Circulation

AHA POLICY STATEMENT

Reducing Nontraumatic Lower-Extremity Amputations by 20% by 2030: Time to Get to Our Feet

A Policy Statement From the American Heart Association

ABSTRACT: Nontraumatic lower-extremity amputation is a devastating complication of peripheral artery disease (PAD) with a high mortality and medical expenditure. There are ≈150 000 nontraumatic leg amputations every year in the United States, and most cases occur in patients with diabetes. Among patients with diabetes, after an ≈40% decline between 2000 and 2009, the amputation rate increased by 50% from 2009 to 2015. A number of evidence-based diagnostic and therapeutic approaches for PAD can reduce amputation risk. However, their implementation and adherence are suboptimal. Some racial/ethnic groups have an elevated risk of PAD but less access to high-quality vascular care, leading to increased rates of amputation. To stop, and indeed reverse, the increasing trends of amputation, actionable policies that will reduce the incidence of critical limb ischemia and enhance delivery of optimal care are needed. This statement describes the impact of amputation on patients and society, summarizes medical approaches to identify PAD and prevent its progression, and proposes policy solutions to prevent limb amputation. Among the actions recommended are improving public awareness of PAD and greater use of effective PAD management strategies (eg, smoking cessation, use of statins, and foot monitoring/care in patients with diabetes). To facilitate the implementation of these recommendations, we propose several regulatory/legislative and organizational/institutional policies such as adoption of quality measures for PAD care; affordable prevention, diagnosis, and management; regulation of tobacco products; clinical decision support for PAD care; professional education; and dedicated funding opportunities to support PAD research. If these recommendations and proposed policies are implemented, we should be able to achieve the goal of reducing the rate of nontraumatic lower-extremity amputations by 20% by 2030.

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Lower-extremity peripheral artery disease (PAD) affects >200 million adults worldwide and 8 to 10 million adults in the United States.[1,2] Its global prevalence increased by 24% from 2000 to 2010 (26% and 23% increase in individuals ≥65 years and <65 years of age, respectively).[1] Among patients with diagnosed PAD, ≈11% are likely to develop critical limb ischemia (CLI; also known as chronic limb-threatening ischemia),[3] a clinical condition in which the blood supply to the limb does not accommodate the resting metabolic needs of the tissue, resulting in persistent foot pain, skin ulceration, and gangrene. A quarter of patients with CLI require limb amputations within a year after the diagnosis to resolve limb pain, nonhealing wounds, and life-threatening infection.[4] Unfortunately, national surveillance data do not distinguish these indications because procedural coding for amputations remains nonspecific.

Nonetheless, several reports have shown that the incidence of nontraumatic lower-extremity amputations declined steadily in the 1990s and 2000s. Using data from Medicare and Medicaid, Goodney et al[5] reported that the rate of lower-extremity amputations decreased by 45%, from 196 procedures per 100 000 patients in 1996 to 119 procedures per 100 000 patients in 2011. The decrease was driven by the decline in the rate of major amputations (above ankle); there was no evident decline in the rate of minor amputations (below ankle). Agarwal et al[6] found a similar declining trend of major amputations among patients hospitalized with CLI. Specifically, the proportion of patients with CLI requiring major amputation declined from ≈17% in 2003 to ≈11% in 2011.

However, using more recent data from the National Inpatient Sample, Geiss et al[7] reported concerning trends in nontraumatic lower-extremity amputations (Figure 1). Among patients with diabetes, after a 43% decline between 2000 and 2009, amputation rates increased by 50% from 2009 to 2015. The increase was seen for both major and minor amputations, although it was more evident for the latter (annual percent change, ≈3% and ≈7%, respectively). For both major and minor amputations, the increasing rates were more pronounced in younger adults (18–64 years) than older adults (≥65 years), with a respective annual percent change of ≈8% versus ≈2%. These data are important because patients with diabetes and PAD are among those at the highest risk for lower-extremity amputations.[8] For patients without diabetes, the rate of nontraumatic lower-extremity amputations appeared to plateau between 2012 and 2015. Accordingly, in 2015, there were ≈150 000 nontraumatic lower-extremity amputations in the United States.

Although amputation is an important and potentially sole treatment option for some patients,[9,10] it often is preventable, even among patients with advanced PAD. Thus, a concerted effort is needed to address the burden of nontraumatic lower-extremity amputation and to institute policies to mitigate its incidence and improve limb outcomes among patients with PAD. Some racial and ethnic groups and those who are living in poverty have an elevated risk of PAD[11] but less access to high-quality vascular care, leading to increased rates of amputation.[12] Improving the diagnosis and management of PAD could have a great impact on health care disparities.

Accordingly, the purpose of this policy statement is to describe the impact of amputation on patients and society, to summarize medical approaches that can prevent amputation, and to propose policy solutions, with a focus on PAD. Among the approaches recommended are improved public awareness of PAD; enhanced clinician education; early detection; optimal use of evidence-based PAD management, including smoking cessation,[13] statins,[14] regular foot monitoring/care in patients with diabetes,[15,16] timely referral to vascular specialists,[17] and improved access to health care[18]; and the elimination of health care disparities surrounding these issues.[19]

To facilitate the implementation of these evidence-based approaches and to achieve the goal of reducing the rate of nontraumatic lower-extremity amputations by 20% by 2030, we propose several regulatory/legislative and organizational/institutional policies: adoption of quality and performance measures for PAD care; screening for PAD in individuals with high risk; coverage for annual foot monitoring of patients with diabetes; robust federal regulation of tobacco products; availability of affordable tobacco cessation therapy; integration of clinical decision support to diagnose and manage PAD; consistent reimbursement for the ankle-brachial index (ABI) diagnostic test across all states; affordable, accessible, and equitable medical care for all patients with PAD; professional education on PAD diagnosis and management; and dedicated funding opportunities to support PAD research.

IMPORTANCE OF AWARENESS OF PAD

Increasing the public awareness of PAD should facilitate conversations between at-risk patients and clinicians and therefore lead to improved detection and management of PAD.[20] At present, knowledge about PAD is limited in American adults; in a population-based telephone survey, only 26% of people ≥50 years of age expressed familiarity with PAD.[21] Awareness of PAD among primary care physicians has also been low. Primary care physicians were aware of a PAD diagnosis among their patients with a history of PAD only 49% of the time.[20]

Suboptimal awareness of PAD by both patients and health care professionals is likely to contribute to lower-than-expected use of guideline-directed medical

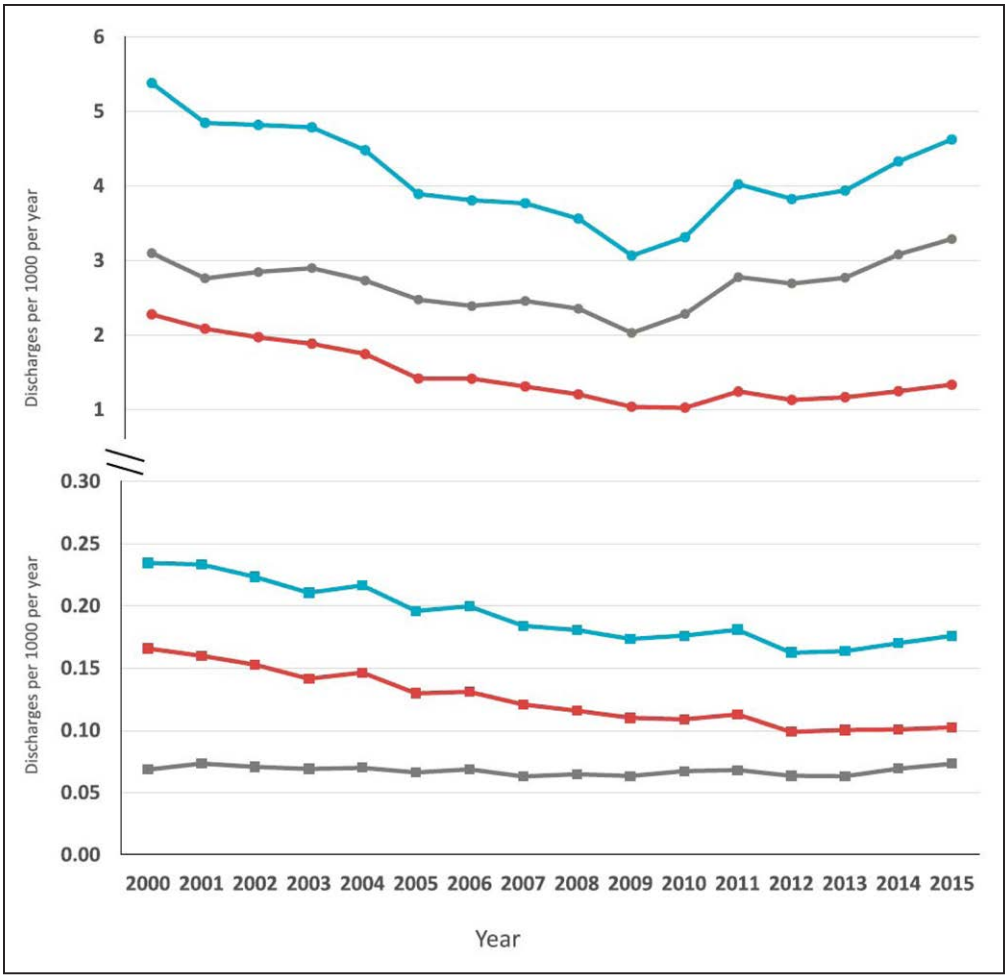

Figure 1. Age-adjusted rates of total (blue lines), major (red lines), and minor nontraumatic (gray lines) lower-extremity amputations in adults with diabetes (top) and without diabetes (bottom).

therapy for those with PAD. Despite the benefit of statins in reducing the risk of cardiovascular events, studies have shown that among individuals with PAD, only ≈30% were taking statins.[22,23] Smoking cessation therapy (counseling or medication) was given to only ≈35% of current smokers with PAD.[23] Of importance, there was no temporal change in the use of preventive therapy and lifestyle counseling among patients with PAD from 2005 to 2012.[23] The situation is similar among patients with diabetes at high risk of PAD and CLI. Although the American Diabetes Association recommends regular foot care in individuals with diabetes,[24] only ≈30% of eligible patients actually receive it.[15]

To the best of our knowledge, no studies have quantified the reduction of nontraumatic amputations attributable to an increasing awareness of PAD. However, because awareness of PAD creates the basis for the diagnosis and management of PAD, it is critical to increase the awareness of PAD among patients and clinicians. For health care professionals, a promising approach is to integrate clinical decision support for PAD into the electronic medical record.[25,26] Of note, a few small studies have shown that understanding the reason for treatment is a major predictor of better adherence to PAD management[27] and that patient education indeed improves patients' knowledge of signs, symptoms, treatment, and complications of PAD.[28]

To improve awareness of PAD, several organizations have conducted PAD awareness campaigns (Stay in Circulation, PAD Awareness Month, Legs for Life, among others).[29–31] In 2021, the American Heart Association (AHA), in conjunction with key stakeholder organizations, will unveil the first National PAD Action Plan, which is a comprehensive road map for a coordinated, enduring approach to vascular health. This collaborative endeavor has 6 major goals that focus on improving the awareness, diagnosis, and treatment of PAD. One of the goals is to reduce the rates of nontraumatic lower-extremity amputations related to PAD by public outcome reporting and focused public health interventions. The long-term success of the PAD National Action Plan depends on the synergistic coordination of the

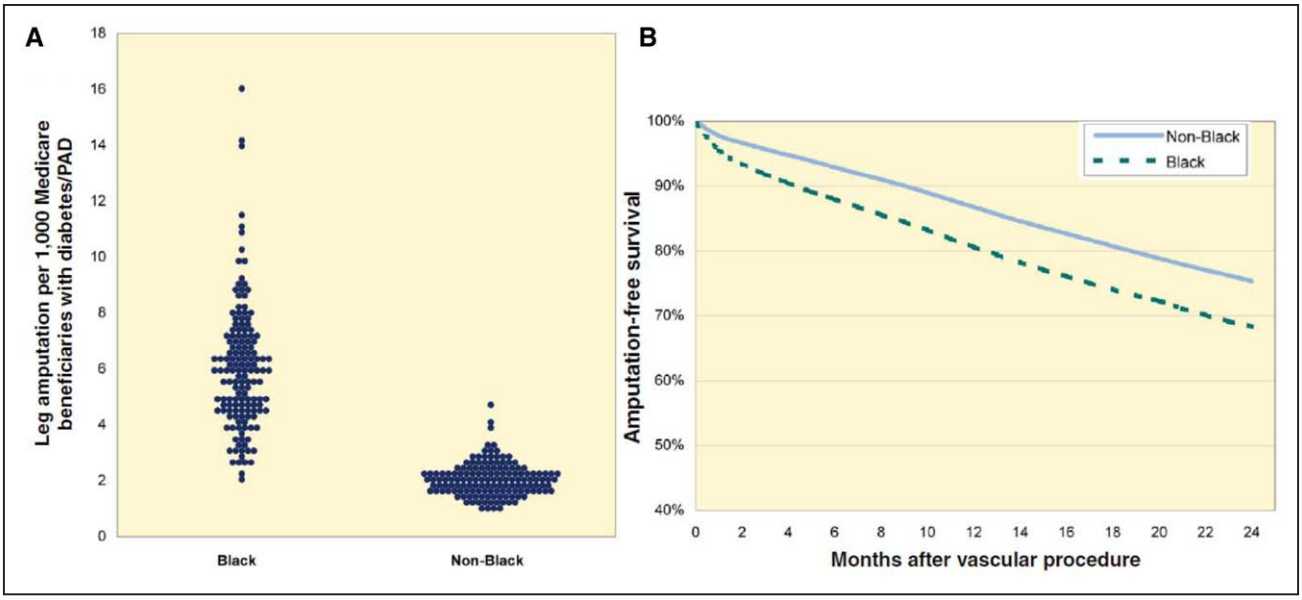

Figure 2. Incidence of any amputation per 1000 individuals (A) and amputation-free survival (B) among Medicare beneficiaries with diabetes and peripheral artery disease (PAD) by race.
Each dot in **A** represents the age- and sex-adjusted rate of lower-extremity amputation among patients with PAD and diabetes in 1 of 306 US hospital-referral regions. Reprinted from Goodney et al[32] with permission. Copyright © 2015, Trustees of Dartmouth College.

activities of many groups committed to preventing PAD complications, treating cardiovascular risk, and improving quality of life (QOL) for those with PAD.

DISPARITIES

The excess risks of amputations attributable to diabetes and PAD are synergistic when combined with poverty, racial disparities, geographic limitations in health care access, and myriad other health challenges.[14] Together, these factors represent many of the most challenging issues facing American health care today. In fact, recent work showed that disparities can increase the risk of amputation many times over, according to whether a patient is Black or White or where they live in the United States.[12,14,32,33]

Racial disparities in the United States are dramatic. Among Medicare beneficiaries with diabetes and PAD, 4-fold differences in amputation risk are recognized between Black Americans and other racial/ethnic groups (Figure 2A).[32] Even after patients receive invasive treatment, these disparities continue to manifest. After similar revascularization treatments, Black patients are more likely to undergo amputation (Figure 2B).

The association of poverty with prognosis in PAD is complex. For example, even in a publically funded health care system such as the Veterans Health Administration, in which an effect of socioeconomic status would be expected to be minimal, lower socioeconomic status (eg, income) was independently associated with higher risk of lower-extremity amputation.[12] Moreover, one might hypothesize that Medicare-Medicaid dual eligibility might be associated with improved outcomes for PAD because dual coverage might eliminate common hurdles to health care access and lessen disparities. However, data from the Vascular Quality Initiative demonstrated that among patients with severe PAD such as CLI, those with dual eligibility actually had higher mortality and amputation risk compared with those eligible only for Medicare.[34] However, this result should not be interpreted to mean that dual eligibility increases the risk but is likely to reflect that people with dual eligibility have a high risk factor profile. Thus, Medicaid expansion may help increase access to care for these patients and minimize PAD-related disparities.

In addition, there is considerable geographic variation within the United States in the rate of lower-extremity amputation.[35] Specifically, per 100 000 patients with PAD, the Mountain region observed 5500 amputations, whereas the East South Central region had 8400 amputations. Geographic variation remained even after accounting for differences in clinical factors such as diabetes.

These findings can be summarized in stark realities, including wide variations in the incidence and severity of PAD, limited health insurance coverage for many high-risk subgroups, and inadequate access to advanced PAD care. In many of these regions, simply expanding the social safety net may not be enough to limit disparities. Improving access to care through insurance expansions and increasing the availability and accessibility to interventions that reduce the risk of amputation would be necessary components to affect amputation rates among high-risk populations.

Table 1. Major Factors Influencing QOL Among Amputees

Patient factors
Higher QOL
Walking with prosthesis
Transtibial (vs transfemoral) amputation
Female sex (especially if <60 y of age)
Living at home
Lower QOL
Age >65 y
Presence of diabetes
Isolation (being homebound)
Physician-controlled factors
Timing of amputation
Informed decision making
Postamputation support

QOL indicates quality of life.
Data derived from Davie-Smith et al[45] and Suckow et al.[46]

Table 2. Unmet Needs Among Amputees

Preparation for living with an amputation
Finding a prosthetist
Knowledge gaps related to prosthetic limb options
Inadequate postdischarge pain control, including postoperative pain, phantom limb pain, and residual limb pain
Inadequate knowledge of medical insurance system
Financial challenges

Data derived from Columbo et al.[42]

IMPACT OF NONTRAUMATIC LOWER-EXTREMITY AMPUTATIONS

Patient Impact

Despite advances in surgical technique and critical care, mortality rates after major amputation for PAD remain high, such that postamputation mortality is often equated to the mortality risk of advanced cancer.[36] A recent meta-analysis reported a 3-year mortality risk of 71% after lower-extremity amputation.[37] Mortality risk increases with older age, proximal amputation level (eg, above the knee), and comorbidities, particularly cardiac and kidney disease. Average 30-day postamputation mortality has remained relatively stable at 5% to 15% across different clinical settings.[38–41]

The decision of whether and when to amputate hinges on the surgeon's judgment and informed decision making by patients. The ultimate goal is to maximize personal outcome priorities and QOL for remaining life. Patient involvement in this process has been shown to enhance postamputation adjustment and recovery.[42] Patients facing "life or limb" decisions must be made fully aware of the available options (eg, palliative care in the case of end-stage disease and high operative mortality risk) and decision support tools (eg, risk assessment tools[43,44]).

Although clinical outcomes such as patient survival are the common focus when patients and physicians consider the decision for amputation, less is known about its impact on QOL. A systematic review has shown that walking ability and use of a prosthesis have the strongest influence on QOL in individuals after amputations (Table 1).[45] For many people, a perceived loss of ability to participate in previous vocational, recreational, social, and sexual activity can have a greater toll on postamputation QOL than the absent limb itself.[47] Return to employment after amputation can be challenging.[48] Accordingly, depression and anxiety are highly prevalent, with rates of 20% to 30% of patients with major depressive disorders.[49] Postdischarge rehabilitation[50] and prosthetic use[46,51] play an important part in both physical and psychological recovery. Focus group interviews have identified unmet needs in patients who have undergone amputations (Table 2) and highlight the importance of patient-centered approaches to address these deficiencies.[42] To address this issue, funding agencies should prioritize research on patient-centered outcomes in PAD, especially in patients with CLI.

Impact on the Health Care System and Health Care Costs

Beyond patient impact, nontraumatic amputations have a significant effect on the health care system and on health care costs more broadly. Although national cost estimates specific to amputation are not well characterized, it is clear from studies of diabetic foot ulcers and limb ischemia that these costs are extremely high. For example, the annual cost of providing inpatient care for patients with a primary diagnosis of diabetic foot ulcers was estimated at >$790 million in 2010, as a consequence of nearly 60 000 admissions annually at a cost per hospitalization exceeding $13 000.[52] Among hospitalizations requiring revascularization or amputation, costs were found to be even higher, with open and endovascular revascularization costing ≈$60 000 per hospitalization and major amputation costing ≈$54 000 per patient in 2010.[52] A study of Medicare patients with CLI undergoing endovascular revascularization, surgical revascularization, or major amputation for 4 years after the procedure found that costs were highest among the amputation group, with an average of $55 700 per patient-year.[53]

Nontraumatic amputations also have implications for health care delivery well beyond the costs of the amputation itself. One major issue is hospital readmissions, which are common after hospitalizations for CLI and for amputation. For example, studies have demonstrated that in patients with a primary diagnosis of CLI, the readmission rate within 30 days is ≈20%, with recurrent

ischemia, infection, and gangrene as major causes.[54,55] A study from the American College of Surgeons National Surgical Quality Improvement Program reported an 18% 30-day readmission rate among patients undergoing lower-extremity amputation, with nearly half resulting from wound-related complications.[56] Medical comorbidities such as heart failure and end-stage kidney disease were potent risk factors of readmission. Accordingly, long-term health care use and costs are high among individuals with CLI and those with nontraumatic amputation. One study estimated that the aggregate costs of readmissions for patients with CLI who undergo revascularization exceed US $300 million annually,[57] and a study from the Partners Research Patient Data Registry showed that patients after amputation had an average of 71 hospital days per year up to 3 years.[58] Similarly, a study in the Veterans Administration found that postamputation patients had high health care use, with an average of 3 hospitalizations per patient during a median follow-up of 32.1 months.[59]

EVIDENCE-BASED MANAGEMENT OF PAD AND POTENTIAL CONTRIBUTION TO REDUCING NONTRAUMATIC AMPUTATION

In this section, we summarize evidence-based management for patients with PAD that can lower the risk of lower-extremity amputations. All of these diagnostic and therapeutic approaches constitute high-quality care, and health management organizations and hospitals should incorporate them as quality measures.

Diagnosis of PAD, Including ABI Evaluation

The ABI is a noninvasive sensitive and specific measurement to detect PAD.[60] The AHA and the American College of Cardiology 2016 PAD guideline recommends screening of PAD with ABI in high-risk populations (eg, older adults, ever-smokers, patients with diabetes).[61] However, the US Preventive Services Task Force does not recommend ABI screening in asymptomatic adults.[62] Because some primary care organizations and insurers follow US Preventive Services Task Force recommendations,[63] this approach may preclude a timely opportunity to diagnose PAD and deliver evidence-based treatment for PAD to prevent adverse limb events, because most patients with PAD are asymptomatic or have atypical leg symptoms.[20]

In this context, the recent VIVA trial (Viborg Vascular) tested the benefit of vascular screening (ABI measurement for PAD detection, ultrasonography for detecting abdominal aortic aneurysm, and blood pressure for hypertension screening) with subsequent relevant medical management (eg, optimizing cardiovascular preventive therapy and referral to a vascular surgeon) in men 65 to 74 years of age. In this trial, vascular screening resulted in a 7% reduction of mortality. Decreased inpatient days attributable to PAD and increased use of guideline-directed medical therapies for PAD were also found.[64]

Of importance, a recent analysis found that 1-time ABI screening among individuals ≥65 years of age followed by optimization of preventive therapies such as statins was cost-effective with an incremental cost-effectiveness ratio of US $88 758 per quality-adjusted life-year over a 35-year period.[65] This analysis shows that screening of high-risk populations is especially cost-effective (eg, incremental cost-effectiveness ratio, US $24 092 per quality-adjusted life-year in smokers).

Although a body of evidence supports the ABI measurement in asymptomatic individuals (especially high-risk populations), an important barrier is the lack of consistent reimbursement for ABI testing across the United States on the basis of abnormal physical findings (eg, diminished or absent pulses). The reimbursement of ABI for an abnormal physical examination varies significantly from permitted to disallowed to unclear across states.[66] Nontraumatic lower-extremity amputation cannot be effectively prevented if its leading cause, PAD, cannot be diagnosed.

In addition to detecting PAD, the ABI is useful for diagnosing CLI and is often used in conjunction with other tests to assess foot perfusion, including toe systolic blood pressure, toe-brachial index, skin perfusion pressure, and transcutaneous oximetry. Details of these modalities are beyond the scope of this policy statement but are provided in a recent AHA scientific statement.[67]

Smoking Cessation

Cigarette smoking is one of the most important modifiable risk factors for PAD. According to data from the Health Professionals Follow-up Study, 44% of PAD risk is attributable to smoking (followed by 41% to hypertension, 17% to hypercholesterolemia, and 14% to diabetes).[68] A recent report from the ARIC study (Atherosclerosis Risk in Communities) demonstrated that smoking is more strongly associated with incident PAD than other major atherosclerotic cardiovascular diseases.[69] Specifically, compared with never-smokers, individuals with ≥40 pack-years of smoking had ≈4 times higher risk for PAD versus ≈2 times higher risk for coronary heart disease and stroke. The impact of smoking on PAD is consistent across racial groups.[69,70] Although data relating other tobacco products (eg, cigars, pipes, and electronic cigarettes) to PAD risk are sparse, they likely contribute; a body of evidence demonstrates that these products increase the risk of other cardiovascular diseases.[71]

In the United States, 20% to 30% of patients diagnosed with PAD are estimated to be active smokers (50%–60% former smokers).[23,72] Although there are limited data on the direct effect of smoking cessation on reducing the risk of lower-extremity amputations, a single-center registry showed that patients with PAD who quit smoking after lower-extremity angiography had significantly improved amputation-free survival at 5 years compared with those who continued smoking (81% versus 60%; hazard ratio, 0.43 [95% CI, 0.22–0.86]).[13]

Given the strong impact of smoking on PAD pathophysiology and other adverse outcomes (eg, lung cancer and other cardiovascular disease), smoking cessation is recommended for all patients with PAD.[61] Contemporary smoking cessation programs consist of physician advice to quit smoking, referral to formal tobacco cessation counseling, and prescription of pharmacological agents (bupropion or varenicline) or nicotine replacement therapies (nicotine patch, gum, lozenge, nasal spray, or inhaler) to aid smoking cessation.[73] Brief smoking cessation counseling by vascular surgeons has been shown to increase patient interest in smoking cessation and awareness of smoking harms, with the effect durable 3 months after intervention.[74]

Pharmacological therapy or formal cessation counseling has been shown to be more cost-effective than physician advice alone.[75,76] In a randomized controlled trial,[76] intensive tailored PAD-specific smoking cessation counseling intervention resulted in significantly higher abstinence rates at the 6-month follow-up versus usual care with verbal advice of smoking cessation by a physician (21.3% versus 6.8%). In this trial, many long-term smokers with PAD were willing to initiate a serious quit attempt and to engage in such a program.

Despite the evidence of efficacy, a US study reported that smoking cessation counseling or medication was used in only 36% of visits among actively smoking patients with PAD.[13] Patients with PAD alone were much less likely to receive smoking cessation counseling compared with those with comorbid PAD and coronary heart disease (odds ratio, ≈0.2). Smoking cessation advice or medications were used more in individuals <65 years of age and in White individuals versus their counterparts.[13] Similar results were shown in an international registry.[72]

In addition to smoking cessation, smoking prevention in adolescents and younger adults is crucial to reduce the long-term risk of PAD and nontraumatic lower-extremity amputations. Indeed, the risk of incident PAD was shown to persist for up to 30 years after smoking cessation in the ARIC study (versus up to 20 years for coronary heart disease).[69] In this context, several trials have shown long-term effects of school-based smoking prevention curricula for keeping adolescents never-smokers.[77]

Diabetes Therapies

Diabetes accounts for 45% to 70% of lower-extremity amputations in the United States[78] and is one of the most potent risk factors for PAD.[79,80] Diabetes preferentially affects the tibioperoneal arteries,[81] reducing revascularization opportunities. Diabetes also causes microvascular disease (retinopathy, nephropathy, and neuropathy, known as the diabetic triopathy).[82] Although PAD is recognized as a macrovascular disease, several recent studies have shown strong associations of microvascular abnormalities with CLI and nontraumatic amputations.[83–85] In addition, diabetes may cause amputation independently of PAD. The diabetic foot, with a series of neuropathic abnormalities, increases the risk of foot ulceration and subsequent need of amputations.[86]

Better glucose control has been linked to lower risk of amputations in patients with diabetes. For example, a recent secondary analysis from the ACCORD trial (Action to Control Cardiovascular Risk in Diabetes) has reported that the hazard ratio of lower-extremity amputations was 0.69 (95% CI, 0.48–0.99) in the intensive glucose control group (target hemoglobin A_{1c} <6.0%) versus the standard glycemic control (target hemoglobin A_{1c}, 7.0%–7.9%).[87] Because ≈35 million Americans have diabetes and this number grows at a rate of ≈1.5 to 2 million individuals per year,[88] glucose control among patients with diabetes is pivotal for reducing the nontraumatic lower-extremity amputation rates in the United States.

Recent pharmacological additions to diabetes management may further affect the risk of amputation. In the LEADER trial (Liraglutide Effect and Action in Diabetes: Evaluation of Cardiovascular Outcome Results), the GLP (glucagon-like peptide)-1 receptor agonist liraglutide was associated with a significantly lower risk of diabetic foot ulceration–related amputations compared with placebo.[89] In contrast, in CANVAS (Canagliflozin Cardiovascular Assessment Study), patients treated with a SGLT (sodium glucose transport protein)-2 inhibitor, canagliflozin, had a 2-fold greater risk of amputation.[90] Although increased risk of amputation has not been reported in trials of other SGLT-2 inhibitors such as empagliflozin and dapagliflozin, an observational study of ≈1 million US patients with diabetes has observed ≈2 times higher risk of leg amputations among new users of SGLT-2 inhibitors compared with users of other antidiabetic medications.[91]

Regular Foot Monitoring/Care in Patients With Diabetes

Although the focus of this policy statement is PAD, diabetic foot ulcer is another major cause of nontraumatic lower-extremity amputation.[92] Indeed, ≈50% of

patients with diabetic ulcers have concurrent PAD. The identification of PAD in patients with diabetic ulcers is important because PAD characterized by poor foot perfusion is an independent predictor of nonhealing of ulcers, whereas infection is a predictor of nonhealing of ulcers in patients with PAD.[93]

The American Diabetes Association and the International Working Group on the Diabetic Foot recommend an annual comprehensive foot examination among patients with diabetes.[86,92] As part of this routine diabetic foot examination, health care professionals should check pulses of the dorsalis pedis and posterior tibial arteries to evaluate whether patients have undiagnosed PAD.[94] In addition, they should ask patients with diabetes about walking impairment, ischemic rest pain, and any exertional leg symptoms. An abnormal pulse examination or any concerning symptoms for PAD would then prompt a diagnostic ABI test.

Despite the American Diabetes Association and International Working Group on the Diabetic Foot recommendations, as mentioned, only ≈30% of patients with diabetes actually receive annual foot care.[15] In this context, the American Association of Diabetes Educators promotes foot self-checks.[95] Teaching patients with diabetes thorough foot self-checks can occur over 10 to 20 minutes and include individualized assessment of foot ulcer risk, instructions about how to inspect their feet, toenail care, footwear selection, moisturizing areas, and a basic understanding of what foot conditions should be evaluated by their health care professional.[96] A 1991 study reported a reduction in diabetic foot–related complications after an intervention to improve foot self-checks.[97] However, a recent systematic review revealed little agreement on the optimal strategy to help patients and family members become proficient with routine foot care at home.[98] Standardization and optimization of foot self-checks are warranted. Although we need more data, technologies are advancing for remote monitoring of foot temperature[99] and pressure.[100]

Statins

Statins are potent lipid-lowering medications and play a pivotal role in the primary and secondary prevention of cardiovascular disease.[101] Indeed, the 2016 AHA/American College of Cardiology PAD guideline recommends statin therapy for all patients with PAD.[61] Although risk reduction of major cardiovascular events with statins is widely known, it is important for policymakers and health care professionals to acknowledge a body of evidence indicating the risk reduction of major limb events such as lower-extremity amputations. In addition, as mentioned, the fact that only ≈30% of patients with PAD are taking statins is a major problem in PAD care.[22,23]

The first clinical trial to show potential benefit of statins on limb prognosis was the Heart Protection Study, which included 20 536 patients with a history of coronary disease, PAD, stroke, diabetes, or hypertension. In this trial, 40 mg daily simvastatin resulted in a 16% reduction of peripheral vascular events (ie, carotid procedures, other arterial revascularization, and amputations) compared with placebo.[102] Similarly, a retrospective analysis of 5861 patients with symptomatic PAD from the REACH registry (Reduction of Atherothrombosis for Continued Health) reported a significantly lower risk of the major limb outcomes (worsening claudication/new episode of CLI, leg revascularization, or amputation) among patients receiving any statin (hazard ratio, 0.82 [95% CI, 0.72–0.92]).[103] A recent large observational cohort study of 155 647 patients with incident PAD in the Veterans Affairs database showed that high-intensity statin users had an ≈30% lower risk of major amputation compared with those not on statins. Low- to moderate-intensity statins showed ≈20% reduced risk of major amputations.[14]

Statin therapy also has been associated with a lower risk of amputations among patients with CLI. In a prospective multicenter registry of 1200 patients with CLI, statin therapy was associated with a lower risk of amputations (hazard ratio, 0.45 [95% CI, 0.34–0.63]).[104] Reduced risk of amputations according to statin therapy was consistent across subgroups by age, diabetes, chronic kidney disease, use of antiplatelet agents, and revascularization procedures.[104] Other studies also have demonstrated a lower risk of amputations with statin therapy among patients with PAD receiving leg revascularization.[105,106]

Novel Lipid-Lowering and Antithrombotic Medications

In recent years, a few novel lipid-lowering and antithrombotic therapies have demonstrated promising results for reducing major adverse limb events, including nontraumatic lower-extremity amputations. However, these therapies are associated with varying degrees of side effects such as bleeding and varying cost. Therefore, the risk and benefit of these therapies should be considered before initiation. It is important to note that these novel therapies are meant to be used in conjunction with current guideline-recommended therapies.

The PCSK9 (proprotein convertase subtilisin-kexin type 9) inhibitor evolocumab is a monoclonal antibody that substantially lowers low-density lipoprotein cholesterol concentrations.[107] Recently, the FOURIER trial (Further Cardiovascular Outcomes Research With PCSK9 Inhibition in Subjects With Elevated Risk) reported ≈40% reduction of major limb outcomes, including acute limb ischemia, major amputation, or urgent peripheral

revascularization, with evolocumab versus placebo in patients with atherosclerotic disease and low-density lipoprotein cholesterol levels ≥70 mg/dL (13% had PAD).[108] Furthermore, the rates of major amputation, defined as above the knee or below the knee, excluding forefoot or toe, were >50% lower among patients with PAD on evolocumab versus placebo.[109]

The COMPASS trial (Cardiovascular Outcomes for People Using Anticoagulation Strategies) demonstrated that low-dose rivaroxaban (a direct factor Xa inhibitor) plus aspirin, compared with aspirin alone, was associated with a 70% reduction in the risk of above-the-forefoot amputation secondary to a vascular event among patients with PAD.[110,111] Although rivaroxaban plus aspirin was associated with 70% increased major bleeding,[110] in terms of net benefit, rivaroxaban and aspirin prevented 27 major adverse cardiovascular and limb events for every fatal or critical bleeding event.[111]

TRA2°P (Trial to Assess the Effects of Vorapaxar in Preventing Heart Attack and Stroke in Patients With Atherosclerosis) showed that vorapaxar (a protease-activated receptor 1 antagonist) versus placebo reduced the risk of acute limb ischemia (caused by arterial emboli, arterial thrombosis, or postrevascularization trauma) by ≈40% and the risk of lower-extremity revascularization by ≈20% among patients with stable atherosclerotic disease, including symptomatic PAD.[112–114] The reduction of acute limb ischemia is of particular importance because nearly 20% of cases of acute limb ischemia resulted in amputation.[113] It is important to note that there was a 66% increased risk of moderate or severe bleeding with vorapaxar versus placebo.[112]

Wound Care

There is increasing recognition of multidisciplinary wound care (MDWC) teams as a vital component of amputation prevention.[115–119] Most MDWC teams comprise a combination of vascular specialists, podiatrists, plastic surgeons, infectious disease specialists, nurses, orthotists/prosthetists, nutritionists, and pharmacists and use established and standardized wound care management protocols. The essential functions of a wound care management program include risk stratification of wounds with visual inspection, foot pulse palpation, skin temperature measurement, and shoe gear, gait, orthopedic, neurological, and vascular examinations. Treatment protocols include weekly wound debridement, management of local and systemic infections, and, for recalcitrant wounds, advanced wound dressings and therapies. Offloading of the affected area should be undertaken when appropriate. Diabetes education and referral to appropriate consultants are important components of the program.[61,120]

Adoption of MDWC has been shown in multiple studies to decrease wound healing times and to increase wound healing rates.[115,118,121] Furthermore, ambulatory status is preserved or improved in three-fourths of patients.[118] The use of MDWC teams decreases major amputation rates by >50%,[115,116,119] whereas reduction in all-cause mortality is variable.[116,119] Use of MDWC management is also associated with a reduction in hospitalizations and overall costs.[118,119]

Timely Referral to Vascular Specialists

The responsibility of medical management of PAD often falls to primary care physicians, general cardiologists, or, for patients with diabetes, endocrinologists. Patients with PAD should receive appropriate cardiovascular preventive therapies such as lipid-lowering therapy with statins, glucose control if they have diabetes, and management of blood pressure if they have hypertension.[61] The 2016 AHA/American College of Cardiology PAD guideline recommends antiplatelet monotherapy with aspirin (range, 75–325 mg) or clopidogrel (75 mg) to reduce the risk of adverse cardiovascular outcomes in patients with symptomatic PAD.[94] When patients have symptomatic PAD, referral to a vascular specialist is appropriate to evaluate the need for additional diagnostic studies, intensive medical management, supervised exercise training, or revascularization. Among the patients who undergo lower-extremity amputation in the United States, 73% and 54% do not undergo diagnostic angiography[122] and revascularization,[123] respectively, before the amputation.

Patients with PAD and a diabetic foot ulcer should be referred to a vascular specialist to determine whether revascularization is indicated to aid in wound healing and to help prevent the risk of amputation. The 2019 Endocrine Society guidelines for care of patients with diabetes who are >65 years of age recommend referral to a podiatrist or orthopedist when patients have peripheral neuropathy and referral to a vascular specialist when patients have PAD in order to reduce the risk of foot ulceration and nontraumatic lower-extremity amputation.[124]

Revascularization

Revascularization is associated with lower amputation rates and improved mortality in patients with CLI.[125,126] One study showed that patients with CLI presenting to a hospital that performed ≤5 lower-extremity revascularization procedures per year compared with hospitals that performed >44 per year had an odds ratio of 33.3 (95% CI, 22.28–49.82) for major amputation and 3.33 (95% CI, 2.1–5.28; $P<0.0001$) for 30-day mortality.[117] In another observational study of Medicare patients with CLI, ≈40% of patients treated with revascularization

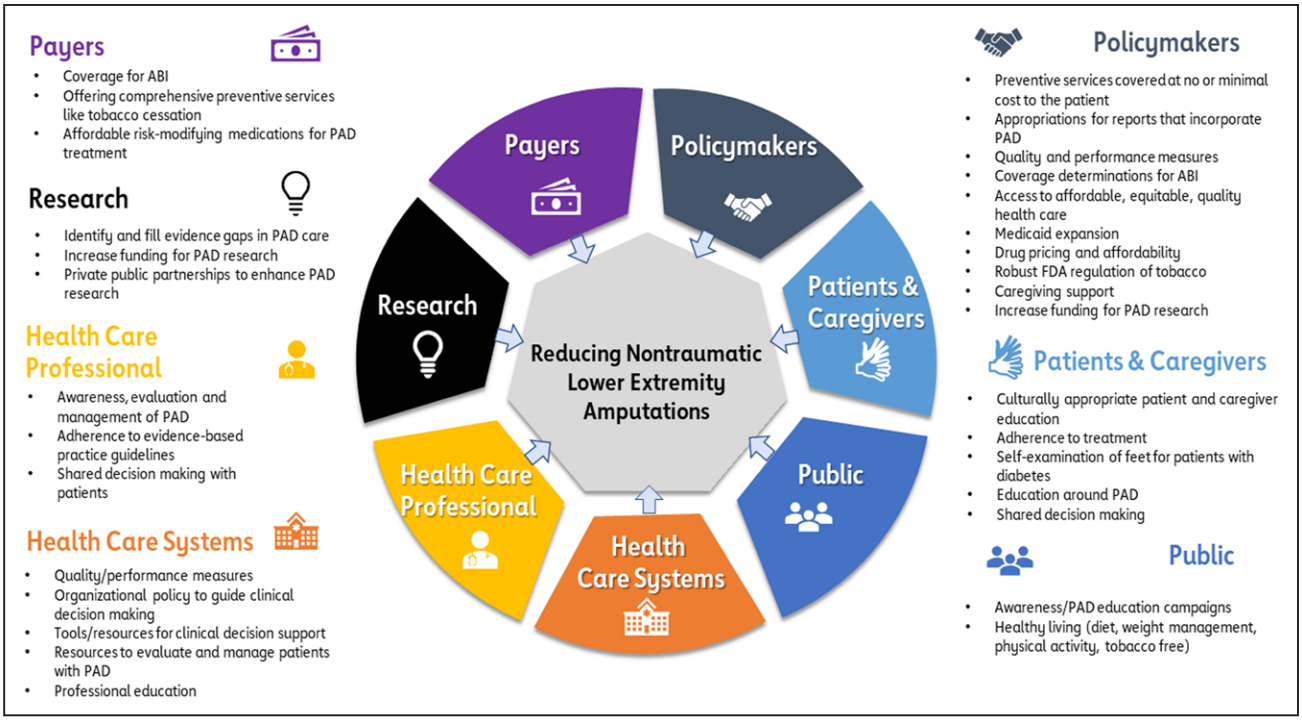

Figure 3. Key roles of each stakeholder for improving peripheral artery disease (PAD) diagnosis and management .
ABI indicates ankle-brachial index; and FDA, US Food and Drug Administration.

were still alive 4 years after treatment, whereas only 22% of patients treated with primary amputation survived for a similar duration.[53]

For several decades, there has been a steady increase in the number of revascularization procedures, with the largest increase in endovascular interventions.[127] Understanding the reasons for the growth in revascularization is challenging because of the variability of practice and preferred techniques, as well as the rapid evolution of endovascular technologies.[128,129] Nonetheless, the increase in the frequency of revascularization has been accompanied by a rise in the number of reinterventions, as might be expected. One recent study reported that the cumulative incidence of a repeat peripheral revascularization procedure or amputation after a median of 2.7 years was ≈42%.[130]

The selection of endovascular revascularization versus open surgical bypass for an individual patient involves assessment of life expectancy, vascular anatomy, comorbid risk factors, probability of needing reintervention, patient preference, and available local skill sets. The "Global Vascular Guidelines on the Management of Chronic Limb-Threatening Ischemia" provide an opportunity to standardize the evaluation and management of these patients.[131] The best results appear to be achieved in higher-volume centers with focused CLI programs.[125] There are conflicting data in specific situations on amputation outcomes in patients who receive open or percutaneous revascularization, but the differences are not large.[126,132] Several trials are ongoing to compare the rate of major adverse limb events in patients undergoing open surgical with those undergoing endovascular treatment.[133–136] Regardless of the outcome of these trials, it is clear that evaluation for revascularization should be considered for all patients at risk for amputation.[137]

IMPORTANCE OF PAD MANAGEMENT FOR ELIMINATING HEALTH CARE DISPARITIES

Improving the management of PAD could have a significant impact on health care disparities among some racial and ethnic groups and those who are living in poverty. These groups have significantly worse limb outcomes and higher rates of amputation and thus are likely to gain the most when guideline-directed diagnostic and therapeutic approaches are implemented for all patients with PAD.

In some cases, when overall quality improves, disparities may diminish. For example, performance on quality measures for acute myocardial infarction, heart failure, and pneumonia has been publicly reported since 2008; improvements in these measures was associated with a reduction in disparities of evidence-based therapies for these diseases between White, Black, and Hispanic adults.[138] Similar findings have been reported for quality measures in the outpatient setting.[139] More recently, reductions in readmissions under the Hospital Readmissions Reduction

Table 3. Policy Guidance

Policy	Recommendations
Legislative/regulatory policy	
ABI	The ABI test should be reimbursed consistently across states.
Quality/performance measures	Performance measures should address the following in patients with PAD: Statins Smoking cessation Glucose control if diabetes is present Annual foot monitoring if diabetes is present
Government reports related to cardiovascular disease (eg, Surgeon General's reports on smoking)	Government reports should acknowledge PAD as an important phenotype of cardiovascular disease.
Access to care	Medical care must be affordable, accessible, and equitable for patients with PAD.
	Medicaid expansion
Drug affordability	Appropriate pharmacological therapy should be available with minimal copay to patients with PAD.
Tobacco	Robust FDA regulation of all tobacco products
	Tobacco cessation therapy should be comprehensive and available in all public and private health care plans at no copay.
Diabetes management	Comprehensive diabetes management, including pharmacotherapies and foot monitoring, should be affordable and accessible.
Research funding	Funding agencies should have dedicated grant opportunities to support PAD research.
	Funding agencies should prioritize research on patient-centered outcomes in PAD, especially in patients with CLI.
Caregiving	Support should be provided to caregivers of patients with PAD.
Organizational/health system policy	
Quality/performance measures	Recommended quality and performance measures should be integrated into electronic heath records and delivery of care.
	Institutions should maintain or participate in a registry that includes outcomes after peripheral revascularization and rates of nontraumatic amputation.
Organizational guideline	Organizational policy should be implemented to guide clinical decision making (eg, referral to vascular specialist).
Clinical decision support	Health care systems should integrate clinical decision support for PAD.
Resource allocation	Resources should be available for evaluating and managing patients with PAD.
Professional education	Educational activities should be provided to health care professionals to develop, maintain, or improve the knowledge, clinical skills, and professional performance for PAD diagnosis and management.
	Clear guidance regarding who and when to be referred to vascular specialists should be implemented.
Patient/caregiver education	Patient education materials for PAD that are culturally relevant and at the appropriate reading level should be available.
	Foot self-checks for patients with diabetes should be standardized, optimized, and implemented.
Barriers to care in high-risk populations (eg, diabetes)	Barriers to PAD-related care should be identified and potential solutions should be implemented (eg, arranging transportation to patients who cannot come to clinics; ensuring that all patients at risk of amputation are seen by a vascular specialist and have access to angiography and revascularization if indicated).
	Screening for social determinants of health

ABI indicates ankle brachial index; CLI, critical limb ischemia; FDA, US Food and Drug Administration; and PAD, peripheral artery disease.

Program were associated with a narrowing of the gap in readmission rates between Black and White patients.[140] The Vascular Quality Initiative, a multistakeholder effort to examine variation and to improve the delivery of vascular care nationwide, could similarly drive improvements in care and perhaps also decrease disparities.[141]

However, in each of these studies, disparities, albeit smaller than baseline, remained between Black and White patients, and similar findings have been shown for poverty. Thus, to narrow the gap further and ultimately to eliminate disparities, efforts to improve PAD care in high-risk groups such as Black patients and those living in poverty will be necessary.

POLICY RECOMMENDATIONS TO DECREASE NONTRAUMATIC AMPUTATIONS BY 20% BY 2030

As described, broad implementation of guideline-directed diagnosis and management of PAD can reduce the rates of lower-extremity amputation. If these approaches are implemented comprehensively, we should be able to

accomplish the goal of reducing lower-extremity nontraumatic amputation by 20% in the next decade. Unfortunately, many individuals with PAD are not receiving these evidence-based approaches because of such barriers as underdiagnosis of PAD, failure to appreciate the importance of PAD, lack of knowledge among health care professionals about PAD management, inadequate access to vascular or foot care specialists, and medical cost. To effectively and efficiently overcome these barriers, key stakeholders should work collaboratively (Figure 3).

To facilitate the process, we propose regulatory/legislative and organizational/institutional policies that would ensure adoption of quality and performance measures to promote optimal medical management of patients with PAD (statins, smoking cessation, glucose control); coverage for annual foot monitoring of patients with diabetes; robust US Food and Drug Administration regulation of all tobacco products[73]; availability of comprehensive tobacco cessation therapy with no copay; integration of clinical decision support to diagnose and manage PAD in electronic health records; consistent reimbursement for the ABI test across all states; affordable, accessible, and equitable medical care for all patients with PAD; professional education on PAD diagnosis and management; and dedicated funding opportunities to support PAD research (see Table 3 for details).

CONCLUSIONS

Nontraumatic lower-extremity amputation is a devastating complication of PAD with a significant impact on patients and society. A recent resurgence of amputation rates in patients with diabetes is a real concern. Low adherence to evidence-based management (eg, smoking cessation, statins, and regular foot monitoring [in diabetes]) among patients with PAD is not acceptable. There is considerable opportunity to improve the care of patients with PAD and thereby reduce the risk of CLI, foot ulceration, and limb amputation. Thus, it is time to take action. We urge that policymakers ranging from regulatory bodies to health systems and individual institutions refer to this policy statement and implement its recommendations to achieve the goal of reducing the rate of nontraumatic lower-extremity amputations by 20% by 2030.

ARTICLE INFORMATION

The American Heart Association makes every effort to avoid any actual or potential conflicts of interest that may arise as a result of an outside relationship or a personal, professional, or business interest of a member of the writing panel. Specifically, all members of the writing group are required to complete and submit a Disclosure Questionnaire showing all such relationships that might be perceived as real or potential conflicts of interest.

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*Modest.

†Significant.

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†Significant.

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