a description of the circumstances associated with the indicated protocol violations/deviation, or other situation indicated—go to Item 3, “Explain circumstances,” (300 characters).

Age < age of consent (known prior to ITD use) or not removed after EMS aware age < age of consent—The ROC PRIMED Trial is being conducted on adults of the legal age of consent. At most sites, this is 18 years of age or older. Know the guidance for ‘age of consent’ given by your local IRB. Mark this section if EMS knowingly applies, or does not remove, the ITD when the patient’s age is first disclosed as being that less than required for consent. Mark this, whether or not EMS was aware of the age-based study exclusion criteria. Mark this if the patient is an obvious young age to whom an ITD was applied where EMS should have recognized a ‘child’ from an adult age-of-consent.

Traumatic arrest/burns and ITD used—An exclusion for ITD use is traumatic arrest such as a blunt or penetrating injury or burns, so if the ITD is used in one of these patients, check this protocol violation.

Other potential protocol violation/protocol deviation—If a protocol violation or deviation other than those listed on this form occurred, check this box.

Known prisoner—Persons known to be prisoners at the time of prehospital care are excluded from the ROC PRIMED Trial, though there may be times when it is not clear that a patient was a prisoner until after the ITD was used. If the EMS providers responded to a cardiac arrest in a jail cell, in which it was clear that the patient was a prisoner, and yet the study intervention was followed, this is considered a protocol violation and this box should be checked. There may be times when the providers treat a patient and later become aware they were a prisoner <u>at the time</u> of treatment—for this situation. An Alert CTC form should be completed and “Other Situation not listed” checked at the bottom of Item 2. Prisoners will need to be followed for safety purposes, but their data will not be included in the analysis.

Known pregnancy prior to starting treatment—Known pregnancy is an exclusion for the ROC Trial. If it was apparent to the EMS providers that the patient was pregnant at the start of the resuscitation attempt, this box should be checked, as a protocol violation has occurred. Like a prisoner, a pregnancy may not be known until after treatment has

occurred, and, in this case, the condition should be recorded as “Other Situation not listed” as the last item in Item 2. Again, this patient would need to be followed for safety data, but they would not be included in the analysis.

ITD opened, but not used—It is possible that one ITD will be opened by an EMS provider prior to confirmation that a cardiac arrest has occurred or the patient had ROSC in the early treatment arm after receiving one shock, and the ITD was not needed. If the one ITD is opened but never used, this box should be checked and the ID number of the unused ITD provided.. Where more than one ITD was opened (whether used or not), do not mark this box—instead mark the box labeled “more than one ITD opened.”

More than one ITD opened—The protocol specifies that only one ITD is to be opened per patient. It is possible that more than one ITD is opened, and if this occurs this box should be checked. There may be a situation where two EMS vehicles arrive at the scene and bring their equipment to the patient’s side and both open up an ITD package. If this occurs, this bubble should be checked and the ID number for each ITD should be entered, along with an indication of whether or not each ITD was used. Since opening the ITD package constitutes randomization of the patient, opening of two packages is considered a protocol violation. The majority of EMS vehicles will only have one ITD on board to prevent the possibility of two ITDs opened from one rig. EMS vehicles in a high traffic area who seldom are able to return to their base after a cardiac arrest may encounter a second cardiac arrest needing an ITD. Because of this, some vehicles will be allowed to carry two ITDs, but the back-up ITD should be stored in an area of the rig which is not easily accessible during a cardiac arrest, so that opening of two packages can be prevented.

Case entered more than 30 days after episode date- An episode is expected to be entered on the Patient Enrollment form within 3 days of the CA. If an episode is entered more than 30 days after the episode occurred, an Alert form will be triggered. Enter the reason for the delay in notification.

Other Situation not listed--

Missing ITD and Date found—Damage to an ITD may occur or they may be stolen or misplaced, and, if so, this box should be checked and the ITD number noted. Recognition of a missing ITD may occur at the time of an arrest or at the time of an inventory check. If the missing ITD is later found, go to the Alert CTC Form used to first notify the CTC of its missing (located on the Alert CTC forms tab, in the section titled ‘Alert forms NOT associated with an episode’), open to edit the form, and enter the date on which the ITD was recovered.

Broken/Damaged ITD—Enter the # of the ITD that was broken or damaged. This may have occurred during shipment from Almac or when in possession of the site or field inventory.

Pregnancy discovered after treatment started or hospital admit—There may be a case when the EMS providers apply study treatment to a patient but the EMS is unaware that the patient is pregnant at the time they begin treatment. This is not a protocol violation, though it is important that we collect this information. Check this box and explain the circumstances in item 3.

Age < age of consent and unknown until after ITD removed—EMS may be unaware of the patient's age until after the ITD has been applied and removed. This is not a protocol violation, though it is important that we collect this information. Check this box and explain the circumstances in item 3. A patient of an obvious young age to whom an ITD was applied should NOT be included in this category (where the EMS should have recognized a 'child' from an adult)—that circumstance should be reported as a Potential Protocol Violation/Deviation.

Other situation—There will be times when a safety issue or an unusual situation occurs in which it is not listed on the Alert CTC form, and for those times "Other situation not listed" should be checked. Explain the circumstances in item 3.

Item 3 – *Explain circumstances*

Any information related to the safety issue, protocol violation/deviation or unusual situation should be noted in Item 3. The Alert CTC database is set up to allow further documentation as more information becomes available. The site Coordinator or Investigator should use the database for entering all information they are aware of in order to help study monitors determine whether the incident was a definite protocol violation/deviation. For safety issues and protocol violations, information will be needed for the regulatory bodies, including the FDA, NIH, local IRB, and CTC IRB. The documentation will need to be submitted in a time line as required by the FDA. The documentation should include a description of the situation; information obtained from the pre-hospital, ED and hospital records, discussion with the EMS providers; whether the circumstance was expected or life threatening and the opinion of the site PI as to whether it was study related.

Person responsible for data on this form

Name of the individual that logged into the electronic data transmission system for clinical study forms or to execute batch up-load of files. This individual will have registered as a member with the CTC for the purpose of participating as a coordinator or investigator in a ROC clinical trial and has designated a user name and password as their "Electronic Signature." The individual has agreed to consider their electronic signature as equivalent to their handwritten signature, to maintain the confidentiality of their user name and password, and to not let others use it. Refer to the "Electronic Signature Agreement" (accessed after logging on to the ROC website) posted at https://roc.uwctc.org/tiki/roc-data-entry.

After verifying the entered data and electronic signature are correct, print the web-forms for your files, or convert the web-forms to PDF format and store electronically. Edits made later to the original web-entered forms or batch up-loaded data posted to forms are associated with the electronic signature of the individual making the changes and are documented in the file's edit history.

Complete this form:
- For each potential Adverse Situation where implementation of study protocol resulted in a potential safety issue to the patient, EMS staff, or bystander
- For public objection to either study
- For Protocol violations/deviations/unusual circumstances

Report this information to the CTC within 1 business day of discovery

Alert CTC

Date: 10-13-2009
Version: 1.09.00

Episode Information:

Date *(mm/dd/yyyy)* ___ / ___ / ___

ROC PRIMED ID ___

Time call received at dispatch *(hh:mm:ss; 24hr clock)* ___ : ___ : ___ ○ From PCR/other ○ From dispatch

○ Unable to obtain *(Non-ROC agency 1st arrival, patient excluded from trial)*

Incident Number *(optional)* ___

Site-linking ID *(optional)* ___

---

0. Is this issue associated with an episode:

○ **No** → Date of Situation: ___ / ___ / ___ *(mm/dd/yyyy)*

○ **Yes** → Episode Id: ___

1. Date reported to CTC (today's date):

___ / ___ / ___ *(mm/dd/yyyy)*

2. Type of situation: *(check all that apply and explain circumstances in item 3*)*

Potential Safety Issues Related to Study Protocol or ITD use

☐ ITD protocol caused delay/interruption of treatment → Estimated delay ___ minutes

☐ Analyze late vs. early protocol caused delay/interruption in treatment → Estimated delay ___ minutes

☐ Public formal objection to Trial

☐ Other potential safety issue

☐ Pulmonary edema found on CXR within 48 hours of arrest

☐ Suspected mechanical failure of ITD → ITD # ___ - ___ - ___ *(nn-nnn-n)*

☐ Failure to immediately remove the ITD after ROSC → number of seconds on with ROSC ___

☐ ITD filled with fluid: ○ once ○ more than once

☐ Airway bleeding → complete ALL **items a, b & c** below:

a. Bleeding occurred?

	Before	After	N/A	
EMS arrival:	○	○	--	
ITD placed:	○	○	○	*(ITD not placed/timing unknown)*
EMS advanced airway:	○	○	○	*(No advanced airway/timing unknown)*
ED/Hospital arrival:	○	○	--	

b. Patient history information:

Yes	No/not noted		
○	○	Anticoagulants/antiplatelets → drug name: ___	*(30)*
○	○	Patient receiving cancer chemotherapy → drug name: ___	*(30)*
○	○	Known lung cancer	
○	○	Known gastrointestinal disease → describe: ___	*(60)*
○	○	Other relevant comorbidity → describe: ___	*(60)*

Complete this form:
- For each potential Adverse Situation where implementation of study protocol resulted in a potential safety issue to the patient, EMS staff, or bystander
- For public objection to either study
- For Protocol violations/deviations/unusual circumstances

Report this information to the CTC within 1 business day of discovery

Alert CTC
Date: 10-13-2009
Version: 1.09.00

Episode Information:

Date *(mm/dd/yyyy)* ___ / ___ / ___

ROC PRIMED ID ___

Time call received at dispatch *(hh:mm:ss; 24hr clock)* ___ : ___ : ___ ○ From PCR/other ○ From dispatch

○ Unable to obtain *(Non-ROC agency 1st arrival, patient excluded from trial)*

Incident Number *(optional)* ___

Site-linking ID *(optional)* ___

c. Site PI/Investigator determination of severity of bleed:

Fluid description: *(mark "Yes" for any applicable - at least one)*

Yes	No				
○	○	Pink, frothy			
○	○	Blood tinged fluid			
○	○	Bloody fluid →	○ Small	○ Moderate	○ Large
○	○	Frank blood →	○ Small	○ Moderate	○ Large
○	○	Bleeding was cause of death			

Life threatening?	Related to study intervention?	Expected?
○ Yes	○ Yes	○ Yes
○ No	○ No	○ No
○ Maybe/Possibly	○ Maybe/Possibly	○ Maybe/Possibly

Potential Protocol Violations/Deviations

☐ Age < age of consent *(e.g. known prior to ITD use or ITD not removed after EMS aware age < age of consent)*

☐ Traumatic arrest/burns and ITD used

☐ Other potential protocol violation/protocol deviation *(e.g. failure to remove the ITD when entering the ED)*

☐ Known prisoner

☐ Known pregnancy prior to starting treatment

☐ ITD opened, but not used → ITD # ___ - ___ - ___ *(nn-nnn-n)*

☐ More than one ITD opened:

ITD # ___ - ___ - ___ *(nn-nnn-n)* → Used? ○ Yes ○ No

ITD # ___ - ___ - ___ *(nn-nnn-n)* → Used? ○ Yes ○ No

☐ Case entered more than 30 days after episode date

Other Situation not listed

☐ Missing ITD # ___ - ___ - ___ *(nn-nnn-n)* → Date found: ___ / ___ / ___ *(mm/dd/yyyy)*

☐ Broken/Damaged ITD # ___ - ___ - ___ *(nn-nnn-n)*

☐ Pregnancy discovered after treatment started or hospital admit

☐ Age < age of consent and unknown until after ITD removed

☐ Other situation → If situation involves an ITD, enter ITD #: ___ - ___ - ___ *(nn-nnn-n)*

3. Explain circumstances *:

___ *(300 char)*

Person responsible for data on this form: ___

6.8.1 Patient/Family Consent Form

The purpose of the Patient Enrollment form is to document family/patient study notification/consent practices for any patient who is enrolled in the trial. FDA regulations regarding exception from informed consent and local IRB requirements must be followed regarding notification of patients/families of any patients who are enrolled in the trial regardless of whether they survived or not. It is recognized that Canadian sites may have differing requirements on notification of patients who die in the field or in the hospital.

Study personnel should attempt to contact the patient or patient's family as soon as feasible as outlined by their local IRB before they are discharged from the hospital in order to notify them of their participation in the trial. This notification attempt would allow time for discussion of study questions as well as consenting to follow-up interviews and to arrange for future contact by study staff. Identifying oneself with the University or the local EMS agency may help to alleviate patient or family concern about the study and participating in the telephone follow-up. Introductions in the ED or hospital will also establish your identity for the one-, three-, and six-month follow-up phone calls, as well as gathering contact information (phone/address) for the patient/family/LAR. The patient's residence may change from the time of hospital discharge to the one-month follow-up if their health status changes in that time period. Obtaining information about the patient's relatives, close friends, work phone number, and other affiliations such as churches or organizations with which the patient is associated may assist you when attempting to locate the patient for follow-up calls during the following six months. The patient and family should be informed of the time required for the follow-up phone calls.

The procedures for notification will vary from site to site—as per local IRB guidance. Depending on the status of the patient, it may be necessary to use more than one type of notification form. For example, if the patient is unable, either physically or mentally, to understand the notification, the "immediate next of kin or legal authorized representative notification form" may be required. If and when, at a later date, the patient recovers to the point where he or she would understand

In all instances, the site must maintain documentation of all failed and successful attempt to notify the patient, family or LAR.

The episode date, time, and episode ID will be pre-filled by the web data entry program, and it will be consistent with the data and time recorded on the Patient Enrollment form. Pre-filled data should be reviewed for accuracy. The incident ID and the site linking ID are optional.

Item 1 – *Was patient and/or family and/or LAR notified that patient was in study?*

Indicate 'yes' or 'no' whether the patient and/or the family and/or legal adult representative (LAR) were notified of the patient's enrollment in the study. If 'yes', check one or more boxes to indicate who was notified, and the date each was notified. If a 'family or LAR was notified, specify their relationship to the patient. If 'no', explain the reason for not notifying the patient, family, or LAR. **Under no circumstances should the "no" bubble be checked if the site is deferring the notification or waiting to send out a notification.** The "no" bubble should be reserved for cases where no address of an LAR can be accessed or a returned letter (no known forwarding address). A reasonable effort should be made to notify, and the method used must be approved by the local IRB.

Item 2 – ***Did the patient (and/or family/LAR) withdraw from hospital record review after notification?***

Indicate 'no' or 'yes' or 'other' as to whether the patient, family or LAR withdrew from hospital record review at the time of notification or after notification of their participation in the study and enter the reason for the withdrawal and the date it occurred. If the family or LAR withdrew, enter their relationship to the patient. Remember that all records up to the time of withdrawal can be reviewed per the FDA. For example, if the patient was entered into the study on June 1 and he was notified of his participation at 10:00 AM on June 3 but decided to withdraw from hospital record review, all records up until 10:00 AM on June 3 can be reviewed and entered on the ROC PRIMED data forms. Refusal of consent for follow-up does not translate into refusal for medical records review. Unless the patient/family withdraws from the medical records review the site can continue to collect the data even if the patient/family decides not to continue with the post discharge follow-up. If 'other', enter the explanation in the box provided on the form. It would be very unusual to have 'other' checked, so please contact the CTC to discuss the situation for which you are checking 'other'.

Item 3 – ***Did patient and/or family and/or LAR consent to follow-up calls?***

Indicate 'no' or 'yes' whether the patient and/or family and/or LAR gave consent for the site to contact them for follow-up calls. If 'yes', indicate who gave the consent and on what date the consent was given. If family/LAR, indicate the relationship of that person to the patient. If 'no', they did not consent to follow-up calls indicate the reason: refused, expired, not required per exclusion on Patient Enrollment form, language barrier, consent deferred until 1 month follow-up, unable to contact patient/family/LAR or other. If refused, provide the reason for the refusal. A deferral could occur because the patient or the family/LAR was not ready to make a decision regarding their participation in the follow-up calls. If 'other', enter the explanation in the box provided on the form.

Item 4- ***Document and explain attempts to contact patient or patient representative:***

Sites need to document attempts made to contact the patient, family or LAR about their participation in the study and the attempt to obtain consent for follow-up. The attempted contacts can be documented on this web form, on the 'Documentation of Patient/Family Contact' from provided by the CTC or in the site episode file. Check either 'Documentation maintained by local log or episode file' or 'Documentation maintained on this form' on the web form. If the site chooses to document the attempted contacts on the 'Documentation of Patient/Family Contact' from provided by the CTC or in the site episode file, the information needs to be available during a site audit or regulatory agency review.

Person responsible for data on this form

Name of the individual that logged into the electronic data transmission system for clinical study forms. This individual will have registered as a member with the CTC for the purpose of participating as a coordinator or investigator in a ROC clinical trial and has designated a user name and password as their "Electronic Signature." The individual has agreed to consider their

electronic signature as equivalent to their handwritten signature, to maintain the confidentiality of their user name and password, and to NOT share it with others. Refer to the “Electronic Signature Agreement” (accessed after logging on to the ROC website) posted at https://roc.uwctc.org/tiki/roc-data-entry.

After verifying the entered data and electronic signature are correct, print the web-forms for your files, or convert the web-forms to PDF format and store electronically. Edits made later to the original web-entered forms are associated with the electronic signature of the individual making the changes and are documented in the file’s edit history.

Complete this form:
- for all patients who were enrolled for which this form shows "R" status on the Episode List.

Patient/Family Consent

Date: 08-11-2009
Version: 1.01.00

Episode Information:

Date *(mm/dd/yyyy)* ___ / ___ / ___

ROC PRIMED ID ___

Time call received at dispatch *(hh:mm:ss; 24hr clock)*
___ : ___ : ___ ○ From PCR/other ○ From dispatch
○ Unable to obtain *(Non-ROC agency 1st arrival, patient excluded from trial)*

Incident Number *(optional)* ___

Site-linking ID *(optional)* ___

---

1. Was patient and/or family and/or LAR notified that patient was in the study?

○ Yes →Who was notified? *(check all that apply)*
- ☐ Family → Date: ___ / ___ / ___ (mm/dd/yyyy) → Relationship: ___ *(20)*
- ☐ Patient → Date: ___ / ___ / ___ (mm/dd/yyyy)
- ☐ LAR → Date: ___ / ___ / ___ (mm/dd/yyyy) → Relationship: ___ *(20)*

○ No → explain:
___ *(60)*
___ *(60)*

2. Did the patient (and/or family/LAR) withdraw from hospital record review after notification?
(Remember all records up to the time of withdrawal can be reviewed)

○ No

○ Yes → Who withdrew? *(check all that apply)*
- ☐ Family/LAR → Date: ___ / ___ / ___ *(mm/dd/yyyy)* → Relationship: ___ *(20)*
- ☐ Patient → Date: ___ / ___ / ___ *(mm/dd/yyyy)*

Reason: ___ *(100)*

○ Other → Explain: ___ *(100)*

3. Did patient and/or family and/or LAR consent to follow-up calls?

○ Yes →Who gave consent? *(check all that apply)*
- ☐ Family → Date: ___ / ___ / ___ (mm/dd/yyyy) → Relationship: ___ *(20)*
- ☐ Patient → Date: ___ / ___ / ___ (mm/dd/yyyy)
- ☐ LAR → Date: ___ / ___ / ___ (mm/dd/yyyy) → Relationship: ___ *(20)*

○ No → Why not? *(check one only)*
- ○ Patient refused consent → Date: ___ / ___ / ___ *(mm/dd/yyyy)*
  Explain: ___ *(60)*
- ○ Family/LAR refused consent → Date: ___ / ___ / ___ *(mm/dd/yyyy)*
  Explain: ___ *(60)*
- ○ Expired - date of death: ___ / ___ / ___ *(mm/dd/yyyy)*
- ○ Not required per exclusion on **Patient Enrollment** form
- ○ Language barrier *(Non-English or Spanish-speaking patient)*
- ○ Consent deferred until 1 month follow-up
- ○ Unable to contact patient/family/LAR *(by phone/consent form not returned/no forwarding address)* as required by the consent/notification plan approved by the IRB/REB. Document the contact attempts in either **item 4**, on the Site's Documentation of Patient/Family Contact form, or in the episode file maintained by the site.
  Explain: ___ *(60)*
- ○ Other → explain: ___ *(60)*

Complete this form:
- for all patients who were enrolled for which this form shows "R" status on the Episode List.

Patient/Family Consent

Date: 08-11-2009
Version: 1.01.00

Episode Information:

Date *(mm/dd/yyyy)*
/ /
ROC PRIMED ID

Time call received at dispatch *(hh:mm:ss; 24hr clock)*
: :
From PCR/other From dispatch
Unable to obtain *(Non-ROC agency 1st arrival,* patient excluded from trial)

Incident Number *(optional)*
Site-linking ID *(optional)*

4. Document and explain attempts to contact patient or patient representative:
(The CTC expects sites to keep a log of attempts made to contact the patient, family or LAR. This can be accomplished by either keeping a local log using the CTC provided Documentation of Patient/Family Contact form, in the site episode file or by using this web form)

- **Documentation maintained by local log or episode file**
- **Documentation maintained on this form**

Date *(mm/dd/yyyy)*	**Type of attempt:** *(Phone, clinic visit, Letter, Certified letter, In person, Email & Other)*	**Results/notes** *(200 characters)*
/ /	If Other, specify: *(30)*	
/ /	If Other, specify: *(30)*	
/ /	If Other, specify: *(30)*	
/ /	If Other, specify: *(30)*	
/ /	If Other, specify: *(30)*	
/ /	If Other, specify: *(30)*	
/ /	If Other, specify: *(30)*	

Person responsible for data on this form

Name:

6.9.1 Follow-up Forms: 1 month, 3 months, 6 months

The purpose of the Follow-up form is to document the patient's participation in follow-up activities at month 1, month 3, and month 6, from the date of discharge from the final acute care hospital (as might occur when the patient is transferred from one hospital to another; not to be confused with a non-acute/rehab/chronic care institution) associated with the cardiac arrest qualifying the patient for enrollment into ROC PRIMED. The Follow-up form captures quality of life measures done at these follow-up periods, who the follow-up was conducted with, or indicates if the patient died since hospital discharge or the last follow-up. This form should be completed on all patients who were discharged alive from the hospital and speak English or Spanish as their primary language.

Coordinators performing the follow-up calls must first view the Quality of Life training video. Go to ROC website > data entry > ROC PRIMED > Training > Quality of Life to view the video. New coordinators should contact the CTC prior to first starting patient follow-up. Please see the additional information on the ALFI-Mini-Mental State Exam and the Modified Rankin Scale at the end of this section.

The ROC PRIMED forms packet is similar to the Epistry and the Hypertonic Saline forms packet, in that each form will have a date and the time call received at dispatch, along with the study ID, incident number, and site linking ID at the top of each page. The incident ID and the site linking ID are optional.

The follow-up calls are due 30 days from patient discharge (1 month call), 90 days (3 month call) and180 days (6 month call). There is a 7 day window on either side of the due date but if you are unable to contact the patient within the time window, contact should be made as soon after as possible. The "R" on the Episode list for the pending form will turn from black to green a week prior to the due date to signal the approaching time frame.

All attempts at contacting the patient for each the month 1, 3, and 6 follow-ups should be documented on the patient care record or the hard copy Patient Contact Documentation form provided by the CTC.

Self-assessed versus Proxy:
Follow-up forms should be conducted with the patient unless the patient scores < 17 on the ALFI-MMSE. If the patient scores < 17, subsequent Follow-Up questionnaires are completed with the proxy.

Example:
1) Month 1-Patient scores > 17 on the ALFI-MMSE.
Month 3-Patient scores > 17 on the ALFI-MMSE. All QOL forms completed using the self-assessed versions (Cerebral Performance Score-Telephone Interview of Patient, Structured Interview for Modified Rankin Scale, Health Utilities Index-self-assessed (HUI) and Geriatric Depression Scale).
Month 6- Patient scores > 17 on the ALFIMMSE. All QOL forms completed using the self-assessed versions (Cerebral Performance Score-Telephone Interview of Patient, Structured Interview for Modified Rankin Scale, Health Utilities Index-self-assessed (HUI) and Geriatric Depression Scale).

2) Month 1-Patient scores > 17 on the ALFI-MMSE.
Month 3-Patient scores > 17 on the ALFI-MMSE > All QOL forms completed using the self-

assessed versions (Cerebral Performance Score-Telephone Interview of Patient, Structured Interview for Modified Rankin Scale, Health Utilities Index-self-assessed (HUI) and Geriatric Depression Scale).
Month 6-Patient scores <17 on the ALFI-MMSE. QOL forms completed using the proxy versions (Cerebral Performance Score-Telephone Interview of Caregiver, Structured Interview for Modified Rankin Scale, Health Utilities Index-by proxy). No Geriatric Depression Scale.

3) Month 1-Patient scores < 17 on the ALFI-MMSE.
Month 3- QOL forms completed using the proxy versions (Cerebral Performance Score-Telephone Interview of Caregiver, Structured Interview for Modified Rankin Scale, Health Utilities Index-by proxy). No Geriatric Depression Scale.
Month 6- QOL forms completed using the proxy versions (Cerebral Performance Score-Telephone Interview of Caregiver, Structured Interview for Modified Rankin Scale, Health Utilities Index-by proxy). No Geriatric Depression Scale.

Item 1 – *Follow-up period*

Confirm the follow-up period for which this form is being completed, either month 1, 3, or 6. The form indicates which follow-up measures are required at each time period.

Item 2 – *Was the patient (or patient representative) successfully contacted?*

If "Yes," indicate the date of the successful contact. If you contact the patient on that day and they request you to contact them on the following (or another) day for the follow-up questions, use the following (or other) day's date for the date of contact if you are successful in completing the follow-up requirements at that time. If the patient or patient representative was not successfully contacted, check "No" and indicate the reason. It is important to have separately documented all unsuccessful attempts to contact the patient or their representatives.

Item 3 – *Was consent obtained?*

Check "Yes, previously" if consent was obtained either while the patient was still hospitalized or after discharge, but prior to the follow-up period that is the subject of this form. If consent was obtained during your follow-up call on the date noted in Item 2, check "Yes" (not to be confused with 'yes, previously'). If during the follow-up call the patient or patient's family/LAR instructed you they did not want to be contacted again, check "No, refused all further contact." If on this contact date in Item 2 the patient or family/LAR indicated they did not want to complete a follow-up at this time (possibly due to ill health or uncertainty regarding further participation), but are willing to be contacted at the next follow-up period, check "No, deferred until the next follow-up period."

The method for obtaining patient or family/LAR consent may be specific to each site and is subject to guidance by the local IRB/REB. The allowance for verbal consent or the requirement for written consent is directed by the local IRB/REB.

Item 4 – *Follow-up conducted with whom?*

Indicate if the follow-up was conducted with the patient, the patient's family, or other. If the follow-up was not with the patient, indicate the relationship to the patient of the person you spoke with.

Item 5 – *Vital status*

If at the time of the call the patient was alive (you either spoke with the patient or the family/LAR told you the patient was alive), check the "Alive" bubble. If you became aware the patient died, indicate the date of death and skip questions 6 and 7.If an indication of alive or dead is obtained during the course of the conversation, that status can be here indicated, regardless of refusal of further contact or deferral until next follow-up period.

Item 6 – *What QOL measures were done?*

Each follow-up period is associated with a specific mix of quality of life measures to be collected. The form for each follow-up period lists the measures required for that period. Check all quality of life measures (CPC, MRS, ALFI-MMSE, HUI, GDS) that were done. If no quality of life measures were done during this follow-up, check "None" and go to Item 7 to provide a narrative reason for not completing the required measure(s).

Item 7 – *If any of the measures listed for this F/U in item 1 were not completed & consent was obtained, why not?*

Indicate which of the required measures noted in Item 1 (and Item 6) were not done and the reason for this. It is possible that several measures were completed and then the patient became tired and declined to answer any more questions. It is also possible that a patient requests that you call them back the following day to complete the questions, and if this occurs, the date that you began the follow-up measures can be noted in Item 2. Where the patient cooperates with some of the initial measures, but asks that you call back a different day to complete some of the others, note in Item 7, the date you called back to complete the interview and the measures reviewed at that time.

Document the efforts—both successful and unsuccessful—made to contact the patient or patient's family/LAR for the follow-up interviews. Multiple calls may be necessary to complete the forms. The documentation of your efforts should be kept in the patient's file, as these will be reviewed on site visits. If a site has a significant number of patients who are either refusing to consent for follow-up or the site is unable to contact the patients, the CTC will work with the site Coordinator on possible methods to increase the follow-up rate.

Questions for Coordinators

When exiting this web-page, whether all items completed with/without errors or portions of the QOL requirements not (yet) fulfilled, indicate the status of 'today's' web-entry of data, selecting one of the three descriptors that best explains the status of the QOL data.

QOL interview guides—ALFI Mini-Mental Sate Examination (ALFI-MMSE), Cerebral Performance Category (CPC), Structured Interview for Assessment of Modified Rankin Scale (MRS), Health Utilities Index (HUI), Geriatric Depression Scale (GDS)

Each follow-up period is associated with a specific mix of quality of life measures to be collected. Following Item 7, the list of period-specific follow-up QOL measures is listed. They are listed in the recommended order of priority. Click on the title of each measure to reveal the related questionnaire form. Read the following pages for directions to conduct the interview for ALFI-Mini-Mental State Examination and the Modified Rankin Scale.

Person responsible for data on this form

Name of the individual that logged into the electronic data transmission system for clinical study forms or to execute batch up-load of files. This individual will have registered as a member with the CTC for the purpose of participating as a coordinator or investigator in a ROC clinical trial and has designated a user name and password as their "Electronic Signature." The individual has agreed to consider their electronic signature as equivalent to their handwritten signature, to maintain the confidentiality of their user name and password, and to not let others use it. Refer to the "Electronic Signature Agreement" (accessed after logging on to the ROC website) posted at https://roc.uwctc.org/tiki/roc-data-entry.

After verifying the entered data and electronic signature are correct, print the web-forms for your files, or convert the web-forms to PDF format and store electronically. Edits made later to the original web-entered forms or batch up-loaded data posted to forms are associated with the electronic signature of the individual making the changes and are documented in the file's edit history.

Complete this form:
- for all patients that were discharged alive from the hospital and consented to follow-up

Follow-up

Version 1.04.00
Date: 01/13/2009

Episode Information:

Date *(mm/dd/yyyy)* ___/___/___

Time call received at dispatch *(hh:mm:ss; 24hr clock)* ___:___:___

- ○ From PCR/other ○ From dispatch
- ○ Unable to obtain *(Non-ROC agency first arrival & no agreement in place to get data, patient is excluded from Trial)*

ROC PRIMED ID: ___-___-___

Incident Number *(optional)* _____

Site Linking ID *(optional)* _____

1. Follow-up period:

- ○ 1 month → Complete **ALFI-MMSE** measures

2. Was the patient (or patient representative) successfully contacted?

- ○ Yes → Date of contact: ___/___/___ *(mm/dd/yyyy)*
- ○ No → Why not? _____ *(30)*

3. Was consent obtained?

- ○ Yes, previously
- ○ Yes
- ○ No, refused all further contact
- ○ No, deferred until next follow-up period

4. Follow-up conducted with whom?

- ○ Patient
- ○ Family → Relationship to patient: _____ *(30)*
- ○ Other → Relationship to patient: _____ *(30)*

5. Vital status:

- ○ Alive
- ○ Dead → Date of death: ___/___/___ *(mm/dd/yyyy)* → If day of death is not available: ___/___ *(mm/yyyy)*
  (Skip the remaining questions)

6. What QOL measures were done? *(check all that apply)*

- ☐ ALFI-MMSE
- ☐ None

7. If any of the measures listed for this F/U in item 1 were not completed & consent was obtained, why not?

_____ *(300 characters)*

Person responsible for data on this form: _____

Complete this form:
for all patients that were discharged alive from the hospital and consented to followup. Target date for completion is 1, 3, and 6 months from the date of hospital discharge.

Follow Up

Date: 08-25-2009
Version: 1.07.00

Episode Information:

Date *(mm/dd/yyyy)* ___ / ___ / ___

ROC PRIMED ID ___

Time call received at dispatch *(hh:mm:ss; 24hr clock)*
___ : ___ : ___ ○ From PCR/other ○ From dispatch
○ Unable to obtain *(Non-ROC agency 1st arrival, patient excluded from trial)*

Incident Number *(optional)* ___

Site-linking ID *(optional)* ___

---

1. **Follow-up period:**
   - ○ 3 month → Complete **CPC**, **MRS**, **ALFI-MMSE**, **HUI**, **GDS** measures

2. **Was the patient (or patient representative) successfully contacted?**
   - ○ Yes → Date of contact: ___ / ___ / ___ *(mm/dd/yyyy)*
   - ○ No → Why not? ___ *(30)*

3. **Was consent obtained?**
   - ○ Yes, previously
   - ○ Yes
   - ○ No, refused all further contact
   - ○ No, deferred until next follow-up period

4. **Follow-up conducted with whom?**
   - ○ Patient
   - ○ Family → Relationship to patient: ___ *(30)*
   - ○ Other → Relationship to patient: ___ *(30)*

5. **Vital status:**
   - ○ Alive
   - ○ Dead → Date of death: ___ / ___ / ___ *(mm/dd/yyyy)* → If day of death is not available: ___ / ___ *(mm/yyyy)*
     (Skip the remaining questions)

6. **What QOL measures were done?** *(check all that apply)*
   - ☐ CPC
   - ☐ MRS
   - ☐ ALFI-MMSE
   - ☐ HUI
   - ☐ GDS
   - ☐ None

7. **If any of the measures listed for this F/U in item 1 were not completed & consent was obtained, why not?**
   ___ *(300 characters)*

Person responsible for data on this form

Name: ___

Complete this form:
for all patients that were discharged alive from the hospital and consented to followup. Target date for completion is 1, 3, and 6 months from the date of hospital discharge.

Follow Up

Date: 08-25-2009
Version: 1.07.00

Episode Information:

Date *(mm/dd/yyyy)* ____ / ____ / ____

ROC PRIMED ID ____

Time call received at dispatch *(hh:mm:ss; 24hr clock)*
____ : ____ : ____ ○ From PCR/other ○ From dispatch
○ Unable to obtain *(Non-ROC agency 1st arrival, patient excluded from trial)*

Incident Number *(optional)* ____

Site-linking ID *(optional)* ____

---

1. **Follow-up period:**
   - ○ 6 month → Complete **CPC**, **MRS**, **ALFI-MMSE**, **HUI**, **GDS** measures

2. **Was the patient (or patient representative) successfully contacted?**
   - ○ Yes → Date of contact: ____ / ____ / ____ *(mm/dd/yyyy)*
   - ○ No → Why not? ____ *(30)*

3. **Was consent obtained?**
   - ○ Yes, previously
   - ○ Yes
   - ○ No, refused all further contact
   - ○ No, deferred until next follow-up period

4. **Follow-up conducted with whom?**
   - ○ Patient
   - ○ Family → Relationship to patient: ____ *(30)*
   - ○ Other → Relationship to patient: ____ *(30)*

5. **Vital status:**
   - ○ Alive
   - ○ Dead → Date of death: ____ / ____ / ____ *(mm/dd/yyyy)* → If day of death is not available: ____ / ____ *(mm/yyyy)*
     (Skip the remaining questions)

6. **What QOL measures were done?** *(check all that apply)*
   - ☐ CPC
   - ☐ MRS
   - ☐ ALFI-MMSE
   - ☐ HUI
   - ☐ GDS
   - ☐ None

7. **If any of the measures listed for this F/U in item 1 were not completed & consent was obtained, why not?**
   ____ *(300 characters)*

Person responsible for data on this form

Name: ____

ALFI Mini-Mental State Examination

Follow-up period: 6 months

1. **What is the year?**
   ☐ *(yyyy)* ○ Cannot answer ○ Other refusal
2. **What is the season?**
   ○ Spring ○ Autumn
   ○ Summer ○ Winter

   ○ Cannot answer ○ Other refusal
3. **What is the date?**
   ☐ *(dd)* ○ Cannot answer ○ Other refusal
4. **What is the day of the week?**
   ○ Monday ○ Wednesday ○ Friday ○ Sunday
   ○ Tuesday ○ Thursday ○ Saturday

   ○ Cannot answer ○ Other refusal
5. **What is the month?**
   ○ January ○ April ○ July ○ October
   ○ February ○ May ○ August ○ November
   ○ March ○ June ○ September ○ December

   ○ Cannot answer ○ Other refusal
6. **Can you tell me where you are right now? For instance, what State/Province are you in?**
   ○ Correct ○ Incorrect ○ Cannot answer ○ Other refusal
7. **What county are you in?**
   ○ Correct ○ Incorrect ○ Cannot answer ○ Other refusal
8. **What town are you in?**
   ○ Correct ○ Incorrect ○ Cannot answer ○ Other refusal
9. **What is the name of the place that you are in?***("home", "house", address, other correct name of a facility or other person's house)*
   ○ Correct ○ Incorrect ○ Cannot answer ○ Other refusal
10. **I shall say three words for you to remember. Repeat them after I have said all three words.** *(Check each bubble if the word was repeated correctly)*
    ☐ Shirt ☐ Brown ☐ Honesty
11. **Please subtract 7 from 100.**
    (Do this 5 times - may coach patient if needed)
    (Count only 1 error if subject makes subtraction error, but subsequent answers are 7 less than the error)
    Number Correct: ○ 5 ○ 4 ○ 3 ○ 2 ○ 1 ○ 0
12. **What are the three words that I asked you to remember?**

Shirt	**Brown**	**Honesty**
○ Spontaneous recall	○ Spontaneous recall	○ Spontaneous recall
○ Cue: **something to wear**	○ Cue: **a color**	○ Cue: **good personal quality**
○ Multiple: **shoes, shirt, socks**	○ Multiple: **blue, black, brown**	○ Multiple: **charity, honesty, modesty**
○ Unable to recall	○ Unable to recall	○ Unable to recall

13. **Repeat what I say: "No ifs, ands, or buts"?**
    ○ Correct ○ 1 out of 3 words in the phrase correct
    ○ 2 out of 3 words in the phrase correct ○ Unable to repeat, or misses the 's'
14. **What is the name of the thing that we are using to talk now?** *(Do not wait for the patient to name it)*
    ○ Telephone, receiver, mouthpiece, etc ○ Cannot answer
    ○ Inaccurate ○ Other refusal
15. **Now I'm going to give you some instructions to follow. I want you to do a 3 step task.**
    First, say "hello", then tap the telephone receiver 3 times with your finger, then say "I'm back" into the phone

    ☐ Hello ☐ Tap ☐ I'm back ☐ Cannot answer ☐ Other refusal

Person responsible for data on this form: ☐

Cerebral Performance Category

Follow-up period: 6 months

Structured Interviews for Assessment of Cerebral Performance Category

Introduction

The research assistant will ask/review the following questions in order to categorize the patient as Cerebral Performance Category (CPC) scale 1 - 4, based upon current status. Telephone questions may be asked of a caregiver, if necessary.

Telephone Interview of Caregiver

1. **Is the patient able to follow simple commands or say a few words (i.e. conscious)?**
   - ○ No → Stop here
   - ○ Yes → Go on
2. **Is the patient able to do normal daily activities without assistance (dressing, preparing meals, local travel, shopping)?**
   - ○ No →Is assistance of another person essential EVERY DAY for some activities of daily living *(i.e. patient cannot be left alone for 24 hours or overnight)* ?
     - ○ Yes → Stop here
     - ○ No → Go on
   - ○ Yes → Go on
3. **Does the patient have any problems that are more than mild, i.e. problems that prevent him/her from doing things that he/she would like to do or have to do (difficulty speaking, moving an arm, or walking; poor memory; getting along with others)?**
   - ○ No → Go on
   - ○ Yes → Stop here
4. **Has the patient returned to a normal life (work, leisure, family activities)?**
   - ○ No → Stop here
   - ○ Yes → Stop here

Telephone Interview of Patient

1. **Are you able to do your normal daily activities without assistance (dressing, preparing meals, local travel, shopping)?**
   - ○ No → Stop here
   - ○ Yes → Go on
2. **Do you have any problems that are more than mild, i.e. problems that prevent you from doing things that you would like to do or have to do (difficulty speaking, moving an arm, or walking; poor memory; getting along with others)?**
   - ○ No → Go on
   - ○ Yes → Stop here
3. **Have you returned to a normal life (work, leisure, family activities)?**
   - ○ No → Stop here
   - ○ Yes → Stop here

Person responsible for data on this form

Name:

Structured Interview for Assessment of Modified Rankin Scale

Follow-up period: 6 months

Please record responses to all questions (unless otherwise indicated in the text), including those concerning status before cardiac arrest. See guidelines on the facing page for further information.

1. Constant Care:

Constant care means that someone needs to be available at all times. Care may be provided by either a trained or untrained caregiver. The patient will usually be bedridden and may be incontinent.	**Now**		**Before cardiac arrest**	
	Yes	No	Yes	No
a. Does the person require constant care?	○	○	○	○

2. Assistance to attend to bodily needs/for walking:

Assistance includes physical assistance, verbal instruction, or supervision by another person.	**Now**		**Before cardiac arrest**	
	Yes	No	Yes	No
a. Is assistance essential for eating? *(Eating without assistance: food and implements may be provided by others)*	○	○	○	○
b. Is assistance essential for using the toilet? *(Using toilet without assistance: reach toilet/commode; undress sufficiently, clean self; dress and leave)*	○	○	○	○
c. Is assistance essential for routine daily hygiene? *(Routine hygiene: washing face, doing hair, cleaning teeth/fitting false teeth. Implements may be provided by others and this should not be considered assistance)*	○	○	○	○
d. Is assistance essential for walking? *(Walking without assistance: able to walk indoors around house or ward, may use any aid (e.g. stick/cane, walking frame/walker), however not requiring physical help or verbal instruction or supervision from another person)*	○	○	○	○

3. Assistance to look after own affairs:

Assistance includes physical assistance, or verbal instruction, or supervision by another person.	**Now**		**Before cardiac arrest**	
	Yes	No	Yes	No
a. Is assistance essential for preparing a simple meal? *(For example, able to prepare breakfast or a snack)*	○	○	○	○
b. Is assistance essential for basic household chores? *(For example, finding and putting away clothes, clearing up after a meal. Exclude chores that do not need to be done every day, such as using a vacuum cleaner)*	○	○	○	○
c. Is assistance essential for looking after household expenses?	○	○	○	○
d. Is assistance essential for local travel? *(Patients may drive or use public transport to get around. Ability to use a taxi is sufficient, provided the person can phone for it themselves and instruct the driver)*	○	○	○	○
e. Is assistance essential for local shopping? *(Local shopping: a least able to buy a single item)*	○	○	○	○

4. Usual duties and activities:

The next sets of questions are about how the patient usually spends his/her day.

a. Work:

i. Before the cardiac arrest, was the person working or seeking work or studying as a student? *(If the person was not employed or seeking work before the cardiac arrest, or the person was retired then indicate "No" and go to **item 4b**)*

- ○ Yes
- ○ No → go to **item 4b**

ii. Since the cardiac arrest has there been a change in the person's ability to work or study? *(Change in ability to work or study includes loss of employment or reduction in level of responsibility; change in education or problems with study)*

- ○ Yes → How restricted are they?
  - ○ Reduced level of work (e.g. change from full-time to part-time or change in level of responsibility)
  - ○ Currently unable to work
- ○ No

b. Family responsibilities:

i. Before the cardiac arrest was the person looking after family at home *(If this was not a major role before the cardiac arrest, indicate "No" and go to **item c**)*

- ○ Yes
- ○ No → go to **item 4c**

ii. Since the cardiac arrest has there been a change in their ability to look after family at home?

- ○ Yes → How restricted are they?
  - ○ Reduced responsibility for looking after family
  - ○ Currently unable to look after family
- ○ No

c. Social & leisure activities:

(Social and leisure activities include hobbies and interests. Includes activities outside the home or at home. Activities outside the home: going to the pub/bar, restaurant, club, church, cinema, visiting friends, going for walks. Activities at home: involving "active" participation including knitting, sewing, painting, games, reading books, home improvements).

i. Before the cardiac arrest did the person have regular free-time activities? *(If the person had very restricted social & leisure activities before the cardiac arrest then indicate "No" and go to **item 4d**)*

- ○ Yes
- ○ No → go to **item 4d**

ii. Since the cardiac arrest has there been a change in their ability to participate in these activities?

- ○ Yes → How restricted are they?
  - ○ Participate a bit less: *at least half as often as before the cardiac arrest*
  - ○ Participate much less: *less than half as often*
  - ○ Unable to participate: *rarely, if ever, take part*
- ○ No

5. Usual duties and activities: *(Continued)*

d. Family & Friendship:

(Problems with relationships include difficulties in relationships with people at home, loss of friendships or increase in isolation. Changes in the person may include: communication problems, quick temper, irritability, anxiety, insensitivity to others, mood swings, depression, and unreasonable behavior).

i. Since the cardiac arrest has the person had problems with relationships or become isolated?

- ○ Yes → What is the extent of disruption/strain?
  - ○ Occasional: *less than weekly*
  - ○ Frequent: *once a week or more, but tolerable*
  - ○ Constant: *daily & intolerable*
- ○ No

ii. Before the cardiac arrest were any similar problems present?

- ○ Yes
- ○ No

6. Symptoms as a result of the cardiac arrest:

(Can be any symptoms or problems reported by the patient or found on neurological examination)

a. Does the patient have any symptoms resulting from the cardiac arrest? *(Record spontaneous answer to the question from respondent)*

- ○ Yes
- ○ No

Structured Interview for Assessment of Modified Rankin Scale

Follow-up period: 6 months

b. Symptom checklist:

	Now		Before cardiac arrest	
	Yes	No	Yes	No
i. Does the person have difficulty reading or writing?	○	○	○	○
ii. Does the person have difficulty speaking or finding the right word?	○	○	○	○
iii. Does the person have problems with balance or coordination?	○	○	○	○
iv. Does the person have visual problems?	○	○	○	○
v. Does the person have numbness (face, arms, legs, hands, feet)?	○	○	○	○
vi. Has the person experienced loss of movement (face, arms, legs, hands, feet)?	○	○	○	○
vii. Does the person have difficulty with swallowing?	○	○	○	○
viii. Any other symptoms? Please record:	○	○	○	○

Person responsible for data on this form:

HEALTH UTILITIES INDEX

Self-Assessed
Follow-up period: 6 months

Start time: [ ] : [ ] *(24-hour clock)*

Read to Patient:

The next set of questions ask about various aspects of your health. When answering these questions we would like you to think about your health and your ability to do things on a day-to-day basis, during the past week. To define the 1 week period, please think about what the date was 7 days ago and recall the major events that you have experienced during this period. Please focus your answer on your abilities, disabilities and how you have felt during the past 1 week.

You may feel that some of these questions do not apply to you, but it is important that we ask the same questions to everyone. Also, a few questions are similar; please excuse the apparent overlap and answer each question independently.

All information you provide is confidential. There are no right or wrong answers; what we want is your opinion about your abilities and feelings.

Interviewer:
For each question, read the entire question/sentence as written following the question number, emphasizing the words in italics, if any. Do not read the response options listed below the question. If the responses are included as part of the question (eg: Q26, Q31 etc) read them as part of the questions. The answer given by the respondent to each question should be clearly marked in the circle beside the one appropriate answer listed below the question.

VISION

1. **During the past week, have you been able to see well enough to read ordinary newsprint *without* glasses or contact lenses?**
   - ○ Yes → Go to **Item 4**
   - ○ No
   - ○ Don't know
   - ○ Refused
2. **Have you been able to see well enough to read ordinary newsprint *with* glasses or contact lenses?**
   - ○ Yes → Go to **Item 4**
   - ○ No
   - ○ Don't know/Didn't wear glasses or contact lenses
   - ○ Refused
3. **During the past week, have you been able to see at all?**
   - ○ Yes
   - ○ No → Go to **Item 6**
   - ○ Don't know
   - ○ Refused
4. **During the past week, have you been able to see well enough to recognize a friend on the other side of the street *without* glasses or contact lenses?**
   - ○ Yes → Go to **Item 6**
   - ○ No
   - ○ Don't know
   - ○ Refused
5. **Have you been able to see well enough to recognize a friend on the other side of the street *with* glasses or contact lenses?**
   - ○ Yes
   - ○ No
   - ○ Don't know/Didn't wear glasses or contact lenses
   - ○ Refused

HEARING

6. **During the past week, have you been able to hear what is said in a group conversation with at least three other people *without* a hearing aid?**
   - ○ Yes → Go to **Item 11**
   - ○ No
   - ○ Don't know
   - ○ Refused

7. **Have you been able to hear what is said in a group conversation with at least three other people *with* a hearing aid?**
   - ○ Yes → Go to **Item 9**
   - ○ No
   - ○ Don't know/Didn't wear a hearing aid
   - ○ Refused
8. **During the past week, have you been able to hear at all?**
   - ○ Yes
   - ○ No → Go to **Item 11**
   - ○ Don't know
   - ○ Refused
9. **During the past week, have you been able to hear what is said in a conversation with one other person in a quiet room *without* a hearing aid?**
   - ○ Yes → Go to **Item 11**
   - ○ No
   - ○ Don't know
   - ○ Refused
10. **Have you been able to hear what is said in a conversation with one other person in a quiet room *with* a hearing aid?**
    - ○ Yes
    - ○ No
    - ○ Don't know/Didn't wear a hearing aid
    - ○ Refused

SPEECH

11. **During the past week, have you been able to be understood *completely* when speaking your own language with people who do not know you?**
    - ○ Yes → Go to **Item 16**
    - ○ No
    - ○ Don't know
    - ○ Refused
12. **Have you been able to be understood *partially* when speaking with people who do not know you?**
    - ○ Yes
    - ○ No
    - ○ Don't know
    - ○ Refused
13. **During the past week, have you been able to be understood *completely* when speaking with people who know you well?**
    - ○ Yes → Go to **Item 16**
    - ○ No
    - ○ Don't know
    - ○ Refused
14. **Have you been able to be understood *partially* when speaking with people who know you well?**
    - ○ Yes → Go to **Item 16**
    - ○ No
    - ○ Don't know
    - ○ Refused
15. **During the past week, have you been able to speak at all?**
    - ○ Yes
    - ○ No
    - ○ Don't know
    - ○ Refused

GETTING AROUND

16. **During the past week, have you been able to bend, lift, jump and run *without difficulty* and *without help or equipment* of any kind?**
    - ○ Yes → Go to **Item 24**
    - ○ No
    - ○ Don't know
    - ○ Refused
17. **Have you been able to walk around the neighborhood *without difficulty* and *without help or equipment* of any kind?**
    - ○ Yes → Go to **Item 24**
    - ○ No
    - ○ Don't know
    - ○ Refused
18. **Have you been able to walk around the neighborhood *with difficulty* but *without help* or *equipment* of any kind?**
    - ○ Yes → Go to **Item 24**
    - ○ No
    - ○ Don't know
    - ○ Refused
19. **During the past week, have you been able to walk at all?**
    - ○ Yes
    - ○ No → Go to **Item 22**
    - ○ Don't know
    - ○ Refused
20. **Have you needed mechanical support, such as braces or a cane or crutches, to be able to walk around the neighborhood?**
    - ○ Yes
    - ○ No
    - ○ Don't know
    - ○ Refused
21. **Have you needed the help of another person to walk?**
    - ○ Yes
    - ○ No
    - ○ Don't know
    - ○ Refused
22. **Have needed a wheelchair to get around the neighborhood?**
    - ○ Yes
    - ○ No
    - ○ Don't know
    - ○ Refused
23. **Have you needed the help of another person to get around in the wheelchair?**
    - ○ Yes
    - ○ No
    - ○ Don't know
    - ○ Refused

HANDS AND FINGERS

24. **During the past week, have you had the *full use* of both hands and ten fingers?**
    - ○ Yes → Go to **Item 28**
    - ○ No
    - ○ Don't know
    - ○ Refused

25. Have you needed the help of another person because of limitations in the use of your hands and fingers?

- ○ Yes
- ○ No → Go to **Item 27**
- ○ Don't know
- ○ Refused

26. Have you needed the help of another person with some tasks, most tasks, or all tasks?

- ○ Some tasks
- ○ Most tasks
- ○ All tasks
- ○ Don't know
- ○ Refused

27. Have you needed special equipment, for example special tools to help with dressing or eating, because of limitations in the use of your hands or fingers?

- ○ Yes
- ○ No
- ○ Don't know
- ○ Refused

SELF-CARE

28. During the past week, have you been able to eat, bathe, dress and use the toilet without difficulty?

- ○ Yes → Go to **Item 31**
- ○ No
- ○ Don't know
- ○ Refused

29. Have you needed the help of another person to eat, bathe, dress or use the toilet?

- ○ Yes
- ○ No
- ○ Don't know
- ○ Refused

30. Have you needed special equipment or tools to eat, bathe, dress or use the toilet?

- ○ Yes
- ○ No
- ○ Don't know
- ○ Refused

FEELINGS

31. During the past week, have you been feeling happy or unhappy?

- ○ Happy
- ○ Unhappy → Go to **Item 33**
- ○ Don't know
- ○ Refused

32. Would you describe yourself as having felt:

- ○ happy and interested in life → Go to **Item 34**
- ○ somewhat happy → Go to **Item 34**
- ○ Don't know
- ○ Refused

33. Would you describe yourself as having felt:

- ○ somewhat unhappy
- ○ very unhappy
- ○ so unhappy that life is not worthwhile
- ○ Don't know
- ○ Refused

34. During the past week, did you ever feel fretful, angry, irritable, anxious or depressed?

- ○ Yes
- ○ No → Go to **Item 37**
- ○ Don't know
- ○ Refused

35. How often did you feel fretful, angry, irritable, anxious or depressed?
(rarely, occasionally, often, or almost always)

- ○ Rarely
- ○ Occasionally
- ○ Often
- ○ Almost always
- ○ Don't know
- ○ Refused

36. During the past week did you feel *extremely* fretful, angry, irritable, anxious or depressed; to the point of needing professional help?

- ○ Yes
- ○ No
- ○ Don't know
- ○ Refused

MEMORY

37. How would you describe your ability to remember things, during the past week:

- ○ Able to remember most things
- ○ Somewhat forgetful
- ○ Very forgetful
- ○ Unable to remember anything at all
- ○ Don't know
- ○ Refused

THINKING

38. How would you describe your ability to think and solve day to day problems, during the past week:

- ○ Able to think clearly and solve problems
- ○ Had a little difficulty
- ○ Had some difficulty
- ○ Had a great deal of difficulty
- ○ Unable to think or solve problems
- ○ Don't know
- ○ Refused

PAIN AND DISCOMFORT

39. Have you had any trouble with pain or discomfort, during the past week?

- ○ Yes
- ○ No → Go to **Item 41**
- ○ Don't know
- ○ Refused

40. How many of your activities, during the past week, were limited by pain or discomfort?

- ○ None
- ○ A few
- ○ Some
- ○ Most
- ○ All
- ○ Don't know
- ○ Refused

41. Overall, how would you rate your health during the past week?

- ○ Excellent
- ○ Very good
- ○ Good
- ○ Fair
- ○ Poor
- ○ Don't know
- ○ Refused

Thank you. That ends this set of questions.

TIME FINISHED: [ ] : [ ] *(24-hour clock)*

Person responsible for data on this form: [ ]

HEALTH UTILITIES INDEX

Proxy-Assessed
Follow-up period: 6 months

Start time: [ ] : [ ] *(24-hour clock)*

Read to proxy:

The next set of questions ask about various aspects of (subject's name)'s health. When answering these questions we would like you to think about (his/her) health and ability to do things on a day-to-day basis, during the past week. To define the 1 week period, please think about what the date was 7 days ago and recall the major events that (he/she) has experienced during this period. Please focus your answer on (subject's name)'s abilities, disabilities and how they have felt during the past 1 week.

You may feel that some of these questions do not apply to (subject's name), but it is important that we ask the same questions about each subject. Also, a few questions are similar; please excuse the apparent overlap and answer each question independently.

All information you provide is confidential. There are no right or wrong answers; what we want is your opinion about (subject's name) abilities and feelings.

Interviewer:
For each question, read the entire question/sentence as written following the question number, emphasizing the words in italics, if any. Do not read the response options listed below the question. If the responses are included as part of the question (eg: Q26, Q31 etc) read them as part of the questions. The answer given by the respondent to each question should be clearly marked in the circle beside the one appropriate answer listed below the question.

VISION

1. **During the past week, has (subject's name) been able to see well enough to read ordinary newsprint *without* glasses or contact lenses?**
   - ○ Yes → Go to **Item 4**
   - ○ No
   - ○ Don't know
   - ○ Refused
2. **Has (subject's name) been able to see well enough to read ordinary newsprint *with* glasses or contact lenses?**
   - ○ Yes → Go to **Item 4**
   - ○ No
   - ○ Don't know/Didn't wear glasses or contact lenses
   - ○ Refused
3. **During the past week, has (subject's name) been able to see at all?**
   - ○ Yes
   - ○ No → Go to **Item 6**
   - ○ Don't know
   - ○ Refused
4. **During the past week, has (subject's name) been able to see well enough to recognize a friend on the other side of the street *without* glasses or contact lenses?**
   - ○ Yes → Go to **Item 6**
   - ○ No
   - ○ Don't know
   - ○ Refused
5. **Has (subject's name) been able to see well enough to recognize a friend on the other side of the street *with* glasses or contact lenses?**
   - ○ Yes
   - ○ No
   - ○ Don't know/Didn't wear glasses or contact lenses
   - ○ Refused

HEARING

6. **During the past week, has (subject's name) been able to hear what is said in a group conversation with at least three other people *without* a hearing aid?**
   - ○ Yes → Go to **Item 11**
   - ○ No
   - ○ Don't know
   - ○ Refused
7. **Has (subject's name) been able to hear what is said in a group conversation with at least three other people *with* a hearing aid?**
   - ○ Yes → Go to **Item 9**
   - ○ No
   - ○ Don't know/Didn't wear a hearing aid
   - ○ Refused
8. **During the past week, has (subject's name) been able to hear at all?**
   - ○ Yes
   - ○ No → Go to **Item 11**
   - ○ Don't know
   - ○ Refused
9. **During the past week, has (subject's name) been able to hear what is said in a conversation with one other person in a quiet room *without* a hearing aid?**
   - ○ Yes → Go to **Item 11**
   - ○ No
   - ○ Don't know
   - ○ Refused
10. **Has (subject's name) been able to hear what is said in a conversation with one other person in a quiet room *with* a hearing aid?**
    - ○ Yes
    - ○ No
    - ○ Don't know/Didn't wear a hearing aid
    - ○ Refused

SPEECH

11. **During the past week, has (subject's name) been able to be understood *completely* when speaking his/her own language with people who do not know (subject's name)?**
    - ○ Yes → Go to **Item 16**
    - ○ No
    - ○ Don't know
    - ○ Refused
12. **Has (subject's name) been able to be understood *partially* when speaking with people who do not know (subject's name)?**
    - ○ Yes
    - ○ No
    - ○ Don't know
    - ○ Refused
13. **During the past week, has (subject's name) been able to be understood *completely* when speaking with people who know (subject's name) well?**
    - ○ Yes → Go to **Item 16**
    - ○ No
    - ○ Don't know
    - ○ Refused
14. **Has (subject's name) been able to be understood *partially* when speaking with people who know (subject's name) well?**
    - ○ Yes → Go to **Item 16**
    - ○ No
    - ○ Don't know
    - ○ Refused

15. **During the past week, has (subject's name) been able to speak at all?**
    - ◯ Yes
    - ◯ No
    - ◯ Don't know
    - ◯ Refused

GETTING AROUND

16. **During the past week, has (subject's name) been able to bend, lift, jump and run *without difficulty* and *without help or equipment* of any kind?**
    - ◯ Yes → Go to **Item 24**
    - ◯ No
    - ◯ Don't know
    - ◯ Refused
17. **Has (subject's name) been able to walk around the neighborhood *without difficulty* and *without help or equipment* of any kind?**
    - ◯ Yes → Go to **Item 24**
    - ◯ No
    - ◯ Don't know
    - ◯ Refused
18. **Has (subject's name) been able to walk around the neighborhood *with difficulty* but *without help or equipment* of any kind?**
    - ◯ Yes → Go to **Item 24**
    - ◯ No
    - ◯ Don't know
    - ◯ Refused
19. **During the past week, has (subject's name) been able to walk at all?**
    - ◯ Yes
    - ◯ No → Go to **Item 22**
    - ◯ Don't know
    - ◯ Refused
20. **Has (subject's name) needed mechanical support, such as braces or a cane or crutches, to be able to walk around the neighborhood?**
    - ◯ Yes
    - ◯ No
    - ◯ Don't know
    - ◯ Refused
21. **Has (subject's name) needed the help of another person to walk?**
    - ◯ Yes
    - ◯ No
    - ◯ Don't know
    - ◯ Refused
22. **Has (subject's name) needed a wheelchair to get around the neighborhood?**
    - ◯ Yes
    - ◯ No
    - ◯ Don't know
    - ◯ Refused
23. **Has (subject's name) needed the help of another person to get around in the wheelchair?**
    - ◯ Yes
    - ◯ No
    - ◯ Don't know
    - ◯ Refused

HANDS AND FINGERS

24. During the past week, has (subject's name) had the *full use* of both hands and ten fingers?

- ○ Yes → Go to **Item 28**
- ○ No
- ○ Don't know
- ○ Refused

25. Has (subject's name) needed the help of another person because of limitations in the use of his/her hands and fingers?

- ○ Yes
- ○ No → Go to **Item 27**
- ○ Don't know
- ○ Refused

26. Has (subject's name) needed the help of another person with some tasks, most tasks, or all tasks?

- ○ Some tasks
- ○ Most tasks
- ○ All tasks
- ○ Don't know
- ○ Refused

27. Has (subject's name) needed special equipment, for example special tools to help with dressing or eating, because of limitations in the use of his/her hands or fingers?

- ○ Yes
- ○ No
- ○ Don't know
- ○ Refused

SELF-CARE

28. During the past week, has (subject's name) been able to eat, bathe, dress and use the toilet without difficulty?

- ○ Yes → Go to **Item 31**
- ○ No
- ○ Don't know
- ○ Refused

29. Has (subject's name) needed the help of another person to eat, bathe, dress or use the toilet?

- ○ Yes
- ○ No
- ○ Don't know
- ○ Refused

30. Has (subject's name) needed special equipment or tools to eat, bathe, dress or use the toilet?

- ○ Yes
- ○ No
- ○ Don't know
- ○ Refused

FEELINGS

31. During the past week, has (subject's name) been feeling happy or unhappy?

- ○ Happy
- ○ Unhappy → Go to **Item 33**
- ○ Don't know
- ○ Refused

32. Would you describe (subject's name) as having felt:

- ○ happy and interested in life → Go to **Item 34**
- ○ somewhat happy → Go to **Item 34**
- ○ Don't know
- ○ Refused

33. Would you describe (subject's name) as having felt:

- ○ somewhat unhappy
- ○ very unhappy
- ○ so unhappy that life is not worthwhile
- ○ Don't know
- ○ Refused

34. During the past week, did (subject's name) ever feel fretful, angry, irritable, anxious or depressed?

- ○ Yes
- ○ No → Go to **Item 37**
- ○ Don't know
- ○ Refused

35. How often did (subject's name) feel fretful, angry, irritable, anxious or depressed?
(rarely, occasionally, often, or almost always)

- ○ Rarely
- ○ Occasionally
- ○ Often
- ○ Almost always
- ○ Don't know
- ○ Refused

36. During the past week did (subject's name) feel *extremely* fretful, angry, irritable, anxious or depressed; to the point of needing professional help?

- ○ Yes
- ○ No
- ○ Don't know
- ○ Refused

MEMORY

37. How would you describe (subject's name) ability to remember things, during the past week:

- ○ Able to remember most things
- ○ Somewhat forgetful
- ○ Very forgetful
- ○ Unable to remember anything at all
- ○ Don't know
- ○ Refused

THINKING

38. How would you describe (subject's name) ability to think and solve day to day problems, during the past week:

- ○ Able to think clearly and solve problems
- ○ Had a little difficulty
- ○ Had some difficulty
- ○ Had a great deal of difficulty
- ○ Unable to think or solve problems
- ○ Don't know
- ○ Refused

PAIN AND DISCOMFORT

39. Has (subject's name) had any trouble with pain or discomfort, during the past week?

- ○ Yes
- ○ No → Go to **Item 41**
- ○ Don't know
- ○ Refused

40. How many of (subject's name)'s activities, during the past week, were limited by pain or discomfort:

- None
- A few
- Some
- Most
- All
- Don't know
- Refused

41. Overall, how would you rate (subject's name)'s health during the past week?

- Excellent
- Very good
- Good
- Fair
- Poor
- Don't know
- Refused

Thank you. That ends this set of questions.

TIME FINISHED: [ ] : [ ] *(24-hour clock)*

Person responsible for data on this form: [ ]

Geriatric Depression Scale

Follow-up period: 6 months

Choose the best answer for how you have felt over the past week:

1. **Are you basically satisfied with your life?**
   ○ Yes ○ No
2. **Have you dropped many of your activities and interests**
   ○ Yes ○ No
3. **Do you feel that your life is empty?**
   ○ Yes ○ No
4. **Do you often get bored?**
   ○ Yes ○ No
5. **Are you in good spirits most of the time?**
   ○ Yes ○ No
6. **Are you afraid that something bad is going to happen to you?**
   ○ Yes ○ No
7. **Do you feel happy most of the time?**
   ○ Yes ○ No
8. **Do you often feel helpless?**
   ○ Yes ○ No
9. **Do you prefer to stay at home, rather than going out and doing new things?**
   ○ Yes ○ No
10. **Do you feel you have more problems with memory than most?**
    ○ Yes ○ No
11. **Do you think it is wonderful to be alive now?**
    ○ Yes ○ No
12. **Do you feel pretty worthless the way you are now?**
    ○ Yes ○ No
13. **Do you feel full of energy?**
    ○ Yes ○ No
14. **Do you feel that your situation is hopeless?**
    ○ Yes ○ No
15. **Do you think that most people are better off than you are?**
    ○ Yes ○ No

Person responsible for data on this form:

6.10.1 ALFI Mini Mental State Examination (ALFI-MMSE) Form

ADULT LIFESTYLE FUNCTIONAL INSTRUMENT: TELEPHONE VERSION OF MINI MENTAL STATE EXAMINATION

Overview

The **Mini Mental State Examination (MMSE)** is a widely-used tool in both clinical and research practice as a brief cognitive screening test to distinguish potential dementia from normal function (Kukull, Larson, Teri, Bowen, McCormick, & Pfanshmidt, 1994).

The **Adult Lifestyles and Function Interview (ALFI)** was initially designed as a telephone-administered follow-up interview of subjects in a research study in St. Louis. The ALFI consists of various tools to test psychological status of study participants (Fischbach, 1990). One of the tools is a telephone version of the Mini Mental State Examination (ALFI-MMSE).

Research has demonstrated that the scores on the ALFI-MMSE correlate strongly with the score of the original version, given face-to-face for subjects undergoing geriatric assessment. Roccaforte et al. (1992) demonstrated through their research that the ALFI-MMSE is a useful and economic tool for screening for cognitive impairment.

For our purposes, we will be using the ALFI-MMSE to evaluate a patient's mental status at 1, 3, and 6 months post-discharge from hospital, in order to determine whether or not to proceed with the subsequent interviews. If a patient scores below a "17," then a proxy for the patient (Power of Attorney, spouse, offspring, etc.) will be asked to carry out the subsequent interviews. You must use the below worksheet to score the interview.

Rules of the ALFI-MMSE

Instructions : The ALFI-MMSE is a **standardized test**; therefore, it is extremely important that all respondents be asked each question in the same format. The questions that you read to the patient are printed **in bold letters**. Please read each question exactly as it is written, taking special care to speak slowly and to enunciate each word. This is especially important for patients with hearing impairments.

> **If the respondent normally wears a hearing aid, make sure that it is in place and turned on!**

Accurate Recording: Some of the questions ask for specific information. Your task is not to obtain the "correct" factual data; instead, you must record *exactly what is said,* even if it is incorrect. Scores on this test should be representative of the patient's ability; therefore, do not help him by giving hints.

Prompting: Do not prompt or help the respondent with any answers unless the directions for the question allow it.

Feedback: Unless specifically indicated, do not comment to the respondent on his performance with respect to the questions. This could create undue stress for the respondent, potentially causing him to lose his train of thought and to spend more time answering, or to answer incorrectly.

Answer Sheet : In administering the test, do not offer extra help or wait too long for responses. Although sometimes it is appropriate to re-read a question, in general, if a subject gives an incorrect answer, you should just score accordingly and proceed to the next item.

Refusal/Cannot Answer : If the respondent refuses to answer a question or states that he cannot, abstain from comment and move on to the next question. In scoring, the respondent would simply receive a score of "0" for that question.

This form is scheduled for completion at the 1, 3 and 6 month follow-up period. If the patient scores less than 17 on the ALFI-MMSE at 1 month, the exam should not be completed at the 3 or 6 month follow-up. If the patient scores ≥17 at the 1 month interview, the ALFI-MMSE should be administered at month 3; and if the patient again scores ≥, it should be administered at month 6. If the patient scores ≤17 at any of the 3 follow-up interviews, it should not be repeated at the subsequent interview. A phone interview by proxy should be completed using the CPC, MRS and HUI QOL tools for any and all subsequent Follow-Up calls once the patient scores <17.

Item 1 – What is the current year? This question is used as a measure of long-term memory and orientation.

- Remember to speak clearly when you ask the question.
- Record exactly what the respondent states, being careful not to give feedback.

- Scoring
  - Correct : 1 point
  - Incorrect : 0 points
  - Refused/Cannot Answer : 0 points
- **Maximum points for this question**: ①

Item 2 – What is the season? This question is used as a measure of long-term memory and orientation.

- Remember to speak clearly when you ask the question.
- Record exactly what the respondent states, being careful not to give feedback.

- Scoring
  - Correct : 1 point
  - Incorrect : 0 points
  - Refused/Cannot Answer : 0 points
- **Maximum points for this question**: ①

Item 3 – What is the date? This question is used as a measure of short-term memory and orientation.

- Remember to speak clearly when you ask the question.
- Record exactly what the respondent states, being careful not to give feedback

- Scoring
  - Correct : 1 point
  - Incorrect : 0 points
  - Refused/Cannot Answer : 0 points

- **Maximum points for this question**: ①

Item 4 – What is the day of the week? This question is used as a measure of short-term memory and orientation.

- Remember to speak clearly when you ask the question.
- Record exactly what the respondent states, being careful not to give feedback.

- Scoring
  - Correct : 1 point
  - Incorrect : 0 points
  - Refused/Cannot Answer : 0 points

- **Maximum points for this question**: ①

Item 5 – What is the month? This question is used as a measure of short-term memory and orientation.

- Remember to speak clearly when you ask the question.
- Record exactly what the respondent states, being careful not to give feedback.

- Scoring
  - Correct : 1 point
  - Incorrect : 0 points
  - Refused/Cannot Answer : 0 points

- **Maximum points for this question**: 1

Item 6 – Can you tell me where you are right now? For instance, what state are you in? This question is used as a measure of spatial orientation.

- Although we cannot verify the respondent's answer, it is the appropriateness of the answer that will key you as to whether the respondent is answering correctly. **For example:** You call a client in California, and he states that he lives in an igloo — Score: 0.
- Remember to speak clearly when you ask the question.
- Record exactly what the respondent states, being careful not to give feedback.

- Scoring
  - Correct : 1 point
  - Incorrect : 0 points
  - Refused/Cannot Answer : 0 points

- **Maximum points for this question**: ①

Item 7 – What county are you in? This question is used as a measure of spatial orientation.

- Remember to speak clearly when you ask the question.
- Record exactly what the respondent states, being careful not to give feedback.

- Scoring — Correct : 1 point; Incorrect : 0 points; Refused/Cannot Answer : 0 points
  - **Maximum points for this question**: ①

Item 8 – What town are you in? This question is used as a measure of spatial orientation.

- Remember to speak clearly when you ask the question.
- Record exactly what the respondent states, being careful not to give feedback.

- Scoring — Correct : 1 point; Incorrect : 0 points; Refused/Cannot Answer : 0 points
  - **Maximum points for this question**: ①

Item 9 – What is the name of the place that you are in? This question is used as a measure of spatial orientation. 'Home', 'house', address, other correct name of a facility or other person's house are acceptable.

- Remember to speak clearly when you ask the question.
- Record exactly what the respondent states, being careful not to give feedback.

- Scoring — Correct : 1 point; Incorrect : 0 points; Refused/Cannot Answer : 0 points
  - **Maximum points for this question**: ①

Item 10 – I will say three words for you to remember. Repeat them after I have said all three words: shirt, brown, and honesty. Later in the interview, the respondent is again asked to recall the words. This question is used to test the respondent's ability to register.

- Because learning these three words affects later questions, please be careful to pronounce each word clearly.
- Most people will learn the three words on the first trial, but those who do not are given up to three trials to learn the words.
- The score is based on the first trial.

- Scoring — **Shirt:** Correct : 1 point; Incorrect : 0 points
  Brown: Correct : 1 point; Incorrect : 0 points

Honesty:	Correct :	1 point
	Incorrect :	0 points
Refused/Cannot answer :		0 points

- Maximum points for this question: ③

Item 11 – Please subtract 7 from 100. The respondent is asked to subtract seven from one hundred, then subtract seven from that answer, and keep going for a total of five trials. This question is used as a measure of attention and calculation.

- This question is easy to administer, but you must take care when scoring.
- A miss/error is classified as an incorrect subtraction (wrong answer).
- If the respondent subtracts incorrectly for one trial, but correctly for the following answers, count that as "1 miss/error." Respondent's score would "4." Count only one error if subject makes a subtraction error, but subsequent answers are 7 less than the error.
- Make sure that you write down exactly what the respondent states in the spaces provided. Compare the answer to the correct answer. You should score it according to the following rules:

- Scoring:

If Correct:	5 points
If 1 miss or error:	4 points
If 2 misses or 2 errors:	3 points
If 3 misses or 3 errors:	2 points
If 4 misses or 4 errors:	1 point
If Refused/Cannot answer:	0 points

- **Maximum points for this question**: ⑤

Item 12 – What are the three words that I asked you to remember? Shirt, Brown, and Honesty. This question is used to test recent memory and recall.
The administration instructions **allow 3 seconds for a response**. After this, you are asked to give a category cue. The respondent does not have to get all 3 words within 3 seconds, but he is given three seconds to initiate each response. This means that his response could go something like this: *(3 seconds)* … "Shirt" … *(3 seconds)* … "Brown" … *(3 seconds)* … "Honesty," and he would receive full credit.

In general, it is best to follow the 3-second rule. However, you may need to be flexible at times. It is important for you to recognize when the subject is in the process of getting the answer and when he needs help. If, for example, you can tell that he is getting the answer, do not interrupt with the category cue, even if the 3 seconds are up. If he then gets the

correct answer, score "1." If, however, it is obvious that he is not working toward an answer, wait only 3 seconds before giving the category cue.

If you start cueing for one word and the respondent gets another one right, give full credit for the one that they got spontaneously.

Scoring: "1" for spontaneous recall. If the respondent asks, "Which three words do you mean?" or "I do not remember three words," start out right away with category cueing. Give the cues in the original order of presentation (shirt, brown, and honesty). You should say "One of the words was something to wear" and then keep on cueing for shirt until the respondent gets it right or until you have to tell him that the word was shirt. Then you should give the cue for brown, and then for honesty. You are allowed to clarify for the respondents, for example, if they ask which question number it was, or how many questions ago you stated these three words.

Shirt:	Spontaneous recall:	1 point
	Cue: **something to wear**:	0 points
	Multiple: **shoes, shirt, socks**:	0 points
	Unable to recall/Refused:	0 points
Brown:	Spontaneous recall:	1 point
	Cue: **a color**:	0 points
	Multiple: **blue, black, brown**:	0 points
	Unable to recall/Refused:	0 points
Honesty:	Spontaneous recall:	1 point
	Cue: **a good personal quality**:	0 points
	Multiple: **charity, honesty, modesty**:	0 points
	Unable to recall/Refused:	0 points

- **Maximum points for this question**: ③

Item 13 – Repeat what I say: **"No ifs, ands, or buts."** State the phrase in a clear voice. This question is used to measure language and attention.

- Because the point of this question is to assess attention, a score of "0" will be given for any extra or incorrect words.
- Remember to speak clearly when you ask the question.
- Document exactly what the respondent states, being careful not to give feedback.
- The interview web-form will ask if the response was correct, if 2 out of 3 words or 1 out of 3 words in the phrase were correct, or if the patient was unable to repeat or missed the 's' on if,and,but.
- Scoring Correct : 1 point

Refused/Cannot Answer : 0 points

- **Maximum points for this question**: ①

Item 14 – What is the name of the thing that we are using to talk now? This question is used to measure a respondent's language skills. The response is expected to be immediate.

- Scoring Correct : 1 point
  Incorrect : 0 points
  Refused/Cannot Answer : 0 points

- Once the ALFI-MMSE has been completed, simply add up the total.
- Maximum score for the ALFI-MMSE is 22 points.
- The cut-off for this tool is a score of 17. If the score is less than 17, a proxy is needed to give consent and to complete the rest of the interview.
- If the respondent scores at least 17, then he may complete the HUI on his own.
- **Maximum points for this question**: ①

Item 15 – Now I'm going to give you some instructions to follow. I want you to do a 3 step task. First, say "hello", then tap the telephone receiver 3 times with your finger, then say "I'm back" into the phone.

Answer Item 15 on the web-data form, but do not include it when scoring the ALFI-MMSE.

ALFI-MMSE Scoring Form

Complete this form:
-at 1 month, 3 month & 6 month follow-up

ALFI Mini-Mental State Examination

Draft Version
Date: xx/xx/2007

Date of contact: ___ / ___ / ___ *(mm/dd/yyyy)*

ROC PRIMED ID: ___ - ___ - ___

Follow-up period:

○ 1 month ○ 3 month ○ 6 month

___ 1. What is the year?

___ *(yyyy)* ○ Cannot answer ○ Other refusal

___ 2. What is the season?

○ Spring ○ Autumn
○ Summer ○ Winter

○ Cannot answer ○ Other refusal

___ 3. What is the date?

___ *(dd)* ○ Cannot answer ○ Other refusal

___ 4. What is the day of the week?

○ Monday ○ Friday
○ Tuesday ○ Saturday
○ Wednesday ○ Sunday
○ Thursday

○ Cannot answer ○ Other refusal

___ 5. What is the month?

○ January ○ July
○ February ○ August
○ March ○ September
○ April ○ October
○ May ○ November
○ June ○ December

○ Cannot answer ○ Other refusal

___ 6. Can you tell me where you are right now? For instance, what State/Province are you in?

○ Correct ○ Incorrect ○ Cannot answer ○ Other refusal

___ 7. What county are you in?

○ Correct ○ Incorrect ○ Cannot answer ○ Other refusal

___ 8. What town are you in?

○ Correct ○ Incorrect ○ Cannot answer ○ Other refusal

___ 9. What is the name of the place that you are in? *("home", "house", address, other correct name of a facility or other person's house)*

○ Correct ○ Incorrect ○ Cannot answer ○ Other refusal

---

continue to next page

Date of contact: ___/___/___ *(mm/dd/yyyy)*

ROC PRIMED ID: ___-___-___

Follow-up period:
○ 1 month ○ 3 month ○ 6 month

___10. **I shall say three words for you to remember. Repeat them after I have said all three words.** *(Check each bubble if the word was repeated correctly)*
- ☐ Shirt
- ☐ Brown
- ☐ Honesty

___11. **Please subtract 7 from 100.**
(Do this 5 times - may coach patient if needed)
(Count only 1 error if subject makes subtraction error, but subsequent answers are 7 less than the error)
Number Correct: ○ 5 ○ 4 ○ 3 ○ 2 ○ 1 ○ 0

___12. **What are the three words that I asked you to remember?**

Shirt	**Brown**	**Honesty**
○ Spontaneous recall	○ Spontaneous recall	○ Spontaneous recall
○ Cue: **something to wear**	○ Cue: **a color**	○ Cue: **good personal quality**
○ Multiple: **shoes, shirt, socks**	○ Multiple: **blue, black, brown**	○ Multiple: **charity, honesty, modesty**
○ Unable to recall	○ Unable to recall	○ Unable to recall

___13. **Repeat what I say: "No ifs, ands, or buts"?**
- ○ Correct
- ○ 2 out of 3 words in the phrase correct
- ○ 1 out of 3 words in the phrase correct
- ○ Unable to repeat, or misses the 's'

___14. **What is the name of the thing that we are using to talk now?** *(Do not wait for the patient to name it)*
- ○ Telephone, receiver, mouthpiece, etc
- ○ Inaccurate
- ○ Cannot answer
- ○ Other refusal

Total_____ (Do not score #15)

15. **Now I'm going to give you some instructions to follow. I want you to do a 3 steps task. First, say "hello", then tap the telephone receiver 3 times with your finger, then say "I'm back" into the phone**
- ☐ ☐ Hello
- ☐ ☐ Tap
- ☐ ☐ I'm back
- ☐ ☐ Cannot answer
- ☐ ☐ Other refusal

ALFI Mini-Mental State Examination

Follow-up period: 1 month

1. **What is the year?**
   ☐ *(yyyy)* ○ Cannot answer ○ Other refusal
2. **What is the season?**
   ○ Spring ○ Autumn
   ○ Summer ○ Winter

   ○ Cannot answer ○ Other refusal
3. **What is the date?**
   ☐ *(dd)* ○ Cannot answer ○ Other refusal
4. **What is the day of the week?**
   ○ Monday ○ Wednesday ○ Friday ○ Sunday
   ○ Tuesday ○ Thursday ○ Saturday

   ○ Cannot answer ○ Other refusal
5. **What is the month?**
   ○ January ○ April ○ July ○ October
   ○ February ○ May ○ August ○ November
   ○ March ○ June ○ September ○ December

   ○ Cannot answer ○ Other refusal
6. **Can you tell me where you are right now? For instance, what State/Province are you in?**
   ○ Correct ○ Incorrect ○ Cannot answer ○ Other refusal
7. **What county are you in?**
   ○ Correct ○ Incorrect ○ Cannot answer ○ Other refusal
8. **What town are you in?**
   ○ Correct ○ Incorrect ○ Cannot answer ○ Other refusal
9. **What is the name of the place that you are in?***("home", "house", address, other correct name of a facility or other person's house)*
   ○ Correct ○ Incorrect ○ Cannot answer ○ Other refusal
10. **I shall say three words for you to remember. Repeat them after I have said all three words.** *(Check each bubble if the word was repeated correctly)*
    ☐ Shirt ☐ Brown ☐ Honesty
11. **Please subtract 7 from 100.**
    (Do this 5 times - may coach patient if needed)
    (Count only 1 error if subject makes subtraction error, but subsequent answers are 7 less than the error)
    Number Correct: ○ 5 ○ 4 ○ 3 ○ 2 ○ 1 ○ 0
12. **What are the three words that I asked you to remember?**

Shirt	**Brown**	**Honesty**
○ Spontaneous recall	○ Spontaneous recall	○ Spontaneous recall
○ Cue: **something to wear**	○ Cue: **a color**	○ Cue: **good personal quality**
○ Multiple: **shoes, shirt, socks**	○ Multiple: **blue, black, brown**	○ Multiple: **charity, honesty, modesty**
○ Unable to recall	○ Unable to recall	○ Unable to recall

13. **Repeat what I say: "No ifs, ands, or buts"?**
    ○ Correct ○ 1 out of 3 words in the phrase correct
    ○ 2 out of 3 words in the phrase correct ○ Unable to repeat, or misses the 's'
14. **What is the name of the thing that we are using to talk now?** *(Do not wait for the patient to name it)*
    ○ Telephone, receiver, mouthpiece, etc ○ Cannot answer
    ○ Inaccurate ○ Other refusal
15. **Now I'm going to give you some instructions to follow. I want you to do a 3 step task.**
    First, say "hello", then tap the telephone receiver 3 times with your finger, then say "I'm back" into the phone

    ☐ Hello ☐ Tap ☐ I'm back ☐ Cannot answer ☐ Other refusal

Person responsible for data on this form:

ALFI Mini-Mental State Examination

Follow-up period: 3 months

1. **What is the year?**
   ☐ *(yyyy)* ○ Cannot answer ○ Other refusal
2. **What is the season?**
   ○ Spring ○ Autumn
   ○ Summer ○ Winter

   ○ Cannot answer ○ Other refusal
3. **What is the date?**
   ☐ *(dd)* ○ Cannot answer ○ Other refusal
4. **What is the day of the week?**
   ○ Monday ○ Wednesday ○ Friday ○ Sunday
   ○ Tuesday ○ Thursday ○ Saturday

   ○ Cannot answer ○ Other refusal
5. **What is the month?**
   ○ January ○ April ○ July ○ October
   ○ February ○ May ○ August ○ November
   ○ March ○ June ○ September ○ December

   ○ Cannot answer ○ Other refusal
6. **Can you tell me where you are right now? For instance, what State/Province are you in?**
   ○ Correct ○ Incorrect ○ Cannot answer ○ Other refusal
7. **What county are you in?**
   ○ Correct ○ Incorrect ○ Cannot answer ○ Other refusal
8. **What town are you in?**
   ○ Correct ○ Incorrect ○ Cannot answer ○ Other refusal
9. **What is the name of the place that you are in?***("home", "house", address, other correct name of a facility or other person's house)*
   ○ Correct ○ Incorrect ○ Cannot answer ○ Other refusal
10. **I shall say three words for you to remember. Repeat them after I have said all three words.** *(Check each bubble if the word was repeated correctly)*
    ☐ Shirt ☐ Brown ☐ Honesty
11. **Please subtract 7 from 100.**
    (Do this 5 times - may coach patient if needed)
    (Count only 1 error if subject makes subtraction error, but subsequent answers are 7 less than the error)
    Number Correct: ○ 5 ○ 4 ○ 3 ○ 2 ○ 1 ○ 0
12. **What are the three words that I asked you to remember?**

Shirt	**Brown**	**Honesty**
○ Spontaneous recall	○ Spontaneous recall	○ Spontaneous recall
○ Cue: **something to wear**	○ Cue: **a color**	○ Cue: **good personal quality**
○ Multiple: **shoes, shirt, socks**	○ Multiple: **blue, black, brown**	○ Multiple: **charity, honesty, modesty**
○ Unable to recall	○ Unable to recall	○ Unable to recall

13. **Repeat what I say: "No ifs, ands, or buts"?**
    ○ Correct ○ 1 out of 3 words in the phrase correct
    ○ 2 out of 3 words in the phrase correct ○ Unable to repeat, or misses the 's'
14. **What is the name of the thing that we are using to talk now?** *(Do not wait for the patient to name it)*
    ○ Telephone, receiver, mouthpiece, etc ○ Cannot answer
    ○ Inaccurate ○ Other refusal
15. **Now I'm going to give you some instructions to follow. I want you to do a 3 step task.**
    First, say "hello", then tap the telephone receiver 3 times with your finger, then say "I'm back" into the phone

    ☐ Hello ☐ Tap ☐ I'm back ☐ Cannot answer ☐ Other refusal

Person responsible for data on this form: ☐

1. **What is the year?**
   ____ *(yyyy)* ○ Cannot answer ○ Other refusal
2. **What is the season?**
   ○ Spring ○ Autumn
   ○ Summer ○ Winter

   ○ Cannot answer ○ Other refusal
3. **What is the date?**
   ____ *(dd)* ○ Cannot answer ○ Other refusal
4. **What is the day of the week?**
   ○ Monday ○ Wednesday ○ Friday ○ Sunday
   ○ Tuesday ○ Thursday ○ Saturday

   ○ Cannot answer ○ Other refusal
5. **What is the month?**
   ○ January ○ April ○ July ○ October
   ○ February ○ May ○ August ○ November
   ○ March ○ June ○ September ○ December

   ○ Cannot answer ○ Other refusal
6. **Can you tell me where you are right now? For instance, what State/Province are you in?**
   ○ Correct ○ Incorrect ○ Cannot answer ○ Other refusal
7. **What county are you in?**
   ○ Correct ○ Incorrect ○ Cannot answer ○ Other refusal
8. **What town are you in?**
   ○ Correct ○ Incorrect ○ Cannot answer ○ Other refusal
9. **What is the name of the place that you are in?***("home", "house", address, other correct name of a facility or other person's house)*
   ○ Correct ○ Incorrect ○ Cannot answer ○ Other refusal
10. **I shall say three words for you to remember. Repeat them after I have said all three words.** *(Check each bubble if the word was repeated correctly)*
    ☐ Shirt ☐ Brown ☐ Honesty
11. **Please subtract 7 from 100.**
    (Do this 5 times - may coach patient if needed)
    (Count only 1 error if subject makes subtraction error, but subsequent answers are 7 less than the error)
    Number Correct: ○ 5 ○ 4 ○ 3 ○ 2 ○ 1 ○ 0
12. **What are the three words that I asked you to remember?**

Shirt	**Brown**	**Honesty**
○ Spontaneous recall	○ Spontaneous recall	○ Spontaneous recall
○ Cue: **something to wear**	○ Cue: **a color**	○ Cue: **good personal quality**
○ Multiple: **shoes, shirt, socks**	○ Multiple: **blue, black, brown**	○ Multiple: **charity, honesty, modesty**
○ Unable to recall	○ Unable to recall	○ Unable to recall

13. **Repeat what I say: "No ifs, ands, or buts"?**
    ○ Correct ○ 1 out of 3 words in the phrase correct
    ○ 2 out of 3 words in the phrase correct ○ Unable to repeat, or misses the 's'
14. **What is the name of the thing that we are using to talk now?** *(Do not wait for the patient to name it)*
    ○ Telephone, receiver, mouthpiece, etc ○ Cannot answer
    ○ Inaccurate ○ Other refusal
15. **Now I'm going to give you some instructions to follow. I want you to do a 3 step task.**
    First, say "hello", then tap the telephone receiver 3 times with your finger, then say "I'm back" into the phone

    ☐ Hello ☐ Tap ☐ I'm back ☐ Cannot answer ☐ Other refusal

6.11.1 Structured Interview for the Modified Rankin Scale
(revised for cardiac arrest pts. in ROC PRIMED)

Introduction

The Modified Rankin Scale (MRS) (van Swieten et al., 1988) is widely used as a functional outcome measure in stroke. The purpose of the Structured Interview is to assign patients to MRS grades in a systematic way. The interview consists of five sections corresponding to the levels of disability on the MRS (see Table).

Modified Rankin Scale		Section of the Structured Interview
5	**Severe disability:** bedridden, incontinent and requiring constant nursing care and attention	1. Constant care
4	**Moderately severe disability:** unable to walk without assistance, and unable to attend to own bodily needs without assistance	2. Assistance for bodily needs/walking
3	**Moderate disability:** requiring some help, but able to walk without assistance.	3. Assistance to look after own affairs
2	**Slight disability:** unable to carry out all previous activities but able to look after own affairs without assistance.	4. Usual duties and activities
1	**No significant disability:** despite symptoms: able to carry out all usual duties and activities.	5. Symptom checklist
0	**No symptoms at all**	

General Instructions

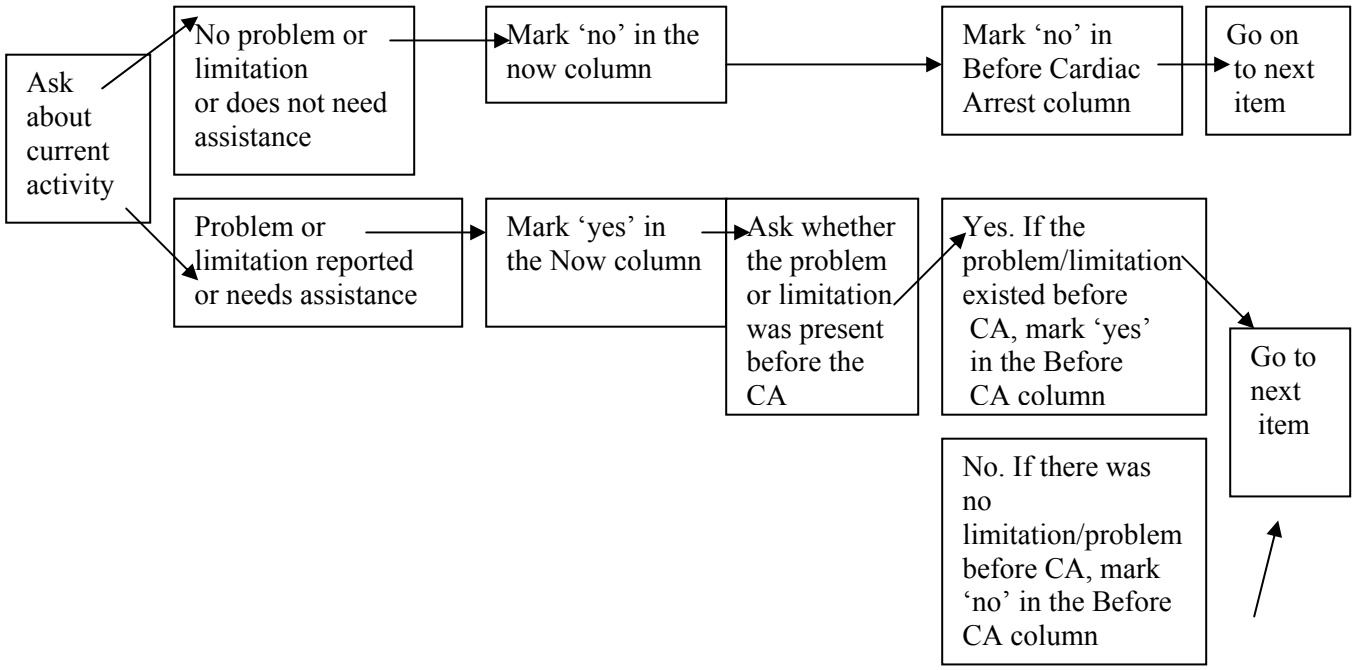
Timing
The interview is intended for use after discharge from hospital at the 3 and 6 month follow-up interviews.

Respondents
Use the best source of information available. Information can be obtained from the patient and/or a person who is familiar with the daily routine of the patient. Interview the patient and a close friend or caregiver whenever possible. If the patient lacks insight into some difficulties, or responses are inconsistent it is often helpful to interview a caregiver or relative independently.

Procedure
The MRS tool asks for assessment of functional status 'now' (current status) and for 'before cardiac arrest' (for comparison purposes). For sections 1, 2, 3, & 5 (as numbered on the MRS web-form) first ask about the current ('now') activities. If there is currently no problem or limitation in a particular activity, it is not necessary to ask about status 'before cardiac arrest,' but please tick the relevant boxes. If the person indicates a problem or limitation on a particular activity, then establish whether this problem or limitation was present before the cardiac arrest and record the response appropriately in the 'before cardiac arrest' column. (This sequence is illustrated in the diagram on the next page.)

Ask each question as it is stated on the form. You may prompt them with examples of what they might consider (see italicized prompts provided on the MRS web-form).

Diagram: Interview procedure for sections 1, 2, 3 & 5



For Section 4, 'Usual duties and activities', ask about ability to perform the activity before CA and then ask about a change in that ability after the CA. If the person did not participate in an activity (e.g. work) before the CA then, mark 'no' and move to the indicated next question as indicated on the questionnaire. Sometimes it can be difficult to establish whether or not someone could do an activity before the CA (particularly if the person had one or more previous CA) – in this case use your judgment and focus on the CA for which the patient was enrolled in the study.

The responses to the separate sections should generally be hierarchical (for example if a person indicates that they require assistance to attend to bodily needs, then it is inconsistent if they then say that they go out alone for social and leisure activities). Thus, responses to later questions may suggest revisions to earlier responses. Check for consistency as you proceed. Ask all questions and go back to clarify, if necessary.

Notes for specific sections of the interview are shown with each item on the data form. The document is formatted so that the notes appear opposite the interview questions.

Sources:-
Section 2 of the interview is adapted from the Barthel Index (Collin et al. 1988), and Section 4 is adapted from the Extended Glasgow Outcome Scale (Wilson et al., 1998).

Collin, C., Wade, D. T., Davies, S., & Home, V. (1988). The Barthel ADL Index: a reliability study. International Disability Studies, 10, 61-63.

Van Swieten, J. C., Koudstaal, P. J., Visser, M. C., Schouten, H. J. A., & van Gijn, J. (1988). Interobserver agreement for the assessment of handicap in stroke patients. Stroke, 19, 604-607.

Wilson, J. T. L., Pettigrew, L. E. L., & Teasdale, G. M. (1998). Structured interviews for the Glasgow Outcome Scale and Extended Glasgow Outcome Scale: Guidelines for their use. Journal of Neurotrauma, 15, 573-585.

Structured Interview for Assessment of Modified Rankin Scale

Follow-up period: 3 months

Please record responses to all questions (unless otherwise indicated in the text), including those concerning status before cardiac arrest. See guidelines on the facing page for further information.

1. Constant Care:

Constant care means that someone needs to be available at all times. Care may be provided by either a trained or untrained caregiver. The patient will usually be bedridden and may be incontinent.	**Now**		**Before cardiac arrest**	
	Yes	No	Yes	No
a. Does the person require constant care?	○	○	○	○

2. Assistance to attend to bodily needs/for walking:

Assistance includes physical assistance, verbal instruction, or supervision by another person.	**Now**		**Before cardiac arrest**	
	Yes	No	Yes	No
a. Is assistance essential for eating? *(Eating without assistance: food and implements may be provided by others)*	○	○	○	○
b. Is assistance essential for using the toilet? *(Using toilet without assistance: reach toilet/commode; undress sufficiently, clean self; dress and leave)*	○	○	○	○
c. Is assistance essential for routine daily hygiene? *(Routine hygiene: washing face, doing hair, cleaning teeth/fitting false teeth. Implements may be provided by others and this should not be considered assistance)*	○	○	○	○
d. Is assistance essential for walking? *(Walking without assistance: able to walk indoors around house or ward, may use any aid (e.g. stick/cane, walking frame/walker), however not requiring physical help or verbal instruction or supervision from another person)*	○	○	○	○

3. Assistance to look after own affairs:

Assistance includes physical assistance, or verbal instruction, or supervision by another person.	**Now**		**Before cardiac arrest**	
	Yes	No	Yes	No
a. Is assistance essential for preparing a simple meal? *(For example, able to prepare breakfast or a snack)*	○	○	○	○
b. Is assistance essential for basic household chores? *(For example, finding and putting away clothes, clearing up after a meal. Exclude chores that do not need to be done every day, such as using a vacuum cleaner)*	○	○	○	○
c. Is assistance essential for looking after household expenses?	○	○	○	○
d. Is assistance essential for local travel? *(Patients may drive or use public transport to get around. Ability to use a taxi is sufficient, provided the person can phone for it themselves and instruct the driver)*	○	○	○	○
e. Is assistance essential for local shopping? *(Local shopping: a least able to buy a single item)*	○	○	○	○

4. Usual duties and activities:

The next sets of questions are about how the patient usually spends his/her day.

a. Work:

i. Before the cardiac arrest, was the person working or seeking work or studying as a student? *(If the person was not employed or seeking work before the cardiac arrest, or the person was retired then indicate "No" and go to **item 4b**)*

- ○ Yes
- ○ No → go to **item 4b**

ii. Since the cardiac arrest has there been a change in the person's ability to work or study? *(Change in ability to work or study includes loss of employment or reduction in level of responsibility; change in education or problems with study)*

- ○ Yes → How restricted are they?
  - ○ Reduced level of work (e.g. change from full-time to part-time or change in level of responsibility)
  - ○ Currently unable to work
- ○ No

b. Family responsibilities:

i. Before the cardiac arrest was the person looking after family at home *(If this was not a major role before the cardiac arrest, indicate "No" and go to **item c**)*

- ○ Yes
- ○ No → go to **item 4c**

ii. Since the cardiac arrest has there been a change in their ability to look after family at home?

- ○ Yes → How restricted are they?
  - ○ Reduced responsibility for looking after family
  - ○ Currently unable to look after family
- ○ No

c. Social & leisure activities:

(Social and leisure activities include hobbies and interests. Includes activities outside the home or at home. Activities outside the home: going to the pub/bar, restaurant, club, church, cinema, visiting friends, going for walks. Activities at home: involving "active" participation including knitting, sewing, painting, games, reading books, home improvements).

i. Before the cardiac arrest did the person have regular free-time activities? *(If the person had very restricted social & leisure activities before the cardiac arrest then indicate "No" and go to **item 4d**)*

- ○ Yes
- ○ No → go to **item 4d**

ii. Since the cardiac arrest has there been a change in their ability to participate in these activities?

- ○ Yes → How restricted are they?
  - ○ Participate a bit less: *at least half as often as before the cardiac arrest*
  - ○ Participate much less: *less than half as often*
  - ○ Unable to participate: *rarely, if ever, take part*
- ○ No

5. Usual duties and activities: *(Continued)*

d. Family & Friendship:

(Problems with relationships include difficulties in relationships with people at home, loss of friendships or increase in isolation. Changes in the person may include: communication problems, quick temper, irritability, anxiety, insensitivity to others, mood swings, depression, and unreasonable behavior).

i. Since the cardiac arrest has the person had problems with relationships or become isolated?

- ○ Yes → What is the extent of disruption/strain?
  - ○ Occasional: *less than weekly*
  - ○ Frequent: *once a week or more, but tolerable*
  - ○ Constant: *daily & intolerable*
- ○ No

ii. Before the cardiac arrest were any similar problems present?

- ○ Yes
- ○ No

6. Symptoms as a result of the cardiac arrest:

(Can be any symptoms or problems reported by the patient or found on neurological examination)

a. Does the patient have any symptoms resulting from the cardiac arrest? *(Record spontaneous answer to the question from respondent)*

- ○ Yes
- ○ No

Structured Interview for Assessment of Modified Rankin Scale

Follow-up period: 3 months

b. Symptom checklist:

	Now		Before cardiac arrest	
	Yes	No	Yes	No
i. Does the person have difficulty reading or writing?	○	○	○	○
ii. Does the person have difficulty speaking or finding the right word?	○	○	○	○
iii. Does the person have problems with balance or coordination?	○	○	○	○
iv. Does the person have visual problems?	○	○	○	○
v. Does the person have numbness (face, arms, legs, hands, feet)?	○	○	○	○
vi. Has the person experienced loss of movement (face, arms, legs, hands, feet)?	○	○	○	○
vii. Does the person have difficulty with swallowing?	○	○	○	○
viii. Any other symptoms? Please record:	○	○	○	○

Person responsible for data on this form:

Structured Interview for Assessment of Modified Rankin Scale

Follow-up period: 6 months

Please record responses to all questions (unless otherwise indicated in the text), including those concerning status before cardiac arrest. See guidelines on the facing page for further information.

1. Constant Care:

Constant care means that someone needs to be available at all times. Care may be provided by either a trained or untrained caregiver. The patient will usually be bedridden and may be incontinent.	**Now**		**Before cardiac arrest**	
	Yes	No	Yes	No
a. Does the person require constant care?	○	○	○	○

2. Assistance to attend to bodily needs/for walking:

Assistance includes physical assistance, verbal instruction, or supervision by another person.	**Now**		**Before cardiac arrest**	
	Yes	No	Yes	No
a. Is assistance essential for eating? *(Eating without assistance: food and implements may be provided by others)*	○	○	○	○
b. Is assistance essential for using the toilet? *(Using toilet without assistance: reach toilet/commode; undress sufficiently, clean self; dress and leave)*	○	○	○	○
c. Is assistance essential for routine daily hygiene? *(Routine hygiene: washing face, doing hair, cleaning teeth/fitting false teeth. Implements may be provided by others and this should not be considered assistance)*	○	○	○	○
d. Is assistance essential for walking? *(Walking without assistance: able to walk indoors around house or ward, may use any aid (e.g. stick/cane, walking frame/walker), however not requiring physical help or verbal instruction or supervision from another person)*	○	○	○	○

3. Assistance to look after own affairs:

Assistance includes physical assistance, or verbal instruction, or supervision by another person.	**Now**		**Before cardiac arrest**	
	Yes	No	Yes	No
a. Is assistance essential for preparing a simple meal? *(For example, able to prepare breakfast or a snack)*	○	○	○	○
b. Is assistance essential for basic household chores? *(For example, finding and putting away clothes, clearing up after a meal. Exclude chores that do not need to be done every day, such as using a vacuum cleaner)*	○	○	○	○
c. Is assistance essential for looking after household expenses?	○	○	○	○
d. Is assistance essential for local travel? *(Patients may drive or use public transport to get around. Ability to use a taxi is sufficient, provided the person can phone for it themselves and instruct the driver)*	○	○	○	○
e. Is assistance essential for local shopping? *(Local shopping: a least able to buy a single item)*	○	○	○	○

4. Usual duties and activities:

The next sets of questions are about how the patient usually spends his/her day.

a. Work:

i. Before the cardiac arrest, was the person working or seeking work or studying as a student? *(If the person was not employed or seeking work before the cardiac arrest, or the person was retired then indicate "No" and go to **item 4b**)*

- ○ Yes
- ○ No → go to **item 4b**

ii. Since the cardiac arrest has there been a change in the person's ability to work or study? *(Change in ability to work or study includes loss of employment or reduction in level of responsibility; change in education or problems with study)*

- ○ Yes → How restricted are they?
  - ○ Reduced level of work (e.g. change from full-time to part-time or change in level of responsibility)
  - ○ Currently unable to work
- ○ No

b. Family responsibilities:

i. Before the cardiac arrest was the person looking after family at home *(If this was not a major role before the cardiac arrest, indicate "No" and go to **item c**)*

- ○ Yes
- ○ No → go to **item 4c**

ii. Since the cardiac arrest has there been a change in their ability to look after family at home?

- ○ Yes → How restricted are they?
  - ○ Reduced responsibility for looking after family
  - ○ Currently unable to look after family
- ○ No

c. Social & leisure activities:

(Social and leisure activities include hobbies and interests. Includes activities outside the home or at home. Activities outside the home: going to the pub/bar, restaurant, club, church, cinema, visiting friends, going for walks. Activities at home: involving "active" participation including knitting, sewing, painting, games, reading books, home improvements).

i. Before the cardiac arrest did the person have regular free-time activities? *(If the person had very restricted social & leisure activities before the cardiac arrest then indicate "No" and go to **item 4d**)*

- ○ Yes
- ○ No → go to **item 4d**

ii. Since the cardiac arrest has there been a change in their ability to participate in these activities?

- ○ Yes → How restricted are they?
  - ○ Participate a bit less: *at least half as often as before the cardiac arrest*
  - ○ Participate much less: *less than half as often*
  - ○ Unable to participate: *rarely, if ever, take part*
- ○ No

5. Usual duties and activities: *(Continued)*

d. Family & Friendship:

(Problems with relationships include difficulties in relationships with people at home, loss of friendships or increase in isolation. Changes in the person may include: communication problems, quick temper, irritability, anxiety, insensitivity to others, mood swings, depression, and unreasonable behavior).

i. Since the cardiac arrest has the person had problems with relationships or become isolated?

- ○ Yes → What is the extent of disruption/strain?
  - ○ Occasional: *less than weekly*
  - ○ Frequent: *once a week or more, but tolerable*
  - ○ Constant: *daily & intolerable*
- ○ No

ii. Before the cardiac arrest were any similar problems present?

- ○ Yes
- ○ No

6. Symptoms as a result of the cardiac arrest:

(Can be any symptoms or problems reported by the patient or found on neurological examination)

a. Does the patient have any symptoms resulting from the cardiac arrest? *(Record spontaneous answer to the question from respondent)*

- ○ Yes
- ○ No

b. Symptom checklist:

	Now		Before cardiac arrest	
	Yes	No	Yes	No
i. Does the person have difficulty reading or writing?	○	○	○	○
ii. Does the person have difficulty speaking or finding the right word?	○	○	○	○
iii. Does the person have problems with balance or coordination?	○	○	○	○
iv. Does the person have visual problems?	○	○	○	○
v. Does the person have numbness (face, arms, legs, hands, feet)?	○	○	○	○
vi. Has the person experienced loss of movement (face, arms, legs, hands, feet)?	○	○	○	○
vii. Does the person have difficulty with swallowing?	○	○	○	○
viii. Any other symptoms? Please record:	○	○	○	○

Person responsible for data on this form:

6.12.1 Cerebral Performance Category

Structured Interviews for Assessment of Cerebral Performance Category

Introduction

The research assistant will ask/review the following questions in order to categorize the patient as Cerebral Performance Category (CPC) scale 1 - 4, based upon current status. Telephone questions may be asked of a caregiver, if necessary.

Telephone Interview of Caregiver

1. **Is the patient able to follow simple commands or say a few words (i.e. conscious)?**
   - ○ No → Stop here
   - ○ Yes → Go on
2. **Is the patient able to do normal daily activities without assistance (dressing, preparing meals, local travel, shopping)?**
   - ○ No →Is assistance of another person essential EVERY DAY for some activities of daily living *(i.e. patient cannot be left alone for 24 hours or overnight)* ?
     - ○ Yes → Stop here
     - ○ No → Go on
   - ○ Yes → Go on
3. **Does the patient have any problems that are more than mild, i.e. problems that prevent him/her from doing things that he/she would like to do or have to do (difficulty speaking, moving an arm, or walking; poor memory; getting along with others)?**
   - ○ No → Go on
   - ○ Yes → Stop here
4. **Has the patient returned to a normal life (work, leisure, family activities)?**
   - ○ No → Stop here
   - ○ Yes → Stop here

Telephone Interview of Patient

1. **Are you able to do your normal daily activities without assistance (dressing, preparing meals, local travel, shopping)?**
   - ○ No → Stop here
   - ○ Yes → Go on
2. **Do you have any problems that are more than mild, i.e. problems that prevent you from doing things that you would like to do or have to do (difficulty speaking, moving an arm, or walking; poor memory; getting along with others)?**
   - ○ No → Go on
   - ○ Yes → Stop here
3. **Have you returned to a normal life (work, leisure, family activities)?**
   - ○ No → Stop here
   - ○ Yes → Stop here

Person responsible for data on this form

Name:

Structured Interviews for Assessment of Cerebral Performance Category

Introduction

The research assistant will ask/review the following questions in order to categorize the patient as Cerebral Performance Category (CPC) scale 1 - 4, based upon current status. Telephone questions may be asked of a caregiver, if necessary.

Telephone Interview of Caregiver

1. **Is the patient able to follow simple commands or say a few words (i.e. conscious)?**
   - ○ No → Stop here
   - ○ Yes → Go on
2. **Is the patient able to do normal daily activities without assistance (dressing, preparing meals, local travel, shopping)?**
   - ○ No →Is assistance of another person essential EVERY DAY for some activities of daily living *(i.e. patient cannot be left alone for 24 hours or overnight)* ?
     - ○ Yes → Stop here
     - ○ No → Go on
   - ○ Yes → Go on
3. **Does the patient have any problems that are more than mild, i.e. problems that prevent him/her from doing things that he/she would like to do or have to do (difficulty speaking, moving an arm, or walking; poor memory; getting along with others)?**
   - ○ No → Go on
   - ○ Yes → Stop here
4. **Has the patient returned to a normal life (work, leisure, family activities)?**
   - ○ No → Stop here
   - ○ Yes → Stop here

Telephone Interview of Patient

1. **Are you able to do your normal daily activities without assistance (dressing, preparing meals, local travel, shopping)?**
   - ○ No → Stop here
   - ○ Yes → Go on
2. **Do you have any problems that are more than mild, i.e. problems that prevent you from doing things that you would like to do or have to do (difficulty speaking, moving an arm, or walking; poor memory; getting along with others)?**
   - ○ No → Go on
   - ○ Yes → Stop here
3. **Have you returned to a normal life (work, leisure, family activities)?**
   - ○ No → Stop here
   - ○ Yes → Stop here

Person responsible for data on this form

Name:

Structured Interviews for Assessment of Cerebral Performance Category

Introduction

The research assistant will ask/review the following questions in order to categorize the patient as Cerebral Performance Category (CPC) scale 1 - 4, based upon current status. Telephone questions may be asked of a caregiver, if necessary.

Telephone Interview of Caregiver

1. **Is the patient able to follow simple commands and say a few words (i.e. conscious)?**
   - ○ No → Stop here
   - ○ Yes → Go on
2. **Is the patient able to do normal daily activities without assistance (dressing, preparing meals, local travel, shopping)?**
   - ○ No → Stop here
   - ○ Yes → Go on
3. **Does the patient have any problems that are more than mild, i.e. problems that prevent him/her from doing things that he/she would like to do or have to do (difficulty speaking, moving an arm, or walking; poor memory; getting along with others)?**
   - ○ No → Stop here
   - ○ Yes → Go on
4. **Has the patient returned to a normal life (work, leisure, family activities)?**
   - ○ No → Stop here
   - ○ Yes → Stop here

Telephone Interview of Patient

1. **Are you able to do your normal daily activities without assistance (dressing, preparing meals, local travel, shopping)?**
   - ○ No → Stop here
   - ○ Yes → Go on
2. **Do you have any problems that are more than mild, i.e. problems that prevent you from doing things that you would like to do or have to do (difficulty speaking, moving an arm, or walking; poor memory; getting along with others)?**
   - ○ No → Go on
   - ○ Yes → Stop here
3. **Have you returned to a normal life (work, leisure, family activities)?**
   - ○ No → Stop here
   - ○ Yes → Stop here

Person responsible for data on this form:

6.13.1 Health Utilities Index – Self Assessed

HEALTH UTILITIES INDEX

Self-Assessed
Follow-up period: 3 months

Start time: [ ] : [ ] *(24-hour clock)*

Read to Patient:

The next set of questions ask about various aspects of your health. When answering these questions we would like you to think about your health and your ability to do things on a day-to-day basis, during the past week. To define the 1 week period, please think about what the date was 7 days ago and recall the major events that you have experienced during this period. Please focus your answer on your abilities, disabilities and how you have felt during the past 1 week.

You may feel that some of these questions do not apply to you, but it is important that we ask the same questions to everyone. Also, a few questions are similar; please excuse the apparent overlap and answer each question independently.

All information you provide is confidential. There are no right or wrong answers; what we want is your opinion about your abilities and feelings.

Interviewer:
For each question, read the entire question/sentence as written following the question number, emphasizing the words in italics, if any. Do not read the response options listed below the question. If the responses are included as part of the question (eg: Q26, Q31 etc) read them as part of the questions. The answer given by the respondent to each question should be clearly marked in the circle beside the one appropriate answer listed below the question.

VISION

1. **During the past week, have you been able to see well enough to read ordinary newsprint *without* glasses or contact lenses?**
   - ○ Yes → Go to **Item 4**
   - ○ No
   - ○ Don't know
   - ○ Refused
2. **Have you been able to see well enough to read ordinary newsprint *with* glasses or contact lenses?**
   - ○ Yes → Go to **Item 4**
   - ○ No
   - ○ Don't know/Didn't wear glasses or contact lenses
   - ○ Refused
3. **During the past week, have you been able to see at all?**
   - ○ Yes
   - ○ No → Go to **Item 6**
   - ○ Don't know
   - ○ Refused
4. **During the past week, have you been able to see well enough to recognize a friend on the other side of the street *without* glasses or contact lenses?**
   - ○ Yes → Go to **Item 6**
   - ○ No
   - ○ Don't know
   - ○ Refused
5. **Have you been able to see well enough to recognize a friend on the other side of the street *with* glasses or contact lenses?**
   - ○ Yes
   - ○ No
   - ○ Don't know/Didn't wear glasses or contact lenses
   - ○ Refused

HEARING

6. **During the past week, have you been able to hear what is said in a group conversation with at least three other people *without* a hearing aid?**
   - ○ Yes → Go to **Item 11**
   - ○ No
   - ○ Don't know
   - ○ Refused

7. **Have you been able to hear what is said in a group conversation with at least three other people *with* a hearing aid?**
   - ○ Yes → Go to **Item 9**
   - ○ No
   - ○ Don't know/Didn't wear a hearing aid
   - ○ Refused
8. **During the past week, have you been able to hear at all?**
   - ○ Yes
   - ○ No → Go to **Item 11**
   - ○ Don't know
   - ○ Refused
9. **During the past week, have you been able to hear what is said in a conversation with one other person in a quiet room *without* a hearing aid?**
   - ○ Yes → Go to **Item 11**
   - ○ No
   - ○ Don't know
   - ○ Refused
10. **Have you been able to hear what is said in a conversation with one other person in a quiet room *with* a hearing aid?**
    - ○ Yes
    - ○ No
    - ○ Don't know/Didn't wear a hearing aid
    - ○ Refused

SPEECH

11. **During the past week, have you been able to be understood *completely* when speaking your own language with people who do not know you?**
    - ○ Yes → Go to **Item 16**
    - ○ No
    - ○ Don't know
    - ○ Refused
12. **Have you been able to be understood *partially* when speaking with people who do not know you?**
    - ○ Yes
    - ○ No
    - ○ Don't know
    - ○ Refused
13. **During the past week, have you been able to be understood *completely* when speaking with people who know you well?**
    - ○ Yes → Go to **Item 16**
    - ○ No
    - ○ Don't know
    - ○ Refused
14. **Have you been able to be understood *partially* when speaking with people who know you well?**
    - ○ Yes → Go to **Item 16**
    - ○ No
    - ○ Don't know
    - ○ Refused
15. **During the past week, have you been able to speak at all?**
    - ○ Yes
    - ○ No
    - ○ Don't know
    - ○ Refused

GETTING AROUND

16. **During the past week, have you been able to bend, lift, jump and run *without difficulty* and *without help or equipment* of any kind?**
    - ○ Yes → Go to **Item 24**
    - ○ No
    - ○ Don't know
    - ○ Refused
17. **Have you been able to walk around the neighborhood *without difficulty* and *without help or equipment* of any kind?**
    - ○ Yes → Go to **Item 24**
    - ○ No
    - ○ Don't know
    - ○ Refused
18. **Have you been able to walk around the neighborhood *with difficulty* but *without help* or *equipment* of any kind?**
    - ○ Yes → Go to **Item 24**
    - ○ No
    - ○ Don't know
    - ○ Refused
19. **During the past week, have you been able to walk at all?**
    - ○ Yes
    - ○ No → Go to **Item 22**
    - ○ Don't know
    - ○ Refused
20. **Have you needed mechanical support, such as braces or a cane or crutches, to be able to walk around the neighborhood?**
    - ○ Yes
    - ○ No
    - ○ Don't know
    - ○ Refused
21. **Have you needed the help of another person to walk?**
    - ○ Yes
    - ○ No
    - ○ Don't know
    - ○ Refused
22. **Have needed a wheelchair to get around the neighborhood?**
    - ○ Yes
    - ○ No
    - ○ Don't know
    - ○ Refused
23. **Have you needed the help of another person to get around in the wheelchair?**
    - ○ Yes
    - ○ No
    - ○ Don't know
    - ○ Refused

HANDS AND FINGERS

24. **During the past week, have you had the *full use* of both hands and ten fingers?**
    - ○ Yes → Go to **Item 28**
    - ○ No
    - ○ Don't know
    - ○ Refused

25. Have you needed the help of another person because of limitations in the use of your hands and fingers?

- ○ Yes
- ○ No → Go to **Item 27**
- ○ Don't know
- ○ Refused

26. Have you needed the help of another person with some tasks, most tasks, or all tasks?

- ○ Some tasks
- ○ Most tasks
- ○ All tasks
- ○ Don't know
- ○ Refused

27. Have you needed special equipment, for example special tools to help with dressing or eating, because of limitations in the use of your hands or fingers?

- ○ Yes
- ○ No
- ○ Don't know
- ○ Refused

SELF-CARE

28. During the past week, have you been able to eat, bathe, dress and use the toilet without difficulty?

- ○ Yes → Go to **Item 31**
- ○ No
- ○ Don't know
- ○ Refused

29. Have you needed the help of another person to eat, bathe, dress or use the toilet?

- ○ Yes
- ○ No
- ○ Don't know
- ○ Refused

30. Have you needed special equipment or tools to eat, bathe, dress or use the toilet?

- ○ Yes
- ○ No
- ○ Don't know
- ○ Refused

FEELINGS

31. During the past week, have you been feeling happy or unhappy?

- ○ Happy
- ○ Unhappy → Go to **Item 33**
- ○ Don't know
- ○ Refused

32. Would you describe yourself as having felt:

- ○ happy and interested in life → Go to **Item 34**
- ○ somewhat happy → Go to **Item 34**
- ○ Don't know
- ○ Refused

33. Would you describe yourself as having felt:

- ○ somewhat unhappy
- ○ very unhappy
- ○ so unhappy that life is not worthwhile
- ○ Don't know
- ○ Refused

34. During the past week, did you ever feel fretful, angry, irritable, anxious or depressed?

- ○ Yes
- ○ No → Go to **Item 37**
- ○ Don't know
- ○ Refused

35. How often did you feel fretful, angry, irritable, anxious or depressed?
(rarely, occasionally, often, or almost always)

- ○ Rarely
- ○ Occasionally
- ○ Often
- ○ Almost always
- ○ Don't know
- ○ Refused

36. During the past week did you feel *extremely* fretful, angry, irritable, anxious or depressed; to the point of needing professional help?

- ○ Yes
- ○ No
- ○ Don't know
- ○ Refused

MEMORY

37. How would you describe your ability to remember things, during the past week:

- ○ Able to remember most things
- ○ Somewhat forgetful
- ○ Very forgetful
- ○ Unable to remember anything at all
- ○ Don't know
- ○ Refused

THINKING

38. How would you describe your ability to think and solve day to day problems, during the past week:

- ○ Able to think clearly and solve problems
- ○ Had a little difficulty
- ○ Had some difficulty
- ○ Had a great deal of difficulty
- ○ Unable to think or solve problems
- ○ Don't know
- ○ Refused

PAIN AND DISCOMFORT

39. Have you had any trouble with pain or discomfort, during the past week?

- ○ Yes
- ○ No → Go to **Item 41**
- ○ Don't know
- ○ Refused

40. How many of your activities, during the past week, were limited by pain or discomfort?

- ○ None
- ○ A few
- ○ Some
- ○ Most
- ○ All
- ○ Don't know
- ○ Refused

41. Overall, how would you rate your health during the past week?

- ○ Excellent
- ○ Very good
- ○ Good
- ○ Fair
- ○ Poor
- ○ Don't know
- ○ Refused

Thank you. That ends this set of questions.

TIME FINISHED: [ ] : [ ] *(24-hour clock)*

Person responsible for data on this form: [ ]

Start time: [ ] : [ ] *(24-hour clock)*

Read to Patient:

The next set of questions ask about various aspects of your health. When answering these questions we would like you to think about your health and your ability to do things on a day-to-day basis, during the past week. To define the 1 week period, please think about what the date was 7 days ago and recall the major events that you have experienced during this period. Please focus your answer on your abilities, disabilities and how you have felt during the past 1 week.

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VISION

1. **During the past week, have you been able to see well enough to read ordinary newsprint *without* glasses or contact lenses?**
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   - ○ No
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2. **Have you been able to see well enough to read ordinary newsprint *with* glasses or contact lenses?**
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3. **During the past week, have you been able to see at all?**
   - ○ Yes
   - ○ No → Go to **Item 6**
   - ○ Don't know
   - ○ Refused
4. **During the past week, have you been able to see well enough to recognize a friend on the other side of the street *without* glasses or contact lenses?**
   - ○ Yes → Go to **Item 6**
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5. **Have you been able to see well enough to recognize a friend on the other side of the street *with* glasses or contact lenses?**
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HEARING

6. **During the past week, have you been able to hear what is said in a group conversation with at least three other people *without* a hearing aid?**
   - ○ Yes → Go to **Item 11**
   - ○ No
   - ○ Don't know
   - ○ Refused

7. **Have you been able to hear what is said in a group conversation with at least three other people *with* a hearing aid?**
   - ○ Yes → Go to **Item 9**
   - ○ No
   - ○ Don't know/Didn't wear a hearing aid
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8. **During the past week, have you been able to hear at all?**
   - ○ Yes
   - ○ No → Go to **Item 11**
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9. **During the past week, have you been able to hear what is said in a conversation with one other person in a quiet room *without* a hearing aid?**
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GETTING AROUND

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22. **Have needed a wheelchair to get around the neighborhood?**
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23. **Have you needed the help of another person to get around in the wheelchair?**
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HANDS AND FINGERS

24. **During the past week, have you had the *full use* of both hands and ten fingers?**
    - ○ Yes → Go to **Item 28**
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SELF-CARE

28. During the past week, have you been able to eat, bathe, dress and use the toilet without difficulty?
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30. Have you needed special equipment or tools to eat, bathe, dress or use the toilet?
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- ○ Often
- ○ Almost always
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36. During the past week did you feel *extremely* fretful, angry, irritable, anxious or depressed; to the point of needing professional help?

- ○ Yes
- ○ No
- ○ Don't know
- ○ Refused

MEMORY

37. How would you describe your ability to remember things, during the past week:

- ○ Able to remember most things
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THINKING

38. How would you describe your ability to think and solve day to day problems, during the past week:

- ○ Able to think clearly and solve problems
- ○ Had a little difficulty
- ○ Had some difficulty
- ○ Had a great deal of difficulty
- ○ Unable to think or solve problems
- ○ Don't know
- ○ Refused

PAIN AND DISCOMFORT

39. Have you had any trouble with pain or discomfort, during the past week?

- ○ Yes
- ○ No → Go to **Item 41**
- ○ Don't know
- ○ Refused

40. How many of your activities, during the past week, were limited by pain or discomfort?

- ○ None
- ○ A few
- ○ Some
- ○ Most
- ○ All
- ○ Don't know
- ○ Refused

41. Overall, how would you rate your health during the past week?

- ○ Excellent
- ○ Very good
- ○ Good
- ○ Fair
- ○ Poor
- ○ Don't know
- ○ Refused

Thank you. That ends this set of questions.

TIME FINISHED: [ ] : [ ] *(24-hour clock)*

Person responsible for data on this form: [ ]

6.14.1 Health Utilities Index – Proxy-Assessed

HEALTH UTILITIES INDEX

Proxy-Assessed
Follow-up period: 3 months

Start time: [ ] : [ ] *(24-hour clock)*

Read to proxy:

The next set of questions ask about various aspects of (subject's name)'s health. When answering these questions we would like you to think about (his/her) health and ability to do things on a day-to-day basis, during the past week. To define the 1 week period, please think about what the date was 7 days ago and recall the major events that (he/she) has experienced during this period. Please focus your answer on (subject's name)'s abilities, disabilities and how they have felt during the past 1 week.

You may feel that some of these questions do not apply to (subject's name), but it is important that we ask the same questions about each subject. Also, a few questions are similar; please excuse the apparent overlap and answer each question independently.

All information you provide is confidential. There are no right or wrong answers; what we want is your opinion about (subject's name) abilities and feelings.

Interviewer:
For each question, read the entire question/sentence as written following the question number, emphasizing the words in italics, if any. Do not read the response options listed below the question. If the responses are included as part of the question (eg: Q26, Q31 etc) read them as part of the questions. The answer given by the respondent to each question should be clearly marked in the circle beside the one appropriate answer listed below the question.

VISION

1. **During the past week, has (subject's name) been able to see well enough to read ordinary newsprint *without* glasses or contact lenses?**
   - ○ Yes → Go to **Item 4**
   - ○ No
   - ○ Don't know
   - ○ Refused
2. **Has (subject's name) been able to see well enough to read ordinary newsprint *with* glasses or contact lenses?**
   - ○ Yes → Go to **Item 4**
   - ○ No
   - ○ Don't know/Didn't wear glasses or contact lenses
   - ○ Refused
3. **During the past week, has (subject's name) been able to see at all?**
   - ○ Yes
   - ○ No → Go to **Item 6**
   - ○ Don't know
   - ○ Refused
4. **During the past week, has (subject's name) been able to see well enough to recognize a friend on the other side of the street *without* glasses or contact lenses?**
   - ○ Yes → Go to **Item 6**
   - ○ No
   - ○ Don't know
   - ○ Refused
5. **Has (subject's name) been able to see well enough to recognize a friend on the other side of the street *with* glasses or contact lenses?**
   - ○ Yes
   - ○ No
   - ○ Don't know/Didn't wear glasses or contact lenses
   - ○ Refused

HEARING

6. **During the past week, has (subject's name) been able to hear what is said in a group conversation with at least three other people *without* a hearing aid?**
   - ○ Yes → Go to **Item 11**
   - ○ No
   - ○ Don't know
   - ○ Refused
7. **Has (subject's name) been able to hear what is said in a group conversation with at least three other people *with* a hearing aid?**
   - ○ Yes → Go to **Item 9**
   - ○ No
   - ○ Don't know/Didn't wear a hearing aid
   - ○ Refused
8. **During the past week, has (subject's name) been able to hear at all?**
   - ○ Yes
   - ○ No → Go to **Item 11**
   - ○ Don't know
   - ○ Refused
9. **During the past week, has (subject's name) been able to hear what is said in a conversation with one other person in a quiet room *without* a hearing aid?**
   - ○ Yes → Go to **Item 11**
   - ○ No
   - ○ Don't know
   - ○ Refused
10. **Has (subject's name) been able to hear what is said in a conversation with one other person in a quiet room *with* a hearing aid?**
    - ○ Yes
    - ○ No
    - ○ Don't know/Didn't wear a hearing aid
    - ○ Refused

SPEECH

11. **During the past week, has (subject's name) been able to be understood *completely* when speaking his/her own language with people who do not know (subject's name)?**
    - ○ Yes → Go to **Item 16**
    - ○ No
    - ○ Don't know
    - ○ Refused
12. **Has (subject's name) been able to be understood *partially* when speaking with people who do not know (subject's name)?**
    - ○ Yes
    - ○ No
    - ○ Don't know
    - ○ Refused
13. **During the past week, has (subject's name) been able to be understood *completely* when speaking with people who know (subject's name) well?**
    - ○ Yes → Go to **Item 16**
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    - ○ Yes → Go to **Item 16**
    - ○ No
    - ○ Don't know
    - ○ Refused

15. **During the past week, has (subject's name) been able to speak at all?**
    - ◯ Yes
    - ◯ No
    - ◯ Don't know
    - ◯ Refused

GETTING AROUND

16. **During the past week, has (subject's name) been able to bend, lift, jump and run *without difficulty* and *without help or equipment* of any kind?**
    - ◯ Yes → Go to **Item 24**
    - ◯ No
    - ◯ Don't know
    - ◯ Refused
17. **Has (subject's name) been able to walk around the neighborhood *without difficulty* and *without help or equipment* of any kind?**
    - ◯ Yes → Go to **Item 24**
    - ◯ No
    - ◯ Don't know
    - ◯ Refused
18. **Has (subject's name) been able to walk around the neighborhood *with difficulty* but *without help or equipment* of any kind?**
    - ◯ Yes → Go to **Item 24**
    - ◯ No
    - ◯ Don't know
    - ◯ Refused
19. **During the past week, has (subject's name) been able to walk at all?**
    - ◯ Yes
    - ◯ No → Go to **Item 22**
    - ◯ Don't know
    - ◯ Refused
20. **Has (subject's name) needed mechanical support, such as braces or a cane or crutches, to be able to walk around the neighborhood?**
    - ◯ Yes
    - ◯ No
    - ◯ Don't know
    - ◯ Refused
21. **Has (subject's name) needed the help of another person to walk?**
    - ◯ Yes
    - ◯ No
    - ◯ Don't know
    - ◯ Refused
22. **Has (subject's name) needed a wheelchair to get around the neighborhood?**
    - ◯ Yes
    - ◯ No
    - ◯ Don't know
    - ◯ Refused
23. **Has (subject's name) needed the help of another person to get around in the wheelchair?**
    - ◯ Yes
    - ◯ No
    - ◯ Don't know
    - ◯ Refused

HANDS AND FINGERS

24. During the past week, has (subject's name) had the *full use* of both hands and ten fingers?

- ○ Yes → Go to **Item 28**
- ○ No
- ○ Don't know
- ○ Refused

25. Has (subject's name) needed the help of another person because of limitations in the use of his/her hands and fingers?

- ○ Yes
- ○ No → Go to **Item 27**
- ○ Don't know
- ○ Refused

26. Has (subject's name) needed the help of another person with some tasks, most tasks, or all tasks?

- ○ Some tasks
- ○ Most tasks
- ○ All tasks
- ○ Don't know
- ○ Refused

27. Has (subject's name) needed special equipment, for example special tools to help with dressing or eating, because of limitations in the use of his/her hands or fingers?

- ○ Yes
- ○ No
- ○ Don't know
- ○ Refused

SELF-CARE

28. During the past week, has (subject's name) been able to eat, bathe, dress and use the toilet without difficulty?

- ○ Yes → Go to **Item 31**
- ○ No
- ○ Don't know
- ○ Refused

29. Has (subject's name) needed the help of another person to eat, bathe, dress or use the toilet?

- ○ Yes
- ○ No
- ○ Don't know
- ○ Refused

30. Has (subject's name) needed special equipment or tools to eat, bathe, dress or use the toilet?

- ○ Yes
- ○ No
- ○ Don't know
- ○ Refused

FEELINGS

31. During the past week, has (subject's name) been feeling happy or unhappy?

- ○ Happy
- ○ Unhappy → Go to **Item 33**
- ○ Don't know
- ○ Refused

32. Would you describe (subject's name) as having felt:

- ○ happy and interested in life → Go to **Item 34**
- ○ somewhat happy → Go to **Item 34**
- ○ Don't know
- ○ Refused

33. **Would you describe (subject's name) as having felt:**
- ○ somewhat unhappy
- ○ very unhappy
- ○ so unhappy that life is not worthwhile
- ○ Don't know
- ○ Refused

34. **During the past week, did (subject's name) ever feel fretful, angry, irritable, anxious or depressed?**
- ○ Yes
- ○ No → Go to **Item 37**
- ○ Don't know
- ○ Refused

35. **How often did (subject's name) feel fretful, angry, irritable, anxious or depressed?**
(rarely, occasionally, often, or almost always)
- ○ Rarely
- ○ Occasionally
- ○ Often
- ○ Almost always
- ○ Don't know
- ○ Refused

36. **During the past week did (subject's name) feel *extremely* fretful, angry, irritable, anxious or depressed; to the point of needing professional help?**
- ○ Yes
- ○ No
- ○ Don't know
- ○ Refused

MEMORY

37. **How would you describe (subject's name) ability to remember things, during the past week:**
- ○ Able to remember most things
- ○ Somewhat forgetful
- ○ Very forgetful
- ○ Unable to remember anything at all
- ○ Don't know
- ○ Refused

THINKING

38. **How would you describe (subject's name) ability to think and solve day to day problems, during the past week:**
- ○ Able to think clearly and solve problems
- ○ Had a little difficulty
- ○ Had some difficulty
- ○ Had a great deal of difficulty
- ○ Unable to think or solve problems
- ○ Don't know
- ○ Refused

PAIN AND DISCOMFORT

39. **Has (subject's name) had any trouble with pain or discomfort, during the past week?**
- ○ Yes
- ○ No → Go to **Item 41**
- ○ Don't know
- ○ Refused

40. How many of (subject's name)'s activities, during the past week, were limited by pain or discomfort:

- None
- A few
- Some
- Most
- All
- Don't know
- Refused

41. Overall, how would you rate (subject's name)'s health during the past week?

- Excellent
- Very good
- Good
- Fair
- Poor
- Don't know
- Refused

Thank you. That ends this set of questions.

TIME FINISHED: [ ] : [ ] *(24-hour clock)*

Person responsible for data on this form: [ ]

Start time: [ ] : [ ] *(24-hour clock)*

Read to proxy:

The next set of questions ask about various aspects of (subject's name)'s health. When answering these questions we would like you to think about (his/her) health and ability to do things on a day-to-day basis, during the past week. To define the 1 week period, please think about what the date was 7 days ago and recall the major events that (he/she) has experienced during this period. Please focus your answer on (subject's name)'s abilities, disabilities and how they have felt during the past 1 week.

You may feel that some of these questions do not apply to (subject's name), but it is important that we ask the same questions about each subject. Also, a few questions are similar; please excuse the apparent overlap and answer each question independently.

All information you provide is confidential. There are no right or wrong answers; what we want is your opinion about (subject's name) abilities and feelings.

Interviewer:
For each question, read the entire question/sentence as written following the question number, emphasizing the words in italics, if any. Do not read the response options listed below the question. If the responses are included as part of the question (eg: Q26, Q31 etc) read them as part of the questions. The answer given by the respondent to each question should be clearly marked in the circle beside the one appropriate answer listed below the question.

VISION

1. **During the past week, has (subject's name) been able to see well enough to read ordinary newsprint *without* glasses or contact lenses?**
   - ○ Yes → Go to **Item 4**
   - ○ No
   - ○ Don't know
   - ○ Refused
2. **Has (subject's name) been able to see well enough to read ordinary newsprint *with* glasses or contact lenses?**
   - ○ Yes → Go to **Item 4**
   - ○ No
   - ○ Don't know/Didn't wear glasses or contact lenses
   - ○ Refused
3. **During the past week, has (subject's name) been able to see at all?**
   - ○ Yes
   - ○ No → Go to **Item 6**
   - ○ Don't know
   - ○ Refused
4. **During the past week, has (subject's name) been able to see well enough to recognize a friend on the other side of the street *without* glasses or contact lenses?**
   - ○ Yes → Go to **Item 6**
   - ○ No
   - ○ Don't know
   - ○ Refused
5. **Has (subject's name) been able to see well enough to recognize a friend on the other side of the street *with* glasses or contact lenses?**
   - ○ Yes
   - ○ No
   - ○ Don't know/Didn't wear glasses or contact lenses
   - ○ Refused

HEARING

6. **During the past week, has (subject's name) been able to hear what is said in a group conversation with at least three other people *without* a hearing aid?**
   - ○ Yes → Go to **Item 11**
   - ○ No
   - ○ Don't know
   - ○ Refused
7. **Has (subject's name) been able to hear what is said in a group conversation with at least three other people *with* a hearing aid?**
   - ○ Yes → Go to **Item 9**
   - ○ No
   - ○ Don't know/Didn't wear a hearing aid
   - ○ Refused
8. **During the past week, has (subject's name) been able to hear at all?**
   - ○ Yes
   - ○ No → Go to **Item 11**
   - ○ Don't know
   - ○ Refused
9. **During the past week, has (subject's name) been able to hear what is said in a conversation with one other person in a quiet room *without* a hearing aid?**
   - ○ Yes → Go to **Item 11**
   - ○ No
   - ○ Don't know
   - ○ Refused
10. **Has (subject's name) been able to hear what is said in a conversation with one other person in a quiet room *with* a hearing aid?**
    - ○ Yes
    - ○ No
    - ○ Don't know/Didn't wear a hearing aid
    - ○ Refused

SPEECH

11. **During the past week, has (subject's name) been able to be understood *completely* when speaking his/her own language with people who do not know (subject's name)?**
    - ○ Yes → Go to **Item 16**
    - ○ No
    - ○ Don't know
    - ○ Refused
12. **Has (subject's name) been able to be understood *partially* when speaking with people who do not know (subject's name)?**
    - ○ Yes
    - ○ No
    - ○ Don't know
    - ○ Refused
13. **During the past week, has (subject's name) been able to be understood *completely* when speaking with people who know (subject's name) well?**
    - ○ Yes → Go to **Item 16**
    - ○ No
    - ○ Don't know
    - ○ Refused
14. **Has (subject's name) been able to be understood *partially* when speaking with people who know (subject's name) well?**
    - ○ Yes → Go to **Item 16**
    - ○ No
    - ○ Don't know
    - ○ Refused

15. **During the past week, has (subject's name) been able to speak at all?**
    - ○ Yes
    - ○ No
    - ○ Don't know
    - ○ Refused

GETTING AROUND

16. **During the past week, has (subject's name) been able to bend, lift, jump and run *without difficulty* and *without help or equipment* of any kind?**
    - ○ Yes → Go to **Item 24**
    - ○ No
    - ○ Don't know
    - ○ Refused
17. **Has (subject's name) been able to walk around the neighborhood *without difficulty* and *without help or equipment* of any kind?**
    - ○ Yes → Go to **Item 24**
    - ○ No
    - ○ Don't know
    - ○ Refused
18. **Has (subject's name) been able to walk around the neighborhood *with difficulty* but *without help or equipment* of any kind?**
    - ○ Yes → Go to **Item 24**
    - ○ No
    - ○ Don't know
    - ○ Refused
19. **During the past week, has (subject's name) been able to walk at all?**
    - ○ Yes
    - ○ No → Go to **Item 22**
    - ○ Don't know
    - ○ Refused
20. **Has (subject's name) needed mechanical support, such as braces or a cane or crutches, to be able to walk around the neighborhood?**
    - ○ Yes
    - ○ No
    - ○ Don't know
    - ○ Refused
21. **Has (subject's name) needed the help of another person to walk?**
    - ○ Yes
    - ○ No
    - ○ Don't know
    - ○ Refused
22. **Has (subject's name) needed a wheelchair to get around the neighborhood?**
    - ○ Yes
    - ○ No
    - ○ Don't know
    - ○ Refused
23. **Has (subject's name) needed the help of another person to get around in the wheelchair?**
    - ○ Yes
    - ○ No
    - ○ Don't know
    - ○ Refused

HANDS AND FINGERS

24. During the past week, has (subject's name) had the *full use* of both hands and ten fingers?
- ○ Yes → Go to **Item 28**
- ○ No
- ○ Don't know
- ○ Refused

25. Has (subject's name) needed the help of another person because of limitations in the use of his/her hands and fingers?
- ○ Yes
- ○ No → Go to **Item 27**
- ○ Don't know
- ○ Refused

26. Has (subject's name) needed the help of another person with some tasks, most tasks, or all tasks?
- ○ Some tasks
- ○ Most tasks
- ○ All tasks
- ○ Don't know
- ○ Refused

27. Has (subject's name) needed special equipment, for example special tools to help with dressing or eating, because of limitations in the use of his/her hands or fingers?
- ○ Yes
- ○ No
- ○ Don't know
- ○ Refused

SELF-CARE

28. During the past week, has (subject's name) been able to eat, bathe, dress and use the toilet without difficulty?
- ○ Yes → Go to **Item 31**
- ○ No
- ○ Don't know
- ○ Refused

29. Has (subject's name) needed the help of another person to eat, bathe, dress or use the toilet?
- ○ Yes
- ○ No
- ○ Don't know
- ○ Refused

30. Has (subject's name) needed special equipment or tools to eat, bathe, dress or use the toilet?
- ○ Yes
- ○ No
- ○ Don't know
- ○ Refused

FEELINGS

31. During the past week, has (subject's name) been feeling happy or unhappy?
- ○ Happy
- ○ Unhappy → Go to **Item 33**
- ○ Don't know
- ○ Refused

32. Would you describe (subject's name) as having felt:
- ○ happy and interested in life → Go to **Item 34**
- ○ somewhat happy → Go to **Item 34**
- ○ Don't know
- ○ Refused

33. Would you describe (subject's name) as having felt:

- ○ somewhat unhappy
- ○ very unhappy
- ○ so unhappy that life is not worthwhile
- ○ Don't know
- ○ Refused

34. During the past week, did (subject's name) ever feel fretful, angry, irritable, anxious or depressed?

- ○ Yes
- ○ No → Go to **Item 37**
- ○ Don't know
- ○ Refused

35. How often did (subject's name) feel fretful, angry, irritable, anxious or depressed?
(rarely, occasionally, often, or almost always)

- ○ Rarely
- ○ Occasionally
- ○ Often
- ○ Almost always
- ○ Don't know
- ○ Refused

36. During the past week did (subject's name) feel *extremely* fretful, angry, irritable, anxious or depressed; to the point of needing professional help?

- ○ Yes
- ○ No
- ○ Don't know
- ○ Refused

MEMORY

37. How would you describe (subject's name) ability to remember things, during the past week:

- ○ Able to remember most things
- ○ Somewhat forgetful
- ○ Very forgetful
- ○ Unable to remember anything at all
- ○ Don't know
- ○ Refused

THINKING

38. How would you describe (subject's name) ability to think and solve day to day problems, during the past week:

- ○ Able to think clearly and solve problems
- ○ Had a little difficulty
- ○ Had some difficulty
- ○ Had a great deal of difficulty
- ○ Unable to think or solve problems
- ○ Don't know
- ○ Refused

PAIN AND DISCOMFORT

39. Has (subject's name) had any trouble with pain or discomfort, during the past week?

- ○ Yes
- ○ No → Go to **Item 41**
- ○ Don't know
- ○ Refused

40. How many of (subject's name)'s activities, during the past week, were limited by pain or discomfort:

- None
- A few
- Some
- Most
- All
- Don't know
- Refused

41. Overall, how would you rate (subject's name)'s health during the past week?

- Excellent
- Very good
- Good
- Fair
- Poor
- Don't know
- Refused

Thank you. That ends this set of questions.

TIME FINISHED: [ ] : [ ] *(24-hour clock)*

Person responsible for data on this form: [ ]

6.15.1 Geriatric Depression Scale

Choose the best answer for how you have felt over the past week:

1. **Are you basically satisfied with your life?**
   ○ Yes ○ No
2. **Have you dropped many of your activities and interests**
   ○ Yes ○ No
3. **Do you feel that your life is empty?**
   ○ Yes ○ No
4. **Do you often get bored?**
   ○ Yes ○ No
5. **Are you in good spirits most of the time?**
   ○ Yes ○ No
6. **Are you afraid that something bad is going to happen to you?**
   ○ Yes ○ No
7. **Do you feel happy most of the time?**
   ○ Yes ○ No
8. **Do you often feel helpless?**
   ○ Yes ○ No
9. **Do you prefer to stay at home, rather than going out and doing new things?**
   ○ Yes ○ No
10. **Do you feel you have more problems with memory than most?**
    ○ Yes ○ No
11. **Do you think it is wonderful to be alive now?**
    ○ Yes ○ No
12. **Do you feel pretty worthless the way you are now?**
    ○ Yes ○ No
13. **Do you feel full of energy?**
    ○ Yes ○ No
14. **Do you feel that your situation is hopeless?**
    ○ Yes ○ No
15. **Do you think that most people are better off than you are?**
    ○ Yes ○ No

Person responsible for data on this form:

Choose the best answer for how you have felt over the past week:

1. **Are you basically satisfied with your life?**
   ○ Yes ○ No
2. **Have you dropped many of your activities and interests**
   ○ Yes ○ No
3. **Do you feel that your life is empty?**
   ○ Yes ○ No
4. **Do you often get bored?**
   ○ Yes ○ No
5. **Are you in good spirits most of the time?**
   ○ Yes ○ No
6. **Are you afraid that something bad is going to happen to you?**
   ○ Yes ○ No
7. **Do you feel happy most of the time?**
   ○ Yes ○ No
8. **Do you often feel helpless?**
   ○ Yes ○ No
9. **Do you prefer to stay at home, rather than going out and doing new things?**
   ○ Yes ○ No
10. **Do you feel you have more problems with memory than most?**
    ○ Yes ○ No
11. **Do you think it is wonderful to be alive now?**
    ○ Yes ○ No
12. **Do you feel pretty worthless the way you are now?**
    ○ Yes ○ No
13. **Do you feel full of energy?**
    ○ Yes ○ No
14. **Do you feel that your situation is hopeless?**
    ○ Yes ○ No
15. **Do you think that most people are better off than you are?**
    ○ Yes ○ No

Person responsible for data on this form:

Quick References

7.1 ROC PRIMED ITD Online Inventory

1. A physical inventory of all ITDs is required every quarter. The ITD must be VISUALLY confirmed by the ROC coordinator or agency contact, and the date of the visual confirmation entered on the online inventory. ITD's are an investigational device and used under Exemption from Consent, so sites are required to keep very close track of the ITD's and to know every patient on whom one was used.

2. Keep your missing, broken, or problem packaging up-to-date real time via ROC PRIMED Alert forms and then they won't be on your lists needing updating later. Entering the ITD number on an Alert form automatically adjusts the online inventory.

3. If you find a previously lost ITD--fabulous--go to the Alert form where you reported it lost and add the date that it was found and the location where it was found. Entering the found date on that same Alert form automatically adds it back into the online inventory.

4. If you are downloading a worksheet of ITDs to be updated, do it on the first date or later of the inventory cycle
so that you don't get confused by an earlier/older list of ITD's that may have more than you really need to follow-up on.

5. The 'date of known status' must be no earlier than the start date listed on the "Inventory Check Dates". No earlier dates are accepted by the system. The update is to be completed by the due date listed in the "Inventory Check Dates". The inventory cycles are scheduled for mid-March, mid-June, mid-September and mid-December. It is targeted for inventory to be complete on the ROC website one month after each date. Plan your inventory cycles accordingly.

6. If you ITD's were shipped to you just prior to the quarterly inventory date, the ITDs will not appear on the list of ITDs that need to be inventoried for the present quarter.

Online Process for Updating Your Inventory-Downloading and Uploading Your File

There are three main ways for updating your inventory:
1. Updating inventory directly through a web interface.
2. Downloading a list of ITDs as a CSV file (comma separated value). You can open the CSV file in Excel for editing, then, re-uploading the updated inventory list through the web. Please follow the CSV file specifications below.
3. Working on your own CSV and uploading it. If you are keeping your inventory in Excel spreadsheets or in an Access database, please convert it to a CSV file before uploading. Please follow the CSV file specifications below.

1. Updating inventory on the web:
This method is best for updating a few ITDs at a time.

1. Click on the "Generate inventory list" tab on top of this section.
2. To see the list of all ITDs assigned to your site, do not fill out anything under "Filter ITD listing by:" section before clicking on the "Inventory List"

There are 2 ways to get a customized list of ITDs:

a. Manually select certain groups of ITDs by choosing the appropriate filter selection before clicking on the "Inventory List" button.

For example: If you only want a list of broken/damaged and missing ITDs that are in allocation A, you can generate that list by

* Selecting allocation A from the "Allocation" drop-down list.
* Check "Broken/Damaged" and "Missing" checkboxes.

b. To get a list of ITDs to work on for the quarterly inventory check, simply click on "Online list" in the "Generate a list of outstanding ITDs for the current inventory period" section.

3. Click on the "Inventory List" button at the bottom of the "Filter ITD listing by:" section.
4. The list of ITDs will be displayed according to your selection in the previous step.
5. Click on the "Edit form" button.
6. Update information on the ITD you wish to update, then click "Save".
7. If there are any errors, the error messages will be displayed at the top of the form. All errors have to be corrected before saving the form.

2. Downloading a list of ITDs as a CSV file to work in Excel:

This method is best for doing many updates at once, and taking advantage of Excel's features such as copy and paste. For example, you can copy a status and apply to many ITDs at once.

1. Click on the "Generate inventory list" tab on top of this section.
2. To see the list of all ITDs assigned to your site, do not fill out anything under "Filter ITD listing by:" section before clicking on the "Generate CSV" button.

There are 2 ways to download a customized list of ITDs:

a. Manually select certain groups of ITDs by choosing the appropriate filter selection before clicking on the "Generate CSV" button.

For example: If you only want a list of missing ITDs that are in allocation A, you can generate that list by

* Selecting allocation A from the "Allocation" drop-down list.
* Check "Missing" checkbox.

b. To get a list of ITDs to work on for the quarterly inventory check, simply click on "CSV list" in the "Generate a list of outstanding ITDs for the current inventory period" section.

3. Click on the "Generate CSV" button.
4. Click "Ok" to save the CSV file.
5. Open the CSV file you have just saved in Excel, and work from there. Make sure you save your work once the ITDs are updated.

3. Uploading the file to the inventory system:

1. Click on the "Update inventory via CSV upload" tab on top of this section.
2. Click on the "Browse" button in the "Upload a new data file:" section to select the file from your computer.
3. Click on "Upload selected file" button.
4. If there are any errors, detailed error messages will be displayed. All errors have to be fixed before saving ITD information.

CSV file specifications:

* Fields separated by commas
* Dates formatted as mm/dd/yyyy

* First line must contain column headings. Each line must have 9 columns:
    - Site - 3 letter site code
    - ITD Number - formatted as xx-xxx-x
    - Allocation - the inventory allocation for a group of ITDs within a site, the major division(s) within a system used for randomization purposes (for those sites with more than one division within the site).
    - Status - the status of the ITD at the time of inventory
    - Status as of (mm/dd/yyyy) - the date that you or your agency contact verified that the ITD was in the location stated in the status code column
    - Episode ID/Alert ID - the episode ID that the ITD was used to enroll a patient or the alert ID that was used to report a problem with the ITD.
    - If missing, previous known location - previous known location if the ITD is missing
    - Previous known date (mm/dd/yyyy) - previous known date before the ITD is missing
    - Note - any additional information on the ITD.

7.2 TIPS For Completing the Time Record and CPR Process Forms

These two detailed forms capture critical detail about the timing of the course of care and the 'real story' about the resuscitation effort. You know what 'they' say about the devil being in the details.

These two forms provide data that, when looked at in aggregate, can help you assess and understand many study and EMS agency related practices.

These two forms are the source for data that the ROC Study Monitoring Committee uses to assess study compliance and to identify areas that might need attention.

These two forms have and will continue to serve as the foundation for many ROC discoveries.

These two forms are inter-related and go together. Though Frank Sinatra may not have anticipated the ROC PRIMED study when he sang a then 1955 popular song, he was so ROC right-on:

Try, try, try to separate them, it's an illusion
Try, try, try and you only come to this conclusion
…like a horse and carriage…
You can't have one without the other

So, in the ROC spirit of continuous improvement, here are devilish details that are good to review:

1. Assemble all source documentation:

This includes all avenues of finding out what really happened at the scene—messages left by EMS on the notification hot-line; your follow-up interviews with EMS crews; review of the ECG download; your review of <u>all</u> the EMS documentation (there can be more than one PCR). Assemble and review all this as soon as possible after the episode. Memories grow dim with time and if you 'strike while the iron is hot' and follow-up on any missing sources or details right away, you just might get all the facts.

Move into action—if defib is not synchronized, think of ways to make sure it gets done and improve someone's processes. If your local forms or interview questions are not getting you solid data, change it up and infuse what you've learned through experience.

2. Enter both watch (charted, PCR) and defib/dispatch times:

Don't cherry pick the watch times entered on the Time Record, enter all you have. When provided side by side with defib/dispatch times, the Time Record web-form is able to help with generating aligned times and adjusting whacky watch times. If charting is electronic, the times are still 'watch' values.

Move into action—if charted times do not make sense, then let EMS know how important the times are for our ROC work to help improve survival. If PDA download times do not make sense, feed that back to agency management and figure out why, then charm them to fix it. If defib download times don't make sense, then evaluate the synch procedures and reinforce a helpful approach.

3. Provide an 'adjusted time' sometimes, but not always:

If no watch or defib/dispatch time is in the source documents, then you may be able to derive a time and provide it in the 'aligned time' column. Do this only when source documentation supports the veracity of that entry. Rarely, would an adjusted time be so precise as to include seconds (such as 13:12:11). Usually, an adjusted time to the minute (such as 13:12) is most appropriate. If adjusting selected a lonely watch time (where there is no defib time) to better reflect the true course of care, then one expects similar changes to be considered for other lonely watch times --for example, if you added 51 seconds to one watch time, it would be odd to subtract 1.09 seconds from a different line item for the same case (unless source documentation supports such an adjustment).

Move into action—if EMS is not providing the needed data to accurately reflect the course of care, let them know. And, work with them to figure out how to capture this data. A big one for many sites is the Time 1st EMS CPR. Another big one is time ITD is placed. Keep working with EMS to get these times better documented.

4. No-time is sometimes better than any-old time:

Better a missing time than entering a time not based on source data or known and confirmed EMS practice. Do not conform entered times to meet an AE or AL assignment, in the absence of reference documentation. If both the watch and defib/dispatch are missing in the all the source documentation, then it would generally be best to not provide an adjusted time for the given line item.

Move into action—let EMS know how much you and ROC appreciate their providing good documentation and recognize them for their work. But, let them know where improvements would have a big impact.

5. NA or Cannot Determine-Important to distinguish:

NA means 'not applicable' (not, not available). Mark NA for line items that do not apply to the course of care that you are reporting. 'Cannot determine' means that the line item would apply to the course of care, but inadequate or unclear documentation prevents you from providing a response.

6. 1st CA EMS rhythm within 10 seconds of pad placement:

It is the intent of this data element to capture the 'presenting rhythm', so a tight 10 second timeframe for 'seeing' this rhythm is defined. Most agencies apply only defib pads, while some agencies apply both defib pads and monitoring electrodes. If you can see a signal and discern a rhythm within 10 seconds of applying either pads or electrodes, enter that rhythm and time on the CPR Process form. But—and this is important—on that same form, be sure the time for 'pads placed' is the time defib pads were placed, because this time floods the CPR process measures table with minutes for which measures would be expected.

Move into action—call the CTC with any questions. This can be confusing.

7. 1st EMS shock assessment:

A shock assessment requires an ECG signal, whether from electrodes or defib pads. If you have derived an 'adjusted' time for shock assessment based on other information (such as an EMS interview) and you have the ECG recording, then double check the recording that

the reported time is plausible. If it is not plausible, then defer to your review of the ECG recording or enter 'no doc time'.

Move into action—evaluate your interview form and consider how to improve. Don't lead 'the witness', but be sure that questions are framed to capture the course of care details. If you are not getting ECG recordings with ECG signals for close to 100% cases, then work with EMS to get there.

8. Cross form errors detect inconsistent responses:

There are several times that are entered on both the Time Record and the CPR Process form. If one is changed, then the other needs to be reviewed and edited. Cross form errors can be frustrating, but read them closely to discern any disconnect in entries.

Move into action—read the messages carefully. Call the CTC with any questions about or suggestions for re-wording.

data→information→knowledge→improved survival

7.3 ROC CTC Resources

04/08

 *Phone*	(206) 685-1302 (800) 332-0586 (toll free) Office Hours: – Weekdays – 7:30am to 5:00pm	**Website: www.uwctc.org** **Click on ROC (must have individual user ID/password to enter internal ROC website)**
 *Mail*	ROC CTC 1107 NE 45th Street, Suite 505 Seattle, WA 98105-4689	
 *email*	General Correspondence: rocctc@u.washington.edu	
 *FAX*	General Correspondence: **(206) 543-0131**	

	Overall Administrative	
	• Meeting arrangements, travel	Art Kerr
	• Subcontracts, site payments	Shirley Joaquin
	• Personnel changes, address and email corrections. Sites should first go to ROC website, click on "Contact Directory," enter username "resus" and password "call911," find your site, and update the information.	Susan Fisher
	• IRB/REB and Regulatory Issues Including approvals, renewals, FWAs, issues related to FDA, CTA (IND, IDE)	Amy Gest
	• Supplies: brochures	Berit Bardarson
	• Web issues – Main ROC website	
	➢ Web and data entry access issues	Umberto Lenzi
	➢ Electronic signature agreements	Umberto Lenzi

	EMS Structures	
	• Questions about protocol/data	Gena Sears
	• Questions about web data entry	Chi Shen, Ben Bergsten-Buret, Rich Moore
	Epistry Protocol	
	• Questions about protocol/data collection	Gena Sears, Judy Powell, Graham Nichol
	• Statistical issues	Cardiac – Trauma –
	• Questions about batch upload	Ben Bergsten-Buret, Bob Ledingham,
	• Questions about web data entry	Chi Shen, Ben Bergsten-Buret, Rich Moore
	• Epistry payment report	Judy Powell
	• Epistry payment (from UW to sites)	Shirley Joaquin
	Hypertonic Saline Protocol	
	• Questions about protocol, data, adverse events	Berit Bardarson, Judy Powell, Eileen Bulger
	• Statistical issues	
	• Questions about web data entry	Chi Shen, Ben Bergsten-Buret, Rich Moore
	• Data payment report	Judy Powell
	• Data payment (from UW to sites)	Shirley Joaquin
	• Questions about supplies	Berit Bardarson
	ROC PRIMED Protocol	
	• Questions about protocol, data, adverse events • CPR process	Lois Van Ottingham, Judy Powell, Graham Nichol
	• Statistical issues	
	• Questions about web data entry	Chi Shen, Ben Bergsten-Buret, Rich Moore
	• Data payment report	Judy Powell
	• Data payment (from UW to sites)	Shirley Joaquin
	• Questions about supplies	Lois Van Ottingham

7.4 ROC PRIMED Coordinators

Site Name:

Name of Coordinator responsible for entering data	Title/Role	Check (√) if responsible for data for specific agency or hospital			
		Regulatory	Pre-Hospital	Hospital	Follow-Up

7.5 Documentation of Patient/Family Contact

Pt. ID	Date	Time	Person Contacted	Relationship to Pt.	Summary of Attempts to Contact & Conversations	Coordinator/Investigator Name

- **This should include the attempts (successful & failed) to notify and consent the pt./family/LAR. If letters sent, indicate if certified.**
- **Returned letters can be kept in the episode file.**

8.1 ECG Transmission

Operational Memos

February 4, 2009

ROC PRIMED Operations Memo No. 1

9.1 Re: Site documentation of receipt of ITD Shipments

Within 3 business days of receipt of an ITD shipment from Almac, the boxes are to be opened and each ITD inspected to ensure that the ITD numbers match those on the ID list sent to the site by the CTC and the packing list sent to the site by Almac.

On the front of each ITD package the top ITD label should be missing (this is taken off at the time of packaging from ACSI and placed on the ITD itself). Each of the remaining pull-off ITD labels (X on the front and X on the back) should have identical ID numbers, and all labels for that package should match the ITD sticker on the ITD inside of the clear bag. Each ITD package should be inspected for tears or damage to the ITD or flexible connector.

If any discrepancies are found on the ID labels or there is any damage to the package or its contents, complete an Alert form at the time of discovery, describing the problem, promptly send the ITD package to the CTC and note this on the Alert form. After inspecting all ITDs in the shipment, sign and date the shipping form, noting any discrepancies or damage on the packing form, and fax to Almac within 3 days of receiving the ITDs.

Return any ITDs, connectors or packages found damaged or with problems at the agency or in the field (whether or not used on a patient) to the CTC.

Operational Memos

February 26, 2009

ROC PRIMED Operations Memo No. 2

9.2 Approach to handling delay of cross-over in ROC PRIMED trial

The coordinating center has received a request to delay by one month the time of cross-over of a cluster in ROC PRIMED. This memo is to explain our approach to handling delay in crossover.

According to the PRIMED protocol, the treatment conditions (Analyze Early versus Analyze Late) are randomly assigned to “clusters” of patients (e.g., agencies) in a cross-over design. Each cluster has a pre-arranged number of crossovers and a crossover schedule starting from the date the cluster enters the evaluable phase. It is expected that the dates for implementing the crossovers will be within 5 days of the target dates. This policy has been generally accepted well and there have been very few exceptions to it.

Because the unit of randomization in a cluster-randomized trial is the cluster rather than the individual patient, delayed cross-over is analogous to non-adherence (non-compliance) of a patient in an individual-randomized trial. The PRIMED protocol handles non-adherence according to the intent-to-treat principle, which means that outcomes for a given arrest are analyzed according to the assigned treatment for the given date on which they occur even if a different treatment is actually delivered. Therefore, the effect of lack of adherence to the assigned cross-over schedule is to dilute the treatment effect and hence to reduce the power of the trial. The design of the trial is such that a certain amount of non-adherence (such as the cluster-unit in question deviating from the target date by as much as one month) can be accommodated without reducing the power of the trial below an acceptable level. However, such deviations clearly have to be strictly controlled in order to avoid significant attenuation of treatment effect in the trial.

Based on the above considerations, the DCC’s approach in the given situation is to urge the cluster-unit to initiate the cross-over within 5 days of the target date, or at the soonest possible date if the 5-day required range is not possible. The unit will also be informed of the consequences to the trial of lack of adherence to the cross-over schedule.

Other

10.1