6.10 Strategies for Monitoring and Promoting Adherence

6.10.1 Statement of Purpose

The AASK Study is intended to evaluate the effects of anti-hypertensive medications and levels of blood pressure control on the progression of renal disease in African-American hypertensive patients with chronic renal insufficiency. Goals of the study, as defined by the Design and Intervention Subcommittee, include the implementation of procedures for the management of blood pressure and the assessment of process-related factors that may influence participant adherence to the protocol.

The **Adherence** Subcommittee will oversee the development of strategies to promote and monitor participant adherence to medication regimens and appointments. This subcommittee will also develop and implement procedures for training project staff in the application of adherence promotion strategies and will monitor participant adherence to established protocols and will investigate ways in which adherence can be facilitated or enhanced.

6.10.2 Principles of Adherence Promotion

A. Components of adherence

Individuals with chronic illness, such as hypertension or renal disease, are typically asked to initiate or modify a range of health-related behaviors that influence disease progression, response to treatment, and quality of life. These behaviors include specific components of traditional medical interventions, such as medication use and attendance at clinic appointments, in addition to numerous behaviors that characterize an individual's life style (e.g. dietary habits, patterns of physical activity, use of alcohol and nicotine). Optimal management of chronic illness is, therefore, dependent upon patient ability to establish or modify these health-related behavior patterns in accordance with specific recommendations made by health care providers.

B. Multi-component intervention strategy

Adherence to various health-behavior regimens can be influenced by complexity of the regimen, treatment duration, patient knowledge and attitudes, social reinforcement, and environmental cues. Although interactions among these factors can be extremely complex, a variety of intervention strategies have been shown to effectively promote adherence. Multi-component interventions are frequently adopted in a stepped care approach to adherence promotion. Various components of these adherence promotion interventions are tailored to address specific aspects of a complex regimen. As a patient masters specific aspects of a health-behavior regimen by attaining a sequence of incremental goals, the pattern of behavior gradually comes to approximate the desired behavioral outcome.

Treatment strategies in the implementation of a multi-component behavioral intervention for the management of adherence can be seen to parallel treatment strategies in the implementation of a multi-component pharmacological intervention for the management of hypertension. As with a pharmacological regimen, the complexity and aggressiveness of a behavioral regimen is determined by patient presentation and response to treatment. In either case, treatment is initiated at a "minimal effective dose", that is, consistent with common practice or an established protocol. The "dose" is then titrated up or down to maintain the desired treatment effect.

If hypertension is not adequately controlled at a given "dose" of a specific pharmacological regimen, the regimen "dose" can be increased by an increment in the level of a particular drug, and/or by the incorporation of additional anti-hypertensive agents into the regimen. The more frequent or more extended patient contact with health care providers that is required to initiate these changes represents another dimension on which the dose of the regimen can be varied and measured. In a similar fashion, if adequate adherence is not obtained with the initial behavioral intervention, the "dose" of that intervention can be altered by increasing the intensity of existing components or by incorporating additional components.

C. Proactive implementation

Each interaction with participants will have an incremental (or decremental) effect on overall adherence to the study protocol. Contacts with study physicians, coordinators, and blood pressure technicians have potential to develop a significant cumulative effect on participants' adherence and retention. Because of this pervasive impact on adherence, it is important for all study personnel to have a working knowledge of behavior management strategies that are used in the adherence promotion procedures. All personnel who **conduct clinical activities** with study participants will therefore be trained and certified in the application of adherence promotion strategies. A description of training and certification procedures is presented in section 6.10.3.

Adherence promotion strategies will be structured to provide intensive intervention with participants early in the study, a time when participants tend to be highly motivated to follow the study protocol and most receptive to the introduction of behavioral strategies to promote adherence. This proactive stance is intended to aggressively reinforce early adherence, and to prevent the development of inappropriate medication use patterns that will be difficult to alter. As participants learn to implement self-management strategies and develop the ability to maintain adequate levels of adherence, the frequency and intensity of the adherence promotion procedures can be reduced to a "maintenance dose".

D. Adherence promotion goals

Adherence promotion strategies utilized in the AASK Study will be structured to help participants develop skills that will enable them to maintain a consistent pattern of health-promoting behaviors. As a primary purpose of the study is to determine if protocol defined blood pressure goals can be attained on specific pharmacological regimens, adherence promotion strategies will be focused on factors that are most directly related to the use of prescribed medications (i.e., temporal patterns of medication use, activities associated with medication use, changes in blood pressure, and attendance at scheduled appointments). Specific procedures will be established to monitor participant behaviors that reflect these dimensions of adherence, participants will be provided with specific feedback regarding their performance of these behaviors, and interactions with participants for the purpose of assessment and feedback will be structured to reinforce progress and to identify and resolve barriers. Strategies to attain these adherence goals are presented in section 6.10.4.

While other health behaviors (e.g., dietary habits, patterns of physical activity, use of alcohol and nicotine) are certainly relevant to the management of hypertension and renal disease, intensive efforts to monitor and modify these behaviors are beyond the scope of the AASK project. A detailed assessment of these health behaviors will not be undertaken. Biochemical assays used in the assessment of hypertension and renal disease provide information relevant to life style modification only when systematically related to specific patient behaviors. Without detailed behavioral data (e.g. food intake records, physical activity schedules) it is not possible to implement treatment strategies to alter relevant behavior patterns.

In the absence of detailed behavioral data needed to facilitate and monitor lifestyle modifications, feedback regarding specific observed lab values and recommended levels for particular assays will not be routinely provided to participants as this limited information will not effectively promote desired behavior changes. Participants with abnormal lab values will be given general recommendations regarding dietary habits and physical exercise. These recommendations will be consistent with recommendations that are routinely made by a primary care physician. Attempts to simultaneously initiate behavior changes on a number of dimensions may jeopardize efforts to promote adequate medication adherence. Therefore, systematic efforts to help a participant modify specific aspects of lifestyle that are relevant to the management of hypertension and renal disease will be undertaken only after adequate adherence to the pharmacological regimen has been established.

Adherence promotion resources

It can be generally recognized that patient adherence to a pharmacological regimen will be proportional to the level of resources allocated to adherence promotion activities. Just as some

patients require higher doses of medication to obtain the desired treatment effect, certain patients will require the allocation of more behavioral resources to obtain adequate levels of adherence. The proposed adherence promotion procedures are designed to emphasize the use of structured procedures that can be implemented on a more or less aggressive basis as dictated by patient presentation and behavioral resources. The structured procedures will ensure that the adherence promotion intervention is consistently applied study-wide while accommodating anticipated patient variability and existing differences in behavioral expertise.

6.10.3 Adherence Promotion Training and Certification

Overview

Effective implementation of adherence promotion strategies is dependent upon a working knowledge of specific communication techniques and behavioral interventions, and also requires the proficient application of these various skills. Training and certification for adherence promotion will be accomplished at two levels. Level I training will provide personnel with the knowledge base that is pre-requisite for adherence promotion. Level II training will utilize modeling and behavior rehearsal strategies to promote the development of communication skills and behavior management strategies that are addressed in the Level I adherence promotion knowledge base. Adherence promotion training will address the development of knowledge and skills relevant to the following areas:

PATIENT EDUCATION
Strategies: Medication instruction
Hypertension information

PERFORMANCE FEEDBACK
Strategies: Pill counts
Global self-report
Medication diaries
Self-monitoring blood pressure
Goal setting

SOCIAL SUPPORT
Strategies: Communication skills
Social reinforcement
Family support
Staff continuity

ENVIRONMENTAL CUES
Strategies: Reminder calls and cards
Daily routines and prompts

Level I Training and Certification

Level I adherence promotion training and certification must be successfully completed by all study personnel who have contact with participants. This can be accomplished at AASK Annual Training Sessions. Personnel unable to attend this training session will be able to obtain this information by reviewing self-study materials provided by the Recruitment and Compliance Subcommittees. A pre-test/post-test assessment format will be utilized in order to certify a working knowledge of key adherence promotion concepts and to evaluate the relative efficacy of the instructor-presented and self-study formats for adherence promotion training.

Level II Training and Certification

Level II adherence promotion training and certification will be conducted only at the AASK Training Session. This training will utilize modeling and behavioral rehearsal strategies to promote the development of communication skills and behavior management strategies. Personnel participating in this training will observe the application of adherence promotion strategies, rehearse participant interactions structured to promote adherence, and receive constructive feedback to improve adherence promotion skills. These activities will be structured to encourage the use of open-ended questions, reflective listening strategies, comments to reinforce adherence, summary statements intended to influence motivation to follow study protocol, and questions to elicit specific statements of intended adherence. Proficiency in these skills will be certified through successful performance of structured adherence promotion exercises.

6.10.4 Monitoring and Promoting Adherence

Overview

All staff interactions with study participants should be consistent with strategies that are presented in Level I adherence promotion training and rehearsed in Level II training. In addition to maintaining a general environment intended to promote adherence to all aspects of the study protocol, it will be important to establish a structured regimen of adherence-promoting activities for each participant. The regimen will be systematically reviewed with study participants at each appointment.

Behavioral adherence regimen

Participants will be expected to maintain a number of behaviors that will influence overall adherence to the study protocol. Each participant will be instructed to bring all anti-hypertensive medications to each appointment and maintain a blood pressure management diary. **Participants may be instructed to self-monitor their blood pressure as an optional component of the behavioral adherence regimen.** This behavioral regimen will be initiated at the onset of the **baseline phase** in order to help each participant develop a consistent pattern of adherence promoting behaviors.

It is important for participants to establish the habit of bringing medications to clinic visits during the baseline phase in order to effectively monitor adherence to randomized drugs during the follow-up phase. The blood pressure management diary is designed as an iconic prescription that illustrates the proper time and dose for prescribed medications. The diary is formatted to allow the entry of relevant information with minimal participant burden. Participants may be instructed in the use of equipment to measure blood pressure or can be instructed to identify locations in their community where blood pressure can be measured on a regular basis.

The performance of each of these health-related behaviors provides participants with an opportunity to practice following recommendations made by a health care professionals. In addition to serving as "adherence rehearsal", the regimen provides a structured format in which the participant can more clearly see the relationship between personal behavior (pill taking) and asymptomatic disease (blood pressure). Providing participants with constructive feedback about their performance of these health-related behaviors will have a direct influence on their adherence to prescribed medication regimens. Establishing this regimen will facilitate participant adherence to drug titration procedures during baseline and will enhance adherence to medication regimens at time of drug randomization.

Adherence criteria

Project staff will meet on a weekly basis to review the records of participants in order to identify potential adherence problems and establish proactive adherence promotion strategies. Adherence will be measured on a number of different dimensions in order to monitor participant performance adequately and initiate corrective action when a participant fails to maintain an acceptable level of adherence. A participant will be considered to fall below an acceptable adherence threshold if any of the following events occur:

1. Pill count shows that the participant took less than 80%**, or more than 110%** of prescribed medication.
2. The participant's blood pressure management diary contains entries for less than 80% of the prescribed doses.
3. The participant fails to bring **all study medications and** the blood pressure management diary to a scheduled appointment.

Adherence promotion procedures (Adherence Review Form 16)

Systematic adherence promotion procedures will be **initiated at randomization** in order to reinforce adequate levels of adherence, identify poor adherence, and establish specific strategies to increase adherence. These procedures include the following components: pill count, self-reported medication adherence, self-reported barriers to adherence, review of blood pressure management diary, structured feedback about performance, review of medication regimen, problem solving to establish or update adherence strategies, and specific goals for medication use and self-monitoring.

Adherence promotion procedures will be systematically conducted in a semi-structured interview format that is outlined in the Adherence Review Form. The form is designed to direct project personnel through critical aspects of the adherence promotion procedures. Thus completion of the Adherence Review Form will serve both as guide for conducting the interview and as a data collection instrument. The review form can be completed by any member of the project staff holding Level I certification for adherence promotion. Each participant will be assigned to a primary adherence manager for the purpose of maintaining continuity across all study contacts.

During the follow up, adherence promotion procedures will be conducted (i.e. the Adherence Review Form will be completed) during all routine protocol appointments beginning at FV2. Each primary adherence manager will complete at least 60% of the adherence review forms for assigned participants. A study physician will conduct adherence promotion procedures (i.e. completed the Adherence Review Form) with each participant at one of the first three baseline appointments. This proactive physician intervention is intended to maximize the influence of recommendations from a professional authority by presenting specific behavioral recommendations to participants while they are highly motivated to follow the study protocol and are most receptive to the introduction of behavioral strategies for adherence promotion.

Adherence Promotion Procedures

1. Drug Compliance Form #05, Blood Pressure Form #10, and Adherence Review Form #16 will be routinely administered at each protocol visit beginning at FV2.
2. Pill count procedures specified in Form #05 will be conducted during each protocol visit in order to calculate adherence rates that are used in the adherence promotion procedures. A range of adherence rates from 80% - 110% for their randomized study drug is defined as an acceptable level of medication adherence.
3. Mean arterial pressure (MAP), documented on Form #10, will be calculated during each protocol visit in order to make informed clinical decisions about the implementation of adherence promotion strategies.
4. Form #16 is an outline for a semi-structured interview that addresses the basic components of the adherence promotion procedures. The form contains decision algorithms that define standard procedures for adapting the content of the adherence promotion interview in response to a participant's clinical presentation.
5. Medications, dose schedules, and adherence promotion strategies will be written on the back of the patient's BP Management Self Monitoring Diary. The participant will also use the diary to self-monitor medication use. Recording self-monitored blood pressure measurements in the diary is optional.
6. When a participant consistently meets medication adherence and blood pressure criteria at three consecutive protocol visits, detailed evaluation of potential barriers to medication adherence and the active development of strategies to overcome identified barriers to medication use may be discontinued.

7. As long as a participant maintains an acceptable level of medication adherence and blood pressure control, and abbreviated interview will be conducted at each monthly protocol visit in order to provide the participant with structured feedback intended to maintain in long term adherence to the treatment regimen and to identify the development of adherence problems as soon as possible.
8. More extensive adherence promotion procedures will be initiated any time a participant fails to meet medication adherence or blood pressure criteria.
9. The individual responsible for managing a participant's medication regimen will be notified any time the participant fails to meets medication adherence or blood pressure criteria. Decisions to change the medication regimen will be informed by a review of the participant's adherence rates.
10. Personnel at each clinical center will meet on a regular basis to review protocol adherence, identify potential problems, and develop proactive strategies to minimize poor adherence.

Follow-up phone contact

During both baseline and follow-up phases, participants will be called 48 hours in advance of all scheduled appointments in order to review appointment time and location, and to identify and resolve any potential barriers. Any participant who fails to attend a scheduled appointment will be contacted within 24 hours of the missed appointment by his/her primary adherence manager in an attempt to reschedule the appointment within the allowed window. All phone interactions with the participant will utilize adherence promotion procedures consistent with those outlined on the Adherence Review Form #16.

During the follow-up phase the participants will be called within one week after each appointment in order to review goals and reinforce adherence. The caller will reinforce the participant for attending the previous appointment, review goals and adherence strategies specified at that appointment, remind the participant of the next scheduled appointment, identify anticipated barriers, and develop strategies to resolve identified barriers. Each primary adherence manager will complete at least 75% of the telephone contacts for assigned participants.

6.10.5 Strategies For Evaluating Adherence

The adherence promotion procedures that are being implemented in the AASK Study utilize a number of measures to evaluate participant adherence to the pharmacological regimens established by the study protocol (e.g. retrospective self-report, prospective self-monitoring, pill count). There are advantages and disadvantages associated with each of these measures and no single measure of adherence can be identified as a "gold standard" Adequate assessment of medication adherence can only be accomplished through the use of multiple measures that characterize various aspects of medication use habits.

A comprehensive battery of adherence measures will be used in the AASK Study in order to adequately evaluate medication use habits and promote adherence to pharmacological regimens established in the study protocol. This assessment battery incorporates a range of self-report and observational data that will be needed to interpret the AASK primary outcome data. Information obtained in the analysis of relationships among adherence measures and primary outcome measures will be used to refine adherence assessment and promotion strategies that will be implemented in the full-scale trial.

6.11 Lifestyle Modifications

6.11.1 Principles and Strategies

The goal of the AASK Study trial is to evaluate the efficacy of different pharmacologic treatment regimens and two different levels of blood pressure control in slowing the progression of renal disease in hypertensive African Americans with chronic renal insufficiency. However, certain lifestyle behaviors are recommended and are important in the general medical care of participants with hypertension and/or renal disease. These include attention to diet, moderate routine physical exercise, and the avoidance of tobacco and excessive ethanol intake. While these modifications will be recommended and encouraged, intensive instruction and assurance of compliance to these modifications is beyond the scope of this trial.

6.11.2 Fundamentals of Lifestyle Modification

Certain lifestyle behaviors that are considered cost effective for health improvement by both the Joint National Commission on Hypertension and the Healthy People 2000 Initiative will be encouraged when medically appropriate. Dietary modifications which are **favorable for blood pressure and overall cardiovascular health will be recommended-taking the renal function status into consideration**. Recommended modifications may include: 1) adjusting caloric intake to achieve a desired body weight 2) a sodium intake as estimated from the 24-hour urinary sodium excretion between 1.5 and 2 grams per day; 3) a potassium intake between 85-95 mEq per day and/or achieving a serum potassium between 3.5 and 5.5 mEq/l. Thus participants whose serum potassium is in the normal range (3.5 -5.5 mEq/L) will have a goal of a potassium intake of 85-95 mEq/day. However, participants whose serum potassium is outside the range of 3.5-5.5 mEq/L will have their potassium intake altered. Participants whose serum potassium is <3.5 mEq/L will have these potassium intake increased and participants whose serum potassium is greater than 5.5 mEq/L will have their potassium intake decreased; 4) a protein intake, as estimated from the 24-hour urinary urea appearance of 0.75 - 1.0 gram/kg/day 5) achieving a serum calcium level between 8.5-10.5 mg/dL; 6) achieving a serum phosphorus level between 2.5-4.5 mg/dL; 7) achieving a LDL cholesterol level <130 mg/dL; 8) alcohol consumption < 1 oz

per day; 9) moderate exercise of 30-45 minutes three times a week; and 10) the cessation of smoking. The primary objective with the lifestyle modification guidelines will be to encourage behavior change and to maintain that change. Within the scope of this study, efforts, although limited by personnel and time, should be made to promote compliance in the maintenance of these lifestyle modifications.

6.11.3 Materials and Equipment Necessary for Implementing Lifestyle Modification

6.11.3.1 Participant Data

Individual participant data should include: A) Current body weight, body mass index. B) Sodium, potassium, and protein intakes based on 24-hour urinary excretion of sodium, potassium and urea respectively. C) Fasting lipid profile. D) Serum calcium, phosphorous and potassium (see CBL Reports). E) History of alcohol and tobacco use, and exercise habits.

6.11.3.2 Lifestyle Modification Educational Materials

6.11.4 Lifestyle Modification Counseling/Assessment

6.11.4.1 Qualification of Study Personnel

Study personnel designated to implement the lifestyle modification must attend the training session at the Data Coordinating Center for instructions on how to use the individualized lifestyle modification plan and educational material. It is anticipated that this will take approximately one-two hours during the training session to familiarize the designated study personnel with these forms and lifestyle goals. Specifically, the study personnel designated at the clinical centers to implement the lifestyle modification guidelines are not required to have had any specialized training in nutritional sciences, menu planning, or in behavior modification.

6.11.4.2 The Environment

It is important that the atmosphere of the clinical setting as well as the attitudes of the study personnel work together to provide an environment that is comfortable and not intimidating to the AASK participants. Attention should be given to participant's privacy, confidentiality, and to a quiet counseling space where the designated study personnel can meet with the participant and his/her family as needed. Thus the study personnel designated for implementing the lifestyle modification should have a private counseling space free of telephone interruptions available to them. Data on the participant and space for filing and storing lifestyle modification data should be readily available. Scales to weigh the participant and measure height should be available.

6.11.4.3 Communication

Implementing of the lifestyle modifications will require communication between

multiple members of the study team. In particular, certain aspects of the lifestyle modification recommendations may be altered by the investigator based on new or ongoing active medical problems in the participant. Also, regularly scheduled staff meetings where the investigator and the multiple members of the study team can discuss the lifestyle modifications in an individual participant will enhance understanding of the importance of the lifestyle modifications and implementing them. Referral to participant's regular doctor or to a registered dietician is appropriate when multiple dietary modifications are needed or extra emphasis needs to be placed on compliance.

6.11.4.4 Schedule of Visits for Lifestyle Modification

The lifestyle modification counseling will occur at visits FV2 and every Protocol follow-up visit after FV2.

6.11.4.5 Preparation for Lifestyle Modification Visits

All data necessary to complete the individualized plan for lifestyle modification for each participant should be available. The individual plan for lifestyle modification will be completed prior to the participant's visit and reviewed by the study personnel.

6.11.4.6 Content of Lifestyle Modification Visit

At each of the scheduled lifestyle modification visits, Form #15 will be completed and reviewed by study personnel. Some participants may be outside the goal range in many of the lifestyle areas while others may be within goal in all areas (Section 6.2). Thus all participants should receive counseling and educational material in areas where they are outside the goal ranges (see Section 6.2) at least once during the study. This does not need to occur at each lifestyle modification visit and it is at the discretion of the study personnel at each clinical center whether or not to counsel and give educational material more than once during the Full-Scale Study to any participant. Form 15 will be completed at each scheduled lifestyle modification visit. At least at one visit during the study, the participant will be counseled and given educational material in areas where they are outside the goal ranges (see Section 6.2) the following will occur.

Lifestyle modification counseling may occur during the GFR visits (G-1, FV-3, FV6, at 3 month intervals thereafter, AND LAST FV) and at the randomization visit. Since the participant will be in the clinical center for approximately four hours during the GFR visit, ample time will be available for lifestyle modification counseling. The format for each lifestyle modification visit will vary depending on

which, if any, of the areas when the participant is outside goal ranges are chosen by the study personnel for counseling and the distribution of educational material in that area at that particular visit. Data from previous visits will be available to develop and update the individualized plan for lifestyle modification. For example, on the lifestyle modification visit that occurs during the FV-3 visit, the estimated sodium intake from the FV-2 visit urine collection will be available for review. During the lifestyle modification visit, the participant will be thanked for having all the necessary tests to complete the individualized plan for lifestyle modification. The individualized plan for lifestyle modification will be reviewed with the participant which will take approximately 5 to 20 minutes. The time required to review the individualized plan for lifestyle modification will vary with each participant and will depend in part on how many of the participant's values need modification. No form is needed. Lastly, if the participant needs to modify any of the lifestyle items, educational materials will be given and reviewed for each item at least once during the study. Review of this educational material with the participant will serve simply to ensure that the participant is able to read the material and understands the meaning of the material. If the participant has questions that go beyond the scope of the actual written material, such as specific dietary menu planning questions, or if it is deemed necessary by the investigator, the participant will be referred to dietitian or health educator for more detailed instructions. The study personnel who implement the lifestyle modification visit will simply review the general goals and guidelines outlined in the participant's individualized plan and educational material. It is anticipated that the review of the educational materials will take between 0 and 20 minutes depending upon the number of modifications required for an individual participant and which areas are addressed at any given visit. Study personnel will not provide in depth individualized counseling to the participant because of lack of training and time.

6.11.5 Compliance with Lifestyle Modification Recommendations

Compliance is an important objective of any lifestyle modification program. However, study personnel will not have the training or time to institute an aggressive program to ensure compliance to the lifestyle modification goals. It is anticipated that the individualized plan for lifestyle modification and the educational materials will provide information that can be utilized to comply with the goals. Since these visits will reoccur at about two month intervals, the repeated review of the lifestyle modification goals and the participant's deviation from those goals should help improve compliance with the dietary and lifestyle recommendations.

The multiple procedures required of participants in the AASK trial, along with the psychological burden associated with chronic renal disease, combine to produce an environment which may make it difficult to engage successfully in any active lifestyle

modifications. As a result, the management of compliance becomes a dynamic process. The study personnel's role are to help minimize the impact of the complex protocol requirements and to individualize the lifestyle modification program to facilitate compliance. The participant will only be given educational material related to the lifestyle(s) that need modification. At the same time the study personnel must remain sensitive to and integrate other factors which may be affecting the participant's overall motivation.