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Original Article

Patient profiles and health status outcomes for peripheral artery disease in high-income countries: a comparison between the USA and The Netherlands

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Aims Peripheral artery disease (PAD) is a global disease. Understanding variability in patient profiles and PAD-specific health status outcomes across health system countries can provide insights into improving PAD care. We compared these features between two high-income countries, the USA and The Netherlands.

Methods and results Patients were identified from the patient-centred outcomes related to treatment practices in peripheral arterial disease: investigating trajectories study—a prospective, international registry of patients presenting to vascular specialty clinics for new onset, or exacerbation of PAD symptoms. PAD-specific health status was measured with the peripheral artery questionnaire. General linear mixed models for repeated measures were used to study baseline, 3, 6, and 12-month PAD-specific health status outcomes (peripheral artery questionnaire summary score) between the USA and The Netherlands. Out of a total of 1114 patients, 748 patients (67.1%) were from the USA and 366 (32.9%) from The Netherlands. US patients with PAD were older, with more financial barriers, higher cardiovascular risk factor burden, and lower referral rates for exercise treatment ($P < 0.001$). They had significantly worse PAD-specific adjusted health status scores at presentation, 3, 6, and 12 months of follow-up (all $P < 0.0001$). Magnitude of change in 1-year health status scores was smaller in the US cohort when compared with The Netherlands.

Conclusion Compared with the Dutch cohort, US patients had worse adjusted PAD-specific health status scores at all time point, improving less over time, despite treatment. Leveraging inter-country differences in care and outcomes could provide important insights into optimizing PAD outcomes.

Clinical trial registration https://clinicaltrials.gov/ct2/show/NCT01419080? term=portrait&rank=1 NCT01419080.

Keywords Peripheral artery disease • High-income countries • Health status outcomes

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Introduction

The burden of cardiovascular disease remains extremely high globally and translates into significant mortality, morbidity, and health-care expenditures.[1] This is particularly the case for peripheral artery disease (PAD), with an estimated 236.62 million people living with PAD in 2015.[2] High morbidity and mortality rates are noted for this disease, with 15–20% of its population at risk of dying in 5 years.[1] Projected rates for PAD are on the rise worldwide, and for high-income countries, in particular, the increase is most notable in its rapidly aging populations.[2] Beyond its high mortality risk, PAD also has a profound impact on patients' health status, symptoms, function, and quality of life due to the chronic nature of this disease.

As the projected burden of disease for PAD is a growing area of concern in the industrialized world,[2–4] it becomes a key to understand its presentation forms across geographical regions and health-care contexts, as diverse socio-ecological impacts may contribute to variability in manifestations and may even contribute to the way this chronic disease is being treated and ultimately how benchmarks for health status targets following treatment may be defined across countries. As an example, not only does the US population face a life-expectancy gap when compared with their European counterparts, but additionally spend their lives in an overall worse health status when compared with individuals living in Western Europe.[5] The USA, when compared with any European country, has a much higher prevalence of cardiovascular disease and its risk factors/comorbidities including diabetes, smoking, and obesity,[6] and their respective health-care systems differ significantly to deal with these challenges. It is unknown whether these contextual factors are also reflected into the presentation of PAD, care received, and subsequent health status outcomes across geographical contexts such as the USA vs. Europe.

We therefore aimed to contrast PAD populations in the USA vs. The Netherlands to (i) examine their patient profiles (demographics, socio-economic, and clinical); (ii) their PAD treatment patterns in the specialty setting; and (iii) their PAD-specific health status outcomes upon PAD presentation and 1 year thereafter. Establishing inter-country differences in the care and health outcomes of patients with PAD may identify areas of clinical improvement and provide future directions in research for addressing PAD as a global health problem.

Methods

Data availability

Because of the sensitive nature of the data collected for this study, requests to access a de-identified data set from qualified researchers trained in human subject confidentiality protocols may be considered on an individual basis by contacting the corresponding author or by contacting the PORTRAIT (Patient-C Outcomes Related to Treatment Practices in Peripheral Arterial Disease: Investigating Trajectories) group on the website.[7]

Study design

This observational prospective cohort study was based on patient data collected from the multi-national PORTRAIT registry. A full description of the PORTRAIT registry has previously been published.[7] Data were collected prospectively from 1275 patients with new or worsening PAD symptoms who were treated at vascular specialty clinics in the USA, The Netherlands, or Australia between June 2011 and October 2015. There were 10, 5, and 1 participating sites, respectively. Patients from Australia were excluded because of their small sample size for this country-specific comparison. Differences in healthcare systems in the USA and The Netherlands are well-known, providing an opportunity for determining the impact of these differences on PAD outcomes.

Trained study-coordinators at each site-documented demographics, clinical history, and treatment from patient's medical records. Standardized interviews were conducted to obtain information about patients' socioeconomic, psychosocial, and health status. Information about race/ethnicity was collected by self-report and age/sex was obtained from patients' medical records. From these records, we also prospectively captured information on cardiovascular risk factors and comorbid conditions as well as disease-severity and PAD care metrics.[8]

Study population

Patients aged 21 years or older, presenting to a PAD specialist (vascular surgeon, vascular medicine specialist, radiologist, or cardiologist), patients with new-onset or recent exacerbation of exertional leg symptoms, and an abnormal resting ankle-brachial index (ABI) ($\leq$0.90),[9] or a significant drop in post-exercise ankle pressure of $\geq$20 mmHg[10] were included. Those with a non-compressible ABI, critical limb ischemia, who did not speak English/Spanish/Dutch, who were hard of hearing, or were unable to provide informed consent were excluded.[7] The study was designed in accordance with the Helsinki Declaration and was approved by the Institutional Review Board at each participating institution. Patients provided informed consent for their study participation.

Study measures

The main variable of interest was country of enrolment—the USA vs. The Netherlands—for the PORTRAIT study. Differences in healthcare systems in the USA and The Netherlands are well-known and provide an opportunity to contrast patient and care profiles and subsequent outcomes, to generate hypotheses about possible quality improvement and care innovation strategies. In the US healthcare system, which does not ensure universal coverage, health insurance plans are mostly covered by a third party through employers, Mediacid (for low-income people and those with disabilities) or Medicare (for patients 65 or older).[11,12] The Netherlands' system for short-term medical care needs, while also mostly privatized, is regulated by the government and its hallmark features are that health insurance is mandatory and premiums are equalized regardless of risk and age. The system for short-term medical care needs is funded by employers, the insured population, and the government. Long-term healthcare and nursing care needs are supported by the government.[11,13]

Lastly four quality metrics as endorsed and retained by guidelines were determined for the two countries.[10,14,15] These are part of the American College of Cardiology/American Heart Association Performance Measures for PAD and include: (i) statin therapy, (ii) antiplatelet therapy, (iii) smoking cessation therapy/counselling, and (iv) referral to a PAD-specified supervised exercise training (SET) programme.

Primary outcomes

The outcomes assessed in this study were health status as measured by the disease-specific and generic health status instruments at baseline, 3, 6, and 12 months. PAD-specific health status was evaluated using the validated peripheral artery questionnaire (PAQ), a 20-item multi-dimensional assessment tool.[16] The PAQ measures six domains relevant to patients with PAD: physical function, symptoms, symptom stability, social limitation, treatment satisfaction, and quality of life. Each domain has a score range 0–100 with higher scores indicating

better health status. PAQ domain scores (excluding the treatment satisfaction and symptom stability scales) can be combined to calculate a PAQ summary score.

Generic health status was evaluated with the EQ-5D questionnaire, a standardized generic measure of health status for clinical assessment. It has two parts: a descriptive section (EQ-5D Index Score) and visual analogue scale (EQ-5D VAS score). For our study, we used the EQ-5D VAS score which represents a patient's assessment of their overall health. Scores range from the worst (a score of 0) to the best (a score of 100) imaginable state, with higher scores indicating better health status.[17]

Other measures collected included age, sex, race, education, employment, living status, and insurance status. In order to assess financial barriers despite having insurance, patients were asked three validated questions[8,18,19] to examine whether, due to cost, patients (i) had avoided obtaining healthcare services; (ii) had not taken a prescribed medication in the past year, and (iii) experienced difficulty to get medical care when needed. Those who answered either 'yes' to the first question, or 'always'/'frequently'/'occasionally' to the second question, or 'extremely difficult'/'moderately difficult'/'somewhat difficult' to the third question were categorized as having 'financial concerns'. This approach has been tested and studied previously in prior acute myocardial infarction and PAD cohorts.[20,21]

Information on clinical comorbidities consisted of history of stroke, hypertension, coronary artery disease, myocardial infarction, percutaneous coronary interventions, coronary artery bypass grafting, chronic kidney disease, chronic lung disease, diabetes, and smoking. For PAD-specific characteristics, we included collected information on indicators of disease burden and severity (ABI, mild/moderate/severe claudication based on Rutherford category), patients' symptom presentation (new symptoms vs. exacerbation of symptoms), duration of pain, and lesion characteristics (lesion location, lesion site, and laterality of symptomatic leg). In addition, we collected history of lower-extremity amputations and history or surgical or endovascular lower-extremity interventions.

Statistical analysis

Baseline patient characteristics and PAD treatment information were described for the overall cohort and by country (USA vs. The Netherlands) (*Table 1*). Continuous variables were compared using Student *t*-tests and categorical variables were compared using the χ^2 test or Mantel–Haenszel trend test, as appropriate. Mean health status scores and standard deviations at baseline, 3, 6, and 12 months were summarized by country. Comparisons were performed using Student's *t*-tests and linear trend tests.

General linear mixed models for repeated measures, with a random effect for provider and site, were used to study baseline, 3-, 6-, and 12-month health status outcomes (including disease-specific PAQ summary scores and generic health-related quality of life using EQ-5D) as a function of country (USA vs. The Netherlands). Covariates in the model included age, sex, race, avoiding care due to cost, work for pay, new onset vs. exacerbation of PAD, bilateral disease, smoking, history of diabetes, CAD, bilateral disease, and sleep apnoea.[22] Estimates for health status differences by country were presented as mean estimates, group differences over time were summarized as least square means. Missingness patterns were examined; of the 1114 patients, 16 patients had missing information on 1 covariate, while only 1 patient had 2 covariates missing. Over follow-up, 101 patients had 1 missing PAQ assessment while 88 had 2 missing PAQ assessments. A value of $P < 0.05$ was considered statistically significant. All analyses were performed using SAS version 9. 4 (SAS Institute, Cary, NC, USA).

Results

Between June 2011 and October 2015, 1275 patients were enrolled in the PORTRAIT registry. Of the 1275 patients, 1162 (91.1%) met the resting ABI inclusion criteria and 113 (8.9%) met the post-exercise ABI pressure decrease criteria. After excluding patients from Australia ($n = 95$), our final study cohort from the USA and The Netherlands consisted of 1180 patients with 748 US (67.1%) and 366 Dutch patients (32.9%) (Supplementary material online, *Figure S1*). We additionally excluded 66 patients who did not have baseline PAQ scores and at least one follow-up assessment.

Patient profiles by country

There were significant differences in patient profiles between the two countries (*Table 1*). The mean age of the entire cohort was 67.5 ± 9.4 years, with the Dutch cohort being significantly younger (65.2 ± 8.5 vs. 68.6 ± 9.6 years) and all White (100.0% vs. 72.1%) when compared with the US cohort. There were significantly more women with PAD in the US cohort when compared with Dutch patients (41.4% vs. 31.1%). From a socio-economic perspective, more US patients reported financial barriers to care (21.1% vs. 8.2%) and were less likely to be married. Significantly more US patients had completed high-school education (85.3% vs. 42.9%). No differences in insurance status were noted by country.

As for the clinical profiles, Dutch patients were more likely to be current smokers (52.3% vs. 30.2%) compared with the US cohort who were more likely to be former smokers (56.8% vs. 42.2%). Overall, the US cohort was higher risk when compared with the Dutch cohort with a higher prevalence of cardiovascular risk factors and comorbidities including hypertension, history of myocardial infarction, percutaneous coronary interventions as well as coronary artery bypass grafting ($P < 0.001$). Similarly, the rates of diabetes, chronic kidney disease, and sleep apnoea were significantly higher across the US cohort when compared with patients from The Netherlands.

As for the PAD severity profile, we observed that, compared with the US cohort, Dutch patients were nearly twice as likely to present with new onset symptoms of PAD (79.0% vs. 40.4%). US patients had more delay of presentation with PAD symptoms as more than half presented with symptoms duration of >12 months and presented with more severe disease as evidenced by more advanced Rutherford class (moderate–severe claudication). There was no difference in ABI values between the two cohorts. Anatomically, Dutch patients had more unilateral disease as well as higher rates of both proximal and distal disease (multilevel) ($P < 0.001$). While there was no difference between the two cohorts in rates of prior amputation, more US patients (approximately one-third) had a history of peripheral vascular intervention (33.8% vs. 15.3%).

PAD treatment patterns after enrolment

US patients were equally likely to be on antiplatelet agents as well as statins when compared with the Dutch cohort. More US patients received smoking cessation counselling compared with The Netherlands cohort (81.3% vs. 71.9%). Most of the Dutch cohort was referred to a 'supervised' exercise programme (69.8% vs. 1.7%) in contrast to the US cohort which was either referred to an 'unsupervised' programme (55.3% vs. 3.8%) or not referred at all. While

Table 1 Patient and treatment characteristics by country

Characteristics	USA *n* = 748	The Netherlands *n* = 366	Total *n* = 1114	*P* value
Demographics and socio-economic status				
Age	68.6 ± 9.59	65.16 ± 8.54	67.47 ± 9.4	<0.001
Mean ± SD				
White	539 (72.1)	366 (100.0)	905 (81.2)	<0.001
Male	438 (58.6)	252 (68.9)	690 (61.9)	<0.001
BMI	29.5 ± 6.3	26.7 ± 4.4	28.9 ± 6.1	<0.001
Health insurance	741 (99.1)	366 (100)	1107 (99.4)	0.10
Education high school or above	638 (85.3)	154 (42.9)	792 (71.5)	<0.001
Married	402 (54.1)	265 (72.4)	667 (60.1)	<0.001
Working for pay	168 (22.6)	98 (26.8)	266 (24.0)	0.12
Financial barriers	158 (21.1)	30 (8.2)	188 (16.9)	<0.001
Risk factors and comorbidities				
Smoke status				
Never	97 (13.0)	20 (5.5)	117 (10.5)	
Former	425 (56.8)	154 (42.2)	579 (52.0)	<0.001
Current	226 (30.2)	191 (52.3)	417 (37.5)	
CAD	402 (53.7)	102 (27.9)	504 (45.2)	<0.001
Dyslipidaemia	663 (88.6)	228 (62.3)	891 (80.0)	0.001
Hypertension	669 (89.4)	224 (61.2)	893 (80.2)	<0.001
Diabetes	286 (38.2)	77 (21.0)	363 (32.6)	<0.001
Chronic kidney disease	112 (15.0)	16 (4.4)	128 (11.5)	<0.001
Chronic back pain	97 (13.0)	52 (14.2)	149 (13.4)	0.57
Sleep apnoea	83 (11.1)	7 (1.9)	90 (8.1)	<0.001
History of MI	168 (22.5)	49 (13.4)	217 (19.5)	<0.001
History of PCI	217 (29.0)	45 (12.3)	262 (23.5)	<0.001
History of CABG	189 (25.3)	35 (9.6)	224 (20.1)	<0.001
History of TIA/CVA	89 (11.9)	44 (12.0)	133 (11.9)	0.95
Chronic lung disease	118 (15.8)	75 (20.5)	193 (17.3)	0.05
PAD treatment history				
Amputation	10 (1.3)	3 (0.8)	13 (1.2)	0.56
Peripheral vascular intervention	253 (33.8)	56 (15.3)	309 (27.7)	<0.001
Cilostazol	74 (9.9)	0 (0)	74 (6.7)	<0.001
Antiplatelet therapy	646 (86.4)	197 (53.8)	843 (75.7)	<0.001
Statin	595 (79.5)	215 (58.7)	810 (72.7)	<0.001
ACE inhibitor	373 (49.9)	87 (24.0)	460 (41.4)	<0.001
PAD characteristics upon presentation				
New onset PAD symptoms	302 (40.4)	289 (79.0)	591 (53.1)	<0.001
ABI	0.67 ± 0.19	0.66 ± 0.18	0.67 ± 0.19	0.12
Mean ± SD				
Rutherford category				
Mild claudication	150 (20.2)	97 (27.2)	247 (22.5)	0.002
Moderate claudication	377 (50.7)	186 (52.2)	563 (51.2)	
Severe claudication	217 (29.2)	73 (20.5)	290 (26.4)	
Duration of pain				
<1 month	9 (1.3)	15 (5.7)	24 (2.5)	
1–6 months	188 (27.4)	95 (36.4)	282 (29.9)	
7–12 months	137 (19.9)	31 (11.9)	168 (17.7)	
>12 months	353 (51.4)	120 (46.0)	473 (49.9)	<0.001
Unilateral disease	323 (43.2)	208 (56.8)	531 (47.7)	< 0.001

Continued

Table 1 *Continued*

Characteristics	USA n = 748	The Netherlands n = 366	Total n = 1114	P value
Lesion site				
Proximal	175 (23.6)	134 (36.9)	309 (28.0)	<0.001
Distal	299 (40.3)	30 (8.3)	329 (29.8)	
Both	268 (36.1)	199 (54.8)	467 (42.3)	
PAD treatment after enrolment				
Cilostazol	141 (18.9)	0 (0)	141 (12.7)	<0.001
Antiplatelet therapy	667 (90.6)	309 (88.8)	976 (90.0)	0.35
Statin	623 (83.3)	304 (83.1)	927 (83.2)	0.92
ACE Inhibitor	381 (51.0)	86 (23.7)	467 (42.1)	<0.001
Smoking cessation physician advice	174 (81.3)	133 (71.9)	307 (76.9)	0.025
Unsupervised PAD exercise therapy	414 (55.5)	14 (3.8)	428 (38.4)	<0.001
Supervised PAD exercise therapy	12 (1.7)	233 (69.8)	245 (23.3)	<0.001
Invasive treatment	140 (20.2)	82 (22.7)	222 (21.1)	0.36
Surgical treatment	12 (1.7)	16 (4.4)	28 (2.7)	0.010
Endovascular treatment	131 (18.9)	68 (18.8)	199 (18.9)	0.95
Provider				
Interventional cardiologist	493 (65.9)	0 (0)	493 (44.3)	<0.001
General cardiologist	138 (18.4)	0 (0)	138 (12.4)	
Vascular surgeon	44 (5.9)	354 (96.7)	398 (35.7)	
Other	73 (9.8)	12 (3.3)	85 (7.6)	

Values are listed as *n* (%), unless otherwise described.
ACE, angiotensin converting enzyme; BMI, body mass index; CABG, coronary artery bypass grafting; CAD, coronary artery disease; CVA, cerebrovascular accident; EQ-5D, European quality of life 5 dimensions; GAD, generalized anxiety disorder; IQR, interquartile range; MI, myocardial infarction; PAD, peripheral artery disease; PAQ, peripheral artery questionnaire; PCI, percutaneous coronary intervention; PHQ-8, patient health questionnaire; SD, standard deviation; TIA, transient ischaemic attack.

overall there were no differences in rates of invasive treatment, patients from The Netherlands were more likely to be referred for surgical treatment (4.4% vs. 1.7%). Of note, most PAD patients in the USA were treated by interventional cardiologists compared with The Netherlands where >96% were treated by vascular surgeons.

Health status profiles in PAD

At presentation, US patients had worse unadjusted and adjusted disease-specific health status outcomes at baseline compared with the Dutch cohort as evident from their PAQ summary scores (unadjusted: 47.1 ± 22.0 vs. 55.3 ± 19.1, $P < 0.001$) (*Table 2*). These differences were not seen in the EQ-5D scores. As for the follow-up, differences in PAQ summary scores between the US and Dutch cohort ranged from ∼6.5 to 13 points (from 3 to 12 months of follow-up) with the US patients consistently having lower scores throughout the year following their PAD diagnosis (*Table 2*). There were no differences in the follow-up EQ-5D scores at any time point.

The adjusted generalized linear mixed repeated measures model, showed a statistically significant difference in PAQ summary scores between countries at each time point, with the US patients having consistently lower scores ($P < 0.01$) than Dutch patients (*Figure 1*). While both Dutch and US patients improved over time ($P < 0.01$), US patients lagged behind Dutch patients in the magnitude of improvement (*P* value for interaction country × time = 0.0001), including at 1 year where the magnitude of improvement was -5.63 for US when compared with the Dutch cohort. Because the differences in EQ-5D were not significant by country (*Table 2*), we did not proceed with modelling for EQ-5D.

Discussion

Our study highlights several differences in patient profiles including risk factors as well as disease specific treatment for PAD between two high-income countries. US patients with PAD were older, presented with more advanced disease, reported more financial barriers, had a higher burden of cardiovascular comorbidities and risk factors in contrast to the Dutch cohort which was younger but with higher rates of smoking. While rates of guideline-directed medical therapy and referrals to invasive treatment were similar between the two cohorts, Dutch patients were more likely to be referred to supervised exercise treatment. When compared with their Dutch counterparts, US patients presented with worse health status upon PAD diagnosis, differences that persisted at all measurement points. Importantly, while 12-month health status improved for both cohorts, Dutch patients made significantly greater improvements over time.

Our study adds to the existing literature on PAD in several ways. Since the REACH (Reduction of Atherothrombosis for Continued Health) registry,[23] this is the first study to comprehensively explore differences in profiles of patients with PAD between two high-income countries. Similarly, to our knowledge, this is also the first

Table 2 Unadjusted peripheral artery questionnaire summary scores and EQ-5D cores at baseline, 6, and 12 months between patients with PAD from the USA and The Netherlands

Time (months)	Country		*P* value
	USA	The Netherlands	
PAQ summary scores (mean ± SD)			
Baseline	47.1 ± 22.0	55.3 ± 19.1	<0.0001
3 months	65.9 ± 25.0	72.4 ± 21.6	<0.0001
6 months	67.8 ± 24.6	76.8 ± 21.3	<0.0001
12 months	67.4 ± 25.6	80.3 ± 20.5	<0.001
EQ-5D scores (mean ± SD)			
Baseline	66.2 ± 20.6	65.1 ± 16.4	0.40
3 months	70.0 ± 19.5	69.9 ± 15.4	0.92
6 months	69.5 ± 19.5	71.7 ± 14.0	0.06
12 months	69.7 ± 19.1	71.8 ± 14.1	0.09

PAD, peripheral artery disease; PAQ, peripheral artery questionnaire; SD, standard deviation; USA, United States of America.

comparative study to present long-term health status outcomes for PAD patient cohorts from two high income countries. Our study is also unique, in comparison with other longitudinal PAD registries including the REACH registry, the Society for Vascular Surgery, Vascular Quality Initiative[24] and National Cardiovascular Data Registry, Peripheral Vascular Intervention,[25] in that it has rich, disease-specific health status profiles documented along with a detailed profiling of patients' social determinants of health.

In our study, US patients with PAD who presented to vascular specialty clinics, presented late for their PAD symptoms and had more severe cardiovascular risk profile, a finding that could be explained by several differences between the two countries.[26] The US healthcare system, largely privatized and partially organized by the government, is among the most expensive globally, yet high uninsurance and underinsurance rates, cost barriers in accessing care, as well as health disparities are some examples of the strains that patient populations in the US face.[26] Whereas the Dutch healthcare system is also largely privatized, the market is strictly regulated with mandatory insurance and a fixed price system, a competition regulating body, and a system where it is illegal to deny individuals health insurance.[27] The impact of these architectural designs of healthcare systems on the affordability and quality of care and outcomes have been well described and are in line with our observations.[28] Examples of financial barriers in accessing care specifically in the USA include high out-of-pocket costs for prescription medications, inpatient, and outpatient hospital care, all of which have also been reported to represent a significant issue for patients with PAD in the USA.[29] Other mechanisms that explain as to why US patients had a more severe cardiovascular risk profile are vastly different lifestyle trends that patients adopt between the two high-income countries especially in terms of physical activity[30] and dietary patterns that translate into differences in cardiovascular disease and metabolic syndrome manifestations.[31,32] These differences were also reflected in our cohort. Interestingly, despite higher observed smoking rates and lower educational status in the Dutch patients, the Dutch cohort's overall cardiovascular risk profile was not as severe when compared with the US cohort.

As far as the management of PAD goes, higher rates of ACE inhibitors reflecting the higher hypertension burden, were observed in the US cohort, as well as about 1/5 of patients in whom Cilostazol was started vs. none in The Netherlands. Differential prescription of cilostazol reflects the differences in European Society of Cardiology/European Society of Vascular Surgery (ESC/ESVS)[33] and American College of Cardiology Foundation/American Heart Association (ACCF/AHA) guidelines[14] as the ESC guidelines do not recommend this therapy because of lack of evidence of efficacy vs. the ACC guidelines which give it a Class I recommendation. Of note, the vast majority of patients being worked up for PAD were referred to SET in The Netherlands, whereas virtually nobody was sent to such programmes in the USA, but had to rely on unstructured forms of exercise therapy or advice. One reason for this low referral rates for SET in US patients may be that the centre for Medicaid and Medicare services (CMS) extended coverage of SET to PAD in early 2017 while our cohort was enrolled between 2011 and 2015 with a follow-up of 1 year, just missing this new reimbursement policy change. It remains to be seen whether this policy change also had an impact on the update of SET in PAD management. As exercise treatment, SET in particular, is known to be a potent intervention to improve quality of life and walking distance in patients with PAD,[34–37] an important question can be raised from our observations: to what extent can systematic referral to SET explain the profound health status discrepancies between the US and Dutch cohorts?

These differences in PAD-related health status both upon presentation and throughout follow-up were striking indeed and clinically relevant. Despite the fact that the US cohort started out with lower health status, and thus had the largest capacity to improve, their Dutch counterparts outperformed the US PAD cohort in terms of the PAD-specific health status improvements following PAD diagnosis. The worse health status outcomes at presentation as well as through 1 year of follow-up among the US cohort could be explained by late presentation, more severe symptoms, as well as financial barriers which are shown to be associated with worse health status outcomes.[28] While the differential PAD management practices—i.e. systematic referral to SET—may partially explain the observed differences in health status improvements over time, wider societal factors, and social determinants of health (e.g. mental health burden, addiction rates in the US population, higher physical activity levels in The Netherlands) may also explain such differences.[30,38,39] Contrasting treatment practices and outcomes across high-income countries may provide us input as to what practice reform could be implemented and tested to obtain wider health status gains in PAD populations and to understand benchmarks for expected health status benefits of routine PAD management.

Our study should be interpreted in the light of several limitations. Given the observational nature of the study, no inference could be drawn about causality as unmeasured clinical and psychologic factors may have contributed to outcomes. In addition, we reported findings on the USA and The Netherlands only and our findings may not be

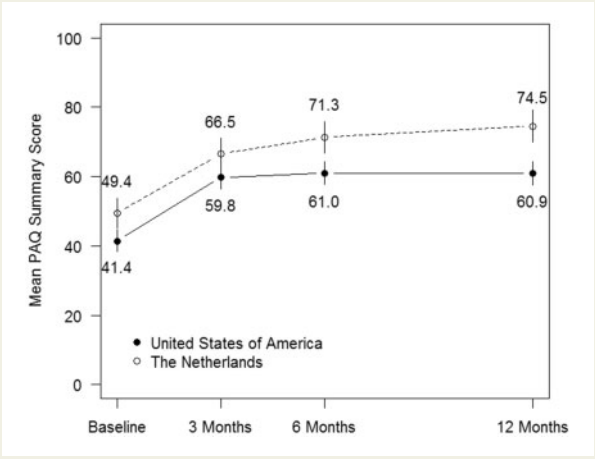

Figure 1 Adjusted peripheral artery questionnaire summary score at baseline, 3, 6 and 12 months between the USA and The Netherlands patients with peripheral artery questionnaire using the general linear mixed model with a time by country interaction. Covariates in the adjusted model include: age, country, sex, white race, avoiding care due to cost, high school education, new or exacerbation of symptoms, bilateral disease, smoking, history of diabetes, coronary artery disease, and sleep apnoea. Lines for each cohort represent standard error.

entirely generalizable to other North American or European geographical areas, respectively. However, the demographics observed and burden of comorbid disease observed within these cohorts are in line with prior reportings.[2,40,41] Related to this limitation, our cohort was drawn from vascular specialty clinics in both countries and thus may not be representative of the entire population in both countries as not all patients may have access to vascular specialty clinics. This study was conducted before CMS approval of SET in the USA, therefore it remains unclear whether practices (especially referral to SET) dramatically changed as well as lack of information on other obstacles including availability of SET centres, time-commitment as well as insurance coverage/out-of-pocket cost issues for SET remain.

In conclusion, stark differences were found in PAD presentation profiles with higher risk profiles and more delayed presentation in the USA as well as differential treatment practices and poor health status scores over the year in the US cohort following their PAD diagnosis when compared with their European counterparts. Differential risk exposure patterns and healthcare systems may uniquely contribute to these observed differences. The findings from our study have several implications for health policy as well as clinical practice in the field of PAD. It is vital that for our health system to be effective in mitigating the mortality and morbidity involved with PAD, preventive care in the form of aggressive risk factor modification is undertaken.[42–44] Central to the care of PAD also is to ensure improved access to care and addressing financial barriers in accessing care[28] which would allow for timely recognition and treatment of the disease. Patient-centred strategies to help support patients in getting access to key treatments such as SET and smoking cessation support are key to maximize health status benefits in this population, and may ultimately translate into more value based care designs for PAD.

Supplementary material

Supplementary material is available at *European Heart Journal – Quality of Care and Clinical Outcomes* online.

Data availability statement

Because of the sensitive nature of the data collected for this study, requests to access a de-identified data set from qualified researchers may be considered on an individual basis by contacting the corresponding author or by contacting the PORTRAIT group on the website.[7]

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Conflict of Interest Statement

The statements in this manuscript are solely the responsibility of the authors and do not necessarily represent the views of the Patient-Centered OutcomesResearch Institute (PCORI), its Board of Governors or Methodology Committee. All manuscripts for the PORTRAIT study are prepared by independent authors who are not governed by the funding sponsors and are reviewed by an academic publications committee before submission.

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