PREVENTION AND TREATMENT OF HYPERTENSION STUDY (PATHS)
VETERANS AFFAIRS COOPERATIVE STUDY #996

A Collaborative Program of the NHLBI, NIAAA, and the
VA Cooperative Studies Program

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January 1991

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ABSTRACT

Alcohol consumption of three or more drinks per day has been recognized as an important correlate of blood pressure in many epidemiologic studies, but few interventional studies have been conducted to examine the effect of a reduction in alcohol intake on blood pressure, and these have been of insufficient size or duration to allow definitive conclusions. Therefore, in collaboration with the National Heart, Lung and Blood Institute (NHLBI) and the National Institute on Alcohol Abuse and Alcoholism (NIAAA) we plan to conduct a prospective randomized controlled VA cooperative study to determine whether blood pressure is lowered over six months of alcohol moderation in nondependent heavy drinkers (three or more drinks per day average) with above average normal (80-89 mm Hg) and mildly hypertensive (90-99 mm Hg) levels of diastolic blood pressure, and to determine whether a reduction in alcohol intake can be maintained for two years. During the first 1.5 years, the study will be initiated (Phase I) at four VA medical centers in order to assess recruitment and alcohol intake reduction success: 116 veterans meeting the entry criteria will be randomized to either an alcohol reduction intervention group or a control observation group. If recruitment and the intervention technique are judged to be successful, then three additional centers will be added in order to randomize 464 additional participants in the seven centers, and complete the study in 3.5 additional years (Phase II), for a total of 580 participants and five years duration. Alcohol intake will be monitored by self-reports using a retrospective diary (Chronological Drinking Record) and by various biochemical markers, such as apolipoproteins, HDL cholesterol, and carbohydrate deficient transferrin, which will be analyzed at a central laboratory. The alcohol intervention technique uses a cognitive - behavioral approach and will be overseen by the NIAAA. Echocardiograms will be performed to assess the effects of blood pressure and alcohol intake changes on left ventricular mass, and will be monitored and analyzed in a central laboratory. Personnel will include a data collector, an interventionist for the alcohol intervention, and a secretary. Separate offices in different locations will be necessary for data collection and intervention sessions.

I. INTRODUCTION

Pharmacologic therapy of hypertension has been demonstrated to lower blood pressure effectively and to reduce all-cause mortality and certain hypertensive complications, such as stroke and congestive heart failure.[1] However, there is concern that antihypertensive medications may have adverse effects that lessen or offset the potential benefits of blood pressure reduction.[2] In addition, antihypertensive medications are not considered an appropriate modality for the prevention of hypertension for a variety of reasons, including cost, the detrimental effects of labeling individuals as having an illness, and the potential adverse effects. Therefore, various nonpharmacologic modalities are being explored for both the prevention and treatment of hypertension.[3]

The initial identification of potential nonpharmacologic interventions for prevention or treatment of hypertension usually emanates from epidemiologic associations. In recent years, alcohol consumption has been recognized as an important independent correlate of blood pressure in many populations, both in the United States and throughout the rest of the world. Of more than 30 cross-sectional epidemiologic studies, the overwhelming majority reported significant elevations in blood pressure in individuals consuming an average of at least three standard drinks per day compared to nondrinkers.[4] [A standard drink contains approximately 14 grams (18 ml) of ethanol and is defined as 12 oz. of beer, 5 oz. of table wine, or 1.5 oz. of distilled spirits.] This relationship generally persists even when controlling for known confounding variables such as age, body mass and smoking.[4,5] The consumption of at least three drinks per day has been estimated to account for 11% of all cases of hypertension in men and for a smaller proportion in women because of their lower alcohol intake.[6,7] On this basis, it can be estimated that as many as three million men in the United States, many of whom are veterans, have elevated blood pressure as a consequence of their consumption of alcohol.[8] Among the known potentially modifiable risk factors for hypertension in men, alcohol is second only to obesity in its observed contribution to the prevalence of hypertension.[9]

These cross-sectional epidemiologic studies suggest that interventions to decrease alcohol consumption have the potential to produce important reductions in blood pressure. Some support for this suggestion derives from prospective observational studies, indicating that reduction in alcohol consumption was associated with reduction in blood pressure,[10,11,12] and from inpatient studies of alcoholics, indicating that detoxification often results in a fall in blood pressure.[13,14]

Further evidence is provided by the results of several short-term crossover studies comparing low alcohol intake or abstinence to high alcohol intake. Potter and Beevers[15] reported that systolic blood pressure was 13 mm Hg lower and diastolic blood pressure was 5 mm Hg lower after 3-4 days of abstinence versus an average of 61 grams/day in a study in 16 moderate hypertensives. Malhotra et al.[16] in a study of five days of an average of 58 grams per day followed by five days of abstinence demonstrated no significant decrease in blood pressure in

10 normotensives, but, in 20 hypertensives, they observed a significant reduction in blood pressure of 12 mm Hg systolic and 6 mm Hg diastolic. Howes[17] reported that systolic blood pressure was 8 mm Hg lower and diastolic blood pressure was 6 mm Hg lower after four days of abstinence compared to four days of an average of 80 grams/day in a randomized crossover study of normotensives. In another randomized crossover study conducted by Puddey et al.,[18] 46 normotensive men drank an average of 61 grams/day in one six-week period and an average of 9.6 grams/day in another six week period; the difference in systolic (3.8 mm Hg, $p<0.01$), but not diastolic (1.6 mm Hg), blood pressure was significant. When the same investigators performed a similarly designed study (65 g vs 9 g per day) in 44 treated hypertensives (baseline diastolic BP 85 mm Hg), they found both systolic (5 mm Hg) and diastolic (3 mm Hg) blood pressure to be significantly lower ($p<0.001$) on the lower alcohol intake.[19] The average net reductions in blood pressure observed in these studies ranged from 3-13 mm Hg for systolic pressure (5-13 mm Hg in hypertensives) and from 1-6 mm Hg for diastolic pressure (3-6 mm Hg in hypertensives), for differences in alcohol intake of 3 1/2 to 6 drinks per day.

The short-term results of these intervention trials are, therefore, encouraging and suggestive of a therapeutic benefit of lowering alcohol intake in hypertensives and a preventive effect in normotensives. These studies and the epidemiologic data have led to recommendations to limit alcohol intake to control hypertension.[20] However, the intervention studies have been too small (10-48 persons) and the follow-up intervals too short (three days to six weeks) to allow definitive conclusions to be drawn about the preventive and therapeutic effects of a reduction in alcohol intake. In addition, even a short-term randomized controlled trial of alcohol moderation or abstention in untreated hypertensives has not been reported. For these reasons, a randomized controlled trial of moderate size and with long-term follow-up in moderate to heavy, nondependent drinkers is needed to determine whether sustained reductions in alcohol consumption will lead to a lower blood pressure, both short-term and with long-term follow-up.

The long-term modification of alcohol consumption in heavy, nondependent drinkers has received increasing attention since the 1970s. Prior to that time the treatment of problem drinkers was almost exclusively aimed at a goal of total abstinence. Over the past 15 years, work by Marlatt and his colleagues and other research groups has demonstrated the effectiveness of cognitive - behavioral interventions in moderating drinking in heavy drinking populations.[21] One important component in these interventions entails the training of individuals in basic self-control procedures including self-monitoring and the functional analysis of drinking behavior. Miller et al.[22] reported that problem drinkers treated by behavioral self-control training showed significant decreases in drinking which were maintained at a three-month follow-up by 70 percent of the clients. Mean consumption levels at baseline decreased from 80 grams to 54 grams of ethanol at termination and were maintained at three-month follow-up. Sanchez-Craig[23] describes a brief intervention program in which participants are taught to identify risk situations, to develop cognitive and behavioral coping skills, and to monitor their behavior. In a study of 70 early-stage problem drinkers, Sanchez-Craig et al. found a reduction in mean daily alcohol consumption from 100 g to

approximately 25 g over six months of follow-up. The reduction in consumption appeared to be maintained for a further 18 months.[24]

Based on the need for a trial of sufficient size and duration to determine the effects of alcohol reduction on blood pressure and the recent experience with interventional modalities in nondependent drinkers, we propose a randomized prospective VA cooperative study of alcohol moderation in nondependent moderate to heavy drinkers. Alcohol is responsible for considerable morbidity and mortality among the veteran population in the United States, and the cost to the Department of Veterans Affairs for treatment of alcohol-related problems is substantial. Alcoholism is twice as prevalent among male veterans compared to nonveterans of the same age, and alcoholism and alcohol-related disorders are among the most frequent reasons for admission to VA medical centers.[25,26] It is therefore likely that, even though they may not be alcohol dependent, more veterans drink excessively compared to their nonveteran contemporaries. Therefore, we believe it is appropriate to test the alcohol-blood pressure hypothesis within VA as a multicenter cooperative trial.

In summary, a clinical trial of the reduction of alcohol intake in lowering blood pressure will permit assessment of the effects of a nonchemical intervention which may prove useful in the treatment of a significant risk factor affecting the nation's health. This study may also provide information about the dose related effects of alcohol on blood pressure and left ventricular mass; compliance with a behavioral intervention to reduce alcohol intake; and the refinement of biochemical markers of alcohol intake.

II. OBJECTIVES OF THE STUDY

A. Primary Objectives

1. To determine whether systolic and diastolic blood pressure are lowered after six months of alcohol moderation compared to no intervention in nondependent moderate to heavy drinkers with diastolic blood pressure between 80 and 99 mm Hg.

2. To determine whether systolic and diastolic blood pressure are lowered independently in the mildly hypertensive stratum (90-99 mm Hg diastolic) over six months.

3. To determine whether a reduction in alcohol intake can be achieved at six months and can be maintained for two years.

B. Secondary Objectives

1. To determine whether a dose response relationship exists between blood pressure change and changes in self-reported alcohol intake and/or biochemical markers of alcohol intake, controlling for weight, heart rate, exercise, urinary sodium and potassium, and dietary intake of calcium and other nutrients, in each treatment group and in both groups combined.

2. To determine whether there is a difference between the treatment and control groups in terms of echocardiographic left ventricular mass changes at six months compared to baseline, and to determine whether a dose response relationship exists between changes in blood pressure, self-reported alcohol intake and/or biochemical markers of alcohol intake and changes in left ventricular mass.

3. To determine if drug treatment for hypertension is required at a lower rate in the intervention group compared to the control group over two years.

4. To determine the relationship between changes in self-reported alcohol intake (by retrospective diary) and changes in the following biochemical markers: apolipoprotein A_1 and A_2, HDL (and HDL_2 and HDL_3) cholesterol, gamma glutamyltransferase (GGT) and carbohydrate-deficient transferrin (CDT).

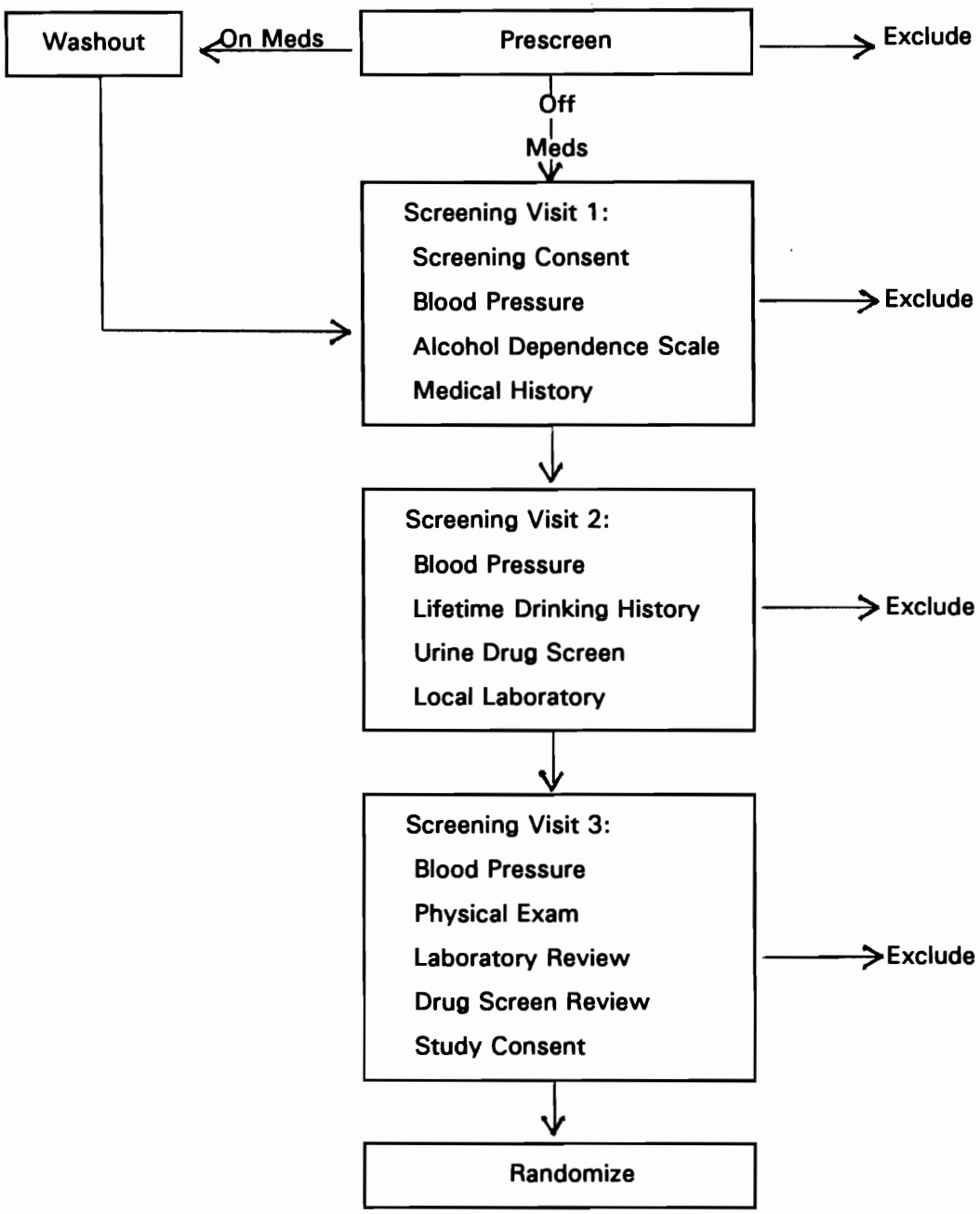
III. STUDY DESIGN

This is a prospective, randomized, parallel study comparing the effects on blood pressure and other end points of an intervention to produce alcohol moderation versus nonintervention in nondependent moderate to heavy drinkers ($\geq$21 drinks/week) with upper normal (80-89 mm Hg) and mildly hypertensive (90-99 mm Hg) levels of diastolic blood pressure off antihypertensive medications. The screening process is summarized in Figure 1 and is described in detail in Section VI. Ambulatory male and female veterans who are considered potential participants, primarily based on a brief self-administered prescreening questionnaire, will be invited to attend three screening visits. If they are on antihypertensive medications prior to entry into the study, these medications will be discontinued before beginning the screening phase (see Section VI.D). Baseline evaluations during this phase will include: medical history; blood pressure, weight and heart rate determinations; physical examination; local and central laboratory studies; psychosocial and health habits assessment; dietary and physical activity assessments; assessment of alcohol intake and alcohol dependence; and echocardiogram. Participants meeting the inclusion criteria will be randomized either to an intervention to reduce alcohol intake (to no more than 14 drinks per week and at least 50 percent less than the baseline level) or to a control condition. All participants will be followed for two years. If blood pressure exceeds certain safety criteria, open treatment of hypertension will be initiated, but the participant will remain in the study (see Section IV.B).

FIGURE 1

Flow Diagram for Screening

(Inclusion/Exclusion Procedures)



Due to the behavioral nature of the alcohol intervention, an open design is required. Those participants randomized to the control group will be scheduled for data collection visits only. Because of this design feature, particular care will be taken to maintain blindness to intervention assignments among clinic personnel involved in collecting the primary study data common to both groups. To avoid differences in response to the BP measurement environment, data collection will take place in the same location for both randomization groups, and participants in the alcohol intervention group will be seen in a different location for the intervention sessions. Data collection visits will be at monthly intervals for the first six months and quarterly for the remaining 18 months. Data collection at each visit is indicated in Table 1.

Table 1

Data Collection Schedule

	VISIT															
	S1[1]	S2	S3		F1[2]	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11	F12
TIME[3]	0	2	4		1	2	3	4	5	6	9	12	15	18	21	24
ITEM				R												
Screening Consent	X			A												
Heart Rate, Blood				N												
Pressure, and				D												
Weight	X	X	X	O	X	X	X	X	X	X	X	X	X	X	X	X
Alcohol Dependence				M												
Scale	X			I												
Medical History	X			Z												
Demographic Charac-				A												
teristics	X			T												
Lifetime Drinking				I												
History		X		O												
Psychosocial and				N												
Health Habits		X								X		X		X		X
Local Lab		X								X		X		X		X
Drug Screen		X								X		X		X		X
ECG		X								X		X				X
Food Frequency																
Questionnaire			X				X			X		X		X		X
Chronological																
Drinking Record			X				X			X		X		X		X
Physical Exam			X													
Study Consent			X													
Central Lab			X				X			X		X		X		X
Overnight Urine			X							X		X		X		X
Echocardiogram				X						X						

[1]S indicates a screening visit.

[2]F indicates a follow-up visit.

[3]Time of visit is weeks after first screening visit for screening visits and months after randomization for follow-up visits.

A self-reported retrospective diary approach will be used to assess alcohol intake. In addition to alcohol intake history and locally determined laboratory measurements, biochemical markers will be determined in a Central Lipid Laboratory for GGT, HDL cholesterol with HDL_2 and HDL_3 subfractions, apolipoproteins A_1 and A_2, and CDT in order to validate changes in alcohol intake. These markers are more sensitive in combination and are more effective in detecting drinkers who report less or no drinking than are collateral reports.[27] In addition, total cholesterol, LDL cholesterol and triglycerides will be measured and a urine drug screen will be performed. Alcohol history and central laboratory tests will be obtained during the baseline assessments and at the 3-, 6-, 12-, 18- and 24-month visits.

Echocardiograms will be performed during the baseline period and six months after randomization in order to assess the relationship between changes in alcohol intake and blood pressure and indices of left ventricular (LV) mass and function which have been shown to have predictive power for cardiovascular events and to be directly affected by heavy drinking (see Section X.E).

The planning and execution of this multicenter VA cooperative study is outlined in Table 2. A 15-month feasibility phase (Phase I), involving four clinical centers, will be used to assess the ability, within a VA medical center setting, to recruit participants at an adequate rate and to achieve a sufficient difference in alcohol intake between the intervention and control groups. The results of this feasibility phase will be reviewed by the Data and Safety Monitoring Committee and the Cooperative Studies Evaluation Committee. If they decide that the recruitment rate is adequate and that the intervention group has achieved a significant reduction in alcohol intake and, if the Directors of the NHLBI, the NIAAA and the VA Medical Research Service concur in this decision, then three additional clinical centers will be added to the study group and the study will be continued in the seven centers for an additional 39-42 months (Phase II). If completed as planned, the duration of the study will be five years (60 months) and 580 participants will be randomized.

IV. BLOOD PRESSURE RANGES AND DEFINITIONS

A. Blood Pressure Definitions

1. A Visit Blood Pressure is defined as the average of two seated systolic and diastolic readings at that visit determined by a random zero sphygmomanometer. (See Section X.A for details of BP measurement.)

TABLE 2

Schedule of Activities for Study Phases

Phase	Activities	Duration	Date
PLANNING	Prepare Protocol	9 months	10/88-6/89
I: FEASIBILITY	Select 4 centers, prepare Operations Manual, train personnel, initiate screening	7 months	8/89- 2/90
	Recruit 116 participants	9 months	3/90-11/90
	Complete follow-up of initial cohort, continue recruitment	6 months	12/90- 5/91
II: FULL SCALE TRIAL	Select 3 more centers, train new personnel	3 months	4/91- 6/91
	Complete recruitment (N=580)	15 months	7/91- 9/92
	Complete 6-month follow-up	6 months	10/92- 3/93
	Complete maintenance follow-up	18 months	4/93- 9/94
REPORTING	Analyze data, prepare manuscripts	6 months	10/94- 3/95

2. The Inclusion Blood Pressure is an untreated blood pressure of 75-109 mm Hg, inclusive, diastolic, with a systolic blood pressure of less than or equal to 199 mm Hg at the first screening visit and for the average of the four readings at the first two screening visits, and 80-99 mm Hg diastolic with a systolic BP less than or equal to 179 mm Hg for the average of the six readings of the three screening visits.

3. The Baseline Blood Pressure is the average of the six blood pressure readings during the three screening visits for randomized participants.

4. The Treatment Blood Pressure is the average of the blood pressures at the last two visits in the six-month postrandomization period except as follows:

a. Use only the last if the next to last is more than two months before the last.

b. If the participant has been placed on BP lowering medications, use only visits prior to initiation of the drug treatment.

c. Use only the last if there are no visits (off BP lowering medications) beyond month three.

B. Safety Monitoring: Blood Pressure Escape

Standard treatment for hypertension will be initiated for participants in the trial, depending on length of follow-up and level of follow-up blood pressure. The criteria are as follows:

1. A diastolic blood pressure (DBP) of 115 mm Hg or greater (mean of 2 readings) or systolic of 220 mm Hg or greater at a single regularly scheduled monthly or nonscheduled visit will require initiation of treatment for hypertension.

2. Visit BP measurements $\geq$105 mm Hg diastolic or $\geq$200 mm Hg systolic at two consecutive visits approximately 1 week apart will require initiation of antihypertensive treatment.

3. After the six-month visit, an average systolic blood pressure, at each of three consecutive visits approximately one week apart, of $\geq$170 mm Hg, or a diastolic BP averaged over three consecutive visits (six readings) of $\geq$95 mm Hg will require initiation of treatment for hypertension. Completion of the three consecutive visits without exceeding these limits is required in order to continue without initiation of antihypertensive drug treatment.

V. HUMAN RIGHTS CONSIDERATIONS

A. Human Studies and Ethical Considerations

The primary ethical issues presented by this study are: the withdrawal of any existing antihypertensive therapy, the risk of mildly elevated levels of blood pressure for six months, the risk of blood pressure going too high, and the risk of continued moderate to heavy alcohol intake.

Participants in this study will have upper normal BP (80-89 mm Hg) or be in the lower two-thirds of the mild hypertension range (90-99 mm Hg). Although the cardiovascular risk for individuals in

the upper normal BP range is more than for those <80 mm Hg, it has not been considered feasible to study the effects on morbidity or mortality of treatment to lower BP in these individuals because of the very large sample sizes that would be required to demonstrate a significant decrease in the very low individual risk for those with BP in this range. Pharmacologic antihypertensive treatment is therefore not currently recommended.[20]

Individuals with mild hypertension tend to develop target organ damage over a period of many years, and some morbidity and mortality trials have failed to demonstrate benefits from treatment, especially for hypertensives with diastolic BP <100 mm Hg. Those studies that suggest benefit show very little difference in risk for several years. Therefore, the potential risk to an individual of six months of blood pressure remaining in the mildly hypertensive range is exceedingly small. Nevertheless, candidates for the study will be advised of that finite risk during the informed consent procedure. Safety criteria are established to initiate treatment with antihypertensive medications if a participant's BP exceeds the mildly hypertensive level during the initial six-month treatment phase or if a participant becomes or remains frankly hypertensive during the maintenance phase.

Alcohol intervention or even advice to modify drinking is rarely pursued in moderate to heavy drinkers who do not present with manifestations of dependence. Therefore, even though our control group will receive no advice concerning their drinking, some of these participants may benefit from their participation in this study, although their changes in alcohol intake should not be nearly as large as for those participants in the intervention group. Many individuals who drink heavily will be recognized by our screening procedures who would not otherwise have been detected. If adverse health consequences of continued drinking are detected within the study, there are safety criteria for withdrawing the participant from the study treatment program and referring him for more intensive alcohol treatment. However, study data collection will continue, if possible.

In summary, we believe this study is organized in such a manner that it is ethically prudent and that the small potential for risk is outweighed by the benefits that may accrue to many individuals participating in the study and for large groups of alcohol drinkers who may be benefited by the results of the study.

B. Informed Consent Procedure

The informed consent documents have been approved by the Perry Point CSPCC Human Rights Committee and must also be approved by the equivalent Institutional Review Board (Human Rights Committee) at each of the participating centers.

Appropriate informed written consent for screening (see Form 87, App. A) will be obtained from all participants prior to entering the screening phase of the study and prior to withdrawing any existing medications, unless the latter is clinically indicated, regardless of the individual's participation in the study. Medication withdrawal may be indicated, for example, in a patient with low blood pressure on little antihypertensive medication or in one for whom medication was begun with inadequate documentation of "hypertension." A separate informed written consent to enter the study (see Form 88, App. A) will be obtained at the end of the screening phase for participants who meet the eligibility criteria for randomization prior to entering the randomization/ intervention phase of the study.

Each candidate will be given ample time to read or have read to him the consent documents. Clinic personnel will summarize for the candidate the nature of the study, including the time commitment involved, the frequency of visits, and the fact that blood samples and overnight urines will be collected and questionnaires about nutrition, health practices and lifestyle will be administered. Possible risks, limitation of benefits, monitoring procedures, confidentiality and right to withdraw from the study will be communicated to the veteran. Study candidates will be advised that they are not required to participate in this experimental protocol, but may avail themselves of "standard" treatment for hypertension (if present). They will also be informed that any VA benefits for which they may be eligible will not be jeopardized by their participation in the study or by their refusal to participate.

At the beginning of each phase, after the candidate has expressed an understanding of what participation requires and a willingness to participate, he will be asked to sign the appropriate consent documents. These forms will also be signed by the participating investigator and a witness. For participants who meet eligibility criteria and are randomized, two sets of consent documents will have been signed: one for screening and, when necessary, washout of antihypertensive medications; and a second for participation in the randomized controlled trial.

VI. SCREENING PROCESS

A. Recruitment of Participants

The clinical centers will use the prescreening questionnaire, the Brief Screening Instrument (BSI), to survey their potential study populations and recruit participants. Table 3 illustrates the variety of sources that may be used for locating eligible participants. Screening may be conducted in hypertension clinics and other ambulatory care areas including medical and nonmedical clinics, admitting/triage/emergency areas, lobbies or waiting rooms, and may involve patients discharged from the participating VA medical centers with conditions not excluded in the protocol. The latter will require

TABLE 3

Participant Recruitment Sources

Mailing Lists of Veterans
VA Hypertension Clinics
Other VA Medical Clinics
VA Dermatology Clinics
VA Surgery and Surgical Subspecialty Clinics
VA Dental Clinics
VA Admissions
VA Discharges
Veterans Service Organizations
VET Centers
Advertising

follow-up screening visits after usual alcohol intake and blood pressure levels are reestablished. Recruitment may involve contact with local veterans organizations, the use of mailings to veterans living reasonably close to the medical center and the use of newspaper, television, radio and other types of advertising. Oncology and cardiology clinics and alcohol and other substance abuse units would be unlikely sources for participants. The most efficient and productive method of recruitment in the feasibility phase (Phase I) has been to mail the BSI with a return envelope and a brief letter of explanation to veterans whose names and addresses have been provided by Information Resource Management Service (IRM) from those registered in the medical center computer.

A large number of veterans will need to be screened in order to recruit the study population. Based on data from veterans entering cooperative hypertension studies or attending general medical clinics, as well as data from community surveys and participants in hypertension prevention or treatment trials, we estimated that 5-10% of veterans screened would meet the alcohol entry criteria and the majority of these would meet the blood pressure criteria. We further estimated that 2-4% of the population screened for this study would be eligible and give consent.

In Phase I, 18% of veterans prescreened with the BSI (Brief Screening Instrument) have been eligible for the first screening visit (SV1). Although about half of these have been excluded prior to SV1, 55% of those completing SV1 have been eligible for SV2, 60% of those completing SV2 visits have been eligible for SV3, and 76% of those completing SV3 visits have been randomized. Overall, 1.1% of those prescreened have been randomized, but 25% of those who come in for an SV1 have eventually been randomized and the largest number of exclusions during screening have taken place at the shortest visit (SV1). Thus far, a higher proportion than estimated are meeting the alcohol intake criteria, but a smaller

proportion are meeting the blood pressure criteria. This experience from feasibility phase indicates that large numbers of veterans should be prescreened and a large volume of SV1 visits scheduled (overbook to account for 50% initial no-shows). In order for a site to randomize four participants per month, they should complete an average of 100 BSI prescreening forms per week (several hundred may need to be mailed) and schedule a minimum of 8 SV1 visits per week. This has varied among sites in the feasibility phase and may change as the study continues, so each site will need to adjust prescreening and screening activities according to recent yields.

The self-administered BSI is used to quickly eliminate a large number of ineligible individuals. Sutdy personnel may make available (e.g., with a poster) or distribute copies of this instrument in areas where large numbers of veterans are accessible, such as VAMC waiting areas or cafeterias and VFW and American Legion posts. This intrument should be mailed to veterans using computer-generated mailing labels and can also be administered to individual veterans. It is estimated that each site may need to prescreen approximately 6,000 veterans in order to randomize the 50-60 participants per center required during the 15-month intake period of the full-scale trial (Phase II). In FY90 one VA medical center in an average size metropolitan area (one million population) had nearly 200,000 outpatient visits and 25-30,000 veterans used that medical center at least once; the veteran population of the metroplitan area was almost 100,000 in 1980. Therefore, it is likely that there are adequate numbers of veterans available for screening, if screening is pursued systematically. The Operations and Executive Committees have monitored recruitment performance at least monthly during the feasibility phase and will continue to monitor frequently. The Data and Safety Monitoring Committee also monitors recruitment.

B. Inclusion Criteria

1. Age and Gender

Male and female veterans aged 25-79 years will be recruited for the study. Even though it may be possible to recruit small numbers of veterans below 25 years of age, drinking patterns are usually not well established. Quantity of alcohol intake is reported to be lower in older people, but some data suggests that alcohol may have a greater impact on blood pressure in men over 50 years of age, so an upper age limit of 79 will be used.[28,29]

2. Moderate to Heavy Drinkers

To qualify for randomization, the consumption of alcohol must average at least 3 drinks per day (21 drinks [294 grams] per week) over the previous six months as documented by the Lifetime Drinking History (LDH)[30] questionnaire at Screening Visit 2.

3. Blood Pressure

Average untreated blood pressure over three visits must be between 80 and 99 mm Hg, inclusive, diastolic and less than or equal to 179 mm Hg systolic.

4. Informed Consent

Appropriate informed consent must be obtained.

C. Exclusion Criteria

Individuals must be excluded for factors or conditions that would interfere with the objectives of the study or which could produce significant morbidity during the course of the study.

1. Alcohol Dependence

Meets criteria for alcohol dependence using the Alcohol Dependence Scale (ADS).[31] Individuals meeting the criteria for alcohol dependence (5 or more symptoms) will be referred for further evaluation and treatment of their alcohol dependence.

2. Psychoactive Substance Dependence

Diagnosed psychoactive substance dependence, at any time during the year prior to recruitment. Participants who test positive on a urine drug screen will be further examined and, if dependence is indicated, excluded.

3. Direct Alcohol-Attributed Medical Conditions

a. Acute or chronic liver disease, including biopsy-proven cirrhosis or alcoholic hepatitis. Specific single exclusionary findings include: jaundice (bilirubin > 2.5 mg %), hypoalbuminemia (albumin < 3.0 g %), hypoprothrombinemia (PT > 3 seconds over control), ascites, encephalopathy or varices.

b. Pancreatitis, acute or chronic: An acute attack within the previous three years or documented chronic pancreatitis.

c. Peripheral neuropathy.

d. Cerebellar dysfunction.

e. Significant cognitive deficits secondary to alcohol excess: Wernicke's or Korsakoff's syndrome or other alcohol-induced organic brain syndrome.

f. Current megaloblastic (or megalocytic) anemia, with both hematocrit < 37% and the MCV > 102 $c\mu$.

g. Alcohol related upper gastrointestinal bleeding in the past year.

4. Diagnosed Psychiatric Conditions (current or history of [by patient or in prior medical record])

a. Major psychotic disorder, requiring medication for control.

b. Major affective disorder, requiring medication for control.

c. Major personality disorder, expected to impair reliable participation in the study.

d. Severe anxiety disorder.

5. Cardiovascular Diseases

a. Unable to withdraw contraindicated medications (see Appendix H).

b. Hypertensive retinopathy greater than K-W group II, current or history of.

c. Cerebral or subarachnoid hemorrhage, history of.

d. Atherothrombotic stroke or myocardial infarction, within the six-month period prior to recruitment.

e. Symptomatic ischemic heart disease.

f. Current atrial fibrillation or other significant dysrhythmia that would preclude accurate blood pressure measurement or is indicative of serious underlying heart disease.

g. Current congestive heart failure (CHF), as evidenced by at least two of the following: recent dyspnea or orthopnea not of pulmonary origin; ventricular diastolic gallop (S_3); basal pulmonary rales; evidence of congestive heart failure on chest x-ray. If signs are controlled with digoxin, patient may be included. However, if a diuretic and/or an angiotensin converting enzyme inhibitor is required or indicated for CHF, the patient must be excluded (since these are also antihypertensive medications).

h. Surgically curable or other secondary forms of hypertension.

6. Other

a. Malignancies or other diseases that are likely to be fatal or disabling during follow-up.

b. Seizure disorder.

c. Coagulopathies, bleeding diatheses or any condition being treated with anticoagulants.

d. Blood pressure outside of screening range.

e. Unable or unwilling to participate.

f. Anticipates moving/relocating out of area within six months.

g. Pregnancy

D. Study Candidates on Antihypertensive Medications

1. If a veteran currently taking antihypertensive medication(s) appears to meet the eligibility criteria (other than blood pressure) and it is anticipated that his diastolic pressure will not rise above 99 mm Hg or his systolic above 179 mm Hg, medications will be discontinued or tapered, if medically indicated, after informed consent is obtained. If he is receiving active care for hypertension by a non-VA physician, permission should be obtained from the physician for drug withdrawal.

2. An individual will not be eligible for screening until he has been off antihypertensive medications for a minimum of two weeks. A longer minimum period of observation, such as 3-4 weeks, should be observed for those individuals who may be on guanethidine or reserpine. All candidates must be seen at least once within one week after medication has been withdrawn for a blood pressure check. If there is uncertainty about how high or how quickly the blood pressure might rise or if a candidate would benefit from reassurance, a blood pressure check in less than seven days may be appropriate. If blood pressure exceeds the entry criteria levels during washout, the individual will be excluded from the study and appropriate antihypertensive therapy will be initiated. As long as blood pressure remains below the entry levels, the candidate may be followed at appropriate intervals in order to monitor for "return" of blood pressure to entry levels: some individuals may have been started on antihypertensive medications previously without adequate documentation of hypertension, some may have altered a risk factor contributing to their hypertension, and some may require months or years for their blood pressure to rise to previous untreated levels.

3. Treated patients may be on minimally effective combinations or doses of antihypertensive medications or may be noncompliant, so the number of medications a patient has been prescribed may not be predictive of his untreated blood pressure. Individuals should be excluded, however, if the screening blood pressure on medication exceeds the entry criteria or the patient seems compliant and his treatment requires more than two appropriately combined antihypertensive medications, including a diuretic, at usual maximal doses. An example of this would be: hydrochlorothiazide 50 mg/day + atenolol 100 mg/day + any appropriate dose of a vasodilator antihypertensive agent (e.g., hydralazine, prazosin, terazosin, a calcium channel blocker, or minoxidil).

E. Screening (Prerandomization) Visits

There will be three biweekly visits during the prerandomization screening phase. Participants will be randomized at the third visit unless they are excluded. Baseline alcohol intake will be assessed before randomization but baseline special (central) laboratory tests and the echocardiogram will be performed only after the participant meets the randomization criteria in order to reduce the volume and expense of unnecessary tests.

F. Exclusions During Screening

In addition to the exclusion criteria described in Section VI.C, individuals will be excluded for the following:

1. Blood pressure exceeding the safety limits described in Section IV.

2. Failure to return to clinic within 30 days of previous visit.

G. Screening Rules for Randomization

1. Blood Pressure

The objective of the screening rule is to identify persons with DBP between 80 and 99 mm Hg on the basis of three visits, and to assign each participant to either the lower stratum (DBP 80-89 mm Hg) or the higher stratum (DBP 90-99 mm Hg). Since recruitment of individuals with the desired ranges of DBP and alcohol consumption may be difficult, a sensible screening rule should try to avoid excluding candidates on the basis of a single visit. Therefore, a relatively wide range of acceptable BPs will be used for the first two visits and the target DBP range (80-99 mm Hg) will be required for the average of the three screening visits. Two measurements will be taken at each visit. The screening process may be terminated if the DBP at the first screening visit is not between 75 and 109 mm Hg or if the DBP averaged over the first two screening visits is not between 75 and 109 mm Hg. An individual is eligible for randomization if the DBP averaged over the three screening visits is between 80-99 mm Hg. The interval between each of these visits must be at least six days and no more than 30 days.

Participants will be classified as either lower stratum (80-89 mm Hg) or higher stratum (90-99 mm Hg) on the basis of the average of the six measurements. This average will also provide the baseline value.

2. Alcohol Consumption

The information required to initially screen individuals for participation in the study is based on a brief self-administered questionnaire that includes several "usual" alcohol intake items. If individuals report having 10 or more drinks per week, e.g., 2 or more drinks per day on 5 or more days per week, they will be kept in the pool of individuals to be screened. These participants will qualify for the first screening visit, at which the Alcohol Dependence Scale will be used to identify and exclude alcohol dependent individuals.[31]

The Lifetime Drinking History[30] questionnaire will be administered at the second screening visit to obtain more detailed information on drinking patterns in terms of typical quantity, frequency, variability (binge drinking) and beverage consumed. It is designed to provide quantitative indices of an individual's alcohol consumption pattern from the onset of drinking to the present. To qualify for randomization, the consumption of alcohol must average at least 3 drinks per day (21 drinks per week) over the prior six months.

H. Alcohol Intake During Screening

No active encouragement to alter alcohol intake will be undertaken during this phase.

I. Procedures for Prescreening and Screening Visits

Before scheduling any screening visits the prescreening questionnaire will be administered. If eligible for formal screening, the first screening visit will be scheduled or, if on antihypertensive medications, the screening consent will be obtained and the washout phase will be initiated.

At Screening Visit 1, the following will be obtained:

1. Screening Consent, if not previously obtained.

2. Two random-zero sitting BPs, standing BP, sitting and standing heart rate, and weight.

3. ADS-10 (Alcohol Dependence Scale), focused medical history and demographics.

At Screening Visit 2, the following will be obtained:

1. Two random-zero sitting BPs, standing BP, sitting and standing heart rate, and weight.

2. Local laboratory tests: standard urinalysis including screen for illicit drugs; CBC (Hgb, Hct, RBC indices, platelets, and WBC); biochemical profile to include: cholesterol, urea nitrogen, creatinine, uric acid, glucose, electrolytes, albumin, total bilirubin, SGOT (AST), LDH, alkaline phosphatase, calcium, and phosphorus.

3. Standard 12-lead electrocardiogram.

4. PA chest x-ray, if it has not been performed within the previous year or if clinically indicated.

5. LDH (Lifetime Drinking History) and psychosocial and health habits questionnaire to assess depression, sexual satisfaction, coping, physical activity/exercise, coffee use, smoking, interpersonal conflict, and recent prescription and nonprescription (OTC) medication use.

The participant will be given instructions and collection materials for an overnight urine sample and will be instructed to avoid meals or other fat intake within 12 hours before the next visit.

At Screening Visit 3, the following will be obtained:

1. Two random-zero sitting BPs, standing BP, sitting and standing heart rate, weight, and height.

2. Overnight urine sample for time of collection, volume, creatinine, sodium, and potassium.

3. Chronological Drinking Record (CDR).

4. Physical examination with review and completion of the focused medical evaluation and review of the local laboratory tests and urine drug screen.

5. Study consent, if participant meets eligibility criteria. The Perry Point VA Cooperative Studies Program Coordinating Center (CSPCC) will be called by the data collector to confirm eligibility.

6. Blood samples, if eligibility confirmed. Plasma and serum will be prepared and will be sent to the Central Lipid Laboratory for determination of biochemical markers.

7. Echocardiogram (or within 1-2 weeks of randomization).

Appointments for the study echocardiogram (if not completed at SV3) and the first postrandomization follow-up data collection visit will be made. Treatment assignment will be revealed to the study interventionist by the CSPCC. Both the data collector and the participating investigator will remain blinded to treatment assignment. The study interventionist will contact the participant to reveal group assignment and to schedule the first intervention visit (if in the intervention group) after the echocardiogram has been obtained. However, the first intervention visit should occur within two weeks of the randomization visit.

J. Participant Randomization

As soon as the screening process has been completed and the participant's eligibility has been established, the Perry Point CSPCC will be called. The participant's eligibility will be confirmed and his treatment group assignment will be determined. Treatment group assignments will be randomly generated using a fixed randomization scheme.[32] Treatment assignments will be independently generated for each level of the blood pressure stratum within each participating medical center.

VII. SIX-MONTH INITIAL TREATMENT PHASE

A. Criteria for Withdrawing Participant from the Treatment Program and/or the Study

Development of any of the following will justify an investigator calling the Chairman about withdrawing a participant from the treatment program at any time after randomization:

1. Any of the exclusion criteria listed in Section VI.C.1.-6., (except 4.c, d, 5.a, b, e, f, g, h, 6.a, d, f), or unrelated intercurrent illness that renders the participant unable to continue in the treatment program. These participants should be referred for appropriate care; however, study data collection should continue, if possible. The participating investigator is responsible for referrals.

2. Participant moves or is lost to follow-up.

3. Participant requests termination from the treatment program or the study. If the former, data collection will be continued, if acceptable to the participant, even if some data collection visits are missed.

4. Death. If a participant dies during the study, a copy of the death certificate will be forwarded to the CSPCC.

If the participant must be withdrawn from the study, the termination form will be completed and, whenever possible, blood pressures, heart rate, weight, local and central laboratory analyses, CDR, food frequency questionnaire, echocardiogram, ECG, psychosocial and health habits assessment, and overnight urine collection will be obtained. Appropriate follow-up or referral should be arranged as clinically indicated. All participants should be seen for a complete six-month visit, whenever possible.

B. Clinic Visits

A participant will have six data collection visits at one-month intervals during this phase. Random zero sitting and standing blood pressure, heart rate, and weight will be determined at each visit.

C. Interim Visits

A minimum of three interim visits at one-week intervals will be scheduled if diastolic BP exceeds 104 mm Hg or systolic BP exceeds 199 mm Hg.

D. Test Procedures

Self-reported alcohol intake (CDR), food frequency questionnaire and central laboratory tests will be obtained at the three-and six-month visits. Echocardiogram, local routine lab, ECG, psychosocial and health habits assessment and overnight urine collection will be repeated only at the six-month visit.

E. Intervention Procedures (See Section IX).

F. Blood Pressure Escape

If blood pressure exceeds the safety limits described in Section IV.B, open treatment for hypertension will be initiated. The participant will continue to be followed according to the study protocol.

VIII. MAINTENANCE PHASE AFTER SIX-MONTH VISIT

A. Criteria for Withdrawing Participant from the Treatment Program and/or the Study

All criteria for termination of a participant are the same as outlined in Section VII.A. All termination procedures outlined in Section VII.A. should be followed, except no echocardiogram will be obtained after the six-month echocardiogram.

B. Clinic Visits

A participant will have six data collection visits at three-month intervals during this phase. Random zero sitting and standing blood pressure and heart rate, and weight will be determined at each visit.

C. Interim Visits

Interim visits will be scheduled at one week intervals if diastolic BP exceeds 94 mm Hg or systolic BP exceeds 169 mm Hg. If the diastolic BP is elevated, a minimum of two interim visits will be required to obtain the diastolic BP averaged over three consecutive visits.

D. Blood Pressure Escape

If blood pressure exceeds the safety limits described in Section IV.B, open treatment for hypertension will be initiated. The participant will continue to be followed according to the study protocol.

E. Test Procedures

Self-reported alcohol intake (CDR), food frequency questionnaire, local and central laboratory tests, overnight urine collection and psychosocial and health habits assessment will be obtained every six months during the maintenance phase. Echocardiograms will not be performed during this phase.

IX. INTERVENTION PROCEDURES

All participants will be told not to reveal their randomization status to the study data collector, but to provide accurate responses to any questions asked by the data collector.

A. Alcohol Reduction Intervention

There are a number of treatment models applied to addictive behaviors. These vary in setting (e.g., inpatient hospital care, outpatient psychiatric treatment, half-way house living, and self-help groups such as AA), in intensity, and in theoretical base. Studies of treatment effectiveness suggest that all work equally well, with length of treatment, usually in an outpatient clinic, being a critical factor.[33,34] An examination of the elements in successful treatment programs indicates certain commonalities, viz. teaching or helping patients to (1) replace drinking with alternative coping behaviors, (2) develop techniques to deal appropriately with emotional states, social pressures, and interpersonal problems, and (3) increase or develop confidence in personal competency. As noted above, the Rand Report found that success in dealing with drinking problems was related to the length of time spent in outpatient treatment but did not require a goal of total abstinence for all patients. In such settings, patients develop a trusting relationship with counselors. They learn to understand reasons for drinking, explore and experiment with alternatives to drinking in the context of this safe relationship, and gradually take on full responsibility for managing their lives with confidence in their self-mastery. These changes are produced by the application of the principles of learning theory, regardless of the theoretical frame of the treatment offered. Unfortunately, therapists are not always aware that they do this or how to go about it effectively.

It is likely that brief, inexpensive, learning theory based treatment approaches, will, in this next decade, supplant the more expensive, and often very long term, outpatient treatment model just as the latter is overtaking the costly "AA illness" model of inpatient hospital care with its goal of abstinence. However, it may always be the case that severely impaired (psychologically or cognitively) or dependent drinkers will require more intensive care. Most of the cognitive-behavioral treatment models developed in the late 60's or 70's are rooted in Bandura's principles of behavior modification. They have been applied with success to a wide range of drinkers. Because they rely heavily on self-mastery (in some ways helping the client to become his own therapist or problem-solver) which necessitates homework assignments or self-paced tutorials and can be applied in group settings, these treatments should prove more successful and cost effective.

In the past 15 years, Miller, Marlatt, Sanchez-Craig, Annis, and others have developed models and studied the outcome of cognitive interventions in heavy drinkers. The components of these interventions are similar and emphasize self-monitoring, self-control, and self-mastery, all of which are developed and enhanced by homework assignments, behavioral record keeping, and practice outside the treatment setting. In each approach, patients are taught to analyze their drinking patterns, to learn alternatives to using drinking as a coping device, and to develop methods of "self-soothing" or relaxation. The most effective treatment models include strategies for initiating and maintaining behavior change, thus

reducing the risk of relapse. The key element in preventing relapse seems to be a strong sense of self-mastery inculcated by the patient gradually assuming more responsibility for planning and implementing change. Thus, he not only experiences and comes to expect success on his own but also is less negatively impacted by occasional lapses or "failures".[35-38] This approach towards self-efficacy may be enhanced by a goal of controlled drinking as opposed to abstinence.[35,36,38] Sanchez-Craig and colleagues[24] found no differences between subjects randomly assigned either to controlled drinking or to abstinence; in both groups, subjects moderated their drinking and generally maintained the improvement through two years of follow-up.

In summary, expanding one's repertoire in personal and social functioning and increasing self-confidence by planning and experiencing effective coping behaviors seems to protect individuals from returning to problem drinking (and other negative habitual behavior, as decreased alcohol consumption often results in improvement in other areas of life). A program based on principles of learning theory and applied in stages that allow progression from increasing motivation to change, initiating change, and maintaining change by preventing relapse through increased self-efficacy seems essential to the goals of this study. Because each segment can be strictly defined and operationalized, it will be a less difficult task to assess the effectiveness of a behavioral model in reducing alcohol consumption than if more "traditional" outpatient treatment modalities were to be applied.

The intervention model to be used will be adapted from the Sanchez-Craig brief treatment program for early intervention in alcohol abuse and alcoholism.[23] Components of other behavioral models (e.g., Marlatt[39], Miller[40]) will be added to ensure sufficient attention to increased self-efficacy and relapse prevention. The self-help materials developed by Sanchez-Craig at the Addiction Research Foundation will be the mainstay for the participants' homework.[41]

Interventionists (GS-11 social workers or masters level psychologists with some clinical experience) will be centrally trained at a one to two-week training workshop in the application of the model and the integrated use of other materials. The trainers, experienced clinicians, will carefully take personnel through the procedures, session by session, using didactic and experiential techniques. After determining that interventionists understand and have some degree of comfort with the materials, a few subjects will be selected who are representative of the patient population at each site. The trainer will then monitor interventionists' application of the procedure with these subjects in a manner similar to that used in clinical supervision. Quality assurance will be maintained throughout the study by periodic checks in the form of clinical supervision, videotaped sessions, conference calls, and/or site visits.

Participants randomized to the alcohol intervention will receive six 60-90 minute individual sessions in the first three months and at monthly intervals for the duration of the initial six-month study phase. During the maintenance stage, they will be seen at one- to three-month intervals for review and booster sessions. This plan of gradually decreasing visits will permit participants to gain control over their own lives and increase their self-confidence in mastering situation specific behaviors which will accrue from learning experiences independent of the treatment.

Participants will learn to analyze their drinking behaviors in personally defined, situation-specific circumstances. They will identify high risk situations and review their current coping methods, generate new cognitive and/or behavioral approaches to these situations and apply these new coping strategies outside the treatment. This method will increase self-confidence towards meeting their drinking goals. The interventionist will be active in the treatment phase but will serve principally as an advisor to the participant who sees himself as the primary change agent. A self-help manual and daily drinking records will be used to assist the participant throughout the intervention.

Intervention Session 1 will include the following:

1. Feedback from assessment (CDR, lab work, baseline assessment).

2. Discussion of relationship between hypertension and level of consumption with an emphasis on reduction, ideally to ≤ 2 drinks per day, whether or not drinking is a "problem."

3. Discussion of the objectives of alcohol intervention which are:

a. To identify, using the CDR, situations where drinking occurs or is excessive (i.e., risk situations) and to begin to explore factors which might account for this.

b. To develop strategies that allow coping with these situations without drinking/overdrinking.

c. To establish a pattern of drinking which meets the study goals and does not interfere with important duties or daily functioning.

d. To learn to monitor progress objectively (i.e., self-monitoring).

4. Review of procedures for self-monitoring of drinking (provide daily drinking record [DDR] forms). These forms may be seen as the equivalent of diaries and are called behavioral records in some studies.

Participant will be requested to monitor his drinking for a week. He will return for a second session in one week.

Intervention Session 2 will include the following:

1. Administration of the CDR (by interview).

2. Review of self-monitoring of drinking (DDR).

3. Request for initial period of abstinence (provide rationale).

4. Dispensing and reviewing self-help manual.

Participant will return for a third session in two weeks.

Intervention Session 3 will include the following:

1. Assessment of progress.

2. Establishment of the long-term goal (using self-help manual as guide): 50% reduction in intake or 14 drinks per week, whichever is less; or abstinence, if preferred by participant.

3. Specification of rules and guidelines for moderate drinking or abstinence (maximum quantity and frequency, beverages, appropriate and inappropriate drinking situations).

4. Identification of aids to facilitate moderate drinking or abstinence (skills for pacing drinking, learning to prepare in advance for drinking events, learning to monitor effects of drinking, developing new recreational activities).

5. Functional analysis of drinking behavior using the CDR, DDR and self-help manual with attention to:

a. Identification of problematic drinking situations.

b. Generation of alternative behaviors and activities to eliminate or moderate drinking.

c. Development of strategies for coping with situations that tend to arise when drinking is significantly reduced (unexpected urges to drink, social pressures and relapses).

THE STUDY INTERVENTIONIST WILL USE THE SELF-HELP MANUAL TO REVIEW EACH OF THESE STEPS.

The participant will be requested to apply the strategies outlined in the manual to achieve his drinking goal. An appointment will be scheduled in two weeks to assess progress.

Intervention Session 4 will include the following:

1. Assessment of drinking status, and modification of goal, if necessary.

2. Encouragement to continue self-monitoring, with emphasis on specific needs as identified in 1 and on self-mastery.

An appointment should be arranged in two weeks to assess progress.

Intervention Session 5 will involve teaching how to deal with high risk situations by encouraging participants to:

1. Make decisions regarding goal in the context of behavior;

2. Problem solve by individually defining risks and developing alternative coping strategies;

3. Make use of rehearsal, modelling, thought control, and self-soothing as relevant to situation and person specific risks of the following nature:

a. Environmental.
b. Interpersonal.
c. Intrapersonal.

An appointment should be arranged in two weeks to assess progress.

Intervention Session 6 will include the following:

1. Review of sessions 1-5 and assessment of progress and goal status. Training for a focus on self-management to head off potential problems by anticipation and rehearsal.

2. Discussion of the Goal Violation Effect and its impact.

3. Discussion of the need to schedule for leisure time and pleasant activities.

4. Discussion of the need for weekly planning to prevent relapse.

Additional intervention follow-up visits will be arranged at one-month intervals during the initial six-month phase and at one to three-month intervals during the maintenance phase.

B. Control Treatment

Control participants will receive the same assessment (data collection) procedures as the intervention group. Otherwise, contact will be minimal to decrease opportunities for "nonspecific" intervention, such as social support or feedback from clinic staff about lifestyle changes initiated by the participant.

Participants randomized to the control group will be informed that they have been assigned to the group which will not receive training to reduce alcohol intake. They will be reminded that we do not know what effects - favorable or unfavorable - changes in alcohol intake will have on blood pressure and other risk factors and, therefore, they are not being advised to change their drinking.

They will also be reminded that study staff will check blood pressures regularly for two years. Unlike the screening phase, the results of the blood pressure checks will not be reported to participants during the study. The rationale for this is that blood pressure can be higher at one visit and lower at another just from normal variation and we wish to control for any psychological effects of this variation. However, a participant will be informed immediately if his blood pressure goes too high (as defined in Section IV.B). If this happens, treatment for hypertension will be initiated.

Control group participants will not have regular contact with the interventionist after randomization. However, the interventionist will be the contact person for all participants in matters not related to data collection or the data collection visits.

C. Behavior Modification vs. Assessment

It may be argued that the control group is receiving a trial of "advice" similar to that described by Orford and Edwards.[42] Or that by calling their attention to both the possible relationship between alcohol consumption and hypertensive disease and the fact that another group in the study will receive training in reducing alcohol intake, the controls may be sensitized to use whatever cues are given during data collection or may be inferred from the information given them at randomization to implement their own "behavioral change programs." Or that, as Emrick[34] argues, 40% of all problem drinkers improve with any treatment and 15% of them abstain. In a manner similar to the presumed impact of assessment on the controls in the present study, they may have been influenced by their physicians, employers, health promotion/ education efforts, etc. Nevertheless, the tools learned in the intervention and the support it affords those receiving it are probably more necessary to the participants in this study who will be drawn from a heavier drinking population than those studied by Miller, Marlatt and others. Relapse prevention models tend to decrease the severity and duration of drinking as well as lengthen the time between drinking episodes.[43] In addition, various levels of intervention, no matter how brief, are better than assessment-only conditions. Marlatt[39] found that heavy drinkers exposed to two intervention models (alcohol information school and skills training program) had significant reductions in alcohol intake at four-month follow-up while changes in a control group (assessment only) were not significant. Similarly, Chick[44] found that, at one-year follow-up, a very brief intervention session (30-60 minutes) by a trained nurse led to significant changes in clients who were seen but not in those in an assessment only condition. Concerned that restrictions on selecting subjects may have slanted the results in this positive direction, Chick[45] randomly assigned patients attending an "alcohol problems clinic" to either a single session of "advice" or to "extended in or outpatient treatment." At the two-year follow-up, those who had had extended treatment were functioning best. Because our sample will be drawn from above average

drinkers, we may expect that a longer intervention such as the one used in our Intervention group will be more effective than a mere suggestion inferred by Control group participants at randomization.

X. LABORATORY EVALUATIONS AND END POINT MEASUREMENTS

A. Blood Pressure Measurements

The BP measurement procedures are adapted from NHLBI and VA protocols, including Monotherapy of Hypertension, Trials of Hypertension Prevention, and The Hypertension Detection and Follow-Up Program.

At each visit of the study, arterial blood pressure will be measured in the right arm by the study data collector using the proper size blood pressure cuff. All participants will have their arm circumference measured at each visit to determine the correct cuff size (small, regular, large or thigh). Blood pressures will be taken with the same random-zero mercury sphygmomanometer, at approximately the same time of the day, and in the same environment. Systolic BP will be determined based upon Phase 1 and diastolic BP as Phase 5 (disappearance of the Korotkoff sounds).

Mental activity, especially talking, causes the blood pressure to rise. Therefore, the participant should not engage in conversation either before or during the blood pressure evaluations. He should be kept as calm and undisturbed as possible. Since smoking can transiently elevate blood pressure, the participant should be advised not to smoke for a minimum of two hours before the blood pressure measurements.

All clinic personnel who examine participants must record the blood pressure in the same manner. Therefore, central training for measurement of blood pressure, including use of the random zero sphygmomanometer, will be conducted at the initiation of the feasibility (I) and full (II) study phases for all participating personnel. Retraining sessions will be scheduled as necessary. This training will involve careful description and demonstration of the techniques involved, discussion of sources of variability in blood pressure measurement, and audio- and/or videotape assessment of accuracy in recording Korotkoff sounds. Local training sessions will also be conducted for all personnel who are involved in recording blood pressure. This will be accomplished using a stethoscope with a "Y" tube to which the earpiece sets from two stethoscopes can be attached to one stethoscope head so that two observers can listen for the Korotkoff sounds in the same individual. Both observers will write down their readings. This procedure should be repeated on succeeding days until all clinic personnel read the same level of blood pressure within 4 mm Hg for any one systolic reading and within 2 mm Hg for any diastolic reading.

B. Alcohol Consumption Quantitation

Self-reports of alcohol consumption are subject to two important sources of error: denial or deliberate deception and forgetting. The relative risks for these two sources of error vary as a function of a number of factors, one of which is the objective of assessment and its influence on the respondent's motivation to respond accurately.

Self-reports of alcohol consumption have been used in two broad categories of research: (1) general population surveys of drinking patterns and (2) as diagnostic and outcome measures in clinical research. The present clinical trial may be seen to lie midway between these two research agendas for the following reasons:

First, in comparison with general population surveys, this study is conducted with populations with above average levels of alcoholic consumption. United States survey data suggest that one-third of the adult population consists of abstainers or of persons who seldom take a drink. Another third consists of people who have up to three drinks per week. The remaining third contains people who consume four or more drinks per week.[46]

Second, the present study also differs from those clinical studies in which drinking has become a major issue; and often the client is coerced to seek treatment. If self-report of consumption is seen in the context of a clinical program, there may be a strong incentive to fabricate drinking to either invite or avoid further clinical intervention.

Three general procedures for obtaining self-reports have evolved over the last few decades:

1. general population survey measures of recall,
2. prospective diary techniques, and
3. retrospective diary or interview listing of drinking events.

Because of its brevity, the first method, sometimes referred to as a "frequency-quantity index" has been favored in the majority of U.S. population surveys and most screening instruments. One problem unique to these "summary judgments" is the fact that the respondent is asked to abstract his or her behavior rather than report it directly (respondents may err in stating what is the "usual" quantity or "averaging" the frequency of drinking over time). In addition to errors of judgment, when asking respondents to recall their drinking over some specified period of time, there is the risk that respondents will not remember accurately. This risk grows as the recall period is lengthened.

Prospective diary techniques serve to counter both of these issues by having the respondent report daily on actual behavior. Prospective diaries are prohibitive in many survey situations because they require additional fieldwork, time and expense and may produce greater changes in drinking behavior.

Retrospective diaries, while avoiding errors in judgment in abstracting behavior, vary by the length of specified reporting periods (from the previous day to several years).

The literature that compares prospective diaries to retrospective recall has not yielded consistent findings. Poikolainen and Karkkainen[47] reported that recall reports were only about 60% as high as prospective diary reports. Sobell et al.,[48] in a study of 40 male outpatient treatment clients, showed that retrospective 30-day diary estimates were significantly higher than beverage specific recall reports. Williams et al.[49] tested both a 27-day and a 14-day recall technique against prospective diaries in a North Carolina household sample and found no differences between all three techniques. More recently, Hilton[50] found that a prospective diary did not differ from two summary recall techniques.

Gerstel et al.[51] randomly assigned a sample of 631 residents in the Boston area to one of two conditions: (prospective, daily drinking record) and (retrospective, chronological drinking record). Respondents were followed for three consecutive weeks. Gerstel et al. achieved better results with retrospective records, despite the conventional wisdom that prospective diaries are less subject to problems of recall. Makela[52] found that a retrospective period of seven days compared to one or more months, minimized the degree of forgetting. This, together with interviewer probes and motivational support, may have offset the recall advantages of the prospective diary.

Most of the studies comparing different assessment techniques of alcohol consumption have indirectly addressed the issue of relative validity. Given that coverage rates are typically low, many studies have assumed that the method that yields the largest amount of reported consumption is the better method. One of the few studies to directly address the accuracy of retrospective diaries compared observations of 100 bar patrons with respondents' reports one week later.[53] Seventy-five percent of the self-reports matched the observed drinking. Of the remainder, the majority erred by 2-3 drinks but there was no significant difference between under-reporting (46%) and over-reporting (54%).

A number of procedures have been developed to address the measurement of response bias and error. The degree of rapport within the interview, the extent of confidentiality, and the nonthreatening evaluative context serve to enhance patient motivation and veracity. In addition, when respondents provide information under conditions where they are led to believe that objective, external validation of the response is available, respondents are motivated to respond accurately.

Procedures for external confirmation of self-reports frequently involve collateral informants and provision for biochemical tests.

In the literature on the validity of self-reports in general populations, Cahalan et al.[54] found that wives and husbands reported very similar distributions in the frequency of wife's drinking, while husband's tended to report a slightly higher frequency for themselves than did their wives. This was confirmed in a 1984 national survey.[55] The findings suggest that the wife might know less about her husband's drinking than the husband knows about hers since men spend more time away from home and women, who generally drink less, do relatively more of their drinking in company with their husbands.

Recently, Ridley and Kordinak,[56] in a comparison of reports of nonalcoholic couples, found that correlations of self and spouse reports on three screening tests ranged from .69 to .99. While Midanik's review[57] yielded contradictory findings on whether the self or spouse was more likely to report problems, more recent reviews of the literature concluded that there is considerable concordance between the alcoholic's and the spouse's reports.[58,59] While spouses are the more frequent source of collateral information, a spouse or co-habitant is unavailable for many patients. Different collateral information sources (relatives, counselors, friends, etc.) have different types and amounts of contact with the subject and these variations introduce an additional source of error that lowers validity estimates.[60] The combination of biological markers and self-report measures has proven more powerful than collateral reports.[27] The inclusion of collaterals with biological markers and self-reports can enhance validity, but must be weighed against such factors as added fieldwork effort and expense, lower response rates, and differential contact with respondents in the study.

Based on the above, a retrospective diary technique will serve as the criterion outcome for self-reported alcohol consumption. The advantages of this technique include reduced demands on recall (seven days), interviewer aids and probes for more accurate detail, non-evaluative reporting of behaviors, and interviewer rapport.

The criterion outcome for self-reported alcohol consumption that will be used in this study is the Chronological Drinking Record (CDR) developed by the Research Triangle Institute in collaboration with the National Institute on Alcohol Abuse and Alcoholism.[61] The CDR provides a listing of the amounts of alcohol by type of beverage, size, and number of drinks consumed on an event-by-event basis for a specified time period. In addition to alcohol, contextual data are recorded for physical location, type and number of persons present, time of day, duration of drinking, and occasion of use. The weekly interview format allows probing for information in chronological order for the entire week ending on the day preceding the interview. By embedding drinking events in a socio-ecological context, the recall of amounts

consumed is enhanced and the profile of an individual's drinking behavior can be used in interventions to deal with drinking. The CDR is a widely tested instrument and has been used in research and clinical settings.[51,53,62] Total alcohol per event is obtained by converting the total reported ounces of a specific beverage into estimated ounces of ethanol and by summing over all beverages in the same event. Ethanol may be summed over events to yield total weekly consumption and average daily consumption.

The CDR will be administered to all participants in both the intervention and control conditions at baseline, at three months, and then again at six months, and at six-month intervals thereafter during the maintenance phase of the study.

C. Biochemical Markers of Alcohol Intake

Because the history of the amount of alcohol ingested is sometimes unreliable, and because compliance with alcohol reduction is necessary to analyze the effect of alcohol on blood pressure, laboratory monitoring of compliance with reduced alcohol intake is a vital part of this study. No single test is an ideal marker of alcohol intake, but the combination of gamma glutamyltransferase (GGT) and high density lipo-protein provides a reasonable correlation with alcohol intake.

GGT is an enzyme produced by the liver, the synthesis of which can be increased by agents (such as ethanol) which induce microsomal enzyme synthesis.[63] GGT is elevated in the blood of the majority of alcoholics, and alcohol intake is the major determinant of GGT levels among the population without evidence of alcohol dependence.[64] GGT has been the most widely used test for diagnosis of alcohol abuse in many parts of the world, and has been used to monitor abstinence in patients undergoing alcohol rehabilitation.[64] GGT has several attributes which make it useful in the current study. There is a direct relationship between alcohol intake and serum GGT activity, with an apparent threshold of 2-3 drinks per day in one study.[65] GGT levels are elevated in persons with or without alcoholic liver disease, although levels are higher in those with liver disease.[66] GGT rises rapidly after alcohol intake, reaching a maximum by about one week after beginning a regular daily intake.[67] GGT activity falls rapidly after decrease in alcohol consumption in most persons, returning to baseline within two weeks after cessation of ingestion.[67]

The limitations of GGT are not minor, however. The sensitivity of GGT is relatively low; in most studies, no more than 67% of alcoholics have elevated GGT, with the percentage being lower in those without addiction.[64] The pattern of alcohol intake appears critical in determining the frequency of elevation; those with daily consumption are much more likely to have elevated GGT than binge drinkers.[68] The duration of regular alcohol consumption is also important; those with alcohol intake of less than two weeks duration have lower levels and less frequent elevations than those drinking heavily for six weeks

or longer.[69] In a minority of individuals, GGT levels do not change significantly even after one month of alcohol abstinence.[66] Thus, although GGT is an indicator of alcohol intake, it could not be used as the sole biochemical marker.

Deglycosylated transferrin as a marker of alcohol consumption was developed by Stibler and her colleagues in Sweden[70] and has been evaluated in Australia[71] and the United States.[72] In the most recent study,[72] 57 patients (79%) had increased serum carbohydrate-deficient transferrin (CDT) levels before detoxification and 15 (21%) did not. In those with abnormally high levels on admission, the CDT levels decreased progressively after the cessation of alcohol intake (half-life, 16 $\pm$ 5 days) in 51 of the 57 patients. Patients whose CDT levels reached normal values after treatment showed an increase within a "few days" after relapse. GGT activities were elevated in only 56% of the 57 men with increased CDT levels at the time of admission but were normal in 80% of the 15 men with normal CDT levels. However, a combination of CDT and GGT had a sensitivity of 95%.

Alterations in the metabolism of lipids by ethanol have been noted for many years.[73-75] The major change in lipid levels with alcohol intake is an increase in the level of high density lipoprotein, both its cholesterol content (HDL-C) and its apoprotein components, Apo A_1 and Apo A_2. There is a direct linear relationship between alcohol intake and serum levels of Apo A_1, Apo A_2, and HDL-C from 0 to approximately 450 mL of ethanol daily.[60] The correlation between changes in reported alcohol intake and changes in Apo A_1 over six weeks in a recent study[19] was 0.76 ($p<0.001$). Blood pressure changes also correlated more highly with apolipoprotein changes than with retrospective alcohol intake diaries. Levels of all three fall rapidly with reduction of alcohol intake; the decline begins within 1-2 days of decreased alcohol use, reaching a new steady-state within 1-2 weeks.[76-80] An increase in alcohol intake appears to cause a slower increase in HDL-C and apoprotein levels, with maximum levels not occurring until 4-5 weeks after an increase in alcohol consumption, although a rise was evident within one week of increasing intake.[67] There appears to be little or no threshold effect, since both HDL-C and apoprotein levels can distinguish alcohol intakes of 2-3 drinks per day and one drink per day in crossover studies.[78-81] The correlation between HDL-C or apoprotein levels and alcohol intake is stronger than that for GGT,[83] and alcohol appears to be a major determinant of variations in HDL-C levels; in one study, the correlation of HDL-C with alcohol intake was stronger than with cigarette smoking and obesity, two factors associated with HDL-C and apoprotein levels.[75] There is no reported data on the effects of the pattern or duration of drinking on HDL-C or apoprotein levels, such as exists for GGT.

The methods for determination of GGT are relatively standard, and it should be possible to perform GGT measurements at any of the test sites available. Methods for determination of HDL-C, apoprotein and CDT are difficult to standardize, since there is no national or international reference

material. For this reason, it is essential that lipid, apoprotein, and CDT measurements be performed in a single laboratory, by a single procedure, to eliminate a potential source of bias. The actual method used is less critical, but should be the same for all samples in the study. Since samples for lipoprotein measurements will be mailed to a central testing facility, it seems reasonable to measure GGT at the same facility to minimize interlaboratory differences in measurement as a source of variation in reporting results.

For visits at which the samples will be drawn for Central Laboratory tests, participants will be instructed not to eat within 12 hours prior to the clinic visit. They may continue their usual beverage intake as long as fats (e.g., milkshakes) are avoided.

Samples for Central Laboratory determinations will be drawn at the third screening visit, after it is determined that the participant meets the eligibility criteria, at the three- and six-month follow-up data collection visits, and every six months thereafter until the end of the two years of follow-up.

D. Illicit Drug Quantitation

All urine samples collected during the study will be analyzed for marijuana, cocaine, amphetamine, benzodiazepine, barbiturate, and opiate use. An immunoassay screen will be used to eliminate true negative specimens from further consideration. The remaining possibly positive samples will be assessed by clinical interview.

E. Echocardiograms

Echocardiographically-determined left ventricular mass (LVM) has been demonstrated to be a more sensitive measure of left ventricular hypertrophy than electrocardiography.[84] Systolic blood pressure is a strong correlate of echo-LVM, along with age and obesity.[85] Findings reported from the Framingham Heart Study indicate that echo-LVM is a strong predictor of total mortality[86] and incidence of clinical coronary heart disease[87] in older men and women, independent of blood pressure measured in the clinic setting. Casale et al. have reported a predictive role of echo-LVM in the risk of cardiovascular events in hypertensives.[88] Left ventricular hypertrophy (LVH) by echocardiogram has been found to be present in 41-52% of chronic alcoholics without overt cardiac disease, compared to a 3% prevalence of LVH in an age and blood pressure matched control group who drank "no more than small amounts of alcohol occasionally".[89,90] In a recently published study of a group of chronic alcoholics, a strong positive correlation between lifetime alcohol intake and echo-LVM was observed.[91] The only data available for nondependent drinkers is preliminary and unpublished. These cross-sectional and longitudinal data demonstrate a direct relationship between alcohol intake and echo-LVM; from these data, a 2-3 drink per

day change in alcohol intake is estimated to exert a 3-4 fold greater effect on echo-LVM than a 2 mm Hg change in diastolic blood pressure. Treatment of hypertension, both by certain antihypertensive drugs[92] and by weight reduction,[93] has been shown to reduce LVM. Since there is a growing consensus that echo-LVM is an important risk factor, it is becoming standard in cardiovascular (especially hypertension) studies to assess echocardiographic indices. Therefore, the medical significance of reducing alcohol intake would be enhanced if it were shown that a reduction in LVM resulted, in addition to an effect on measured blood pressure. However, since the longitudinal data on BP change and echocardiographic variables is limited and the data on levels of alcohol intake and echocardiographic variables is even more limited, this will be a secondary objective of the study.

After meeting the randomization criteria, all participants will undergo or be scheduled for an echocardiogram as soon as possible (within 1-2 weeks of the randomization visit), but before being told their randomization assignment. Those participants with interpretable baseline echocardiograms (estimated to be 75%) will have a repeat echocardiogram at the end of the six-month initial treatment phase. Six-month echocardiograms will also be obtained for the few participants for whom baseline echocardiograms cannot be obtained for scheduling reasons.

The participating investigator for the central echocardiogram laboratory will oversee the performance of echocardiograms, which includes the following responsibilities: the training and monitoring of echo technicians from the local VA medical centers in order to standardize the methodology/techniques for obtaining the echocardiographic recordings, the mailing of echo tracings, the reading and interpretation of the echocardiograms, supplying the CSPCC with data in a timely manner, and development and implementation of quality control procedures. Performance assessments will be communicated to the echo technician, the participating investigator and the supervising cardiologist at the local station. He will also participate in the analysis, interpretation and reporting of the echocardiographic data.

F. Measurement of Sodium, Potassium, Magnesium, and Creatinine Excretion

At baseline and every six months thereafter, each participant will bring an overnight urine sample for determination of sodium, potassium, magnesium, and creatinine. The purpose is to determine if there are potential confounding effects on BP by changes in sodium and potassium intake. Creatinine will be used as a check on the adequacy of urine collection. Several studies have shown that overnight sodium and potassium collections are significantly correlated with 24-hour collections.[94-96] Overnight collections should avoid a bias toward weekend collections and facilitate compliance because they place much less of a burden on the participant. On the night of each collection, the participant will be instructed to void before retiring and record the time he went to bed. He will not save this void. Each void during the night

and the first morning void will be saved in the container provided. He will also record the time of the first morning void so the total hours of collection are known. Duplicate samples will be retained: one will be sent to the local VA lab for analysis, the other will be stored for backup for lost specimens and for quality control purposes.

For quality control purposes, duplicate samples will be cross-analyzed for at least 5% of the participants. For each phase (I and II) of the trial, duplicate samples from the first 10 participants will be sent to the VA Renal Laboratory for analysis. Subsequently, at least every 15th sample will be sent for duplicate analysis.

G. Diet Assessment

Development of food frequency questionnaire methodology for use in large-scale studies has been ongoing since the 1960's.[97-99] Its appeal lies in its ease of administration, low time burden for participants, and relatively low cost for investigators compared to other methods of assessing dietary intake. The food frequency questionnaire with its many variations has undergone many validation studies in which more time-consuming methods such as food records, 24-hour recalls, or diet history were used as a basis for comparison.[100-104] In general, correlation coefficients between food frequency questionnaires and the other methods varied with the studies and with the nutrients of interest. However, it is generally agreed based on these validation studies that although food frequency questionnaires are not sufficiently accurate or precise to characterize an individual in terms of nutrient intake, they are useful in describing dietary intake of a group and in estimating relative consumption of nutrients through classification of individuals into broad categories or percentiles.[105,106]

Recently the Block food frequency questionnaire[103] was designed and validated for its ability to quantify nutrient intake by means of a self-administered instrument. The foods selected were based on the contribution of that food to the total dietary intake of specific nutrients observed in NHANES II.[107,108] Portion sizes for each food item was similarly determined from NHANES II data. The Block food frequency questionnaire was subsequently field tested and validated for assessment of calcium intake[109] and is being tested for assessment of beta carotene intake. Thus, the Block food frequency questionnaire has been well-developed and amply validated in a number of settings and would be an appropriate tool to be used.

XI. BIOSTATISTICAL CONSIDERATIONS

A. Outcome Variables

The primary outcome measurements are changes in systolic blood pressure and in diastolic blood pressure from baseline to the six-month visit. Analysis of covariance adjusting for baseline values will be used to determine statistically significant differences between the two treatment groups. The analysis will be performed using the intention-to-treat principle; all randomized participants with any follow-up data will be included. The final treatment blood pressure will be as defined in Section IV.A.4. For individuals who are put on antihypertensive medication during the study, even if for another indication, their final blood pressure will be calculated using the BP measurements prior to medication. A secondary analysis using the six-month visit data for all participants, regardless of protocol status, will also be performed. Differences in six-month blood pressure will also be tested in the higher blood pressure stratum alone. Furthermore, the treatment differences in the two strata (a strata by treatment interaction) will be tested.

Evaluation of differences in blood pressure at two years will be difficult because there may be a substantial difference between groups with regard to initiation of antihypertensive medication. However, we will be able to compare the proportions and determine if the difference is statistically significant. Survival analysis techniques will also be used to evaluate this data.

The alcohol intervention will be evaluated using self-report. Individuals will be asked to quantify their alcohol use at baseline, at six months, and at two years. Those participants who have at least a 50% reduction in alcohol consumption between baseline and evaluation will be labelled "successes," those with less than a 50% reduction will be labelled as "failures." Participants with missing data will be labelled as "failures." Tests comparing the proportion of successes in the two groups will be conducted for both the six-month and two-year evaluations. Techniques of regression analysis will be useful in exploring the dose-reponse relationship between change in blood pressure and change in alcohol intake. Partial correlations will be used to examine the strength of this relationship after adjusting for other changes (such as weight) that may also occur.

In addition, a series of biochemical markers of alcohol use will be measured at baseline, at six months, and at two years. The following measurements will be taken: apolipoprotein A_2, apolipoprotein A_1, gamma GT, CD transferrin, and HDL. Analysis of covariance will be used to evaluate differences in these measurements between the two groups. The primary biochemical marker of interest will be apolipoprotein A_2. In addition, relationships among the alcohol intake indices will be explored.

Analysis of covariance will be used to evaluate differences in left ventricular mass between the two groups. Participants who are not "echoable" at baseline will be excluded from analysis. The dose-response relationship between changes in blood pressure and alcohol intake and changes in left ventricular mass will be examined.

Participants who go on antihypertensive medication will continue to be followed in the study. For both the alcohol and echocardiogram variables, they will be treated the same as the other participants. However, for evaluation of blood pressure, measurements obtained after the start of antihypertensive medication will not be used.

Since some subgroups may respond more than others, subgroup analyses will be performed to tentatively identify some of them. Such analyses are exploratory and not confirmatory and will be reported as such. One interesting subgroup would be those participants who are at least 55 years old.

B. Sample Size

All sample sizes are calculated to provide 90% power for two-sided tests at the alpha = .05 level.

1. Blood Pressure

The main end point is the change in blood pressure from baseline to the six-month visit. Blood pressure will be measured two times at each visit. Using estimates of variance components from Rosner,[110,111] we can expect a standard deviation (s) in diastolic blood pressure change of about 7 mm Hg. The corresponding standard deviation for systolic blood pressure is about 11 mm Hg. We are interested in detecting differences (δ) of two mm Hg in DBP and of three mm Hg in SBP for the entire sample. We also require good power for detecting differences of 3 and 4.5 mm Hg for DBP and SBP respectively for those participants in the upper stratum (baseline DBP 90-99 mm Hg). Total sample size requirements can be calculated using the formula,

$$N = 4\left(\frac{(z_{.025} + z_{.1})s}{\delta}\right)^2$$

problem $z_{.025}$ and $z_{.1}$ are obtained from the standard normal distribution. Requirements would be 516 for DBP and 566 for SBP for the entire sample and 230 for DBP and 252 for SBP for the upper stratum.

2. Self-Report of Alcohol Intake

In order to assess the effectiveness of the intervention in reducing alcohol, participants will be asked about their changes in drinking behavior. If 20% of the control group participants and 60% of the intervention group participants report a 50% decrease in alcohol consumption after six months, we would need 78 participants in both groups combined to detect this difference with 90% power.[112] A difference of this magnitude would be detected during the feasibility phase of the study. A smaller difference would be expected after two years of follow-up. If half of these participants (10% vs. 30%) maintain this reduction after two years, then 202 participants would be required.

3. Biochemical Marker of Alcohol Intake: Apolipoprotein A_2

From Camargo et al.[54] we estimate that the correlation (r) between change in alcohol intake and change in apolipoprotein A_2 is .61, the standard deviation in change in apolipoprotein is about 5 mg %, and the standard deviation in change in alcohol intake is about 18 g/day. Since the slope (b) of a linear regression equation relating two variables, x and y, can be calculated using the formula, $b = r_{xy} \frac{s_x}{s_y}$, then we can also calculate that a change of 30 g/day in alcohol intake would imply a change in apolipoprotein A_2 of 5.1 mg %. In order to detect a difference of 5.1 mg % with a standard deviation of 5 mg %, a total sample size requirement of 42 can be obtained from the formula in Section XI.B.1.

4. Conclusions

It appears from these sample size calculations that a total sample size of about 580 will be sufficient to test blood pressure changes. Since all randomized participants with any follow-up data will be included in this analysis, as discussed in Section XI.A, the dropout rate is expected to be very low (< 2%) and to have little effect on power. Therefore, no adjustment for dropouts is necessary. Furthermore, if the upper stratum includes at least 260 participants, there will be good power for detecting the desired difference within this stratum. It also appears that the alcohol intervention can be assessed with ample power after the first 80 participants have completed the six-month study. Generalizability of the study results will be limited if there are few participants in the lower stratum. To obtain adequate power in the upper stratum and to support generalizability with regard to the lower stratum, recruitment will be monitored so that at least 200 participants will be in the lower stratum and at least 260 in the upper stratum.

XII. ORGANIZATION AND ADMINISTRATION

The Perry Point Cooperative Studies Program Coordinating Center under the leadership of the study biostatistician is responsible for coordinating all study activities. A participating investigator at each participating medical center will be responsible for providing leadership at that center. The investigator's most important responsibilities will include recruitment of participants and supervision of study personnel, including a study data collector, a study interventionist and a secretary. The study data collector will assist in recruitment, schedule visits and will complete most of the data collection forms. The study interventionist will assist in recruitment and will administer the alcohol consumption reduction intervention. The study secretary will assist in recruitment, scheduling, data collection, correspondence, and forms management. Several computer assistants at the coordinating center will review study data and enter the data from the study forms into the center's computer. A database management programmer will prepare software for editing data and monitoring data flow. A statistical programmer will develop software for data analysis and presentation. The study chairman will provide overall leadership for the study. The study coordinator in the chairman's office will review completed study forms and will be a liaison between the study chairman, the coordinating center, the participating centers, and the project offices at NHLBI and NIAAA.

The group of investigators will be known collectively as the Study Group. They will meet at least once a year to discuss, with the study chairman, study biostatistician and representatives from NHLBI and NIAAA, problems with recruitment and retention of participants and other study problems. They will initially meet prior to the start of intake to discuss the protocol and to learn about the unique characteristics and constraints associated with cooperative multihospital research. A second meeting will occur near the end of the initial intake period. A third meeting will occur when the second group of centers joins the study. Additional meetings will occur periodically for the duration of the study.

A group chaired by the study chairman and known as the Executive Committee will be responsible for making most management decisions. They also will meet periodically and will review the activity of the Study Group, approve protocol changes and discipline participating centers that fail to follow the protocol or fail to recruit and retain enough participants. Publication policy will be determined by this committee. However, all manuscripts must be approved by the Chief of the Coordinating Center before being submitted for publication. The membership of this committee will include the study chairman, study biostatistician, several investigators from participating medical centers, the project officers and other representatives from NHLBI and NIAAA, and the investigators overseeing the central laboratories and the intervention. An Operations Committee will more frequently monitor the progress of the study. It will

consist of the study chairman, study biostatistician, project officers, Chief of the Coordinating Center, intervention coordinator, and study coordinator.

An independent monitoring committee known as the Data and Safety Monitoring Committee will be responsible for reviewing the progress of the study and making recommendations about any significant changes such as early termination. They will review the data collected during the initial feasibility phase of the study and will be particularly concerned at that time with the effect of the alcohol intervention and with recruitment of participants. If they decide to recommend that the study should continue, they will then review the Executive Committee's decision about adding additional centers. The Data and Safety Monitoring Committee will include a biostatistician, a cardiovascular epidemiologist, experts in clinical hypertension, alcohol research and nutrition, a behavioral scientist and ex-officio, nonvoting representatives of the supporting agencies. The Data and Safety Monitoring Committee will meet periodically and, unlike the Study Group and Executive Committee, will have access to all study data as it is accumulated during the study. The study chairman, biostatistician and project officers for NHLBI and NIAAA will also have access to all study data.

A Human Rights Committee will be responsible for reviewing this study at least once a year to ensure that participants' rights and safety are protected in this study. They are independent of, but will meet with, the Data and Safety Monitoring Committee.

One additional group, the Cooperative Studies Evaluation Committee (CSEC), will exercise an important responsibility in monitoring this study. This committee is responsible for reviewing all proposed VA cooperative studies. Its approval was required before initiating this study. In addition, CSEC will review the recommendations of the Data Monitoring Board at the conclusion of the feasibility phase. A positive recommendation from CSEC and the concurrence of the Directors of the NHLBI, NIAAA and the VA Medical Research Service will be required before proceeding to the full-scale trial.

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APPENDIX A

Informed Consent

DVA COOPERATIVE STUDY #996 - Information About the DVA Cooperative Study "Prevention and Treatment of Hypertension Study" (PATHS)

FORM 87 - SCREENING CONSENT

Medical Center Name _____ Medical Center No. __ __ __

Participant Name_____ Participant No. __ __ __ __ __

PURPOSE: The Department of Veterans Affairs is conducting a study designed to determine how alcohol intake is related to blood pressure and other risk factors for diseases of the heart and blood vessels ("cardiovascular" diseases). You may be eligible for this study depending on your general health, drinking practices and the level of your blood pressure. You are being asked to participate in a screening program that will determine if you are eligible to participate in this study.

PROCEDURES: If you are currently on medications for high blood pressure, you will be asked to stop taking them. Depending on the medication, we may gradually taper the dosage downward. You will be seen at appropriate intervals to monitor your blood pressure. Once the effect of any medicine has worn off or if you have not been taking any medication for high blood pressure, you will be asked to return for three (3) visits about two (2) weeks apart. You will be given $10.00 per visit for your attendance at the second and third screening visits to help defray expenses related to the visits. At these visits, you will have your blood pressure, pulse and weight measured. We will also ask you questions about various health practices, obtain standard laboratory tests, including blood (about a tablespoon) and urine samples and an electrocardiogram (EKG), and perform a physical examination. In addition to standard laboratory tests, your urine will be tested for the presence of several drugs (including cocaine, marijuana and opiates) that might have an effect on your blood pressure. These results will be kept confidential and will not be revealed to anyone outside this study.

RISKS: There is a very small possible risk of a medical complication occurring when you discontinue any blood pressure drugs. We will watch you very closely during this time and will allow you to start taking blood pressure medicine if your blood pressure rises above the mild hypertension range. Drawing blood may cause pain or bruising at the site of the needle stick.

BENEFITS: No benefits can be promised from your participation in this screening program. However, you may benefit from information obtained about your health. You may also feel some satisfaction from knowing you have contributed to medical research which may benefit others in the future.

MONITORING: Your medical and study records may be monitored by a member of the DVA Cooperative Studies Program. At all times, your records will be kept confidential and your identity will not be revealed to anyone outside the program.

WITHDRAWAL/REFUSAL: You do not have to participate in this program if you do not want to. You may also withdraw at any time without jeopardizing the medical care to which you may be entitled.

_____
(Participant's Signature)

YOU WILL RECEIVE A COPY OF THIS FORM.

I HAVE HAD MY QUESTIONS ANSWERED SATISFACTORILY TODAY. I UNDERSTAND THE NATURE OF THE PROGRAM AND AGREE TO TAKE PART IN IT. I UNDERSTAND THAT I AM FREE TO WITHDRAW MY CONSENT AND DISCONTINUE PARTICIPATION AT ANY TIME.

(Participant's Signature)	(Date)
(Witness' Signature)	(Date)
(Participating Investigator's Signature)	(Date)

DVA COOPERATIVE STUDY #996 - Information About the DVA Cooperative Study

"Prevention and Treatment of Hypertension Study" (PATHS)

FORM 88 - STUDY CONSENT

Medical Center Name _____ Medical Center No. ___ ___ ___

Participant Name _____ Participant No. ___ ___ ___ ___ ___

PURPOSE: Researchers are currently studying the relationship of many "lifestyle" factors, such as diet, smoking, drinking alcohol, and exercise, to diseases of the heart and blood vessels ("cardiovascular" diseases). You are being asked to participate in a study designed to determine how alcohol intake is related to blood pressure and other risk factors for cardiovascular diseases. The information learned from this study should be useful in treating people with mild high blood pressure as well as in "public health" recommendations and measures to reduce cardiovascular disease risk. Approximately 600 individuals will participate in this study.

PROCEDURES: All participants in this study will be randomized (by chance, like the flip of a coin) to one of two groups. One group will be asked to lower the amount of alcohol they drink each week and will attend sessions with an instructor where strategies and methods to reduce drinking are taught. The first five (5) sessions will be scheduled during the first three months and will take about one hour for each session. Then sessions may be scheduled at one to three month intervals for the remainder of the study. If you are randomized to the second group you will not attend the instruction sessions nor will you be asked to change the amount of alcohol that you drink.

For all participants there will be six visits one month apart over a period of six months. At these visits, you will have your blood pressure, pulse and weight measured. Occasionally, we will ask you questions about various health practices. At three visits, you will have blood samples drawn (about 4 teaspoons). You will also undergo two (2) echocardiograms (ultrasound examinations of your heart); at the beginning and near the end of the six-month period. This test takes pictures of the heart using sound waves, is safe, and requires about 45 minutes.

After the initial six-month period, you will be followed every three months for an additional eighteen (18) months. During this time, you will come to the clinic six times, at three-month intervals, for measurements and questions similar to the first part of the study. Blood samples will be drawn three times during the 18-month follow-up period.

At each of the visits described above, you will be given $10.00 for your attendance to help defray expenses related to the visit.

During your participation in this study, we will check your blood pressure many times but will not inform you of the results except at the beginning of your participation in the study. However, if your blood pressure goes above the mildly hypertensive range at any time or rises into or remains in the frankly hypertensive range after the initial six-month period, we will notify you and begin or refer you for appropriate treatment, but we will continue to follow you in the study. If any other medical or psychological problems occur during the course of the study, the participating investigator will refer you for appropriate treatment.

_____

(Participant's Signature)

RISKS: The intervention sessions and the evaluation sessions offer no risks to you other than the possibility of tiredness, frustration or anxiety on answering questions. The staff will provide you rest time as needed. Drawing blood may cause pain or bruising at the site of the needle stick. You will be monitored for physical or psychological health problems that might pose a risk for you. There is a very small possible risk of a medical complication occurring during the time when your blood pressure may be mildly elevated. If your blood pressure rises into or remains in the frankly hypertensive range we will watch you very closely and, if necessary, will refer you for appropriate treatment or treat your blood pressure ourselves.

BENEFITS: No benefits can be promised from your participation in this study. However, you may benefit from information derived by monitoring of your health and from the special tests (such as the echocardiogram). You may also feel some satisfaction from knowing you have contributed to medical research which may benefit others in the future.

MONITORING: In order to insure your safe participation during the course of the study, your medical and study records may be monitored by a member of the DVA Cooperative Studies Program. At all times, your records will be kept confidential and your identity will not be revealed to anyone outside the program.

WITHDRAWAL/REFUSAL: You do not have to participate in this study if you do not want to. You may also withdraw at any time during the study and discontinue participation without jeopardizing the medical care to which you may be entitled.

ALTERNATIVE TREATMENT: If you have a cardiovascular risk factor such as high blood pressure, abnormal blood fats (such as cholesterol), or cigarette smoking, there are many ways to improve your risk, including medications.

YOU WILL RECEIVE A COPY OF THIS FORM.

ALL OF MY QUESTIONS RELATING TO THIS STUDY HAVE BEEN ANSWERED TO MY SATISFACTION. I UNDERSTAND THAT IF I HAVE ANY ADDITIONAL QUESTIONS, I MAY CALL:

_____ AT _____.

IF I HAVE ANY QUESTIONS ABOUT MY RIGHTS AS A STUDY PARTICIPANT OR ABOUT A STUDY RELATED INJURY, I CAN CALL:

_____ AT _____.

HAVING READ AND UNDERSTOOD THE ABOVE INFORMATION, I FREELY AGREE TO PARTICIPATE IN THIS STUDY.

_____ _____

(Participant's Signature) (Date)

_____ _____

(Witness' Signature) (Date)

_____ _____

(Participating Investigator's Signature) (Date)

APPENDIX B

Budget

Position Descriptions

01/91

VA-NHLBI-NIAAA COOPERATIVE STUDY 996
Prevention and Treatment of Hypertension Study

Estimated Study Budget for Participating Centers

	FY 91	FY 92	FY 93	FY 94	FY 95	TOTAL
Personnel:						
GS-11, 1.0	10,650	43,200	45,300	47,500	4,000	150,650
GS-7, 1.0	6,300	25,400	26,700	28,000	2,350	88,750
GS-5, 1.0	5,025	20,400				25,425
Other Operating Costs:						
Misc supplies	200	880	920	960	100	3,060
Participant payment	500	4,000	3,000	1,550	250	9,300
Total	22,675	93,880	75,920	78,010	6,700	277,185

NOTE: GS-5's would be funded until 09/92.
GS-11's and GS-7's would be funded until 10/94.

INTERVENTIONIST, (GS-11) 1.0, PARTICIPATING CENTERS

DESCRIPTION

An interagency collaborative study of the effects of alcohol use on hypertension will require an "interventionist" who will be responsible for training participants assigned to the "treatment" condition to alter their drinking behaviors in a face-to-face clinical interview format consisting of hourly sessions spaced over a period of months. This will be done by analyzing participants' drinking-related behaviors, identifying high-risk situations, strengthening coping skills, and helping participants learn to problem solve in order to learn and maintain alternate strategies and behaviors.

DUTIES

Meet individually with participants in regularly scheduled sessions.

Transmit study data in an integrated, knowledgable, and nonthreatening manner. This data will include medical, laboratory, psychological, and alcohol-related information.

Instruct participants in proper use of study materials to self-monitor their drinking and other related life-style behaviors.

Assist participant in setting and achieving appropriate drinking and other life-style change goals and in maintaining his motivation for behavior change.

KNOWLEDGE

Minimum of B.S. or A.B. degree with previous health care experience or a candidate in training for an advanced degree in a health-related area.

Experience with clinical interviewing and at least short-term prolonged contact.

Familiarity with medical vocabulary with understanding of the relationship of alcohol use/abuse to various health problems, especially hypertension and its concomitants; some knowledge of the various tests and biological markers to be used in this study.

SUPERVISION

Candidate should be able to function independently and creatively within appropriate guidelines after a brief training period.

INTERVENTIONIST, (GS-11) 1.0, PARTICIPATING CENTERS (cont)

PERSONAL CONTACTS AND QUALITIES

Will participate and communicate with all study personnel as appropriate.

Works in a kind, empathic, honest manner.

Has sufficient status within the agency.

Impresses one as highly credible and authoritative.

Is interested in the study.

Is able to maintain a caring but objective professional demeanor.

STUDY DATA COLLECTION TECHNICIAN (GS-7) 1.0, Participating Centers

DESCRIPTION

This position encompasses a broad range of clinical care and administrative duties related to VA Cooperative Study #996, "Trial of Reduction of Alcohol Intake in Lowering Blood Pressure." The study technician holds a unique and important position with regard to the implementation of the study design. This individual will serve as a clinical research technician with broad responsibilities in the conduct of this multicenter cooperative study. This individual will be primarily responsible for all activities related to data collection, other than the performance of the physical examinations, and will carry a primary responsibility in recruitment of participants. In this regard, the position will encompass a wide variety of administrative, interpersonal, clinical and scientific skills. In addition, this person must achieve an understanding of the basic pathophysiology of hypertensive- and alcohol-related disorders and the details of treatment and participant follow-up procedures to adequately serve the needs listed above.

MAJOR DUTIES

The principal duties of the data collection technician will be as follows:

Administrative Responsibilities:

Data Collection and maintenance of all participant records related to screening and data collection visits, including study forms and questionnaires, home telephone and address, and pertinent laboratory data.

Transmission of forms to the Chairman's office and to the Perry Point CSPCC.

Appointment and laboratory scheduling with study participants and coordination of visits with participating investigators, when indicated.

Preparation and mailing of plasma and serum samples and echocardiographic tapes to the central laboratories.

Data Collection:

It will be the responsibility of the study technician to obtain the data necessary to complete every study screening and data collection form for each participant. This will include obtaining review of the medical history from interviews with the participant and from medical records, and consulting with appropriate physicians if indicated regarding inclusion and exclusion criteria.

All data will be recorded and filed for access at the participating institution and duplicate copies sent to the Chairman's office and the Perry Point CSPCC.

STUDY DATA COLLECTION TECHNICIAN (GS-7) 1.0, Participating Centers (Cont.)

Procedures:

The study technician will be responsible for obtaining history of participant complaints or illnesses; all random-zero blood pressure determinations and other vital signs; administering all lifestyle and alcohol intake (CDR) questionnaires; with the assistance of the interventionist carrying out the prescreening and screening procedures, administering the screening alcohol intake and dependency instruments, and obtaining informed consent.

The study technician will instruct participants on the collection of overnight urines, draw blood samples (or arrange for blood to be drawn) for local laboratory studies, draw blood samples and process them for the plasma and serum to be sent to the Central Laboratory.

The study technician will maintain contacts with inpatient services, outpatient clinics, emergency services and other sources to locate and identify potential participants for the study.

The technician will initiate and oversee the prescreening and screening process, including medical evaluation and tests.

The study technician will schedule diagnostic tests, consultations, and all screening and data collection visits.

The technician will bring all potential study participants to the attention of the participating investigator(s) at the institution for their evaluation.

Following randomization, the technician will schedule and conduct all data collection visits according to the study protocol.

The technician will schedule appropriate tests at regular designated intervals, or additional tests when necessary.

The technician will visit the patient during hospitalization for reasons other than those related to the study.

The technician will serve as a source of information to patients for questions which arise during the course of the study related to data collection or data collection visits.

The technician will notify the participating investigator of any protocol violations, intercurrent illness or event, or blood pressure escape criteria being met, so proper evaluation and/or treatment may be initiated.

Secretarial and Organizational Activities:

The study technician will be available during regular hours for all questions directed to the participating investigator regarding the study. These may originate from the Chairman's office, from other physicians in or outside the hospital, nursing staff or patients. The

STUDY DATA COLLECTION TECHNICIAN (GS-7) 1.0, Participating Centers (Cont.)

individual will answer those questions of which he or she is capable and refer the remaining questions to the participating investigator or study interventionist. All questions related to the intervention or randomization status will be referred.

A small amount of correspondence related to the study will be organized and administered by the study technician.

FACTOR I - KNOWLEDGE

An understanding of the basis of scientific experimentation with appropriate attention to the reliability and objectivity of data acquisition will be necessary. A knowledge of the theories and principles of physiology, biology, chemistry or related discipline equivalent to a bachelor's degree or nursing degree is necessary, with some exposure to undergraduate science or comparable experience. The candidate will be expected to achieve a detailed understanding of blood pressure measurement, and pathophysiology of hypertensive- and alcohol-related diseases. He/She should understand the medical tasks utilized in the screening, evaluation, and follow-up of participants. Specific knowledge pertaining to the techniques of random-zero blood pressure determinations, venipuncture and processing of blood and overnight urine specimens, and administration of questionnaires and Chronological Drinking Record.

FACTOR II - SUPERVISORY CONTROLS

The data collection technician regularly and independently performs the duties listed above under the supervision of the participating investigator. He or she will monitor the information sent to the Chairman's office and with the assistance of the participating investigator, determine discrepancies in data, deviations from protocol, administrative or scheduling difficulties, and other problems which may arise. For the most part, however, the technician must achieve a large degree of independent and self-sufficient activity in order to interpret the requests of participants and physicians and insure that all data required is collected.

FACTOR III - GUIDELINES

The guidelines will include the operations manual for the study and those VA regulations covering patient management. Additional guidelines regarding the details of the study operation at the individual participating centers will be determined and elaborated by the participating investigators.

FACTOR IV - COMPLEXITY

This position requires skills in organization, interpersonal relationships, communications, and the understanding and knowledge of fairly complex clinical and technical factors related to the study. The individual must be able to understand the scientific basis for the study and the details of the study protocol. In addition, the individual will

STUDY DATA COLLECTION TECHNICIAN (GS-7) 1.0, Participating Centers (Cont.)

serve as the spokesperson for the participating investigator in several situations, and must be able to explain both detailed and broader aspects of the study protocol to a variety of individuals.

FACTOR V - SCOPE AND EFFECT

The individual must be flexible enough to deal with many aspects of the day-to-day administration of the project, organized enough to maintain all the data, schedules and participant identification, and insightful enough to identify and call to the participating investigator's attention those problems that arise within any aspect of the study.

FACTOR VI - PERSONAL CONTACTS

The major personal contacts will be with the participants enrolled in the study. The skill of the data collection technician at expressing care and concern for these participants will determine in large part the success of the study in following all participants to the conclusion of the protocol. In addition, the technician must maintain affable working relationships with the interventionist, nurses, radiographers, laboratory technicians, physicians, secretarial staff and the participating investigator. The interpersonal skills needed to maintain such relationships with this varied group of people will require an individual who has considerable talent in this area.

FACTOR VII - PURPOSE OF PERSONAL CONTACTS

The main purpose of the participant contact is to facilitate continued follow-up and acquisition of data throughout the study protocol. The participants must be kept informed as to the nature of their participation in the study, the importance of compliance to study protocol, and the necessity to notify the study technician should there be any change in status. In terms of the contact with medical staff, good relationships with these individuals will facilitate the smooth operation of scheduling and data acquisition during the study.

FACTOR VIII - PHYSICAL DEMANDS

The work is mostly sedentary with some walking and periods of standing. No heavy physical labor is required.

FACTOR IX - WORK ENVIRONMENT

The work will be performed primarily in the office and ambulatory care setting.

APPENDIX E

Study Forms

STUDY FORMS

FORM 1 - BRIEF SCREENING INSTRUMENT LOG

FORM 2 - DATA COLLECTION FORM

FORM 3 - DEMOGRAPHIC CHARACTERISTICS

FORM 4 - ALCOHOL USE QUESTIONNAIRE (ADS-10)

FORM 5 - MEDICAL HISTORY

FORM 6 - LIFETIME DRINKING HISTORY

FORM 7 - PHYSICAL ACTIVITY

FORM 8 - PSYCHOSOCIAL AND HEALTH HABITS QUESTIONNAIRE

FORM 9 - BECK INVENTORY

FORM 10 - LOCAL LABORATORY DATA

FORM 10A- QUALITY CONTROL SAMPLES - OVERNIGHT URINES

FORM 11 - PHYSICAL EXAMINATION

FORM 12 - DIET QUESTIONNAIRE

FORM 13 - CHRONOLOGICAL DRINKING RECORD

FORM 14 - CENTRAL LABORATORY DATA

FORM 15 - ECHOCARDIOGRAM REPORT FORM

FORM 15A- ECHOCARDIOGRAM WORKSHEET

FORM 16 - ASSESSMENT OF INTERVENTION SESSIONS

FORM 17 - INTERVENTIONIST OR PARTICIPANT GLOBAL ASSESSMENT FORM

FORM 18 - ASSESSMENT OF FOLLOW-UP INTERVENTION SESSIONS

FORM 19 - INTERCURRENT ILLNESS

FORM 20 - EXCLUSION/TERMINATION FORM

DVA COOPERATIVE STUDY #996 - PATHS

FORM 1 - BRIEF SCREENING INSTRUMENT LOG

Medical Center Name ______________________

Medical Center No. __ __ __

Form Completed By ______________________

Date Completed __ __ / __ __ / __ __
Mo Day Yr

Participant Number	Q.1 Veteran 1=Yes, 2=No	Q.2 Age	Q.3 Sex 1=Male 2=Female	Alcohol Use: Q.9 1=Yes 2=No	Alcohol Use: Q.10 (Enter No.)	Alcohol Use: Q.11 (Enter No.)	Race 1=Black 2=Nonblack	Source (Code)	Eligible 1=Yes 2=No
__ __ __ __ __	__	__ __	__	__	__ __	__	__	__ __	__
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PI's Signature ______________________

VA FORM 10-29010(NR)a
AUGUST 1990

DVA COOPERATIVE STUDY #996 **FORM 2**
PATHS **DATA COLLECTION FORM**

Medical Center Name _____ Medical Center No. __ __ __

Participant Name _____ Participant No. __ __ __ __ __

Form Completed By _____ Date Completed __ __ __ __ __ __
Mo Day Yr

CODE APPROPRIATE RATING PERIOD ..... __ __

SCREENING: S1=91 S2=92 S3=93 FOLLOW-UP MONTH: 01 02 03 04 05 06 09 12 15 18 21 24

IF INTERIM VISIT, ENTER INTERIM VISIT NUMBER ..... __ __

1. DID PARTICIPANT COME IN FOR THIS VISIT? (1=Yes, 2=No) ..... ____

IF NO, EXPLAIN _____

2. PREPARATION FOR BLOOD PRESSURE MEASUREMENTS

a.	Time of day	__ __:__ __ AM / PM
	WAIT FIVE MINUTES	
b.	Room temperature	__ __ °F
c.	Arm circumference .. (Code: 1=Right arm, 2=Left arm)	__ __ cm ____
d.	Cuff size (code) ..... 1=Small adult (<25 cm) 2=Adult (25-32 cm) 3=Large adult (33-41 cm) 4=Thigh (>41 cm)	_____
e.	Resting 30-second heart rate	__ __ / 30 sec.
f.	Resting one-minute heart rate (2 x e)	__ __ __ / 1 min.
g.	Pulse obliteration pressure (using standard mercury manometer)	__ __ __ mm Hg
		+ 3 0
h.	Maximum zero	+ __ __ mm Hg
i.	Random zero peak inflation level	__ __ __ mm Hg
j.	Certification number of random zero device	__ __ __ __

3. FIRST RANDOM ZERO SITTING BLOOD PRESSURE — SBP / DBP

a.	Reading	__ __ __ / __ __ __ mm Hg
b.	Zero value	__ __ / __ __
c.	Corrected value (a - b)	__ __ __ / __ __ __ mm Hg

WAIT 30 SECONDS

4. SECOND RANDOM ZERO SITTING BLOOD PRESSURE — SBP / DBP

a.	Reading	__ __ __ / __ __ __ mm Hg
b.	Zero value	__ __ / __ __
c.	Corrected value (a - b)	__ __ __ / __ __ __ mm Hg

STAND PARTICIPANT AND WAIT 60 SECONDS

5. RANDOM ZERO STANDING BLOOD PRESSURE — SBP / DBP

a.	Reading	__ __ __ / __ __ __ mm Hg
b.	Zero value	__ __ / __ __
c.	Corrected value (a - b)	__ __ __ / __ __ __ mm Hg

6. SUM OF 2 SITTING BLOOD PRESSURES (3c + 4c) ..... __ __ __ / __ __ __ mm Hg

7. MEAN BLOOD PRESSURES (item 6 ÷ 2) ..... __ __ __ / __ __ __ mm Hg

8. IF SCREENING VISIT, Does participant meet blood pressure inclusion criteria? (1=Yes, 2=No) ..... ____

9. HEIGHT (Screening Visit 3 ONLY) ..... __ __ inches

10. WEIGHT ..... __ __ __ lbs.

CONCURRENT MEDICATION:

Drug Name	A. Drug Code	B. Daily Dose (mg/day)
11. _____	__ __ __	__ __ __ __
12. _____	__ __ __	__ __ __ __
13. _____	__ __ __	__ __ __ __
14. _____	__ __ __	__ __ __ __
15. _____	__ __ __	__ __ __ __
16. _____	__ __ __	__ __ __ __

INTERCURRENT ILLNESS:

17. Has participant been ill, had any medical or psychiatric treatment initiated, or been hospitalized since last visit? (1=Yes, 2=No) ..... ___

IF YES, complete Form 19.

18. DATE OF NEXT VISIT ..... Mo __ __ Day __ __ Yr __ __

_____
Participating Investigator's Signature

DVA COOPERATIVE STUDY #996 **FORM 3**
PATHS **DEMOGRAPHIC CHARACTERISTICS**

Medical Center Name _____ Medical Center No. __ __ __

Participant Name _____ Participant No. __ __ __ __ __

Form Completed By _____ Date Completed __ __ __ __ __ __
Mo Day Yr

1. Please tell me your date of birth, starting with the month, the day, and then the year ..... Mo __ __ Day __ __ Yr __ __

2. Which of the following best describes your racial/ethnic background? ..... ___
   1=White, not of hispanic origin
   2=Black, African American
   3=Hispanic or Latino
   4=Asian
   5=American Indian
   6=Other, specify _____

3. Marital status ..... ___
   1=Married and living with spouse
   2=Not married, living with another
   3=Separated
   4=Widowed
   5=Divorced
   6=Never married, not living with someone

4. Including yourself, how many persons are now living in your household?
   a. Adults (18 and older) ..... ___
   b. Children (17 and younger) ..... ___

5. Are you currently self-employed or employed outside the home? (1=Yes, 2=No) ..... ___

   IF YES, ANSWER QUESTIONS 6 AND 7 AND GO TO QUESTION 11.
   IF NO, SKIP TO QUESTION 8.

6. How many hours do you work each week? ..... ___
   1=35 hrs or more 3=Less than 10 hrs
   2=10-34 hrs 4=Variable

7. What kind of work are you doing now?

   _____

8. IF NOT EMPLOYED, code main reason ..... ___
   1=Retired
   2=Permanently disabled (but not hospitalized)
   3=Temporarily disabled (but not hospitalized)
   4=Temporarily laid off
   5=Looking for a job but none available
   6=Doesn't want to work
   7=Other, specify _____

Medical Center No. ___ ___ ___

Participant No. ___ ___ ___ ___ ___

9. When was the last time you were employed? ..... Mo ___ ___ Yr ___ ___

10. What kind of work did you do then? _____

11. In some households, it is difficult to pay for basic expenses like food, transportation, and heating. How hard would you say it is for you to find money for these basics? ..... ___
    1=Very hard
    2=Somewhat hard
    3=Not very hard at all

12. How many years of education have you finished? ..... ___ ___

13. Do you have a high school diploma? (1=Yes, 2=No) ..... ___

14. Do you have a GED? (1=Yes, 2=No) ..... ___

15. Do you have an associate's degree, a bachelor's degree or study beyond a bachelor's degree? ..... ___
    1=No
    2=Associate's degree
    3=Bachelor's degree
    4=Beyond bachelor's degree
    Specify _____

16. Have you moved residence in the past year? (1=Yes, 2=No) ..... ___

17. Do you expect to move within the next six months? (1=Yes, 2=No) ..... ___

INTERVIEWER SHOULD NOTE EASE OF LANGUAGE ABILITY AND ANY POSSIBLE LITERACY PROBLEMS:

_____

_____

_____

_____
Participating Investigator's Signature

VA FORM 10-29010(NR)c
AUGUST 1990

DVA COOPERATIVE STUDY #996 **FORM 4**
PATHS **ALCOHOL USE QUESTIONNAIRE (ADS-10)**

Medical Center Name _____ Medical Center No. __ __ __

Participant Name _____ Participant No. __ __ __ __ __

Form Completed By _____ Date Completed __ __ __ __ __ __
Mo Day Yr

1. HAVE YOU HAD "SHAKES" WHEN SOBERING UP (HANDS TREMBLE, SHAKE INSIDE) AS A RESULT OF DRINKING? ..... _____
   0 = No
   1 = Yes, sometimes
   2 = Yes, almost every time I drink

2. DO YOU GET PHYSICALLY SICK (E.G., VOMIT, STOMACH CRAMPS) AS A RESULT OF DRINKING? ..... _____
   0 = No
   1 = Sometimes
   2 = Almost everytime I drink

3. DO YOU PANIC BECAUSE YOU FEAR YOU MAY NOT HAVE A DRINK WHEN YOU NEED IT? ..... _____
   0 = No 1 = Yes

4. HAVE YOU HAD BLACKOUTS ("LOSS OF MEMORY" WITHOUT PASSING OUT) AS A RESULT OF DRINKING? ..... _____
   0 = No, never 2 = Often
   1 = Sometimes 3 = Almost every time I drink

5. DO YOU CARRY A BOTTLE WITH YOU OR KEEP ONE CLOSE AT HAND? ..... _____
   0 = No
   1 = Some of the time
   2 = Most of the time

6. HAVE YOU PASSED OUT AS A RESULT OF DRINKING? ..... _____
   0 = No
   1 = Sometimes
   2 = Almost every time

7. AS A RESULT OF BEING DRUNK, HAS YOUR THINKING BEEN FUZZY OR UNCLEAR? ..... _____
   0 = No 2 = Yes, for one or two days
   1 = Yes, but only for a few hours 3 = Yes, for many days

8. CAN YOU DRINK MORE THAN YOU USED TO BEFORE GETTING DRUNK? ..... _____
   0 = No 1 = Yes

9. HAVE YOU HAD WEIRD AND FRIGHTENING SENSATIONS WHEN DRINKING? ..... _____
   0 = No
   1 = Yes, perhaps once or twice
   2 = Yes, often

10. AFTER TAKING ONE OR TWO DRINKS, CAN YOU USUALLY STOP? ..... _____
    0 = Yes 1 = No

_____
Participating Investigator's Signature

VA FORM 10-29010(NR)d
AUGUST 1990

Medical Center Name _____ Medical Center No. __ __ __

Participant Name _____ Participant No. __ __ __ __ __

Form Completed By _____ Date Completed __ __ __ __ __ __
Mo Day Yr

1. HAVE SCREENING CONSENT AND VA 10-1086 BEEN SIGNED? (1 = Yes, 2 = No) ..... ___

2. PARTICIPANT'S SOCIAL SECURITY NUMBER ..... __ __ __ __ __ __ __ __ __

MEDICAL HISTORY IS THERE A HISTORY OF:	CODE: 1=YES 2=NO	COMMENTS
3. Cirrhosis	___	_____
4. Alcoholic hepatitis	___	_____
5. Pancreatitis	___	_____
6. Alcohol-related UGI bleeding	___	_____
7. Varices	___	_____
8. Peripheral neuropathy	___	_____
9. Cerebellar dysfunction	___	_____
10. Encephalopathy	___	_____
11. Significant cognitive deficits	___	_____
12. Psychoactive substance dependence	___	_____
13. Major psychotic disorder	___	_____
14. Major affective disorder	___	_____
15. Severe anxiety disorder	___	_____
16. Major personality disorder	___	_____
17. Malignancy (active)	___	_____
18. Seizure disorder	___	_____
19. Clotting or bleeding disorder	___	_____
20. Stroke	___	_____
21. Cerebral or subarachnoid hemorrhage	___	_____
22. Myocardial infarction	___	_____
23. Symptomatic ischemic heart disease	___	_____
24. Congestive heart failure	___	_____
25. Atrial fibrillation or other dysrhythmia	___	_____
26. Retinopathy (grade III-IV: hypertensive hemorrhages and/or exudates with or without papilledema)	___	_____
27. Surgically curable or secondary hypertension	___	_____

28. Are there any reasons for excluding the participant? (1=Yes, 2=No) ..... ___

IF YES:

a. Summary of significant medical/psychiatric diagnoses and findings that would exclude participant: _____

_____

_____

IF YES, STOP HERE. PARTICIPANT NOT ELIGIBLE FOR THE STUDY. COMPLETE FORM 20.

 Medical Center No. __ __ __ Participant No. __ __ __ __ __

HYPERTENSION TREATMENT HISTORY

29. Has the participant been previously diagnosed as having hypertension? (1=Yes, 2=No) ..... ___

IF YES:

A. How long ago was participant's hypertension first detected? (years) ..... __ __

B. How long ago was participant first treated for hypertension? (years) ..... __ __

C. When screened, was participant currently being treated for hypertension? (1=Yes, 2=No) ..... ___

LIST ALL MEDICATIONS USED FOR HYPERTENSION AT TIME OF INITIAL SCREENING.

	Drug Name	A. Drug Code	B. Daily Dose (mg/day)	C. Duration 1=<1 mo 2=1 mo-6 mo 3=>6 mo <1 yr 4=>1 yr
30.	_____	__ __ __	__ __ __ __	____
31.	_____	__ __ __	__ __ __ __	____
32.	_____	__ __ __	__ __ __ __	____
33.	_____	__ __ __	__ __ __ __	____
34.	_____	__ __ __	__ __ __ __	____
35.	_____	__ __ __	__ __ __ __	____
36.	_____	__ __ __	__ __ __ __	____
37.	_____	__ __ __	__ __ __ __	____

_____
Participating Investigator's Signature

VA FORM 10-29010(NR)e
AUGUST 1990

DVA COOPERATIVE STUDY #996 - PATHS

FORM 6 - LIFETIME DRINKING HISTORY

MEDICAL CENTER NAME _____ MEDICAL CENTER NO. ____ PARTICIPANT NAME _____ PARTICIPANT NO. _____

FORM COMPLETED BY _____ DATE COMPLETED Mo ___ Day ___ Yr ___ TOTAL NUMBER OF PHASES ___

PHASE	FREQUENCY	QUANTITY Drinks/Day	TYPE (%)	STYLE (Circle One)	LIFE EVENT OR CHANGES Code: 1=Positive, 2=Negative	CONTEXT (%)	TIME (%)
PAST WEEK From Date _____ To Date _____	_____ Days/Wk.	Average ___ Maximum ___	Beer ___ Liquor ___ Wine ___	1 Occasional 2 Weekend 3 Binge 4 Frequent	___ 1 Family ___ 7 Financial ___ 2 Work ___ 8 Peer Group ___ 3 School ___ 9 Drug Use ___ 4 Medical ___10 Treatment ___ 5 Residence ___11 Death ___ 6 Legal-Jail ___12 Emotional	Alone ___ With Others ___	Morning ___ Afternoon ___ Evening ___
PAST SIX MO. From Date _____ To Date _____	___ Days/Mo.	Average ___ Maximum ___	Beer ___ Liquor ___ Wine ___	1 Occasional 2 Weekend 3 Binge 4 Frequent	___ 1 Family ___ 7 Financial ___ 2 Work ___ 8 Peer Group ___ 3 School ___ 9 Drug Use ___ 4 Medical ___10 Treatment ___ 5 Residence ___11 Death ___ 6 Legal-Jail ___12 Emotional	Alone ___ With Others ___	Morning ___ Afternoon ___ Evening ___

1 Drink (approx.) = 12 oz. beer
1-1/2 oz. liquor
5 oz. wine
3 oz. fortified wine
13.6 g absolute alcohol

Liquor: 1 mickey (12 oz.) = 8 drinks
1 bottle (25 oz.) = 17 drinks

Wine: 1 bottle (25 oz.) = 5 drinks
1 bottle fortified = 8 drinks

To Calculate Drinks/Week: FREQUENCY (___ Days/Mo.) x Average QUANTITY (___ Drinks/Day) ÷ 4.3 = _____.__ Drinks/Week

PARTICIPANT MEETS ALCOHOL CONSUMPTION INCLUSION CRITERION? (CIRCLE ONE) YES NO

IF YES, COMPLETE DRINKING HISTORY. IF NO, STOP.

VA FORM 10-29010(NR)t
AUGUST 1990

MEDICAL CENTER NAME ______________ MEDICAL CENTER NO. _ _ _ PARTICIPANT NAME ______________ PARTICIPANT NO. _ _ _ _ _ _

FORM COMPLETED BY ______________ DATE COMPLETED Mo _ _ Day _ _ Yr _ _

PHASE	FREQUENCY Days/Month	QUANTITY Drinks/Day	TYPE (%)	STYLE (Circle One)	LIFE EVENT OR CHANGES Code: 1=Positive, 2=Negative		CONTEXT (%)	TIME (%)
PHASE _ _ From _ _ Younger Age To _ _ Older Age	_ _	Average _ _ Maximum _ _	Beer _ _ _ Liquor _ _ _ Wine _ _ _	1 Occasional 2 Weekend 3 Binge 4 Frequent	_ 1 Family _ 2 Work _ 3 School _ 4 Medical _ 5 Residence _ 6 Legal-Jail	_ 7 Financial _ 8 Peer Group _ 9 Drug Use _ 10 Treatment _ 11 Death _ 12 Emotional	Alone _ _ _ With Others _ _ _	Morning _ _ _ Afternoon _ _ _ Evening _ _ _
PHASE _ _ From _ _ Younger Age To _ _ Older Age	_ _	Average _ _ Maximum _ _	Beer _ _ _ Liquor _ _ _ Wine _ _ _	1 Occasional 2 Weekend 3 Binge 4 Frequent	_ 1 Family _ 2 Work _ 3 School _ 4 Medical _ 5 Residence _ 6 Legal-Jail	_ 7 Financial _ 8 Peer Group _ 9 Drug Use _ 10 Treatment _ 11 Death _ 12 Emotional	Alone _ _ _ With Others _ _ _	Morning _ _ _ Afternoon _ _ _ Evening _ _ _
PHASE _ _ From _ _ Younger Age To _ _ Older Age	_ _	Average _ _ Maximum _ _	Beer _ _ _ Liquor _ _ _ Wine _ _ _	1 Occasional 2 Weekend 3 Binge 4 Frequent	_ 1 Family _ 2 Work _ 3 School _ 4 Medical _ 5 Residence _ 6 Legal-Jail	_ 7 Financial _ 8 Peer Group _ 9 Drug Use _ 10 Treatment _ 11 Death _ 12 Emotional	Alone _ _ _ With Others _ _ _	Morning _ _ _ Afternoon _ _ _ Evening _ _ _
PHASE _ _ From _ _ Younger Age To _ _ Older Age	_ _	Average _ _ Maximum _ _	Beer _ _ _ Liquor _ _ _ Wine _ _ _	1 Occasional 2 Weekend 3 Binge 4 Frequent	_ 1 Family _ 2 Work _ 3 School _ 4 Medical _ 5 Residence _ 6 Legal-Jail	_ 7 Financial _ 8 Peer Group _ 9 Drug Use _ 10 Treatment _ 11 Death _ 12 Emotional	Alone _ _ _ With Others _ _ _	Morning _ _ _ Afternoon _ _ _ Evening _ _ _

1 Drink (approx.) = 12 oz. beer
1-1/2 oz. liquor
5 oz. wine
3 oz. fortified wine
13.6 g absolute alcohol

Liquor: 1 mickey (12 oz.) = 8 drinks
1 bottle (25 oz.) = 17 drinks

Wine: 1 bottle (25 oz.) = 5 drinks
1 bottle fortified = 8 drinks

____
Participating Investigator's Signature

VA FORM 10-29010(NR)f
AUGUST 1990

MEDICAL CENTER NAME _____ MEDICAL CENTER NO. __ __ __

PARTICIPANT NAME _____ PARTICIPANT NO. __ __ __ __ __

FORM COMPLETED BY _____ DATE COMPLETED Mo __ __ Day __ __ Yr __ __

CODE APPROPRIATE RATING PERIOD (MONTH) 00 (PRE) 06 12 18 24 ..... __ __

READ TO PARTICIPANT: These questions are about physical exercise. In the PAST SEVEN DAYS, have you done any of the following exercises, sports, or physically active hobbies?

	CODE: 1 = YES 2 = NO	A. How many TIMES in the past week did you (play/go/do) this activity? CODE: TIMES	B. On the average, about how many MINUTES did you actually spend on this activity on each occasion? CODE: MINUTES	C. What usually happened to your heart rate or breathing when you did this activity? Did you have a small, moderate, or large increase, or no increase at all in your heart rate or breathing? CODE: 1 = SMALL 2 = MODERATE 3 = LARGE 4 = NONE
1. WALKING FOR EXERCISE ...	____	1A. __ __	1B. __ __ __	1C. ____
2. JOGGING/RUNNING	____	2A. __ __	2B. __ __ __	2C. ____
3. HIKING	____	3A. __ __	3B. __ __ __	3C. ____
4. GARDENING/YARD WORK	____	4A. __ __	4B. __ __ __	4C. ____
5. AEROBICS/AEROBIC DANCING	____	5A. __ __	5B. __ __ __	5C. ____
6. OTHER DANCING	____	6A. __ __	6B. __ __ __	6C. ____
7. CALISTHENICS OR GENERAL EXERCISE	____	7A. __ __	7B. __ __ __	7C. ____
8. GOLF	____	8A. __ __	8B. __ __ __	8C. ____
9. TENNIS	____	9A. __ __	9B. __ __ __	9C. ____
10. BOWLING	____	10A. __ __	10B. __ __ __	10C. ____
11. BIKING	____	11A. __ __	11B. __ __ __	11C. ____
12. SWIMMING/WATER EXERCISES	____	12A. __ __	12B. __ __ __	12C. ____
13. YOGA	____	13A. __ __	13B. __ __ __	13C. ____
14. WEIGHT LIFTING/TRAINING	____	14A. __ __	14B. __ __ __	14C. ____
15. BASKETBALL	____	15A. __ __	15B. __ __ __	15C. ____
16. BASEBALL/SOFTBALL	____	16A. __ __	16B. __ __ __	16C. ____
17. FOOTBALL	____	17A. __ __	17B. __ __ __	17C. ____
18. SOCCER	____	18A. __ __	18B. __ __ __	18C. ____
19. VOLLEYBALL	____	19A. __ __	19B. __ __ __	19C. ____
20. HANDBALL, RACQUETBALL, OR SQUASH	____	20A. __ __	20B. __ __ __	20C. ____
21. SKATING	____	21A. __ __	21B. __ __ __	21C. ____
22. SKIING	____	22A. __ __	22B. __ __ __	22C. ____
Have you done any (other) exercises, sports or physically active hobbies in the past week (that I haven't mentioned)? (1=Yes, 2=No)				
23. Anything else?	____ (IF YES, DESCRIBE BELOW)			
24. _____		24A. __ __	24B. __ __ __	24C. ____
25. _____		25A. __ __	25B. __ __ __	25C. ____

Signature of Participating Investigator _____

VA FORM 10-29010(NR)g
AUGUST 1990

FORM 8
PSYCHOSOCIAL AND HEALTH HABITS QUESTIONNAIRE

Medical Center Name _____ Medical Center No. __ __ __

Participant Name _____ Participant No. __ __ __ __ __

Form Completed By _____ Date Completed __ __ __ __ __ __
Mo Day Yr

CODE APPROPRIATE RATING PERIOD (MONTH) ..... __ __

CODE: 00 (PRE) 06 12 18 24

1. How would you rate your general state of health during the past six months? ..... ___
   1=Excellent 4=Fair
   2=Very good 5=Poor
   3=Good

SMOKE HABITS

2. Have you ever smoked? (1=Yes, 2=No) ..... ___
   IF NO, skip to Q. 10.

3. Do you currently smoke cigarettes? (1=Yes, 2=No) ..... ___
   a. IF NO, when did you stop smoking? ..... Mo __ __ Yr __ __
   (SKIP TO Q. 10)

4. How many cigarettes do you smoke each day? ..... __ __ __

5. Do you inhale? (1=Never, 2=Sometimes, 3=Always) ..... ___

6. Do you smoke more during the morning than during the rest of the day? (1=Yes, 2=No) ..... ___

7. How soon after you wake up do you smoke your first cigarette? ..... ___
   1=Less than 15 minutes 3=Within 2 hours
   2=Within 1 hour 4=Greater than 2 hours

8. Do you find it difficult to refrain from smoking in places where it is forbidden (work, cinema, airplanes, etc.)? (1=Yes, 2=No) ..... ___

9. Do you smoke if you are so ill that you are in bed most of the day? (1=No, 2=Yes, but lesser amount, 3=Yes, the same) ..... ___

10. Do you use chewing tobacco, snuff or other smokeless tobacco? (1=Yes, 2=No) ..... ___
    a. How often each day? ..... __ __

CAFFEINE

11. On a typical day, how many cups of regular coffee do you drink? ..... __ __
    1=One or two 4=Seven +
    2=Three or four 5=None
    3=Five or six

12. On a typical day, how many cups of tea do you drink? ..... __ __
    1=One or two 4=Seven +
    2=Three or four 5=None
    3=Five or six

13. On a typical day, how many glasses of cola or caffeine-containing soft drinks do you drink? ..... __ __

1=One or two
2=Three or four
3=Five or six
4=Seven +
5=None (GO TO Q.15)

14. How often did you drink this much coffee/tea/cola per day in the last six months? ..... ___

1=Every day or almost every day
2=About once a week
3=About once a month
4=Several times in the last six months

EXERCISE

15. What kind of exercise do you get during a typical day AT WORK? ..... ___

1=Do not work
2=Usually sit during the day and do not walk very much
3=Stand or walk about quite a lot but do not lift or carry things very often
4=Usually lift or carry light loads or have to climb stairs or hills often
5=Often lift or carry heavy loads

16. What kind of exercise do you get during a typical day when you are not at work or if you are not working now? ..... ___

1=Usually sit during the day and do not walk very much
2=Stand or walk about quite a lot but do not lift or carry things very often
3=Usually lift or carry light loads or have to climb stairs or hills often

17. About how many flights of stairs do you climb each day? ..... __ __

18. How many times per week do you engage in any regular physical activity such as brisk walking, jogging, bicycling, etc. long enough to work up a sweat? ..... __ __

19. Compared to other men your age, how would you rate your physical activity? ..... ___

1=Not very active
2=Moderately active
3=Very active

20. Has your physical activity changed during the past three months? ..... ___

1=No, remains the same
2=Less active, explain _____
3=More active, explain _____

MEDICATIONS

During the past six months, how often have you used any of the following medications or drugs: USE CODES BELOW

(0=Never, 1=Less than monthly, 2=Monthly, 3=Weekly, 4=Daily or almost daily)

21. Allergy pills ..... ___
22. Amphetamines (uppers) ..... ___
23. Antibiotics ..... ___
24. Antidepressants ..... ___
25. Aspirin ..... ___
26. Diet pills ..... ___
27. Laxatives ..... ___
28. Pain killers ..... ___
29. Sleeping pills ..... ___
30. Medicine for indigestion ..... ___
31. Tranquilizers ..... ___
32. Vitamins ..... ___
33. Marijuana ..... ___
34. Cocaine ..... ___

STRESS

35. Some people live a calm, predictable life. Others find themselves facing unexpected changes, frequent interruptions, inconveniences, or "things going wrong." How often are you faced with these minor (or major) annoyances or frustrations? ..... ___
    1=Once a month or less
    2=Once a week
    3=A few times a week
    4=About once a day
    5=Several times a day

36. When you are under pressure or stress, what do you usually do? ..... ___
    1=Do something about it immediately
    2=Plan carefully before taking any action
    3=Do nothing at all

37. Some people easily get angry with others around them because of problems or just because they are not feeling happy. During the past six months, how often have you gotten into an argument with a fellow worker, friend, or family member that ended in yelling or loud shouting? ..... ___
    1=Once a month or less
    2=Once a week
    3=A few times a week
    4=About once a day
    5=Several times a day

38. During the past six months, about how often have you been in an argument or disagreement in which you or another person hit, slapped or shoved? ..... ___
    1=Once a month or less
    2=Once a week
    3=A few times a week
    4=About once a day
    5=Several times a day

SOCIAL NETWORKS

39. About how many friends do you have, people you know more than just casually? ..... __ __

40. How many close friends do you have, people you feel at ease with and can talk with about personal problems? ..... __ __

41. How many people do you know from whom you can expect real help in times of trouble? (include family and friends) ..... __ __

42. Is there a member of your family, other than those in your household, who lives less than 1 hour's travel (car, bus) from you? (1=Yes, 2=No) ..... ___

43. How many clubs and organizations (e.g., church group, VFW, PTA, bowling team, etc.) do you belong to? ..... __ __

44. In the last month, how often did you attend religious services? ..... __ __

45. In the last month, how often did you read a book, magazine, or newspaper? ..... __ __

46. During the last month, how many times did you get together with one or more friends? ..... __ __

47. During the last month, how many times did you visit with relatives? ..... __ __

COPING FUNCTION AND ALCOHOL

Here are some different reasons people have for drinking alcohol. Thinking of yourself and your reasons, how true are each of these reasons for you personally? (Choices are very true, true, not true.)

1=Very True 2=True 3=Not True

48. A drink helps me relax ..... ___
49. I drink to be sociable ..... ___
50. A drink helps me to forget my worries ..... ___
51. A drink helps me gain self-confidence ..... ___
52. A drink helps cheer me up when I am in a bad mood ..... ___
53. A drink helps me when I am lonesome ..... ___
54. I like the way a drink tastes ..... ___
55. I drink when I am bored ..... ___
56. I am used to drinking often ..... ___

SLEEP

In the past six months:

57. On the average, how many hours of sleep have you gotten each night? ..... __ __

58. Do you have difficulty falling asleep? (1=Yes, 2=No) ..... ___

59. Do you find yourself waking up during the night? (1=Yes, 2=No) ..... ___

60. Do you snore? (1=Never, 2=Rarely, 3=Sometimes, 4=Often) ..... ___

SEXUAL FUNCTION

61. Thinking of your current sex life, how would you describe it? ..... ___

1=Could not be better	6=Somewhat inadequate
2=Excellent	7=Poor
3=Good	8=Highly inadequate
4=Above average	9=Could not be worse
5=Adequate	

62. How often do you have sexual intercourse now? ..... ___

1=Not at all	5=More than once a week
2=Less than once per week	6=Once a day
3=Once or twice a month	7=More than once a day
4=Once a week	

63. How often would you like to have sexual intercourse now? ..... ___

1=Not at all	5=More than once a week
2=Less than once per week	6=Once a day
3=Once or twice a month	7=More than once a day
4=Once a week	

Participating Investigator's Signature

DVA COOPERATIVE STUDY #996
PATHS

FORM 10
LOCAL LABORATORY DATA

Medical Center Name _____ Medical Center No. __ __ __

Participant Name _____ Participant No. __ __ __ __ __

Form Completed By _____ Date Completed __ __ __ __ __ __
Mo Day Yr

CODE APPROPRIATE RATING PERIOD (MONTH) ..... __ __

CODE: 00 (PRE) 06 12 18 24

1. Hemoglobin (g) ..... __ __.__
2. Hematocrit (%) ..... __ __.__
3. WBC (total neutrophils, lymphocytes) ($x10^3$ cells/mm^3) ..... __ __.__
4. Platelets ($x10^3/mm^3$) ..... __ __ __ __
5. Mean cell volume (MCV) (μ^3) ..... __ __ __
6. Mean cell hemoglobin (MCH) ($\mu\mu g$) ..... __ __
7. Mean cell hemoglobin concentration (MCHC) (%) ..... __ __

8. Creatinine (mg %) ..... __ __.__
9. Urea nitrogen (BUN) (mg %) ..... __ __ __
10. Sodium (mEq/L) ..... __ __ __
11. Potassium (mEq/L) ..... __ __.__
12. Bicarbonate (HCO_3 or CO_2) (mEq/L) ..... __ __.__
13. Chloride (mEq/L) ..... __ __ __
14. Glucose (mg %) ..... __ __ __
15. Cholesterol (mg %) ..... __ __ __
16. Uric acid (mg %) ..... __ __.__
17. Calcium (mg %) ..... __ __.__
18. Phosphorus (mg%) ..... __ __.__
19. Magnesium (mg %) ..... __ __.__
20. AST (SGOT) (U/L) ..... __ __ __
21. Alkaline phosphatase (U/L) ..... __ __ __ __
22. LDH (U/L) ..... __ __ __ __
23. Albumin (g %) ..... __ __.__
24. Bilirubin (mg %) ..... __ __.__
25. Prothrombin time (sec.) ..... __ __.__ / __ __.__
(patient) (control)

VA FORM 10-29010(NR)j
AUGUST 1990

Medical Center No. __ __ __

Participant No. __ __ __ __ __

Urinalysis:

26. Glucose (1=None, 2=Trace, 3=1+, 4=2+, 5=3+, 6=4+) ..... ___

27. Protein (1=None, 2=Trace, 3=1+, 4=2+, 5=3+, 6=4+) ..... ___

COMMENT ON ANY SIGNIFICANT ABNORMALITIES: _____

_____

_____

Overnight Urine:

28. Date of specimen ..... Mo __ __ Day __ __ Yr __ __

29. Time begun/time completed ..... __ __:__ __ am/pm TO __ __:__ __ am/pm

30. Urine volume (ml) ..... __ __ __ __

31. Urine creatinine concentration (mg/dl) ..... __ __ __

32. Urine sodium concentration (mEq/L) ..... __ __ __

33. Urine potassium concentration (mEq/L) ..... __ __ __

34. Urine magnesium concentration (mEq/L) ..... __ __.__

Urine Drug Screen: (CODE: 1=Positive, 2=Negative)

35. Marijuana ..... ___

36. Cocaine ..... ___

37. Opiates ..... ___

38. Amphetamines ..... ___

39. Barbiturates ..... ___

40. Benzodiazepines ..... ___

Electrocardiogram: (NOT TO BE DONE AT 18-MONTH FOLLOW-UP VISIT)

41. Date obtained ..... Mo __ __ Day __ __ Yr __ __

42. ECG (1=Normal, 2=Abnormal) ..... ___

43. Mechanism ..... ___

1=Sinus 2=Other, specify _____

44. ST-T wave abnormalities (1=Absent, 2=Present) ..... ___

a. If present, specify _____

45. Old MI (1=Absent, 2=Present) ..... ___

a. If present, specify _____

46. LVH (1=Absent, 2=Present) ..... ___

47. SV_1 (mV) ..... __.__

48. $RV_{5 \text{ or } 6}$ (mV) ..... __.__

49. Strain (1=Yes, 2=No) ..... ___

50. Other abnormality? (1=Yes, 2=No) ..... ___

a. If yes, specify _____

_____

Participating Investigator's Signature

VA FORM 10-29010(NR)j
AUGUST 1990

DVA CSP #996 - PATHS

FORM 10A - QUALITY CONTROL SAMPLES - OVERNIGHT URINES

MEDICAL CENTER NO. ___ ___ ___

DATE SENT: MO ___ ___ DAY ___ ___ YR ___ ___

PARTICIPANT NO.	RATING PERIOD	CONCENTRATIONS CREATININE (mEq/L)	SODIUM (mEq/L)	POTASSIUM (mEq/L)	MAGNESIUM (mEq/L)
___ ___ ___ ___ ___	___ ___	___ ___ ___	___ ___ ___	___ ___ ___	___ ___.___
___ ___ ___ ___ ___	___ ___	___ ___ ___	___ ___ ___	___ ___ ___	___ ___.___
___ ___ ___ ___ ___	___ ___	___ ___ ___	___ ___ ___	___ ___ ___	___ ___.___
___ ___ ___ ___ ___	___ ___	___ ___ ___	___ ___ ___	___ ___ ___	___ ___.___
___ ___ ___ ___ ___	___ ___	___ ___ ___	___ ___ ___	___ ___ ___	___ ___.___
___ ___ ___ ___ ___	___ ___	___ ___ ___	___ ___ ___	___ ___ ___	___ ___.___
___ ___ ___ ___ ___	___ ___	___ ___ ___	___ ___ ___	___ ___ ___	___ ___.___
___ ___ ___ ___ ___	___ ___	___ ___ ___	___ ___ ___	___ ___ ___	___ ___.___
___ ___ ___ ___ ___	___ ___	___ ___ ___	___ ___ ___	___ ___ ___	___ ___.___
___ ___ ___ ___ ___	___ ___	___ ___ ___	___ ___ ___	___ ___ ___	___ ___.___
___ ___ ___ ___ ___	___ ___	___ ___ ___	___ ___ ___	___ ___ ___	___ ___.___
___ ___ ___ ___ ___	___ ___	___ ___ ___	___ ___ ___	___ ___ ___	___ ___.___
___ ___ ___ ___ ___	___ ___	___ ___ ___	___ ___ ___	___ ___ ___	___ ___.___
___ ___ ___ ___ ___	___ ___	___ ___ ___	___ ___ ___	___ ___ ___	___ ___.___
___ ___ ___ ___ ___	___ ___	___ ___ ___	___ ___ ___	___ ___ ___	___ ___.___
___ ___ ___ ___ ___	___ ___	___ ___ ___	___ ___ ___	___ ___ ___	___ ___.___
___ ___ ___ ___ ___	___ ___	___ ___ ___	___ ___ ___	___ ___ ___	___ ___.___
___ ___ ___ ___ ___	___ ___	___ ___ ___	___ ___ ___	___ ___ ___	___ ___.___
___ ___ ___ ___ ___	___ ___	___ ___ ___	___ ___ ___	___ ___ ___	___ ___.___
___ ___ ___ ___ ___	___ ___	___ ___ ___	___ ___ ___	___ ___ ___	___ ___.___
___ ___ ___ ___ ___	___ ___	___ ___ ___	___ ___ ___	___ ___ ___	___ ___.___
___ ___ ___ ___ ___	___ ___	___ ___ ___	___ ___ ___	___ ___ ___	___ ___.___
___ ___ ___ ___ ___	___ ___	___ ___ ___	___ ___ ___	___ ___ ___	___ ___.___
___ ___ ___ ___ ___	___ ___	___ ___ ___	___ ___ ___	___ ___ ___	___ ___.___
___ ___ ___ ___ ___	___ ___	___ ___ ___	___ ___ ___	___ ___ ___	___ ___.___
___ ___ ___ ___ ___	___ ___	___ ___ ___	___ ___ ___	___ ___ ___	___ ___.___
___ ___ ___ ___ ___	___ ___	___ ___ ___	___ ___ ___	___ ___ ___	___ ___.___
___ ___ ___ ___ ___	___ ___	___ ___ ___	___ ___ ___	___ ___ ___	___ ___.___
___ ___ ___ ___ ___	___ ___	___ ___ ___	___ ___ ___	___ ___ ___	___ ___.___
___ ___ ___ ___ ___	___ ___	___ ___ ___	___ ___ ___	___ ___ ___	___ ___.___

VA FORM 10-29010(NR)j(a)

AUGUST 1990

DVA COOPERATIVE STUDY #996
PATHS

FORM 11
PHYSICAL EXAMINATION

Medical Center Name _____ Medical Center No. __ __ __

Participant Name _____ Participant No. __ __ __ __ __

Form Completed By _____ Date Completed __ __ __ __ __ __
Mo Day Yr

1. Review of medical history with participant, including medications, nonalcohol substance use. Record relevant data and any reason(s) for exclusion:

_____

_____

PHYSICAL FINDINGS. Indicate within normal limits (1=WNL or absent) or abnormal findings (2=Abnormal). Please comment on abnormal findings below.

2. Head, ears, nose, throat, eyes (including optic fundi) (1=WNL, 2=Abnormal) ..... ___
3. Neck (1=WNL, 2=Abnormal) ..... ___
4. Lungs (1=WNL, 2=Abnormal) ..... ___
5. Heart:
   a. Rhythm (1=Regular, 2=Other) ..... ___
   b. Murmur (1=None, 2=Systolic, 3=Diastolic, 4=Both) ..... ___
   c. Gallop (1=None, 2=S_3 only, 3=S_4 only, 4=S_3 and S_4) ..... ___
6. Abdomen (1=WNL, 2=Abnormal) ..... ___
   a. Record liver span (cm) in mid-clavicular line ..... __ __
7. Rectal, prostate (if indicated) (1=WNL, 2=Abnormal, 3=Not Done) ..... ___
8. Extremities (1=WNL, 2=Abnormal) ..... ___
   a. Edema (1=Present, 2=Absent) ..... ___
   b. Peripheral pulses (1=WNL, 2=Abnormal) ..... ___
9. Lymphatics (1=WNL, 2=Abnormal) ..... ___
10. Neurological (1=WNL, 2=Abnormal) ..... ___
11. Skin (1=WNL, 2=Abnormal) ..... ___
12. Mental status (1=WNL, 2=Abnormal) ..... ___
13. Chest x-ray (1=Normal, 2=Abnormal) ..... ___
14. Date of chest x-ray ..... Mo __ __ Day __ __ Yr __ __

COMMENTS: _____

_____

_____

_____

15. Have study consent and VA Form 10-1086 been signed? (1=Yes, 2=No) ..... ___
16. Are there any reasons for excluding the participant? (1=Yes, 2=No) ..... ___

IF YES:

a. Summarize significant medical/psychiatric diagnoses and findings that would exclude participant: _____

_____

_____

COMPLETE FORM 20 FOR ALL EXCLUDED PARTICIPANTS.

_____
Participating Investigator's Signature

VA FORM 10-29010(NR)k
AUGUST 1990

DVA COOPERATIVE STUDY #996 - PATHS

FORM 12 - DIET QUESTIONNAIRE

Medical Center Name _____ Medical Center No. __ __ __

Participant Name _____ Participant No. __ __ __ __ __

Form Completed By _____ Date Completed __ __ __ __ __ __
Mo Day Yr

CODE APPROPRIATE RATING PERIOD (MONTH) 00 (PRE) 03 06 12 18 24 __ __

This form asks you a variety of questions about your background, environment, and habits, which may affect or be related to your health. The information you provide will help scientists to understand more about the causes of disease. This questionnaire will take about 12-15 minutes to complete. Please fill in the information requested, or place a check in the appropriate space. If you are not sure about an answer, please estimate.

THIS SPACE FOR OFFICE USE

TODAY'S DATE: Month __ __ (11) - Day __ __ - Year __ __ (16)

Please PRINT YOUR NAME (name of study participant)

(17) LAST _____ (31) FIRST _____ (40) MIDDLE _____ (48)

A (79 80)

1-10*

ADDRESS: (11) STREET _____ (34)

(35) CITY _____ (49) STATE __ __ (52) ZIP _____ (61)

62 __ __ State Code

TELEPHONE: (__ __ __) __ __ __ - __ __ __ __ (64 ... 73)

B (79 80)

1. When were you born? ____/____/____ Month Day Year (11)

2. How old are you? ____ years (18)

3. Sex: 1 ___ Male 2 ___ Female (20)

4. Race or ethnic background: (21)
   1 ___ White, not of Hispanic origin
   2 ___ Black, not of Hispanic origin
   3 ___ Hispanic
   4 ___ American Indian/Alaskan native
   5 ___ Asian
   6 ___ Pacific Islander

5. Please circle the highest grade in school you have completed: (22)
   1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17+

6. How tall are you? ____ feet ____ inches 7. How much do you weigh? _____ pounds (24)

8. Do you smoke cigarettes now? 1 ___ No 2 ___ Yes (30)
   IF YES: On the average, about how many cigarettes a day do you smoke now? ____ cigarettes (31)

9. During the past year, have you taken any vitamins or minerals?
1 ___ No 2 ___ Yes, fairly regularly 3 ___ Yes, but not regularly If Yes, → 33 ___

What do you take fairly regularly?	# of PILLS per DAY, WEEK, etc.		
Multiple Vitamins			
One-a-day type	_____ pills per _____		34 ___
Stress-tabs type	_____ pills per _____		37 ___
Therapeutic, Theragran type	_____ pills per _____	How many milligrams or IUs per pill?	40 ___
Other Vitamins			
Vitamin A	_____ pills per _____	_____ IU per pill	43 ___
Vitamin C	_____ pills per _____	_____ mg per pill	47 ___
Vitamin E	_____ pills per _____	_____ IU per pill	51 ___
Calcium or dolomite	_____ pills per _____	_____ mg per pill	55 ___

Other (What?) 1 ___ Yeast 2 ___ Selenium 3 ___ Zinc 4 ___ Iron 5 ___ Beta-carotene
6 ___ Cod liver oil 7 ___ Other _____ 59 ___

Please list the brand of multiple vitamin/mineral you usually take: _____

C
79 80

10. This section is about your *usual* eating habits. Thinking back over the past year, how often do you usually eat the foods listed on the next page?

First, check (✓) whether your usual serving size is small, medium or large. (A small portion is about one-half the medium serving size shown, or less; a large portion is about one-and-a-half times as much, or more.)

Then, put a *NUMBER* in the most appropriate column to indicate *HOW OFTEN*, on the average, you eat the food. You may eat bananas *twice a week* (put a *2 in the "week"* column). If you never eat the food, check "Rarely/Never." Please DO NOT SKIP foods. And please BE CAREFUL which column you put your answer in. It will make a big difference if you say "Hamburger once a day" when you mean "Hamburger once a week"!

One item says "in season." Indicate how often you eat this just in the 2-3 month time when that food is in season. (Be careful about overestimating here.)
Please look at the *example* below. This person
1) eats a medium serving of cantaloupe once a week, in season.
2) has ½ grapefruit about twice a month.
3) has a small serving of sweet potatoes about 3 times a year.
4) has a large hamburger or cheeseburger or meat loaf about four times a week.
5) never eats liver.

EXAMPLE:

	Medium Serving	Your Serving Size			How often?				
		S	M	L	Day	Week	Month	Year	Rarely/ Never
Cantaloupe (in season)	¼ medium		✓			1			
Grapefruit	(½)		✓				2		
Sweet potatoes, yams	½ cup	✓						3	
Hamburger, cheeseburger, meat loaf	1 medium			✓		4			
Liver	4 oz.								✓

FOR OFFICE USE
Q 9, mg or IU: 1 = 50-100 2 = 200-250 3 = 400-500 4 = 1000 5 = 5000 6 = 10,000 7 = 20,000-25,000 8 = 50,000 9 = Unk.

On the following two pages, code the four characters for each food as follows:

___ S-1 M-2 L-3 NS-9

___ ___ No. Times NS-99

___ Da-1 Wk-2 Mo-3 Yr-4 Nev-5 NS-9

If respondent places a checkmark in the "How often" columns, **do not** impute "01", once. Instead, code "99", Not Stated. If respondent does not check a portion size, **do not** impute medium, but code "9".

	Medium Serving	Your Serving Size			How often?					OFFICE USE
					Day	Week	Month	Year	Rarely/ Never	
FRUITS & VEGETABLES		S	M	L						
EXAMPLE – Apples, applesauce, pears	(1) or ½ cup		✓			4				
Apples, applesauce, pears	(1) or ½ cup									11
Cantaloupe (in season)	¼ medium									15
Oranges	1 medium									19
Orange juice or grapefruit juice	6 oz. glass									23
Grapefruit	(½)									27
Other fruit juices, fortified fruit drinks	6 oz. glass									31
Beans such as baked beans, pintos, kidney, limas, or in chili	¾ cup									35
Tomatoes, tomato juice	(1) or 6 oz.									39
Broccoli	½ cup									43
Spinach	½ cup									47
Mustard greens, turnip greens, collards	½ cup									51
Cole slaw, cabbage, sauerkraut	½ cup									55
Carrots, or mixed vegetables containing carrots	½ cup									59
Green salad	1 med. bowl									63
Salad dressing, mayonnaise (including on sandwiches)	2 Tblsp.									67
French fries and fried potatoes	¾ cup									71
Sweet potatoes, yams	½ cup									75 D 79 80
Other potatoes, incl. boiled, baked, potato salad, mashed	(1) or ½ cup									11
Rice	¾ cup									15
MEAT, MIXED DISHES, LUNCH ITEMS		S	M	L	Da	Wk	Mo	Yr	Nv	
Hamburgers, cheeseburgers, meat loaf	1 medium									19
Beef—steaks, roasts	4 oz.									23
Beef stew or pot pie with carrots, other vegetables	1 cup									27
Liver, including chicken livers	4 oz.									31
Pork, including chops, roasts	2 chops or 4 oz.									35
Fried chicken	2 sm. or 1 lg. piece									39
Chicken or turkey, roasted, stewed or broiled	2 sm. or 1 lg. piece									43
Fried fish or fish sandwich	4 oz. or 1 sand.									47
Other fish, broiled, baked	4 oz.									51
Spaghetti, lasagna, other pasta with tomato sauce	1 cup									55
Hot dogs	2 dogs									59
Ham, lunch meats	2 slices									63
Vegetable soup, vegetable beef, minestrone, tomato soup	1 med. bowl									67
BREADS / SALTY SNACKS / SPREADS		S	M	L	Da	Wk	Mo	Yr	Nv	
White bread (including sandwiches), bagels, etc., crackers	2 slices, 3 cracks									71
Dark bread, including whole wheat, rye, pumpernickel	2 slices									75 E 79 80
Corn bread, corn muffins, corn tortillas	1 med. piece									11
Salty snacks (such as chips, popcorn)	2 handfuls									15
Peanuts, peanut butter	2 Tblsp.									19
Margarine on bread or rolls	2 pats									23
Butter on bread or rolls	2 pats									27
BREAKFAST FOODS		S	M	L	Da	Wk	Mo	Yr	Nv	
High fiber, bran or granola cereals, shredded wheat	1 med. bowl									31
Highly fortified cereals, such as Product 19, Total, or Most	1 med. bowl									35
Other cold cereals, such as Corn Flakes, Rice Krispies	1 med. bowl									39
Cooked cereals	1 med. bowl									43
Eggs (1 egg = small, 2 eggs = medium)										47
Bacon	2 slices									51
Sausage	2 patties or links									55

	Medium Serving	Your Serving Size			How often?					OFFICE USE
SWEETS		S	M	L	Day	Week	Month	Year	Rarely/ Never	
Ice cream	1 scoop									59
Doughnuts, cookies, cakes, pastry	1 pc. or 3 cookies									63
Pies	1 med. slice									67
Chocolate candy	small bar, 1 oz.									71
DAIRY PRODUCTS, BEVERAGES		S	M	L	Da	Wk	Mo	Yr	Nv	
Cheeses and cheese spreads, not including cottage	2 slices or 2 oz.									75
Whole milk and bevs. with whole milk (not incl. on cereal)	8 oz. glass									11
2% milk and bevs. with 2% milk (not incl. on cereal)	8 oz. glass									15
Skim milk, 1% milk or buttermilk (not incl. on cereal)	8 oz. glass									19
Regular soft drinks (not diet)	12 oz. can or bottle									23
Beer	12 oz. can or bottle									27
Wine	1 med. glass									31
Liquor	1 shot									35
Milk or cream in coffee or tea	1 Tblsp.									39
Sugar in coffee or tea, or on cereal	2 teaspn.									43

F 79 80

	1 Seldom/Never	2 Sometimes	3 Often/Always	OFFICE USE
11. How often do you eat the skin on chicken?	_____	_____	_____	47 _
How often do you eat the fat on meat?	_____	_____	_____	48 _
How often do you add salt to your food?	_____	_____	_____	49 _
How often do you add pepper to your food?	_____	_____	_____	50 _

12. Not counting salad or potatoes, about how many servings of vegetables do you eat per day or per week? _____ vegetables per _____ day, week — OFFICE USE 51 _ _ _

13. Not counting juices, how many servings of fruits do you usually eat per day or per week? _____ fruits per _____ day, week — OFFICE USE 54 _ _ _

G 79 80

THANK YOU VERY MUCH for taking the time to fill out this information.

Reviewed by _____

DVA COOPERATIVE STUDY #996 - PATHS

FORM 13 - CHRONOLOGICAL DRINKING RECORD

Medical Center Name _____ Medical Center No. __ __ __

Participant Name _____ Participant No. __ __ __ __ __

Form Completed By _____ Date Completed __ __ __ __ __ __
Mo Day Yr

CODE APPROPRIATE RATING PERIOD (MONTH) CODE: 00 (PRE) 03 06 12 18 24 __ __

1. WEEK (complete for Event 1 only) ..... BEGINNING: Mo __ Day __ ENDING: Mo __ Day __ Yr __ __

2. EVENT NUMBER ..... __ __

3. DAY OF WEEK (1=Sun., 2=Mon., 3=Tues., 4=Wed., 5=Thurs., 6=Fri., 7=Sat.) ..... ___

4. TIME OF DRINKING ..... FROM: __ : __ am/pm TO: __ : __ am/pm

5. WHERE WERE YOU DRINKING? (see codes) ..... __ __

6. WHAT WAS THE OCCASION? (see codes) ..... __ __

7. WHAT WERE YOU DRINKING? (List in order from first to last for event.)
CODE: 1=Beer 3=Table Wine 5=Cordial
2=Wine Cooler 4=Fortified Wine 6=Liquor

a. Type _____ ___ Size __ __.__ (oz.) Number __ __

b. Type _____ ___ Size __ __.__ (oz.) Number __ __

c. Type _____ ___ Size __ __.__ (oz.) Number __ __

d. Type _____ ___ Size __ __.__ (oz.) Number __ __

e. Type _____ ___ Size __ __.__ (oz.) Number __ __

f. Type _____ ___ Size __ __.__ (oz.) Number __ __

8. DID YOU EAT WHILE YOU WERE DRINKING? (1=Full meal, 2=Snacks only, 3=No food) ..... ___
a. If snacks only, specify _____

9. TIME OF LAST FULL MEAL ..... __ __ : __ __ am/pm

10. WERE YOU ALONE WHILE YOU WERE DRINKING? (1=Yes [Go to Q.15], 2=No) ..... ___

11. WHO WAS WITH YOU? (CODE: 1=Yes, 2=No)
a. My spouse/significant other ..... ___
b. Other relatives ..... ___
c. A date ..... ___
d. People from work ..... ___
e. Neighbors ..... ___
g. Other friends ..... ___
h. People I knew on sight, but didn't know very well ..... ___
i. People I met there ..... ___
j. Other ..... ___

12. HOW MANY PEOPLE WERE WITH YOU (don't count yourself)? ..... __ __

13. DID THESE OTHER PEOPLE DRINK? (1=Yes, 2=No) ..... ___

14. COMPARED TO THESE OTHER PEOPLE, HOW MUCH DID YOU DRINK? ..... ___
1=Drank more 2=Drank less 3=Drank the same 4-Don't know

15. TOTAL NUMBER OF EVENTS (complete if last event) ..... __ __

Participating Investigator's Signature _____

VA FORM 10-29010(NR)m
AUGUST 1990

CODES FOR QUESTION 5

PRIVATE HOME (including back yard):
01 - In my own home
02 - Home of someone I work with
03 - Neighbor's home
04 - Relative's home
05 - Friend's home
NOT IN PRIVATE HOME:
06 - Night Club (dinner and entertainment, floor show)
07 - Restaurant (serves lunch/dinner with drinks. May have a bar in same room. No live entertainment.)
08 - Restaurant/cocktail lounge (patrons often drink here while waiting for dinner)
09 - Bar/cocktail lounge (no food other than snacks)
10 - Neighborhood bar, pub, or tavern (snacks and/or light lunch)
11 - Private club or bar (for members and guests)
12 - Parks, picnic areas, street, etc.
13 - Other

CODES FOR QUESTION 6

IN HOME:
01 - Listening to radio, watching TV, reading
02 - With or before a meal
03 - Just relaxing
04 - Party for friends, acquaintances, etc.
05 - Other
AWAY FROM HOME:
06 - Sports event
07 - With or before a meal
08 - On the way to or from work, a party, etc.
09 - Party
10 - Special event (wedding, awards, etc.)
11 - Other

Medical Center Name _____ Medical Center No. __ __ __

Participant Name _____ Participant No. __ __ __ __ __

Form Completed By _____ Date Completed __ __ __ __ __ __
Mo Day Yr

TO BE COMPLETED BY PARTICIPATING CLINIC

CODE APPROPRIATE RATING PERIOD (MONTH) ..... __ __

CODE MONTH: 00 (PRE) 03 06 12 18 24

1. DATE SPECIMEN COLLECTED ..... Mo __ __ Day __ __ Yr __ __

TO BE COMPLETED BY THE CENTRAL LABORATORY

2. DATE SPECIMEN ANALYZED ..... Mo __ __ Day __ __ Yr __ __
3. Total triglycerides (mg %) ..... __ __ __ __
4. Total cholesterol (mg %) ..... __ __ __
5. LDL cholesterol (mg %) ..... __ __ __
6. HDL cholesterol (mg %) ..... __ __
7. HDL_2 cholesterol (mg %) ..... __ __
8. HDL_3 cholesterol (mg %) ..... __ __
9. Apo - A_1 (mg %) ..... __ __ __
10. Apo - A_2 (mg %) ..... __ __ __
11. GGT (u/l) ..... __ __ __
12. CDT (mg/l) ..... __ __ __

COMMENTS: _____

_____

_____

_____

_____
Signature of Laboratory Director

DVA COOPERATIVE STUDY #996
PATHS

FORM 15
ECHOCARDIOGRAM REPORT FORM

Medical Center Name _____ Medical Center No. __ __ __

Participant Name _____ Participant No. __ __ __ __ __

Form Completed By _____ Date of Reading __ __ __ __ __ __
Mo Day Yr

CODE APPROPRIATE RATING PERIOD: 00 (PRE) 06 (MONTH) ..... __ __

1. BLOOD PRESSURE ..... __ __ __ / __ __ __ mmHg
2. HEART RATE ..... __ __ __ BPM
3. STUDY QUALITY (Grade 0, 1, 2, 3, 4 [Excellent]) ..... ____

M-MODE MEASUREMENTS (ASE)	AVERAGE	S.D.
4. SEPTUM	__ __.__ mm	__.__
5. POSTERIOR WALL DIASTOLE	__ __.__ mm	__.__
6. POSTERIOR WALL SYSTOLE	__ __.__ mm	__.__
7. LEFT ATRIUM	__ __.__ mm	__.__
8. AORTIC DIMENSION	__ __.__ mm	__.__
9. LEFT VENTRICAL DIMENSION DIASTOLE (LVDD)	__ __.__ mm	__.__
10. LEFT VENTRICAL DIMENSION SYSTOLE (LVDS)	__ __.__ mm	__.__
11. RIGHT VENTRICLE WALL (ANTERIOR)	__ __.__ mm	__.__
12. RIGHT VENTRICLE WALL (EPICARDIAL)	__ __.__ mm	__.__

DIASTOLIC LEFT VENTRICULAR FUNCTION	AVERAGE	S.D.
13. MITRAL VALVE SLOPE	__ __ __.__ mm	__ __.__
14. E VELOCITY	__ __ __.__ cm/sec	__ __.__
15. A VELOCITY	__ __ __.__ cm/sec	__ __.__
16. Q-INFLOW	__ __ __.__ ms	__ __.__
17. Q-CC	__ __ __.__ ms	__ __.__

SYSTOLIC LEFT VENTRICULAR FUNCTION	AVERAGE	S.D.
18. EJECTION TIME (ET)	__ __.__ __ sec	__.__ __

19. REGIONAL LEFT VENTRICULAR WALL MOTION ..... ____
(CODE: 1=Normal, 2=Mildly Abnormal, 3=Markedly Abnormal)

COMMENTS: _____

_____

ECHO REPORT SUBMITTED BY (PRINT) _____

SIGNATURE _____

VA FORM 10-29010(NR)o
AUGUST 1990

DVA COOPERATIVE STUDY #996
PATHS

FORM 15A
ECHOCARDIOGRAM WORKSHEET

Medical Center Name _____ Medical Center No. __ __ __

Participant Name _____ Participant No. __ __ __ __ __

Form Completed By _____ Date of Echo __ __ __ __ __ __
Mo Day Yr

CODE APPROPRIATE RATING PERIOD: 00 (PRE) 06 (MONTH) ..... __ __

SEND TO ECHO CENTRAL LAB ONLY; RETAIN COPY AT HOSPITAL.

1. HEIGHT ..... __ __ inches
2. WEIGHT ..... __ __ __ lbs.
3. BLOOD PRESSURE (SUPINE) AFTER ECHO

   (Record two measurements, supine, taken at end of echo)

   Reading 1 __ __ __ / __ __ __

   Reading 2 __ __ __ / __ __ __

4. SONOGRAPHER'S NAME: _____
5. ECHO MACHINE MANUFACTURER: _____
6. SERIAL NUMBER: _____

M-MODE MEASUREMENTS (ASE):

7. LEFT VENTRICAL DIMENSION DIASTOLE (LVDD) ..... __ __ mm
8. LVDS ..... __ __ mm
9. POSTERIOR WALL ..... __ __ mm
10. SEPTUM ..... __ __ mm
11. LEFT ATRIUM ..... __ __ mm

DOPPLER MEASUREMENTS:

12. E VELOCITY ..... __ __ __ cm/sec
13. A VELOCITY ..... __ __ __ cm/sec

REGIONAL LEFT VENTRICULAR WALL MOTION:

14. CODE: 1=Normal, 2=Abnormal ..... ____

    Describe: _____

    _____

	2-DE	M-Mode	Doppler
15. ECHO QUALITY (code each item using codes below)	____	____	____

CODES: 1=Good-Excellent, 2=Fair, 3=Poor

VA FORM 10-29010(NR)p
AUGUST 1990

DVA COOPERATIVE STUDY #996
PATHS

FORM 16
ASSESSMENT OF INTERVENTION SESSIONS

Medical Center Name _____ Medical Center No. _ _ _

Participant Name _____ Participant No. _ _ _ _ _

Form Completed By _____ Date Completed _ _ _ _ _ _
Mo Day Yr

	SESSIONS					
	1	2	3	4	5	6
	CODING: 1=YES 2=SOME 3=NO					
1. DATE	_ _ _ _ _ _ (Mo Day Yr)	_ _ _ _ _ _	_ _ _ _ _ _	_ _ _ _ _ _	_ _ _ _ _ _	_ _ _ _ _ _
2. APPOINTMENT KEPT	_____	_____	_____	_____	_____	_____
3. LENGTH OF VISIT[1]	_ _	_ _	_ _	_ _	_ _	_ _
4. COVERED ALLOCATED MATERIAL	_____	_____	_____	_____	_____	_____
5. PARTICIPANT GRASPED MATERIAL	_____	_____	_____	_____	_____	_____
6. PARTICIPANT COMPLETED ASSIGNMENTS	_____	_____	_____	_____	_____	_____
7. PARTICIPANT KEPT DDRs	_____	_____	_____	_____	_____	_____
8. PROGRESS MADE	_____	_____	_____	_____	_____	_____
9. GOAL STATUS	_____	_____	_____	_____	_____	_____
10. GOAL MODIFICATION[2]	_____	_____	_____	_____	_____	_____
11. INTERVENTION MODIFICATION[2]	_____	_____	_____	_____	_____	_____

[1] RECORD IN 15 MINUTE BLOCKS UP TO 90 MINUTES.

[2] WHERE THERE HAS BEEN MODIFICATION, SPECIFY EXACT TERMS ON A SEPARATE SHEET FOR EACH SESSION.

_____
Interventionist's Signature

VA FORM 10-29010(NR)q
AUGUST 1990

STUDY #996 - FORM 16 (Continuation) Medical Center No. __ __ __ Participant No. __ __ __ __ __

SESSION NO.	SESSION DATE (MO) (DAY) (YR)	GOAL/INTERVENTION MODIFICATION
____	__ __ - __ __ - __ __	
____	__ __ - __ __ - __ __	
____	__ __ - __ __ - __ __	
____	__ __ - __ __ - __ __	

DVA COOPERATIVE STUDY #996
PATHS

FORM 17

INTERVENTIONIST OR PARTICIPANT GLOBAL ASSESSMENT FORM

Medical Center Name _____ Medical Center No. __ __ __

Participant Name _____ Participant No. __ __ __ __ __

Form Completed By _____ Date Completed __ __ __ __ __ __
Mo Day Yr

PLEASE GIVE BRIEF AND SPECIFIC ANSWERS TO THE FOLLOWING QUESTIONS.

1. GOAL TO BE MAINTAINED:

	1	2	3	4	5
a. Satisfaction with Goal	Not at all Satisfied	Slightly Satisfied	Moderately Satisfied	Very Satisfied	Extremely Satisfied
b. Confidence in Maintaining Goal	Not at all Confident	Slightly Confident	Moderately Confident	Very Confident	Extremely Confident

2. RULES/GUIDELINES THAT WILL HELP YOU (PARTICIPANT) MAINTAIN THE GOAL:

A. _____

B. _____

C. _____

D. _____

3. AIDS TO MODERATE DRINKING (OR ABSTENTION):

A. _____

B. _____

C. _____

D. _____

4. IDENTIFY YOUR (PARTICIPANT'S) PROBLEM DRINKING RISKS:

INTERPERSONAL	SOCIAL PRESSURES: PEOPLE/PLACES/SITUATIONS	EMOTIONS
A. _____	A. _____	A. _____
B. _____	B. _____	B. _____
C. _____	C. _____	C. _____
D. _____	D. _____	D. _____

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AUGUST 1990

Medical Center No. __ __ __

Participant No. __ __ __ __ __

12. LIST PROBLEMS (FROM QUESTION 6) AND HOW YOU PLAN TO DEAL (OR HAVE DEALT) WITH THEM.

_____

_____

_____

_____

_____

_____

_____

_____

_____

_____

_____
Interventionist's Signature

DVA COOPERATIVE STUDY #996
PATHS

FORM 19
INTERCURRENT ILLNESS

Medical Center Name _____ Medical Center No. __ __ __

Participant Name _____ Participant No. __ __ __ __ __

Form Completed By _____ Date Completed __ __ __ __ __ __
Mo Day Yr

	HAS THE PARTICIPANT DEVELOPED OR BEEN TREATED FOR:	CODE: 1=YES 2=NO	COMMENTS
1.	Alcohol dependence	___	
2.	Psychoactive substance dependence	___	
3.	Cirrhosis	___	
4.	Alcoholic hepatitis	___	
5.	Pancreatitis	___	
6.	Alcohol-related UGI bleeding	___	
7.	Varices	___	
8.	Peripheral neuropathy	___	
9.	Cerebellar dysfunction	___	
10.	Encephalopathy	___	
11.	Significant cognitive deficits	___	
12.	Psychoactive substance dependence	___	
13.	Major psychotic disorder	___	
14.	Major affective disorder	___	
15.	Severe anxiety disorder	___	
16.	Major personality disorder	___	
17.	Malignancy (active)	___	
18.	Seizure disorder	___	
19.	Clotting or bleeding disorder	___	
20.	Stroke	___	
21.	Cerebral or subarachnoid hemorrhage	___	
22.	Myocardial infarction	___	
23.	Symptomatic ischemic heart disease	___	
24.	Congestive heart failure	___	
25.	Atrial fibrillation or other dysrhythmia	___	
26.	Retinopathy (grade III-IV: hypertensive hemorrhages and/or exudates with or without papilledema)	___	
27.	Surgically curable or secondary hypertension	___	
28.	Other illness	___	
	a. Specify _____		
	b. Specify _____		
	c. Specify _____		

_____
Participating Investigator's Signature

VA FORM 10-29010(NR)t
AUGUST 1990

DVA COOPERATIVE STUDY #996
PATHS

FORM 20
EXCLUSION/TERMINATION FORM

Medical Center Name _____ Medical Center No. __ __ __

Participant Name _____ Participant No. __ __ __ __ __

Form Completed By _____ Date Completed __ __ __ __ __ __
Mo Day Yr

EXCLUSION

1. Date excluded ..... Mo __ __ Day __ __ Yr __ __

2. Code up to 3 reasons for exclusion ..... a. __ __ __
in order of importance, starting
with the most important. b. __ __ __

c. __ __ __

TERMINATION

3. Date terminated ..... Mo __ __ Day __ __ Yr __ __

Reasons for Termination	1=YES 2=NO
4. Participant completed scheduled follow-up	____
5. Participant moved or lost to follow-up	____
6. Participant requests termination	____
7. Death ..... (Send copy of Death Certificate to Coordinating Center.)	____
8. Other, specify _____	____

COMMENTS: _____

_____

_____

_____

_____

_____

_____
Participating Investigator's Signature

VA FORM 10-29010(NR)u
AUGUST 1990

APPENDIX H

List of Contraindicated Medications

LIST OF CONTRAINDICATED MEDICATIONS

INTRODUCTION

The purpose of this section is to provide the investigator with a list of drugs that are contraindicated because of possible hypotensive effects.

The reason for contraindication is given after each class of drugs.

The final decision as to whether the patient should be included in the study will be that of the investigator. The investigator is advised to seek the consent of the Study Chairman.

TABLE OF CONTENTS

I. ANTIPSYCHOTIC DRUGS

I-A. Phenothiazines:

Drug (Generic Name)	Trade Name(s)
Acetophenazine	Tindal®
Butaperazine	Repoise®
Carphenazine	Proketazine®
Chlorpromazine	Thorazine®
Fluphenazine	Permitil, Prolixin®
Mesoridazine	Serentil®
Perphenazine	Trilafon®
Prochlorperazine	Compazine®
Promazine	Sparine®
Promethazine	Phenergan®
Thiethylperazine	Torecan®
Thioridazine	Mellaril®
Trifluoperazine	Stelazine®
Triflupromazine	Vesprin®

Reason: These drugs produce alpha-adrenergic blockade which produces a decrease in peripheral resistance and a decrease in arterial pressure.

I-B. Thioxanthenes:

Drug (Generic Name)	Trade Name(s)
Chlorprothixene	Taractan®
Thiothixene	Navane®

Reason: Same as I-A.

I-C. Butyrophenones:

Drug (Generic Name)	Trade Name(s)
Droperidol	Inapsine®
Haloperidol	Haldol®

Reason: Same as I-A.

I-D. Dihydroindolone:

Drug (Generic Name)	Trade Name(s)
Molindone	Moban®, Lidone®

Reason: Same as I-A.

I-E. Dibenzoxazepine:

Drug (Generic Name)	Trade Name(s)
Loxapine	Loxitane®

Reason: Postural hypotension may occur.

I-F. Diphenylbutylpiperidine:

Drug (Generic Name)	Trade Name(s)
Pimozide	Orap®

Reason: Postural hypotension may occur.

I-G. Miscellaneous:

Drug (Generic Name)	Trade Name(s)
Lithium Carbonate	Lithane®, Eskalith®, Others

Reason: Lithium may cause hypotension.

II. ANTIDEPRESSANT DRUGS

II-A. Tricyclics:

Drug (Generic Name)	Trade Name(s)
Amitriptyline	Elavil®
Amoxapine	Asendin®
Desipramine	Norpramin®, Pertofrane®
Doxepin	Sinequan®, Adapin®
Imipramine	Presamine®, Tofranil®
Maprotiline	Ludiomil®
Nortriptylline	Aventyl®, Pamelor®
Protriptyline	Vivactil®
Trimipramine	Surmontil®

Reason: Orthostatic hypotension are commonly observed with therapeutic doses.

II-B. Monoamine Oxidase Inhibitors:

Drug (Generic Name)	Trade Name(s)
Isocarboxazid	Marplan®
Pargyline	Eutonyl®
Phenelzine	Nardil®
Tranylcypromine	Parnate®

Reason: A major side effect of these drugs has been postural hypotension. Under certain conditions, the ingestion of foods containing tyramine (fermented cheeses, herring, broad beans, chicken liver and certain fermented beverages) and these drugs will produce a hypertensive crisis.

II-C. Miscellaneous:

Drug (Generic Name)	Trade Name(s)
Carbamazepine	Tegretol®
Fluoxetine	Prozac®
Trazodone	Desyrel®

Reason: Hypertension and hypotension have been reported with these drugs.

III. AMPHETAMINES

Drug (Generic Name)	Trade Name(s)
Amphetamine	Benzedrine®
Dextroamphetamine	Dexedrine®
Hydroxyamphetamine	Paradrine®
Methamphetamine	Desoxyn®

Reason: Their CNS stimulation in addition to peripheral alpha and beta action common to sympathomimetic drugs will raise both systolic and diastolic blood pressure.

IV. VASODILATOR DRUGS

IV-A. Nitrites and Nitrates:

Drug (Generic Name)	Trade Name(s)
Amyl Nitrite	Amyl Nitrite®
Erythrityl Tetranitrate	Cardilate®
Isosorbide Dinitrate	Isordil®, Sorbitrate®,Others
Nitroglycerin	Nitro-Bid®, Nitrol®, Nitrostat®, Transderm Nitro®, Others
Pentaerythritol Tetranitrate	Duotrate®, Metranil®, Pentritol®, Peritrate®, Vasitol®

Reason: Decreases blood pressure.

IV-B. Miscellaneous:

Drug (Generic Name)	Trade Name(s)
Diazoxide	Hyperstat®
Hydralazine	Apresoline©
Minoxidil	Loniten®
Sodium Nitroprusside	Nipride®
Trimethaphan Camsylate	Arfonad®

Reason: Decreases blood pressure.

V. ANTIADRENERGIC DRUGS

V-A. Antiadrenergic Drugs - Centrally Acting:

Drug (Generic Name)	Trade Name(s)
Clonidine	Catapres®
Guanabenz	Wytensin®
Guanfacine	Tenex®
Methyldopa	Aldomet®

Reason: These drugs decrease blood pressure.

V-B. Antiadrenergic Drugs - Peripherally Acting:

Drug (Generic Name)	Trade Name(s)
Alseroxylon	Rauwiloid®
Deserpidine	Harmonyl®
Guanadrel	Hylorel®
Guanethidine	Ismelin®
Mecamylamine	Inversive®
Phenoxybenzamine	Dibenzyline®
Phentolamine	Regitine®
Prazosin	Minipress®
Rauwolfia, Whole root	Raudixin®
Rescinnamine	Moderil®
Reserpine	Serpasil®
Terazosin	Hytrin®

Reason: These drugs decrease blood pressure.

V-C. Antiadrenergic Drugs - Beta Adrenergic Blockers:

Drug (Generic Name)	Trade Name(s)
Acebutolol	Sectral®
Atenolol	Tenormin®
Betaxolol	Betoptic®
Esmolol	Brevibloc®
Labetalol	Normodyne®, Trandate®
Metoprolol	Lopressor®
Nadolol	Corgard®
Pindolol	Visken®
Propranolol	Inderal®
Timolol Maleate	Timoptic®, Blocadren®

Reason: These drugs have been reported to produce hypotensive effects.

VI. CALCIUM CHANNEL BLOCKING AGENTS

Drug (Generic Name)	Trade Name(s)
Diltiazem	Cardizem®
Nifedipine	Procardia®, Adalat®
Verapamil	Isoptin®, Calan®

Reason: Decreases blood pressure.

VII. DIURETIC AGENTS

Drug (Generic Name)	Trade Name(s)
Amiloride	Midamor®
Bumetanide	Bumex®
Ethacrynic Acid	Edecrin®
Furosemide	Lasix®
Spironolactone	Aldactone®
Thiazide Diuretics	Naturetin®, Diuril®, Others
Triamterene	Dyrenium®

Reason: Decreases blood pressure.