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## **Summary of Edits**

### **Summary of changes between Version 1.0 and 1.1:**

- Changed p.5 text “high normal BP and borderline HTN” to “above optimal BP and stage 1 HTN”
- Added statement that personal physicians of all participants eligible for randomization are sent a letter describing the trial and asking them to contact the site if they have any questions or concerns about their patient’s participation in PREMIER.

## **5. Recruitment**

### ***Study Population***

Study participants (n = 800) will be 25 years of age or older, with systolic BP of 120-159 mmHg and diastolic BP of 80-95 mmHg. Approximately 400 (50%) of the participants will be female, 320 (40%) will be African-American, and 240 (30%) will have stage 1 hypertension. After three screening visits, participants will be randomly assigned to one of the two lifestyle behavioral interventions or a group that receives advice. Follow-up will last 18 months after randomization. The primary outcome variable is systolic BP (SBP). Other outcomes include diastolic BP (DBP), adherence to dietary and physical activity regimens, and the onset of hypertension.

### ***Eligibility Criteria***

The eligibility criteria for this trial (Table 2) have been selected to yield a reasonably representative sample of adults with above optimal BP and stage 1 hypertension. Most of these criteria exclude individuals for whom the interventions would be inappropriate, or those who have health problems requiring immediate attention. Inclusion and exclusion criteria are defined in detail below:

### ***Contact with Personal Physicians***

In addition to the requirement for physician notification for a positive Rose questionnaire in order to determine study eligibility, clinical center staff must notify the personal physician of otherwise eligible study candidates to see if she has any concerns about her patient's participation. This notification can be in the form of a fax-back request for concerns, if any. A positive response from the provider is not required in order to randomize the participant. The absence of a negative response is sufficient. In the event that the study candidate does not have a personal physician, has a negative Rose questionnaire, and is otherwise eligible to participate, no further action is required.

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**Table 2. Eligibility Criteria**

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**Inclusion Criteria**

Baseline SBP 120-159 mmHg and DBP 80-95 mmHg  
Age 25 or older as of the PSV visit  
Willing and able to participate fully in all aspects of the intervention  
Provide informed consent  
BMI 18.5-45 kg/m<sup>2</sup>  
Access to telephone

**Medication Exclusions**

Regular use of antihypertensive drugs or other drugs that raise or lower BP  
(any in previous three months prior to SV1)  
Current use of insulin or oral hypoglycemic agents  
Use of oral corticosteroids >5 days/month on average  
Current use of medications for treatment of psychosis or manic-depressive illness  
Use of oral breathing medications other than inhalers > 5 days/month on average  
Use of weight-loss medications in the 3 months prior to SV1

**Medical History Exclusions**

Cardiovascular event (stroke, MI, PTCA, CABG, or ASCVD-related therapeutic procedure)  
Congestive heart failure  
Current symptoms of angina or peripheral vascular disease by Rose Questionnaire (Rose et al., 1977), unless approved by both participant's personal physician and a PREMIER clinician. If no personal physician, must be referred.  
Cancer diagnosis (except for non-melanoma skin cancer) or treatment in past two years  
Renal insufficiency (GFR<60 ml/min as estimated using Cockcroft-Gault formula)  
Random glucose  $\geq$  160mg/dL or FBS  $\geq$  126 mg/dL  
Psychiatric hospitalization within the last 2 years

**Other Exclusions**

Unable to provide acceptable BP measurements  
Consumption of more than 21 alcoholic drinks per week  
Consumption of 6 or more drinks on one occasion twice or more per week  
Planning to leave the area prior to the anticipated end of participation  
Body weight change > 15 pounds in the 3 months prior to SV1  
Pregnant, breast feeding, or planning pregnancy prior to the end of participation  
Current participation in another clinical trial  
Investigator discretion for safety or adherence reasons  
Household member of another PREMIER participant or of a PREMIER staff member

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### *Inclusion Criteria*

- SBP 120–159 mm Hg and DBP 80-95 mm Hg

Two blood pressure measurements are taken at each of the first three formal screening visits (SV1, SV2, and SV3), and the average of these six measurements must fall within the stated limits for both SBP and DBP. An additional set of measurements is taken at a later visit; however, this set does not determine eligibility.

**Table 3. PREMIER Blood Pressure Eligibility Criteria**

Visit	Measure	Eligible Range (mm/Hg)*
SV1	SBP	118-170
	DBP	78-100
SV2	SBP	119-165
	DBP	79-98
SV3	SBP	120-159
	DBP	80-95

\*Cumulative average of SV measurements (see measures section)

In order to identify participants not likely to meet these limits, somewhat wider eligibility limits are also established for the average cumulative blood pressures at each of SV1 and SV2 (see MOP Chapters 7 and 8).

Participants who are excluded from the screening process because of blood pressure may re-start the screening process at a later date, but only as part of screening for a separate cohort.

- Age  $\geq$  25 years

Participants must be 25 years of age or older at the prescreening visit. This is assessed by asking, at the prescreening visit, whether the participant is currently 25 years of age or older. Date of birth is also collected for confirmation.

- Willing and able to participate fully in all aspects of the intervention

The staff repeatedly emphasize this issue with potential participants. A participant's willingness to complete the extensive battery of screening tests and visits is an indication of their overall commitment to the project and possibly their willingness to make lifestyle changes. Since next to blood pressure limits, this is likely to account for the majority of study exclusions, it is imperative that participants understand the nature and demands of the study as early into the screening process as possible.

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- Body mass index 18.5-45 Kg/m<sup>2</sup>

The weight screening criteria have been selected to exclude those who are seriously underweight (they may not respond well to the dietary change interventions) and those who are massively obese.

- Willing and able to provide written informed consent

In order to participate in the study, all subjects must provide written informed consent using procedures that are reviewed and approved by each center's local IRB. Typically, this will involve separate consent forms prior to screening and again prior to randomization.

- Easy access to telephone

Participants must have easy access to a telephone in order to complete telephone diet recalls, and for other study-related contacts.

### *Exclusion Criteria*

*Medication Exclusions: use of any of the following:*

Unless noted otherwise, current medication use is defined as any use within 21 days of the PSV visit or at any time thereafter. All participants are expected to bring their medication bottles to the SV2 visit for review by a clinic staff member.

“Unstable doses” of medications are operationally defined by the participant having either started, stopped, or changed the dosage of these medications during the past six months, except where noted below

- Antihypertensive drugs, and other drugs that raise or lower BP  
Defined as any use in 3 months prior to SV1
- Current use of any of the following:
  - ▶ Insulin or oral hypoglycemic agents
  - ▶ Oral corticosteroids (> 5 days/month on average)
  - ▶ Medications for treatment of psychosis or manic-depressive illness
  - ▶ Oral breathing medications other than inhalers (> 5 days/month on average)
- Weight loss medications  
Defined as use in the 3 months prior to SV1.

The Eligibility Questionnaire (Form #4) and the Medication Use Questionnaire (Form #11) contain lists of medications in each of these categories of excluded medications. In addition to these medications that are not allowed, the Medications Allowed During PREMIER Form (#102)

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lists other medications that are approved for treatment of constipation, indigestion, and other minor conditions.

### *Medical History Exclusions:*

- Cardiovascular event, congestive heart failure, angina, or peripheral vascular disease

Participants are excluded if they report a prior CVD event (defined as stroke, heart attack, balloon angioplasty, bypass operation, or other vascular procedure) or if they report a clinical diagnosis of congestive heart failure. Confirmation is not necessary unless the participant is uncertain of the diagnosis and the clinical center still wishes to include him/her. A Rose Questionnaire for angina and peripheral vascular disease will be used to identify persons with these conditions. Because of the possibility of false positive tests, persons with a positive Rose Questionnaire can be enrolled if they have had a negative stress test within the past 6 months and both their physician and a study physician agree to let the person in the study.

- Cancer diagnosis (except non-melanoma skin cancer) within the past 2 years

Participants are excluded if they report a prior diagnosis of cancer (other than non-melanoma skin cancer) within 2 years prior to SV1. The diagnosis of cancer and the status of therapy are based on the participant's self-report and do not need to be confirmed with the participant's physician unless a question exists about whether the cancer is currently active. Participants currently on cancer chemotherapy or with evidence of active malignancy or radiation therapy within the past two years are excluded.

- Renal insufficiency

If the serum creatinine level is >1.5 mg/dL (men) or > 1.2 mg/dL (women) AND the calculated GFR is < 60 ml/min, the participant is ineligible. The GFR is calculated using the Cockcroft-Gault formula as listed below:

Men:  $GFR = [(Wt \text{ in Kg}) * (140 - \text{Age in years})] / [72 * \text{serum creatinine in mg/dl}]$

Women:  $GFR = 0.85 * [(Wt \text{ in Kg}) * (140 - \text{Age in yrs})] / [72 * \text{serum creatinine in mg/dl}]$

- Diabetes

Defined as either nonfasting or random glucose  $\geq 160$  mg/dL or fasting blood sugar  $\geq 126$  mg/dL. Repeat testing to confirm the diagnosis may include either a non-fasting or fasting blood sugar.

- Psychiatric hospitalization within the last 2 years

Defined as psychiatric hospitalization within 2 years prior to SV1

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### *Other Exclusions:*

- Unable to provide acceptable blood pressure measurements

As detailed in MOP Chapter 17, individuals for whom valid and reliable measurements of blood pressure cannot be obtained are excluded from participation in the trial. This criterion applies only to blood pressure measurements taken with a random zero sphygmomanometer.

- Consumption of more than 21 alcoholic drinks per week and/or consumption of 6 or more drinks on one occasion twice or more per week

This is determined at the prescreening visit and confirmed subsequently as part of the Eligibility Review that takes place between SV1 and SV2. In both cases the information is based on self-report. One drink of alcohol is defined as one can or bottle of beer, one glass of wine, or one shot of liquor.

- Planning to leave the area prior to the anticipated end of participation
- Body weight change >15 pounds in the 3 months prior to SV1

This is determined by self-report.

- Pregnant, breast feeding, or planning pregnancy prior to the anticipated end of participation (women only)

Any woman who is pregnant or trying to conceive a child at the time of the prescreening visit is excluded from the study, as are women who are breast feeding at the time of the prescreening visit .

- Current participation in another clinical trial
- Investigator discretion for safety or adherence reasons

In addition to the trial's mandatory blood pressure escape levels, individual centers always have the option of excluding participants for reasons of safety as determined locally. At any time prior to randomization, each clinical center has the option of excluding participants for noncompliance with the study protocol. Noncompliance may include, for example, repeated no-shows or reschedules for clinic visits, poor attitude, or any other aspect of the participant's behavior that would suggest he/she is a poor candidate for the trial.

- PREMIER staff or household member of PREMIER staff

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### ***Overview of Recruitment***

Each PREMIER clinical center recruits its participants in four separate cohorts. Specific recruitment approaches include: 1) targeted mailings to specific groups (e.g., employees of local industries, previous screenees), 2) mass mailings (e.g., vis-à-vis inserts in coupon packs and brochures to registered voters or licensed drivers), 3) community and worksite screenings, 4) mass media advertising (e.g., radio and television advertisements and public service announcements), and 5) electronic mail (e.g., to lists of employees) or Web site advertisement. Other approaches can be used, as long as the local IRB approves the new strategy.

Each clinical center has a recruitment coordinator who oversees recruitment efforts and who serves on the recruitment subcommittee. The recruitment coordinator is the primary liaison with the coordinating center for issues related to recruitment.

The coordinating center monitors recruitment activities and facilitates recruitment efforts by providing regular recruitment reports, organizing meetings and conference calls, and distributing meeting/call minutes. In addition to these regular trial monitoring reports, the coordinating center will develop additional reports (either on a regular or ad hoc basis) as requested by the recruitment committee or by the Data and Safety Monitoring Board. The coordinating center also facilitates, where appropriate, the preparation of recruitment materials for common use at the clinical sites.

### ***Record Keeping***

Other than for basic demographic information (e.g., gender and race), data collected at PSV are not considered study data and are not incorporated into the study database. The demographic data are entered only for participants who are eligible for SV1 and who remain interested. Individual clinical centers wishing to track demographic data on all participants will have to create their own system for entering data on ineligible PSV visits.

Beginning with SV1, all data collected on prospective eligible participants must be entered into the data management system. Data for all subjects who become ineligible must be entered up to the point at which they are identified as ineligible. All subjects who drop out of screening, become ineligible, or who are otherwise lost to follow-up must be formally closed out.