Health Care Resources and Costs for Treating Peripheral Artery Disease in a Managed Care Population: Results From Analysis of Administrative Claims Data

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ABSTRACT

OBJECTIVE: Peripheral arterial disease (PAD) is associated with high rates of morbidity and mortality and serves as an important marker for advanced systemic atherosclerosis accompanied by symptomatic or asymptomatic ischemia of the coronary, cerebral, and visceral vasculature. There are little published data on the use of health care resources and costs attributable to PAD. The objectives of this study were to evaluate, from a societal perspective, PAD-related health care resource utilization and to determine the total annualized costs and cost components for patients with PAD, with particular attention to the key outcomes of myocardial infarction (MI), transient ischemic attacks (TIA), stroke, and amputations.

METHODS: This study examined medical, hospital and outpatient, and pharmacy claims from a large managed care database with dates of service from January 1, 1999, through August 31, 2003. Patients with PAD were identified from claims using *International Classification of Diseases, Ninth Revision, Clinical Modification* (ICD-9-CM) diagnosis codes (primary or secondary codes), ICD-9-CM procedure codes, current procedural terminology (CPT) codes, or by a pharmacy claim for cilostazol or pentoxifylline. The index date for each patient was the first occurrence of either a medical claim for PAD or a pharmacy claim for 1 of the 2 drugs. Patients were required to be a minimum of 18 years old with continuous plan eligibility. The prevalence of PAD in adults in a managed care setting was also determined, as were annual rates for the key outcomes of MI, TIA, stroke, and amputations. Health care resource utilization and costs were calculated for PAD patients after the index date for a period of at least 12 months per patient for medications, outpatient/physician office visits, laboratory/diagnostic procedures, emergency department visits, and hospitalization. Cost was defined as the allowed charge on each administrative claim, including the amount paid by the insurer plus the amount paid by the health plan members (copay, deductible, and coinsurance).

RESULTS: Prior to application of exclusion criteria for patients aged 18 years or older and the minimum period of continuous eligibility, the overall prevalence of PAD was 1.18% of the total managed care organization population's 6.67 million members. The PAD study cohort consisted of 30,561 patients with a mean age of 70.7 years at index. The most common comorbidities identified in the preindex period for these PAD patients included hypertension (67% of patients); metabolic disorders/hypercholesterolemia (57%); heart disease including cardiomyopathy, dysrhythmias, and heart failure (55%); and ischemic heart disease (47%). Over a mean postindex period of 25.2 months (median 23.4 months), the total mean annualized PAD-related cost was \$5,955 per patient per year (PPPY). Hospitalizations accounted for the largest component cost category, averaging \$4,442 PPPY or 75% of the total annualized PAD-related cost per PAD patient. PAD-related noncoronary procedures averaged \$729 PPPY (12.2% of total annual PAD-related costs), and PAD-related medications (including antihypertensives and lipid-lowering therapy) totaled \$610 (10.2% of total annual costs), including \$313 PPPY for antihypertensives and \$207 for lipid-lowering therapy. For the subgroup of 24,075 newly identified PAD patients, 8,479 (35.2%) were hospitalized during an average 25.2 months of follow-up, with the mean time to first hospitalization of 8.9 months.

CONCLUSIONS: Approximately 75% of the total PAD-related patient cost in an average of 25 months of follow-up is contributed by hospital costs, and 35% of patients newly diagnosed with PAD experienced a hospitalization in a mean of 8.9 months after the index diagnosis. Based upon mean annual health and member costs of only \$313 PPPY for antihypertensives and \$207 for lipid-lowering therapy, drug therapy in PAD patients may be underutilized.

KEYWORDS: Peripheral arterial disease, Peripheral artery disease, Atherosclerosis, Managed care, Prevalence, Resource utilization, Costs

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The systemic atherosclerosis triad of peripheral arterial disease (PAD), coronary artery disease (CAD), and cerebrovascular disease (CVD) together account for approximately half of the rates of morbidity and mortality in the adult population aged 50 years and older.¹ Through the convergence of these diseases, PAD patients suffer significantly higher morbidity and mortality than comparable unaffected patients, with estimates of a 2- to 6-fold increase in the relative risk of cardiovascular events.^{2,4} PAD serves as an important marker for advanced systemic atherosclerosis, yet despite its prevalence and association with high rates of morbidity and mortality, PAD still remains underdiagnosed and undertreated.^{3,6}

PAD may be defined as obstructive and vasospastic conditions of the arterial vessels outside of the heart and thoracic aorta. There are an estimated 8 to 12 million people in the United States who have PAD, with prevalence estimates as high as 30% in patients older than 70 years or in patients older than 50 years with a history of diabetes, smoking, or both.^{6,7} The symptoms of PAD, ranging from muscle cramping or numbness to intermittent claudication to critical limb ischemia, are exacerbated by activities that increase the oxygen demand, usually resolving with rest. The prevalence of asymptomatic disease is substantial, with estimates of the ratio of asymptomatic to symptomatic disease at about 3 to 1.^{8,9} Risk factor and comorbidity profiles have been found to be similar between symptomatic and asymptomatic PAD patients.⁹

Management of patients with PAD appears to be moving in the direction of more aggressive lifestyle modifications and medical therapy, to provide earlier identification and treatment similar to CAD with the clear goal of decreasing cardiovascular risk.⁵ It has been noted that "best medical treatment" of PAD has

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lagged behind that of CAD due to (1) a less robust body of evidence on effective treatments, (2) lack of awareness of the increased cardiovascular risk, and (3) lack of cost justification for medical management.¹⁰

Medical management currently involves smoking-cessation interventions, lipid-lowering therapies, blood pressure control, antiplatelet therapy, and promoting regular exercise as well as appropriate diabetes/blood sugar control and/or weight loss. While recent surveys have uncovered the need to increase physician knowledge and change attitudes about medical management of PAD,¹¹ there is growing support that medical management for the PAD patient can dramatically reduce the cardiovascular risk as well as improve the patient's functional status.^{7,12}

Economic evaluations of preventative therapies for CAD are relevant for patients with vascular disease since CAD and peripheral arterial occlusive disease commonly occur together and share risk factors, pathophysiology, and response to preventative therapy. Cost-effectiveness analysis has shown that modification of vascular risk factors like tobacco use, hypertension, and hypercholesterolemia improve clinical outcomes at cost-effectiveness ratios usually less than \$20,000 per year of life saved, making medical management for reduction of cardiovascular risk factors generally cost effective.¹³ To our knowledge, this paper is the first to provide a view of the health care resources and costs attributable to PAD from a societal perspective using managed care resource utilization and costs. The results from the present study provide a basis for future comparisons of cost-effective disease management interventions.

The objectives of this study were to determine from a societal perspective the health care resource utilization and total annualized costs and cost components for patients with PAD, using managed care organization (MCO) costs and patient cost-share amounts. Health care resources included medications, outpatient/physician office visits, laboratory/diagnostic procedures, emergency department visits, and hospitalization. The prevalence of PAD in adults in a managed care setting was also determined, as were annual rates for the key outcomes of myocardial infarction (MI), transient ischemic attack (TIA), stroke, and amputations.

Methods

Data were collected from 2 health plans in the southeast and western United States. Both health plans were able to provide medical claims, pharmacy claims, and eligibility information for members during the entire study period, from January 1, 1999, through August 31, 2003. These plans contained 6.67 million MCO members for which complete data existed, including medical, hospital, pharmacy, and eligibility data.

Patients were identified with PAD by the following criteria: (1) an *International Classification of Diseases, Ninth Revision, Clinical Modification* (ICD-9-CM) diagnosis code of 440.xx (any ICD-9 code beginning with 440, atherosclerosis) or 443.9

(peripheral vascular disease, not otherwise specified) on a medical claim (medical claims include all inpatient hospital, outpatient hospital, medical visit, and emergency room); (2) an ICD-9-CM procedure code of 38.08 (incision of vessel, embolectomy or thrombectomy, lower-limb arteries), 38.13 (endarterectomy, upper-limb vessels), 38.18 (endarterectomy, lower-limb arteries), 39.25 (aorta-iliac-femoral bypass), 39.26 (other intra-abdominal vascular shunt or bypass), 39.29 (other peripheral vascular shunt or bypass), 39.50 (angioplasty or atherectomy of other noncoronary vessel, incl. percutaneous transluminal angioplasty of noncoronary vessel), or 39.90 (insertion of non-drug-eluting peripheral vessel stent) on a medical claim; (3) a PAD-related surgical procedure (noncoronary thrombectomy, embolectomy, angioplasty, atherectomy, bypass graft, or stenting) on a medical claim; or (4) a pharmacy claim for cilostazol (Pletal¹⁴) or pentoxifylline (Trental¹⁵). (Cilostazol was approved by the U.S. Food and Drug Administration [FDA] on January 15, 1999, for the indication of reduction of symptoms of intermittent claudication as indicated by an increased walking distance,¹⁴ and pentoxifylline was approved by the FDA on August 30, 1984, for intermittent claudication on the basis of chronic occlusive arterial disease of the limbs.¹⁷) Pharmacy claims for other drugs used in PAD (aspirin, clopidogrel, dipyridamole, etc.) were not used to identify PAD patients due to their use in other disease states.

Patients with PAD were identified from medical, hospital, and pharmacy claims with dates of service from January 1, 2000, through August 31, 2002. The date of the first medical, hospital, or pharmacy claim using the criteria for PAD, listed above, was identified as that patient's index date. Study patients were required to have continuous enrollment for at least 12 months prior to their index date and at least 12 months after their index date to permit comparison for equally continuous periods. They were not required to be newly diagnosed with PAD.

Resource utilization was determined for all patients who qualified for the study cohort by evaluating medical, hospital, and pharmacy claims for all study patients postindex through the earlier of the end of the patient's insurance eligibility (minimum of 12 months postindex date required), or August 31, 2003. Medical and hospital claims were identified from both primary and secondary diagnoses and by the PAD-related procedure codes on the claims. Patients were deemed to be newly identified with PAD if they had no PAD-qualifying drugs or claims, as described above, prior to the index date back to the time of their enrollment (minimum 12 months prior to index).

Comorbidities were identified using the ICD-9-CM codes, at the 3-digit level (e.g., 401.xx-405.xx for hypertensive disease), found in medical claims. In addition to ICD-9-CM codes, pharmacy claims for antidiabetic medication were also used to identify patients with diabetes mellitus. Patients could have had

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more than one comorbidity.

Hospitalizations were identified from the 3-digit ICD-9-CM codes (e.g., 410.xx for acute MI) found in medical claims for the hospitalization, including both primary and secondary diagnoses. Patients were included in more than one hospitalization category if the diagnoses on the hospitalization claim qualified them for more than one category; (e.g., 250.xx for diabetes and 401.xx-405.xx for hypertension).

Costs were derived from claims for office/outpatient visits, outpatient prescriptions, laboratory/diagnostic tests, medical procedures, emergency facility visits, and hospitalizations. Cost was defined as the allowed charge for hospital, medical, and pharmacy claims, comprising the amount paid by the insurance plan plus the patient's copay, deductible, and coinsurance amounts.

Statistical analyses were performed using SAS version 8.02 (SAS Institute Inc., Cary, NC). Means, standard errors, and medians were reported for interval and ratio scaled data. Frequencies and percentages were reported for nominal (categorical) and ordinal scaled variables. For all analyses, an a priori 2-tailed level of significance (alpha value) was set at the 0.05 level.

Since this observational study used de-identified data from retrospective claims without using protected health information, it did not involve patient intervention, and, therefore, Institutional Review Board approval was not necessary.

Results

A total of 30,561 patients met all inclusion criteria for PAD (Table 1). These patients were observed after their index date for an average of 25.2 months (SD $\pm$ 9.3 months, median 23.4 months). The majority of the study cohort of 24,075 patients (79%) was considered newly identified PAD, not having a PAD-distinguishing diagnosis, procedure, or PAD-related medication at any time prior to their index date (minimum 12 months, from the date of enrollment in one of the health plans).

The demographics of this PAD study cohort are shown in Table 2. The mean age at index was 70.7 years (SD $\pm$ 14.3 years, median 73 years), with 78% of the PAD patients older than 60 years and 59% of patients older than 70 years. While 54% of PAD patients were female, there was a greater number of female health plan members overall and, thus, the prevalence for females was lower than for males.

Table 3 presents the prevalence of PAD in the managed care population of 6.67 million members. Overall PAD prevalence was 10.8 patients per 1,000 health plan members. The prevalence was higher among males than among females (11.3 per 1,000 male PAD patients compared with 10.4 per 1,000 female PAD patients). Prevalence increased 6-fold with age group (13.9 per 1,000 patients aged 50 to 59 years increased to 92.7 per 1,000 patients aged 70 years and older).

The 10 most common comorbidities (Table 4) found in the

TABLE 1 Patient Selection Criteria

Inclusion Criteria	No. of Patients Excluded (%)	No. of Patients Retained (%)
Patients with only PAD-related diagnosis or procedure*	—	69,046 (87.3)
Patients with only pharmacy claim(s) for cilostazol or pentoxifylline	—	9,681 (12.2)
Patients with PAD-related diagnosis or procedure and pharmacy claim(s) for cilostazol or pentoxifylline	—	331 (0.4)
Total PAD patients identified		79,058 (100.0)
Patients aged 18 years and older	6,804 (8.6)	72,254† (91.4)
Patients with continuous enrollment for 12 months before and 12 months after index date	41,693 (52.7)	30,561 (38.7)
Patients without a PAD-related diagnosis or pharmacy claim for cilostazol or pentoxifylline in the preindex period (i.e., patients without prior PAD)	6,486 (8.2)	24,075 (30.5)

* Medical claims include inpatient hospital and outpatient hospital and medical visits. Patients were identified with PAD by the following criteria: (1) an ICD-9-CM diagnosis code of 440.xx (atherosclerosis) or 443.9 (peripheral vascular disease, unspecified) on a medical claim; (2) an ICD-9-CM procedure code of 38.08 (incision of vessel, embolectomy or thrombectomy, lower-limb arteries), 38.13 (endarterectomy, upper-limb vessels), 38.18 (endarterectomy, lower-limb arteries), 39.25 (aorta-iliac-femoral bypass), 39.26 (other intra-abdominal vascular shunt or bypass), 39.29 (other peripheral vascular shunt or bypass), 39.50 (angioplasty or atherectomy of other noncoronary vessel incl. percutaneous transluminal angioplasty of noncoronary vessel), or 39.90 (Insertion of non-drug-eluting peripheral vessel stent) on a medical claim; or (3) CPT codes for a PAD-related surgical procedure (noncoronary thrombectomy, embolectomy, angioplasty, atherectomy, bypass graft, or stenting) on a medical claim. (The 30 different CPT codes are available from the authors upon request.)

† 1.08% of the 6,665,787 enrollees in the available data as of August 31, 2002.

CPT=current procedural terminology; ICD-9-CM=International Classification of Diseases, Ninth Revision, Clinical Modification; PAD=peripheral arterial disease.

TABLE 2 Demographics of the PAD Patient Study Cohort

Population	All PAD Patients N = 30,561	Newly Identified* PAD Patients N = 24,075 (78.8% of all PAD)
Patient age (years)		
Mean $\pm$ SD	70.7 $\pm$ 14.3	69.5 $\pm$ 14.6
Median	73	72
<40	826 (2.7%)	784 (3.3%)
40-49	1,927 (6.3 %)	1,754 (7.3%)
50-59	3,927 (12.9%)	3,417 (14.2%)
60-69	5,996 (19.6%)	4,858 (20.2%)
70+	17,885 (58.5%)	13,262 (55.1%)
Patient gender		
Male	13,978 (45.7%)	11,073 (46.0%)
Female	16,583 (54.3%)	13,002 (54.0%)

* PAD patients were designated as "Newly Identified" if they did not have a PAD-related diagnosis, procedure, or medication of interest from the time of their enrollment (12 months minimum) until their index date.

PAD=peripheral arterial disease.

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TABLE 3 Prevalence of PAD in Patients Aged 18 Years or Older per 1,000 Members in a Managed Care Population (N = 6,665,787)

Population	PAD Patient Count	PAD Prevalence*
Male	36,068	11.325
Female	36,186	10.395
Age (years)		
18-40	3,401	0.100
40-49	6,605	0.442
50-59	11,511	13.925
60-69	17,756	37.531
70+	32,981	92.718
Total	72,254	10.840

* The PAD prevalence rate is based on the number of patients per 1,000 members within the indicated population category. For example, there were 3,184,813 males, of which 36,068 qualified as PAD patients, to yield a prevalence rate of 11.325 PAD patients per 1,000 members.

PAD=peripheral arterial disease.

TABLE 4 Common Comorbid Conditions in PAD Patients in the 12-Month Period Prior to Index Date (N = 30,561)

Comorbidity	ICD-9-CM Code	No. of Patients (%)
Symptoms, signs, and ill-defined conditions	780-789	26,189 (85.7)
Hypertensive disease	401-405	20,560 (67.3)
Metabolic/immunity disorders	270-279	17,497 (57.3)
Other heart disease	420-429	16,769 (54.9)
Rheumatism (excluding the back)	725-729	15,709 (51.4)
Ischemic heart disease	410-414	14,359 (47.0)
Arthropathies and related disorders	710-719	15,759 (51.6)
Disorders of the eye and adnexa	360-379	15,875 (51.9)
Diseases of skin and subcutaneous tissue	700-709	4,695 (48.1)
Diabetes mellitus*	250.xx	8,605 (28.1)

* Diabetes mellitus identified by claims with ICD-9=250.xx or antidiabetic drug therapy.

ICD-9-CM=International Classification of Diseases, Ninth Revision; Clinical Modification; PAD=peripheral arterial disease.

30,561 PAD patients prior to the patients' index date included hypertension (67% of patients); metabolic/immunity disorders and hypercholesterolemia (57%); heart disease/cardiomyopathy, dysrhythmias, and heart failure (55%); and ischemic heart disease (47%). Rheumatism and arthropathies were also prevalent in at least half of the patients, and diabetes mellitus was documented in 28.1% of the study patients.

All-cause hospitalization was examined for newly identified PAD patients after the patient's index date to determine the frequency of hospitalization events and the length of time to a first event for key outcomes. Overall, 35% of these PAD patients were hospitalized during their observation period, with a mean time to the first hospitalization at approximately 9 months postindex (Tables 5 and 6). The 8,479 hospitalized PAD

patients incurred 14,642 hospitalizations over the average 25-month observation period to yield an annualized rate of 321.7 hospitalizations per 1,000 PAD patients.

Hospitalizations were analyzed for the key events of MI, stroke, TIAs, and amputations. Stroke was the most common diagnosis (on hospital claims, in any diagnosis field), occurring for 8.0% of the newly identified PAD patients during their observation period, nearly double that of MI, which occurred in 4.1% of the newly identified PAD patients. The percentage of PAD patients hospitalized for limb amputation was the lowest, at 1.1%. Among those PAD patients who were hospitalized, again the most common reason was for stroke, occurring in 22.7% of those hospitalized, nearly double that of MI, which occurred in 11.5% of the hospitalized PAD patients.

As displayed in Figure 1, measuring the key PAD-related outcomes of stroke, MI, TIA, and amputation over time, stroke was the most commonly occurring event over time and amputation was the least common. Mean time to the first hospitalization for these events was lowest for amputation (8 months), followed by stroke (10 months), and TIA and MI (11 months).

The most common hospitalization diagnoses for PAD patients involved respiratory/chest symptoms (dyspnea, stridor, chest pain, abnormal chest sounds, or sputum), seen in 46.5% of hospitalized patients. Cardiovascular diseases were the next most common hospitalization diagnoses, led by essential hypertension in 34.6% of hospitalized patients and ischemic heart disease in 30.0% of hospitalized patients. Since the average patient's observation period was approximately 25 months, event rates were annualized giving the following annual hospitalization event rates per 1,000 PAD patients: all cause—322 events, respiratory/chest symptoms—123 events, essential hypertension—82 events, ischemic heart disease—76 events, and stroke—52 events. The average time to first hospitalization was shortest for atherosclerosis-associated events (4.5 months), followed by ischemic heart disease (10 months), essential hypertension (10.6 months), and respiratory/chest symptoms (11 months).

The total average annualized cost of PAD-related patient care was \$5,955 per PAD patient per year (PPPY), which includes the amount paid by the insurer plus the patient's copayments, deductibles, and coinsurances. Of the individual components of care (Table 7), hospitalizations for the PAD-related outcomes of MI, stroke, TIA, and amputations were the highest single item, averaging \$4,442 PPPY or 75% of the total PAD-related cost of care for this managed care study cohort. Hospitalizations for the PAD-related outcomes of MI, stroke, TIA, and amputations represented 49% of the average all-cause hospitalization total of \$9,149. Costs for PAD-related procedures were confined to non-coronary procedures (bypasses, angioplasty, atherectomy, embolectomy, and stents), which, in aggregate, averaged \$729 PPPY (12.2%). Of these procedures, arterial bypass had the highest average cost at \$240 PPPY (4.0%). The total of PAD-

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TABLE 5 Hospitalizations for Any Cause* in Newly Identified PAD Patients (N = 24,075)

Event	No. of Patients	% of All PAD Patients (N = 24,075)	% of Hospitalized PAD Patients (N = 8,479)	No. of Events	% of Events (N = 14,642)
All-cause hospitalizations†	8,479	35.2	100	14,642	100
MI	979	4.1	11.5	1,148	7.8
Stroke	1,927	8.0	22.7	2,307	15.8
TIA	625	2.6	7.4	686	4.7
Amputation	274	1.1	3.2	371	2.5
Other causes of hospitalizations (most common ICD-9-CM codes)					
Respiratory/chest symptoms	3,941	16.4	46.5	5,599	38.2
Essential hypertension	2,937	12.2	34.6	3,720	25.4
Other chronic IHD	2,542	10.6	30.0	3,525	24.1
Atherosclerosis	1,772	7.4	20.9	2,035	13.9
Cardiac dysrhythmias	2,300	9.6	27.1	3,099	21.2
General symptoms	2,334	9.7	27.5	2,930	20.0
Heart failure	1,924	8.0	22.7	2,945	20.1
Diabetes mellitus	1,557	6.5	18.4	2,456	16.8
Other diseases of lung‡	1,747	7.3	20.6	2,069	14.1
Abdomen/pelvis symptoms	1,674	7.0	19.7	2,051	14.0

* Hospitalizations occurred on or after the patient's index date. A given hospitalization may be included in more than one category, for each diagnosis category attributed to the event.

† All-cause hospitalizations in this row in the table = the number of unique hospitalization events for the study cohort, where each hospitalization is only counted once regardless of the number of diagnosis categories attributed to it.

‡ Other diseases of lung—includes pulmonary insufficiency, pulmonary collapse, emphysema, acute edema, and respiratory failure.

ICD-9-CM = International Classification of Diseases, Ninth Revision; Clinical Modification; IHD = ischemic heart disease; MI = myocardial infarction;

PAD = peripheral arterial disease; TIA = transient ischemic attack.

attributable emergency department visits, office visits, and laboratory/diagnostic testing resulted in an average of \$173 PPPY (2.9%) in aggregate.

PAD-related medications were divided into the following drug classes: antiplatelet agents (aspirin, cilostazol, clopidogrel, dipyridamole, pentoxifylline, and ticlopidine), antihypertensives (ACE inhibitors, angiotensin receptor blockers, beta-blockers, calcium channel blockers, diuretics, and other antihypertensives), and lipid-lowering therapy. The average annualized expense for these classes of medication totaled \$610, or 10.2% of the average annual PAD patient-related expenditures. Antihypertensives were used by 67% of the patients and comprised \$313 of the annualized medication costs. Lipid-lowering therapy was used by 38.8% of patients, at an annualized cost of \$207.

Antiplatelet medications were used in 26.9% of patients and comprised \$90 of the annualized medication costs (not including over-the-counter aspirin). Of the antiplatelet medications (Table 8), clopidogrel was the most commonly prescribed, used by 12.9% of patients and accounting for 41% of antiplatelet prescription volume. Pentoxifylline was used by 12.2% of patients and accounted for 40% of antiplatelet prescription volume. The other antiplatelet medications were used by 7% of the patients.

Note that these costs capture actual usage patterns rather than optimal or guideline patterns. Costs for the injectable antiplatelet drugs were usually incorporated into the hospital charges.

Discussion

The total average annualized PAD-related cost of care for patients in this managed care study cohort of \$5,955 reflects only the PAD-attributed drugs, procedures, diagnostics, and office visits and so may understate the overall total costs for these patients, which can be higher due to significant comorbidities. As expected, the costs for PAD-related hospitalizations were the highest single expense item, averaging 75% of the patient's total cost of PAD-related care. The hospital costs as a percentage of the total bill were much higher for PAD patients than the typical rate of 36% reported by the Health Care Financing Administration (now the Centers for Medicare and Medicaid Services),¹⁶ which may be indicative of the higher comorbidity and cardiovascular risk profile of the PAD patients but may also be due, in part, to the use of PAD-attributable costs.

It is noteworthy that approximately 1 of 3 PAD patients in the study cohort ended up in the hospital within 2 years of their index date. Further, the 8,479 hospitalized PAD patients incurred 14,642 hospitalizations, which is nearly 2 hospitaliza-

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TABLE 6 Mean Time to Event and Annual Event Rate of Hospitalization for Any Cause in Newly Identified PAD Patients (N=24,075)

Event	Mean Time to First Event (Months ± SD)	Annual Event Rate* per 1,000 PAD Patients
All-cause hospitalizations	8.9 ± 9.2	321.7
MI	11.5 ± 9.4	25.3
Stroke	10.0 ± 8.8	52.0
TIA	11.1 ± 10.0	15.2
Amputation	8.0 ± 9.9	8.8
Other causes of hospitalizations (most common ICD-9-CM codes)		
Respiratory/chest symptoms	11.2 ± 12.6	122.9
Essential hypertension	10.6 ± 10.8	82.1
Other chronic IHD	10.0 ± 10.1	76.1
Atherosclerosis	4.5 ± 8.4	46.7
Cardiac dysrhythmias	11.9 ± 9.6	67.4
General symptoms	12.5 ± 9.7	63.6
Heart failure	12.4 ± 8.8	64.7
Diabetes mellitus	9.5 ± 7.9	54.2
Other diseases of lung	12.2 ± 8.4	46.2
Abdomen/pelvis symptoms	11.7 ± 8.1	45.9

* Annual event rates are computed by summing all events over each patient's observation period (12 months minimum). The total number of events is divided by the total number of months in the patient's observation period and multiplied by 12.

ICD-9-CM=International Classification of Diseases, Ninth Revision Clinical Modification; IHD=ischemic heart disease; MI=myocardial infarction; PAD=peripheral arterial disease; TIA=transient ischemic attack.

FIGURE 1 Kaplan-Meier Survival Curve of Patients

Note: The figure shows the Kaplan-Meier survival curve of patients remaining over time who were not hospitalized for stroke (CVA), myocardial infarction (MI), transient ischemic attack (TIA) or amputation; incident cases only displayed, N=24,075. Data was censored at the length of each patient's postindex eligibility, with a maximum postindex period of 44 months (January 1, 2000, to August 31, 2003).

tions per patient, on average, throughout the mean 25-month observation period, with 49% of the hospitalization costs attributable to the outcomes of MI, stroke, TIA, or amputation. Thus, interventions resulting in reduced hospitalizations in this population can have significant PPPY cost impacts. Since PAD is an indicator of a disease process within the entire circulatory system, it is not surprising that leading reasons for hospitalization were respiratory-, cardiovascular-, or cerebrovascular-related.

The average time to first hospitalization was shortest for atherosclerotic events. However, that timing may be affected by those patients whose index event was a hospitalization with a PAD diagnosis. Limb amputation was uncommon (1.1%) in this cohort, resembling percentages seen in recent literature.⁸

PAD-related drug costs were 10.2% of the patient's total cost of PAD-related care, averaging \$610 per patient per year. The antihypertensive agents accounted for the largest chunk (51%) of the average annual prescription costs, followed by the antihyperlipidemics (34%). Antiplatelet agents accounted for \$90

(15%) of the annual drug costs. The prescription antiplatelet agents were being taken by 26.9% of the PAD patients, which appears to be low drug utilization in light of the current TransAtlantic Inter-Society Consensus Working Group treatment recommendations for PAD, which state that all patients with PAD (whether symptomatic or asymptomatic) should be considered for treatment with low-dose aspirin or other approved antiplatelet agents to reduce the risk of cardiovascular morbidity and mortality.⁸ Similarly, 39% of patients were receiving antihyperlipidemics, which assumes the remainder are able to meet their low-density lipoprotein cholesterol targets using diet alone. It seems reasonable to suggest that antiplatelet, antihyperlipidemic, and antihypertensive medications can provide the possibility of decreasing hospitalizations by optimizing the number of patients taking appropriate pharmacotherapy. Future research may be directed at exploring relationships between appropriate pharmacotherapy and the frequency of hospitalization.

While PAD-attributable office visits, emergency department charges, and laboratory/diagnostic costs appeared low, PAD contribution to nonhospital health care resources may be reflected in utilization attributed to related cardiovascular or cerebrovascular morbidity and not attributed to the diagnoses selected to identify PAD.

The demographics of this managed care PAD cohort appeared reflective of prior studies, with 78% of sufferers older than 60 years, a mean age of 70 years, and a slightly higher prevalence in men (1.13% versus 1.04% in women).^{8,17,18} Prevalence may be understated in this study because of the use of diagnoses originating from claims and surrogate markers compared with other studies that base their epidemiology on

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TABLE 7 Annualized Cost* per PAD Patient per Year, by Components (N=30,561)

Cost Component	Mean (\$)	SD (\$)
Total PAD-related pharmacy claims	610	786.10
Antiplatelet drugs† and pentoxifylline	90	253.30
Antihypertensives	313	473.40
Lipid-lowering therapy	207	373.83
Total PAD-related procedures	729	7,272.26
Arterial bypasses	240	3,507.74
Angioplasty	155	3,617.79
Embolectomy, atherectomy	186	3,754.05
Stents	148	3,568.88
All-cause hospitalizations‡	9,149	28,072.36
PAD-related hospitalizations (MI, stroke, TIA, or amputation)	4,442	29,592.15
Other hospitalizations	4,707	40,789.65
PAD-attributable emergency room§	36	448.95
PAD-attributable outpatient office visits§	65	363.35
PAD-attributable laboratory/diagnostic§	72	255.04
Total PAD-related health care costs‡	10,662	33,739

* Annualized cost includes the amount allowed by the insurance plan plus the patient's cost-share (copay, deductible and coinsurance amount) for the indicated PAD-related health care resource, summed over the observation period (minimum 12 months per patient), divided by the length of the observation period and then multiplied by 365 days. Costs and resource utilization were determined by evaluating claims with dates of services from the patient's index date (occurring between January 1, 2000, and August 31, 2002) through the earlier of the end of the patient's insurance eligibility (minimum of 12 months postindex date) or August 31, 2003.

† Antiplatelet drugs included aspirin, cilostazol, clopidogrel, dipyridamole, and ticlopidine.

‡ Only hospitalizations attributed to the key PAD-related events of MI, stroke, TIA, and amputation were included in the total PAD-related health care costs. All-cause hospitalizations are provided to the reader as a reference, to show the magnitude of hospitalization expenses in the PAD patient population. Attributing hospitalizations for MI, stroke, TIA, and amputation as PAD-related events was done for 2 reasons: (1) the diagnosis codes used for a hospitalization are generally not going to be attributed to a PAD-related code such as 440.0 (atherosclerosis) or 443.9 (peripheral vascular disease) and (2) broad sequelae result from peripheral artery disease.

§ PAD-attributable costs for emergency room, office visits, and laboratory utilization include those claims with an ICD-9-CM diagnosis or procedure code or CPT code for PAD.

ICD-9-CM=International Classification of Diseases, Ninth Revision, Clinical Modification; IHD=ischemic heart disease; MI=myocardial infarction; PAD=peripheral arterial disease; TIA=transient ischemic attack.

TABLE 8 Annualized Outpatient Drug Utilization for 30,561 PAD Patients

Medication Class	No. of Patients (% of Cohort)	No. of Rxs (% of class)*
Antiplatelets	8,212 (26.9)	35,028 (100.0)
Cilostazol	1,799 (5.9)	5,385 (15.4)
Clopidogrel	3,955 (12.9)	14,337 (40.9)
Dipyridamole	250 (0.8)	1,008 (2.9)
Ticlopidine	97 (0.3)	419 (1.2)
Pentoxifylline	3,736 (12.2)	13,879 (39.6)
Antihypertensives	20,497 (67.1)	272,464 (100.0)
ACE inhibitors	9,957 (32.6)	55,848 (20.5)
ARBs	4,555 (14.9)	23,689 (8.7)
Beta-blockers	9,581 (31.4)	54,100 (19.9)
CCBs	8,807 (28.8)	50,902 (18.7)
Diuretics	12,868 (42.1)	70,412 (25.8)
Other AHTNs	3,465 (11.3)	17,513 (6.4)
Antihyperlipidemics	11,867 (38.8)	69,267 (100.0)

* Pharmacy claim (Rx) counts were summed over each patient's entire observation period (minimum 12 months), divided by the length of the observation period and multiplied by 365 days. Resource utilization and costs were determined by evaluating claims with dates of services from the patient's index date (occurring between January 1, 2000, and August 31, 2002) through the earlier of the end of the patient's insurance eligibility (minimum of 12 months postindex date) or August 31, 2003.

ACE=angiotensin-converting enzyme; AHTN=antihypertensive; ARB=angiotensin receptor blocker; CCB=calcium channel blocker; PAD=peripheral arterial disease; Rx=prescription.

although typical of older patients, can result in impairing or discouraging physical activity and therefore may contribute to stasis-inspired worsening of cardiovascular symptoms.

Limitations

Foremost among the limitations of this study is the attribution of hospitalizations associated with primary or secondary diagnoses of MI, stroke, TIA, or amputation in the cost and event rate calculations for PAD. This method may have resulted in over-estimation of the costs and resource utilization attributed to PAD. However, this method was necessary for 2 reasons: (1) the principal diagnosis code (i.e., the reason for the hospitalization) is generally not going to be attributed to a PAD-related code such as 440.0 (atherosclerosis) or 443.9 (peripheral vascular disease), and (2) broad sequelae result from PAD. For example, thrombotic heart disease may very well result from peripheral obstructive lesions. Thus we chose to investigate the magnitude of mean all-cause hospital utilization in patients with PAD, with a focus on the key events of MI, stroke, TIA, and amputation. For similar reasons, we did not distinguish primary hospital diagnoses from secondary diagnoses.

confirmed diagnoses.⁹

The comorbidity profile of these patients, similar to data from other studies,^{6,12,19,20} indicates a high percentage of patients with cardiovascular and other comorbidities, particularly for hypertension and heart disease. The clinical picture represented by the [coding of] comorbid conditions is one of diffuse disease processes throughout the circulatory system. The high comorbidity with diseases like rheumatism and arthropathies,

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Second, PAD patients could have been included in this study on the basis of a single medical or hospital claim with a PAD primary or secondary diagnosis or a single pharmacy claim for either pentoxifylline or cilostazol. A more rigorous method to identify PAD patients would have required at least 2 medical claims with relevant diagnosis or procedure codes or at least 1 relevant medical claim and 1 relevant pharmacy claim (for pentoxifylline or cilostazol). On the other hand, prevalence rates may be understated since physicians do not consistently code claims specifically for PAD.

Despite the limitations of claims data to estimate resource utilization and costs related to PAD, our results compare favorably with the findings reported by Migliaccio-Walle et al. in their analysis of 16,440 Canadian patients with PAD compared with 15,590 reference patients with a diagnosis of MI.²¹ The average annualized postdiagnosis cost in the 5-year follow-up period was \$CN8,394 in 2002 currency (approximately \$US5,400 in 2002) compared with \$CN9,716 (approximately \$US6,300 in 2002) for the MI patients. The authors concluded that by the end of year 1, the health care resource burden for PAD is comparable with a diagnosis of MI.

Conclusions

The overall prevalence of PAD was 1.18% of the total MCO population of 6.67 million members. Over a mean postindex period of 25.2 months (median 23.4 months), the total mean annualized PAD-related cost was \$5,955 PPPY in 2001-2003 dollars for 30,561 PAD patients. Hospitalizations accounted for the largest component cost category, averaging \$4,442 PPPY or 75% of the total annualized PAD-related cost per PAD patient. For a subgroup of 24,075 newly identified PAD patients, 8,479 (35.2%) were hospitalized during an average 25.2 months of follow-up with the mean time to first hospitalization of 8.9 months. Based upon mean annual health and member costs of only \$313 PPPY for antihypertensives and \$207 for lipid-lowering therapy, drug therapy in PAD patients may be underutilized.

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