Modification of Diet in Renal Disease Study

Manual of Operations

Volume I, Chapter 4

Recruitment Coordinators' Chapter

October 1988

MDRD Manual of Operations

Volume I, Chapter 4

Recruitment Coordinators' Chapter

TABLE OF CONTENTS

APPENDICES

MANUAL OF OPERATIONS
Volume I, Chapter 4
Recruitment Coordinators' Chapter

Section 4.1 INTRODUCTION

The Recruitment Coordinator is a member of a multidisciplinary team involved in the MDRD Study. The coordinator will be a part of the team for approximately 21 months as a part-time position. The Recruitment Coordinator should be thoroughly familiar with all details of the Protocol, with appropriate chapters from Volume I of the Manual of Operations.

Section 4.2 RESPONSIBILITIES

The individual will be responsible for coordinating all patient recruitment activities in cooperation with the Principal Investigator and other MDRD team members. The functions include:

1. Medical Chart screening, including the retrieval from patient's charts of relevant information needed for completing screening forms
2. Interviewing physicians and patients to determine patient eligibility for study
3. Following up on all patient referrals or telephone inquiries about the MDRD Study
4. completing all forms required for recruitment
5. Maintaining logs of patient calls, and files and records on all aspects of recruitment
6. Preparing (composing) all necessary correspondence to referring professional and lay persons
7. Participating in local MDRD team meetings
8. Attending all necessary training meetings and study-wide meetings of recruitment personnel

Section 4.2 RESPONSIBILITIES

9. Using (interacting with) all forms of media (TV, newspaper, radio, mailing list, etc) as necessary to recruit patients

10. Making presentations before professional and lay groups

11. Developing materials (in addition to those provided by the national MDRD organization) for use in the local recruitment area

12. Monitoring recruitment goals for the clinical center and assisting the Principal Investigator in meeting these recruitment goals.

Section 4.3 QUALIFICATIONS

Each center will be required to assign the above responsibilities (duties) to an individual, who may presently be a member of the MDRD staff or who may be an individual hired for this position. It is recommended that this individual be a health professional who has experience with clinical trials, research studies and/or patient recruitment. It will be helpful for the individual to have computer knowledge, writing and presentation skills along with strong organizational abilities.

This position is most essential to the study, for the proper number of patients must be enrolled at each center; without participants, the data can not be collected to complete the study.

Section 4.4 CERTIFICATION

All Recruitment Coordinators must be certified in Forms Completion if they wish to complete any form other than Form 01, the Chart Screening Form.

(Additional certification requirements may be developed by NIH as part of a Recruitment Coordinator Training Session.)

Baseline Enrollment Quotas

Month *	Baseline Enrollment of Study A Patients Per Clinical Center	Baseline Enrollment of Study B Patients Per Clinical Center
JAN 1989	3	1
FEB 1989	6	2
MAR 1989	9	3
APR 1989	12	4
MAY 1989	15	5
JUN 1989	18	6
JUL 1989	21	7
AUG 1989	24	8
SEP 1989	27	9
OCT 1989	30	10
NOV 1989	33	11
DEC 1989	36	12
JAN 1990	39	13
FEB 1990	42	14
MAR 1990	45	15
APR 1990	48	16
MAY 1990	51	17
JUN 1990	54	
JUL 1990	57	
AUG 1990	60	
SEP 1990	End of Enrollment Period	

Protocol Requirements:

Overall, each center should enroll 77 patients into Baseline, 60 in the Study A range and 17 in the Study B range. Each center should randomize 53 patients for Follow-Up, 40 in Study A and 17 in Study B.

* Quotas are for the end of each month listed.

Randomization Quotas

Month *	Number of Study A Patients Randomized Per Clinical Center	Number of Study B Patients Randomized Per Clinical Center
JAN 1989	0	0
FEB 1989	0	0
MAR 1989	0	0
APR 1989	0	0
MAY 1989	2	1
JUN 1989	4	1
JUL 1989	6	2
AUG 1989	8	3
SEP 1989	10	3
OCT 1989	12	4
NOV 1989	14	5
DEC 1989	16	5
JAN 1990	18	6
FEB 1990	20	7
MAR 1990	22	7
APR 1990	24	8
MAY 1990	26	9
JUN 1990	28	9
JUL 1990	30	10
AUG 1990	32	11
SEP 1990	34	11
OCT 1990	36	12
NOV 1990	38	13
DEC 1990	40	13

Protocol Requirements:

Each clinical center should randomize 53 patients in Follow-Up, 40 in Study A and 13 in Study B. All patients must be enrolled in Baseline by September 30, 1990.

* Quotas are for the end of each month listed.

XXXXXXXXXXXXXXXX HOSPITAL
UNIVERSITY CITY, MYSTATE

CERTIFICATION OF SUBJECT CONSENT

MODIFICATION OF DIET IN RENAL DISEASE STUDY

Screening Phase

Principal Investigator: XXXXXXXXXX X. XXXXXXXXXX, M.D.

1. I have been told that I have kidney disease and that I may be eligible to participate in a clinical research study called the Modification of Diet in Renal Disease (MDRD) Study. The purpose of this research is to determine the effectiveness of a diet low in protein and phosphorus and of strict control of blood pressure in reducing the chances that my kidney disease will progress to the point where dialysis or a kidney transplant is needed. I have been told that I do not have to participate in this study. This research study is being carried out in 15 medical centers in the United States under the sponsorship of the National Institutes of Health (NIH) and the Health Care Financing Administration (HCFA).

2. I understand that to find out whether I am eligible to participate in this study I need to have some blood tests performed within the next month. This will require drawing blood from my arm 1 - 3 times. The total amount of blood that will be drawn will be about 2 ounces (4 tablespoonsful). When these tests are done, I will be told whether I am eligible for the study, and if not why not.

3. I understand that there is no risk from the drawing of blood except for the slight pain of the needle stick and the small chance that I will get a bruise from the needle. The study doctors will send copies of the test results to my regular doctor. These results may or may not be helpful in my care. The results of my tests will not be revealed to anyone else outside of the MDRD Study. In any case, I will not be charged for these tests.

4. I understand that if I am found to be eligible for the study, the study doctors will explain the study to me in much greater detail. I will then be asked to sign a second consent form, indicating my agreement to enter the study. If on the other hand, I am eligible but do not wish to participate in the study, I agree to have my regular doctor provide my blood sample results to the MDRD team or come to the MDRD Clinic to have a blood sample drawn on an annual basis.

5. I understand that I am free to decline to allow these extra blood and urine tests and to decline to participate in the study even if I am eligible. If I do not choose to participate, this will not in any way compromise my care by the doctors at this medical center or by my regular doctor. I am also free to end my participation at any time without affecting my care.

6. I understand that I have the right to ask questions at any time and that I should contact Dr. XXXXXXXXXXX at (XXX) XXX-XXXX, ext. XXXXX, for answers about the research and my rights. In addition, I may contact the Human Investigation Review Committee at (XXX) XXX-XXXX, ext. XXXXX to discuss my concerns.

7. I understand that I will not be paid anything for my participation in this study. In addition, there will be no compensation for a physical or psychological injury that might occur as a result of this study other than coverage of medical costs as discussed below. On the other hand, neither I nor my insurance company will be charged for any of the clinic visits or tests done as part of this study. These charges will all be paid for by NIH and HCFA.

8. I have read this consent form. Dr. _____ has discussed this study with me and has given me the opportunity to ask questions and to have them answered to my satisfaction. My signature below shows that I understand all of the above and that I freely and voluntarily consent to participate in the screening phase of this research study.

_____
Participant

I have fully explained to _____ the nature and purpose of the MDRD Study described in this consent form, including the risks that are involved in its performance. I have answered all questions to the best of my ability.

_____
Principal Investigator or Representative

_____ _____
Date Witness

XXXXXXXXXXXXXXXX HOSPITAL
UNIVERSITY CITY, MYSTATE

CERTIFICATION OF SUBJECT CONSENT

MODIFICATION OF DIET IN RENAL DISEASE STUDY

Follow-up Phase

Principal Investigator: XXXXXXXXXX X. XXXXXXXXXX, M.D.

1. I have been told that I have kidney disease. I have previously agreed to participate in the Baseline Phase of the Modification of Diet in Renal Disease (MDRD) Study. I have now been told that I am eligible to participate in the Follow-up Phase. I understand that the MDRD Study is a clinical research study to determine the effectiveness of a diet low in protein and phosphorus and of strict control of blood pressure in reducing the chances that my kidney disease will progress to the point where dialysis or a kidney transplant is needed. I have been told that I do not have to participate in this study.

2. I have been given a copy of the MDRD Study Information Handbook. I have read this handbook, and I have had my questions answered to my satisfaction. I now understand all the specific purposes of the study and the nature of a clinical trial. I understand that the Follow-up Phase of this study will last until the winter of 1993.

3. I understand that I may be assigned to Study A or Study B depending upon my kidney function. If my kidney filtering function is between about one half and one quarter of normal, I will be assigned to Study A, which will compare the effects of a diet composed of natural foods, but quite restricted in protein and phosphorus content (Diet L), with the effects of a diet having more normal amounts of protein and phosphorus (Diet M). If my kidney filtering function is less than one quarter of normal, I will be assigned to Study Group B, which will compare the effects of Diet L (as described above), with the effects of a diet even more restricted in protein and phosphorus, but supplemented with a mixture of essential ketoacids and amino acids, the building blocks of normal protein (Diet K). These diets have been described in the MDRD Study Information Handbook, which I have read.

4. I understand that I will be assigned to one of two diets, Diet M or L if I am assigned to Study A, or Diet L or K if I am assigned to Study B. The diet assignment will be made purely by chance by a process called randomization, which is like flipping a coin. I agree to do my best to follow my assigned diet during the entire Follow-up Period.

5. I understand that the possible advantages of the diets containing more protein are that there will be fewer restrictions in the foods that I can eat and that there is less risk of any nutritional deficiencies. The possible disadvantage is that, if reduction of dietary protein is shown to be effective, I will not have the benefit of a low protein diet. The risks and benefits of the lower protein diets are just the opposite. If a low protein diet is effective, my kidney disease may progress less than it

would have otherwise. On the other hand, it is possible that these diets may lead to deficiencies of protein, phosphorus, or other nutrients. The diet will be more restrictive than a normal diet and may be harder to follow. In either case, both my renal function and my nutritional state will be followed very carefully by the study doctors to be sure that any risks are minimized.

6. I understand that if I have a serious illness unrelated to my assigned diet, or if I have any serious problems related to my diet, I will no longer be asked to follow my assigned diet. Then my regular doctor will be free to choose whatever diet (s)he and I think will be best for me.

7. I understand that adequate blood pressure control is important for everyone, and especially for people with kidney disease. But it is not known what blood pressure target is best. This study will also compare the effects of two levels of blood pressure control. I understand that I will be assigned in the same way, purely by chance, either to a group in which the blood pressure is lowered to levels usually aimed for in patients with high blood pressure, or to group with stricter blood pressure control to achieve levels closer to the average value found in healthy people. These two blood pressure control regimens are described further in the MDRD Study Information Handbook.

8. I understand that the benefits of usual blood pressure control are that it has been used widely in thousands of patients and is generally well tolerated. However it may be that usual therapy, which accepts blood pressures higher than the average value in normal people, may permit kidney disease to progress faster than a blood pressure closer to the normal average. The risks and benefits of the stricter blood pressure are just the opposite. Lowering blood pressure to this level may give more protection to the kidneys of patients with existing kidney disease. But this degree of blood pressure lowering may be associated with symptoms of dizziness on standing, a sense of fatigue or weakness, or with excessive sleepiness. It may even be that in some patients kidney function will be poorer with lower blood pressure.

9. I understand that if I have a serious illness unrelated to my assigned blood pressure treatment, or if I have any serious problems related to my blood pressure treatment, I will no longer be asked to follow my assigned blood pressure. Then my regular doctor will be free to choose whatever blood pressure treatment (s)he and I think will be best for me.

10. I understand that there is no way for doctors to know now which of these proposed treatments for my kidney disease will be better, or to choose which will be better for me. It is the purpose of this study to answer these questions. But I understand that the progress of this study will be followed closely by a national board of experts, and that if one treatment is shown to be better than another, all study patients will be put on the better treatment. In addition, I will have tests periodically to check for any signs of nutritional deficiencies or problems related to blood pressure control.

11. For women: I understand that because of the potential risks to an unborn child of some of the study procedures as well as the protein and phosphorus restricted diets, I should not continue to participate in the study if I become pregnant. I am not now planning to get pregnant before the end of the study in the winter of 1993. I agree to report any missed menstrual period or symptoms of pregnancy (such as "morning sickness," breast tenderness, unusually short or light menstrual period) immediately to the study physician. If pregnancy is confirmed then I will be immediately withdrawn from the study, and my regular doctor will prescribe the diet and other therapy (s)he thinks is best for me.

12. If for any reason I am released from my diet or blood pressure goal assignment, I will still be asked to visit the study clinic every four months to see the study dietitian and physician until the national study is completed. At those visits a blood sample will be drawn to measure my kidney function and nutritional state. A GFR test will also be performed if you are not on dialysis or have not received a kidney transplant.

13. I agree to visit the clinic monthly until the end of the study. I also agree to visit the clinic for two additional visits with the study dietitian at the beginning of the follow-up period. I will be seen each time by the study doctor and team to evaluate my diet, my blood pressure, my kidney function, my general nutritional state, and my sense of well-being. I understand and specifically give my consent for the following: The study doctor will take a brief history and do a physical examination, and the nurse will measure my blood pressure at each visit. My blood pressure will be carefully controlled to my assigned target, set as described in the MDRD Study Information Handbook. The study dietitian will ask me about my diet, chosen as described above, and will make suggestions to make it easier for me to follow my diet. On some days I will have to keep accurate records of all the food that I eat. I will have blood drawn for tests every other month and will have to bring in complete 24 hour urine collections each month. An electrocardiogram will be done twice a year. This information may be useful to me and my regular doctor. Periodically I will complete questionnaires asking how I feel about my diet and any symptoms that I might have. I will be phoned at home to ask about my general sense of well-being. This phone interview will be tape recorded. There is no risk from any of these procedures other than the possibility of bruising at the place where blood has been drawn.

14. I understand that, in addition to the above, I will have a special test performed, called a GFR test, which measures the filtering ability of my kidneys very accurately. This test will be done four times in the first year and three times a year thereafter. A small amount of a radioactive substance will be injected under the skin of my arm, I will be asked to drink lots of water, and then six blood samples will be drawn and six timed urine collections will be obtained. The blood samples are taken through a small tube inserted into a vein by a needle stick, so that this test will require only one needle stick. The radiation exposure that I will receive from this test is less than I would get from a chest X-ray. It is very unlikely that this amount of radiation will have any harmful effect, though the long term effects of very low levels of radiation such as this are not completely known.

FOR WOMEN: I understand that it is important for me not to have the GFR test if I am pregnant, because even the low level of radioactivity that I would be exposed to might be harmful to my unborn child. Therefore if I am of an age where pregnancy is possible, a pregnancy test will be done before each GFR test. I agree also to report any missed periods or other symptoms of pregnancy such as morning sickness or breast tenderness to the study doctor.

15. I understand that my identity and all the medical records of my participation in this study will be kept confidential. I am aware that a qualified representative of the NIH or of the Food and Drug Administration may inspect these research records. In any reports or publications no results or information identifiable with specific individuals will be discussed. I understand that my social Security or Medicare numbers will be recorded to help the MDRD Study team and HCFA find out if I have been hospitalized or have gone onto dialysis or received a transplant.

16. I understand that I am free to decline to participate in the study. If I do not choose to participate, this will not in any way compromise my care by the doctors at this medical center or by my regular doctor. I am also free to end my participation at any time without affecting my care.

17. I understand that I have the right to ask questions at any time and that I should contact Dr. XXXXXXXXXXX at (XXX) XXX-XXXX, ext. XXXXX, for answers about the research and my rights. In addition, I may contact the Human Investigation Review Committee at (XXX) XXX-XXXX, ext. XXXXX to discuss my concerns.

18. I understand that I will not be paid anything for my participation in this study. In addition, there will be no compensation for a physical or psychological injury that might occur as a result of this study other than coverage of medical costs as discussed below. On the other hand, neither I nor my insurance company will be charged for any of the clinic visits or tests done as part of this study, nor for the vitamin and calcium supplements provided. These charges will all be paid for by NIH and HCFA. Costs of blood pressure medications (except for enalopril) or any other drugs will not be paid for. HCFA will also pay any other medical costs directly related to my kidney disease during my participation in this study, or to any medical complications of my treatment in this study that are not payable by other third party payers (insurance companies). Payment will only be made for services provided by the clinic participating in the MDRD Study, or by others under arrangement with that clinic.

19. I have read this consent form and the MDRD Study Information Handbook. Dr. _____ has discussed this study with me and has given me the opportunity to ask questions and to have them answered to my satisfaction. My signature below shows that I understand all of the above and that I freely and voluntarily consent to participate in this research study.

_____
Participant

I have fully explained to _____ the nature and purpose of the MDRD Study described in this consent form, including the risks that are involved in its performance. I have answered all questions to the best of my ability.

_____
Principal Investigator or Representative

_____ _____
Date Witness

XXXXXXXXXXXXXXXX HOSPITAL
UNIVERSITY CITY, MYSTATE

CERTIFICATION OF SUBJECT CONSENT

MODIFICATION OF DIET IN RENAL DISEASE STUDY

Baseline Phase

Principal Investigator: XXXXXXXXXX X. XXXXXXXXXX, M.D.

1. I have been told that I have kidney disease and that I may be eligible to participate in a clinical research study called the Modification of Diet in Renal Disease (MDRD) Study. The purpose of this research is to determine the effectiveness of a diet low in protein and phosphorus and of strict control of blood pressure in reducing the chances that my kidney disease will progress to the point where dialysis or a kidney transplant is needed. I have been told that I do not have to participate in this study. This research study is being carried out in 15 medical centers in the United States under the sponsorship of the National Institutes of Health (NIH) and the Health Care Financing Administration (HCFA).

2. I have been given a copy of the MDRD Study Information Handbook. I have read this handbook, and I have had my questions answered to my satisfaction. I now understand all the specific purposes of the study and the nature of a clinical trial.

3. I understand that by signing this form I show my agreement to enter the Baseline Period of the study, which will last for three to five months. During this period I agree to visit the clinic monthly, where I will be seen by the study doctor and team to evaluate my diet, my blood pressure, my kidney function, my general nutritional state, and my sense of well-being. I agree to visit the clinic for two additional appointments with the dietitian.

4. I understand and specifically give my consent for the following: The study doctor will perform a complete medical history and physical examination at the first visit, and the nurse will measure my blood pressure at each visit. My blood pressure will be carefully controlled. The study dietitian will ask me about my usual diet and will prescribe a diet very similar to my usual diet. On some days I will have to keep accurate records of all the food that I eat. I will have blood drawn for tests on three occasions and will have to bring in complete 24 hour urine collections on four occasions. An electrocardiogram will be done. This information may be useful to me and my regular doctor. I will complete questionnaires asking how I feel about my diet, any symptoms that I might have, and about my general sense of well-being. I will be phoned at home to answer a well-being questionnaire. There is no risk from any of these procedures other than the possibility of bruising at the place where blood has been drawn.

5. I understand that, in addition to the above, I will have a special test called a GFR test performed. This test measures the filtering ability of my kidneys very accurately, and will be done twice in the Baseline Period. A small amount of a radioactive substance will be injected under the skin of my arm, I will be asked to drink lots of water, and then six blood samples will be drawn and six timed urine collections will be obtained. The blood samples are taken through a small tube inserted into a vein by needle stick, so that this test will require only one needle stick. The radiation exposure that I will receive from this test is less than I would get from a chest X-ray. It is very unlikely that this amount of radiation will have any harmful effect, though the long term effects of very low levels of radiation such as this are not completely known.

   FOR WOMEN: I do not plan to get pregnant during the study. I understand that it is important for me not to have the GFR test if I am pregnant, because even the low level of radioactivity that I would be exposed to might be harmful to my unborn child. Therefore, if I am of an age where pregnancy is possible, a pregnancy test will be done before each GFR test. I agree also to report any missed periods or other symptoms of pregnancy such as morning sickness to the study doctor.

6. I understand that at the end of this Baseline Period I will be told whether I am eligible to enter the Follow-up Period of the Study. If I am eligible I will be asked to sign a third consent form for entry into the Follow-up Period, which is described in the MDRD Study Information Handbook, and which will be described in detail at that time. If I am not eligible, I will be told why. If I turn out not to be eligible, I agree to either have my regular doctor provide my blood sample results to the MDRD team or come to the MDRD Clinic every four months and to have a blood sample drawn at those visits.

7. I understand that my identity and all the medical records of my participation in this study will be kept confidential. I am aware that a qualified representative of the NIH or of the Food and Drug Administration may inspect these research records. In any reports or publications no results or information identifiable with specific individuals will be discussed. I understand that my social Security or Medicare numbers will be recorded to help the MDRD Study team and HCFA find out if I have been hospitalized or have gone onto dialysis or received a transplant.

8. I understand that I am free to decline to participate in this study. If I do not choose to participate, this will not in any way compromise my care by the doctors at this medical center or by my regular doctor. I am also free to end my participation at any time without affecting my care.

9. I understand that I have the right to ask questions at any time and that I should contact Dr. XXXXXXXXXXX at (XXX) XXX-XXXX, ext. XXXXX, for answers about the research and my rights. In addition, I may contact the Human Investigation Review Committee at (XXX) XXX-XXXX, ext. XXXXX to discuss my concerns.

10. I understand that I will not be paid anything for my participation in this study. In addition, there will be no compensation for a physical or psychological injury that might occur as a result of this study other than coverage of medical costs as discussed below. On the other hand, neither I nor my insurance company will be charged for any of the clinic visits or tests done as part of this study, nor for the vitamin and calcium supplements provided. These charges will all be paid for by NIH and HCFA. HCFA will also pay any other medical costs directly related to my kidney disease during my participation in this study, or to any medical complications of my treatment in this study that are not payable by other third party payers (insurance companies). Payment will only be made for services provided by the clinic participating in the MDRD Study, or by others under arrangement with that clinic.

11. I have read this consent form and the MDRD Study Information Handbook. Dr. _____ has discussed this study with me and has given me an opportunity to ask questions and to have them answered to my satisfaction. My signature below shows that I understand all the above and that I freely and voluntarily consent to participate in this research study.

_____
Participant

I have fully explained to _____ the nature and purpose of the MDRD Study described in this consent form, including the risks that are involved in its performance. I have answered all questions to the best of my ability.

_____
Principal Investigator or Representative

_____ _____
Date Witness

MODIFICATION OF DIET IN RENAL DISEASE STUDY
INFORMED CONSENT FORM FOR ENTRY INTO STUDY C

Institution:
Principal Investigator:

1. I have volunteered as a study for the Modification of Diet in Renal Disease Study (MDRD). I completed the Baseline Period, and I was assigned to Study Group A on the basis of my kidney function and then randomized to Diet M or L and either a moderate or low mean arterial blood pressure goal. During the Follow-up Period my kidney disease worsened to a predetermined level of severity such that I am now withdrawn from the study.

2. I have been told that I am eligible to enter a separate study, Study C. The purpose of this study is to determine whether patients with progressive kidney disease whose kidney function has been shown to worsen on a diet with moderate or low protein and phosphorus content might benefit from eating a diet with less protein and phosphorus and supplemented with a mixture of essential amino acids and keto acid analogues (Diet K). Specifically, Study C is being conducted to answer the following questions:

   A. Can dietary protein and phosphorus restriction supplemented with a mixture of essential amino acids and keto acid analogues slow or stop the progressive loss of kidney function in patients with chronic kidney disease?

   B. Is this diet safe?

   C. Is this reduction in dietary protein and phosphorus with supplementation practical? In other words, can patients control their diets and change their eating habits in this way for the "long run"?

   D. Will lowering blood pressure slow or stop the progressive loss of kidney function in patients with kidney disease?

   E. Does strict blood pressure control increase side effects from the medication?

3. I have been given a copy of the MDRD Study Information Handbook. I have read this handbook, and I have had my questions answered to my satisfaction. I now clearly understand the following:

   A. My participation in Study C will last until the winter of 1993.

   B. At the beginning of Study C I will be assigned to Diet K with a very low protein and phosphorus content supplemented with keto acid/amino acid supplements.

   C. I will continue to receive blood pressure therapy as needed to achieve the control target I was assigned to when initially randomized. I understand that if I have a serious illness unrelated to my assigned blood pressure treatment, or if I have any

C. (continued)
serious problems related to my blood pressure treatment, I will no longer be asked to follow my assigned blood pressure. Then my regular doctor will be free to choose whatever blood pressure treatment (s)he and I think will be best for me.

D. A daily vitamin and mineral supplement will be provided free of charge.

E. The possible benefits and risks of the diet and blood pressure medications have been explained to me.

i. Diet K: The potential benefit of eating this diet is the possible increased chance of slowing or stopping the progression of my kidney disease. The keto acid/amino acid supplements are intended to prevent protein malnutrition.

Reduced protein and phosphorus diets with keto acid/amino acid supplements similar to Diet K have been tested in patients with chronic kidney disease and have been found safe when used up to 4 years. However, it is possible that this diet when followed for long periods may lead to nutritional deficiencies of protein, phosphorus, vitamins, minerals or other substances. To date, there are no known risks specifically associated with the use of keto acid/amino acid supplements except for the unpleasant taste and odor. Diet K may result in weight loss or gain, and there my be an increased risk of developing high blood sugar and/or fat levels. It is also possible that the course of my kidney disease will not be changed by following this diet.

ii. The benefits of usual blood pressure control are that it has been used widely in thousands of patients and is generally well tolerated. However it may be that usual therapy, which accepts blood pressures higher than the average value in normal people, may permit kidney disease to progress faster than a blood pressure closer to the normal average. The risks and benefits of the stricter blood pressure are just the opposite. Lowering blood pressure to this level may give more protection to the kidneys of patients with existing kidney disease. But this degree of blood pressure lowering may be associated with symptoms of dizziness on standing, a sense of fatigue or weakness, or with excessive sleepiness. It may even be that in some patients kidney function will be poorer with lower blood pressure.

iii. There is no way for doctors to know now which of these proposed treatments for your kidney disease will be better, or to choose which will be better for you. It is the purpose of this study to answer these questions. But the progress of this study will be followed closely by a national board of experts. If one treatment is shown to be better than another, all study patients will be offered the better treatment. In addition, you will have tests periodically to check for any signs of nutritional deficiencies or problems related to blood pressure control.

F. **FOR WOMEN:** I understand that because of the potential risks to an unborn child of some of the study procedures as well as the protein and phosphorus restricted diets, I should not continue to participate in the study if I become pregnant. I am not now planning to get pregnant before the end of the study in 1993. I agree to report any missed menstrual period or symptoms of pregnancy (such as "morning sickness," breast tenderness, unusually short or light menstrual period) immediately to the study physician. If pregnancy is confirmed then you will be immediately withdrawn from the study, and your regular doctor will prescribe the diet and other therapy (s)he thinks is best for me.

G. I agree to visit the clinic monthly until the end of the study. I also agree to visit the clinic for two additional visits with the study dietitian at the beginning of the follow-up period. I will be seen each time by the study doctor and team to evaluate my diet, my blood pressure, my kidney function, my general nutritional state, and my sense of well-being. I understand and specifically, give my consent for the following: The study doctor will take a brief history and do a physical examination, and the nurse will measure my blood pressure at each visit. My blood pressure will be carefully controlled to my assigned target, set as described in the MDRD Study Information Handbook. The study dietitian will ask me about my diet and will make suggestions to make it easier for me to follow my diet. On some days I will have to keep accurate records of all the food that I eat. I will have blood drawn for tests every other month and will have to bring in complete 24 hour urine collections each month. An electrocardiogram will be done twice a year. This information may be useful to me and my regular doctor. Periodically, I will complete questionnaires asking how I feel about my diet and any symptoms that I might have. I will be phoned at home to ask about my general sense of well-being. There is no risk from any of these procedures other than the possibility of bruising at the place where blood has been drawn.

H. I understand that in addition to the above, I will have a special test performed, called a GFR test, which measures the filtering ability of kidneys very accurately. This test will be done at most four times a year. A small amount of a radioactive substance will be injected under the skin of my arm, I will be asked to drink lots of water, and then six blood samples will be drawn and six timed urine collections will be obtained. The blood samples are taken through a small tube inserted into a vein by a needle stick, so that this test will require only one needle stick. The radiation exposure that I will receive from this test is less than I would get from two chest X-rays. It is very unlikely that this amount of radiation will have any harmful effect, though the long term effects of very low levels of radiation such as this are not completely known.

FOR WOMEN: I understand that it is important for me not to have the GFR test if I am pregnant, because even the low level of radioactivity that I would be exposed to might be harmful to my unborn child. Therefore if you are of an age where pregnancy is possible, a pregnancy test will be done before each GFR test. You should also report any missed periods or other symptoms of pregnancy such as morning sickness to the study doctor.

I. If for any reason I am released from my diet or blood pressure goal assignment, I will still be asked to visit the study clinic every four months to see the study dietitian and physician until the national study is completed. At those visits a blood sample will be drawn to measure my kidney function and nutritional state. A GFR test will also be performed if I am not on dialysis and have not received a kidney transplant.

4. I understand that my identity and all the medical records of my participation in this study will be kept confidential. I am aware that a qualified representative of the NIH or of the Food and Drug Administration may inspect these research records. In any reports or publications, no results or information identifiable with specific individuals will be discussed. I understand that my Social Security or Medicare numbers will be recorded to help the MDRD Study team and HCFA find out if I have been hospitalized or have gone onto dialysis or received a transplant.

5. I understand that I am free to decline to participate in the study. If I do not choose to participate, this will not in any way compromise my care by the doctors at this medical center or by my regular doctor. I am also free to end my participation at any time without affecting my care.

6. I understand that I have the right to ask questions at any time and that I should contact Dr. XXXXXXXX at (XXX)-(XXXX), ext. XXXX, for answers about the research and my rights. In addition, I may contact the Human Investigation Review Committee at (XXX) XXX-XXXX, ext. XXXX to discuss my concerns.

7. I understand that I will not be paid anything for my participation in this study. In addition, there will be no compensation for a physical or psychological injury that might occur as a result of this study other than coverage of medical costs as discussed below. On the other hand, neither I nor my insurance company will be charged for any of the clinic visits or tests done as part of this study, nor for the vitamin and calcium supplements provided. These charges will all be paid for by NIH and HCFA. HCFA will also pay any other medical costs directly related to my kidney disease during my participation in this study, or related to any medical complications of my treatment in this study that are not payable by other third party payers (insurance companies). Payment will only be made for services provided by the clinic participating in the MDRD Study, or by others under arrangement with that clinic.

8. I have read this consent form and the MDRD Study Information Handbook. Dr. _____ has discussed this study with me and has given me the opportunity to ask questions and to have them answered to my satisfaction. My signature below shows that I understand all of the above that I freely and voluntarily consent to participate in this research study.

_____
Participant

I have full explained to _____ the nature and purpose of the MDRD Study described in this consent form, including the risks that are involved in its performance. I have answered all questions to the best of my ability.

_____
Principal Investigator

_____ _____
(Date) Witness