MOP 9

Endpoints Outcome Ascertainment Procedures

Version 1.1

September 22, 2015

Outcome Ascertainment Procedures
TABLE OF CONTENTS

1.0 OUTCOME ASCERTAINMENT PROCEDURES 2

1.1 Overview 2
1.2 Specific Disease Outcomes 2
1.3 Ascertaining Potential Events 2
1.4 Collection and Abstraction of Medical Information ..... 3~~4~~
1.5 Death Investigations 7
1.6 Review and Validation 8
1.7 Clinical Site Procedures for Identifying and Processing Events for Outcome Classification 8
1.8 Medical Records Processing 9

2.0 OUTCOME SURVEILLANCE FOR EXACERBATIONS DUE TO CHRONIC OBSTRUCTIVE PULMONARY DISEASE, PNEUMONIA, MECHANICAL VENTILATION OR LUNG TRANSPLANT ..... 11~~12~~

2.1 Introduction 11
2.2 Event Identification 11
2.3 Diagnostic criteria for pulmonary events 11

3.0 OUTCOME SURVEILLANCE OF FATAL EVENTS 13

3.1 Event Identification 13
3.2 Diagnostic Criteria 13

4.0 EVENT CLASSIFICATION COMMITTEE 14

4.1 Introduction 14
4.2 Review Process 14
4.3 Disagreement Resolution 14
4.4 Confidentiality 14

1.0 Outcome Ascertainment Procedures

1.1 Overview

The mission of the Morbidity and Mortality (M&M) Committee is to design and implement a system for event ascertainment, including review and validation of a variety of outcomes to facilitate the classification of incident events occurring among the SPIROMICS participants. The specific objectives of the outcomes procedure manual are to clearly describe how the committee will:

- identify cause of death as respiratory, cardiovascular, cancer, sudden death, other or unknown;
- identify acute exacerbations of COPD requiring hospitalization or Emergency Department (ED) visits;
- identify incidence of pneumonia occurring in the hospital or ED setting;
- identify incidence of mechanical ventilation in the setting of acute respiratory failure;
- identify when lung transplantation occurs; and
- review and evaluate clinical information collected from medical records from hospitals and emergency departments to classify each event type.

The identification and classification of health events in SPIROMICS outlined in this manual follows standard principles of population-based surveillance. These principles include ascertaining potential events, gathering medical information about these events, and reviewing collected data to validate the types of events of interest. The aim of surveillance in SPIROMICS is to identify all hospitalizations and emergency department visits for each participant (regardless of reason) and validate the diagnosis of COPD exacerbations and/or pneumonia that occur between baseline exam and the subsequent follow up. We will also investigate deaths to validate cause of death. The general approach to defining outcomes of interest, ascertainment of potential cases, gathering medical records, and review/validation of events is outlined below. Details of each of these steps are provided in the proceeding chapters of this manual.

1.2 Specific Disease Outcomes

The specific outcomes of primary consideration in SPIROMICS are: 1) hospitalizations and ED visits for COPD exacerbations, 2) hospitalizations and ED visits for pneumonia, 3) lung transplantation, and 4) death. The cause of death of any participant will be adjudicated by the M&M committee and is a primary outcome. A certain percentage of hospitalizations and ED visits will be reviewed for exacerbations and pneumonia and will also be considered primary outcomes. The final percentage of visits to be reviewed will be determined by the M&M Committee. See Section 2.0 for more detailed discussion.

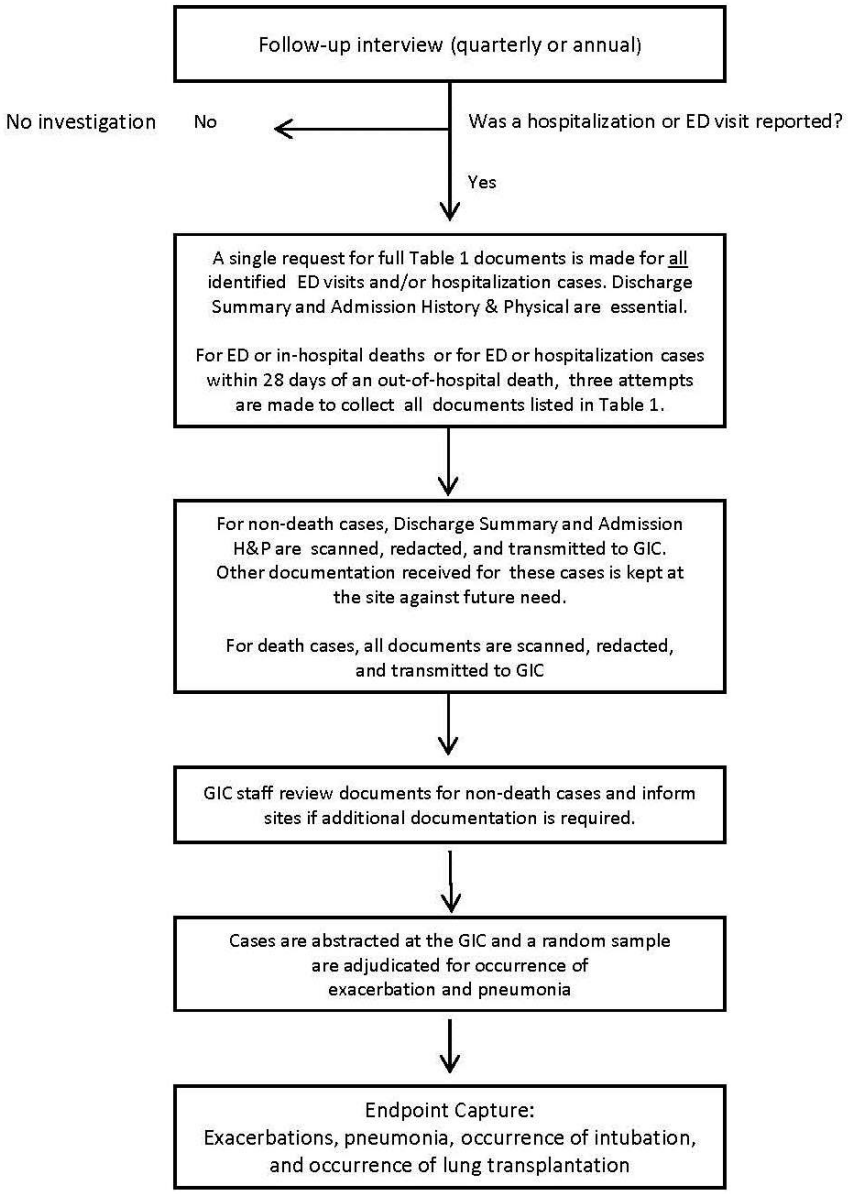
In addition to the above primary outcomes, the following outcomes will also be abstracted at the GIC if they are found to be a primary cause of an ED visit or hospitalization upon record review: lung cancer, diabetes, venous thrombosis, pulmonary embolus, osteoporosis, hip fracture, myocardial infarction, coronary artery disease, and stroke or transient ischemic attack.

1.3 Ascertaining Potential Events

Event surveillance of the cohort uses information obtained from the annual visit or quarterly phone follow-up interview. When any interview indicates that the participant has died, been seen in the Emergency Department, or admitted to a hospital, mechanisms to obtain the appropriate medical records or death certificate are initiated. Fatal events are also ascertained from review of vital statistics lists and obituaries for the state in which the community is located. SPIROMICS records the occurrence of all hospitalizations and all ED visits and captures the discharge diagnoses and ICD-9 or -10 codes if available but only conducts detailed investigations for selected types of medical events as noted above. Detailed investigation of recalled hospitalization events and ED visits will be triggered initially by participant report but verification of specific discharge diagnoses or codes (see Figure 1 below and Tables 2 & 3) may trigger additional record collection if not already received (see Table 1). Death investigation will be

conducted in all cases, and investigation of hospitalized and of out of hospital deaths will include interviews with next of kin and mailing questionnaires to appropriate physicians, medical examiners, or coroners.

Figure 1. Summary of event investigation based on initial reason for hospitalization or emergency department visit as reported by participant.



1.4 Collection and Abstraction of Medical Information

A detailed abstraction form specific to the type of event will be used by trained staff at the GIC to record relevant data from the medical records of eligible events. A single request for all documents listed in Table 1 below will be made for all identified hospitalization or ED visit cases.

In SPIROMICS, a hospitalization will be defined as admission into an acute care hospital, either by direct admit or via ED arrival and subsequent admit to a hospital unit. Direct admit to a hospital unit for overnight stay following planned surgery will be considered a hospitalization. Admission to inpatient

rehab, outpatient rehab, nursing home, or hospice facility will not be considered a hospitalization. ED observation or 23 hour observation stays will be considered an ED visit. Treatment received in a doctor's office, walk-in clinic, and outpatient/day surgery will not be investigated.

Of the case documents received in response to the single request, site coordinators will transmit only the following to the GIC: Admission History & Physical and Discharge Summary reports in the case of hospitalizations or ED notes including a Visit or Discharge Summary for ED-only visits. Other documents received in response to the single request will be held at the site against future need.

An Event Tracking Form will be completed for each qualifying visit and the records transmitted to the GIC. If these records reveal a diagnosis or ICD code from Tables 2 or 3, or the Discharge Summary lists keywords for outcomes of importance to the study (see Section 1.1), additional records retained at the site including chest imaging reports, consult reports, and other pertinent documents may be requested by the GIC. In some instances coordinators may receive additional records they did not request. If they are related to the event and are germane, these may be retained or sent to the GIC upon request. For time and cost purposes, please do not collect or transmit non-essential progress notes, unrelated test results or unrelated procedure reports (urinalyses, bunionectomy procedures), etc.

Medical records will be centrally abstracted by trained and certified abstractors. Abstractors follow detailed question by question instructions for the standardized abstraction of medical record information into a database. A brief summary (1-2 pages) of information abstracted from these materials will be provided to the M&M Committee for their review when classifying the event. See Supplement 1 for an example of this event summary form. Note that diagnoses and codes in Tables 2 and 3 represent a comprehensive list that captures both events that will be adjudicated in addition to several other diagnoses identified by the steering committee as important for potential future use (listed under "For abstraction but not adjudication"). If there is ever any doubt as to whether additional records should be collected or transmitted, err on the side of additional records. Tables 1-3 are available individually in Supplement 4.

Table 1. Documents to be requested once for all identified events, obtained in full for all deaths, or obtained in full if requested by the GIC for relevant diagnoses (Tables 2 and 3) or study keywords.

1	Coding summary with ICD-9 or ICD-10 codes
2	Admission History and Physical
3	Discharge Summary (#2 and #3 maybe one note for ED visits)
4	General labs (blood)
5	Microbiology labs (blood, sputum, tracheal and bronchial fluid)
6	Procedure or surgical reports
7	Spirometry report
8	Echo report
9	Pulse oximetry report
10	Arterial blood gas report
11	Discharge medication report
12	Chest X-ray report
13	Chest CT scan report
14	Pulmonary angiography
15	V/Q Lung scan
16	Autopsy or Medical examiner report
17	Death Certificate

Table 2. ICD-9-CM codes and diagnoses that will require attainment of Table 1 records (see Table 1).

Diagnoses requiring abstraction	
Acute upper respiratory infection	465.X
Acute bronchitis	466.X
Viral Pneumonia	480.X
Pneumococcal pneumonia	481.X
Other bacterial pneumonia	482.X
Pneumonia due to other specified organism	483.X
Bronchopneumonia, organism unspecified	485.X
Pneumonia, organism unspecified	486.X
Influenza	487.X
Influenza	488.X
Bronchitis	490.X
Chronic bronchitis 491 With acute exacerbation 491.21	491.X
Emphysema	492.X
Asthma 493 Unspecified 493.0 With status asthmaticus 493.1 With acute exacerbation 493.2	493.X
Bronchiectasis	494.X
COPD	496.X
Pneumonitis due to solids and liquids	507.X
Empyema	510.X
Pleurisy	511.X
Pneumothorax	512.X
Abscess of lung and mediastinum	513.X
Pulmonary congestion and hypostasis (includes pulmonary edema NOS)	514.X
Other diseases of lung including but not exclusive to: Acute pulmonary edema of lung, unspecified 518.4 Pulmonary insufficiency following trauma and surgery 518.5 Acute respiratory failure 518.81	518.X
Heart Failure	428.X
Additional procedures if listed on coding summary or reported by patient where additional records are needed	Mechanical Ventilation not in the setting of a surgical procedure Lung Transplantation, or any hospitalization where the patient reports they were treated for a respiratory problem
For abstraction but not adjudication	
Lung cancer	162.X or 163.X
Diabetes	249.X 250.X
Venous thrombosis (DVT)	453.X
Pulmonary embolus	415.X
Osteoporosis	733.X
Hip Fracture	820.X 821.X
Myocardial Infarction	410.X, 411.X
Coronary artery disease	414.X
Stroke or transient ischemic attack	433.X, 434.X, 435.X

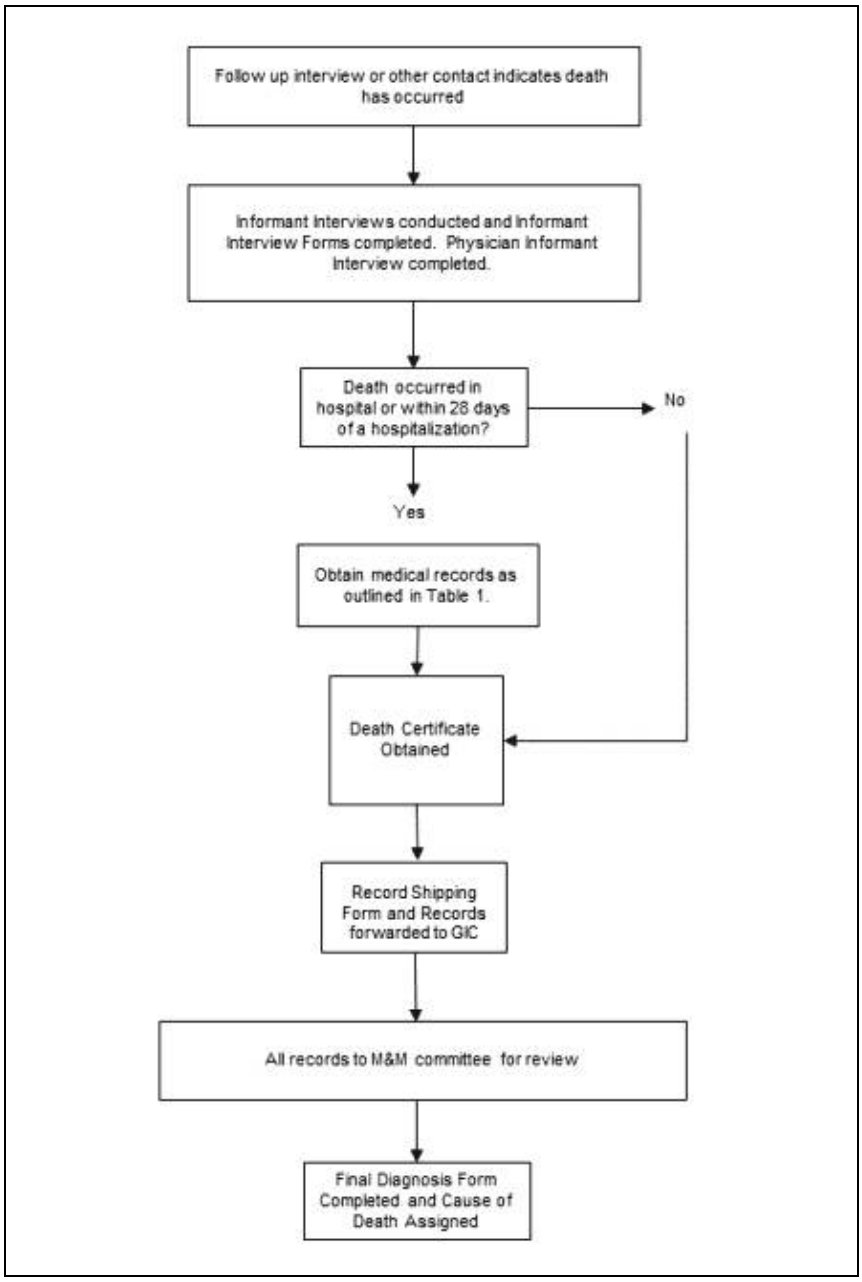
Table 3. ICD-10-CM codes and diagnoses that will require attainment of Table 1 records (see Table 1).

Diagnoses requiring abstraction	
Acute upper respiratory infections of multiple and unspecified sites	J06.X
Influenza due to identified avian influenza virus	J09.X
Influenza due to identified influenza virus	J10.X
Influenza, virus not identified	J11.X
Viral pneumonia	J12.X
Pneumonia due to Streptococcus pneumonia	J13.X
Pneumonia due to Haemophilus influenza	J14.X
Bacterial pneumonia, not elsewhere classified	J15.X
Pneumonia due to other infectious organisms, not elsewhere classified	J16.X
Pneumonia in disease classified elsewhere	J17.X
Pneumonia, organism unspecified	J18.X
Acute bronchitis	J20.X
Acute bronchiolitis	J21.X
Unspecified acute lower respiratory infection	J22.X
Bronchitis, not specified as acute or chronic	J40.X
Simple and mucopurulent chronic bronchitis	J41.X
Unspecified chronic bronchitis	J42.X
Emphysema	J43.X
Other chronic pulmonary disease which includes but is not exclusive to: COPD with acute lower respiratory infection (J44.0) excluding influenza COPD with acute exacerbation (J44.1) Other specified COPD (J44.8)	J44.X
Asthma	J45.X
Status asthmaticus (includes acute severe asthma	J46.X
Bronchiectasis	J47.X
Respiratory conditions due to inhalation of chemicals, gases, fumes and vapors	J68.X
Pneumonitis due to solids and liquids	J69.X
Respiratory conditions due to other external agents	J70.X
Adult respiratory distress syndrome	J80.X
Pulmonary edema	J81.X
Abscess of lung and mediastinum	J85.X
Pyothorax	J86.X
Pleural effusion, not elsewhere classified	J90.X
Pleural effusion in conditions classified elsewhere	J91.X
Pneumothorax	J93.X
Other pleural conditions	J94.X
Postprocedural respiratory disorders, not elsewhere classified	J95.X
Respiratory failure, not elsewhere classified	J96.X
Other respiratory disorders	J98.X
Heart Failure	I50.X
Additional diagnoses or procedures if listed on coding summary or reported by patient where additional records are needed	Mechanical Ventilation not in the setting of a surgical procedure
	Lung Transplantation, or any hospitalization where the patient reports they were treated for a respiratory problem
For abstraction but not adjudication	
Lung cancer	C33.X, C34.X, C38.4
Diabetes	E1X.X
Venous thrombosis	I80.X, I81.X, I82.X
Pulmonary embolus	I26.X
Osteoporosis	M80.X, M81.X, M82.X
Hip fracture	S72.X
Myocardial infarction	I20.X, I21.X, I22.X, I23.X, I24.X
Coronary artery disease	I25.X
Stroke or transient ischemic attack	I63, I64, G45.X

1.5 Death Investigations

Once a clinical center becomes aware that a death has occurred, a death certificate will be obtained and the Death Certificate Form completed. For all deaths, the Informant Interview will also be completed by seeking information from the decedent's family within 6 months after death. The informant is contacted by telephone or if this is not possible then the form can be completed by mail. For all in-hospital deaths and any death occurring within 28 days of a hospitalization or ED visit, all records from Table 1 will be collected and efforts summarized on the Event ID Tracking Form. The records collected will be reviewed by the GIC central abstractor and a Hospital Record Abstraction Form completed if the death occurred while hospitalized. All of these forms and records for every death will be reviewed by the M&M committee to assign a cause of death.

Figure 2. Summary of death investigation



1.6 Review and Validation

Diagnostic information obtained through abstraction of the medical record combined with documents copied from the medical records are second-blinded and prepared for review by members of the M&M Committee. M&M committee members will complete an Event Review Form which indicates their judgment as to the diagnosis of each event. M&M reviewers will follow the Principles of Mortality Adjudication as guidance in determining cause of events (see Supplement 2). Reviewers will follow criteria outlined in Section 2.3 for determining whether an exacerbation or pneumonia has occurred.

1.7 Clinical Site Procedures for Identifying and Processing Events for Outcome Classification

During the completion of the quarterly follow-up interview and during annual clinic visits, study coordinators will ask the participant whether they had been admitted to a hospital or seen in an emergency department (ED) at any time since their last SPIROMICS contact. If no events are reported there will be no events to be investigated. If participants respond 'Yes' they are then asked to identify the type of event (i.e., whether the event was a visit to the ED or an admission to the hospital, or both). The information on event type appears on the Event IDs List and can be useful in field center efforts to obtain medical records.

Event Identification (ID) Numbers

When an event eligible for investigation is reported during a SPIROMICS follow-up call or clinic visit and the data are entered into the data management system, a unique event ID number is assigned by the GIC to each reported event. This Event ID is derived from the participant ID number and the reported hospitalization by computer algorithm. For example, for a given participant ID number there may be several Event IDs. Information about the reported event and the associated Event ID is imported biweekly into the Event IDs List.

The Event ID is composed of the participant's 8 digit study ID number, followed by 4 digits. The first two digits indicate the last in-person clinic visit (e.g., 01, 02) the last two digits indicate the sequentially numbered events. (re: 01, 02, 03, 04, etc.)

Examples:

Visit 1 (Baseline) event labeling for San Francisco participant id SFXXXXXX:
SFXXXXXX0101, SFXXXXXX0102, SFXXXXXX0103, SFXXXXXX0104

Visit 2 (Year 1) follow-up event labeling for San Francisco participant id SFXXXXXX:
SFXXXXXX0201, SFXXXXXX0202, SFXXXXXX0203, SFXXXXXX0204

Updating Events

There may be instances when the participant has reported an incorrect or incomplete event date, which is discovered when the medical records are obtained. The study coordinator may correct the appropriate form associated with the event. It is very important to select and update the correct form of interest by going into the existing entry, not by creating a new entry (which is default for entering forms). NOTE: In the event that a change to the data collection form changes the order of events, the Event ID **will not** be changed to reflect the revised order. Event IDs should be treated as ordering by identification rather than time of occurrence.

Events Not Reported During Quarterly Contacts or Annual Clinic Visits

Additional events, not self-reported at annual follow-up, may be identified when medical records are obtained for a self-reported event. These newly-discovered events must be assigned their own Event IDs and will remain distinct from self-reported events identified during a visit. Newly-discovered events will

be added to the form they should have originally been reported on (i.e., if an event took place on 4/1/2011 and a quarterly contact was completed on 5/2/11, that quarterly contact should be updated to include the newly-discovered event information).

To correctly capture this information: 1) Open the quarterly follow-up or annual clinic visit in edit mode, 2) Go to the last hospitalization or ED reporting question, and change that from a "No" to a "Yes" which will "unlock" the information fields for the event, 3) enter the information for the newly discovered event, 4) Create a note log on the Date of Event field, that says: "Detected after [Quarterly Follow-up or Annual Clinic visit]", and 5) Save the changes.

Numbering Events

If a participant has an ED or hospitalized event where he/she was transferred directly to another facility, this is considered one (1) event only.

If a participant has discrete admission and discharge dates that are not continuous (with intervening days not in the hospital), these are considered two (2) events.

1.8 Medical Records Processing

Medical Record Release Forms and Request Cover Form

In order to obtain medical records for a specific event, a current and signed medical record release form will be sent to each medical facility identified (as indicated on the Event IDs List) for each event. Medical record release forms are valid for 90 days from the time the patient signs and dates the form. Keeping in mind that a patient may have more than one event or may have been seen in more than one institution; it may be helpful to have the participant sign several release forms at one time, or to sign one and leave the date blank. Alternatively, some institutions may release medical records with a copy of the participant's signed HIPAA consent form. Sites should follow local institutional policy for medical records release.

The medical records release form must include the specific dates of the event and the name of the PI or Co-PI requesting the records. The DMS-generated Medical Record Request with pre-populated demographics and participant's self-reported reason for the event should accompany each request for medical records.

When records are received, the clinical center (CC) determines if the records are sufficient to ascertain the event. The first step is to directly compare what was received to what was requested.

ICD Codes (International Classification of Diseases)

Obtaining discharge diagnoses and ICD codes, if available, for all events is critical for the standardized ascertainment of potential events. Originally developed to provide comparable international data on causes of death, today ICD codes are used in many countries for coding hospital discharge diagnoses for billing purposes. For both hospitalizations and ED visits, an ICD code is assigned for each diagnosis. Usually there is one primary discharge diagnosis/ICD Code for each hospitalization or ED visit, but there may be several secondary diagnoses listed as well. The secondary diagnoses may include old and new diagnoses.

An ICD coding summary sheet is usually part of the medical records for any event, often as a separate document but codes can be found on the medical record face sheet, embedded in the records (particularly ED records), or even hand-written on the Discharge Summary. Generally, the ICD code sheet must be specifically requested in addition to the other needed records. ICD codes for each event are important to our abstraction efforts, so if a coding summary is not received for a specific event, the CC is asked to follow-up with the medical records department to obtain it if they are already requesting more records. If the ICD-9 or -10 code summary is not available from the medical records department, an attempt to obtain it from the hospital's billing department may be made.

Ordering, Scanning, and Redacting Medical Records

Sites will be provided a document scanner. Verify that each scanner is set up locally and connected to your network following the security protocol guidelines established by each institution related to data collection and archive for confidential information. Scanned medical records output must be saved on a secure server at your host institution. The GIC has also provided sites with Adobe Acrobat Professional Version 9.5 or higher to create PDFs of your electronic files. This ensures the proper level of file security.

Place all documents for each event, including the generated Medical Record Shipping Cover Letter, in Table 1 order and scan using the scanner set to black and white document and save as a PDF in a secure location using Adobe Acrobat Professional 9.5 or higher. Insert a header with the appropriate Event ID from the Event IDs List in the upper right-hand corner. This header should appear on every page of the document.

In order to comply with the de-identification rules for research conducted under HIPAA, field centers are to redact (blind) the scanned records using the Adobe Acrobat Pro software. See Supplement 3 for more information.

Each page of the scanned medical records or death certificates must be checked and the following items redacted:

Participant and family member names and/or initials, addresses, and telephone numbers
Participant birth date and Social Security number
Hospital and healthcare system names, facility initials, street addresses, and telephone numbers
Institutional letterheads and/or logos
All healthcare staff names, initials, provider numbers, pager and extension numbers
Medical record numbers
Health plan ID numbers
Account numbers
Lab, test, or procedure accession numbers, order numbers, or exam numbers
Dictation job and confirmation numbers
Electronic mail addresses
Web addresses or URLs, IP addresses

The following items should *not* be redacted:

Participant age, gender
Admission and Discharge dates
Healthcare staff titles or departments (i.e., MD, RT, Cardiology)
On death certificates, do not blind date and time of or causes of death

Sending Materials to the GIC

Sites should send files to the GIC at least once a month. Files will be transferred using FileZilla FTP. Please see Supplement 5 for more information.

Support Contacts at the GIC

Supplement 6 has current contact information for questions.

2.0 Outcome Surveillance for Exacerbations due to Chronic Obstructive Pulmonary Disease, Pneumonia, Mechanical Ventilation or Lung Transplant

2.1 Introduction

All cases of exacerbation due to COPD resulting in an ED visit or hospitalization among SPIROMICS participants will be identified through the annual clinic visits or quarterly follow-up calls. All of these eligible events will be investigated and processed through the SPIROMICS M&M Committee. Self-reported COPD exacerbations resulting in outpatient treatment without ED visit or hospitalization will also be identified through the quarterly follow up calls but outpatient records will not be obtained for verification.

2.2 Event Identification

At a minimum, the Admission History and Physical and Discharge Summary should be obtained for all hospitalizations and transmitted to the GIC. A Discharge or Visit Summary should be obtained for all Emergency Department visits and this data transmitted to the GIC. For visits where study keywords or ICD-9 or -10 codes or diagnoses listed on Tables 2 and 3 are found, additional record collection may be necessary as determined by the GIC. For all cases, clinical centers shall make one request for all the records outlined in Table 1 as their first data request. Of the documents received, the Admission H&P and Discharge Summary or Visit Summary will be scanned, redacted, and transmitted to the GIC, with any other case documents stored at the clinical center against future need. The transmitted documents will be reviewed by GIC staff for Table 2 or 3 diagnoses or ICD codes or study keywords. If any of these are present and listed in the Discharge Summary as a primary cause of the event, the GIC may request that the clinical center to redact and transmit any remaining Table 1 documents they have retained on file.

Data from hospitalizations and ED visits will be abstracted centrally at the GIC using the SPIROMICS Hospital Record Abstraction (HRA) form. Exacerbations will be diagnosed based on record abstraction and review.

2.3 Diagnostic criteria for pulmonary events

By consensus of the SPIROMICS M&M committee, for an event to qualify as an exacerbation, the event must meet all of the following criteria:

1) There is evidence that the subject experienced an increase for ≥2 consecutive days in any 2 "major" symptoms (increase in dyspnea, sputum purulence, or sputum volume) or an increase in 1 "major" and 1 "minor" symptom (increase in nasal discharge, wheeze, sore throat, cough, or fever).
2) The subject was prescribed antibiotics and/or steroids for this respiratory event.
3) The subject has no radiographic abnormalities to suggest pneumonia.

OR

We will also accept acute respiratory failure in a subject without other known cause.

A diagnosis of COPD (either in the medical record or based on baseline SPIROMICS data) is not required for an event to be classified as an exacerbation.

For an event to qualify for pneumonia, the event must meet all of the following criteria:

1) The subject has a radiographic abnormality consistent with pneumonia (Chest X-ray or CT)
2) The subject was prescribed anti-infective for respiratory abnormality.

Criteria for Lung Transplantation are as follows:

1) The subject undergoes either single or double lung transplant.

Criteria for Noninvasive Mechanical Ventilation for respiratory failure are as follows:

1) The subject receives positive pressure ventilation delivered through a noninvasive interface (nasal mask, facemask, or nasal plugs) for respiratory failure.
2) The subject is not receiving noninvasive mechanical ventilation solely for the purpose of sleep apnea.

Criteria for Invasive Mechanical Ventilation are as follows:

1) The subject receives positive pressure ventilation delivered via an invasive interface (endotracheal tube or tracheostomy) for respiratory failure.
2) The subject is not receiving invasive mechanical ventilation solely as part of procedure that requires general anesthesia.

Other hospitalizations for which the participant reports treatment for a respiratory problem other than the above will also be reviewed by the M&M committee individually.

3.0 Outcome Surveillance of Fatal Events

3.1 Event Identification

Deaths will be identified using several methods including (1) questions asked during the quarterly follow up contact and annual visit to be performed by the clinical centers, (2) periodic review of local obituaries by the study coordinators, and (3) query of the National Death Index (NDI) and Social Security Death Index (SSDI) to be performed by the GIC annually or monthly. Once a death is identified, clinical center staff will obtain a death certificate and send a blinded copy to the GIC for processing and abstraction. Death certificates will be obtained in all cases. If a death certificate cannot be obtained, it will be stated in the documentation on the Event ID Tracking Form. For all deaths, the Informant Interview will also be completed by seeking information from the decedent's family within 6 months after death. The informant is contacted by telephone or if this is not possible then the form may be completed by mail. If additional informants are identified through this process who may have additional information regarding the cause of death, additional Informant Interviews should be conducted and submitted. A minimum of three attempts should be made to contact the informant to perform the interview before determining the Informant Interview cannot be obtained. If no informant can be contacted, the clinical center should attempt to contact the patient's physician and complete the Physician Questionnaire either by mail or by phone. A minimum of two attempts should be made to obtain a completed Physician Questionnaire before determining that it cannot be obtained. For hospitalizations within 28 days of the death or for in-hospital or ER deaths, medical records from Table 1 will be obtained and record collection efforts summarized on the Event Tracking Form. A minimum of three attempts should be made to obtain hospital records in such cases before determining that they cannot be obtained. Records collected will be reviewed by the GIC central abstractor and a Hospital Record Abstraction Form completed if the death occurred while hospitalized. All of these forms and records will be reviewed by the M&M committee to assign a cause of death.

3.2 Diagnostic Criteria

Ascertainment of cause-specific mortality in patients with COPD will be determined by the M&M committee and guided by the Principles of Mortality Adjudication (Supplement 2). If medical records are inadequate and a death certificate cannot be obtained, a cause of death will be adjudicated based on the

best available evidence of record. If a probable cause cannot be adjudicated, it will be classified as "Unknown". In general, the primary cause of death will be attributed to the disorder that causes the patient to present for medical treatment and should be distinguished from terminal events that are the immediate cause of death. For example, if a patient is admitted to the hospital with a COPD exacerbation and during the exacerbation subsequently develops complications such as pneumonia, respiratory failure, renal failure, sepsis or myocardial infarction, the primary cause of death should be attributed to COPD.

Included within cardiovascular causes of death will be two subcategories, "sudden death" and "sudden cardiac death." Sudden Death is defined as death that occurs within 24 hours of being observed alive and without evidence of a deteriorating medical condition. Sudden Cardiac Death is defined as death that occurs within 1 hour of being observed alive and without evidence of a deteriorating medical condition. If the interval between death and last being observed alive is greater than 24 hours, and there is no other known cause of death, the cause of death will be classified as "Unknown." The diagnosis of myocardial infarction will require pathologic evidence, or evidence of medical record including electrocardiographic tracings, blood enzyme measurements, and compatible clinical findings.

4.0 Event Classification Committee

4.1 Introduction

This committee will be comprised of a minimum of one member from each primary clinical center.

4.2 Review Process

The GIC will assemble and disseminate all review packets which will include essential medical records and an Event Summary Form (Supplement 1) to the appropriate Physician Reviewers through an online system accessible through the SPIROMICS website. The reviewers will have two weeks from the date notified that a set of cases is ready to complete a set of reviews. A reviewer's classification of an event applies only to the specific hospitalization or emergency department visit or outpatient event under review. The reviewer should not be concerned if there is a history of prior events or records unless it is a hospitalization occurring within 28 days of a death. Each event should be judged separately. Each case will be reviewed independently by two reviewers. Reviewers will not be assigned cases from their own clinical center.

4.3 Disagreement Resolution

Cases that produce a disagreement among the two independent reviews will be sent to the chair of the appropriate review group for resolution. The chair will have access to results of each reviewer's decisions and will make a third and final classification for these cases.

4.4 Confidentiality

Several procedures are in place to protect the security of the personal identifying information obtained from medical records and used in the event ascertainment process. Personal identifying information (name, SSN, date of birth, etc.) from participants is used for the purpose of linkage to the National Death Index. This information is needed to determine vital status of participants who are lost to follow up. All participant personal identifiers, treating physicians, hospital names and locations, and other identifying information are redacted on medical records sent to the GIC and double-checked for appropriate blinding before distribution to the Event Classification Committee (ECC). ECC members are instructed to complete proper confidential destruction of any medical record information they are provided in order to carry out their reviews. Study personnel involved in processing the medical record information, from abstraction to handling of these data have been trained on the protection of human subjects in research.