PARTNERS PROGRAM
CLINICIAN'S MANUAL

Enrolling Your Patients in the PARTNERS Program

PARTNERS

PAD Awareness, Risk, and Treatment: New Resources for Survival

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Dear Colleague:

Thank you for your participation in the PARTNERS national screening survey. Data gathered in the PARTNERS Program will help physicians nationwide better understand the real-world prevalence of peripheral arterial disease (PAD) in the primary care setting. The program is also designed to increase patient understanding of the factors that place them at increased risk of heart attack and stroke. Additionally, by promoting early identification and treatment of PAD, we hope to contribute to a reduction in mortality and an improvement in the quality of life of patients who suffer from PAD.

> If you are a local program director or local program coordinator who did not attend the regional PARTNERS start-up meeting, STOP READING this manual, and PLEASE see your regional program director for a copy of the clinician's questionnaire before reading further.

PAD is a prevalent, morbid, and mortal atherosclerotic syndrome that too often goes unrecognized and untreated in the United States. It is a marker of increased risk of myocardial infarction and stroke, and the cardiovascular prognosis without medical intervention remains poor. Epidemiological studies have reported high rates of ischemic events (heart attack, stroke, and transient ischemic attack) in the PAD population, approximately 50% higher in men with PAD and three times higher in women with PAD than in men and women without PAD, respectively.[1] These data support the clinical value of PAD screening programs. The PARTNERS Program is designed to serve as a national investigation to detect PAD prevalence in a defined patient population, to assess and increase both physician and patient awareness of PAD, and to assess the magnitude of atherosclerotic risk factors in this group. The goal is to foster improved community-prescribed treatment of PAD, including both medical treatment and life-style modifications. Twenty-eight Regional Coordinating Centers will

If you have any questions about the PARTNERS Program, please feel free to contact your regional program coordinator (see insert), or call PPD Pharmaco at the toll-free number below.

Thank you for your commitment to the PARTNERS Program. You are taking part in an important effort to increase national awareness of PAD and its risk factors. Through this partnership, we anticipate greater awareness, detection, and treatment of PAD. We hope to increase the number of patients treated, and to improve outcomes for these patients. In particular, the goals are to improve functional status, reduce rates of amputation, and reduce PAD-associated risks of heart attack, stroke, and vascular death.

Sincerely,

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PPD Pharmaco

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PERIPHERAL ARTERIAL DISEASE: A PREVALENT DISORDER IN OUR COMMUNITIES

Arterial occlusive disease of the lower extremities is a prevalent but insufficiently recognized illness that causes significant morbidity and mortality. In Western societies, the most common cause of lower extremity arterial occlusive disease is atherosclerosis. The clinical presentation of PAD (asymptomatic, mild to severe claudication, critical limb ischemia, or a vascular emergency) depends upon the rate of disease progression, the severity of decrease in limb blood flow, and the propensity for development of collateral blood flow and/or sudden thrombosis. Thus, patients with anatomically comparable degrees of arterial occlusive disease may present with symptoms that range from mild claudication to rest pain to more severe outcomes, such as frank gangrene. All of these patients are at increased risk for myocardial infarction and stroke.

The natural history of lower extremity arterial occlusive disease has been carefully examined in several studies.[2-5] Progression of disease may be slow, but in patients presenting with intermittent claudication, there is eventual symptomatic worsening in 15% to 20% of patients over a 5- to 10-year period after diagnosis.[4,5] Tissue necrosis and/or progression to rest pain requiring vascular surgery is needed in 2.7% to 5.0% of limbs with claudication annually, and amputation is ultimately required in 1% of these cases per year.[2] This amputation rate may seem low; however, when the number of amputations is totaled over a 5- to 10-year follow-up, there is a 5% to 10% amputation rate for this prevalent disease.[3,4] New data suggest that risk factor modification can alter the rate of disease progression in symptomatic individuals and may thereby avert adverse outcomes, including amputation.

The risk of death for individuals with PAD is as high as for many common cancers. In fact, the results of one study suggest that patients with a very low ABI (<0.40) have a 5-year probability of survival of only 44%, a rate lower than the survival rates for colon cancer and non-Hodgkin's lymphoma.[6] Risk of heart attack and stroke is also an important issue for the PAD patient. Criqui et al have reported an approximately sixfold increase in relative risk of cardiovascular mortality for patients with large-vessel PAD compared to those with no evidence of PAD.[7] Heart attack, stroke, transient ischemic attack (TIA), angina, and congestive heart failure all occur at increased rates in individuals with PAD. Criqui et al found that total cardiovascular morbidity rates were approximately 50% higher in men with PAD than those without PAD, and 300% higher in women with PAD.[1] The implication is that there are substantial costs to the patient in terms of quality of life as well as potential loss of employment.

Unfortunately, the associations between the diagnosis of PAD and its accompanying risks remain relatively unknown in our communities, and patients often do not receive intensive medical treatment until severe symptoms or limb-threatening gangrene is observed. Aggressive medical therapies, however, as well as life-style interventions, may forestall disease progression in both the affected limb and in other systemic circulations and reduce risk of myocardial infarction and stroke. The PARTNERS Program proposes that a physician and nursing partnership may be ideal to carry out long-term interventions.

— How PARTNERS Can Help: Program Design —

Early diagnosis of PAD and risk assessment offer a significant opportunity for primary prevention of future complications and associated cardiovascular events. Since the underlying disorder in PAD is atherosclerosis, findings of the ankle-brachial index (ABI) may also suggest the presence of atherosclerosis in the cardiovascular and cerebrovascular beds. Increased awareness, diagnosis, risk assessment, and early treatment can offer the powerful benefits of improving quality of life and preventing costly, debilitating, and mortal events, especially myocardial infarction and stroke.

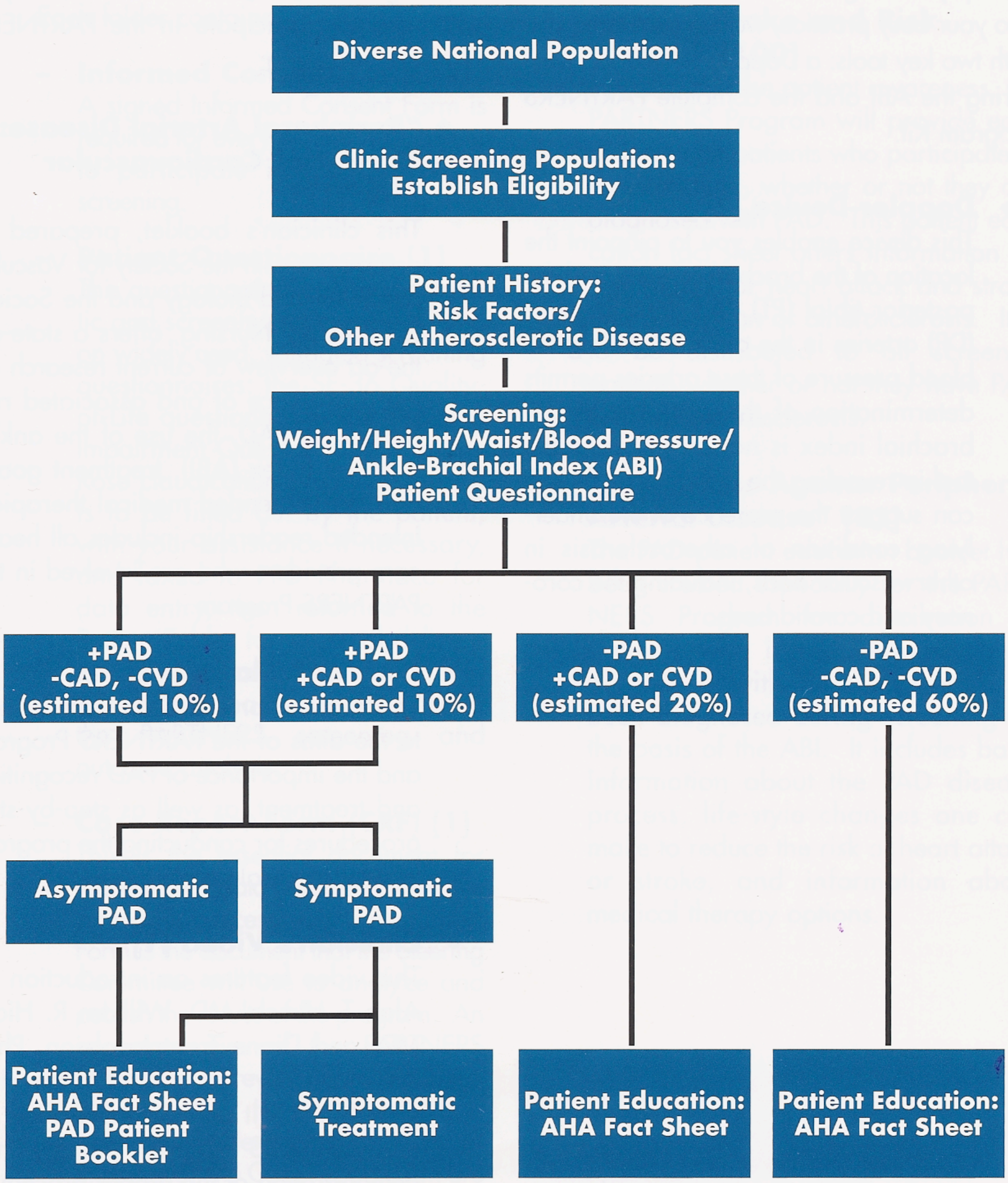
Approximately 10,000 high-risk patients will be screened in the program and divided into four groups:

- PAD and no other atherosclerotic disease
- PAD plus other atherosclerotic disease
- non-PAD plus other atherosclerotic disease
- non-PAD and no other atherosclerotic disease

PAD prevalence will be correlated with cardiovascular risk factors and treatment intensity. Patients will receive targeted patient education to support appropriate treatment. Inclusion and exclusion criteria for the study reflect the focus on patients at high risk for PAD. The program will include all patients aged 70 or older and all patients 50 or older who have diabetes or a history of smoking. An anticipated 15% positive PAD diagnosis rate will yield approximately 1,500 patients in the two PAD groups.

Figure 1 (page 5) outlines the flow of patients through the program.

Figure 1. PARTNERS Screening Flow



PARTNERS: THE PROGRAM KIT

To help you integrate the PARTNERS Program into your busy practice, we are providing you with two key tools: a Doppler device for measuring the ABI and the complete PARTNERS Program Kit.

- **Doppler Device [1]**
  This device enables you to pinpoint the location of the brachial arteries and the posterior tibial (PT) and dorsalis pedis (DP) arteries in the ankle. Reading the blood pressure of these arteries permits determination of the ABI. The ankle-brachial index is not only a valuable tool in revealing the presence of PAD, it can suggest the presence of the underlying condition of atherosclerosis in other vascular beds, including the coronary and carotid beds.

The Program Kit contains all the elements you will need to participate in the PARTNERS Program, including:

- **"Peripheral Arterial Disease: Marker of Cardiovascular Risk" [1]**
  This clinician's booklet, prepared in association with the Society for Vascular Medicine and Biology and the Society for Vascular Nursing, offers a state-of-the-art overview of current research on the prevalence of and associated risk factors for PAD, the use of the ankle-brachial index (ABI), treatment goals, and recommended medical therapies. Intended readership includes all health care providers who are involved in the PARTNERS Program.

- **Clinician's Manual [1]**
  This manual provides an introduction to the aims of the PARTNERS Program and the importance of PAD recognition and treatment, as well as step-by-step procedures for conducting the program in your medical practice.

- **Clinician's Video [1]**
  This video features an introduction by Alan T. Hirsch, MD, William R. Hiatt, MD, and Diane Treat-Jacobson, PhD, RN, of the PARTNERS Steering Committee. It gives an overview of the PARTNERS Program, along with a demonstration of the proper procedure for determining ABI. All clinical staff who are involved in the PARTNERS Program can benefit from viewing this video. It will be especially useful for your staff who have not attended the regional PARTNERS meeting and as a resource for confirming ABI procedure.

- **Patient Folder [12]**
  Each folder contains:

  - **Informed Consent Form [1]**
    A signed Informed Consent Form is required for every patient who agrees to participate in the PARTNERS screening.

  - **Patient Questionnaire [1]**
    This questionnaire is a key diagnostic and screening instrument, based on widely used, validated screening questionnaires: the SF-36 Quality-of-Life questionnaire, the Walking Impairment Questionnaire, and the Rose claudication questionnaire. It is to be filled out by the patient, with your assistance if necessary, and faxed to PPD Pharmaco for data entry, then returned to the Patient Folder for eventual delivery to your regional center. The data in this questionnaire are essential to the PARTNERS screening and outcome analysis.

  - **Case Report Form (CRF) [1]**
    This is the essential document for recording all data collected during the screening process. The Case Report Form is the document that the Steering Committee will use to analyze and publish the results of the program. An important aim of the PARTNERS Program is to reveal the relationships between PAD, its risk factors, and other atherosclerotic risks. Many of the items on the Case Report Form are designed to elicit this information. It is to be completed by the local program coordinator and physician, faxed or mailed to PPD Pharmaco along with the accompanying patient questionnaire, and returned to the Patient Folder, for eventual delivery to your regional center.

- **AHA "Fact Sheet on Heart Attack, Stroke and Risk Factors" [100]**
  In order to raise patient awareness, the PARTNERS Program will provide education to all patients who participate in the screening, whether or not they are diagnosed with PAD. This patient education fact sheet offers information on risk factors for heart attack and stroke and prevention of atherosclerosis. It is to be distributed to all screened patients whether or not they have PAD or other atherosclerosis.

- **"Take Steps Against Peripheral Arterial Disease" [25]**
  The PAD patient education booklet has been created especially for the PARTNERS Program for distribution to patients who have previously been diagnosed with PAD or who have been diagnosed during screening on the basis of the ABI. It includes basic information about the PAD disease process, life-style changes one can make to reduce the risk of heart attack or stroke, and information about medical therapy options.

(continued)

- **Spanish-Language Patient Folder [1]**
  This single copy of a Spanish version of the Patient Folder (with a Spanish-language Informed Consent Form, Patient Questionnaire, an English CRF, and Spanish-language patient education materials) is included as a sample. If you require additional copies for conducting the PARTNERS screening in your practice, please use the reorder form. Please order an ample supply of these folders, according to anticipated need, in advance of screening.

  - The sample Spanish-language AHA booklet "Ataque al corazón y derrame cerebral: Señales y acción" (Heart Attack and Stroke: Signals and Actions) provides Spanish-language patient education on risk factors for heart attack and stroke and prevention of atherosclerosis.

- **Enrollment Tracking Log [2]**
  This form is optional and for your own use in identifying and listing patients in your practice who are eligible for screening, and to note which patients were invited to enroll and which agreed.

- **Reorder Form [5]**
  To order additional Patient Folders or other materials, this form can be faxed or mailed to: Sunbelt Graphics, Inc., 55 Avenue of the Americas, New York, NY 10013. Fax: 212-226-1623

- **Pre-Addressed Envelopes [5]**
  These envelopes can be used to return completed Case Report Forms to PPD Pharmaco at 3900 Paramount Parkway, TCC 1400, Morrisville, NC 27560, if a fax machine is unavailable.

- **Plavix® (clopidogrel bisulfate) full prescribing information.**