

Editor's Choice — Carotid Stenosis Treatment: Variation in International Practice Patterns

M. Venermo^{a,*}, G. Wang^{b,o}, A. Sedrakyan^c, J. Mao^c, N. Eldrup^d, R. DeMartino^e, K. Mani^f, M. Altreuther^g, B. Beiles^h, G. Menyheiⁱ, G. Danielsson^j, I. Thomson^k, G. Heller^l, C. Setacci^m, M. Björck^{f,p}, J. Cronenwett^{n,p}

^a University Hospital, Helsinki, Finland

^b Hospital of the University of Pennsylvania, Division of Vascular Surgery, Philadelphia, PA, USA

^c Department of Healthcare Policy and Research, Weill Cornell Medical College, New York, NY, USA

^d Aarhus University Hospital, Aarhus, Denmark

^e Mayo Clinic, Rochester, MN, USA

^f Department of Surgical Sciences, Uppsala University, Uppsala, Sweden

^g Department of Vascular Surgery, St Olavs Hospital, Trondheim, Norway

^h Australian and New Zealand Society for Vascular Surgery, East Melbourne, Australia

ⁱ Department of Vascular Surgery, University Pecs Medical School, Pecs, Hungary

^j National University Hospital of Iceland, Department of Surgery, Reykjavik, Iceland

^k Vascular Surgery, Dunedin School of Medicine, Dunedin Hospital, Dunedin, New Zealand

^l Department of Surgery, Kantonsspital Graubünden, Chur, Switzerland

^m Vascular and Endovascular Surgery Unit, Department of Medicine, Surgery and Neuroscience University of Siena, Italy

ⁿ Section of Vascular Surgery, Dartmouth-Hitchcock Medical Centre, Lebanon, NH, USA

WHAT THIS PAPER ADDS

The treatment of carotid stenosis is one of the best studied disease processes in vascular surgery, and several societies have published guidelines and recommendations about the indications for CEA and CAS. However, considerable variation exists between countries and centres. In this study, variation in the treatment patterns in over 400 centres in the United States, Europe, Australia, and New Zealand are analysed. The main focus is on indications and the proportion of stenting. Furthermore, an analysis on the influence of the reimbursement system on indications was performed.

Objectives: The aim was to determine current practice for the treatment of carotid stenosis among 12 countries participating in the International Consortium of Vascular Registries (ICVR).

Methods: Data from the United States Vascular Quality Initiative (VQI) and the Vascunet registry collaboration (including 10 registries in Europe and Australasia) were used. Variation in treatment modality of asymptomatic versus symptomatic patients was analysed between countries and among centres within each country.

Results: Among 58,607 procedures, octogenarians represented 18% of all patients, ranging from 8% (Hungary) to 22% (New Zealand and Australia). Women represented 36%, ranging from 29% (Switzerland) to 40% (USA). The proportion of carotid artery stenting (CAS) among asymptomatic patients ranged from 0% (Finland) to 26% (Sweden) and among symptomatic patients from 0% (Denmark) to 19% (USA). Variation among centres within countries for CAS was highest in the United States and Australia (from 0% to 80%). The overall proportion of asymptomatic patients was 48%, but varied from 0% (Denmark) to 73% (Italy). There was also substantial centre level variation within each country in the proportion of asymptomatic patients, most pronounced in Australia (0–72%), Hungary (5–55%), and the United States (0–100%). Countries with fee for service reimbursement had higher rates of treatment in asymptomatic patients than countries with population based reimbursement (OR 5.8, 95% CI 4.4–7.7).

Conclusions: Despite evidence about treatment options for carotid artery disease, the proportion of asymptomatic patients, treatment modality, and the proportion of women and octogenarians vary considerably among and within countries. There was a significant association of treating more asymptomatic patients in countries with fee for service reimbursement. The findings reflect the inconsistency of the existing guidelines and a need for cooperation among guideline committees all over the world.

© 2017 European Society for Vascular Surgery. Published by Elsevier Ltd. All rights reserved.

Article history: Received 11 November 2016, Accepted 24 January 2017, Available online 6 March 2017

Keywords: Carotid endarterectomy, Carotid artery stenting, Carotid stenosis

^o These authors are joint first authors. ^p These authors are joint last authors.

* Corresponding author. Helsinki University, Helsinki University Hospital, Helsinki University Hospital, PO Box 340, FI00029 HUS, Finland.
E-mail address: Maarit.venermo@hus.fi (M. Venermo).

1078-5884/© 2017 European Society for Vascular Surgery. Published by Elsevier Ltd. All rights reserved.

<http://dx.doi.org/10.1016/j.jvs.2017.01.012>

INTRODUCTION

Carotid artery disease has long been associated with ischaemic stroke. In the early 1990s, large randomised trials clarified the indications for carotid endarterectomy (CEA) treatment of symptomatic disease. Surgical intervention in patients with carotid artery stenosis of $\geq 50\%$ in the presence of symptoms was found to be highly beneficial, provided that the complication rates were low.^{1,2} Indeed, the absolute risk reduction of CEA compared with best medical treatment (BMT) in patients with 50–69% and 70–99% symptomatic carotid stenosis was shown to be 7.8% and 15.6% respectively.^{3,4} Carotid artery stenting (CAS) as a treatment modality for carotid stenosis has also been studied and compared with CEA. In a recent pooled analysis of 3433 randomised patients, CEA was safer in the short term than CAS because of the increased risk of stroke in CAS patients over the age of 70 years, although no difference was apparent in younger patients.⁵

Treatment of asymptomatic carotid stenosis is more controversial. In two large randomised trials with more than 4700 patients with asymptomatic carotid stenosis, the absolute risk reduction of stroke when CEA was compared with BMT was 5.3–5.9% after 5 years.^{6,7} Furthermore, in the 10 years since these trials, BMT has improved to the point where the annual stroke risk from asymptomatic stenosis is now estimated by some to be as low as 0.5%.⁸ Current guidelines regarding asymptomatic patients recommend careful patient selection, primarily offering CEA or CAS to those under 75 years of age⁹ or those with life expectancy more than 5 years.^{10,11}

Despite several randomised controlled trials (RCTs) being available, there are still differences between medical society guidelines regarding the treatment of carotid stenosis.¹² Registries provide a real world view and can demonstrate variation in how practice guidelines are translated into clinical practice.¹³ Registries also permit analysis of variation among different geographical regions and among centres. In a previous study, variation has been shown to exist between European countries, New Zealand, and Australia,¹⁴ but no centre level analysis has been performed.

The present study included data from 11 countries on three continents: Australasia, Europe, and North America. Variations in treatment of carotid artery stenosis were examined over a 4 year period (2010–2013). Trends were analysed in the treatment of asymptomatic versus symptomatic carotid stenosis and the distribution of treatment modality (CEA vs. CAS) for each patient group, focusing on variation among countries and among centres within countries. Data were analysed for difference in treatment among octogenarians and by gender. In asymptomatic patients the association of treatment and fee for service versus population based reimbursement was analysed. The authors sought to describe how actual practice compares with society guidelines in an international cohort of patients.

MATERIALS AND METHODS

To achieve these objectives, the International Consortium of Vascular Registries (ICVR, www.icvr-initiative.org) was formed in 2014 as a collaboration of the US Food and Drug Administration Medical Device Epidemiology Network (MDEpiNet) Science and Infrastructure Centre at Cornell University and 11 vascular registries from Australasia, Europe, and North America. This represents a collaboration of national registries in VASCUNET, based on the European Society for Vascular Surgery, and the Vascular Quality Initiative (VQI), based on the Society for Vascular Surgery. Registries contributing data to this ICVR project are from Australia, Denmark, Finland, Hungary, Iceland, Italy, New Zealand, Norway, Sweden, Switzerland, and the United States. De-identified individual patient data from 10 national registries and aggregated patient data from Italy were submitted to the Cornell Analytic Centre for analysis.

In six of the participating countries, registry is national, covering all hospitals in the country (Australia, Denmark, Hungary, Iceland, New Zealand, Norway, and Sweden). The Finnish registry captured all treatment from three hospital regions (Helsinki, South Savonia, and South Karelia). Italy and the United States captured all data from selected centres in voluntary national registries. Switzerland captured all procedures performed within their public but not private healthcare sector. Thus, data that are presented represent 15–100% of all procedures performed in the countries surveyed (Table 1). The percentage of CAS procedures enrolled was lower than CEA procedures because in

Table 1. The capture rate of the registers in the participating countries (comparison of number of procedures registered in the registry compared with the procedures registered in the official health dataset of the country).

	Registry coverage CEA	Registry coverage CAS	Number of the procedures included
Australia	70%	37%	8025
Denmark	> 95%	> 95%	1519
Finland ^a	40% (100%)	40% (100%)	938
Hungary	80%	60%	5388
Iceland	100%	100%	78
Italy	70%	40–50%	6937
Norway	80%	80%	1033
Sweden	> 98%	> 90%	4047
Switzerland ^b	50%	< 10%	1811
New Zealand	85%	< 5%	1478
USA ^c	15% (100%)	15% (100%)	27,353

AAA = abdominal aortic aneurysm; CAS = carotid artery stenting; CEA = carotid endarterectomy.

^a In Finland the registry is regional and covers 100% of the procedures in the regions, audited using hospital records.

^b The Swiss vascular registry includes patients undergoing surgery for AAA in public hospitals, and captures 85% of all open and 70% of all endovascular procedures in the country.

^c US data represent an estimated 15% of all CEA and CAS procedures over the study period. All participating centres capture 100% of their consecutive cases, audited using billing data.

many countries CAS is performed by specialists other than vascular surgeons who don't always participate in these registries.

Patients undergoing CEA or CAS from January 1, 2010, to December 31, 2013, were included for all countries except Italy, which submitted data for 2012–2013. A dataset was created on the basis of common variables across the registries, including country, de-identified hospital number, patient's age, gender, and risk factors (diabetes, cardiac disease, stroke history, pulmonary disease, hypertension), indication for surgery (symptomatic vs. asymptomatic), type of the procedure (CAS or CEA), and year of the procedure. The grade of stenosis was categorized by the criteria of each centre as a percentage of the diameter of stenosis compared with the distal internal carotid artery (ICA) (NASCET), except in Italy, where there is a variation between the hospitals (some centres use NASCET, other centres ECST).

For analyses comparing the proportion of CAS versus CEA used to treat carotid stenosis, only those centres entering data for both CAS and CEA were included (all centres contributing data were included in separate CEA and CAS analyses). Italy and Norway were excluded from centre level analysis because centre level information was not available.

Description of regions and centres

Variation across countries and among centres within countries was analysed. Because of its large size and number of participating centres, the United States was further divided into five regions (New England, East, South, Midwest, and West) for comparison. Eleven countries and 418 centres were included in the analyses. In the analysis of

time trends, only those centres that submitted data for all 4 years (2010–2013) were included. Countries were also grouped and analysed by whether they primarily use fee for service or population based reimbursement for these procedures. In countries that have largely fee for service reimbursement, physician payment is proportional to the number of procedures performed, and in countries with population based reimbursement, physician payment is independent of the number of procedures performed.

Statistical methods

Variations in symptom status and patient age, gender, and carotid stenosis severity were first identified within the entire cohort at the country and centre level and represented graphically. Data are presented as percentages and 95% confidence intervals (CI). Small centres (with number of procedures < 10) were excluded when describing centre level variation due to unstable estimates. After excluding the centres that were not participating in both CAS and CEA modules, the proportion of CAS procedures relative to CEA was examined across countries among both asymptomatic and symptomatic patients. Differences in patient characteristics and use of CAS were compared between symptomatic and asymptomatic patients and across countries with chi-square tests. Trends in indication, patient demographics, and use of CAS were analysed over time. The Cochran–Armitage test for trend was used to assess the significance. Comparison between countries using fee for service and population based reimbursement methods were made to assess compliance with guidelines. Proportions of asymptomatic patients treated and proportion

Table 2. Characteristics of patients undergoing carotid procedures.

	Asymptomatic CEA (n = 24952)	CAS (n = 3135)	p	Symptomatic CEA (n = 27482)	CAS (n = 3038)	p
Year			< .01			< .01
2010	2844 (11.4%)	261 (8.3%)		5167 (18.8%)	308 (10.1%)	
2011	3713 (14.9%)	416 (13.3%)		5796 (21.1%)	449 (14.8%)	
2012	7901 (31.7%)	1071 (34.2%)		7699 (28.0%)	1005 (33.1%)	
2013	10,494(42.1%)	1387 (44.2%)		8820 (32.1%)	1276 (42.0%)	
Age						
65+	18,983 (76.1%)	2386 (76.1%)	.98	20,447 (74.4%)	2096 (69.0%)	< .01
80+	3987 (16.0%)	561 (17.9%)	< .01	5295 (19.3%)	550 (18.1%)	.12
Gender			< .01			.02
Female	9372 (37.6%)	1061 (33.8%)		9475 (34.5%)	1111 (36.6%)	
Male	15,571 (62.4%)	2074 (66.2%)		17,992 (65.5%)	1927 (63.4%)	
Comorbidities						
Diabetes	8018 (32.2%)	1031 (33.1%)	.29	7385 (27.2%)	999 (33.1%)	< .01
Cardiac	9323 (37.4%)	1372 (44.1%)	< .01	10,093 (37.2%)	1255 (41.8%)	< .01
Pulmonary	3421 (18.9%)	423 (20.2%)	.15	3161 (16.5%)	555 (25.3%)	< .01
Stroke	101 (0.7%)	223 (12.2%)	< .01	5353 (50.9%)	758 (52.7%)	.20
Hypertension	21,781 (87.4%)	2745 (88.1%)	.25	23,125 (85.1%)	2566 (85.1%)	.95
Stenosis ≥ 70%	22,615 (95.2%)	2924 (94.3%)	.03	20,241 (87.8%)	2692 (91.1%)	< .01
General anaesthesia	20,025 (83.1%)	296 (10.1%)	< .01	17,739 (79.4%)	343 (12.3%)	<0 .01

Note. Missing data: 0.7% of diabetes, 0.8% of cardiac history, 29.1% of pulmonary history, 48.7% of stroke, 0.8% of hypertension, 12.1% of stenosis grade, 13.9% of anaesthesia. CAS = carotid artery stenting; CEA = carotid endarterectomy.

of patients over 75 years old among asymptomatic patients were compared. A generalised linear model, accounting for country and centre clustering, was used to evaluate the difference between the two groups of countries. Patients with missing values for a specific characteristic were excluded for analysis of that part. Statistical analyses were performed using SAS v9.3 (SAS Institute Inc., Cary, NC, USA) and Microsoft Excel 2013.

RESULTS

There were 58,607 procedures conducted for carotid stenosis; the majority (89.5%) were CEA ($n = 52,434$) with only 10.5% CAS ($n = 6173$). Patients were predominantly male (64%), and 75% were over 65 years of age. The indication for treatment was asymptomatic stenosis in 48% and

symptomatic stenosis in 52%. The majority of patients (92%) had $\geq 70\%$ stenosis of the ICA. Baseline characteristics of the patients are presented in Table 2.

Risk factors

The most common risk factor among all patients treated for carotid stenosis was hypertension, with a prevalence of 63% in Norway and 92% in Hungary. The prevalence of cardiac risk factors was highest in Australia (52%) and lowest in the Denmark (24%). The proportion of diabetic patients was highest in the United States (35%) and lowest in Iceland (15%). The prevalence of pulmonary disease was only 9% in Switzerland but as high as 21% in the United States. Risk factors among asymptomatic patients and symptomatic patients were similar (Supplementary material, Tables S1 and S2).

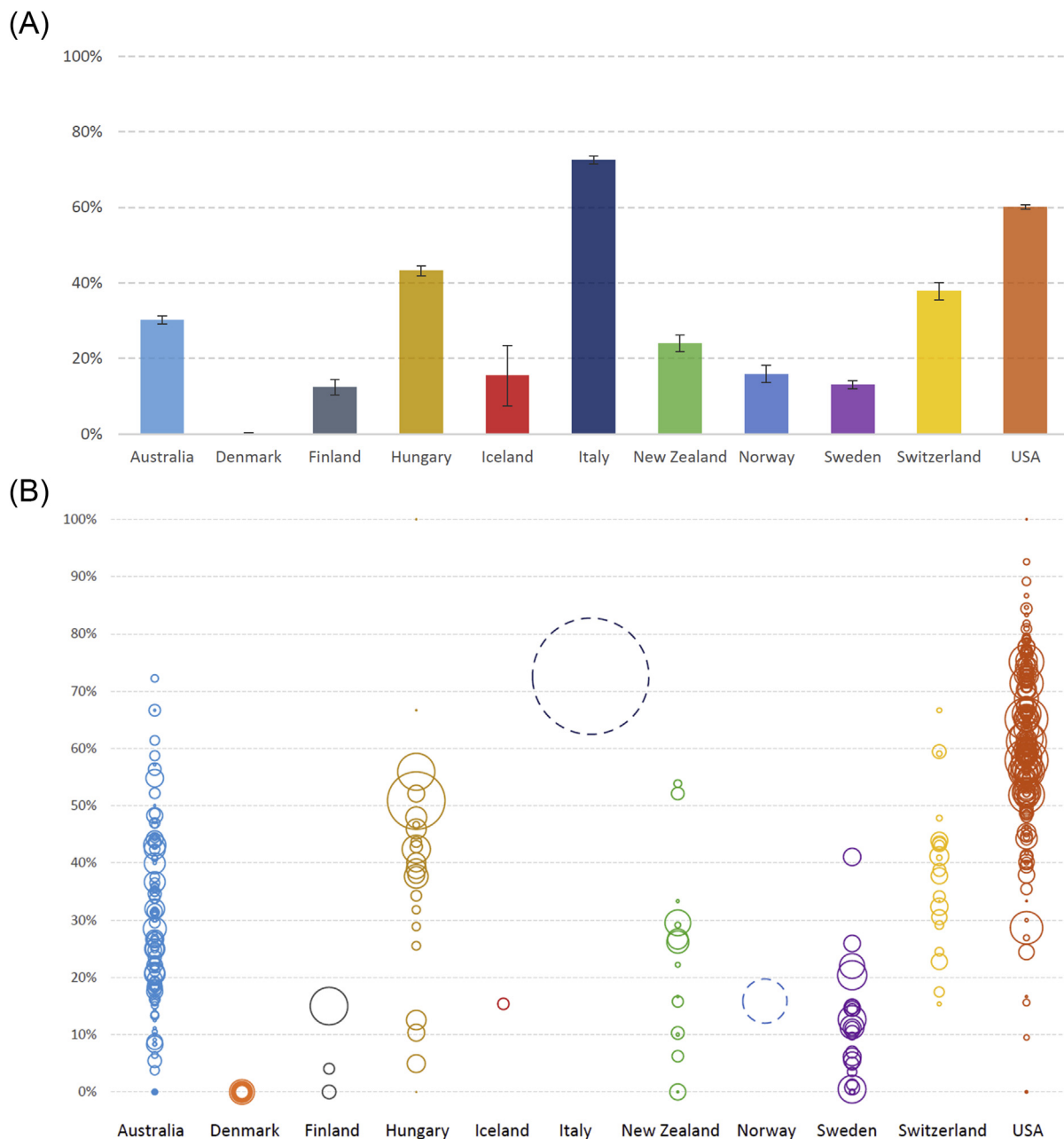


Figure 1. The proportion of asymptomatic patients in 11 participant countries (A) and in the participating hospitals in each country (B).

Variation and trends in treatment of asymptomatic versus symptomatic patients

The percentage of asymptomatic patients varied between 0.0% in Denmark and 73% in Italy (Fig. 1A). The majority of the procedures in the United States were performed on asymptomatic patients (60.1%), with minor variation among its five regions (Fig. 1A). In Australia, the proportion of asymptomatic patients was lower at 30%. The lowest proportion of asymptomatic patients was reported from the Nordic countries, varying between 0.0% in Denmark and 16% in Norway. The proportion of severe (> 70%) stenosis among asymptomatic patients was 94.3% and varied from 93.8% in USA to 100% in Iceland.

The variation in the percentage of asymptomatic patients between hospitals in most countries was as large as the variation between countries. The largest national variation was noted in the United States, with the proportion of asymptomatic patients varying from 0% to 100% among centres, followed by Australia from 0% to 72% and Hungary from 5% to 55%. In Denmark, there was no variation noted, as all treated patients were symptomatic. The variation in indication between the hospitals in each country is presented in Fig. 1B.

There was no overall trend noted with regard to the proportion of symptomatic patients treated between 2010 and 2013. Interestingly, a significant trend was seen in two countries: in Sweden the proportion of symptomatic patients increased from 81% in 2010 to 90% in 2013 ($p < .01$). In Hungary, in contrast, the proportion of symptomatic patients decreased from 61% in 2010 to 56% in 2013 ($p < .01$).

Treatment of asymptomatic patients

The majority of asymptomatic patients were treated by CEA (88%) and a minority were treated by CAS (12%). The proportion of asymptomatic patients treated by CAS varied from 0% in Finland and Iceland to 26% in Sweden (Fig. 2). The proportion of CAS procedures in asymptomatic patients

in the United States was 12%, with little variation across regions. Variation between centres was highest in the United States (0–80%), followed by Australia (0–70%), whereas in Iceland and Finland none of the centres performed CAS in asymptomatic patients (Fig. 3A).

Octogenarians made up 16% of individuals treated for asymptomatic stenosis. Among all asymptomatic patients undergoing CAS, 18% were octogenarians, with variation between countries noted from 0% in Norway to 23% in Italy. Among asymptomatic patients undergoing CEA, 16% were octogenarians with variation among countries and regions being from 0% in Finland to 20% in Italy (Supplementary Material Fig. S1). Thus, CAS was performed as often in octogenarians as in younger patients (13% vs. 12%, $p = .23$).

Women constituted 37% of all asymptomatic patients. The percentage of women treated for asymptomatic carotid stenosis varied among the countries, from 12% in Finland to 41% in the United States (Supplementary Material Fig. S2). The percentage of women treated was similar for CAS (34%) and CEA (38%) procedures.

Treatment of asymptomatic stenosis and reimbursement system

In countries with fee for service reimbursement (Australia, Italy, Switzerland, United States), 56% of all carotid procedures were performed on asymptomatic patients, in contrast to countries with population based reimbursement, where 24% of all carotid procedures were done for asymptomatic stenosis ($p < .01$) (Fig. 4). After using hierarchical analysis to account for country and centre level clustering, fee for service countries were more likely to perform procedures in asymptomatic patients than population based reimbursement countries (OR 5.8, 95% CI 4.4–7.7). Furthermore, in countries with fee for service reimbursement, 37% of the asymptomatic patients were older than 75 years compared with 20% in population based reimbursement countries, indicating a higher likelihood of treatment being offered to this group (OR 2.7, 95% CI 1.4–5.2).

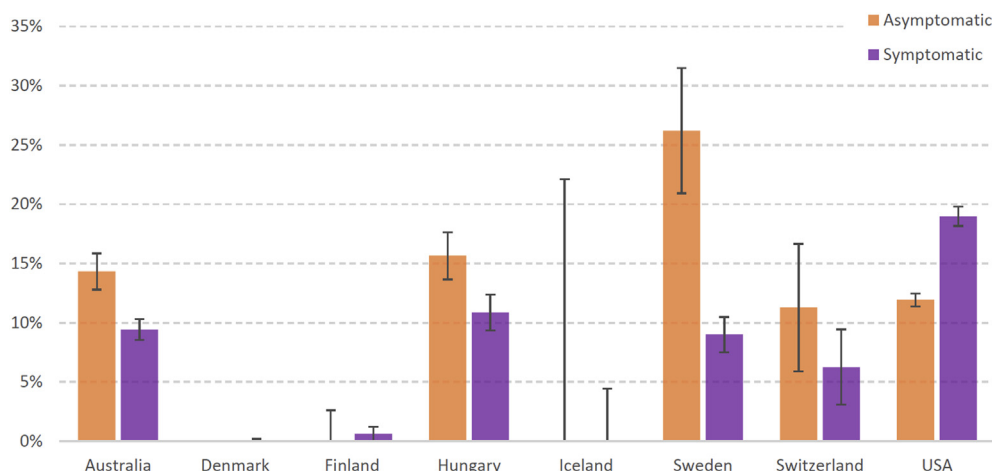


Figure 2. The proportion of carotid artery stenting for all procedures in asymptomatic and symptomatic patients in the 10 participating countries. *Note.* New Zealand and Norway were excluded from the analyses because of the absence of carotid artery stenting reporting in the registry.

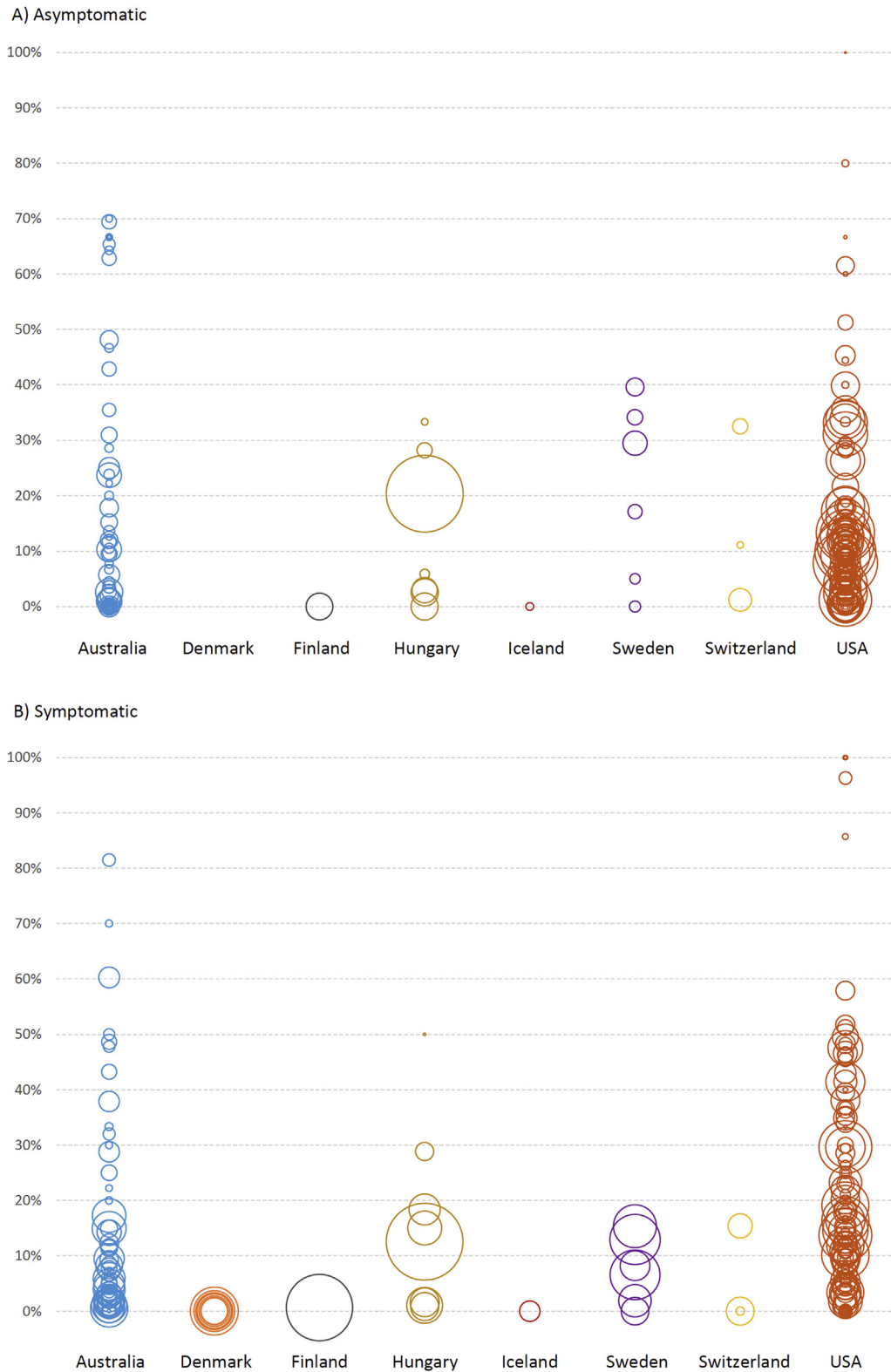


Figure 3. Variation between the hospitals in the proportion of carotid artery stenting for all carotid procedures (CAS vs. CEA). (A) Asymptomatic. (B) Symptomatic. Note. New Zealand and Norway were excluded from the analyses because of the absence of CAS reporting in the registry. CAS = carotid artery stenting; CEA = carotid endarterectomy.

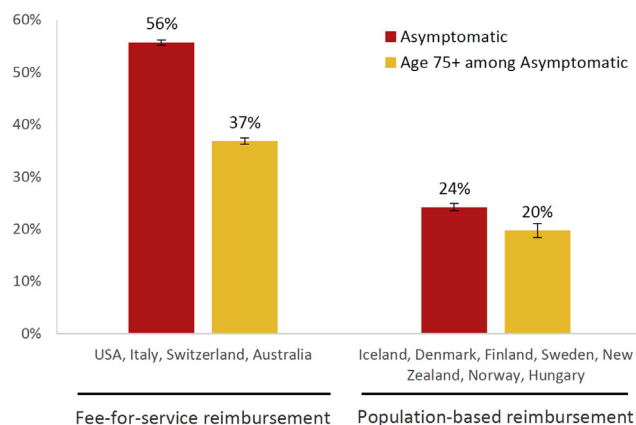


Figure 4. Treatment of asymptomatic stenosis and reimbursement system.

Treatment of symptomatic patients

In symptomatic patients, the majority of patients were treated by CEA (88%) and the minority of patients were treated by CAS (12%). This percentage of CAS treatment varied between 0% in Denmark and Iceland and 19% in the United States (Fig. 2). Variation between centres was highest in Australia (0–81%) and the United States (0–96%) whereas in Denmark and Iceland CAS was not performed to treat symptomatic patients (Fig. 3B). In Europe the variation between the centres was highest in Hungary (0–29%), and Sweden and Switzerland (0–15%).

Of all symptomatic patients, 19% were octogenarians; the proportion was similar in CAS (18%) and CEA (19%) patients. The variation between countries was higher among CAS patients (0% in Norway to 29% in Switzerland) than CEA patients (8% in Hungary to 25% in New Zealand) (Supplementary Material Fig. S1).

Variation in the percentage of women treated for symptomatic disease overall was high, with the percentage of women lowest in Switzerland (29%) and Australia (30%) and highest in the United States (38%) (Supplementary Material Fig. S2).

CAS treatment of symptomatic versus asymptomatic patients

There was considerable variation in the selection of patients for CAS treatment in different countries. CAS was used more frequently in the asymptomatic than in the symptomatic cohort in Australia ($p < .01$), Hungary ($p < 0.01$), Sweden ($p < 0.01$), and Switzerland ($p = .09$) (Fig. 2). In contrast, CAS was used more often to treat symptomatic than asymptomatic patients in Finland ($p < .40$) and the United States ($p < .01$). Denmark and Iceland did not utilise CAS at all.

Trends over time

Overall, there was a 1.2% (from 10.5% to 9.3%, $p = .02$) decrease in the proportion of CAS utilised over time, with this change occurring in both asymptomatic (from 12.2% to 10.7%, $p = .13$) and symptomatic (from 9.4% to 8.4%,

$p = .09$) patients. The biggest decrease in asymptomatic patients was seen in Australia, where the proportion of CAS decreased from 15.5% to 11.9% ($p = .07$) and in the United States, from 11.3% to 7.9% ($p < .01$). The most remarkable increase in the proportion of CAS in asymptomatic patients was noted in Hungary (from 7.6% to 17.2%; $p < .01$). In symptomatic patients the proportion of stenting decreased in two countries: Australia (from 10.9% to 8.4%, $p = .02$) and Sweden (from 11.8% to 6.5%, $p = .06$), and in other countries there were no significant trends. The proportion of CAS procedures among octogenarians varied between 9.0% and 9.6% over the time period studied, and did not show a significant trend.

DISCUSSION

The treatment of carotid stenosis is one of the best studied disease processes in vascular surgery. Several societies have published guidelines and recommendations about the indications for CEA and CAS; however, there is considerable variability among those recommendations.¹² In an analysis of 44 guidelines from 23 different regions/countries, the recommendation for the treatment of asymptomatic severe carotid stenosis varied from “CEA should be provided” to “medical treatment alone.”¹² Although based on the same RCTs, the recommendations by the Society for Vascular Surgery, the European Society for Vascular Surgery, the American Heart Association, and the European Society for Cardiology are not similar (Supplementary Material Table S3). Perhaps not surprisingly, there exist large variations in the practice of CEA and CAS among the countries and centres analysed in the current study. In this study, which is the largest registry survey reported to date, including 59,000 procedures from over 400 centres in the United States, Europe, Australia, and New Zealand, the biggest variation was seen in the treatment of patients with asymptomatic carotid stenosis. Here, the percentage of asymptomatic patients varied between 0 and 100% among centres and between 0 and 60% among countries. Furthermore, over 15% of the asymptomatic patients who underwent CEA or CAS were 80 years or older, a population that was excluded from most RCTs, and with sparse data to support their treatment. In this registry, CAS remained relatively uncommon in the treatment of carotid stenosis during the 4 year period, and the proportion of stenting was observed to decrease slightly in a few countries. This may have been a consequence of the publication of short-term results of the International Carotid Stenting Study (ICSS) in 2010, where the risk of procedure related stroke of any severity was higher following CAS than after CEA, and where the authors concluded that, until long-term results were available, CEA should remain the treatment of choice for patients who were suitable candidates for surgery.¹⁵ Because of the inconsistency of the existing guidelines and thus their failure to truly steer the clinical practice patterns, deeper collaboration between the guideline committees and consensus on the recommendations should be achieved.

The reason behind the variation in the proportion of asymptomatic patients selected for carotid treatment in different countries and centres is likely multifactorial. One major reason could be related to the physician reimbursement system in each country. In countries with fee for service reimbursement many more asymptomatic patients were treated than in countries with population based reimbursement. This is in line with recent findings regarding variations in management of abdominal aortic aneurysms in countries participating in the ICVR, indicating that patients are more likely to be treated at a lower diameter threshold for an aneurysm in countries with a fee for service reimbursement system.¹⁶ Since treatment of asymptomatic patients is less beneficial, this suggests a more aggressive approach motivated in part by reimbursement. With an undercurrent of possible overtreatment and excessive healthcare costs, the American Academy of Family Physicians began a “Choosing Wisely” campaign to reduce screening for carotid stenosis in asymptomatic patients, which was in turn supported by the United States Preventative Services Task Force statement recommending against the routine screening for carotid artery stenosis in asymptomatic patients.¹⁷ The impact of this recommendation will need to be assessed in future studies. However, it may be that these actions are insufficient and in the end the only truly effective steering force would be the change in reimbursement system so that ineffective, or even potentially harmful, procedures would not be reimbursed.

Within symptomatic patients, there was variation in the utilisation of CAS among countries. In general, CEA was preferred over CAS, but the proportion of patients undergoing CAS for symptomatic carotid stenosis varied from 0% to 9%. Furthermore a relatively high proportion (19%) of symptomatic patients treated were octogenarians, with a high fraction (18%) undergoing CAS. In randomised trials comparing CAS with CEA for symptomatic carotid stenosis, CAS was associated with a higher risk of procedure related stroke than CEA, particularly in elderly patients, but had lower attendant risks of myocardial infarction, cranial nerve palsy, and access site (vs. incision) haematomas.^{15,18–20} In a separate analysis of ICSS patients who were randomised to and received CAS, increasing age was an independent predictor of stroke, myocardial infarction, or death within 30 days of stenting, with a relative increase in risk of 17% for every 5 years of increasing age. In contrast, the long-term results of RCTs comparing CAS and CEA showed that the 5 and 10 year risk of stroke was low after either treatment in both symptomatic and asymptomatic patients, with no difference in restenosis rates.^{21,22} These conflicting data are probably responsible for influencing these variations in practice observed between centres and countries. Based on similar efficacy long term, the utilisation of CAS may increase in the future; however, this must be weighed against the increased peri-procedural complications associated with CAS in those of advanced age. Further study should be dedicated to the appropriateness of CAS in the treatment of patients ≥ 75 years of age, taking into account peri-procedural risks, long-term outcomes and life expectancy.

In this study, the proportion of asymptomatic patients in the United States was significantly lower than that in earlier reports, where over 90% of carotid artery interventions were performed in asymptomatic patients based on claims data.^{23,24} This is probably because the United States data in this study were derived from the VQI, and this registry has a more accurate representation of pre-operative symptoms than is present in administrative claims data. The unreliability of administrative data in determining symptom status has been studied and reported previously.^{25,26} These differences underscore the importance of using registry data to accurately ascertain symptom status when evaluating variations in practice and the appropriateness of intervention for carotid stenosis.

This study has several limitations. First, different degrees of validation are used in each country’s registry to assure that all relevant procedures are included, but most have a high level of capture within participating hospitals.^{27–31} Second, not all registries include all hospitals or procedures performed in the country, so this cannot be considered a population based analysis. This especially affects the proportion of CAS procedures in some countries where CAS is performed by specialists who do not participate in these vascular registries. Nonetheless, the variations observed are probably real and not biased in a particular direction. Finally, details of patient co-morbidities were not harmonized across the registries, so these factors can only be compared in general context.

CONCLUSIONS

Despite significant evidence on treatment options for carotid artery disease internationally, there is large variation in the proportion of asymptomatic patients selected for CEA/CAS among countries and centres participating in ICVR, which may be influenced by reimbursement systems. The proportion of CAS remained low during the study period in the registries of all countries. Interestingly, the variation between centres was much higher than among countries in the utilisation of CAS. Additional variation exists in the treatment of women and octogenarians. Registry collaborations spanning the globe such as ICVR can provide important data to inform and unify best practice and treatment guidelines.

CONFLICT OF INTEREST

None.

FUNDING

The project and efforts were funded in part by the US Food and Drug Administration through grant 1U01FD005478 (PI Sedrakyan). Views expressed in the publication do not necessarily reflect the official policies of the Department of Health and Human Services; nor does any mention of trade names, commercial practices, or organization imply endorsement by the US government.

APPENDIX A. SUPPLEMENTARY DATA

Supplementary data related to this article can be found at <http://dx.doi.org/10.1016/j.ejvs.2017.01.012>.

REFERENCES

- 1 North American Symptomatic Carotid Endarterectomy Trial Collaborators. Beneficial effect of carotid endarterectomy in symptomatic patients with high-grade carotid stenosis. *N Engl J Med* 1991;**325**:445–53.
- 2 The European Carotid Surgery Trials' Collaborative Group. MRC European Carotid Surgery Trial: interim results for symptomatic patients with severe (70–99%) or with mild (0–29%) carotid stenosis. *Lancet* 1991;**337**:1235–43.
- 3 Rothwell PM, Gutnikov SA, Warlow CP. European Carotid Surgery Trialists' Collaboration. Reanalysis of the final results of the European carotid surgery trial. *Stroke* 2003;**34**:514–23.
- 4 Rothwell PM, Eliasziw M, Gutnikov SA, Warlow CP, Barnett HJ. Carotid Endarterectomy Trialists Collaboration. Endarterectomy for symptomatic carotid stenosis in relation to clinical subgroups and timing of surgery. *Lancet* 2004;**363**:915–24.
- 5 Bonati LH, Fraedrich G. Carotid Stenting Trialists' Collaboration. Age modifies the relative risk of stenting versus endarterectomy for symptomatic carotid stenosis—a pooled analysis of EVA-3S, SPACE and ICSS. *Eur J Vasc Endovasc Surg* 2011;**41**:153–8.
- 6 Executive Committee for the Asymptomatic Carotid Atherosclerosis Study. Endarterectomy for asymptomatic carotid artery stenosis. *JAMA* 1995;**273**:1421–8.
- 7 Halliday A, Mansfield A, Marro J, Peto C, Peto R, Potter J, et al. Prevention of disabling and fatal strokes by successful carotid endarterectomy in patients without recent neurological symptoms: randomized controlled trial. *Lancet* 2004;**363**:1491–502.
- 8 den Hartog AG, Achterberg S, Moll FL, Kappelle LJ, Visseren FL, van der Graaf Y, et al. Asymptomatic carotid artery stenosis and the risk of ischemic stroke according to subtype in patients with clinical manifest arterial disease. *Stroke* 2013;**44**:1002–7.
- 9 Ricotta JJ, AbuRahma A, Ascher E, Eskandari M, Faries P, Lal BK. Society for vascular surgery. Updated society for vascular surgery guidelines for management of extracranial carotid disease. *J Vasc Surg* 2011;**54**:e1–31.
- 10 CD1 Liapis, Bell PR, Mikhailidis D, Sivenius J, Nicolaidis A, Fernandes e Fernandes J, et al. ESVS Guidelines Collaborators. ESVS guidelines. Invasive treatment for carotid stenosis: indications, techniques. *Eur J Vasc Endovasc Surg* 2009;**37**(4 Suppl.).
- 11 European Stroke Organisation, Tendera M, Aboyans V, Bartelink ML, Baumgartner I, Clément D, et al. ESC Committee for Practice Guidelines. ESC Guidelines on the diagnosis and treatment of peripheral artery diseases: document covering atherosclerotic disease of extracranial carotid and vertebral, mesenteric, renal, upper and lower extremity arteries: the task force on the diagnosis and treatment of peripheral artery diseases of the European Society of Cardiology (ESC). *Eur Heart J* 2011;**32**:2851–906.
- 12 Abbott AL, Paraskevas KI, Kakkos SK, Gollidge J, Eckstein HH, Diaz-Sandoval LJ, et al. Systematic review of guidelines for the management of asymptomatic and symptomatic carotid stenosis. *Stroke* 2015;**46**:3288–301.
- 13 Altman DG, Schulz KF. Statistics notes: concealing treatment allocation in randomised trials. *BMJ* 2001;**323**:446–7.
- 14 Vikatmaa P, Mitchell D, Jensen LP, Beiles B, Björck M, Halbakken E, et al. Variation in clinical practice in carotid surgery in nine countries 2005–2010. Lessons from VASCUNET and recommendations for the future of national clinical audit. *Eur J Vasc Endovasc Surg* 2012;**44**:11–7.
- 15 Ederle J, Dobson J, Featherstone RL, Bonati LH, van der Worp HB, de Borst GJ, et al. International Carotid Stenting Study investigators. Carotid artery stenting compared with endarterectomy in patients with symptomatic carotid stenosis (International Carotid Stenting Study): an interim analysis of a randomised controlled trial. *Lancet* 2010;**375**:985–97.
- 16 Beck A, Sedrakyan A, Mao J, Venermo M, Faizer R, Debus S, et al. Variations in abdominal aortic aneurysm care: a report from the International consortium of vascular registries. *Circulation* 2016;**134**(24):1948–58.
- 17 Langer-Gould AM, Anderson WE, Armstrong MJ, Cohen AB, Eccher MA, Iverson DJ, et al. The American Academy of Neurology's top five choosing wisely recommendations. *Neurology* 2013;**81**:1004–11.
- 18 Mas JL, Chatellier G, Beyssen B, Branchereau A, Moulin T, Becquemin JP, et al. EVA-3S Investigators. Endarterectomy versus stenting in patients with symptomatic severe carotid stenosis. *N Engl J Med* 2006;**355**:1660–71.
- 19 SPACE Collaborative Group, Ringleb PA, Allenberg J, Brückmann H, Eckstein HH, Fraedrich G, Hartmann M, et al. 30 day results from the SPACE trial of stent-protected angioplasty versus carotid endarterectomy in symptomatic patients: a randomised non-inferiority trial. *Lancet* 2006;**368**:1239–47.
- 20 Brott TG, Hobson 2nd RW, Howard G, Roubin GS, Clark WM, Brooks W, et al. CREST Investigators. Stenting versus endarterectomy for treatment of carotid-artery stenosis. *N Engl J Med* 2010;**363**:11–23.
- 21 Bonati LH, Dobson J, Featherstone RL, Ederle J, van der Worp HB, de Borst GJ, et al. International Carotid Stenting Study investigators. Long-term outcomes after stenting versus endarterectomy for treatment of symptomatic carotid stenosis: the International Carotid Stenting Study (ICSS) randomised trial. *Lancet* 2015;**385**:529–38.
- 22 Brott TG, Howard G, Roubin GS, Meschia JF, Mackey A, Brooks W, et al. CREST Investigators. Long-term results of stenting versus endarterectomy for carotid-artery stenosis. *N Engl J Med* 2016;**374**:1021–31.
- 23 Eslami MH, McPhee JT, Simons JP, Schanzer A, Messina LM. National trends in utilization and postprocedure outcomes for carotid artery revascularization 2005 to 2007. *J Vasc Surg* 2011;**53**:307–15.
- 24 Rockman CB, Garg K, Jacobowitz GR, Berger JS, Mussa FF, Cayne NS, et al. Outcome of carotid artery interventions among female patients, 2004 to 2005. *J Vasc Surg* 2011;**53**:1457–64.
- 25 Hertzner NR. The Nationwide Inpatient Sample may contain inaccurate data for carotid endarterectomy and carotid stenting. *J Vasc Surg* 2012;**55**:263–6.
- 26 Bensley RP, Yoshida S, Lo RC, Fokkema M, Hamdan AD, Wyers MC, et al. Accuracy of administrative data versus clinical data to evaluate carotid endarterectomy and carotid stenting. *J Vasc Surg* 2013;**58**:412–9.
- 27 Venermo M, Lees T. International Vascunet validation of the Swedvasc registry. *Eur J Vasc Endovasc Surg* 2015;**50**:802–8.
- 28 Bergqvist D, Björck M, Lees T, Menyhei G. Validation of the VASCUNET registry — pilot study. *Vasa* 2014;**43**:141–4.
- 29 Troeng T, Malmstedt J, Björck M. External validation of the Swedvasc Registry: a first-time individual cross-matching with the unique personal identity number. *Eur J Vasc Endovasc Surg* 2008;**36**:705–12.
- 30 Cronenwett JL, Likosky DS, Russell MT, Eldrup-Jorgensen J, Stanley AC, Nolan BW. VSGNNE. A regional registry for quality assurance and improvement: the vascular study group of Northern New England (VSGNNE). *J Vasc Surg* 2007;**46**:1093–101.
- 31 Beiles B, Bourke BM. Validation of Australian data in the Australasian vascular audit. *Charles Barry ANZ J Surg* 2014;**84**:624–7.