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Peripheral Artery Disease Screening in the Community and 1-Year Mortality, Cardiovascular Events, and Adverse Limb Events

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Introduction: This study aimed to examine all-cause mortality, 1- and 2-year major cardiovascular events, and major adverse limb events in individuals aged ≥65 years who received an in-home health visit with peripheral artery disease screening. In addition, we compared 1-year healthcare utilization before and after peripheral artery disease screening for those who screened positive.

Setting/Participants: Medicare Advantage beneficiaries aged ≥65 years participating in the Optum HouseCalls program in the U.S. between April 1, 2017 and February 1, 2019 were included.

Intervention: The intervention consisted of a peripheral artery disease screening program using a plethysmography system.

Main outcome measures: One-year all-cause mortality as a landmark analysis, 1- and 2-year major cardiovascular events, and major adverse limb events after screening were compared by peripheral artery disease screen status using claims data. We compared cardiovascular medications and revascularization procedures between the year before and after the peripheral artery disease screening event for those with peripheral artery disease.

Results: Of 192,500 beneficiaries, 27.7% screened positive. One-year all-cause mortality rates for those who screened positive for peripheral artery disease versus those who screened negative were higher (1.51% vs 0.89%; $p<0.001$; adjusted hazard ratio=1.21; 95% CI=1.08, 1.36) as well as 1-year major cardiovascular events (5.54% vs 3.60%; adjusted hazard ratio= 1.22; 95% CI=1.15, 1.30) and major adverse limb events (0.23% vs 0.04%; adjusted hazard ratio=3.15; 95% CI=2.10, 4.73). Similar risks were observed for 2-year results. Before and after peripheral artery disease screening, medications remained stable for those who screened positive (e.g., statin therapy=54.2% vs 56.6%); rates of peripheral vascular interventions remained stable (0.0% vs 0.1%).

Conclusions: A national peripheral artery disease screening effort is feasible. Detecting previously undiagnosed peripheral artery disease is a way to risk stratify a population that would benefit from further cardiovascular risk management.

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INTRODUCTION

In the U.S. alone, it is estimated that more than 8.5 million Americans have peripheral artery disease (PAD).[1] In patients who experience major adverse limb events (MALEs) after a PAD diagnosis, 1-year mortality rates of 14%, and 1-year cardiovascular-related hospitalizations of 55% have been noted.[2] This burden of disease translates into a decreased quality of life and a high cost to society.[1,3]

Despite estimates of rising PAD incidence and systematic underdetection and undertreatment,[4–7] there is a relative lack of contemporary efforts that illustrate the PAD burden at the population level in at-risk subpopulations, including individuals aged ≥65 years. Current epidemiologic studies estimate that symptomatic PAD is present in 12.4% of individuals aged ≥65 years. Up to half of the patients with PAD present with asymptomatic disease, and thus, these estimates may be an underrepresentation of the true PAD burden.[8]

Because existing data on PAD estimates are quickly becoming outdated,[9] there is a need to better understand the magnitude of the PAD burden in the overall population. Recognition of PAD is necessary to prescribe evidence-based cardiovascular treatments and lifestyle changes to reduce cardiovascular events.[10] We therefore studied data from a nationwide sample and perform a landmark analysis on 1-year mortality rates, examining 1-year and 2-year major cardiovascular events (MACEs) and MALEs in Medicare Advantage beneficiaries aged ≥65 years who received an in-home health visit with PAD screening. We additionally examined the patterns of healthcare utilization (cardiovascular medications, rates of PAD revascularization) in the year before and the year after the PAD screening. Current estimates of PAD burden would inform potential future population health strategies that can target preventive interventions to those with the highest burden in the community.

METHODS

Study Sample

This study used deidentified claims data from the OptumLabs Data Warehouse,[11] including medical and pharmacy claims, and enrollment records for commercial and Medicare Advantage beneficiaries as well as data elements originating from the in-home health visits (Optum HouseCalls program), which included a count of previous HouseCalls visits, information on refusals or those in whom PAD screening could not be performed, PAD screening results for both limbs, height, weight, aspirin use, and smoking status.

Eligible records were those of beneficiaries with coverage and claims information between January 1, 2014 and March 28, 2020. Exclusion criteria were individuals who (1) did not have 1-year continuous enrollment for Medical and Pharmacy plan benefits before and after the in-home visit, (2) had pre-existing vascular disease (Centers for Medicare & Medicaid Services hierarchical condition categories [HCCs]-106, atherosclerosis of the extremities with ulceration or gangrene; HCC-107, vascular disease with complications; or HCC-108, vascular disease in the year before the visit), (3) had end-stage renal disease and dialysis codes (N181x-N185x and N191x-N195x) (because of lack of Medicare Advantage Outcomes Claim data), (4) were in long-term care facilities >90 days during the year before the index in-home visit (because of lack of Medicare Advantage Outcomes Claim data), (5) had no valid vital status information, (6) were missing sex or year of birth information, (7) were aged <65 years at the start of the continuous enrollment period 1 year before the index visit, or (8) had missing height and/or weight.

In-home visits are organized by OptumCare, which offers annual health assessments by advanced healthcare practitioners.[12] Health screenings, educational materials, and medication reviews are offered during these 45–60 minute visits. For individuals who received >1 in-home visit, the first visit in which PAD screening occurred was used. HouseCalls visit data from 2014 to 2016 was only used to calculate the number of previous house call visits. The study timeline around the index house call visit was 1 year before the index and 1 year after the index for all.

This study protocol was designed a priori. It was deemed exempt from IRB approval.

Measures

Outcomes. Outcomes information was derived from the OptumLabs Data Warehouse as deidentified claims data. The primary outcome was 1-year all-cause mortality, after a year of continuous enrollment after the in-home visit with PAD screening, set up as a landmark analysis.

Additional outcomes were 1- and 2-year MACE and 1- and 2-year MALE. MACE included ischemic stroke (ICD-10-CM Codes I63 and 164) and acute myocardial infarction (ICD-10-CM Codes I21 and 122).[13–15] For MALE, a cross-walk of previous work[16,17] was conducted, resulting in codes for peripheral vascular interventions, lower limb amputation, and admissions with diagnostic PAD codes (Appendix Table 1, available online).

Healthcare utilization was documented as the use of cardiovascular medications (antidiabetic agents, anticoagulant therapy, antiplatelet therapy, proprotein convertase subtilisin/Kexin type 9 [PCSK9] inhibitors, tobacco cessation medications, statin therapy), count of guideline-recommended medication classes used, and rates of peripheral vascular interventions (Appendix Tables 1 and 2, available online).

PAD Screening. PAD screening was implemented between April 1, 2017 and February 1, 2019 in those aged ≥65 years[18] within the HouseCalls visits program, designed to be national in reach, with a complete rollout to 45 states (Appendix Figure 1, available online). Certified and licensed advanced practice clinicians trained to perform the PAD screening test conducted the screening. Integrated within their in-home visits, beneficiaries received PAD screening through a QuantaFlo (Semler Scientific, Inc, San Jose, CA) assessment.[19] This noninvasive test derives a digital ankle–brachial index and was selected because of its ease of use in a community setting. The test relies on a plethysmography system resulting in a blood volume waveform visualization. A QuantaFlo score (ratio) is provided for each leg. The lowest score

is used in the diagnosis. In calculating the ratio, a volume waveform is obtained from both upper arms. The calculation is performed by a standardized algorithm comparing the ankle volume waveform with the volume waveform of the 2 arms. A ratio of the index of leg-to-arm pulse volume is generated, with plethysmography index values >0.99 indicating no abnormality, 0.99−0.91 indicating mild disease, 0.90−0.61 indicating moderate disease, 0.60−0.31 indicating significant disease, and ≤0.30 indicating severe disease.[19] Using contrast angiography as the reference, a plethysmography index value ≤0.99 has a sensitivity of 86.0%, a specificity of 100%, and an accuracy of 87.5% to detect PAD.[19] As a conservative approach, individuals with plethysmography index values ≤0.90 were considered as screened positive for PAD. The prognostic validity of the plethysmography test was established for the primary outcomes, and a dose–response relationship (log-rank test $p<0.0001$) for severity by plethysmography thresholds was noted for all outcomes (Appendix Figure 2, available online) and in previous validation efforts in a regional community screening effort among the same age group.[20]

After a positive PAD screening, beneficiaries and their primary care physicians received the results. If screened positive, beneficiaries also received PAD educational materials (Appendix Figure 3, available online).

Other Variables. Follow-up days were calculated since the index in-home visit. To be able to report on the same cohort for all endpoints, including healthcare utilization, a continued enrollment 1 year after the PAD screening event was enforced. As a consequence of the requirement of continuous enrollment, landmark analysis was pursued for the 1-year mortality endpoint.[21] For the landmark analysis, individuals who survived in the first year after their PAD screening were subsequently followed to model their mortality risk in the subsequent year, censoring at the earliest occurrence of death, disenrollment, or 730th day of observation. For the 1- and 2-year MACE and MALE events, time to first event analyses were performed, censoring at the earliest event or the 365th and 730th days, respectively.

Demographic variables included age, sex, race, and ethnicity. Information about the geographic region of the beneficiaries was categorized as Northeast, Midwest, South, West, and others, including the District of Columbia and unknown state. Health plan enrollment characteristics included the number of previous in-home visits received since 2014. Risk factor information assessed at the index visit included BMI (kg/m^2) and tobacco use. Medical history information in the year before the index in-home visit was derived according to Elixhauser comorbidity variables; a modified Elixhauser comorbidity index; and claims-based comorbidities, including atrial fibrillation, dyslipidemia, stroke, and coronary artery disease.[22,23]

Statistical Analysis

Beneficiary characteristics were described for the overall sample and by PAD screening status. Continuous variables were summarized as means and SDs and medians and IQRs, and categorical variables were summarized as frequencies and percentages. Standardized differences were calculated to quantify the effect sizes of the differences between the groups. For all descriptive comparisons, standardized differences <10% or <20% were considered negligible or small, respectively.[24,25]

Crude event rates by PAD screen result (positive versus negative) were described for all-cause mortality (1-year landmark analysis), MACE (1 year and 2 years), and MALE (1 year and 2 years). Kaplan−Meier curves were constructed separately by screen status, and PAD severity and differences were tested using the log-rank test. MACE and MALE rates were also provided by PAD severity. Hazard ratios (HRs) and 95% CIs were derived from Cox proportional hazards models for the association between PAD screen status (positive versus negative) and all-cause mortality, MACE, and MALE. We adjusted our models for age, sex, race, region, number of previous house call visits, BMI, cigarette usage, other tobacco usage, Elixhauser comorbidities (chronic heart failure, valvular disease, pulmonary circulatory disease, uncomplicated hypertension, complicated hypertension, other neurologic disorder, chronic obstructive pulmonary disease, uncomplicated diabetes, complicated diabetes, hypothyroidism, renal failure, liver disease, acid peptic disorder, HIV, lymphoma, metastatic cancer, cancer solid tumor, rheumatoid arthritis, coagulopathy, weight loss, fluid/electrolyte, blood loss, anemia, substance abuse, psychosis, depression), additional comorbidities (atrial fibrillation, dyslipidemia, stroke, coronary artery disease), PAD laterality, baseline hypoglycemic agents, baseline anticoagulant medication, baseline antiplatelet therapy, baseline PCSK9 therapy, baseline smoking-cessation medication, baseline statin therapy, and baseline aspirin as well as geographic region and race. The proportionality of hazards assumption was tested and met using weighted Schoenfeld residuals. To examine the robustness of our analyses and to rule out whether any of the findings were driven by the most severe PAD cases, we replicated the Cox models for all the outcomes while excluding those with severe PAD (plethysmography index values ≤0.30).

Among the cohort that screened PAD positive, we compared medication usage patterns (hypoglycemic agents, anticoagulant therapy, antiplatelet therapy, PCSK9 therapy, smoking-cessation medications, and statin therapy) through total counts in the 12-month period before and after the index in-home visit using a difference-in-difference analysis and did the same for admissions for MALE. To accommodate these comparisons, difference-in-differences analysis used generalized linear models with a Poisson distribution for the count outcome. We used generalized estimating equation to account for within-subject correlation of outcome before and after PAD screening.[26] The group classified as having a negative PAD screen was used as the reference group. This approach has the advantage of adjusting for both baseline treatments and unobserved confounding that remain fixed over time.

Complete case analysis was performed with SAS, version 9.4 (SAS Institute, Cary, NC). Analyses were performed by OA, and independent data replication was performed for all analyses by a separate analyst.

RESULTS

After applying the inclusion and exclusion criteria, 192,500 individuals who underwent PAD screening within the context of their house call visit were identified. The only missing covariate information was observed for the BMI, which had a missing rate of 0.56%. For comorbidities, medication treatments, and outcomes, there were no missing data because the

Table 1. Characteristics for the Total Sample and by PAD-Positive Versus Negative Screen Status

Characteristics	Total N=192,500	PAD-positive screen *n*=53,343 (27.7%)	PAD-negative screen *n*=139,157 (72.3%)	Standardized difference
Demographics				
Age in years, mean (SD)[a]	74.3 (5.8)	75.7 (6.1)	73.8 (5.6)	0.32
Age in years, median (IQR)	73.0 (70.0–78.0)	75.0 (71.0–80.0)	73.0 (69.0–77.0)	
Age, categories				
65–69 years	46,326 (24.1)	(9,743) 18.3	(36,583) 26.3	−0.19
70–74 years	63,580 (33.0)	(15,613) 29.3	(47,967) 34.5	−0.11
75–79 years	43,286 (22.5)	(15,613) 23.9	(30,520) 21.9	0.05
80–84 years	25,039 (13.0)	(15,613) 17.0	(15,997) 11.5	0.16
≥85 years	14,269 (7.4)	(15,613) 11.6	(8,090) 5.8	0.21
Female sex[a]	117,996 (61.3)	34,731 (65.1)	83,265 (59.8)	0.11
Race				
Asian	4,382 (2.28)	1,186 (2.2)	3,196 (2.3)	−0.00
Black	39,332 (20.4)	12,700 (23.8)	26,632 (19.1)	0.11
White	120,489 (62.6)	32,283 (60.5)	88,206 (63.4)	−0.06
Other/unknown	12,044 (6.3)	3,372 (6.3)	8,672 (6.2)	0.00
Hispanic	16,253 (8.4)	3,802 (7.1)	8,672 (9.0)	−0.07
Geographical region				
Northeast	25,728 (13.4)	7,822 (14.7)	17,906 (12.9)	0.05
Midwest	13,323 (6.9)	3,783 (7.1)	99,540 (6.9)	0.01
South	140,837 (73.2)	38,542 (72.3)	102,295 (73.5)	−0.03
West	12,568 (6.5)	3,184 (6.0)	9,384 (6.7)	−0.03
Other/unknown	44 (0.1)	12 (0.1)	32 (0.1)	−0.00
Enrollment characteristics				
Previous number of in-home visits, mean (SD)[a]	1.9 (1.3)	2.0 (1.3)	1.9 (1.3)	0.05
Previous number of in-home visits, median (IQR)[a]	2.0 (1.0–3.0)	2.0 (1.0–3.0)	2.0 (1.0–3.0)	
Risk factors				
BMI, mean (SD)[a]	28.6 (5.8)	28.0 (5.8)	28.9 (5.7)	−0.16
BMI, median (IQR)[a]	27.8 (24.7–31.6)	27.1 (24.0–31.0)	28.1 (25.0–32.0)	
Cigarette use[a]				
Never smoked cigarettes	119,470 (62.1)	31,193 (58.5)	88,277 (63.4)	−0.10
Current cigarette smoker	119,470 (6.6)	4,873 (9.1)	7,808 (5.6)	0.14
Former cigarette smoker	60,349 (31.4)	43,072 (32.4)	43,072 (31.0)	0.03
Other				
Other tobacco usage				
Never	186,362 (96.8)	51,535 (96.6)	134,827 (96.9)	−0.02
Current	3,234 (1.7)	971 (1.8)	2,263 (1.6)	0.01
Former	2,904 (1.5)	837 (1.6)	2,067 (1.5)	0.01
Medical history				
Elixhauser comorbidity index score, mean (SD)	2.8 (2.2)	3.0 (2.2)	2.8 (2.2)	0.10
Elixhauser comorbidity index score, median (IQR)	2.0 (1.0–4.0)	3.0 (1.0–4.0)	2.0 (1.0–4.0)	
Chronic heart failure[a]	31,193 (6.6)	4,109 (7.7)	8,498 (6.1)	0.06
Cardiac arrhythmias	30,840 (16.0)	9,568 (17.9)	21,272 (15.3)	0.07
Valvular disease[a]	17,892 (9.3)	5,603 (10.5)	12,289 (8.8)	0.06
Pulmonary circulatory disease[a]	5,603 (1.4)	906 (1.7)	1,781 (1.3)	0.03
Hypertension, uncomplicated[a]	136,606 (71.0)	39,915 (74.8)	96,691 (69.5)	0.12
Hypertension, complicated[a]	17,849 (9.3)	5,648 (10.6)	12,201 (8.8)	0.06
Other neurologic disorder	9,631 (5.0)	2,956 (5.5)	6,675 (4.8)	0.03
COPD[a]	32,614 (16.9)	9,485 (17.8)	23,129 (16.6)	0.03
Diabetes, uncomplicated[a]	54,993 (28.6)	15,897 (29.8)	39,096 (28.1)	0.04

(*continued on next page*)

Table 1. Characteristics for the Total Sample and by PAD-Positive Versus Negative Screen Status (*continued*)

Characteristics	Total N=192,500	PAD-positive screen *n*=53,343 (27.7%)	PAD-negative screen *n*=139,157 (72.3%)	Standardized difference
Diabetes, complicated[a]	32,980 (17.1)	9,866 (18.5)	23,114 (16.6)	0.05
Hypothyroidism[a]	40,186 (20.9)	11,277 (21.1)	28,909 (20.8)	0.01
Chronic kidney disease (Stages 1–5)[a]	17,809 (9.3)	5,864 (11.0)	11,945 (8.6)	0.08
Liver disease[a]	7,591 (3.9)	1,814 (3.4)	5,777 (4.2)	−0.04
Acid peptic disorder	1,818 (0.9)	531 (1.0)	1,287 (0.9)	0.01
HIV/AIDS[a]	222 (0.1)	59 (0.1)	163 (0.1)	−0.00
Lymphoma	1,470 (0.8)	413 (0.8)	1,057 (0.8)	0.00
Metastatic cancer	1,860 (1.0)	499 (0.9)	1,361 (1.0)	−0.00
Cancer solid tumors	19,011 (9.9)	5,069 (9.5)	13,942 (10.0)	−0.02
Rheumatoid arthritis collagen vascular[a]	10,666 (5.5)	3,022 (5.7)	7,644 (5.5)	0.01
Coagulopathy[a]	4,236 (2.2)	1,145 (2.2)	3,091 (2.2)	−0.01
Obesity	24,702 (12.8)	5,816 (10.9)	18,886 (13.6)	−0.08
Weight loss	5,361 (2.8)	1,900 (3.6)	3,461 (2.5)	0.06
Fluid/electrolyte disorder	15,034 (7.8)	4,689 (8.8)	10,345 (7.4)	0.05
Deficiency anemia[a]	12,540 (6.5)	3,828 (7.2)	8,712 (6.3)	0.04
Blood loss	2,012 (1.1)	645 (1.2)	1,367 (1.0)	0.02
Alcohol abuse disorder	1,937 (1.0)	552 (1.1)	1,385 (1.0)	0.00
Substance use disorder[a]	1,989 (1.0)	518 (1.0)	1,471 (1.1)	−0.01
Psychosis[a]	816 (0.4)	209 (0.4)	607 (0.4)	−0.01
Depression[a]	23,896 (12.4)	6,496 (12.2)	17,400 (12.5)	−0.01
Acute myocardial infarction	5,438 (2.8)	1,817 (3.4)	3,621 (2.6)	0.05
Atrial fibrillation[a]	15,089 (7.8)	4,804 (9.0)	10,285 7.4	0.06
Dyslipidemia[a]	135,490 (70.4)	37,626 (70.5)	97,864 (70.3)	0.00
Stroke (all types)[a]	6,983 (3.6)	2,352 (4.4)	4,631 (3.3)	0.06
Coronary artery disease	29,593 (15.4)	9,776 (18.3)	19,817 (14.2)	0.11
Screened no or mild PAD (plethysmography index >0.90)	139,157 (72.3)	0 (0.0)	139,157 (100.0)	n/a
Moderate PAD (plethysmography index of 0.61–0.90)	35,918 (18.7)	35,918 (67.3)	0 (0.0)	n/a
Significant PAD (plethysmography index of 0.31–0.60)	12,967 (6.7)	12,967 (24.3)	0 (0.0)	n/a
Severe PAD (plethysmography index ≤0.30)	4,458 (2.3)	4,458 (8.4)	0 (0.0)	n/a
Bilateral PAD	25,218 (13.1)	25,218 (47.3)	0 (0.0)	n/a

Note: All values are presented as *n* (%) unless otherwise specified.
[a]Denotes variables included in the calculation of propensity weight for receiving PAD screening versus not.
COPD, chronic obstructive pulmonary disease; n/a, not applicable; PAD, peripheral artery disease.

variables were defined by the presence of a claim with eligible diagnosis or procedure codes or prescription fills. The absence of such claims was interpreted as the absence of the condition or treatment. Those missing region (<0.1%) or race/ethnicity (5%) were classified as other and retained in analyses.

Overall, 17% presented with chronic obstructive pulmonary disease, almost half of the cohort had diabetes mellitus, obesity was present in 13%, and 15% had a history of coronary artery disease. A complete overview of characteristics is presented in Table 1. Those with a positive screen were older, were female, had a somewhat lower BMI, were more likely to smoke, and were more likely to have a history of hypertension and coronary artery disease.

A total of *n*=3,228 died in the first year and were excluded from the cohort (1.5% mortality rate in those with PAD-positive screen vs 0.9% mortality among those who screened negative). In the 1-year landmark analysis for all-cause mortality, those who screened positive had a mortality rate that was higher than that of those who screened negative (1.51% vs 0.89%, $p<0.001$; adjusted HR=1.21, $p=0.0011$). Similarly, MACE risk at 1 year was higher among those with a positive screen (5.54% vs 3.60%; adjusted HR=1.22; $p<0.0001$) and similarly in the second year after PAD screening (8.45% vs

Table 2. Crude Event Rates Presented as Numbers (%) at 1 Year for All-Cause Mortality, 1-Year and 2-Year MACEs, and MALEs for the Total Sample and by PAD-Positive Versus Negative Screen Status

Characteristics		Total	PAD screen positive *n*=53,343 (27.7%)	PAD screen negative *n*=139,157 (72.3%)	*p*-value
1-year mortality[a]					
Number of enrollees	*n*	2,047	808	1,239	
	%	1.06	1.51	0.89	<0.001
MACE					
1-year follow-up period	*n*	7,972	2,956	5,016	
	%	4.14	5.54	3.60	<0.001
2-year follow-up period	*n*	12,280	4,510	7,770	
	%	6.38	8.45	5.58	<0.001
MALE					
1-year follow-up period	*n*	182	125	57	
	%	0.09	0.23	0.04	<0.001
2-year follow-up period	*n*	337	233	104	
	%	0.18	0.44	0.07	<0.001

[a]Landmark analysis after 1-year post-PAD screening survival.
MACE, major cardiovascular event; MALE, major adverse limb event; PAD, peripheral artery disease.

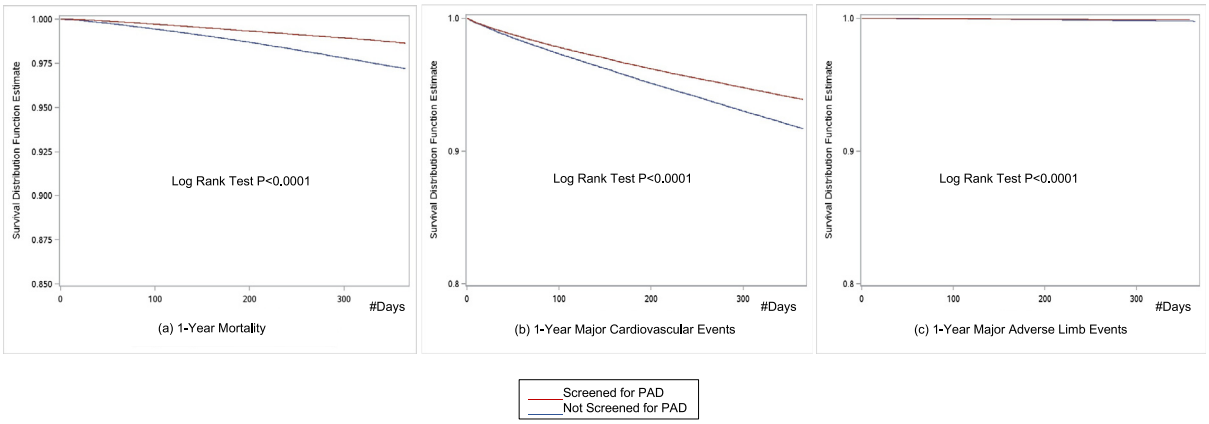
5.58%, $p<0.001$; adjusted HR=1.20, $p<0.0001$). The rate of MALE events was also higher in those screened positive than in those screened negative (0.23% vs 0.04%; adjusted HR=3.15; $p<0.0001$) and further increased after 2 years of follow-up (0.44% vs 0.07%; adjusted HR=3.37; $p<0.0001$). Among the PAD-screened cohort, 27.7% had a positive PAD screen (Tables 2 and 3 and Figure 1). Appendix Table 3 (available online) provides the overview of MACE and MALE event rates by PAD severity, showing an increased event rate by increasing PAD severity ($p<0.001$). The sensitivity analyses examining the association between a PAD-positive and negative screen and PAD outcomes (MACE, MALE, and mortality), excluding those with plethysmography index values ≤0.30, were essentially replicated, with risk estimates remaining relatively similar (Appendix Table 4, available online).

In the year before versus after PAD screening, the use of cardiovascular medications remained relatively stable for both the positively and negatively screened groups (difference-in-difference betas for a count of cardiovascular medications: 0.009 [95% CI=0.003, 0.015,

Table 3. Hazard Ratios and 95% CIs Associated With PAD-Positive Versus Negative Screen Status and All-Cause Mortality, MACEs, and MALEs

	Year 1			Year 2		
	Hazard ratio (95% Wald CIs)			Hazard ratio (95% Wald CIs)		
Endpoints	Unadjusted	Adjusted	*p*-value	Unadjusted	Adjusted	*p*-value
MACE[a,b]	1.55 (1.48, 1.63)	1.22 (1.15, 1.30)	<0.0001	1.53 (1.48, 1.59)	1.20 (1.14, 1.26)	<0.0001
MALE[a,c]	5.73 (4.19, 7.83)	3.15 (2.10, 4.73)	<0.0001	5.87 (4.65, 7.40)	3.37 (2.50, 4.53)	<0.0001
All-cause mortality[c,d,e]				1.69 (1.54, 1.84)	1.21 (1.08, 1.36)	0.0011

[a]All the 3 outcomes were conditional on 12-month post-index survival because of the continuous enrollment requirement.
[b]MACE does not include death. Models were adjusted for age, sex, race, region, number of previous house call visits, BMI, smoking, other tobacco use, chronic heart failure, uncomplicated hypertension, complicated hypertension, uncomplicated diabetes, complicated diabetes, hypertension, renal disease, HIV, substance use disorder, psychosis, depression, atrial fibrillation, dyslipidemia, stroke, coronary artery disease, hypoglycemic agents use, anticoagulant use, antiplatelet use, statin use, PCSK9 use, aspirin use, nicotine dependence mediations, and bilateral PAD.
[c]Models were adjusted for age, sex, race, region, number of previous house call visits, BMI, smoking, other tobacco use, chronic heart failure, uncomplicated hypertension, complicated hypertension, uncomplicated diabetes, complicated diabetes, hypertension, renal disease, substance use disorder, psychosis, depression, atrial fibrillation, dyslipidemia, stroke, coronary artery disease, hypoglycemic agents use, anticoagulant use, antiplatelet use, statin use, aspirin use, nicotine dependence mediations, and bilateral PAD.
[d]Models were adjusted for age, sex, race, number of previous house call visits, BMI, smoking, other tobacco use, chronic heart failure, uncomplicated hypertension, complicated hypertension, uncomplicated diabetes, complicated diabetes, hypertension, renal disease, human immunodeficiency virus, lymphomas, metastatic cancer, solid tumor, substance use disorder, psychosis, depression, atrial fibrillation, dyslipidemia, stroke, CAD, hypoglycemic agents use, anticoagulant use, antiplatelet use, statin use, PCSK9 use, aspirin use, nicotine dependence mediations, and bilateral PAD.
[e]Landmark analysis after 1-year post-PAD screening survival.
CAD, coronary artery disease; MACE, major cardiovascular event; MALE, major adverse limb



N at risk	Follow-up day_1	Day_200	Day_400	Day_600	Day_730*
PAD Negative	139,157	135,996	127,523	70,623	30,688
PAD Positive	53,343	51,431	47,493	27,776	10,485

N at risk	Follow-up day_1	Day_200	Day_400	Day_600	Day_730*
PAD Negative	139,157	139,123	132,573	74,576	32,590
PAD Positive	53,343	53,275	50,337	30,023	11,348

Figure 1. Kaplan–Meier curves of (A) 1-year major adverse cardiovascular events and (B) 1-year major adverse limb events by PAD screen status.
PAD, peripheral artery disease.

p=0.0054] equivalent to 0.9% excess improvement in the number of drug classes used). In the year before and after the screening, about 1 in 5 patients with a positive PAD screen were on hypoglycemic agents, around 6%–8% were on anticoagulant therapy, 7%–8% were on antiplatelet therapy, very few people were on PCSK9 therapy, <1% were on smoking-cessation medications, and statins were prescribed in roughly half of the patients. As for MALE rates, those remained relatively low and rare events in the year before and after the PAD screening (all <0.2%) (Table 4).

DISCUSSION

In a national Medicare Advantage population aged ≥65 years, the feasibility of a national PAD screening effort was shown using in-home house call visits. Prevalence of PAD was substantial, with almost 1 in 3 screening positive for PAD. Through linked national claims data, those with previously undetected PAD who screened positive and survived their first year after the screening had a 20% increased mortality risk in the year after. Similarly, for MACE, they experienced a risk >20% for the 2 subsequent years after their screening. For MALE risk, despite being an overall rare event, those who screened positive had a greater than threefold risk of experiencing 1 in the 2 years after the screening event than those who screened negative. MALE risk was relatively similar before and after PAD screening. For those who screened positive, the rates of cardiovascular risk management medications remained the same in the year before versus the year after PAD screening. Overall, undertreatment of guideline-recommended therapies was noted, for example, statins were only prescribed in about half of the patients.

Evidence on the undetected burden of PAD in the community is rather scarce or becoming quickly outdated. Our study adds to the field because it is the largest study to date reporting on a national PAD screening effort and with documentation of the subsequent burden associated with this undetected risk.[27] Population-level screening for PAD is not widely available[18,28–31] and is logistically challenging to obtain. However, population health approaches to chronic disease risk have become more appealing to identify the highest-risk groups in the community and to be able to tailor resources to individuals in need. Therefore, combining claims data with real-world screening programs such as ours becomes critical to documenting chronic disease burden and can help to prioritize future healthcare resource allocation and spending.

Our study documented that one third of individuals previously unknown to have PAD screened positive in this national screening effort using plethysmography methodology. Recent estimates state that symptomatic PAD is present in 12.4% of individuals aged ≥65 years, leaving many with asymptomatic disease potentially undetected because up to half of the patients with PAD are thought to have asymptomatic disease.[8] Although the argument can be made that these individuals may not have experienced severe clinical disease that warranted PAD-related admissions, the screening efforts

Table 4. Medications and MALEs 1 Year Before and After PAD Screening

Medication/event	Total N=192,500	PAD-Positive Screen *n*=53,343 (27.7%)	PAD Screen Negative *n*=139,157 (72.3%)	*p*-value	Standardized difference
Medications, *n* (%)					
Hypoglycemic agents, *n* (%)					
1-year before PAD screening	45,318 (23.5)	13,062 (24.5)	32,256 (23.2)	<0.001	0.03
1-year after PAD screening	46,380 (24.1)	13,248 (24.8)	33,132 (23.8)	<0.001	0.02
Anticoagulant therapy, *n* (%)					
1-year before PAD screening	10,871 (5.7)	3,332 (6.3)	7,539 (5.4)	<0.001	0.04
1-year after PAD screening	13,760 (7.2)	4,256 (8.0)	9,504 (6.8)	<0.001	0.04
Antiplatelet, *n* (%)					
1-year before PAD screening	9,850 (5.1)	3,521 (6.6)	6,329 (4.6)	<0.001	0.09
1-year after PAD screening	11,024 (5.7)	4,147 (7.8)	6,877 (4.9)	<0.001	0.12
PCSK9, *n* (%)					
1-year before PAD screening	154 (0.1)	55 (0.1)	99 (0.1)	0.026	0.01
1-year after PAD screening	251 (0.1)	84 (0.2)	167 (0.1)	0.041	0.01
Smoking-cessation medications, *n* (%)					
1-year before PAD screening	1,158 (0.6)	369 (0.7)	789 (0.6)	0.002	0.02
1-year after PAD screening	1,215 (0.6)	410 (0.8)	805 (0.6)	<0.001	0.02
Statin therapy, *n* (%)					
1-year before PAD screening	102,239 (53.1)	28,900 (54.2)	73,339 (52.7)	<0.001	0.03
1-year after PAD screening	106,118 (55.1)	30,174 (56.6)	75,944 (54.6)	<0.001	0.04
Medication count, mean (SD)					
1-year before PAD screening	0.87 (0.8)	0.91 (0.9)	0.86 (0.3)	<0.001	0.07
1-year after PAD screening	0.92 (0.9)	0.96 (0.9)	0.90 (0.8)	<0.001	0.08
Difference-in-differences					Beta (log of count)
				0.0054	0.009 (0.003−0.015)
					1.009 (1.003−1.016)
MALE, *n* (%)					
1-year before PAD screening	Masked[a]	Masked[a]	Masked[a]	0.371	0.00
1-year after PAD screening	182 (0.1)	125 (0.2)	57 (0.1)	<0.001	0.05
					Beta (log of count)
Difference-in-differences				–	Model did not converge owing to a multitude of zero cells in the 1 year before PAD screening

[a]Cell counts <11 were masked according to OLDW data policy.
MALE, major adverse limb event; OLDW, OptumLabs Data Warehouse; PAD, peripheral artery disease; PCSK9, proprotein convertase subtilisin/Kexin type 9.

were able to successfully risk stratify these individuals in terms of their future prognostic risk, including death, MACE, and MALE.

For both mortality and MACE risk, individuals who screened positive suffered a >20% risk of mortality and a similar risk of MACE in the 1−2 years after their screening. For MALE risk, the study documented a threefold increased risk among participants who screened positive compared with their counterparts who had a negative screening result. The study also indicated a dose–response relationship between the severity of PAD as detected by the plethysmography screening and subsequent risk of mortality, MACE, and MALE. As a next step, performing cost–benefit studies to see how events potentially could be prevented through further implementation of PAD-screening efforts in the community would help to inform healthcare policy.

It is thought that because of the generalized nature of PAD and overlap with other major cardiovascular diseases, patients would already have been recommended lifestyle modifications and medications to lower their cardiovascular risk.[28] Our data do not support this because those who screened positive for PAD were undertreated for their cardiovascular risk management medications, leaving opportunities open for further intensification of cardiovascular risk management. As far as potential excess

lower extremity peripheral diagnostics and procedures are concerned, there was no evidence of increasing rates in the year after screening compared with the rates in the year before the screening. Collectively, those findings show a need for targeted prevention strategies directed to those who further stand to benefit from them.

Preventive strategies should entail pathways that offer linkage to care to ensure access to guideline-recommended therapy and support to make lifestyle modifications,[10] especially among individuals who previously did not have another diagnosis of cardiovascular disease. Importantly, the PAD-screening intervention was combined with an educational pamphlet offered to beneficiaries who screened positive, and both the beneficiary and primary care physician were notified of the results. The effect of educational interventions and the impacts of screening on improving health behaviors have been described before and could potentially be the levers for change.[32,33] However, future studies will need to examine how these mechanisms may have impacted patients' behavior and what the most effective formats of preventive programs after PAD screening would be.

Limitations

Our study has several limitations. First, although the plethysmography screening test has promising accuracy, sensitivity, and specificity metrics[33] and established prognostic validity in a previously published regional effort,[20] the technology will benefit from ongoing validation. Sensitivity analyses detected a dose–response relationship between the plethysmography index disease severity categorizations and all the endpoints, underscoring the prognostic validity of these assessments in our nationwide study. Next, the study findings are only generalizable to individuals aged ≥65 years and to a population who received HouseCalls visits. Another limitation is that the study could not verify the cause of death and assess what proportion of deaths were attributed to cardiovascular causes. Finally, follow-up information on the use of aspirin was not available because this information was not captured through the claims data, thereby potentially underdocumenting the risk management strategies in this population.

CONCLUSIONS

This study provides evidence for the feasibility of a nationwide PAD-screening program among individuals aged ≥65 years to assess previously undetected PAD burden, which allowed for further risk stratification in terms of their future all-cause mortality, MACE, and MALE risk. Despite uncovering this PAD burden at the population level, targeted programs are needed to ensure that the surplus risk can be mitigated. Future studies will further need to explore the cost–benefit ratio of population-based screening programs against a growing interest in population health approaches to manage growing chronic disease risks and growing healthcare costs.

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CREDIT AUTHOR STATEMENT

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SUPPLEMENTARY MATERIALS

Supplementary material associated with this article can be found in the online version at doi:10.1016/j.focus.2022.100016.

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