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ACTIVITY COUNSELING TRIAL (ACT) PROTOCOL

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SUMMARY OF ACTIVITY COUNSELING TRIAL

The Activity Counseling Trial (ACT) is a randomized clinical trial to evaluate the efficacy of two primary care, practice-based physical activity behavioral interventions. Approximately 810 sedentary men and women 35-75 years of age will be enrolled in the study, including substantial minority representation. Each participant will receive two years of intervention and follow-up. Participants will be enrolled over a period of 15 months or less.

The three study groups, simultaneously implemented at three clinical centers (located in California, Texas, and Tennessee) will consist of the same initial physician assessment and advice. Participants assigned to the two intervention groups also will receive varying levels of practice-based intervention. The interventions are based on behavior change theory, but they differ in the amount of resources required for implementation. The three study groups are as follows:

GROUP A: STANDARD CARE

This group will provide physician assessment and advice and written materials. It will not offer behavioral counseling.

GROUP B: STAFF ASSISTANCE

This intervention is a subset of the Staff-Counseling Intervention and requires fewer resources and less staff time. A guiding principle in developing this intervention was for it to be feasible for delivery in a wide variety of primary care settings without requiring extensive staff support. The intervention employs brief in-person counseling, video, interactive mail, referral to community resources, and occasional telephone contact.

GROUP C: STAFF COUNSELING

This intervention is designed to be an optimal intervention that could be delivered in a primary care setting. It requires substantial staff involvement and employs on-site interpersonal counseling, regular telephone follow-up counseling, in-clinic follow-up counseling, written and visual materials, interactive mail, onsite classes, and referral to community resources.

There will be two primary study outcomes: (1) maximal oxygen uptake (VO_2max) ($L \cdot min^{-1}$) measured by a maximal treadmill test using a standardized protocol, and (2) kilocalories expended in physical activity ($kcal \cdot kg^{-1} \cdot min^{-1}$) measured by a standardized and validated self-report instrument, the seven-day physical activity recall. To determine the relative efficacy of the interventions, comparison between groups for mean changes in the outcome measures will be performed. All analyses will be done separately for men and women. Change from baseline to two years will be the primary outcome analysis. Short-term effects will be examined by change from baseline to six months. Secondary outcomes related to cardiovascular disease risk include plasma lipids/lipoproteins (e.g., triglycerides and HDL), blood pressure, body composition (body mass index, skinfolds, waist-to-hip ratio), plasma insulin, fibrinogen, dietary intake, smoking, heart rate variability, cost-effectiveness, and psychosocial factors. Subgroup analyses also will be conducted.

1. INTRODUCTION

1.A. Background and Significance

Sedentary habits and low levels of cardiorespiratory fitness are important risk factors for cardiovascular disease (Blair, 1989,1992,1993,1994; Blair, McCloy 1993; Ekelund, 1988; Morris, 1990; Kaplan, 1987; Shaper, 1991), non-insulin-dependent diabetes (Helmrick, 1991; Manson, 1992; Gudat, 1994), some cancers (Lee, 1994), and functional limitations (Wagner, 1992; Buchner, 1992). All-cause death rates are approximately doubled in sedentary as compared with active individuals (Blair, 1994; Paffenbarger, 1986), and range up to three times higher in unfit men and women when compared with their physically fit peers (Blair, 1989; Blair, 1994). The relative risk of cardiovascular disease mortality is as high as 7.0 or 8.0 in the least physically fit quartile or quintile when compared with the most fit quartile or quintile of men and women (Blair, 1989; Blair, 1994).

Less than one quarter of adults are active at the level recommended for health benefits in objective 1.3 of Healthy People 2000 (DHHS, 1991), and approximately 25% of adult Americans are essentially totally sedentary (CDC, 1990). The strength of the association between inactivity and cardiovascular disease deaths, and the high prevalence of sedentary lifestyles lead to a high population attributable risk. Population attributable risk estimates for sedentary habits for coronary heart disease (CHD) death range from 29% to 40% across the several states that participate in the Behavioral Risk Factor Surveillance System (CDC, 1990). A report from the U.S. Centers for Disease Control and Prevention (Hahn, 1990) presented estimates of excess deaths in the U.S. from nine chronic diseases (based on 1986 national mortality data). The number of excess deaths for the diseases that could be attributed to several risk factors also was estimated. Smoking had the greatest impact, and was estimated to have caused 361,911 excess deaths in 1986. High levels of cholesterol or blood pressure, obesity, and sedentary habits were comparable in estimated number of excess deaths, with about 250,000 deaths attributed to each of these risk factors.

Increases in physical activity confer several important health benefits, such as reductions in elevated blood pressure (Duncan, 1985; ACSM, 1993), improvements in the lipoprotein profile (Stefanick, 1994), increases in cardiorespiratory fitness (Blomqvist, 1983; Duncan, 1991), improvements in carbohydrate metabolism (King, 1987; Rodnick, 1987; Sato, 1986), and reductions in body fat (Blair, 1993; MacKeen, 1985; MacKeen 1983). Physical activity and cardiorespiratory fitness provide protection against cardiovascular disease mortality in men and women who are at high risk based on the other major risk factors of hypertension, elevated cholesterol, and cigarette smoking (Blair, 1989; Blair, 1993; Shaper, 1991). Recent prospective population studies show a reduction in cardiovascular and all-cause mortality in initially sedentary men who become physically active (Paffenbarger, 1993; Blair, 1993). The reduction in mortality risk in these two studies with increases in physical activity is substantial (on the order of a 50% reduction) and is comparable to risk reductions associated with other beneficial changes, including stopping smoking, losing weight, and lowering blood pressure and cholesterol.

The convincing evidence for health benefits of a physically active way of life in conjunction with the high prevalence of inactivity in the U.S. population has led various groups to identify physical inactivity as a target for interventions designed to improve the public's health. Recent statements on physical activity include reports by the American Heart Association (Fletcher, 1992) and the U.S. Surgeon General (DHHS, 1991). A recent recommendation from the Centers for Disease Control and Prevention and the American College of Sports Medicine (CDC-ACSM) is that every American adult should accumulate 30 minutes or more of moderate intensity physical activity on most,

preferably all, days of the week (Pate, 1995). Moderate-intensity physical activity is defined as 3-5 Metabolic Equivalents (METS), the equivalent of brisk walking at 3-4 miles per hour for most healthy adults. Increases in physical activity can lead to increases in cardiorespiratory endurance, the component of physical fitness that is important for reducing cardiovascular disease risk (Blair, 89; Blair 93; Ekelund, 88).

Patterns of physical activity vary with demographic characteristics (Pate, 1995). Men are more likely than women to engage in physical activity (Dishman, 1991) and the total amount of time spent engaging in physical activity declines with age (Caspersen, 1992). African-Americans and other ethnic minority populations are somewhat less active than White Americans and this disparity is more pronounced for women (Caspersen, 1992). People of higher socioeconomic status participate in more leisure time physical activity than those of lower socioeconomic status. Some of the racial and ethnic differences in physical activity may reflect differences in socioeconomic status.

Characteristics of the individual and of the type of activity are related to participation in physical activity. Lack of time and concerns about injury are common reasons people do not participate in regular physical activity (Martin, 1982). Persons who are obese are often inactive (Bouchard, 1993). An intention to exercise and awareness of the benefits of exercise are weakly related to participation in physical activity; on the other hand, confidence in one's ability to be physically active and to overcome barriers to inactivity and enjoyment of activity are strongly related to participation (Sallis, 1989). Low to moderate intensity activities are more likely to be continued than high intensity activities. Self-regulatory skills, social support, and conducive environments are also associated with increased physical activity.

Physicians and other health care providers have been identified as important avenues for reaching sedentary individuals and encouraging increases in their physical activity. Healthy People 2000 includes an objective on physician counseling for physical activity (DHHS, 1991), and the U.S. Preventive Services Task Force recommends counseling by physicians for all sedentary patients (Harris, 1989). Despite the recommendations, data show that relatively few primary care physicians routinely inquire about their patients' exercise habits and attempt to intervene in the sedentary (Williford, 1992; Taylor, 1983). Although physicians express an interest in physical activity counseling, they often lack the time to enter into discussions about exercise with their patients and may not feel they have the skills to provide physical activity counseling.

Despite difficulties and barriers, physical activity intervention in primary care practices offers promise. Most middle-aged and older adults who are at high risk for premature mortality see a physician at least once a year (Williford, 1992; Taylor, 1983; Kelly, 1992; Valente, 1982). Physicians have high credibility regarding health recommendations, and surveys show that patients are inclined to act on their doctors' advice (Williford, 1992; Taylor, 1983; Kelly, 1992; Valente, 1982). Physical activity interventions in the community and other sites, such as work sites, need to be supported, but intervention in primary care practices should be viewed as an important part of the overall public health effort to get more adults to be more active more of the time.

National recommendations advise health-care professionals to intervene to increase physical activity levels of their patients, but strategies of how to intervene have yet to be tested thoroughly in studies of interventions delivered in health-care settings. Physical activity intervention studies demonstrate increases in activity in adult men and women (King, 1991; Sedgwick, 1980; Sedgwick, 1988; MacKeen, 1985; MacKeen, 1983). A few controlled studies have tested intervention approaches for

long-term change in physical activity, which is important for risk reduction, and have achieved success in promoting long-term increases in physical activity (Kriska, 1986; Juneau, 1987; King 1991). No studies, however, have tested intervention approaches delivered in primary health-care settings directly to patients for primary prevention.

This clinical trial will develop and test interventions to increase and maintain physical activity and cardiorespiratory fitness specifically in health-care settings for primary-care patients. Thus, the goal of ACT is to develop and test the efficacy of physical activity interventions delivered in a primary-care setting. This trial will demonstrate whether interventions delivered in a primary care clinical setting can be successful in long-term increases in physical activity and cardiorespiratory endurance. The ultimate goal is to develop successful strategies that can be implemented in medical practices, with the end result of an increase in physical activity by adults in the U.S. and an improvement in public health.

1.B. Objectives of the Activity Counseling Trial (ACT)

The goal of ACT is to develop and evaluate two intervention models of primary-care, practice-based activity counseling to determine their effectiveness in increasing and maintaining physical activity and cardiorespiratory endurance in previously sedentary participants from primary-care practices.

1. Primary Objectives

   Since the goal of the two interventions is to increase physical activity, quantification of the amount of energy expended in physical activity is a primary outcome of ACT. The 7-day Physical Activity Recall (PAR) remains the most accepted method for estimating kilocalories expended through physical activity in population-based studies. Self-report measures of behaviors such as physical activity, however, may be imprecise and self-report changes can be exaggerated. Cardiorespiratory endurance is an important health-related component of fitness that reduces cardiovascular disease risk and is increased by physical activity. Maximal oxygen consumption (VO_2max) does not measure energy expenditure or physical activity, *per se*, but is an accurate and reliable measure of cardiorespiratory endurance and usually increases with increased physical activity at the level targeted for this study. Although physical activity is related to cardiorespiratory endurance, increases in some types of physical activity may result in greater expenditure of kilocalories while having a lesser effect on cardiorespiratory endurance (for example moderate-intensity activities).

   Thus, both self-report of physical activity as measured by the 7-day PAR and the more precise measure of cardiorespiratory endurance, maximal oxygen consumption, will be coequal primary outcomes.

   The need to maintain increases in physical activity to achieve health benefits has been documented, so the relatively long-term time frame of 24 months has been selected for the primary outcomes. In addition, the primary objectives will be addressed separately in the two genders because of some evidence that intervention effects may differ in men and women.

   Two models of varying degrees of intervention are based on feasibility for delivery in a primary-care setting, behavioral principles previously shown to be effective, and the desire to provide options for intervention delivery.

Primary objectives are to determine:

a. the effects in sedentary men and women of two primary-care based activity counseling regimens (B and C, representing the staff-assisted and staff-counseling interventions, respectively) on physical activity (defined as energy expenditure) ($kcal \cdot kg^{-1} \cdot day^{-1}$) after 24 months when compared to a Standard Care control (Group A) and to each other; and

b. the effects in sedentary men and women of the two primary-care based activity counseling regimens (B and C) on cardiorespiratory endurance (defined as maximum oxygen consumption or VO_2max) ($L \cdot min^{-1}$) after 24 months when compared to Standard Care control and to each other.

2. Secondary Objectives

Although the primary purpose of ACT is to increase physical activity and cardiorespiratory endurance, a variety of secondary outcomes are important for assessing the effects of the interventions. These include short-term intervention effects, alternate measures of physical activity and fitness, levels of factors related to cardiovascular disease risk, psychosocial factors, and cost-effectiveness. These outcomes may be important for medical care practices to assess their relative enthusiasm for implementing physical activity intervention programs for their patients. In addition, intervention effects in different types of participants are important to assess. The interventions may be successful in some groups but not in others for a variety of reasons such as different perceptions, needs, abilities, or cultural factors.

Secondary objectives are to compare the relative effectiveness of the two primary-care based counseling regimens (Interventions B and C) to each other and vs. Standard Care (Group A) control on:

a. the effects on physical activity and cardiorespiratory endurance after 6 months;

b. the effects on submaximal treadmill test performance and shifts from sedentary to light and moderate activity after 6 and 24 months;

c. the effects on factors related to cardiovascular disease risk (HDL-cholesterol, LDL-cholesterol, total cholesterol, triglycerides, blood pressure, plasma insulin, fibrinogen, body composition, dietary fat intake, smoking status, and heart rate variability) after 6 and 24 months;

d. the effects on psychosocial factors (mood, self-efficacy, quality of life) after 6 and 24 months;

e. the relative cost-effectiveness of the two regimens after 24 months;

f. the effects after 6 and 24 months by subgroups categorized by the following factors:
   - age
   - ethnicity
   - body mass index
   - medication use (beta blockers or calcium channel blockers)

- smoking status
- psychosocial variables (mood, self-efficacy, social support); and

g. the relationship between adherence to the intervention protocols across the initial 6 month and overall 2 year periods and changes in cardiorespiratory fitness, physiological outcomes of interest, and quality of life outcomes.

2. TRIAL DESIGN AND METHODS

2.A. Study Design

ACT is a multicenter, randomized controlled trial designed to test the effects of two primary-care practice-based physical activity interventions on the adoption and maintenance of physical activity in sedentary participants. The two interventions (B and C) will be compared to a Standard Care control group (Group A) and to each other. The primary outcomes of physical activity ($kcal \cdot kg^{-1} \cdot day^{-1}$) and VO_2max ($L \cdot min^{-1}$) will be analyzed separately for men and women. Participants will be randomly allocated and stratified by gender, race, and clinical site.

Eight hundred ten participants from three clinical centers (CCs) will each be randomly assigned to one of three study groups: A- Standard Care Control; B- Staff-Assistance Intervention; C- Staff-Counseling Intervention. In all three conditions, participants will receive physician advice to increase their physical activity and will be provided with current recommendations for physical activity (the CDC/ACSM recommendation of accumulating 30 minutes of moderate physical activity on most days of the week and the ACSM prescription for cardiorespiratory endurance). In Interventions B and C, behavior-change programs will be implemented that have been designed to help participants increase their physical activity in order to meet the recommendations. The major difference between these two interventions is the degree of resources and staff burden required. The interventions will be delivered by health educators throughout the two-year intervention period.

2.B. Study Population

Inclusion Criteria

The study population for ACT will consist of participants who are:

- community-dwelling men and women;
- 35-75 years of age;
- receiving primary care from a participating study physician;
- scheduled to see a study physician during the recruitment phase of the study;
- exhibiting a sedentary lifestyle, defined as energy expenditure of ≤ 35 $kcal \cdot kg^{-1} \cdot day^{-1}$ measured by 7-day PAR;
- willing and able to participate in all aspects of the trial;
- in stable health;
- independent in activities of daily living;
- able to alter physical activity in accordance with the intervention program;
- if on medication for chronic disease, on a stable dose for the last 3 months; and
- willing and able to give informed consent.

Exclusion Criteria

Exclusion criteria were selected based on four general principles: an overall focus on primary care and primary prevention, appropriateness of the ACT physical activity recommendations, safety, and the need to minimize study dropouts.

1. Active Medical Conditions

   Individuals with the following conditions by self-report, medical record review, or clinic physician judgement will be excluded:

   - *Coronary Heart Disease:* diagnosis of angina and treatment by antianginal medications, or history of myocardial infarction, angioplasty or bypass surgery;
   - *Cerebral Vascular Disease:* history of stroke or transient ischemic attack;
   - *Peripheral Vascular Disease:* diagnosis of peripheral vascular disease;
   - Arrhythmias: diagnosis of serious arrhythmias, such as atrial fibrillation, complex ventricular arrhythmias, or second or third-degree heart block;
   - *Valvular Heart Disease:* diagnosis of heart valve replacement or significant valvular heart disease;
   - *Cancer:* diagnosis of cancer or receiving active treatment for cancer, including melanoma but excluding other forms of skin cancer, during the past five years;
   - *Diabetes Mellitus:* diagnosis of insulin-requiring diabetes;
   - *Pulmonary Disease:* active treatment for asthma, defined as current daily medication or asthma attacks triggered by physical activity, or a diagnosis of chronic obstructive pulmonary disease, emphysema or restrictive lung disease;
   - *Psychiatric Illness:* "treatment in the last five years for a diagnosis of major depression, manic-depressive illness or schizophrenia. Defined as self-reported treatment for manic-depressive illness or schizophrenia, currently receiving lithium or neuroleptics, hospitalization within the last 5 years for depression, or clinical judgment of treatment for major depression";
   - *Severe Systemic Disease:* diagnosis of Parkinson's disease, chronic liver disease (cirrhosis, chronic hepatitis, etc.), systemic rheumatic condition (rheumatoid arthritis, psoriatic arthritis, Reiter's disease, systemic lupus erythematosus, etc.), kidney failure or other systemic diseases or abnormal laboratory values which would preclude the participant from safely participating in the protocol or impair ability to complete the study;
   - *Blood Pressures:* Resting diastolic BP >100 mmHg or resting systolic BP >180 mmHg to assure stable BP meds and to exclude those with BP levels that would contraindicate a maximal exercise stress test;
   - *Pregnancy, lactation or not practicing contraception.*

2. Abnormal findings on ACT screening exercise treadmill test
   - $\geq$ 1 mm ST segment depression at $\leq$ 5 METS or with symptoms;
   - atrial fibrillation;
   - complex ventricular arrhythmias; and
   - 3rd degree heart block.

3. Inability to Comply with Protocol/Other Reasons
   Individuals with the following conditions by self-report, medical record review, or physician or ACT staff judgement will be excluded:

- *Hearing or Sight Impairments:* significant visual or hearing impairment resulting in inability to use the telephone, hear normal conversation or read forms;
- *Impaired Cognitive Function:* dementia, delirium or impaired cognitive function;
- *Anticipated Move or Distance From Clinic:* persons living >50 miles from the clinical center, except under special circumstances as judged by the clinical center's Principal Investigator, or plans to move within two years;
- *Participation in Other Trials:* currently participating in or planning to participate in another medical intervention study;
- *Women who are pregnant or of childbearing potential who are not practicing contraception*;
- *Participation of Another Household Member in ACT:* living with someone who is an ACT participant;
- *Alcohol Intake:* consuming more than 21 alcoholic drinks per week or alcoholism;
- *Functional Limitations:* difficulty walking one-quarter mile or climbing ten stairs;
- *English Illiteracy:* unable to speak or read English; and
- *Judgement of Clinical Center Staff:* judged to be unsuitable for the trial by the clinic staff for any reason.

Physician Notification of ACT Measures

Physicians will be provided exam and lab results (baseline, 6 months, 24 months) for:
- Lipids; total cholesterol, LDL, HDL, triglycerides
- Blood pressure

Physicians will also be notified when study measurements indicate:
- new cardiovascular events or symptoms
- injuries
- depression or suicidal threat

Inclusion of Women and Minorities

The ACT study was designed with "The NIH Guidelines on Inclusion of Women and Minorities as Subjects in clinical Research" (Federal Register, Vol. 59, No. 59, March 29, 1994) in mind. Based on previous studies, there is a possible differential effect by gender of behavioral interventions to increase physical activity. Therefore, the ACT sample size was estimated separately in men and women to enable the study to answer the research question separately in the two genders. For race/ethnicity, however, results from previous studies fall into the NIH Guidelines category of "neither support[ing] strongly nor negate[ing] strongly the existence of significant differences of clinical or public health importance in intervention effect between subgroups." Under those circumstances the NH policy requires "sufficient and appropriate entry of...subgroups, so that valid analysis of the intervention effect in subgroups can be performed." ACT will have broad representation by race/ethnicity, with approximately 1/3 of the subjects being minority subjects. Minority subjects will be randomly assigned to intervention and control groups to allow valid analysis of the effects of intervention by minority subgroup.

2.C. Recruitment/Screening and Setting

ACT recruitment will take place over approximately a one-year period. The population pool for ACT will consist of patients of those primary-care physicians who are participating in ACT. The

three clinical sites represent a diverse cross section of primary care facilities:

One of the two **Dallas** clinics is a large multispecialty group practice with three participating primary care physicians. It is estimated that 80% of this clinic's population is non-Hispanic White, with the other 20% divided approximately equally between Hispanic, African-American, and Asian. The second practice is a community outpatient clinic associated with Parkland Hospital. There are six primary care physicians who practice in this facility. The patient profile of Bluitt Flowers is 82% African-American, 15% Hispanic and 2.5% non-Hispanic White and the remainder is equally divided between Asian/Pacific Islander and American Indian.

Memphis consists of two community, primary care, internal medicine practices, which reflect diverse primary care populations. Six physicians at these two sites will participate in the study. The sites will enroll approximately 40% African Americans and 60% Caucasians.

Stanford has affiliations with two county-owned, ambulatory care clinics, each having five physicians. The patient populations of these facilities consist of about 50% White, 5% Black, 20% Hispanics, and 5% Asians and other ethnic groups who speak English.

Specific recruitment targets have been set to ensure adequate participation of men and women and minorities and to answer the research questions separately in men and women. The goal of recruitment is to randomize approximately 393 women and 417 men, of which 67% will be Caucasians, 20% African Americans, 10% Hispanics, and 3% other minorities (Asians, Native Americans). Each clinical center has set goals for minority recruitment. Regular monitoring will be done by the Clinical Coordinating Center (CCC) to track overall and minority recruitment goals.

Prior to beginning recruitment, participating primary care physicians at the three CCs will be asked to sign an ACT Physician "Letter of Understanding," which outlines their commitments to the study (Protocol Appendix A).

Recruitment staff will obtain lists of individuals who are regular patients of a participating primary care physician and who have a regularly scheduled follow-up visit, or who are eligible for a follow-up visit at least two months in the future. The two-month minimum time limit is necessary to ensure that potential participants can complete the screening process for enrollment before they see their primary-care physician.

Screening will proceed through a multi-step process, which may vary across sites. First, recruitment staff at some sites will obtain demographic information (age, race and gender) from computerized databases or appointment logs at the clinic. Other sources of information such as medical record review, computerized databases and physician review of potential participants will also be used to identify exclusion criteria.

Telephone Prescreen

Recruitment staff will then call potential participants to 1) inform them of the study, 2) determine interest in participation, and 3) determine if they are eligible to proceed. If subjects meet entry criteria and are interested in participating, they will be asked to come to a pre-screening visit (termed SV0) as soon as possible.

Screening Visit 0 (SV0)

Screening Visit 0 is designed to determine the level of interest and commitment of participants and if participants meet eligibility requirements. During SV0 (all performed as individual sessions), informed consent for this visit will be obtained. The details and demands of the study will be described to potential participants, and screening information will be obtained on the participant's level of physical activity, so as to exclude persons because of a high level of physical activity. Subjects who are eligible and show continuing interest in the study will be invited back for Screening Visit 1 (SV1). Some data collection forms will be sent home with participants to be completed before returning for SV1. A second informed consent for the duration of screening and for trial participation (should the screenee be randomized) will also be sent home for review.

Screening Visit 1 (SV1)

Subjects will return for SV1 within a recommended window of 8-30 days after SV0. SV1 will also be an individual visit. Baseline questionnaires will be collected and reviewed with clinic staff. A symptom-limited maximum stress test will be obtained to determine if subjects have occult coronary disease and to measure VO_2max. Table 1 shows measurements to be made at SV1. Participants who meet all eligibility criteria at SV1 will be invited back for Screening Visit 2.

Screening Visit 2 (SV2)

Subjects will return to the clinic within a recommended window of 4-30 days for SV2. Data to be obtained at this visit are shown in Table 1.

2.D. Informed Consent

During SV0, the clinic coordinator or other appropriate clinic staff members will describe this first screening visit and the forms to be completed. The candidate will then be given a copy of the ACT Preliminary Screening Visit Informed Consent (Protocol Appendix C) to review. The candidate will be given an opportunity to ask questions about the screening process. After all questions have been satisfactorily answered, the candidate will be asked to sign the Preliminary Screening Consent so that screening may begin. Participants will be given a copy of the form and the original will be filed at the clinical site.

At the end of SV0, screenees remaining eligible for and interested in attending SV1 are given a second informed consent to take home and review. This describes SV1 and SV2 procedures as well as the actual study control and intervention groups, visit schedule, measurements and specimens to be taken, and the forms to be completed for the duration of the study, should the screenee be randomized. At the beginning of SV1, the candidate will be given an opportunity to ask questions about the study. After all questions have been satisfactorily answered, the candidate will be asked to sign the Screening and Randomization/Participation Informed Consent (Protocol Appendix C). Participants will be given a copy of this second informed consent and the original will be filed at the clinical site.

ACT informed consent documents will be based on the central models in Appendix C. These may be revised to comply with requirements of local Institutional Review Boards.

2.E. Randomization

Following recruitment, eligible participants will be randomized at their primary care physicians offices to one of three treatment groups: Intervention Groups B or C, or Standard Care Control (Group A). It is recommended that no more than 30 days elapse between SV2 and this first study clinic visit. Randomization will be carried out using a centralized computer-automated system located at the CCC, accessed via touchtone telephone during the participant's physician visit.

After participant eligibility and strata criteria are verified by the distributed data entry system implemented by the Clinical Center staff, the computer will issue an access code that is unique to the participant ID. The health educator will then call in to the central database, enter the access code using the numbers on their touchtone telephone and obtain the assigned treatment group for that participant. The touchtone system will be password protected to secure the randomization information from unauthorized users. Confirmation of the randomization will be sent to the health educator via a faxed report containing the participant's ID, acrostic and group assignment.

The randomization process will be stratified by Clinical Center, race and gender to ensure an even distribution of the number of participants per group for males and females and for each of the three races within each CC. Eighteen computerized randomization lists (a sequence of treatment assignments of about 300% more than the expected enrollment in a given clinic) will be generated using permuted block randomization with random block size.

2.F. Participant retention

A systematic effort will be made to maximize retention of subjects in the trial. Participants will be given a clear, detailed explanation of the procedures and time commitments of the trial prior to randomization. Randomized participants will receive written reminders of data collection appointments two weeks prior to the scheduled appointment. Participants who cancel appointments or who do not show up for data collection appointments will be called and the appointment rescheduled. Participants will be offered free transportation to data collection visits. Participants will receive periodic information about the progress of the study and individual communications such as birthday cards. Each CC will develop an incentive program for participants who complete data collection visits by awarding token prizes and other incentives, such as gift certificates.

2.G. Schedule of Follow-up Visits

Major data collection visits will occur at baseline and at 6 and 24 months after randomization. At these clinic visits, data to determine primary and secondary outcomes will be obtained as well as data on adherence to the physical activity interventions and adverse events. (See Table 1). A 12-month phone contact will be utilized to collect data on 7-day Physical Activity Recall.

2.H. Study Timetable

ACT consists of three phases:

Phase I represents the planning phase for ACT, which will run from September 30, 1994 until September 29, 1995. During these 12 months, the ACT Steering Committee will meet six times. The four subcommittees to the Steering Committee (Recruitment/Eligibility, Design and Analysis,

Measurement, and Intervention), will also meet at these times, and will also have regular conference calls to develop recommendations to the Steering Committee concerning study endpoints, the target population, recruitment and screening strategies, statistical issues, forms development, variables to be measured and study interventions.

Other activities during Phase I will include development and approval of the ACT protocol, development of the Manual of Procedures and study forms, establishment of the ACT data management system, and central and local training of study staff.

Phase II, running from September 30, 1995 until March 31, 1999, will include recruitment, screening, intervention implementation, follow-up, quality control monitoring, and closeout of study participants. During this time, the ACT database will be assembled, study-wide quality control measures will be implemented, and the conduct of ACT and participant safety will be monitored. The ACT Steering Committee and its Subcommittees will continue to meet regularly.

Phase III will focus on data cleanup, finalization of the database, analyses of study data, and publication of the trial results. This phase runs from April 1, 1999 until September 29, 1999.

3. INTERVENTIONS AND CONTROL

3.A. Participant Physical Activity Goals

Participants in all study conditions will be given the same recommendations for physical activity. Current national recommendations for physical activity, which are consistent with recommendations in Healthy People 2000, will form the basis of the ACT physical activity behavioral goals, which will also be consistent with the study goal of increasing the total caloric expenditure by ≥ 2 kcal$\cdot$kg$^{-1}\cdot$day^{-1}.

There are many different ways to meet the goal of increasing total daily energy expenditure by ≥ 2 kcal$\cdot$kg$^{-1}\cdot$day^{-1}. Two examples are a "**Moderate Activity**" approach and a "**Vigorous Exercise**" approach.

- The moderate activity method of becoming more physically active is described by the recent ACSM/CDC recommendation on physical activity (Pate et al, 1995): "Every American adult should accumulate 30 minutes of moderate intensity physical activity over the course of most, preferably all, days of the week." Moderate intensity activity is perhaps best described as brisk walking (3 to 4 mph). This approach encourages fitting more physical activity into the daily routine by taking more short walks, climbing stairs, and engaging in more active pursuits at home, on the job, and in leisure time. Multiple episodes of moderate intensity physical activity can be accumulated in sessions of at least 10 minutes to reach the total of 30 minutes a day.

- The vigorous exercise method of increasing total daily energy expenditure typically involves more formal exercise modes such as jogging, swimming, cycling, or strenuous sports play. This method is summarized as various combinations of frequency, intensity, and duration of exercise sessions (ACSM, 1990). In order to achieve an increase in total daily energy expenditure of ≥ 2 kcal$\cdot$kg$^{-1}\cdot$day^{-1}, a person would have to exercise 3 days a week for 30 minutes per session, at an intensity of 60 to 70% of maximal oxygen uptake (equivalent to approximately 70 to 80% of maximal heart rate).

The goal of 2 kcal•kg^{-1}•day^{-1} is consistent with the amount of activity that will produce significant increases in physical fitness and substantial health benefits. Additional health and functional benefits can be expected from participation in a greater amount or intensity of exercise, at least up to a point. Participants who are willing and able will therefore be encouraged to increase their activity level beyond the basic goal of 2 kcal•kg^{-1}•day^{-1}. This further increase can be achieved most realistically by adding some vigorous exercise to a moderate activity approach, or by increasing the frequency or duration or both for participants following the vigorous exercise approach.

Choices regarding type of physical activities will be allowed and encouraged. The moderate activity goal could be met by any activities consistent with a moderate intensity (3-5 METS), for example brisk walking, gardening, dancing, and/or bicycling. The exercise prescription goal could be met by any endurance activity meeting the prescription intensity, for example jogging, swimming, or class aerobics.

3.B. Group A: Standard Care

The Standard Care control group will receive physician advice consistent with national recommendations for physical activity counseling by physicians and other health care providers. Participants in the standard care control condition will not receive behavioral counseling. Behavior change programs that build on the physician's recommendations will be implemented in the other two conditions.

For participants in all conditions, physicians will assess and recommend physical activity and refer to the health educator in a three-step process:

1. Assess. The physician will assess the participant's current level of activity with a simple self-report tool.

2. Advise and Motivate. The physician will compare the participant's current activity level with ACT physical activity goals and make specific recommendations, as follows:

   a. review the goals with the participant and comment on the extent to which the participant is meeting the goals. Advise the participant how physical activity will likely reduce his/her risk factors for cardiovascular disease;

   b. for a participant not meeting the ACT goals, encourage him/her to increase activity levels, recommend a general category of physical activity (i.e., the moderate activity approach or vigorous exercise approach), and provide examples of activities in these categories. For participants meeting the ACT goals, provide reinforcement and encouragement to continue.

3. Refer. The physician will then refer the participant to an on-site ACT health educator for further information and will tell the participant that this information constitutes an important part of medical care. In the control condition, the health educator will provide existing written materials that summarize the physical activity guidelines and include suggestions for increasing activity gradually to avoid injuries.

This process will be repeated at each non-acute physician visit for the duration of the intervention period of the study.

This simple protocol has the following benefits:

a. It can be completed in a short time (estimated 2-3 minutes);

b. It provides current and specific physical activity guidelines to all participants;

c. It provides recommendations that are tailored to the participant's needs and risks, based on an individual assessment;

d. It is more than the current usual care and is consistent with Healthy People 2000 (USDHHS, 1991) and U.S. Preventive Services Task Force (Harris, 1989) recommendations;

e. It does not entail the use of multiple behavior change techniques that would contaminate the other conditions;

f. It assigns a role for physicians with which they are comfortable (conducting risk assessments and giving recommendations) and which the participants value;

g. It is highly generalizable to most or all primary care settings; and

h. The physicians will receive training in implementing the protocol, which they will probably perceive as improving their practices.

The physical activity recommendations will be recorded in the medical chart so that the physician can review the recommendations at subsequent visits, and so that the behavior change programs in the other two conditions can build on the physician recommendations.

No additional physician visits will be scheduled specifically for physical activity advice. If subsequent clinic visits are scheduled for routine care, the physician will ask about progress in physical activity. If the patient reports increasing activity, the physician will provide praise. If the patient reports no increase, the physician will restate the recommendations. Behavioral counseling will not be provided.

In the Standard Care condition, the health educator will provide existing written materials on physical activity guidelines. No materials will be developed by ACT for this group. The health educator will answer questions about type/amount of physical activity and health benefits. Questions about behavior change will not be answered and behavioral counseling will not be provided.

3.C. Theoretical Background for the ACT Interventions

Consistent with many other effective health behavior change studies, the theoretical basis for the ACT interventions and conceptualization of the intervention mediating factors is Social Cognitive Theory (Bandura, 1986). Social Cognitive Theory draws from the fields of operant learning, social psychology, and cognitive psychology. The theory describes a complex web of determination in which behavior reciprocally influences, and is influenced by, factors within the person and factors in the social and physical environments.

Key personal factors include cognitions, emotions, and physiology. Self-efficacy cognitions, in this case perceptions of one's confidence to be physically active in multiple situations, have been shown to be important predictors of physical activity (Dishman & Sallis, 1994.) Therefore, the interventions are designed to enhance self-efficacy through promoting a series of successful experiences in meeting realistic physical activity goals. Other documented personal factors include enjoyment of physical activity, mood, and perceptions of benefits of and barriers to physical activity. Perceptions of the intensity of physical activity are also related to participation, so ACT goals can be met through a variety of intensity levels.

Key social environmental factors include modeling and social support directly related to physical activity. Though it is consistent with Social Cognitive Theory that access to appropriate activity facilities (e.g., health clubs), resources (e.g., safe space for walking & jogging), and programs (e.g., affordable aerobics classes) promote regular physical activity, compelling data are lacking. Nevertheless, the interventions take into consideration the probable role of environmental influences on physical activity.

The self-regulation model of behavior change is derived from Social Cognitive Theory and has been applied to many behaviors (Karoly & Kanfer, 1988). Teaching the participants to apply self-monitoring, self-evaluation, and self-reinforcement through goal-setting, positive self-talk, and problem-solving enhance the effectiveness of their abilities to integrate physical activity into their daily lives.

The Transtheoretical Model (Prochaska, DiClemente, & Norcross, 1992) combines the common features of several approaches to behavior with the goal of specifying the most appropriate interventions to the participant at the proper time. The Stages of Change concept is used to guide assessment of readiness to adopt a new behavior and to select intervention techniques for each stage of change. This model has been successfully applied to physical activity assessment and intervention.

The ACT Intervention Subcommittee has drawn from all these models and theories to develop two intervention approaches. By necessity, the complex theories have been simplified to allow interventions to be realistic. Virtually all the specific intervention components have been used in previous studies, and there is support for the efficacy of the components (Dishman & Sallis, 1994; King, 1992). In most previous studies, effective multicomponent interventions have been developed directly by staff, and this model serves as the basis for the Staff Counseling Intervention. The Staff Assistance intervention will include key theoretical constructs while minimizing staff time and resources.

Providing both interventions in the context of an ongoing physician-patient relationship is expected to augment the effectiveness of both approaches.

The relationship between the two interventions and the Standard Care Control is shown in Table 2.

3.D. Group B: Staff Assistance Intervention

This intervention builds on the physician advice and, at the same time, is a subset of Intervention C (Staff-Counseling) and requires fewer resources and less staff time. A guiding principle in developing this intervention is for it to be feasible for delivery in a wide variety of primary care

settings without requiring extensive staff support. The intervention relies on mediated interventions to extend clinic staff efforts, yet provides substantial tailoring to individual needs and continued contact to promote maintenance. The components of the Staff Assistance intervention are as follows:

1. Initial session

After referral by the physician during the same clinic visit, the health educator will:

a. show a 15-20 minute video that provides background on the importance of physical activity, presents physical activity goals, provides role modeling, and provides guidance in setting realistic goals;

b. review the physical activity goals as presented by the physician and reiterate the physician's recommendations;

c. individualize the importance of physical activity health and quality of life benefits for the participant in particular;

d. evaluate with the participant the different options for physical activity participation based on the participant's abilities, needs, and preferences, and develop an activity plan;

e. review with the patient the community resource guide (to be developed for each ACT site) to facilitate the matching of programs to participants and inform the participant about the range of options for classes and other programs currently available in the participant's community;

f. describe the importance of the ACT newsletters and use of physical activity self-monitoring logs (mail back cards) for the participant to complete during the course of the study, and the method and schedule by which the cards are to be returned to ACT staff; and

g. schedule one telephone follow-up. This follow-up will assess whether participants met their short-term goals, prompt participants to continue to gradually increase their activity, provide necessary support and problem solving during the crucial first couple of weeks of behavior change, and identify barriers and methods for resolution of those barriers.

2. Interactive mail

An interactive mail-based component will be used that is designed for low-literate patients, uses simple concepts, and has an emphasis on graphics. The mail-based component will consist of:

- monthly mailings (newsletters) that will include activity information and behavior-change assignments;

- a mail-back card including: activity log, short checklist to identify barriers, readiness to change assessment;

- feedback sheets sent in response to the mail-back card between monthly mailings

The monthly mailings will be newsletters and will provide information targeted to different stages of change. New data on health benefits and testimonials on personal success and benefits might be relevant for those in early stages. Features on trying and improving on behavioral skills will address needs of those at later stages. Methods for overcoming seasonal barriers or interruptions will assist in relapse prevention. Features on an activity of the month will promote trying diverse activities. Tips on fun during activity will enhance enjoyment. There will be three or four "columns" each month, and each will contain a specific behavioral assignment. Participants will be encouraged to choose an assignment from one of these options and report their experience or send evidence of completing the assignment to the project office. The mailings will use site-specific inserts to highlight upcoming activity events or activity-related organizations (e.g., Walkabout International). Announcements about milestones reached by individual participants will serve as incentives to recognize and reward physical activity and participation in intervention components. Thus, part of the newsletter will be site-specific.

Each newsletter will be accompanied by a postage-paid, mail-back card. The card will contain a report of minutes and type(s) of activity over the past week, an indication of whether the participant is ready to increase activity in the near future, and a checklist of possible barriers. Feedback sheets will be sent based on the responses.

Staff response to mail-back cards will be individualized based on participant data entered into a laptop PC.

3. Telephone contact

A small amount of telephone follow-up will occur, consisting of:

- one health educator-initiated follow-up phone call after the initial session
- participant-initiated calls to the health educator for questions
- health educator-initiated calls to subjects who are out of touch every 6 months

A relatively low level of phone contact will be allowed in the Staff-Assistance intervention. One staff-initiated call will be made within 1 or 2 weeks after the initial visit. The purposes are to assess success in meeting the first goal, set subsequent goals, provide social support, and problem solve. This will be a 5-10 minute call.

Participants will be encouraged to call the health educator to answer questions or to request assistance with problem-solving. These calls will be limited to 5-10 minutes.

Participants who do not make contact with the project will be pursued by the health educator once every six months. Phone calls will be made to the participant and others who may know how to make contact. The primary purpose of these calls is to stimulate involvement in the intervention program. Reasons for lack of involvement are assessed, and involvement in at least some intervention components will be encouraged and planned.

4. Incentives

A simple and low-cost incentive system will be used to promote continued involvement with the intervention. The incentives will consist of:

- Points for sending in mail-back cards/logs
- Reinforcers, including recognition in monthly mailings (bronze, silver, gold clubs), discounts for activity-related supplies or services, and inexpensive items

Reinforcers will be simple (but effective enough) to be feasible in primary care, such as recognition in newsletters, discount coupons, and inexpensive items. Reinforcers such as t-shirts, sports bottles, gym bags (in the $2-10 range) are realistic. Winners could be announced in newsletters. Formative research will be conducted in the near future to identify reinforcers in this population.

5. Follow-up in-clinic counseling

Brief, structured counseling sessions with the health educator will be conducted in conjunction with scheduled physician visits. The sessions will last 10-15 minutes.

3.E. Group C: Staff-Counseling Intervention

The Staff-Counseling Intervention represents an optimal intervention approach for promoting physical activity across a two-year period via the primary care setting. Drawing on the current intervention literature in the physical activity field, the intervention will include those behavioral elements that have demonstrated efficacy in the physical activity area (or related health behavior areas), and which can be delivered by on-site trained clinic personnel.

Participants assigned to this group will receive all the components of the physician assessment and recommendation, as described for the control condition, as well as all the components of the Staff Assistance intervention plus additional components that provide substantially more individual counseling as well as group classes. The components of this intervention are as follows:

1. Initial session

The initial session will consist of the same components as in the Staff Assistance intervention, with the following additions:

a. apprise the participant of the schedule and nature of the subsequent telephone follow-up counseling sessions with the health educator;

b. determine whether the participant desires additional in-person clinic visits; and

c. encourage attendance at the group classes, and work with the patient to make a commitment to attend classes for at least 3 months;

2. In-person counseling sessions

Additional in-person counseling sessions will be offered throughout the intervention period, particularly during the first few months, to meet individual participant needs. The sessions will be recommended by the health educator, as needed, or requested by the participant. The counseling sessions will have the following objectives:

a. evaluation of success in meeting physical activity goals;
b. updating of physical activity goals;
c. problem-solving around barriers to adherence;
d. discussion of future barriers and plans to effectively cope with them (i.e., relapse prevention); and
e. provision of reinforcement and social support.

3. Group classes

Group classes will be ongoing throughout the intervention phase, will have primarily a behavior change focus, will address adoption and maintenance issues, and will facilitate group support.

To avoid delays in starting new participants in classes, and because of limited resources for specific types of classes for different needs, group classes will be designed to meet the needs of all participants. At least two meetings will be held each week at each clinical center (i.e., Stanford, Dallas, Memphis). Group classes will be held throughout the intervention so they can address both adoption and maintenance issues. Some physical activity will be incorporated into the class session as the site characteristics allow. The amount and type of physical activity will be able to be done in a classroom setting and will be standardized across sites.

Content of the class sessions will focus on behavior change methods. Each week a new topic will be presented by the leader. This may be presentations on using a new behavior change technique, safe and effective participation in a specific physical activity, injury prevention methods, more detailed information on the health benefits of physical activity, or other topics requested by participants. Participants will be encouraged to apply the new information to their activity program.

Participants will report on progress in achieving activity goals. Those meeting goals will be praised and asked to indicate the behavior change methods they used to meet the goals. Those who did not meet goals will be assisted by the group in problem solving. Each class will incorporate a discussion of the next week's goals. Each participant will share the goals and receive feedback and encouragement from the group and leader.

Several elements will make the classes relevant for those in the early stages of change. Group leaders will be trained to be sensitive to providing extra encouragement and assistance to those in contemplation and preparation stages, and to shape their activity goals in small increments.

Those who are already active will be able to get something out of the groups as well. The topics presented in each class will vary, so a participant can attend over a long period and not feel the classes are repetitive. The application of behavior-change methods and group problem solving are relevant for this group as is relapse prevention. Long-term participants can be recruited to be assistant leaders and provide assistance to new members, those having difficulty getting started in regular activity, or those having a relapse.

4. Telephone counseling

Approximately 15 health educator-initiated telephone counseling sessions will occur during the first year. Information provided by the participant on the mail-back card/log will be used in the counseling. The counseling will have the following objectives:

a. evaluation of success in meeting physical activity goals;
b. updating of physical activity goals;
c. problem-solving around barriers to adherence;
d. discussion of future barriers and plans to effectively cope with them (i.e., relapse prevention); and
e. provision of reinforcement and social support.

Feedback sheets and other materials will be mailed out after the phone counseling session, as appropriate.

Group C

The basic schedule of telephone contacts will be flexible to meet the needs of individual participants (e.g., somewhat more frequent if adherence is low or marginal). The frequency can be negotiated with the participant. The general schedule for telephone contacts is:

a) once weekly for the initial two weeks;
b) bi-weekly for the following six-seek period; and
c) once a month for the remainder of the first year.

At the beginning of the second year of counseling with the participant, the health educator and participant will jointly decide how frequent subsequent contacts will be. The recommended frequency of contacts will be monthly for participants with adequate adherence, potentially bimonthly for outstanding adherers who prefer somewhat less contact, and more frequent than once a month for those participants for whom it is deemed necessary.

5. Additional components, as resources allow

The feasibility of providing transportation and child care for group classes and individual counseling sessions will be evaluated at each clinical site. The availability of community transportation will also be assessed for each individual clinical site. The mode of transportation to educational sessions and physical activity programs will be discussed with each participant.

Home visits by the health educator and credit for exercise equipment or club membership will be considered on an individual basis depending on the participant's needs, barriers, and preferences, and on availability of staff and resources.

3.F. Staff and Participant Intervention Adherence

Methods will be employed to enhance protocol adherence by ACT intervention staff and participant adherence to intervention delivery. Methods for monitoring adherence and providing feedback will be employed.

1. Intervention Protocol Adherence by ACT Staff

Adherence to the study protocol by ACT intervention staff is crucial to the integrity of the ACT study. Numerous methods for monitoring and promoting adherence and providing feedback will be employed. Methods to enhance protocol adherence will include:

a. use of standardized intervention materials that are centrally developed;

b. structured guides for patient contacts that include checklists of items to covered in the contact;

c. standardized training of intervention staff with certification and recertification;

d. detailed training manuals given to physicians and health educators that describe procedures and highlight common problems and their solutions;

e. use of a computerized tracking system to enable measurement of various aspects of protocol adherence; and

f. feedback to ACT staff.

2. **Participant Adherence to Intervention**

Participant adherence to intervention delivery includes participants attending clinic sessions, accepting phone calls and participating in follow-up phone counseling, completing intervention forms, and completing various other aspects of the interventions. Methods to enhance adherence to treatment delivery will include:

a. presentation of the intervention under the auspices of the participant's primary care medical institution;

b. frequent contact with participants;

c. reminders to participants to complete forms (e.g., mailback cards);

d. newsletters; and

e. reinforcement for completion of self-monitoring logs and other intervention-specific materials.

Since physical activity is one outcome of this trial, the two active intervention groups are designed to increase patient adherence to treatment outcome, and monitoring adherence to treatment outcome is addressed under measurement of the primary and secondary outcomes.

3.G. Process Evaluation

Documentation of the process by which the interventions are delivered and the extent to which they are received by patients serves many purposes, especially when the interventions are complex, as in ACT. Process data will be used to document the quantity of intervention components delivered, the extent to which the intervention protocol is followed, barriers to full implementation, the quality of the interventions, participant evaluations of each intervention component, and physician and health educator satisfaction with the intervention components.

Three types of process measures will be collected: intervention quantity, intervention quality, and participant evaluation.

1. Intervention quantity

The purpose of these measures will be to document the extent to which the participants are exposed to different intervention components. A computerized tracking system will be used to collect measures of items related to intervention quantity, including delivery of advice by physicians, time and number of contacts with the health educator, attendance at classes, and time and number of telephone counseling sessions. These data will be used to determine which intervention components were utilized by different participant subgroups.

2. Intervention quality

Measures will be made to assess whether the intervention procedures are being implemented as planned. In addition, barriers to full and successful implementation will be identified, and assessment of physicians' and health educators' satisfaction with the interventions will be made. These data will be useful in improving future interventions. Data will include content of sessions, ratings of intervention components by health educators and participants, and completeness of materials, such as self-monitoring logs.

3. Participant evaluation

The purpose of this type of process evaluation is to obtain the participants' subjective evaluations of each intervention component. This evaluation is particularly important in multi-component interventions such as in ACT. Data obtained from participant ratings can be used to predict outcomes and to inform modifications to the program for later studies of dissemination.

The general procedure is to develop simple Likert-type rating scales that can be used to assess patient perceptions of "satisfaction" and "usefulness" of each intervention component, including the physician information and advice, the health educator in-person and telephone contacts materials, classes, and other intervention components.

3.H. Intervention Training

ACT will provide intervention training for physicians, primary care center staff, and health educators. For physicians and primary care staff, the "training the trainers" approach will be used, where central training will be provided to "master trainers" from each clinical center who will then return to his/her site to train others. The health educators will be trained centrally. Each site, in conjunction with the coordinating center, will develop a system to train and certify local ACT staff.

Methods of instruction will be based on a sequence of steps that have been shown to be effective in a wide variety of applications. Similar methods will be used in training "trainers", physicians, and intervention staff. After an overview of the objectives of the training, the content and skills will be explained in a clear and concise manner. Audiovisual aids will be used to present the materials. Counseling methods will be demonstrated by the trainers in a role-play context. "Learners" will role-play the skills using written scenarios, and feedback will be provided by trainers. Role-plays will be conducted in small groups, so each learner has ample opportunity to practice under supervision and receive feedback. Trainers will emphasize verbal praise of effective responding and will use specific and constructive corrective feedback.

Training will emphasize standardization of delivery of the various phases of the intervention and of collection of process measures. Training manuals will be used and each ACT staff will keep a copy for future reference.

1. Physicians will be trained to:

   a. understand the importance of regular physical activity for health;

   b. provide information on the health benefits of physical activity that is relevant to each participant's health status and to specific CVD risk factors;

   c. provide recommendations regarding physical activity that are appropriate to the participant's health status;

   d. deliver the three-step participant assessment and advice protocol;

   e. document physical activity assessment and advice in the medical record; and

   f. know appropriate responses to patient's medical concerns about physical activity.

2. ACT health educators will be trained to:

   a. deliver Interventions B and C, and avoid behavioral counseling for Group A;

   b. use decision rules to determine which intervention components are appropriate for each participant;

   c. use the computerized tracking system, developed for ACT, to keep records regarding number and type of sessions delivered for individual participants and groups, and time spent in intervention delivery;

   d. maintain a clear distinction between methods delivered to participants in the three groups; and

   e. complete process evaluation forms.

3. Primary care office staff will be trained to:

   a. work with ACT health educators to implement procedures for participant flow that will assure appropriate notification of the health educator of appointments and arrival of ACT participants;

   b. provide ACT health educators with patient charts so the health educator can flag charts of study participants to prompt the physician to deliver advice; and

   c. maintain medical records that identify a participant's physical activity goals and document physician assessment and advice.

4. MEASUREMENT (See Table 1)

4.A. Primary Outcomes

1. **Energy expenditure from physical activity** ($kcal \cdot kg^{-1} \cdot day^{-1}$)

   Energy expenditure in physical activity will be estimated using a **seven-day Physical Activity Recall (PAR)** (Blair, 1985). Energy expenditure is assessed by a structured interview in which the participant is asked to estimate the amount of time spent each 24-hour period during the last seven days in five categories of activities classified according to their estimated energy expenditure expressed as metabolic equivalents (METS, or $kcal \cdot kg^{-1} \cdot hr^{-1}$). The MET values used for activities are updated based on Ainsworth et al. (1993). The five categories are sleep, light, moderate, hard, and very hard activity. The amount of time spent in each category is multiplied by that category's average MET value and the results are summed for the 24-hour period to obtain one day's estimate ($kcal \cdot kg^{-1} \cdot day^{-1}$). Interviewers will be centrally trained to follow a standardized protocol for administering the recall questionnaire. To improve precision in the estimate of physical activity, the recall questionnaire will be administered twice, at least eight days apart, at SV0 and SV1. It will then be administered at 6, 12 and twice at 24 months follow-up.

2. **Cardiorespiratory endurance** ($L \cdot min^{-1}$)

   Cardiorespiratory endurance will be assessed by measuring **maximal oxygen uptake** (VO_2 max, $L \cdot min^{-1}$) using a graded maximal treadmill exercise (GXT) protocol (Figure 1). Upon arrival, the participant will be connected to a 12-lead channel electrocardiograph monitor. After a short period of familiarization with walking on the treadmill, the participant will undergo a warm-up period. Speed will be increased to a comfortable pace at which the participant's steady-state heart rate is 60% of age-predicted maximum, or rating of perceived exertion (RPE) level is 11-13 (fairly light to somewhat hard), and maintained for 4 minutes. After a brief recovery, the participant will be fitted with an apparatus for gas exchange measurements. The GXT commences with the treadmill at zero percent grade and at the speed performed during the warm-up. The treadmill is elevated by 2% in 2-minute stages and subsequently by 1% when RPE is 17 (very hard) or above. Blood pressure, heart rate, and RPE are measured during the last 30 seconds of each stage. The test continues until the participant requests to stop because of fatigue or until any one of the criteria listed under ASCM "Indications for Stopping an Exercise test" (ACSM 1991) is met. VO_2max is determined from standardized criteria including any two of the following:

   a. plateau of VO_2max with increased grade;
   b. respiratory exchange ratio >1.1 or ventilation:maximal oxygen uptake ratio ($VE_{btps}/VO_2max > 35$);
   c. fatigue as evidenced by participant distress or loss of coordination; and
   d. attainment of age-predicted maximal heart rate.

   The exercise testing will be supervised by a physician. All staff administering the test will be centrally trained and certified and follow a standardized protocol. The maximal exercise test will be performed at baseline (SV1) and at 6 and 24 months.

4.B. Secondary Outcomes:

Secondary outcomes for ACT include alternate measures of physical activity or fitness, factors related to cardiovascular disease risk, psychosocial factors, and cost effectiveness of the interventions. The following secondary outcomes will be measured (see Table 1, Section IX).

- Heart rate during submaximal exercise test
- Resting blood pressure
- Plasma lipids and lipoproteins (triglycerides, HDL-cholesterol, LDL-C, total cholesterol)
- Plasma insulin
- Plasma fibrinogen
- Body composition: body mass index, skinfolds, waist and hip circumferences
- Psychosocial variables including mood, self-efficacy, social support, and quality of life
- Cost effectiveness
- Dietary intake
- Adoption of light intensity physical activity
- Smoking
- Heart rate variability

1. Submaximal exercise test

   Based on maximal treadmill test results from SV1, the treadmill workload at 50% and at 75% of VO_2max will be determined for each individual and a submaximal exercise test will be performed at the second screening visit (SV2). The participant will be fitted to a heart rate monitor and heart rate, blood pressure, and RPE will be measured as the participant walks on the treadmill for five minutes at 50% and 75% of VO_2max (Figure 1, Section X). This same workload will be used for the submaximal exercise test at the 6 and 24 month visits.

2. Blood pressure

   Resting systolic and diastolic blood pressure will be measured with a standard sphygmomanometer, using the appropriate cuff size. After five minutes of rest, three readings of blood pressure, spaced 60 seconds apart, will be taken while the participant is seated. Blood pressure will be measured at both screening visits (SV1 and SV2) and the average of the six readings will be the baseline blood pressure. Blood pressure measurers will be centrally trained and certified to follow a standardized protocol. Blood pressure will be taken at baseline, and at the 6 and 24 month follow-up visits.

3. Blood measures

   Blood will be collected after at least 12 hours fasting, and at least 8-12 hours after vigorous exercise. Plasma will be analyzed for triglycerides, HDL-cholesterol, total cholesterol, LDL-cholesterol (calculated from the Friedewald equation, 1972), insulin, and fibrinogen. Plasma will be processed and stored for analyses to be performed by a central lab.

4. Anthropometry

   Height will be measured in centimeters using a wall-mounted stadiometer and weight will be measured in kilograms using a balance beam scale with the participant wearing light indoor

clothing and no shoes. One measurement of height and weight will be taken. Following a standardized protocol, circumferences using a nonstretchable tape will be taken in centimeters at the waist and hips. Skinfolds using Lange calipers will be taken in millimeters at the chest (men only), triceps, subscapular, suprailiac, abdominal, and thigh sites. Two readings of circumferences and skinfolds at each site will be made and averaged.

5. Health-Related Quality of Life

Psychosocial measures include a health-related quality of life (HRQL) test battery which includes psychometrically sound measures for depression, anxiety, positive affect, physical well-being, and life satisfaction. HRQL dimensions will be assessed with the following validated instruments: the Beck Depression Inventory (Beck, 1979), the Speilberger Trait Anxiety Scale (Speilberger, 1983), the Exercise-Induced Feeling Inventory (Gauvin & Rejeski, 1993), the Perceived Quality of Life Scale (Patrick, 1988). Pain and well-days will be measured with items taken from general health surveys (MOS Short-Form 36 Health Survey, and the Behavioral Risk Factor Surveillance System).

6. Measurement of mediators

Multicomponent interventions are designed to have an impact on several of the hypothesized mediators of behavior change. In many studies the impact on mediators is not assessed, so the construct validity of the interventions cannot be tested. In ACT we will assess key mediators that are targeted by the interventions and that can be measured adequately. These include environmental constraints, self-efficacy, outcome expectancies, outcome values and social support. Methodologies to measure the mediating variables will be adopted from social cognitive theory. These measures will be used to evaluate the construct validity of the interventions by examining intervention effects on mediators. They will also be used in exploratory analyses to determine which mediators appear to be correlated with changes in physical activity outcome measures.

7. Dietary intake

Dietary intake will be measured to assess changes in diet associated particularly with Interventions B and C and also to control for potential confounding in secondary outcome measures of blood pressure and lipids, should dietary changes occur differentially among the three intervention groups. The nutrients of interest are those related to blood cholesterol or blood pressure, and include:

kilocalories	sodium
total fat	potassium
saturated fat	alcohol
monounsaturated fat	fiber
polyunsaturated fat	

Diet will be assessed using a self-administered diet questionnaire based on the National Cancer Institute Health History and Habits Questionnaire (Block, 1990) and its associated software package (HHHQ-DIETSYS Analysis Software, Version 3.-10, NCI, 1993). Modifications of the questionnaire include a shortened time frame of one month, added foods, particularly ethnic foods, additional nutrients, and expanded sodium intake

The diet questionnaire will be distributed to all participants at SV1 and reviewed by interviewers face-to-face at SV2. Follow-up assessments will occur at the 6 and 24 month follow-up visits. Interviewers will be centrally trained and certified.

8. Adoption of light-intensity physical activity

   Light intensity physical activity will be measured by both a brief self-report instrument and by dividing the amount of time spent in the light activity category of the 7-day PAR into two subcategories: activities that involve very little body movement (approximately <2.0 METS) and those that do involve body movement (≥ 2.0 METS). From these measures, shifts in energy expenditure from sedentary to light intensity physical activity will be quantified.

9. Smoking

   Smoking will be measured by a standardized self-report instrument at baseline, 6 months and 24 months.

10. Heart rate variability

    A number of studies have demonstrated increases in heart rate variability with exercise training in normal athletes (Seals, 1989, deMeersman, 1993), fit non-athletes of all ages (Dixon, 1992) and patients with hypertension (Pagani 1988), myocardial infarction (La Rovere, 1992), or congestive heart failure (Coats, 1992). These and other studies support the hypothesis that changes in autonomic tone, particularly of the parasympathetic nervous system, may be an important mechanism for the reduction in sudden death caused by exercise training. One of the most important mechanisms by which exercise reduces cardiovascular mortality in primary prevention may also be by altering autonomic balance.

    ACT will measure heart rate variability under controlled conditions in all ACT participants at baseline and at 6 and 24 months post-randomization. Participants will be instrumented with standard 12-leads for ECG monitoring in preparation for their maximal exercise test at SV1. No specific changes in lead configuration will be required to measure heart rate variability.

4.C. Safety Monitoring

The primary safety concerns in ACT are cardiovascular and musculoskeletal events that may be associated with engaging in physical activity. Because blood pressure, lipoprotein levels, and depression will be measured as secondary outcomes, they will also be addressed in safety monitoring.

All randomized participants will be free of overt cardiovascular disease at baseline. Follow-up contacts at 6, 12, 18, and 24 months will include assessment of adverse events, with particular attention to cardiovascular events, cardiovascular symptoms, and musculoskeletal injuries. Blood pressure and lipoprotein measurements will be taken at baseline and at the 6 and 24 months follow-up visits. During contacts with the ACT health educator in the two intervention conditions, barriers to physical activity will be identified, including injuries or health problems.

When any cardiovascular events or symptoms or injuries are reported, the participant's physician will be notified and follow-up care will be tracked. Blood pressure and lipoprotein levels taken at baseline, 6 months, and 24 months will be reported to the participant's physician along with a brief summary of national recommendations.

at baseline, 6 months, and 24 months will be reported to the participant's physician along with a brief summary of national recommendations.

Physicians will be notified in a timely manner of the following alert values:

- Beck Depression Inventory score greater than 17
- Beck Depression Inventory item #9, with a confirmed positive response 1, 2 or 3

Because ACT participants will be recruited within primary care settings, contact with the participants' physicians will be achieved easily. Participants and their physicians will be unmasked if safety measures surpass alert levels.

4.D. Cost Analysis

The cost analysis will document the provider's expense of implementing the interventions, capturing both the direct and indirect expenses to the provider by intervention at each site. These "costs", when averaged per sub-group (i.e., each group of the trial), can then be combined with the sub-group's "effect" measures to obtain each intervention's relative cost-effectiveness ratio at the study-group level. These measures will be made in comparison to the "routine care" group. Thus, the cost analysis will also document the medical practice resources required for replication, excluding research related expenses, an important contribution to the future use of the trial's results.

The perspective guiding the cost analysis is that of the provider's, requiring a restricted view of the investments made to produce the intervention which may increase physical activity among a group of participants, who visit their physician. However, since the trial's results will be highly important to the managed care community of providers, the approach taken will be to capitalize on economic information that would be useful to that type of provider as well.

Medical Practice's Direct Expenditures will be those resources invested to produce and deliver the intervention components in the three groups. Actual operational expenditures and units of resources required to implement the trial's interventions will be extracted from administrative records at the three sites and the coordinating center. Personnel time and fringe during the conduct of the trial will be obtained from the intervention sites and allocated to each group by a patient-specific "time management" log. The value of supplies and materials, including pamphlets, videos, participant forms, etc., will be tracked and allocated to specific groups either by actual use when logically determined or by patient-load imputation. Direct research related expenses, (e.g., data collections and data entry, monitoring) will be excluded consistent with the perspective. Intervention training sessions and expenditures for health educators and the physicians will be documented so that these non-operational expenses can be excluded, too.

Medical Practice's Indirect Expenditures are those additional resources invested because of participation in the trial but not directly related to the intervention process (e.g., any increased insurance coverage, increase in utilities, etc.) Estimation of these indirect practice-based expenditures associated with the implement of the trial's interventions will be extracted from administrative records at the three sites.

Since the goal of ACT is to isolate the effect of medical practice-based interventions, and the participant is an integral part of the production of the exercise activity, the "patient's costs"

could be viewed as part of the indirect medical practice expense. Logically, if these costs are too high, the "prescription" will result in non-compliance.

Participants' Direct and Indirect expenses will be those medical and non-medical expenses required of the participants during the trial and directly related to the interventions. In the case of the direct medical expenses, the participant's expenses for injuries and adverse conditions will be tracked by participant-reported data, and the value imputed from regional health expenditure data. As for the indirect non-medical expenses, there are two components that will be documented: adverse event work-loss expenses, and exercise activity expenses. The participants' time losses from work due to injuries will be self-reported, and the value for each event imputed from self-reported income data and corroborated by regional occupation-specific wage estimates. The participants' exercise time would be similarly valued and discounted according to the participant's self-report of "enjoyment" in this time allocation.

All dollar values will be appropriately adjusted to the trial's initial year to remove inflation and regional variations of values will be adjusted using local wage data. Trial findings will be reported by individual sites and overall means. Sensitivity analysis will be conducted to examine the findings' sensitivity to any assumed or imputed values.

4.E. Data Management

ACT will use a distributed data entry system whereby each CC enters ACT data on its participants. Data from CC personal computers (PCs) will be transferred to the CCC according to prespecified schedules.

1. Security

Data security in a distributed data entry system requires strict adherence to backup protocols and careful monitoring of data traffic. The distributed data entry system to be used in ACT facilitates data verification and error corrections and it will contain logic and range checks. ACT will employ a remote data management system that allows direct access to the ACT microcomputer at each CC. Using this technique, it is possible for the Clinical Coordinating Center to take control of the local device and query the system for any number of parameters, i.e., date of last back-up, physical device status, and other diagnostic procedures. This allows the CCC to correct any conditions that have disaster potential. Features of this system, such as the use of an unpublished telephone number, multi-level structure and password-protection, prevent access by unauthorized individuals.

2. Confidentiality

All records kept on the CCC computer will be identified by participant ID number only. Computer files containing names, addresses or other identifiers will not be transferred to the CCC. Participant records at the CCs will be stored in secured areas. Only authorized personnel will have access to the computer area.

3. Computer Entry

a. Programming

Data entry screens will closely mimic hard-copy forms. FoxPro, a relational database software package, will be utilized in programming these screens, which are part of a menu-driven system.

b. Verification

The data entry system will contain internal logic and range checks to ensure the quality of data as they are keyed. Each CC will submit one copy of the two-copy forms to the CCC for selective double-data entry. This will provide an increased measure of data quality. Comprehensive checks will be performed at the CCC on the central database to assess the serial integrity of the data. These procedures will identify and correct entry and transcription errors that, due to the limits of the intra-form logic and range checks, were not detected when keyed.

c. Disaster plan

If a CC must recover from disasters such as natural phenomena (water, fire, or electrical), it will be possible to reconstruct both the database management system and the data up to the last back-up through the use of micro diskettes kept in a secure area remote to the PC's location at each CC. The CCs database management system will have backup procedures incorporated to facilitate this process.

At the CCC level, routine backup procedures will be performed, such as nightly incremental back-up to tape (4mm or 9-track) and monthly full back-ups, to ensure optimal recovery of data systems in the event of disaster. Back-up tapes will be kept in a locked, fire and waterproof storage cabinet away from the computer room.

d. Storage

Several copies of ACT study data will exist in various formats. As mentioned above, each CC will keep a set of back-up diskettes from the clinics. The CCC will archive those files both on the PC server as well as on one of the CCC VaxCluster disks via the local area network using Digital Electronics Corporation's Pathworks for DOS. In this configuration, the mainframe computer's disk resources are shared by the PCs participating in the local area network.

4.F. Masking

A concerted effort will be made to keep the measurement staff masked to the treatment assignment of each participant. The measurement staff will not participate in any intervention activities and vice versa, except for the logging of intervention activity by the intervention staff. The physical sites at each clinic where intervention and measurement occur will be separate. Participants will be instructed not to tell their physicians or the measurers which intervention they are receiving.

4.G. Measurement Training and Certification

At the central training, a "master trainer" at each CC will be trained to conduct training of additional people at his/her site.

Staff training and certification procedures will be developed and implemented for data collection, data management, and intervention. Certification procedures will be developed for measurement training of the two primary outcome variables and selected secondary outcomes. Procedures for training and certification will be part of the ACT Manual of Procedures. Training issues to be addressed in physical activity assessment include interviewer training and certification and the development of support materials for standardization and maintenance of protocol standards.

Each CC will appoint a training and quality control liaison. This person will be responsible for the maintenance of measurement and training standards at that center, including the recertification and training of new personnel in the event of staff turnover. Individuals from the Measurement Subcommittee and/or Clinical Coordinating Center will routinely visit each center throughout the study period to oversee overall maintenance of training and quality control standards.

5. STATISTICAL CONSIDERATIONS

5.A Primary Analyses

Two primary (null) hypotheses have been defined for testing in ACT:

H_1: there are no differences among the mean levels of $V0_2max$ among persons randomized to the three groups of the clinical trial at 24 months post-randomization, and

H_2: there are no differences among the mean levels of seven-day self-reported physical activity levels among persons randomized to the three groups of the clinical trial at 24 months post-randomization.

Each hypothesis will be tested according to the intention-to-treat philosophy (Friedman, 1985) in which all randomized participants will be grouped according to their intervention assignment at randomization, regardless of compliance. All primary comparisons will be two-sided (Fleiss, 1987). A Bonferroni adjustment for multiple comparisons will be used to control the Type I error across the two primary hypotheses: individually, each hypothesis will be tested at significance level 0.025. Separate hypothesis tests will be performed on women and men.

General linear models will be used to model the serial data collected on each primary outcome measure. Time since randomization will be grouped by targeted exams (i.e. 6 or 24 month) and parameterized as a fixed class effect. The primary hypotheses will be tested using linear contrasts for interactions between treatment assignment and the indicator variable for the 24 month exam. No *a priori* parametric structure will be assumed for serial correlation. The baseline level of the measure (i.e. VO_2max or seven-day physical activity recall) will be included as a covariate in models, as will terms for the stratification factors: clinical center and race (African-American, Hispanic, Other).

Extensive attempts are planned to promote the retention of ACT participants; however it is expected that not all randomized participants will be evaluated at 24 months. Including interim

data on VO_2max and seven-day physical activity in analyses testing the 24-month differences is expected to reduce the potential biases that may be associated with missing data. This approach allows all participants who have post-randomization measures to contribute to the analysis, and therefore does not exclude persons who are missing 24-month data.

Secondary analyses will be performed to explore the effect that assumptions about missing data have on trial results. Sensitivity analyses will be conducted in which analysis of results will be performed based on 1) assuming the missing data are missing at random, conditioned on the value of covariates and intermediate results, and 2) assuming that all the unobserved missing data in the intervention and control groups have the same distribution as the observed data in the control group. If these analyses indicate that the results differ substantially, depending on the assumptions one makes about the missing data mechanism, further analyses involving model-based alternatives to the planned primary analyses (e.g. Schluchter, 1992; Shih, 1992; Diggle and Kenward, 1994) and post-hoc stratification (e.g. D'Agostino, 1994) will be explored.

Based on analyses from the Stanford-Sunnyvale Health Improvement Project (SSHIP-I) trial, VO_2max measurements are anticipated to have a right-skewed distribution with the variance increasing with the mean; if this pattern emerges in ACT, a logarithmic transformation will be used, as in the sample size calculations presented below. Each of the three pairwise comparisons of the intervention groups will be tested using a Bonferroni-adjusted significance level of α=0.0083 (0.025/3), as is specified in the sample size calculations.

5.B. Secondary Analyses

A series of publications based on the baseline data will be developed to provide the investigators with a first opportunity for a systematic exploration of the central databases; to assist in developing definitions of new variables for future analyses; to begin the development of scientific collaborations; and to cement the protocol for trial publications. Baseline analyses will include descriptions of recruitment, the baseline characteristics of the participants, and cross-sectional analyses of relationships among study variables.

Although the primary hypotheses only address 24-month change, it will be important to examine how the interventions may affect VO_2max and seven-day physical activity recall across the full 24 month period. Secondary analyses will be performed to track these measures across time using mixed effects analysis of covariance models to allow for both time-varying changes in covariates, and varying covariance structures (Laird and Ware, 1982; Jennrich and Schluchter, 1986; Diggle, 1988; Laird, 1992; Wolfinger, 1992).

Important secondary outcome measures include other measures of fitness and activity, factors related to cardiovascular risk (e.g. levels of lipoproteins, blood pressure, insulin, glucose, and fibrinogen), health related quality of life and cost. Methods similar to those described above will be used for continuous measures. For other types of response variables (categorical, ordered categorical, or counts), we will use the generalized estimating equation (GEE) approach to fit logistic or log-linear models that account for the dependency between repeated measures (Zeger and Liang, 1986; Liang and Zeger, 1986; Prentice, 1988; Zeger, 1988; Lipsitz, 1991; Liang, Zeger and Qaqish, 1992; Miller, 1993). Nonparametric approaches may also be adopted in some settings, as well (e.g. Zerbe and Walker, 1977; Raz, 1988).

A full description of compliance, predictors of compliance, and attrition comprise important

secondary analyses that will allow a more complete understanding of study results. Other important secondary analyses include descriptions of the effectiveness of interventions in pre-defined subgroups formed by race, age, and baseline measures of activity or fitness, body mass index, education, use of beta blockers, pre-existing co-morbid conditions, elevated ST segments, mood disorders, smoking, psychosocial factors and menopausal status. In some secondary analyses, data from women and men may be combined. Cross-sectional and longitudinal relationships among individual outcome measures, and between measures of adherence and outcomes, will also be described.

Importantly, the cross-sectional and longitudinal relationships between VO_2max and other measures of treadmill exercise performance and seven-day physical activity recall will be examined for internal consistency. The robustness of these relationships across study groups and participant subgroups will be assessed using regression analyses.

5.C. Sample Size Considerations

Sample size calculations for the ACT trial were based on recruitment of an equal number of participants to each of its three groups. The two primary outcomes in these calculations are logarithmic-transformed VO_2max measurements (unadjusted for weight) and total kilocalorie expenditure per kilogram body weight by seven-day physical activity recall, including light, moderate and heavy activities, but not including sleep. For each primary outcome, the hypotheses to be tested will investigate 24-month differences between all intervention groups; thus a total of six pairwise comparisons will be performed. Preliminary data used for estimating standard deviations of outcomes were obtained from the SSHIP-I trial run by investigators at Stanford University. Based on the SSHIP-I information, we estimated that the standard deviations of log transformed, 24-month VO_2max measurements adjusted for baseline measurements were 0.1214 for men and 0.1215 for women, respectively. Standard deviations for total kilocalorie expenditure were only available for 12 months of follow-up. The 12-month standard deviations of total kilocalorie expenditure were 2.0894 for men and 2.0206 for women, after adjustment for baseline measurements. Sample size calculations were performed separately for men and women.

To ensure an overall, two-sided, Type I error rate ,α, of 0.05, each pairwise comparison will be performed at the 0.0083 level (0.05/6), thus using critical regions containing 0.00417 probability in each tail. Assuming equal variances of 24-month outcomes for all intervention groups, the general formula used to determine the appropriate sample size to detect a difference of δ with 1-β power is

$$N = \left(\frac{1}{r}\right) V \left(\frac{1}{P_1} + \frac{1}{P_2}\right) \frac{\left(Z_{1-\alpha/2/m} + Z_{1-\beta}\right)^2}{\delta^2},$$

where r is the proportion of participants that will not be lost to follow-up prior to 24 months, V is the baseline adjusted variance of the outcome variable, P_1 and P_2 are the proportion of subjects in the groups being compared, m is the number of trial groups times the number of primary outcomes, and $Z_{1-\alpha/2/m}$ and $Z_{1-\beta}$ are percentiles from a standard normal distribution. For the calculations reported below, we assume 20% loss to follow-up (r = 0.8) and have allowed equal numbers in each group. $Z_{1-\alpha/2/6}=Z_{0.00417}=2.64$ and, for 90% power, $Z_{1-0.1}=1.282$.

The sample size of the trial is based on being able to detect a 7% difference in VO_2max and a 1.1 kcal•kg^{-1}•day^{-1} difference in total energy expenditure with 90% power. The 7% difference would equal a difference of 2000 ml•min^{-1} versus 1869 ml•min^{-1}. The goal of the intervention groups is to target an increase in energy expenditure equal to approximately 2 kcal•kg^{-1}•day^{-1}. The trial is designed to detect an intervention that would obtain this increase on some but not all participants. It is anticipated that a successful intervention would cause some individuals to exceed these goals and some would not improve from baseline. The trial was designed to be able to detect an intervention that results in the following distribution of effects:

No increase in 25% of subjects
1 kcal•kg^{-1}•day^{-1} increase in 25% of participants
2 kcal•kg^{-1}•day^{-1} increase in 45% of participants
3 kcal•kg^{-1}•day^{-1} increase in 5% of participants

for an average increase of 1.3 kcal•kg^{-1}•day^{-1}. The control subjects are assumed to have a distribution of:

1 kcal•kg^{-1}•day^{-1} decrease in 10% of control participants
0 kcal•kg^{-1}•day^{-1} change in 85% of control participants
1 kcal•kg^{-1}•day^{-1} increase in 10% of control participants
2 kcal•kg^{-1}•day^{-1} increase in 5% of control participants

for an average increase of 0.2 kcal•kg^{-1}•day^{-1}. Based on the above assumptions, it will be necessary to randomize 393 women and 417 men to have 90% power to detect a 1.1 kcal•kg^{-1}•day^{-1} difference in total energy expenditure. These sample sizes will also allow ACT to detect a 7% change in VO_2max with approximately 91% power in women and 93% power in men.

5.D. Interim Analysis and Early Stopping

Major interim statistical reports will be prepared biannually for the Steering Committee so as to keep investigators blinded to outcomes. Statistical reports of unblinded results will be circulated to the Data and Safety Monitoring Board and the Project Office. In addition to data that will be reported more frequently (e.g., biweekly recruitment reports and other special reports), these major reports will be developed to provide a comprehensive picture of the status of the study.

Monitoring of clinical trials is generally required on ethical grounds, although it can be further justified by a number of practical considerations. Once the scientific and medical questions of primary interest have been answered, stopping the trial avoids expending additional time, money and effort (Friedman, 1985). The primary outcomes of ACT center on the effect of interventions at 24 months. Recruitment will be completed by the time appreciable information has been collected on these outcomes, so the advantages of early stopping rules based on the primary 24-month outcome measures are considered unprofitable to use in formal stopping rules for ACT. Instead, the Data and Safety Monitoring Board for ACT will assess the need for early stopping based on safety or on the likelihood that a statistically significant difference between treatment groups by the end of the study is improbable based on 6-month data. Group sequential testing using a Type I error spending function for multiple endpoints and longitudinal measures of effectiveness (Reboussin, 1992) will be recommended.

6. QUALITY CONTROL

6.A. Data Collection

All data collected at the ACT CCs will be gathered by trained and certified staff using standardized procedures, questionnaires and forms. All equipment used for data collection will be routinely calibrated. Reporting forms will be checked for accuracy and completeness prior to the participant leaving the clinic. All staff collecting data will be assigned an ID number that will be used to document who collected each piece of data. Data collected by external sites (e.g., central laboratory) will be transferred electronically to the CCC.

6.B. Reports and Site Visits

Reports generated from the CCC will focus on summarizing: recruitment, screening and enrollment progress, protocol violations, missing/delinquent forms, keying errors, data edits, participant missed visits and participant compliance to the study protocol. Some reports will be issued every 2 weeks (screening/recruitment/enrollment) while others will be prepared and circulated every two to four weeks. Results in these reports will be subclassified by clinical center. No information on study endpoints will be included in these reports. In addition, reports of the intervention process and patient adherence to intervention will be issued.

Site visits to the three clinical sites will occur on an annual basis, with options for additional visits, should the need arise (in instances of poor clinic performance, lagging recruitment, poor quality data, etc.). The purposes of these site visits will be to 1) provide a means for continual training, retraining and reinforcement of standard study procedures, 2) enhance communication between the clinical sites and the CCC, and 3) detect and document the extent of problems in implementing the protocol. Site visits to ACT subcontractors will occur on an "as needed" basis.

7. TRIAL ORGANIZATION

The organizational structure of ACT is shown in Figure 2 (Appendix A). Appendix A also lists participating centers and investigators.

7.A. Clinical Centers (CC)

The Principal Investigator at each CC is responsible for clinic operations and performance. (S)he or co-investigators will actively participate in the protocol and Manual of Procedures development and in the entire recruitment effort, from establishing a system for getting access to participants to informing potential participants about the trial and obtaining informed consent. These investigators will be particularly crucial in recruiting study physicians. They are also responsible for implementing the interventions and follow-up data collection. Close working relationships with the staff are essential to the success of the program. This may include weekly staff meetings. The Principal Investigator and his/her Co-Investigators are also expected to contribute to the conduct and progress of the trial by attending Steering Committee meetings and by serving on and chairing subcommittees and proposing scientific papers and serving on writing teams.

7.B. Clinical Coordinating Center (CCC)

In its role as the Clinical Coordinating Center, Bowman Gray School of Medicine/Wake Forest University (WFU) will perform the following functions in support of the study:

1. develop the study forms and the Manual of Procedures with the guidance of the Steering Committee, Subcommittees, and NHLBI staff;
2. purchase and set up the distributed data entry system;
3. train and certify clinic personnel in the use of the data collection forms and the operation of the microcomputer system for data transmission and management support systems;
4. receive data from all centers, edit the data for errors, and double key a subset of data items;
5. analyze the data;
6. generate regular recruitment and quality control reports to the Steering Committee and Project Office, and in addition to these, endpoint reports for the Data and Safety Monitoring Board (DSMB);
7. serve on study committees;
8. propose papers and assist in the preparation and authorship of papers, including providing statistical support;
9. provide and facilitate communication support among the CCs. It is important that the data coordinators in each CC and the Project Manager at the CCC develop close communications. Electronic mail media will be employed for the transmission of routine messages and for resolution of data problems. Telephone conference calls are also to be used for addressing larger problems; and
10. in collaboration with the Project Office, solicit and select organizations for subcontracts to the CCC for: a Central Lab, and an intervention video. The CCC will monitor the progress and quality control of the subcontracts.

7.C. NHLBI Project Office

The NHLBI Project Office will establish an ACT team consisting of the Project Officer, Deputy Project Officer, Contracting Officer, and other professionals in the NHLBI Division of Epidemiology and Clinical Applications, including a statistician and nutritionist, to perform the following functions:

1. provide direction to the CCs and the CCC regarding budgetary considerations, contracting, and subcontracting, and fund the centers through contracts for each phase of the study;
2. serve on the ACT Steering Committee and subcommittees to contribute to the scientific decisions and conduct of the study;
3. represent NHLBI at Protocol Review Committee and Data Safety Monitoring Board meetings;
4. review data monitoring and other quality control reports;
5. conduct site visits to the CCC and to the CCs on an as needed basis;
6. propose papers and serve on writing groups for publications and presentations;
7. review all ACT manuscripts for publication and abstracts for presentation (approval is required if an NHLBI staff member is a co-author);
8. aid the CCC in soliciting proposals, selecting organizations, and monitoring the progress and quality of work for subcontracts; and

9. provide updates of the status of the study as requested to NHLBI and NIH.

7.D. Steering Committee

The Steering Committee provides the leadership for the study and establishes scientific as well as administrative policy. The Steering Committee will be the main governing body of the trial. The five voting members of the Steering Committee include the Principal Investigators from the CCC and CCs and the NHLBI Project Officer. All major scientific decisions will be determined by consensus or vote of the Steering Committee. Except during the organizational period, the Steering Committee will meet approximately semi-annually.

7.E. Steering Committee Subcommittees

The Steering Committee has appointed subcommittees to make recommendations to the Steering Committee and to conduct major activities of the trial. Designated investigators from the CCC, CCs, and Project Office serve on the subcommittees.

Subcommittees will meet regularly either by conference call or in conjunction with the Steering Committee Meetings. Good cross-site representation on the subcommittees will allow for effective communication between the subcommittees. Subcommittees will report their recommendations to the Steering Committee for consideration. The subcommittees have the following responsibilities:

1. **Measurement/Quality Control Subcommittee will:**

   Define baseline and follow-up outcome data to be collected; determine the means for collecting these data (forms development); determine which data need special monitoring by the CCC (outcomes/events, recruitment, laboratory, etc.); formulate needs for staff training and certification; define coronary heart disease and cardiovascular disease events and methods for reporting them; define potential adverse effects and devise systems to report them; and develop alert values.

2. **Design & Analysis/Publications & Presentations Subcommittee will:**

   Develop recommendations for the major aspects of study design, including the definition of outcome measures, sample size, randomization strategies and analysis plans; review and approve all trial-related publications, presentations and ancillary studies; and ensure fair site representation, as well as high quality reporting and timeliness for all publications and presentations.

3. **Intervention Subcommittee will:**

   Formulate the content and approach for the trial interventions; devise systems to monitor them; and develop measures to follow participant and staff adherence to intervention delivery and receipt.

4. **Recruitment/Eligibility Subcommittee will:**

   Develop eligibility criteria; determine what data will be collected during trial screening; formulate viable recruitment strategies; develop the informed consent; and monitor retention during follow-up.

5. **Trial Coordinator Subcommittee will:**

   Discuss implementation of the Manual of Procedures and the impact of protocol changes, ancillary studies, etc. on clinic operations (participant flow, data collection, recruitment, compliance, etc.); propose streamlining procedures that would facilitate clinic operations and data collection efforts; collaborate with the Measurement/Quality Control Subcommittee on staff training, certification and recertification needs.

7.F. Protocol Review Committee (PRC)/Data and Safety Monitoring Board (DSMB)

The PRC/DSMB is appointed by the NHLBI and advises the NHLBI on the conduct of the study. The PRC/DSMB consists of a non-trial chairperson and additional non-trial voting members appointed by the NHLBI. The PRC/DSMB meetings will be attended by the NHLBI Project Office and the PI of the CCC, and the Steering Committee Chair. The PRC will make a formal recommendation to the NHLBI regarding whether the study protocol should be implemented. Meetings of the DSMB (either face-to-face or conference calls) will be held two times per year. Specific responsibilities of the DSMB include:

1. conducting reviews on the progress of the trial, including evaluating participant recruitment and compliance to the protocol;
2. reviewing and approving any subsequent changes to the protocol;
3. reviewing outcome data and making recommendations to the NHLBI on continuation of the study and possible termination, should it become necessary to protect the safety and welfare of the participants; and
4. assisting the NHLBI in resolving problems referred by the Principal Investigators.

7.G. Clinical Coordinating Center Subcontracts

1. Central Blood Laboratory:

   A Central Blood Laboratory will be used to analyze the fasting lipid profile (total cholesterol, triglycerides, HDL and calculated LDL), fasting plasma insulin, and fibrinogen levels. Employment of the Central Laboratory should reduce analytical variance and permit convenient performance monitoring and (if required) remediation. Preparation, storage and shipping of blood samples will be performed according to a standard protocol. Detailed instructions on all aspects of collection, processing and shipping will be written into the ACT Manual of Procedures.

2. Video Subcontractor:

   The video subcontractor to the CCC represents a short-term (during the ACT planning phase) cost reimbursement subcontract to develop and implement a 15-20 minute video that will serve as part of Interventions B and C. The subcontractor will collaborate with the

ACT CCC, the NHLBI Project Office and the ACT Intervention Subcommittee to develop, produce, test, adapt and implement the video that will be based on behavioral principles promoting initiation and maintenance of physical activity.

Contact the "Summaries of ACT P+P Policies," which is located directly behind the protocol.

7.H. Publications & Presentations Policy Objectives

The ACT Publications and Presentations (P+P) policy is in Appendix C. The objectives of the publications and presentations editorial policy are to assure and uphold:

- Expeditious and timely dissemination to the scientific community of all pertinent data resulting from ACT;
- Accurate and scientifically sound publications and presentations from ACT and its collaborating investigators;
- Promotion of and encouragement for analysis and submission of manuscripts among the ACT investigators;
- Establishment of a system for fair determination of authorship on ACT collaborative publications;
- That investigators from all participating ACT centers, particularly those of junior faculty rank and other junior investigators, have the opportunity to participate and be recognized in studywide publications and presentations;
- That press releases, interviews, promotional materials and other circulated ACT documents are accurate and objective, and do not compromise the collaborative trial and the acceptance of its results; and
- Establishment of procedures that allow the NHLBI to review in a timely fashion publications and presentations summarizing data collected during the course of the trial.

7.I. Ancillary Studies

1. General Policy:

ACT investigators are encouraged to propose and conduct ancillary studies. Such studies enhance the value of ACT and ensure the continued interest of the diverse group of investigators who are critical to the success of the study. To protect the integrity of ACT, ancillary studies must be reviewed and recommended by the Design and Analysis (D&A) Subcommittee and approved by the Steering Committee before their initiation. By definition, ancillary studies will require outside (non-ACT) funding.

2. Definition:

An ancillary study is one based upon information from ACT participants in an investigation which is not described in the ACT protocol and involves additional data which are not collected as part of the routine ACT data set, or additional biologic specimens for analysis or storage. Separate informed consent must be obtained from all ancillary study participants, and should clearly identify the ancillary study as one being performed in addition to the main study. An ancillary study may also use ACT data in the analysis (e.g., demographic information, medication use, etc.). An ACT principal investigator or co-investigator must be included as a co-investigator in every ancillary study proposal, to promote continuity with ACT. An investigator from the ACT CCC should be included as an investigator in every

ancillary study proposal to ensure the necessary access to the database and to facilitate data analyses, unless the CCC deems this unnecessary.

3. Approval Process:

   The Design and Analysis (D&A) Subcommittee will be responsible for initial review of ancillary study proposals. Investigators will provide a three to six page summary of the proposed ancillary study to the D & A Subcommittee, which will discuss the proposal in light of the following approval criteria. Before an ancillary study can be approved, it must be demonstrated that the ancillary study will have scientific merit and will not unduly:

   a. interfere with the completion of the main objectives of ACT or complicate interpretation of the ACT results;
   b. result in unmasking of staff assessing study outcomes;
   c. adversely affect participant burden or cooperation in ACT; or
   d. jeopardize the public image of ACT.

4. Publications resulting from ancillary studies will follow the same policies as described in the ACT Publication and Presentation Policy (Appendix C), except that the writing committee will be determined by the ancillary study investigators. *

Consult App D for details of policy.

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TABLE 1.
SCHEDULE OF ACTIVITIES

	Clinic Chart Review	Phone Prescreen	SV0 Orient. Visit	SV1	SV2	Initial MD Visit	6mo FU Visit	12mo Phone Call	18 Month Ph Mail	24mo(a) FU Visit	24mo(b) FU Visit
Eligibility and Recruitment/Tracking											
Age and other eligibility data	X										
Telephone recruitment		X									
Informed Consent			X	X							
Demographics and Medical Hx and health habits			X								
7-Day Physical Activity Recall			X	X			X	X		X	X
Contact information; distribute at SV0				X							
Medications Inventory				X			X			X	
Physical exam				X							
Randomization						X					
Primary/Secondary Outcomes											
VO2max during GXT				X			X			X	
Submaximal Exercise Test (HR @ 50 & 75% V02max)					X		X				X
Heart Rate Variability				X			X			X	
Total Chol, HDL-C					X		X				X
Triglycerides, LDL-C (calculated)					X						X
Fibrinogen/clotting factors					X		X				X
Fasting insulin					X						X
SBP, DBP, resting HR				X	X		X			X	X
BMI					X		X				X
Anthropometrics (skinfolds, girths)					X						X
Diet Questionniare; distribute at SV1; mail for FU					X		X				X
Follow-up Health Habits							X	X		X	
HRQL/IOA; distribute at SV1; mail for FU					X		X				X
Activities Inventory Form								X			X
Initiate ACT Interventions						X					
Process Evaluation/Measures of Compliance	**collected regularly 0-24 mo.**										
Self report: Physical Activity Logs (IntGrpOnly)											
Documentation of Interventions Delivered (IntGrpOnly)											
Cost analysis data collection											
Safety and Adverse Effects											
Musculoskeletal, cardiovascular							X	X	X		X
Hospitalizations/deaths							X	X	X		X

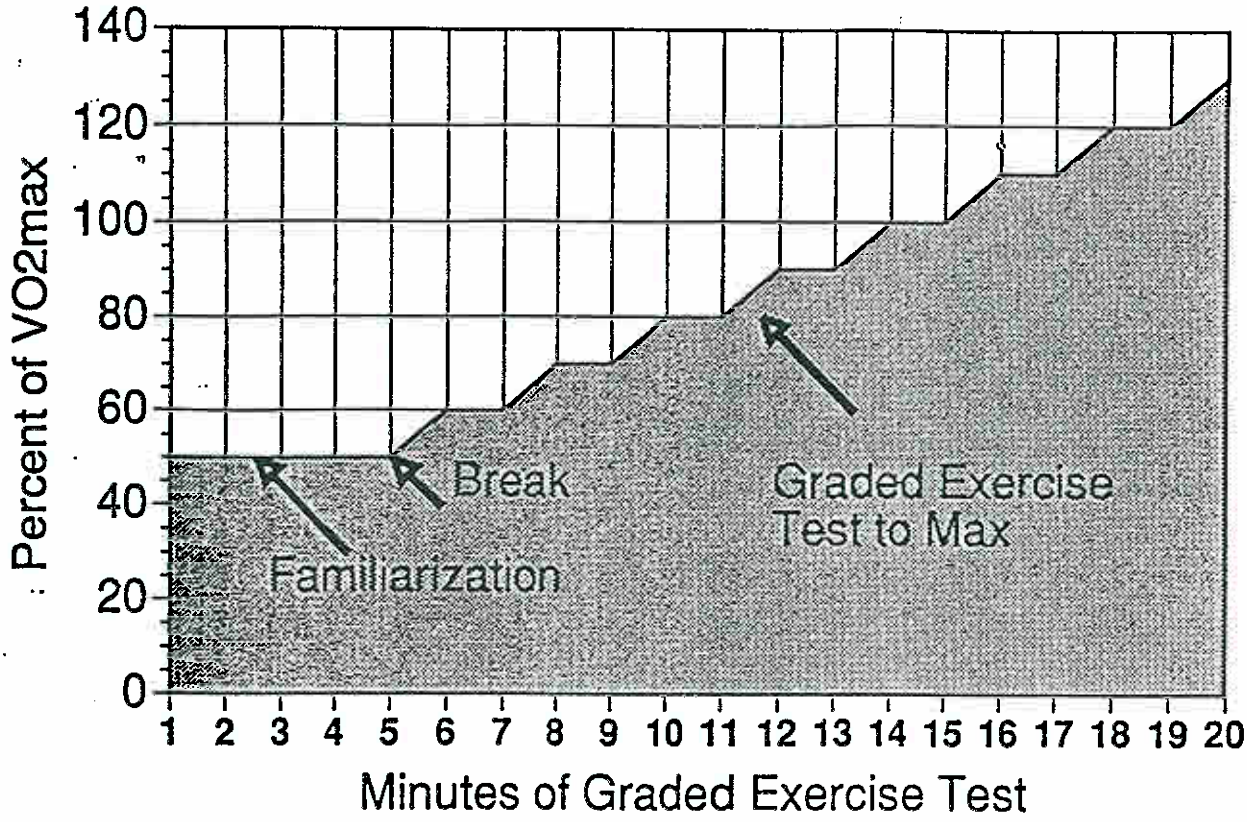
TABLE 2

The three groups of the ACT study indicating their hierarchical relationship.

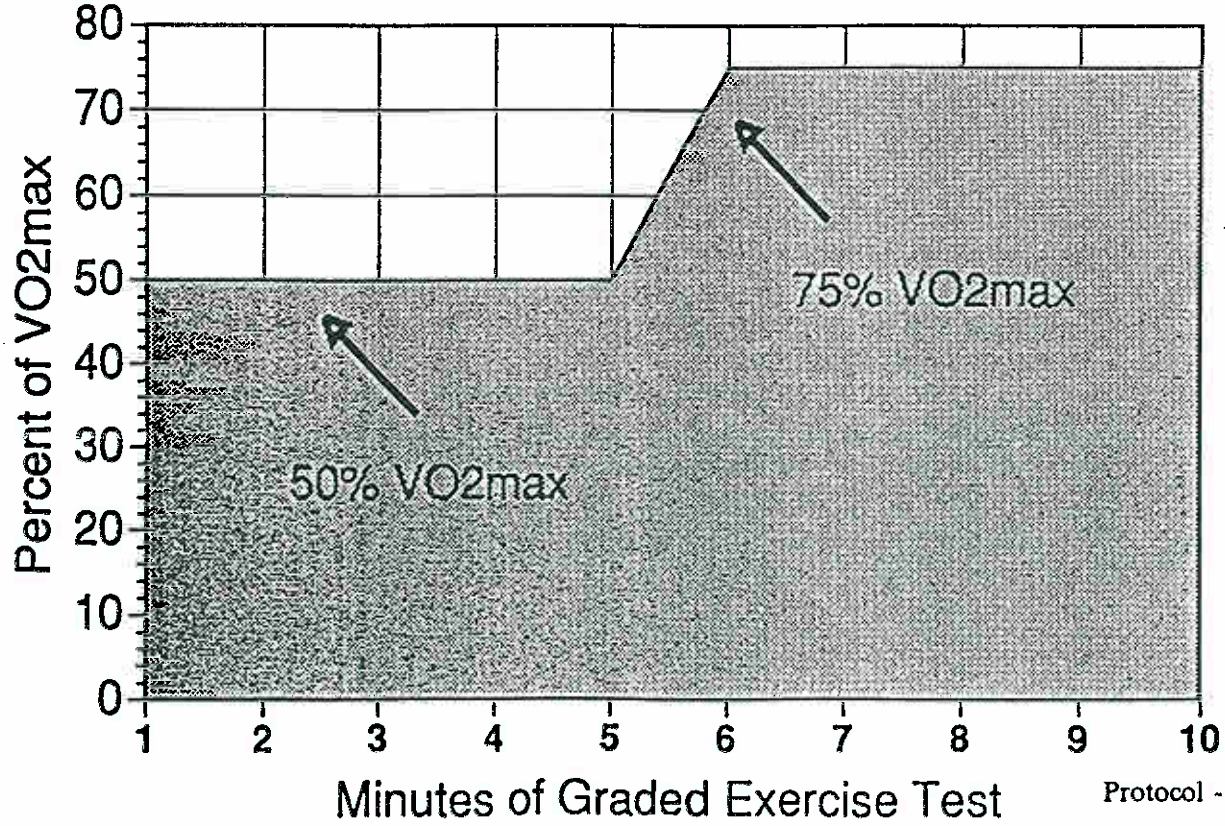
Component	Standard Care	Staff Assistance	Staff Counseling
Initial encounter			
Physician advice	yes	yes	yes
Written materials	limited	yes	yes
Activity logs	no	yes	yes
Behavioral video	no	yes	yes
Personal counseling	no	yes	yes
Encourage/schedule group classes	no	no	yes
Schedule additional in-person sessions	no	no	yes
Mail components			
Monthly newsletters	no	yes	yes
Mail-back cards	no	yes	yes
Incentives for mailing mailing back cards	no	yes	yes
ACTion sheets	no	yes	yes
Telephone components			
Patient-initiated calls calls for questions	limited	yes	yes
Calls every 6 months to re-establish contact, if needed	no	yes	yes
Counselor-initiated calls	no	one	frequent
Regular telephone counseling	no	no	yes
Subsequent clinic visits			
Personal counseling	no	yes	yes
Ongoing group classes	no	no	yes
Individual counseling sessions	no	no	yes
Other components			
Home visits	no	no	possible
Transportation and child care	no	no	possible

FIGURE 1

Protocol for Maximal Graded Exercise Test
(Screening Visit 1)



Protocol for Submaximal Graded Exercise Test
(Screening Visit 2)



APPENDIX A

ACT PHYSICIAN

"LETTER OF UNDERSTANDING"

APPENDIX A
ACT Physician "Letter of Understanding"

Dear Dr. _____:

I would like to take this opportunity to thank you for your willingness to collaborate in the Activity Counseling Trial (ACT). You, your patients and your staff will be instrumental in helping to determine whether or not primary healthcare providers can contribute to increased levels of physical activity in sedentary men and women aged 35-75 years. Eligible patients from your clinic will be randomized to one of three study groups: A) physician counseling and some written materials, B) the same physician counseling, written and other intervention materials, some mailings, occasional phone contact and brief counseling from a trained interventionist (health educator) or C) the same physician counseling, a wider selection of intervention materials and more mailings than in B, regular phone contact and more frequent counseling from the health educator.

As you know, all ACT tests are free of charge to your participating patients. These results will remain unknown to both you and your patient for the duration of the study; thus performance of these tests will not reduce the number of clinical tests to be conducted as part of your patients' normal physician visits. You will be informed of any ACT test results that would call for patient follow-up by your clinic for safety reasons.

Not only is it expected that any increase in physical activity in ACT patients will benefit their general health and cardiovascular status, but it is also possible that ACT monitoring and tests may lead to the early diagnosis of disease, if present. All ACT patients will receive some counseling to support increasing their levels of physical activity.

The ACT staff working in your clinic will make every effort to integrate ACT activities into your clinic as non-intrusively as possible. We will provide the necessary materials to smoothly implement the program for the duration of the study. ACT staff will assume principal responsibility for recruiting, screening, enrolling and administering the study interventions.

We appreciate your staff's cooperation with study personnel efforts to review patient appointment lists/medical records for recruitment purposes, to administer questionnaires in your office and to provide space so that the ACT health educator can conduct the interventions.

I would like to recognize and clarify your willingness: 1) to undergo on-site training to assess and advise on physical activity, 2) to spend 2-3 minutes of the first visit for your ACT participants performing the assessment/advising protocol, without your knowledge of intervention assignment, 3) to provide clinic space for the ACT health educator, 4) to confirm your day-to-day support of the study, even in the temporary absence of ACT staff in your clinic and 5) to forgo any compensation for participation in the project.

By co-signing this letter, you acknowledge our joint participation and cooperation in this important study. I look forward to collaborating with your over the next several years.

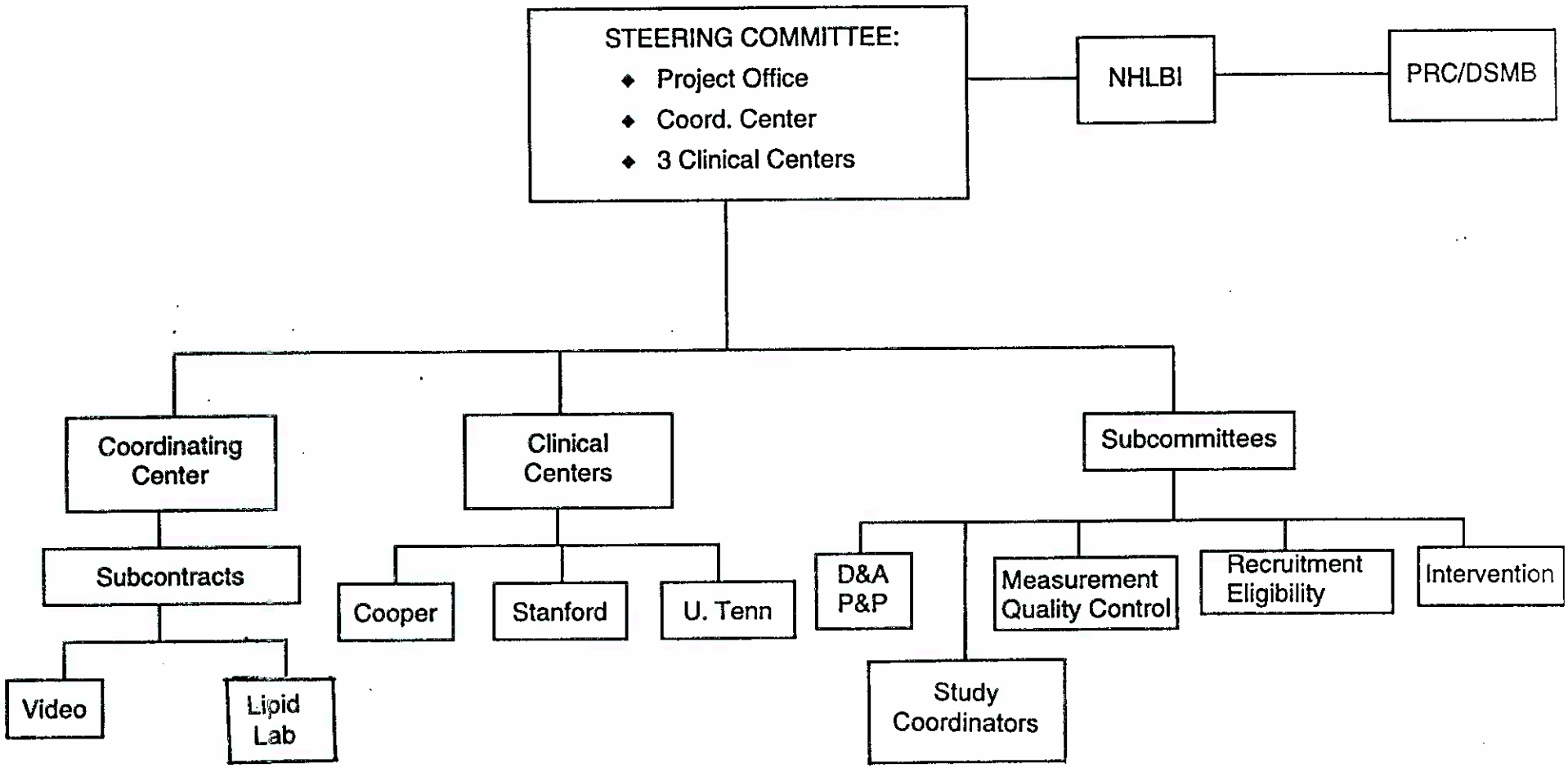
_____ _____
ACT Investigator Date

_____ _____
Participating ACT Physician Date

APPENDIX B

ORGANIZATIONAL STRUCTURE AND PARTICIPATING CENTERS

ACT Organizational Structure



PARTICIPATING CENTERS

Project Office

National Heart, Lung, and Blood Institute
Denise Simons-Morton, M.D., Ph.D.

Coordinating Center

Bowman Gray School of Medicine
Timothy Morgan, Ph.D.

Clinical Centers

Cooper Institute For Aerobics Research
Steven Blair, P.E.D.

Stanford Center For Research in Disease Prevention
Abby King, Ph.D.

University of Tennessee
William Applegate, M.D.

APPENDIX C

MODEL INFORMED CONSENTS

ACTIVITY COUNSELING TRIAL (ACT)

Preliminary Screening Visit Consent

Your doctor has agreed that you can be asked to participate in the research study called "The Activity Counseling Trial" (ACT), a study of physical activity counseling in persons who are involved in limited physical activity.

Purpose of the study

This study will test the effectiveness of physical activity counseling in the physician office setting on the health status of persons who are sedentary (involved in limited physical activity). Approximately 810 men and women 35-75 years of age will be enrolled at three centers, located in California, Texas and Tennessee. Everyone will be encouraged to remain in the study for 2 years. Legal authority to conduct this research is provided by Section 419 [285b-1] of the Public Health Service Act.

Screening procedures

If you agree to participate in ACT, you will be asked to attend a total of three screening visits (counting today's visit) to determine your continued eligibility. The entire screening process could take up to about 2 months to complete, and the three screening visits will last approximately 4-5 hours in all.

At today's initial screening visit we will give you more detailed information about ACT. You will also be asked to provide some general personal information (so that we can keep in touch with you) and more detailed information about your medical history and level of physical activity. If you remain eligible after today's visit, we will give you one form (contact questionnaire) to take home, fill out and bring back for your next screening visit. If you are not eligible, the reason(s) will be explained to you.

Risks/Discomforts

There are no physical risks or discomforts associated with this visit.

Benefits

Continued eligibility may enable you to participate in ACT. Participation could benefit your general health and cardiovascular status.

Alternatives to participation

You may choose to discontinue this preliminary screening process.

Voluntary participation

Participation in the ACT screening process is voluntary. Refusal to participate will involve no loss of benefits to which you are entitled. Further, you may withdraw from any of the screening visits at any time without penalty.

Significant findings

You will be told of any significant findings that may occur during the course of this study that could relate to your willingness to continue to participate. The investigator and the sponsor reserve the right to terminate the study and discontinue your participation at any time for any reason, in order to ensure your safety.

Confidentiality

Personal medical data will be kept confidential as required by the Privacy Act, 5 U.S.C. 552a. Details from your medical records will be stored on a private computer system, but your name will not be used in any computer files. Information stored on the computer may be seen by ACT clinic study staff or government staff at the National Heart, Lung and Blood Institute, which funds the study.

Questions

If you have any questions at any time during your screening for ACT or if you believe you have sustained an injury related to the screening process, you can contact either Dr. _____ at _____ or the Health Educator at _____. If you have any questions about your rights as a research subject, contact Dr. _____, the Institutional Review Board Chairman, at _____.

Consent summary

I understand that I am not waiving any legal rights or releasing the local institution sponsoring this study or its agents from liability for negligence. I understand that in the event of physical injury during the ACT screening process, the local institution sponsoring this study does not have funds budgeted for compensation either for lost wages or for medical treatment. Therefore, the local institution does not provide for treatment or reimbursements for such injuries.

I have read the description of the first ACT screening visit and I freely volunteer to participate in it. I have had known possible side effects and adverse reactions (none for this visit) explained as well as having had alternative procedures explained. I have had an opportunity to ask questions to the ACT clinical staff and I have received acceptable answers. I understand that I may withdraw from the ACT screening program at any time and I will still receive standard treatment for my condition.

_____	_____
Signature of participant	Date
_____	_____
Signature of witness	Date
_____	_____
Signature of Principal Investigator	Date

ACTIVITY COUNSELING TRIAL (ACT)

Screening and Randomization/Participation Consent

Purpose of the study

The objective of this study is to test the effectiveness of physical activity counseling in the physician office setting on the health status of persons who are sedentary (involved in limited physical activity). Approximately 810 men and women 35-75 years of age will be enrolled at three centers, located in California, Texas and Tennessee. Everyone will be encouraged to remain in the study for 2 years. Legal authority to conduct this research is provided by Section 419 [285b-1] of the Public Health Service Act.

Remaining screening procedures

During the remaining two screening visits to determine your eligibility for ACT, you will have a physical examination and will have your blood pressure measured. Blood will be drawn from a vein in your arm (less than 2 tablespoons) to check your levels of cholesterol, insulin, and specific blood clotting factors. Some of this blood will be frozen for later analysis and studies. In preparation for these blood tests, you will be asked to fast (to stop eating and drinking anything except water) for 12 hours before you come in for your third screening visit. At the next two visits, you will walk on an exercise treadmill, which is like walking on a conveyor belt. The treadmill will start going uphill very slowly. You will continue to walk on the treadmill as the uphill increases in steepness. For the first visit this will continue until you cannot proceed further. At the next visit you will walk on the treadmill but it will not be as hard. During this test, you will have your heart rate monitored and you will breath into a breathing tube. Your reactions to the exercise tests will be monitored to assure your safety. We will also ask you to complete some questionnaires that ask about your level of physical activity, what medications you are taking, the types of foods you eat, your smoking history and your quality of life. You will also have height and weight measurements taken.

Study procedures

If you are not eligible to participate in this study, the reason(s) will be explained to you. If you remain eligible for ACT after these next two screening visits, and you agree to participate in the study, you will be assigned by chance to one of the following programs, which involve:

A. Advice from your doctor concerning increasing your level of physical activity and provision of written materials on how to increase your level of physical activity.

B. Advice from your doctor concerning increasing your level of physical activity, provision of written materials on how to increase your level of physical activity, in-person counseling, viewing a video promoting increased physical activity, mailings, occasional phone calls, and referral to community resources. You will be asked to keep track of your physical activity on written "logs" over the two-year course of the study.

C. Advice from your doctor concerning increasing your level of physical activity, provision of written materials on how to increase your level of physical activity, in-person counseling, viewing a video promoting physical activity, phone calls, mailings, written and visual materials, group classes and referral to community resources. You will be asked to keep track of your physical activity on written "logs" over the two-year course of the study.

For all three programs, if you ever have questions about your physical activity program, you can call your Health Educator, who will give you his/her phone number at the time of your first health educator visit.

For all three programs, you will need to return to have several special "measurement" visits. You will also be contacted by study staff by phone at 12 months to provide some information. During the one 6

and two 24 months visits, you will have the same types of tests and procedures that you will have during the next 2 screening visits. The 6- and 24-month "measurement" visits will last approximately 3 to 4 hours. These visits will include the following:

- completion of various questionnaires asking you about your current level of physical activity, your diet, smoking history and quality of life;
- blood pressure measurement;
- height and weight measurements taken;
- a blood test, where blood will be drawn from a vein in your group (less than 2 tablespoons) to check your levels of cholesterol, insulin, and specific blood clotting factors. In preparation for these blood tests, you will be asked to fast (to stop eating and drinking anything except water) for 12 hours before coming in for this visit; and
- exercise treadmill tests, which involve walking on a conveyor belt that starts going uphill very slowly. During these tests, you will have your heart rate monitored and you will breath into a breathing tube. These tests will be the same as at the beginning of the study.

  In addition, a test to determine the degree of stiffness of the main arteries will be done. This test involves placing a pencil-like instrument over the blood vessels of the chest, groin, and/or neck. Recordings will be made on a computer while a partial electrocardiogram is being done. The measurements use high frequency sound waves that are harmless. The procedure will take about 10 minutes while you are lying down in a resting position. You can decline this optional test by crossing out this paragraph.

Risks/Discomforts

The risks of participating in ACT are small. You may experience temporary pain during the blood drawing, with later bruising at the puncture site. Only specially trained staff will be responsible for collection of blood samples. There exists the possibility of certain changes occurring during the treadmill test. These include abnormal blood pressure, fainting, disorder of heart beat and, in rare instances, heart attack, stroke and death. Every effort will be made to minimize these risks by reviewing information about your health and fitness before the test and by closely observing you during the treadmill procedure. Emergency equipment and trained personnel are available to deal with unusual situations that may arise.

Possible risks associated with increasing physical activity include but are not limited to, injuries to the muscles, ligaments, tendons and joints of the body. Other risks associated with exercise include, but are not limited to, abnormal blood pressure, fainting, dizziness, disorders of heart rhythm, and very rare instances of heart attack, stroke, or even death.

Benefits

The physical examination, laboratory tests and treadmill tests may lead to the early diagnosis of disease, if present. The physical examination and the laboratory studies are all free of charge. It is expected that any increase in physical activity in people who are non-active will benefit their general health and cardiovascular status.

Alternatives to participation

To determine your blood levels of cholesterol, insulin and some clotting factors, you could visit your personal health care provider. You may choose to increase your activity level on your own without enrolling in this study. You may choose to have your own health trainer.

Voluntary participation

Participation in the ACT study is voluntary. Refusal to participate will involve no loss of benefits to which you are entitled. Further, you may withdraw from the study at any time without penalty.

Significant findings
You will be told of any significant findings that may occur during the course of this study that could relate to your willingness to continue to participate. Your blood pressure and blood cholesterol results will be sent to your physician. The investigator and the sponsor reserve the right to terminate the study and discontinue your participation at any time for any reason, in order to ensure your safety.

Confidentiality
Personal medical data will be kept confidential as required by the Privacy Act, 5 U.S.C. 552a. Details from your medical records will be stored on a private computer system, but your name will not be used in any computer files. Information stored on the computer may be seen by ACT clinic study staff or government staff at the National Heart, Lung and Blood Institute, which funds the study.

Questions
If you have any questions at any time during the study or if you believe you have sustained an injury related to the study, you can contact either Dr. _____ at _____ or the Health Educator at _____. If you have any questions about your rights as a research subject, contact Dr. _____, the Institutional Review Board Chairman, at _____.

Consent summary
I understand that I am not waiving any legal rights or releasing the local institution sponsoring this study or its agents from liability for negligence. I understand that in the event of physical injury resulting from the research procedures, the local institution sponsoring this study does not have funds budgeted for compensation either for lost wages or for medical treatment. Therefore, aside from the emergency care previously described, the local institution does not provide for treatment or reimbursements for such injuries.

I have read the description of this study and I freely volunteer to participate in it. I have had known possible side effects and adverse reactions explained as well as having had treatment alternatives explained. I have had an opportunity to ask questions to the ACT clinical staff and I have received acceptable answers. I understand that I may withdraw from this study at any time and I will still receive standard treatment for my condition.

_____ _____
Signature of participant Date

_____ _____
Signature of witness Date

_____ _____
Signature of Principal Investigator Date

APPENDIX D

PUBLICATIONS AND PRESENTATIONS POLICIES

APPENDIX D

PUBLICATIONS AND PRESENTATIONS

The Design and Analysis Subcommittee of ACT also serves as the Publications and Presentations Subcommittee (P&P). Major decisions of the Publications and Presentation Subcommittee are subject to approval by the ACT Steering Committee. See Section VII.H. for P & P Policy Objectives. The three major types of ACT publications are as follows:

- **Group-authored Publications and Presentations**

  There will be only one group-authored publication/presentation: the primary outcome paper. All participating investigators and key personnel will be identified in an appendix to this publication, and acknowledged members of the actual writing team will either remain anonymous or, as appropriate, be acknowledged in a footnote on the title page.

- **Individually-authored Studywide Publications and Presentations**

  Individually-authored studywide publications and presentations are all others reporting baseline, design, and results of methodological studies based on the studywide common data set.

- **Other Publications and Presentations**

  Other publications and presentations are those not encompassed by the above two categories; they relate to work done in substudies or ancillary studies by a subset of CCs or in a single CC. This category also includes publications and presentations that use ACT data solely to illustrate new methodologies or procedures.

A. Review of ACT Publications and Presentations

To minimize the possibility that published materials may be based on faulty data, it is the ACT policy that all definitions, criteria and data used in 1) group-authored, 2) individually-authored studywide and 3) other publications and presentations be submitted to the Publications and Presentations (P&P) Subcommittee for review. As part of the review, the P&P Chair will send a copy of the final manuscript to a P&P Liaison at the CCC, who will forward the manuscript for review to a CCC representative to verify accuracy and consistency with other ACT documents and publications. At the same time, the Chair will assign the paper to 2-3 members of the Subcommittee for final P&P review. Also the final draft must be submitted to the NHLBI Project Officer for approval. Although the draft may be submitted through the P&P Subcommittee, each institution involved in the paper/presentation remains individually responsible for obtaining Project Officer approval.

Final drafts should be circulated to all ACT PIs for information purposes. The Publications and Presentations Chair will monitor turn-around times for all reviews, to guard against undue delays. Publications and presentations shall be in compliance with the rules and procedures of disclosure set forth in the Privacy Act. Confidential or proprietary information shall not be disclosed without the prior written consent of the individual or institution. Privacy Act compliance and documentation of written disclosure consents are the responsibility of each

institution involved in the paper/presentation.

B. Authorship for Group-Authored and Individually-Authored Studywide Publications and Presentations

1. Publications and presentations from these two categories will be identified by the P&P Subcommittee based on suggestions from ACT investigators. For each report identified, a writing committee of volunteers -- selected from investigators at all participating institutions -- is to be appointed by the P&P Subcommittee and charged with the responsibility of preparing the report within stated time limits that conform to a production timeline schedule that includes intermediate deadlines as well as a final deadline for journal submission. The P&P Subcommittee is charged with the task of periodic, systematic review of the work of all writing committees; aiding and encouraging them as appropriate; revising their membership or reconstituting them when indicated (with written notification and right of appeal). Appeals should be addressed to the chair of the Steering Committee.

2. It is the intent that selection of writing committee members be equitable and fair to all groups and individuals participating in this collaborative program, especially with regard to junior faculty colleagues and junior investigators.

3. For individually-authored papers, the writing group chair determines the order of authorship. A major criterion for the order of authorship is the level of effort and contribution made by the members of the writing committee.

4. At the request of the writing committee chair, if members of a writing committee have shown little or no interest in participating in the work of the committee or have failed to contribute to the task of preparing the manuscript, their names may be left off the list of authors, pending review by the P&P Subcommittee. The chair of the P&P Subcommittee is to make the final decision upon receipt of a written request from the chair of the respective writing committee; the affected individuals are to be informed in writing that they have the right to appeal the decision to the P&P Subcommittee as a whole.

5. For all group-authored and for most individually-authored papers and "other" publications, based on study wide data, an acknowledgment of all ACT Centers with their PIs and a list with a reasonable number of key personnel are to appear in each publication, printed in an appendix per journal guidelines. NHLBI support and contract numbers are to be on the front page of the manuscript.

6. All requests for reprints are to be directed to the CCC.

C. Authorship for Other Publications and Presentations

1. Proposals for publications and presentations based on special data sets collected on ACT participants by CCs involved in substudies or ancillary studies are also to be submitted to the P&P Subcommittee. In general, the writing committee preparing such a report is to consist of individuals designated by the participating study investigators, but it may include ACT investigators from other sites who wish to collaborate. All ACT PIs will be informed of such ancillary proposals through periodic circulation of P&P progress reports (see Section M of this Appendix). The authorship of such a report is to be designated in the usual manner for

a scientific report, with the order of names appearing after the title to be decided upon by the participating CCs. In addition to a statement of authorship, such a paper is to have a clear statement that this work was a substudy or ancillary study of ACT and the support from NHLBI is to be acknowledged.

2. Requests to use ACT data for purely illustrative purposes should be directed to the chair of the P&P Subcommittee. The subcommittee will act on the request with due attention to the requester's link to ACT and to the potential impact on other ACT-related publications and presentations. Also all requests to discuss ACT in non-data papers such as editorials or reviews should be discussed with the chair of the P&P Subcommittee.

3. Where appropriate, a listing of participating study centers and participants who are not authors is to be included. This decision is to be made by the participating institutions.

4. ACT Centers are encouraged to write papers on local data and other experiences. A local paper addressing material that will be dealt with in a studywide paper should be prepared only after publication of the studywide paper, or only after the studywide paper has been officially accepted for publication. Authorship for a local paper is to be handled by the PI of the local center where the data or experiences originated. Intent to publish should be conveyed to the CCC and the P&P Subcommittee.

5. All substudy, ancillary study, and local manuscripts must be reviewed and approved by the P&P Subcommittee and NHLBI before submission for publication. ACT PIs are also to receive copies of these manuscripts prior to their submission for information purposes. The manuscripts should give a clear reference, on the front page of the article, to ACT and the collaborative nature of the program, including the contract number with the NHLBI. A reprint of every published paper should be sent to the NHLBI Project Office and the CCC for archival purposes.

6. All requests for reprints of these types of publications and presentations are to be directed to the appropriate individual, usually the primary author.

D. Clearance of Abstracts and Presentation of Reports

1. The ACT P&P Subcommittee is to maintain a current list of all relevant meetings and their deadlines for submission of abstracts. It is strongly advised that abstracts submitted for oral presentations be based on a corresponding paper of the same topic.

2. All such abstracts must be approved by the P&P Subcommittee and the Project Officer before they are submitted to any national and/or international organizations. Proposed abstracts must be submitted to the P&P subcommittee at least one week prior to their due date to allow time for review. Approved abstracts will be periodically circulated among the ACT PIs for information purposes. If the abstract is accepted for presentation, the P&P Subcommittee is to be notified. Paper copies of slides to be used should, except under unusual circumstances, be submitted to the subcommittee prior to the presentation. It is permissible to submit previously cleared abstracts to other meetings; copies should be sent to the CCC for inclusion in the listings of publications and presentations.

3. In terms of selecting a presenter, preference is given to members of the writing committee

for the corresponding paper.

4. Once a paper has been published or a report presented at a scientific meeting, data can be used at other scientific meetings by ACT investigators.

5. In the case of papers scheduled for presentation before organizations issuing press releases, the presenter may submit the text of the presentation or other materials after they have been approved by the P&P Subcommittee and the Project Officer for release to the press. If the presentation is based on a manuscript not yet accepted for publication in a peer review journal, a sentence must be included on the front page indicating the preliminary nature of the results. The same principles of notification and acknowledgment apply to both abstracts/presentations and publications (see Section B of this Appendix).

6. Also the Chair must be notified of all editorials and review articles in which ACT may be discussed by an ACT investigator.

E. Invitations to ACT for Presentation of Papers

The ACT investigators welcome opportunities to participate and present reports at national and international scientific meetings. When an invitation is received by an ACT investigator, ACT policies with regard to publications and presentations are as follows:

1. When an invitation is directed to the Chair of the Steering Committee or the Chair of the P&P Subcommittee, the P&P Subcommittee will decide who is to represent ACT. Invitations directed to the NHLBI will be reviewed and approved by the NHLBI Project Office, which will, in turn, notify the P&P Subcommittee.

2. When an ACT investigator receives a personal invitation to make a presentation, he/she should notify the P&P Subcommittee to ensure listing of the presentation on behalf of the ACT Research Group.

3. All presentations in response to such invitations should be based on published ACT reports unless prior approval is granted by the P&P Subcommittee and the Project Officer.

4. Requests received by PIs or their staff to present or discuss at local meetings any previously published ACT data need no prior clearance by the P&P Subcommittee and acceptance of such invitations is encouraged. It is requested that PIs receiving such requests notify the P&P Subcommittee so that the subcommittee can keep records of these presentations. Any publication of such presentations or discussions must be approved by the subcommittee before publication.

5. ACT investigators must notify P&P Subcommittee of any media requests to comment on the progress or results of the ACT study. This of course does not include local media promotion of the ongoing ACT trial.

F. Procedures for Identifying Studywide Publications

1. At periodic intervals, the P&P Subcommittee is to distribute to all participating ACT

institutions an updated progress report of all approved ACT publications (e.g., approved, in preparation, submitted, in press, published; see Section M of this Appendix.

2. New proposals for publications can be identified by the P&P Subcommittee or by an ACT investigator, committee investigator or ACT staff.

3. Requests for proposed publications should include a 2-5 page document, to be submitted to the P&P Chair, that includes:
   - tentative title;
   - name of convener (proposer);
   - introduction;
   - objectives;
   - analysis plan (pertinent variables, analysis definitions, characteristics of population to be analyzed, table shells limited to a reasonable number);
   - tentative conclusions; and
   - pertinent references.

G. Identification of Writing Committees, Selection of Writing Committee Chair, and Work of Writing Committees

1. Once a studywide publication has been identified and approved for preparation by the P&P Subcommittee, the Chair of the subcommittee is to communicate with all ACT investigators via regularly issued P&P Progress Report (see Section M of this Appendix), requesting nominees qualified to participate as members of the writing committee for that paper. The request for nominees is to include a specific date (deadline) for submission of nominations, and should specifically solicit the collaboration of junior faculty members and staff. In general a writing committee should consist of 5-7 members.

2. The P&P Subcommittee is to select, from the submitted list of nominees, the membership of the writing committee for that paper, after which it appoints a Chair of the Writing Group. In most circumstances, the investigator submitting the proposal for approval, i.e., the convener, will be appointed Chair of the Writing Group. Criteria for selection of writing group members will include level of expertise (related to the publication topic), balanced representation across ACT sites, and consideration of individual commitments to other ACT writing group endeavors (to ensure that no one person is "overloaded" with ACT writing responsibilities). On occasion, the convener may suggest names for consideration as writing group members. Such requests should include a statement indicating the rationale for these nominations. The P&P Subcommittee shall make the final decision on a case-by-case basis concerning these special requests. Suggested nominations of non-ACT personnel will also be considered individually. Writing Groups for all papers involving analyses of ACT data must include one CCC representative, usually with statistical expertise.

3. The Chair of the P&P Subcommittee is to contact the newly appointed Chair of the Writing Group and to send him/her a list of the expected responsibilities of 1) the Writing Group Chair, 2) the Writing Group members and 3) the P&P Subcommittee. See Sections N and O of this Appendix. Copies of these communications should also be sent to all Writing Group members.

4. As soon as the chair is identified, it is his/her responsibility to communicate with other committee members to identify data needed from the CCC, and to establish a plan for writing the manuscript. To expedite publication, one or more meetings of the writing committee may be necessary, but in view of cost consideration, it is recommended that such meetings be held to a minimum and, to the degree possible, be incorporated as part of other scheduled meetings, such as Steering Committee meetings or national scientific meetings or by means of conference calls. The following steps should be followed in the preparation of the manuscript. The chair of the writing committee should:

   a. Contact each writing committee member to identify tasks for members of the writing committee;
   b. Submit a reasonable number of table shells to the CCC for data analyses;
   c. Coordinate additional data analyses requests (e.g., additional dummy tables) with the CCC representative who is on the writing committee;
   d. Convene the first meeting or conference call of the writing committee at a time when the CCC has completed the preliminary analyses; and
   e. Keep the Chair of the P&P Subcommittee informed of the paper's progress, notify the Chair of any delays or departures from the established production schedule and provide explanations for any delays that do occur.

5. If a problem of overlap emerges, the P&P Subcommittee will confer with the involved writing committee chairs to resolve the situation.

6. Members of each ACT writing committee should participate actively in preparation of the publication assigned to that committee. The chair has the responsibility to obtain input from every member of his/her committee. The input from every member of the writing committee is essential. If any member of the writing committee does not respond to the chair's request or does not contribute to the writing of the paper, the chair must take immediate action, through the P&P Subcommittee, to replace that individual, who has the right to receive written notice of this action and to appeal to the P&P Subcommittee. It is the responsibility of the chair of the writing committee to approve the final version of the paper before its submission to the P&P Subcommittee. All members of the writing committee should have seen the final draft before its submission to the P&P Subcommittee. The chair of the writing committee should inform the P&P Subcommittee of any substantial minority opinions or reports within the writing group so that serious concerns are not arbitrarily overruled by the writing committee chair without the knowledge of the P&P Subcommittee.

7. If in the judgment of the P&P Subcommittee, a writing committee is not working well and there is an unjustifiable delay in writing the paper assigned to it, the P&P Subcommittee is empowered to change either the chair or the entire membership, to expedite the writing of that particular paper. Affected members of the writing committee are to be informed in writing of this action and have the right of appeal to the Steering Committee.

H. Preparations and Submission of Abstracts

1. All abstracts must be approved by the P&P Subcommittee and the Project Officer before they submitted to any national and/or international organizations. Approval involves a two-stage process: 1) P & P approval of the abstract proposal, and 2) P & P and NHLBI approval of the final version of the abstract.

   a. Abstract proposals not based on a P & P- approved paper must be submitted to the P&P Office ≥2 months prior to the meeting submission deadline, to allow the CCC adequate time to meet the need for data requests and to ensure sufficient time for writing the abstract. The final version of the abstract must be submitted for P & P/NHLBI approval ≥10 days prior to the abstract submission deadline.

   b. For an abstract addressing the same topic as an already approved paper, the final draft of the abstract should be submitted for P & P/NHLBI approval ≥ 10 days before the abstract submission deadline. There is no need to submit a preliminary proposal.

   c. For abstracts dealing with a topic that relates to, but differs somewhat, from an already approved paper, the preliminary proposal does need to be approved by the P & PS/C. However, the 2-month time frame needed for approval of abstracts as discussed in Section "a" above will be relaxed in this situation. The proposer is encouraged to allow ample time before abstract deadline submission for this preliminary approval process. The final draft of the abstract needs to be submitted for P & P/NHLBI approval ≥ 10 days before the abstract submission deadline.

The writing committees should plan well in advance and be selective in their data requests to the CCC. Only tables which relate to the major topics of the abstract should be requested. Paper copies of slides should, except under unusual circumstances, be submitted prior to presentation. The CCC will assist in the development of statistics to be used in slides to ensure uniformity.

2. Upon submission of the abstract proposal to the P & PS/C, the proposer may suggest co-authors. However, P & P members can nominate additional individuals. "For the ACT Investigators" should follow the list of abstract authors on the final version of the abstract.

3. Abstracts will not report ACT baseline data until at least 50% of the baseline data have been collected. For all abstracts reporting on <100% of the baseline data, a statement must be included in the abstract indicating that the present analyses reflect preliminary findings.

4. If acknowledgment of support is required by the meeting organization, the abstract should list the four contract numbers of the four ACT sites:

   N01-HC-45135 (Cooper)
   N01-HC-45136 (Stanford)
   N01-HC-45137 (Memphis)
   N01-HC-45138 (Coordinating Center)

5. All abstracts (as well as one set of the actual slides plus one set of paper copies for each abstract) should be submitted to the CCC for archival purposes so that these can be periodically circulated to ACT investigators.

6. The CCC will periodically circulate sets of paper copies from approved presentations to all Ccs for information purposes. This will keep the ACT investigators abreast of all slide preparations and will minimize duplication of effort.

REMAINDER OF THIS PAGE INTENTIONALLY LEFT BLANK.

I. Preparation and Submission of Papers for Publication

1. Clearance and approval through the P&P Subcommittee and through the NHLBI Project Office are required for all ACT publications prior to their submission for publication.

2. All ancillary and local publications are to include an acknowledgment that approximates the following:

   The research upon which this publication is based was performed pursuant to Contract No. N01-HC-45138 with the National Heart, Lung, and Blood Institute.

3. All review and clearance functions of the P&P Subcommittee and of the NHLBI are to be done judiciously and expeditiously and solely to help fulfill the Policy Objectives set forth in Section VII.H. of the ACT Protocol; and are in no sense censorship functions.

J. Identification of Additional Papers

1. ACT investigators who identify additional studywide publications that draw on data collected by all CCs should submit a written proposal to the Chair of the P&P Subcommittee. Upon receipt of the proposal, the policies and procedures described in Section G of this Appendix are to apply.

2. If a specific writing committee decides that the topic or charge to that writing committee is too broad and should be divided into two or more papers rather than the one paper originally assigned, that writing committee (through its chair) is to communicate with the Chair of the P&P Subcommittee indicating the writing committee's recommendation for the division of the paper into two or more components. The writing committee is to identify which of the components it feels are to be its responsibilities and is to suggest titles and outlines for the other components. The P&P Subcommittee is to consider these recommendations and, when appropriate, redefine the charge to the existing writing committee. The additional papers are to be specified, following procedures as outlined in Section G of this Appendix.

3. If in its deliberation, any writing committee identifies other topics or titles, either directly or indirectly related to the charge of that specific writing committee, the Chair of the Writing Committee is to communicate these suggestions to the Chairperson of the P&P Subcommittee.

Subcommittee.

K. Use of ACT Data for Theses by Graduate Students

1. All requests for use of ACT data by students are to be reviewed by the P&P Subcommittee and the Project Officer.

2. It is required that the student requesting use for ACT data is associated with the study through the ACT investigator who is acting as the student's "sponsor" with regard to the data.

3. ACT data may not be used by students if the data relate to major ACT papers in progress or if the P&P Subcommittee deems that data to be necessary for a future major paper.

4. If the P&P Subcommittee recommends approval for the use of the requested data, a writing committee is to be established and is to include the student as convener of the committee.

5. The writing committee is to take no action regarding the paper until the student has completed and defended the thesis, provided this occurs in a reasonable length of time, to be determined on a case-by-case basis. The student's sponsor is to report the student's progress to the P&P Subcommittee at least annually.

6. The student must include in the completed thesis:

   a. a statement acknowledging ACT for use of the data, and

   b. a statement indicating that opinions, ideas, and interpretations included in the thesis are those of the student alone and not those of the ACT investigators.

7. When the thesis has been completed, as determined by the sponsor, the entire writing committee is to proceed to prepare the paper(s) for publication. It is the responsibility of the ACT PI "sponsor" to ensure that the thesis accurately reflects the conduct and data from ACT, as dissertations are technically available to the public without having gone through the P&P review process.

8. The standard ACT publication policy is to apply to any material published from the thesis.

9. ACT reserves the right to proceed with preparing a paper for publication on the thesis topic if, in the view of the P&P Subcommittee and the student's sponsor, the student has not made reasonable progress in completing the thesis.

L. Use of ACT Data for Grant Application or Contract Proposal

ACT data which have not been previously published but which are needed for grant applications or contract proposals must have prior approval for use by the ACT Steering Committee and Project Office.

M. ACT Publications and Presentations Subcommittee Progress Report (Example)

Paper #1:	"Title"
Writing Group members:	Jones, Allen, Cartwright, Bland, Ayers, Kline
Status:	Submitted to P&P Subcommittee for final approval before submission to target journal
Paper #2:	"Title"
Writing Group members:	Smith, Heller, Forman, Cannon, Flick, Zeller
Status:	First draft in preparation
Paper #3:	"Title"
Writing Group members:	Doe, Shook, Cranston, Brooks, Lorentz
Status:	Undergoing second round of analyses
Paper #4:	"Title"
Writing Group members:	Blitsky, ...
Status:	Accepting nominations for writing group

N. Letter of Intent

Section P of this appendix shows a sample letter of intent sent from the P&P Chair to the Writing Group Chair after P&P Subcommittee approval of the: 1) paper proposal, 2) Writing Group membership and 3) Writing Group Chair appointment.

O. ACT Responsibilities of Writing Group Chair and Writing Group Members

Responsibilities Writing Group Chair[1]

Overall responsibilities:

During all phases of manuscript development, coordinate writing group efforts and ensure timely preparation of the manuscript according to the production timeline.

Detailed charges:

- Communicate with the Writing Group members, the CCC, the Publication & Presentation Subcommittee, the NIH ACT Office, and the target journal editors.
- Prepare outlines.
- Request data analyses from CCC.
- Assign tasks/set deadlines for Writing Group members.
- Conduct periodic Writing Group meetings or conference calls.
- Circulate manuscript drafts to Writing Group members.
- Establish consensus among Writing Group members concerning target journal, subject to final approval by P & P Subcommittee.

- Prepare and send quarterly progress reports to P & P Subcommittee.
- Establish authorship order based on level of effort/input.
- Submit final manuscript draft to P & P Subcommittee and to Project Officer.
- Submit approved manuscript to target journal following final approval by Project Officer.
- Submit reprint of published article to CCC.

Responsibilities Writing Group Members[2]

Overall responsibilities:

- Actively participate in preparation of the manuscript.
- Fulfill assigned writing group tasks in a timely manner.
- Complete all appropriate responsibilities noted above.

[1] Failure of the Writing Group Chair to meet these responsibilities could result in dismissal as Chair and replacement with another Writing Group member or ACT Investigator committed to fulfilling these functions.

[2] Failure of a Writing Group member to meet these responsibilities could result in dismissal from the Writing Group and replacement with another ACT Investigator committed to fulfilling these functions.

P. "Letter of Intent"

(Sent from P & P Chair to Writing Group Chair after P & P Subcommittee approval of: 1) paper proposal, 2) Writing Group membership and 3) Writing Group Chair appointment)

Dear _____:

On behalf of the ACT Publications and Presentations Subcommittee, I would like to congratulate you on your appointment to Chair of the Writing Group for ACT manuscript # __, tentatively entitled "_____."

Our mutual goal is the orderly and expeditious publication of this manuscript. Towards this end, we look forward to working with you and members of your Writing Group to facilitate preparation of the first draft.

As Chair of a writing group, you assume responsibility for coordinating analysis and writing efforts and ensuring that the manuscript is completed according to the pre-determined production timeline. The P & P Subcommittee will monitor your progress and will offer assistance, should you encounter any problems in adhering to the production schedule.

The enclosed attachment, entitled "ACT Responsibilities of Writing Group Chair and Writing

Group Members," details the responsibilities involved in preparing the approved paper. Please review these guidelines carefully. A copy of this letter and the enclosed guidelines have been sent to members of your Writing Group so that they too will be aware of their responsibilities.

High quality and credible publications represent the ultimate goal of ambitious projects such as ACT. As scientists and study investigators, we have a responsibility to disseminate relevant information to the scientific community in a timely manner. Your efforts support these goals.

Sincerely,

Chair, ACT P & P Subcommittee

cc: Writing Group members (names listed alphabetically)
Encl: "ACT Responsibilities of Writing Group Chair and Writing Group Members"