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Manuscript Details

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Title	The relationship between hospital or surgeon volume and outcomes in lower limb vascular surgery in the United Kingdom and Europe
Article type	Short review

Abstract

Introduction Peripheral vascular disease is a major cause of death and disability. The extent to which volume influences outcome of lower limb (LL) vascular surgery remains unclear. This review evaluated the relationship between hospital/surgeon volume and outcome in LL surgery. Methodology Electronic databases; Medline, Embase, the Cochrane Library Databases, Science Citation Index, and CINAHL, proceedings from conferences, citations, and references of included studies were searched. Studies from Europe, of adults undergoing LL vascular surgery reporting outcomes by hospital or surgeon volume were included. Quality of studies was assessed using a modified ACROBAT-NRSI(Robins1) tool. Association between hospital/surgeon volume and outcome were summarised using tables. Results Nine studies from different European countries, comprising 67,445 patients who had undergone diverse LL surgeries were included. Increase in hospital/surgeon volume was associated with a decrease in amputations. The evidence on association between hospital/surgeon volume and mortality was contradictory, but mortality and amputations may co-vary by hospital volume. There were an insufficient number of studies reporting on hospitals/surgeons repeated surgeries but their results suggest an association between high volume hospitals/surgeons and high volume of repeated revascularisations. The associations between hospital/surgical volume on adverse events and length of hospitalisation were inconclusive. Conclusion This review found an association between high volume hospitals/surgeons and fewer amputations. This finding has implications on re-organisation of vascular surgery services, however due to the small number and poor quality of some of the included studies, decisions on reorganisation of LL vascular surgery services should be supplemented by results from clinical audits. There is need for standardisation of definition of volume stratification of outcomes by patient's clinical conditions.

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1 **Title page**

2 **The relationship between hospital or surgeon volume and outcomes in**
3 **lower limb vascular surgery in the United Kingdom and Europe**

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11 **Abstract**

12 **Introduction**

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14 influences outcome of lower limb (LL) vascular surgery remains unclear. This review evaluated the
15 relationship between hospital/surgeon volume and outcome in LL surgery.

16 **Methodology**

17 Electronic databases; Medline, Embase, the Cochrane Library Databases, Science Citation Index,
18 and CINAHL, proceedings from conferences, citations, and references of included studies were
19 searched. Studies from Europe, of adults undergoing LL vascular surgery reporting outcomes by
20 hospital or surgeon volume were included. Quality of studies was assessed using a modified
21 ACROBAT-NRSI(Robins1) tool. Association between hospital/surgeon volume and outcome were
22 summarised using tables.

23 **Results**

24 Nine studies from different European countries, comprising 67,445 patients who had undergone
25 diverse LL surgeries were included. Increase in hospital/surgeon volume was associated with a
26 decrease in amputations. The evidence on association between hospital/surgeon volume and
27 mortality was contradictory, but mortality and amputations may co-vary by hospital volume. There
28 were an insufficient number of studies **reporting on hospitals/surgeons repeated surgeries but their**
29 **results suggest an association between high volume hospitals/surgeons and high volume of repeated**
30 **revascularisations**. The **associations between** hospital/surgical volume on adverse events and length
31 of hospitalisation **were inconclusive**.

32 **Conclusion**

33 **This review found an association between high volume** hospitals/surgeons **and** fewer amputations.
34 This finding has implications on re-organisation of vascular surgery services, **however** due to the

35 small number and poor quality of some of the included studies, decisions on reorganisation of LL
36 vascular surgery services should be supplemented by results from clinical audits. There is need for
37 standardisation of definition of volume stratification of outcomes by patient's clinical conditions.

38

39 **Key words:** Peripheral vascular disease; Critical leg ischaemia; Claudication; Hospital or surgeon
40 volume; Amputation; Mortality.

41 **1. Introduction**

42 Health care service commissioning groups in the United Kingdom (UK), Europe, and globally are
43 faced with the complex challenge of organizing the health delivery service so as to minimise cost,
44 maximise cost-effectiveness, local access, service quality, effectiveness in achieving better clinical
45 outcomes, and improving patients quality of life. A 2008 study by Holt et al¹ reported that higher-
46 volume hospitals/surgeons achieve better outcomes for high-risk procedures, and suggested the
47 reconfiguration of health care services based on the volume model.

48 Some researchers; Awopetu et al², Killeen et al³, Gandjour et al⁴, and Shackley et al⁵ have reviewed
49 the association between hospital/surgeon volume and outcome in lower limb vascular surgery.
50 However, of the four reviews²⁻⁵, only one² drew firm conclusions; reporting that high volume
51 hospitals (HVH) had significantly lower mortality compared with low volume hospitals (LVH). The
52 other three³⁻⁵, found inconclusive or ambiguous results, due to the small number of identified
53 studies, and the heterogeneity in their findings.

54 **1.1. Rationale for conducting the review**

55 Among previous reviews on the association between volume in LL surgery and outcome, Shackley
56 et al.,³ focused mainly on abdominal aortic aneurism (AAA) and carotid endarterectomy; including
57 only four studies considering LL surgery which found contradictory results and authors failing to
58 reach conclusions due to the small number of studies. The other reviews²⁻⁴, included studies mostly
59 conducted in the United States of America (USA), making the outcomes more relevant to USA
60 context. The significance of hospital/surgeon volume in lower limb (LL) vascular surgery, in
61 influencing outcomes, in UK and Europe, has therefore not been clearly elucidated. There is need
62 for an up-to-date evidence relevant to European settings, to aid in the planning and delivery of
63 healthcare in a manner which will maximise local access, viability, and service quality, in the UK
64 and Europe, hence the importance of this review.

65 1.2. Objectives of the review

66 This study aimed to investigate:

- 67 1. The relationship between the volume of LL vascular surgery undertaken by individual
68 surgeons and risk of mortality, amputation, repeat surgery, length of hospitalisation, and
69 adverse events (AEs).
- 70 2. The relationship between the volume of LL vascular surgery undertaken in individual hospitals
71 and risk of mortality, amputation, repeat surgery, length of hospitalisation, and AEs.

72 2. Methodology

73 2.1. Search strategy

74 The review followed the PRISMA guideline and a protocol as registered on PROSPERO
75 (http://www.crd.york.ac.uk/PROSPERO/display_record.asp?ID=CRD42014014850).

76 Comprehensive literature searches were conducted on Medline and Medline in Process, Embase, the
77 Cochrane Library Databases, Science Citation Index, and CINAHL. Proceedings from five key
78 conferences held between 2010 and 2015, and citations and references of included studies were also
79 searched. Literature searching involved two phases; an initial strategy based on a 2000 systematic
80 review by Michaels et al⁶, was adapted and run in MEDLINE and other electronic databases as
81 detailed in Appendix 1. A second search extended the initial strategy using the keywords and index
82 terms focussing on surgical procedures and patient outcomes. Further relevant terms for these
83 concepts were generated by consulting with the clinicians in the project team. Details of data
84 sources and the search strategies are provided in Appendix 1.

85 2.2. Inclusion and exclusion criteria

86 The research question was focused using the PICOS criteria. Study selection was based on pre-
87 specified criteria summarised in Table 1.

88 2.3. Study selection and quality assessment

89 Titles and abstracts of all records were screened by EG and PP. Full text papers were retrieved for
90 studies that appeared to meet inclusion criteria. When needed, a third reviewer (EP or ME) was
91 consulted to resolve disagreements. Data was extracted using a pre-piloted Excel form. Abstracted
92 data included study characteristics (e.g. year and place of publication, study design, and
93 characteristics of participants), and relevant outcomes reported according to specified strata of
94 hospital or surgeon volume. Study quality was assessed using a modified version of A Cochrane
95 Risk Of Bias Assessment Tool: for Non-Randomized Studies of Interventions (ACROBAT-NRSI;
96 now known as Robins1)⁷ tool. Details of the tool and the domains used in the assessment are
97 provided in Appendix 2. A second reviewer double-checked data from all included studies (EG/PP).
98 Disagreements were resolved by discussion with a third reviewer (EP/ME).

99 2.4. Data analysis

100 Due to the heterogeneity in the types of procedures carried out in included studies (endarterectomy,
101 bypass, stents, or angioplasty), and case-mix (gangrene, ischaemia or claudication), a meta-analysis
102 could not be conducted; therefore a narrative synthesis was undertaken. Odds ratios and other raw
103 data of outcomes by hospital or surgeon volume were summarised using tables.

104 3. Results

105 The search from all sources identified 16,719 records. After removing duplicates, the abstracts and
106 titles of 14,486 were screened for eligibility. Twenty seven (27) full articles seemed to meet the
107 inclusion criteria, and were retrieved and read in full. Nine studies⁸⁻¹⁶ met the inclusion criteria and
108 were included (Figure 1). A list of studies excluded at full text level and reasons for exclusion is
109 given in Appendix 3.

110 3.1. Characteristics of included studies

111 3.1.1. Study design and location: All studies were from Europe, of which three^{8,9,13} were from the
112 United Kingdom, one¹² from UK and the Ireland, two^{10,14} from Sweden, two^{11,16} from Finland, and

113 one¹⁵ from Denmark. Studies included in this review were mainly observational studies that utilised
114 clinical/administrative data (Table 2); two studies^{9,13} retrospectively analysed data on vascular
115 procedures extracted from the Hospital Episodes Statistic (HES) database (for 2002 to 2006; and
116 2007 to 2011), the other seven studies^{8,10-12,14-16} analysed retrospectively collected data from
117 different vascular projects. Together the nine studies recruited 67,445 patients, with 439 as the
118 lowest number and 31,821 as the highest, and varied in duration from 3 months to 20 years. Only
119 one of the nine studies¹¹ reported both hospital and surgeon specific volume outcomes. Five
120 studies^{8-10,13,15} reported outcomes by hospital volume only, whereas three^{12,14,16} reported surgeon
121 volume only. There was heterogeneity with regard to the definition of surgeon and hospital volume
122 by studies. Six studies^{9,11-14,16} classified volume as quantiles, whereas three^{8,10,15} used continuous
123 volume. The designation of a low-volume hospital ranged from 2 to <20 procedures, and a high-
124 volume institution from >20 to >67. Low volume surgeons were defined as those performing 10 up
125 to 20 surgeries annually, and high-volume surgeons as those performing >10 to >50 surgeries per
126 year (Table 2).

127 3.1.2. Case and procedure mix: Patients who had LL surgeries in the included studies had a mean
128 age range of 62 to 74.5 years (median 66 to 71 years), and mostly male; percentage male range 46%
129 to 70% (Table 2). The types of procedures and indications for surgery greatly differed by studies;
130 Moxey et al⁹ analysed data for femoropopliteal and femorodistal bypasses in patients with
131 intermitted claudication or gangrene, whereas Troeg et al¹⁴ investigated outcomes after
132 femoropopliteal grafting in patients with chronic leg ischaemia or claudication. The procedures in
133 Kantonen et al¹¹ included endarterectomies, patch-angioplasties, and percutaneous transluminal
134 angioplasties (PTA). Other procedures included infrainguinal reconstructions in patients with
135 critical leg ischaemia^{10,12}, elective and non-elective stenting of the iliac artery¹³, and unspecified
136 vascular surgeries in patients with critical leg ischaemia⁸ (Table 2).

137 3.1.3. Assessment of bias: Study quality was assessed using a modified version of the ACROBAT-
138 NRSI (Robins1)⁷. All the studies were considered to have high risk of selection bias (Figure 2).

139 Studies that had used quantiles to define hospital/surgeon volume^{9,11-14} were considered to have
140 high risk of volume measurement bias. Four studies^{8-10,14}, did not report details of number of
141 patients not included in the final analysis, and were therefore classified as having unclear risk of
142 attrition. Studies that had prospectively recorded outcomes^{11,12,14-16} were considered to have low
143 risk of bias of outcome measurement, especially for mortality; however those which had used
144 healthcare administrative databases^{8,9,13}, were classified as having high risk of outcome
145 measurement bias. Five studies^{9,11,14-16} adjusted for, or compared prevalence of various confounders
146 at baseline¹², and were deemed to have low risk of confounding, whereas the others, either did not
147 adjust for confounders, or adjusted for only age and sex, and were thought to be highly to
148 moderately confounded. Most of the studies^{8,9,11-16}, did not mention whether analyses conducted
149 were based on a prior published protocol, and were therefore classified as having unclear risk of
150 reporting bias.

151 **3.2. Volume and post-operative amputations**

152 3.3.1. Hospital volume and amputations: Three studies⁹⁻¹¹ investigated this outcome and all found
153 an association between volume and amputation (Table 3). Specifically, Moxey et al⁹, reported that
154 at 1 year, high volume hospitals had lower secondary major amputations, in patients who had
155 femoropopliteal bypass surgery (OR: 0.955, 95% CI: 0.928–0.983 p=0.002), and femorodistal bypass
156 (OR: 0.658 (0.517–0.838, p= < 0.001). Kantonen et al¹¹ reported a similar outcome 30 days post-
157 operation (OR: 1.49, 95% CI: 1.0 - 2.25, p = 0.05), whereas Elfstrom et al¹⁰ found significant
158 association at both 30 days and 1 year post-operation (OR: 5.01, 95% CI: 2.24 – 3.41, p = 0.01, and
159 OR: 2.05, 95% CI: 1.24 – 3.42, p = 0.01 respectively).

160 3.3.2. Surgeon volume and amputations: Three studies^{11,12,16} reported the association between
161 surgeon volume and post-operative amputations 30 days post-surgery and all found a correlation
162 between surgeon volume and secondary amputations. Kantonen et al¹¹ and Biancari et al¹⁶, who
163 adjusted for most of the confounders, found that experienced surgeons performed fewer post-
164 operative amputations (OR: 1.89, 95% CI: 1.15 - 2.80, p = 0.01 and OR: 0.40, 95% CI: 0.18–0.91, p

165 = 0.03 respectively). Further, the VSGBI¹² study, which did not adjust for confounders, reported a
166 similar outcome (OR: 0.41, 95% CI: 0.24 – 0.69, p = 0.0006) (see Table 3). The indication for
167 surgery in all the three studies^{11,12,16} was critical leg ischaemia.

168 3.3. Volume and mortality

169 3.2.1. Hospital volume and mortality: Five studies^{9-11,13,15}, reported data on hospital volume and
170 mortality (Table 4). Four of these^{9-11,15}, adjusted for most confounders, whereas one¹³, adjusted only
171 for age and sex.

172 The evidence on this outcome was contradictory, with two of the five studies reporting an
173 association; Moxey et al⁹ found an association between increase in hospital volume and a decrease
174 in mortality during index admission (OR: 0.960, 95% CI: 0.929–0.992, p = 0.014), but not at 1 year
175 (OR: 0.987, 95% CI: 0.966–1.007, p = 0.197), in femoropopliteal bypass but not in femorodistal
176 procedures (Table 4). Elfstorm et al¹⁰, reported an association between an increase in hospital
177 volume and decrease in mortality at 1 year (OR: 1.66, 95% CI: 1.06 - 2.60). Over half of the
178 patients in Moxey et al⁹ (55% femoropopliteal/54% femorodistal) had surgery due to intermittent
179 claudication whereas all patients in Elfstorm et al¹⁰ were operated on because of chronic critical
180 limb ischaemia. The definition of volume ranged from 11.2 to 110.7 patients per annum in Moxey
181 et al⁹ and 85 to 115 patients per annum in Elfstorm et al¹⁰; these might confound the outcome. The
182 insignificant finding in femorodistal bypass surgeries suggests poor outcome in lower extremity
183 vascular disease.

184 The other three studies, Kantonen et al¹¹, Bredahl et al¹⁵ and Goode et al¹³, found no association
185 between hospital volume and 30 day mortality post-operative (Table 4). The indications for surgery
186 in^{11,15} were chronic critical limb ischaemia or intermittent claudication, but Goode et al¹³ did not
187 report the conditions that necessitated surgery. The definition of volume also differed among these
188 studies; Kantonen et al¹¹ using a cut-off of 20, Goode et al¹³ a range of 1 to 111 in elective and 613
189 for non-elective, while Bredahl et al¹⁵ used continuous annual number of cases; these might
190 confound the outcome. The result could also be obscured by patient-mix.

191 3.2.2. Surgeon volume and mortality: Three studies^{11,12,16}, reported data on surgeon volume and
192 mortality (Table 3). Of these two Kantonen et al¹¹, and Biancari et al¹⁶, adjusted for most of the
193 confounders, whereas VSGBI¹², did not adjust for confounders. All found no association between
194 surgeon volume and in-hospital or 30 days mortality (Table 4). Patients in all the three studies^{11,12,16}
195 presented with critical leg ischaemia, but the definition of volume quantiles differed; Kantonen et
196 al¹¹ and the Vascular Society of Great Britain and Ireland (VSGBI)¹² used a cut-off of 10, whereas
197 Biancari et al¹⁶ used 40 and this might have affected outcome. In all the three studies^{11,12,16}, outcome
198 was within 30 days post-surgery. It is possible that the outcomes could be different if they were
199 measured 1 year post surgery.

200 3.4. Volume and number of re-operations

201 3.4.1. Hospital volume and volume of re-operations: Only one study Moxey et al⁹ reported
202 association between hospital volume and number of repeated surgery in patients with intermittent
203 claudication and other conditions. They found that high volume hospitals conducted more revisional
204 bypass procedures at 1 year (OR: 1.031, 95% CI: 1.005–1.057, p=0.018), but not during index
205 admission (OR: 1.017, 95% CI: 0.965–1.070, p=0.532). No such association was observed in
206 femorodistal surgeries, suggesting poor outcome in lower extremity bypasses (Table 5).

207 3.4.2. Surgeon experience and volume of revascularisations: Two studies, the VSGBI¹² and
208 Biancari et al¹⁶ investigated the association between surgeon volume and rates of revascularisation
209 or limb salvage. The VSGBI¹² found that surgeons with a lower annual experience tended to
210 undertake fewer revascularisations (60.6% vs. 74.9%; $\chi^2= 8.9$, $p = 0.003$), and that low
211 volume/experienced surgeons had a lower mean limb salvage rate than high volume/experienced
212 surgeons (65.4 vs. 81.3, $\chi^2= 12.8$, $p = 0.0003$). In addition, Biancari et al¹⁶ also reported a similar
213 finding (Table 5).

214 The small number and poor quality of the included studies, included in the above two analyses,
215 makes it difficult to draw any firm conclusions on association between volume and repeated
216 surgery.

217 3.5. Volume and any adverse events

218 Surgical operations for peripheral vascular disease are associated with a number of adverse events
219 including systemic or wound infection/patency, bleeding/haemorrhage, lesions and gangrene,
220 cardiac and pulmonary comorbidities, renal failure, or prolonged hospitalisations which might result
221 in bed sores (pressure ulcers)^{17,18}. In this review, four of the included studies investigated the impact
222 of hospital^{9,13,15} and surgeon volume¹⁴, respectively, on occurrence of any adverse events (Table 6),
223 while three studies reported the impact of hospital^{8,13} and surgeon volume¹⁶ on length of
224 hospitalisation (LOS)-(Table 7).

225 3.5.1. Hospital volume and AEs: Evidence from three studies^{9,13,15} that reported this outcome was
226 inconclusive; Moxey et al⁹ found that an increase in volume was associated with a decrease in AEs
227 during index admission in femoropopliteal bypass surgeries (OR: 0.968; 95% CI, 0.940–0.998;
228 $p=0.034$), but not in femorodistal surgeries (ORs not reported). A similar finding was reported by
229 Bredahl et al¹⁵. On the contrary, Goode et al¹³, who adjusted only for age and sex, found no
230 association between hospital volume and AEs occurring during admission (OR: 1.0, 95%CI: 1.0 –
231 1.0) for both elective and non-elective surgery (Table 6). The conflicting outcomes here may be
232 either due to differences in patient-mix, volume quantiles used, or locality of vascular insufficiency.

233 3.5.2. Surgeon volume and AEs: Only Troeg et al¹⁴ analysed the association between surgeon
234 volume and AEs. They found no association between volume and any AEs (Table 6). It is difficult
235 to draw any conclusions on the association between surgeon volume and AEs as only one study had
236 data on this outcome.

237 3.6. Volume and length of hospitalisation (LOS)

238 3.6.1. Hospital volume and LOS: Two studies^{8,13} analysed the association between hospital volume
239 and LOS and reported contradicting results. Goode et al¹³ found no association between hospital
240 volume and LOS, regression coefficient -0.010, 95% CI: -0.045 – 0.26 for elective, and -0.310, 95%
241 CI: -0.642 – 0.022 for non-elective iliac artery operations. However Berridge et al⁸ found clearly

242 marked difference in LOS between high and low volume hospitals among patients who had major
243 amputations (Table 7). The association between hospital volume and LOS cannot therefore be
244 determined.

245 3.6.2. Surgeon volume and LOS: Only one study Biancari et al¹⁶ reported on surgeon volume and
246 LOS, and found no association (Table 7). Since only one study reported on this outcome, it is
247 difficult to ascertain the significance of surgeon volume on LOS.

248 **4. Discussion and conclusion**

249 This review found an association between an increase in hospital⁹⁻¹¹ or surgeon^{11,16} volume and
250 decrease in post-operation amputations. **There may be an association between high volume**
251 **hospitals/surgeons and number of repeated surgeries, but we did not find enough studies to enable**
252 **us draw firm conclusions on this outcome.** The direction of association between hospital volume
253 and risk of mortality is inconclusive; whilst some studies found that high volume hospitals had
254 lower mortality rates^{9,10}, others^{11,13,15} found no such association. **However, the evidence suggests**
255 **that mortality and amputations may co-vary by hospital volume. Also,** the association between
256 volume and length of hospitalisation and AEs **was inconclusive.** Our finding on association between
257 volume and amputations agrees with previous studies^{2,6,19,20}, **and** that about hospital volume and
258 mortality is similar to reviews by Awopetu et al², Gandjour et al⁴, Killeen et al³, and Shackley et al⁵;
259 who also found **inconclusive** or ambiguous results on association between volume and mortality.

260 The heterogeneity in findings could be confounded by the diverse case-mix (including, among
261 others; chronic/critical leg ischaemia, or chronic/intermittent claudication²¹, and different types of
262 procedures (endarterectomies, angioplasties, elective or non-elective stenting, infrainguinal
263 reconstructions, femoropopliteal or femorodistal bypasses) in LL vascular surgery. The type of
264 procedure a patient receives largely depends on the severity of their illness^{22,23}. Some studies have
265 reported that patients with chronic leg ischaemia are more likely to undergo amputations^{22,23}. In
266 some of the studies, indication for surgery and type of procedure were adjusted for, and were found

267 to be independent significant predictors of amputation and mortality^{10,11,15}, apart from hospital
268 volume. Given that the type of procedure a patient receives is dependent on the patients clinical
269 presentation^{22,23}, the possibility that differences in the findings in the studies included in this review,
270 were confounded by differences in case-mix between hospitals and differences in types of
271 procedures patients received, should be borne in mind when interpreting our results. **Unfortunately,**
272 **studies included in this review did not provide outcome data (on the relationship between**
273 **hospital/surgeon volumes) stratified by indication for surgery and therefore we could not carry out a**
274 **stratified analysis on the effect of volume on this variable. Also, the conclusions, in the included**
275 **studies, relate to a range of different surgical and endovascular procedures and to earlier and more**
276 **recent publications, but none of the papers looked specifically at how the balance between**
277 **endovascular and open procedures varied over time and whether this was related to hospital or**
278 **clinician volume. Thus the changing mix of procedures, particularly if the uptake of new procedures**
279 **is related to hospital volume, may be a confounding factor, but, since the papers, did not provide**
280 **data on patient outcomes, stratified by the type of procedure, we could not conduct a stratified**
281 **analysis on this variable.**

282 Included studies used different sources of data. The majority of the studies were observational using
283 administrative databases and as such lack clinical detail. For studies that used historical data such as
284 the HES database, where major diagnosis codes were used to identify LL surgery, there may be
285 variability in coding by different hospitals, or different departments, even prospectively collected
286 data, sometimes do not capture all the available cases¹⁰, and variables of all confounding factors,
287 and this may have introduced selection bias. Also, studies included in this review were drawn from
288 a number of different countries, which might have different regional health systems and referrals
289 within those regions, and this might have further introduced selection bias. Therefore the existence
290 of selection bias, and confounding due to inability to control for all important confounders, in the
291 included studies, should be borne in mind. However, the strengths of this study include that a

292 comprehensive literature search, focusing on studies conducted in the UK and Europe, and a
293 rigorous systematic review of the identified studies, were conducted.

294 The definition of mortality varied from in-hospital mortality^{12,13}, to 30-days⁹⁻¹¹ and 1-year^{9,10} post-
295 operatives. However, no consistency was observed between the mortality proxy measure used and
296 outcome. Thus the two studies that analysed in-hospital mortality^{12,13} found no association between
297 volume and mortality, whereas the three that employed 30-day mortality⁹⁻¹¹ found conflicting
298 results. The difference in findings in⁹⁻¹¹ could as well be due to case-mix. Some authors have argued
299 that the aim of vascular surgery is to improve long term quality of life of the patient, and 30-day
300 follow-up would only give an indication of the technical validity of the procedure; suggesting that a
301 1-year follow-up may give the true benefit of the surgery²⁴. However, in this review, there was a
302 contradiction; Elfstorm et al.,¹⁰ found a significant variation in mortality by hospital volume at 1
303 year, whereas Moxey et al⁹ found no association. More research is needed to determine the best
304 mortality time points in LL vascular surgery.

305 The quantification of hospital or surgeon volume has not been standardised. Six studies^{9,11-14,16}
306 classified volume as quantiles, whereas three^{8,10,15} used continuous volume. The justification for
307 choosing the different volume cut-off points has varied from study to study. Kantonen et al¹¹ chose
308 the cut-off point of 10 cases per surgeon and 20 cases per hospital based on the VSGBI¹² report
309 which suggested that surgeons who conducted >10 operations per year had better results. In
310 summarising the results of the SWEDVASC study, Bergqvist et al²⁴ suggested that confidence
311 intervals are likely to be wide unless there are at least 50 operations, and urged that comparisons of
312 surgeon/hospital volume <50 should not be conducted. In this review, the findings among the six
313 studies that used volume quantiles^{9,11-14,16}, and the three^{8,10,15} that employed continuous volume,
314 varied. As the significance of the various volume quantiles has not been clearly demonstrated, we
315 recommend continuous volume be used as a standard volume measure in future volume research.

316 We could have constructed funnel plots to investigate the existence of publication bias in this
317 review. However, for each outcome, we only had three to four studies reporting that outcome. Such

318 a funnel plot would therefore not give any meaningful result. But only studies published in the
319 English language were included in this review, and this may have introduced publication bias. Also
320 five^{10-12,14,16} of the nine included studies in the final analysis are 18 years old or more. Therefore,
321 the possibility of publication bias should therefore be borne in mind when interpreting our results.
322 However, this review was systematic and was based on rigorous methods of literature search, and
323 we hope that this might have eliminated most of **this** bias.

324 **5. Conclusion**

325 **This review found an association between** high volume hospitals/surgeons **and** fewer post-operative
326 amputations. **There might also be an association between high hospital/surgeon volume** and more
327 repeated surgeries. The **association** between hospital/surgeon volume and mortality is still unclear,
328 but mortality and **number of post-operative** amputations may co-vary by hospital volume. **An**
329 **association between high** hospital and surgeon volume **and less number of post-operative**
330 amputations has implications on re-organisation of vascular surgery services. However due to the
331 small number and poor quality of some of the included studies, decisions on reorganisation of lower
332 limb vascular surgery services should be supported by clinical audits, **where outcomes in vascular**
333 **surgery are stratified by indications for surgery and types of procedures;** prospective mandatory
334 clinical audits on this subject, commissioned and funded through national registries and quality
335 improvement programmes, could aid in generating more evidence. There is need for the
336 standardisation of reporting and definition of volumes in vascular research.

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343

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1 **Title page**

2 **The relationship between hospital or surgeon volume and outcomes in**
3 **lower limb vascular surgery in the United Kingdom and Europe**

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11 **Abstract**

12 **Introduction**

13 Peripheral vascular disease is a major cause of death and disability. The extent to which volume
14 influences outcome of lower limb (LL) vascular surgery remains unclear. This review evaluated the
15 relationship between hospital/surgeon volume and outcome in LL surgery.

16 **Methodology**

17 Electronic databases; Medline, Embase, the Cochrane Library Databases, Science Citation Index,
18 and CINAHL, proceedings from conferences, citations, and references of included studies were
19 searched. Studies from Europe, of adults undergoing LL vascular surgery reporting outcomes by
20 hospital or surgeon volume were included. Quality of studies was assessed using a modified
21 ACROBAT-NRSI(Robins1) tool. Association between hospital/surgeon volume and outcome were
22 summarised using tables.

23 **Results**

24 Nine studies from different European countries, comprising 67,445 patients who had undergone
25 diverse LL surgeries were included. Increase in hospital/surgeon volume was associated with a
26 decrease in amputations. The evidence on an association between hospital/surgeon volume and
27 mortality was contradictory, but mortality and amputations may co-vary by hospital volume. There
28 were an insufficient number of studies reporting on the other variables to draw firm conclusions;
29 but their results suggest high volume hospitals may undertake more repeated
30 surgeries/revascularisations and limb salvage. The impact of hospital/surgical volume on adverse
31 events and length of hospitalisation could not be determined.

32 **Conclusion**

33 High volume hospitals/surgeons may undertake fewer amputations and mortality and amputations
34 may co-vary. The finding that hospital and surgeon volume affected the number of secondary

35 amputations has implications on re-organisation of vascular surgery services. However due to the
36 small number and poor quality of some of the included studies, decisions on reorganisation of LL
37 vascular surgery services should be supplemented by results from clinical audits. There is need for
38 standardisation of definition of volume stratification of outcomes by patient's clinical conditions.

39

40 **Key words:** Peripheral vascular disease; Critical leg ischaemia; Claudication; Hospital or surgeon
41 volume; Amputation; Mortality.

42 **1. Introduction**

43 Health care service commissioning groups in the United Kingdom (UK), Europe, and globally are
44 faced with the complex challenge of organizing the health delivery service so as to minimise cost,
45 maximise cost-effectiveness, local access, service quality, effectiveness in achieving better clinical
46 outcomes, and improving patients quality of life. A 2008 study by Holt et al¹ reported that higher-
47 volume hospitals/surgeons achieve better outcomes for high-risk procedures, and suggested the
48 reconfiguration of health care services based on the volume model.

49 Some researchers; Awopetu et al², Killeen et al³, Gandjour et al⁴, and Shackley et al⁵ have reviewed
50 the association between hospital/surgeon volume and outcome in lower limb vascular surgery.
51 However, of the four reviews²⁻⁵, only one² drew firm conclusions; reporting that high volume
52 hospitals (HVH) had significantly lower mortality compared with low volume hospitals (LVH). The
53 other three³⁻⁵, found inconclusive or ambiguous results, due to the small number of identified
54 studies, and the heterogeneity in their findings.

55 **1.1. Rationale for conducting the review**

56 Among previous reviews on the association between volume in LL surgery and outcome, Shackley
57 et al.,³ focused mainly on abdominal aortic aneurism (AAA) and carotid endarterectomy; including
58 only four studies considering LL surgery which found contradictory results and authors failing to
59 reach conclusions due to the small number of studies. The other reviews²⁻⁴, included studies mostly
60 conducted in the United States of America (USA), making the outcomes more relevant to USA
61 context. The significance of hospital/surgeon volume in lower limb (LL) vascular surgery, in
62 influencing outcomes, in UK and Europe, has therefore not been clearly elucidated. There is need
63 for an up-to-date evidence relevant to European settings, to aid in the planning and delivery of
64 healthcare in a manner which will maximise local access, viability, and service quality, in the UK
65 and Europe, hence the importance of this review.

66 1.2. Objectives of the review

67 This study aimed to investigate:

- 68 1. The relationship between the volume of LL vascular surgery undertaken by individual
69 surgeons and risk of mortality, amputation, repeat surgery, length of hospitalisation, and other
70 adverse events (AEs).
- 71 2. The relationship between the volume of LL vascular surgery undertaken in individual hospitals
72 and risk of mortality, amputation, repeat surgery, length of hospitalisation, and other AEs.

73 2. Methodology

74 2.1. Search strategy

75 The review was undertaken according to the PRISMA guideline and followed a registered protocol
76 on PROSPERO
77 (http://www.crd.york.ac.uk/PROSPERO/display_record.asp?ID=CRD42014014850).

78 Comprehensive literature searches were conducted on Medline and Medline in Process, Embase, the
79 Cochrane Library Databases, Science Citation Index, and CINAHL. Proceedings from five key
80 conferences held between 2010 and 2015, and citations and references of included studies were also
81 searched. Literature searching involved two phases; an initial strategy based on a 2000 systematic
82 review by Michaels et al⁶, was adapted and run in MEDLINE and other electronic databases as
83 detailed in Appendix 1. A second search iteration extended the initial strategy using the keywords
84 and index terms focussing on surgical procedures and patient outcomes. Further relevant terms for
85 these concepts were generated by consulting with the clinicians in the project team. Details of data
86 sources and the search strategies are provided in Appendix 1.

87 2.2. Inclusion and exclusion criteria

88 The research question was focused using the PICOS criteria. Study selection was based on pre-
89 specified criteria summarised in Table 1.

90 **2.3. Study selection and quality assessment**

91 Titles and abstracts of all records were screened by PP and EG. Full text papers were retrieved for
92 studies that appeared to meet inclusion criteria. When needed, a third reviewer (EP or ME) was
93 consulted to resolve disagreements. Data was extracted using a pre-piloted Excel form. Abstracted
94 data included study characteristics (e.g. year and place of publication, study design, and
95 characteristics of participants), and relevant outcomes reported according to specified strata of
96 hospital or surgeon volume. Study quality was assessed using a modified version of A Cochrane
97 Risk Of Bias Assessment Tool: for Non-Randomized Studies of Interventions (ACROBAT-NRSI)⁷
98 (Robins1) tool. Details of the tool and the domains used in the assessment are provided in Appendix
99 2. A second reviewer double-checked data from all included studies (PP/EG). Disagreements were
100 resolved by discussion with a third reviewer (EP/ME).

101 **2.4. Data analysis**

102 Due to the heterogeneity in the types of procedures carried out in included studies (endarterectomy,
103 bypass, stents, or angioplasty), and case-mix (gangrene, ischaemia or claudication), a meta-analysis
104 could not be conducted; therefore a narrative synthesis was undertaken. Odds ratios and other raw
105 data of outcomes by hospital or surgeon volume were summarised using tables.

106 **3. Results**

107 The search from all sources identified 16,719 records. After removing duplicates, the abstracts and
108 titles of 14,486 were screened for eligibility. Twenty seven (27) full articles seemed to meet the
109 inclusion criteria, and were retrieved and read in full. Nine studies⁸⁻¹⁶ met the inclusion criteria and
110 were included (Figure 1). A list of studies excluded at full text level and reasons for exclusion is
111 given in Appendix 3.

112 **3.1. Characteristics of included studies**

113 3.1.1. Study design: Studies included in this review were mainly observational studies that utilised
114 clinical/administrative data (Table 2); two studies^{9,13} retrospectively analysed data on vascular

115 procedures extracted from the Hospital Episodes Statistic (HES) database (for 2002 to 2006; and
116 2007 to 2011), the other seven studies^{8,10-12,14-16} analysed retrospectively collected data from
117 different vascular projects. All studies were from Europe, of which three^{8,9,13} were from the United
118 Kingdom, one¹² from UK and the Ireland, two^{10,14} from Sweden, two^{11,16} from Finland, and one¹⁵
119 from Denmark. Together the nine studies recruited 67,445 patients, with 439 as the lowest number
120 and 31,821 as the highest, and varied in duration from 3 months to 20 years. Only one of the nine
121 studies¹¹ reported both hospital and surgeon specific volume outcomes. Five studies^{8-10,13,15} reported
122 outcomes by hospital volume only, whereas three^{12,14,16} reported surgeon volume only. There was
123 heterogeneity with regard to the definition of surgeon and hospital volume by studies. Six
124 studies^{9,11-14,16} classified volume as quantiles, whereas three^{8,10,15} used continuous volume. The
125 designation of a low-volume hospital ranged from 2 to <20 procedures, and a high-volume
126 institution from >20 to >67. On the other hand, low volume surgeons were defined as those
127 performing 10 up to 20 surgeries annually, and high-volume surgeons as those performing >10 to
128 >50 surgeries per year (Table 2).

129 3.1.2. Case and procedure mix: Patients who had LL surgeries in the included studies had a mean
130 age range of 62 to 74.5 years (median 66 to 71 years), and mostly male; percentage male range 46%
131 to 70% (Table 2). The types of procedures and indications for surgery greatly differed by studies;
132 Moxey et al⁹ analysed data for femoropopliteal and femorodistal bypasses in patients with
133 intermitted claudication or gangrene, whereas Troeg et al¹⁴ investigated outcomes after
134 femoropopliteal grafting in patients with chronic leg ischaemia or claudication. The procedures in
135 Kantonen et al¹¹ included endarterectomies, patch-angioplasties, and percutaneous transluminal
136 angioplasties (PTA). Other procedures included infrainguinal reconstructions in patients with
137 critical leg ischaemia^{10,12}, elective and non-elective stenting of the iliac artery¹³, and unspecified
138 vascular surgeries in patients with critical leg ischaemia⁸ (Table 2).

139 3.1.3. Assessment of bias: Study quality was assessed using a modified version of the ACROBAT-
140 NRSI (Robins1)⁷. All the studies were considered to have high risk of selection bias (Figure 2).

141 Studies that had used quantiles to define hospital/surgeon volume^{9,11-14} were considered to have
142 high risk of volume measurement bias. Four studies^{8-10,14}, did not report details of number of
143 patients not included in the final analysis, and were therefore classified as having unclear risk of
144 attrition. Studies that had prospectively recorded outcomes^{11,12,14-16} were considered to have low
145 risk of bias of outcome measurement, especially for mortality; however those which had used
146 healthcare administrative databases^{8,9,13}, were classified as having high risk of outcome
147 measurement bias. Five studies^{9,11,14-16} adjusted for, or compared prevalence of various confounders
148 at baseline¹², and were deemed to have low risk of confounding, whereas the others, either did not
149 adjust for confounders, or adjusted for only age and sex, and were thought to be highly to
150 moderately confounded. Most of the studies^{8,9,11-16}, did not mention whether analyses conducted
151 were based on a prior published protocol, and were therefore classified as having unclear risk of
152 reporting bias.

153 **3.2. Volume and mortality**

154 3.2.1. Hospital volume and mortality: Five studies^{9-11,13,15}, reported data on hospital volume and
155 mortality (Table 3). Four of these^{9-11,15}, adjusted for most confounders, whereas one¹³, adjusted only
156 for age and sex.

157 The evidence on this outcome was contradictory, with two of the five studies reporting an
158 association; Moxey et al⁹ found an association between increase in hospital volume and a decrease
159 in mortality during index admission (OR: 0.960, 95% CI: 0.929–0.992, $p = 0.014$), but not at 1 year
160 (OR: 0.987, 95% CI: 0.966–1.007, $p = 0.197$), in femoropopliteal bypass but not in femorodistal
161 procedures (Table 3). Similarly, Elfstorm et al¹⁰, reported an association between an increase in
162 hospital volume and decrease in mortality at 1 year (OR: 1.66, 95% CI: 1.06 - 2.60). Over half of
163 the patients in Moxey et al⁹ (55% femoropopliteal/54% femorodistal) had surgery due to
164 intermittent claudication whereas all patients in Elfstorm et al¹⁰ were operated on because of
165 chronic critical limb ischaemia. The definition of volume ranged from 11.2 to 110.7 patients per
166 annum in Moxey et al⁹ and 85 to 115 patients per annum in Elfstorm et al¹⁰; these might confound

167 the outcome. The insignificant finding in femorodistal bypass surgeries suggests poor outcome in
168 lower extremity vascular disease.

169 On the other hand the other three studies, Kantonen et al¹¹, Bredahl et al¹⁵ and Goode et al¹³, found
170 no association between hospital volume and 30 day mortality post-operative (Table 3). The
171 indications for surgery in^{11,15} were chronic critical limb ischaemia or intermittent claudication, but
172 Goode et al¹³ did not report the conditions that necessitated surgery. The definition of volume also
173 differed among these studies; Kantonen et al¹¹ using a cut-off of 20, Goode et al¹³ a range of 1 to
174 111 in elective and 613 for non-elective, while Bredahl et al¹⁵ used continuous annual number of
175 cases; these might confound the outcome. The result could also be obscured by patient-mix.

176 3.2.2. Surgeon volume and mortality: Three studies^{11,12,16}, reported data on surgeon volume and
177 mortality (Table 3). Of these two Kantonen et al¹¹, and Biancari et al¹⁶, adjusted for most of the
178 confounders, whereas VSGBI¹², did not adjust for confounders. All found no association between
179 surgeon volume and in-hospital or 30 days mortality (Table 3). Patients in all the three studies^{11,12,16}
180 presented with critical leg ischaemia, but the definition of volume quantiles differed; Kantonen et
181 al¹¹ and the Vascular Society of Great Britain and Ireland (VSGBI)¹² used a cut-off of 10, whereas
182 Biancari et al¹⁶ used 40 and this might have affected outcome. In all the three studies^{11,12,16}, outcome
183 was within 30 days post-surgery. It is possible that the outcomes could be different if they were
184 measured 1 year post surgery.

185 **3.3. Volume and post-operative amputations**

186 3.3.1. Hospital volume and amputations: Three studies⁹⁻¹¹ investigated this outcome and all found
187 an association between volume and amputation (Table 4). Specifically, Moxey et al⁹, reported that
188 at 1 year, high volume hospitals had lower secondary major amputations, in patients who had
189 femoropopliteal bypass surgery (OR: 0.955, 95% CI: 0.928–0.983 p=0.002), and femorodistal bypass
190 (OR: 0.658 (0.517–0.838, p= < 0.001). Kantonen et al¹¹ reported a similar outcome 30 days post-
191 operation (OR: 1.49, 95% CI: 1.0 - 2.25, p = 0.05), whereas Elfstorm et al¹⁰ found significant

192 association at both 30 days and 1 year post-operation (OR: 5.01, 95% CI: 2.24 – 3.41, p = 0.01, and
193 OR: 2.05, 95% CI: 1.24 – 3.42, p = 0.01 respectively).

194 3.3.2. Surgeon volume and amputations: Three studies^{11,12,16} reported the association between
195 surgeon volume and post-operative amputations 30 days post-surgery and all found a correlation
196 between surgeon volume and secondary amputations. Kantonen et al¹¹ and Biancari et al¹⁶, who
197 adjusted for most of the confounders, found that experienced surgeons performed fewer post-
198 operative amputations (OR: 1.89, 95% CI: 1.15 - 2.80, p = 0.01 and OR: 0.40, 95% CI: 0.18–0.91, p
199 = 0.03 respectively). Similarly, the VSGBI¹² study, which did not adjust for confounders, reported
200 a similar outcome (OR: 0.41, 95% CI: 0.24 – 0.69, p = 0.0006) (see Table 4). The indication for
201 surgery in all the three studies^{11,12,16} was critical leg ischaemia.

202 **3.4. Volume and re-operation, revascularisations, or limb salvage**

203 3.4.1. Hospital volume and re-operation: Only one study Moxey et al⁹ reported association between
204 hospital volume and repeated surgery in patients with intermitted claudication and other conditions.
205 They found that high volume hospitals conducted more revisional bypass procedures at 1 year (OR:
206 1.031, 95%, CI: 1.005–1.057, p=0.018), but not during index admission (OR: 1.017, 95% CI:
207 0.965–1.070, p=0.532). No such association was observed in femorodistal surgeries, suggesting
208 poor outcome in lower extremity bypasses (Table 5).

209 3.4.2. Surgeon experience and volume of revascularisations and limb salvage: Two studies, the
210 VSGBI¹² and Biancari et al¹⁶ investigated the association between surgeon volume and rates of
211 revascularisation or limb salvage. The VSGBI¹² found that surgeons with a lower annual experience
212 tended to undertake fewer revascularisations (60.6% vs. 74.9%; $\chi^2= 8.9$, p = 0.003), and that low
213 volume/experienced surgeons had a lower mean limb salvage rate than high volume/experienced
214 surgeons (65.4 vs. 81.3, $\chi^2= 12.8$, p = 0.0003). In addition, Biancari et al¹⁶ also reported a similar
215 finding (Table 5). The small number and poor quality of the included studies, makes it difficult to
216 draw any firm conclusions.

217 3.5. Volume and any adverse events

218 Surgical operations for peripheral vascular disease are associated with a number of adverse events
219 including systemic or wound infection/patency, bleeding/haemorrhage, lesions and gangrene,
220 cardiac and pulmonary comorbidities, renal failure, or prolonged hospitalisations which might result
221 in bed sores (pressure ulcers)^{17,18}. In this review, four of the included studies investigated the impact
222 of hospital^{9,13,15} and surgeon volume¹⁴, respectively, on occurrence of any adverse events (Table 6),
223 while three studies reported the impact of hospital^{8,13} and surgeon volume¹⁶ on length of
224 hospitalisation (LOS)-(Table 7).

225 3.5.1. Hospital volume and AEs: Evidence from three studies^{9,13,15} that reported this outcome was
226 inconclusive; Moxey et al⁹ found that an increase in volume was associated with a decrease in AEs
227 during index admission in femoropopliteal bypass surgeries (OR: 0.968; 95% CI, 0.940–0.998;
228 $p=0.034$), but not in femorodistal surgeries (ORs not reported). A similar finding was reported by
229 Bredahl et al¹⁵. On the contrary, Goode et al¹³, who adjusted only for age and sex, found no
230 association between hospital volume and AEs occurring during admission (OR: 1.0, 95%CI: 1.0 –
231 1.0) for both elective and non-elective surgery (Table 6). The conflicting outcomes here may be
232 either due to differences in patient-mix, volume quantiles used, or locality of vascular insufficiency.

233 3.5.2. Surgeon volume and AEs: Only Troeg et al¹⁴ analysed the association between surgeon
234 volume and AEs. They found no association between volume and any AEs (Table 6). It is difficult
235 to draw any conclusions on the association between surgeon volume and AEs as only one study had
236 data on this outcome.

237 3.6. Volume and length of hospitalisation (LOS)

238 3.6.1. Hospital volume and LOS: Two studies^{8,13} analysed the association between hospital volume
239 and LOS and reported contradicting results. Goode et al¹³ found no association between hospital
240 volume and LOS, regression coefficient -0.010, 95% CI: -0.045 – 0.26 for elective, and -0.310, 95%
241 CI: -0.642 – 0.022 for non-elective iliac artery operations. However Berridge et al⁸ found clearly

242 marked difference in LOS between high and low volume hospitals among patients who had major
243 amputations (Table 7). The association between hospital volume and LOS cannot therefore be
244 determined.

245 Surgeon volume and LOS: Only one study Biancari et al¹⁶ reported on surgeon volume and LOS,
246 and found no association (Table 7). Since only one study reported on this outcome, it is difficult to
247 ascertain the significance of surgeon volume on LOS.

248 **4. Discussion and conclusion**

249 This review found an association between an increase in hospital⁹⁻¹¹ or surgeon^{11,16} volume and
250 decrease in post-operation amputations. The direction of association between hospital volume and
251 risk of mortality is inconclusive; whilst some studies found that high volume hospitals had lower
252 mortality rates^{9,10}, others^{11,13,15} found no such association. The results suggest that high volume
253 hospitals may undertake more revascularisations, limb salvage, and repeated surgeries, but the
254 association between volume and length of hospitalisation and AEs could not be determined. Our
255 finding on association between volume and amputations agrees with previous studies^{2,6,19,20}.
256 Whereas that about hospital volume and mortality is similar to reviews by Awopetu et al², Gandjour
257 et al⁴, Killeen et al³, and Shackley et al⁵ who also found inclusive or ambiguous results on
258 association between volume and mortality.

259 The heterogeneity in findings could be confounded by the diverse case-mix (including, among
260 others; chronic/critical leg ischaemia, or chronic/intermittent claudication²¹, and different types of
261 procedures (endarterectomies, angioplasties, elective or non-elective stenting, infrainguinal
262 reconstructions, femoropopliteal or femorodistal bypasses) in LL vascular surgery. The type of
263 procedure a patient receives largely depends on the severity of their illness^{22,23}. Some studies have
264 reported that patients with chronic leg ischaemia are more likely to undergo amputations^{22,23}.
265 Unfortunately, studies included in this review did not provide outcome data (on the relationship
266 between hospital/surgeon volumes) stratified by indication for surgery or type of procedure

267 conducted, and therefore we could not carry out a stratified analysis on the effect of volume by
268 these variables. However, in some of the studies, indication for surgery and type of procedure were
269 adjusted for, and were found to be independent significant predictors of amputation and
270 mortality^{10,11,15}, apart from hospital volume. Given that the type of procedure a patient receives is
271 dependent on the patients clinical presentation^{22,23}, the possibility that differences in the findings in
272 the studies included in this review, were confounded by differences in case-mix between hospitals
273 and differences in types of procedures patients received, should be borne in mind when interpreting
274 our results.

275 Included studies used different sources of data. The majority of the studies were observational using
276 administrative databases and as such lack clinical detail. For studies that used historical data such as
277 the HES database, where major diagnosis codes were used to identify LL surgery, there may be
278 variability in coding by different hospitals, or different departments, even prospectively collected
279 data, sometimes do not capture all the available cases¹⁰, and variables of all confounding factors,
280 and this may have introduced selection bias. Also, studies included in this review were drawn from
281 a number of different countries, which might have different regional health systems and referrals
282 within those regions, and this might have further introduced selection bias. Therefore the existence
283 of selection bias, and confounding due to inability to control for all important confounders, in the
284 included studies, should be borne in mind. However, the strengths of this study include that a
285 comprehensive literature search, focusing on studies conducted in the UK and Europe, and a
286 rigorous systematic review of the identified studies, were conducted.

287 The definition of mortality varied from in-hospital mortality^{12,13}, to 30-days⁹⁻¹¹ and 1-year^{9,10} post-
288 operative. However, no consistency was observed between the mortality proxy measure used and
289 outcome. Thus the two studies that analysed in-hospital mortality^{12,13} found no association between
290 volume and mortality, whereas the three that employed 30-day mortality⁹⁻¹¹ found conflicting
291 results. The difference in findings in⁹⁻¹¹ could as well be due to case-mix. Some authors have argued
292 that the aim of vascular surgery is to improve long term quality of life of the patient, and 30-day

293 follow-up would only give an indication of the technical validity of the procedure. Suggesting that a
294 1-year follow-up may give the true benefit of the surgery²⁴. However, in this review, there was a
295 contradiction; Elfstorm et al.,¹⁰ found a significant variation in mortality by hospital volume at 1
296 year, whereas Moxey et al⁹ found no association. More research is needed to determine the best
297 mortality time points in LL vascular surgery.

298 The quantification of hospital or surgeon volume has not been standardised. Six studies^{9,11-14,16}
299 classified volume as quantiles, whereas three^{8,10,15} used continuous volume. The justification for
300 choosing the different volume cut-off points has varied from study to study. Kantonen et al¹¹ chose
301 the cut-off point of 10 cases per surgeon and 20 cases per hospital based on the VSGBI¹² report
302 which suggested that surgeons who conducted >10 operations per year had better results. In
303 summarising the results of the SWEDVASC study, Bergqvist et al²⁴ suggested that confidence
304 intervals are likely to be wide unless there are at least 50 operations, and urged that comparisons of
305 surgeon/hospital volume <50 should not be conducted. In this review, the findings among the six
306 studies that used volume quantiles^{9,11-14,16}, and the three^{8,10,15} that employed continuous volume,
307 varied. As the significance of the various volume quantiles has not been clearly demonstrated, we
308 recommend continuous volume be used as a standard volume measure in future volume research.

309 We could have constructed funnel plots to investigate the existence of publication bias in this
310 review. However, for each outcome, we only had three to four studies reporting that outcome. Such
311 a funnel plot would therefore not give any meaningful result. But only studies published in the
312 English language were included in this review, and this may have introduced publication bias. Also
313 five^{10-12,14,16} of the nine included studies in the final analysis are 18 years old or more. Therefore,
314 the possibility of publication bias should therefore be borne in mind when interpreting our results.
315 However, this review was systematic and was based on rigorous methods of literature search, and
316 we hope that this might have eliminated most of the bias.

317 **5. Conclusion**

318 The evidence from this review suggests that high volume hospitals/surgeons may undertake fewer
319 post-operative amputations. They might also undertake more revascularisations, and repeated
320 surgeries. The relationship between hospital/surgeon volume and mortality is still unclear, but
321 mortality and amputations may co-vary by hospital volume. The finding that hospital and surgeon
322 volume affected the number of secondary amputations has implications on re-organisation of
323 vascular surgery services. However due to the small number and poor quality of some of the
324 included studies, decisions on reorganisation of lower limb vascular surgery services should be
325 supported by clinical audits. Prospective mandatory clinical audits on this subject, commissioned
326 and funded through national registries, and quality improvement programmes funded using standard
327 definitions, could aid in generating more evidence. There is need for the standardisation of reporting
328 and definition of volumes in vascular research.

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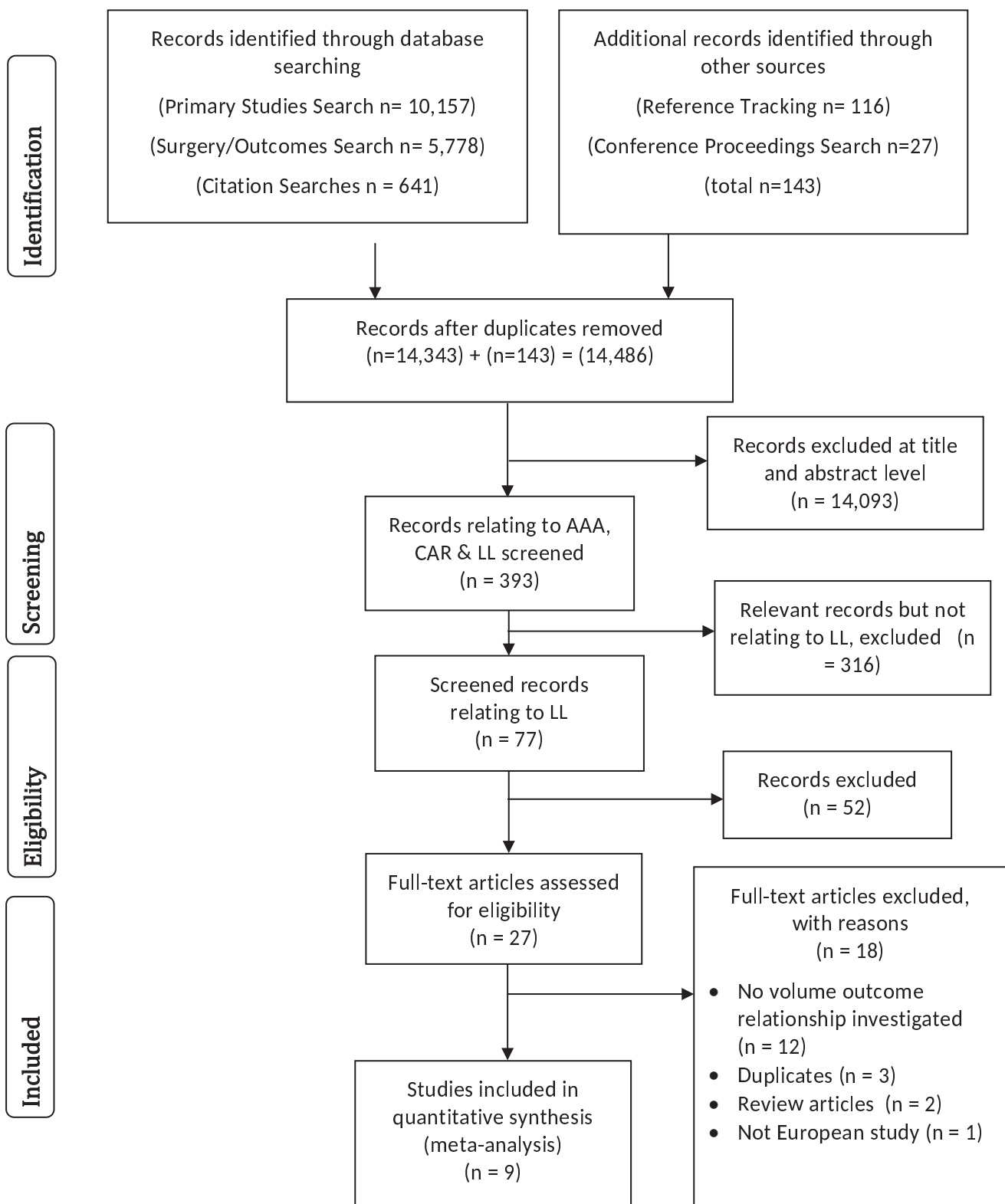
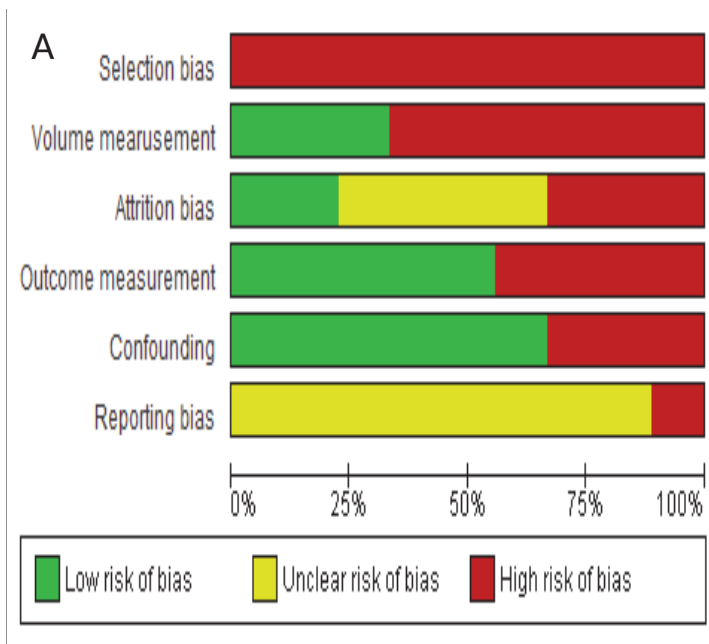


Figure 1: PRISMA diagram of search results and study selection

Notes: The search strategy combined terms for surgeries for three vascular conditions; abdominal aortic aneurysm repair (AAA), carotid endarterectomy (CER) or stenting (CAS), and lower limb vascular surgeries (LL). Three hundred and ninety three (393) abstracts and titles were screened to tag the studies whether they related to AAA, CAR, or LL and whether they were conducted in Europe or not. Among the 77 studies tagged as relating to LL, 25 were deemed relevant and full texts downloaded and assessed for eligibility for inclusion into the LL review.



B

	Selection bias	Volume measurement	Attrition bias	Outcome measurement	Confounding	Reporting bias
Berridge 1998	-	+	?	-	-	?
Biancari 2000	-	-	+	+	+	?
Bredahl 1997	-	+	-	+	+	?
Elfstorm 1996	-	+	?	-	+	-
Goode 2013	-	-	+	-	-	?
Kantonen 1998	-	-	-	+	+	?
Moxey 2012	-	-	?	-	+	?
Troeg 1992	-	-	?	+	+	?
VSGBI 1995	-	-	-	+	-	?

Figure 2: Risk of bias assessment of the included studies, A) summary for all the studies, B) bias by category in the 9 studies. Notes: Studies that had used quantiles to define hospital/surgeon volume were considered to have high risk of volume measurement bias, as the accuracy of the applied volume quantiles to correctly predict outcome cannot be ascertained. Studies that had prospectively recorded outcomes were considered to have low risk of bias of outcome measurement especially for mortality, however the measurement of other outcomes, other than mortality could still be biased. Those which had used healthcare administrative database were classified as having high risk of outcome measurement bias, because of the possibility that inter-hospital variation in codes for a similar condition and coding errors might have introduced bias.

Table 1: Inclusion and exclusion criteria

PICOS	Inclusion criteria	Exclusion criteria
Population	Studies recruiting adults (aged 18 years and over) undergoing elective or emergency peripheral vascular surgery	Studies in patients <18 years old, undefined/ mixed groups of vascular patients or mixed vascular and non-vascular populations, where data cannot be extracted separately for the population of interest.
Intervention	Patients who had undergone invasive procedures intended to maintain and repair blood vessels external to the heart and brain such as endarterectomies, bypasses, angioplasties	Patients who had undergone procedures to blood vessels of the heart or brain, such as coronary artery bypass grafting or repairs to subarachnoid haemorrhages; thoracic-aortic aneurysm repairs; renal or visceral artery procedures; interventions that are intended primarily as an aid to diagnosis; vascular surgical procedures related to acute traumatic injury
Comparator	Low vs. high volume hospitals or surgeons	Did not report outcomes by hospital/surgeon volume
Outcome	Mortality, amputation after surgery, repeated surgery, re-admission, length of hospital stay, any adverse events	Any other outcomes other than these risk factors to surgery
Study design	Prospective or retrospective designs with a contemporaneous comparison between low and high volume hospitals or surgeons.	Reviews, case reports, studies where allocation to group on the basis of outcome – (e.g. case-control studies)

Table 2: Characteristics of included studies

	Berridge et al ⁸	Elfstrom et al ¹⁰	Goode et al ¹³	Kantonen et al ¹¹	Moxey et al ⁹	Troeg et al ¹⁴	VSGBI ¹²	Bredahl et al ¹⁵	Biancari et al ¹⁶
Study design and country	Retrospective analysis of data from the CHKS database, UK	Retrospective analysis of the SWEDVASC database, Sweden	Retrospective analysis of data from HES database, UK	Retrospective analysis of data from the Finnvasc database, Finland	Retrospective analysis of data from HES database, UK	Retrospective analysis of data from the SWEDVASC database, Sweden	Clinical audit, prospective survey, UK and Ireland	Retrospective analysis of data from the Danish Vascular Registry database, Denmark	Observational study of outcomes of vascular procedures, Finland
Study duration	1995 (8 months; April-Dec)	1988-1990 (1 yr)	2007-2011 (4 yrs)	1991-1994 (3 yrs)	2002-2006 (1 yr)	1987-1989 (2 yrs)	1993 (3 months)	1993-2012 (20 yrs)	1991-1997 (6 yrs)
Sample size & (No of hospitals/ surgeons)	2,780 (3 hospitals)	809 (6 hospitals)	23,308 (262 hospitals)	2,296 (25 hospitals) No of surgeons not reported	31,821; FP (27,660, 160 hospitals), FD (4161, 140 hospitals)	809 (23 hospitals) No of surgeons not reported	590 (57 surgeons)	3767 (No of hospitals not reported)	439 (single centre study)
Definition of volume	HA, HB, HC, number of revascularisations and amputations performed by each hospital (continuous)	H1 (85) H2 (83) H3 (117) H4 (189) H5 (175), H6 (115) number of surgeries performed by each hospital (continuous)	Q1 (1-17) Q2 (18-27) Q3 (28-41) Q4 (42-66) Q5 (67-111) the total number of procedures conducted at the hospital over the 4 year period	H <20 vs >20 S <10 vs >10 operations by each hospital or surgeon/ year	FP, Q1 (11.2) Q2 (40.4) Q3, 50.0) Q4 (70.4) Q5 (110.7) FD, Q1 (2) Q2 (6.9) Q3 (10.0) Q4 (13.4) Q5 (19.0) median number of procedures performed by each hospital/ year	S1 (<20), S2 (20-50), S3 (>50), number of surgeries performed by each surgeon over the 2 years	S1 (0-10) S2 (11-20) S3 (21-30) S4 (>30) number of infrainguinal reconstructions performed by each surgeon annually	Continuous annual hospital case load	>40 during the entire study period (6 years) = experienced surgeon

Table 2: Characteristics of included studies, continued

	Berridge et al ⁸	Elfstrom et al ¹⁰	Goode et al ¹³	Kantonen et al ¹¹	Moxey et al ⁹	Troeg et al ¹⁴	VSGBI ¹²	Bredahl et al ¹⁵	Biancari et al ¹⁶
Mean/Median age/ years (SD/range)	Not reported	74.5	Elective median 66 (59 - 74), non-elective median 61.6 (62 - 78)	70.5	FP (69), FD (71)	Intermittent claudication median 66 (55-86), critical ischaemia 73 (61-96)	Not reported	62 (SD, 9)	71.8 (range, 24-96)
Sex (Males)%	Not reported	54% (410/764)	67.2% (13,456/20,027)	58% (10,21/1761)	FP (68%), FD (70%)	Intermittent claudication (65.5), critical ischaemia (50.0)	60.0% (406/679)	46% (1734/3767)	51.9% (223/430)
Indications for surgery & procedures carried out	Vascular/venous surgeries in patients with critical leg ischaemia	Infrainguinal operations in patients with ulcer or gangrene, rest pain, claudication and other conditions	Elective/non-elective iliac artery angioplasty and stenting. (conditions not stated)	Endarterectomies and angioplasties in patients with chronic critical leg ischaemia	Femoropopliteal and femorodistal bypass in patients with intermittent claudication or gangrene)	Vascular surgeries in patients with chronic leg ischaemia or claudication	Infrainguinal reconstructions in patients with critical leg ischaemia	Aortobifemoral (ABF) or an aortobiliac (ABI) bypass for chronic critical limb ischemia or intermittent claudication	Revascularization procedures (infrapopliteal bypass grafts) to the infrapopliteal arteries in patients with critical leg ischemia.
Adjustment for confounders	Unadjusted	Adjusted for most confounders; only odds ratios for hospital 1 vs. 6 reported	Age and sex	Adjusted for most confounders	Adjusted for most confounders	Adjusted for most confounders	Unadjusted but confounders equally distributed	Adjusted for most confounders	Adjusted for most confounders

Notes: HA-hospital volume A, HB – volume B, and HC volume C, S-surgeon volume, Q1-quantile 1-Q2, quantile 2 etc, FP-Femoropopliteal bypass procedures, FD-femorodistal bypass procedures, HES-hospital episodes data, FINVASC-National vascular registry in Finland, SWEDVASC-Swedish National Registry for Vascular Surgery, CHKS-National Comparative Database (UK).

Table 3: Hospital and surgeon volume in lower limb vascular surgery and mortality

Study	Definition of volume	Indication for surgery	Time of event					
			30 days post-surgery			1 year post-surgery		
			OR	95% CI	p	OR	95% CI	p
A. Hospital volume and mortality								
<i>Adjusted for most confounders</i>								
Moxey 2012 ⁹	FP q1(<11.2), q2(40.4), q3(50.0), q4(70.4), q5(110.7)	Intermittent claudication 55.0%, gangrene 24%, others not stated	0.96	0.93-0.99	0.014*	0.99	0.97-1.0	0.197
	FD q1(2), q2(6.9), q3(10.0), q4(13.4), q5(19)	Intermittent claudication 54.2%, gangrene 24%, others operation not stated	No association			No association		
Elfstorm 1996 ¹⁰	q1(<85), q2(83), q3(117), q4(189), q5(175), q6(115)	Ulcer/gangrene (38%), rest pain 36%, Claudication (11%), other (14%)	1.82	0.83 - 4.00	-	1.66	1.06 - 2.60	0.05*
Kantonen 1998 ¹¹	<20 vs. >20	Chronic critical leg ischaemia	No association			-	-	-
Bredahl 1997 ¹⁵	Continuous annual number of cases	Chronic critical limb ischaemia or intermittent claudication	No association			-	-	-
<i>Adjusted for only Age and Sex</i>								
Goode 2013 ¹³	EL q1(1-17), q2(18-27), q3(28-41), q4(42-66), q5(67-111)	Conditions that necessitated operation not stated	1	1.00 - 1.00	-	-	-	-
	Non-EL q1(1-113), q2(114-163), q3(164-202), q4(202-349), q5(350-613)		1	1.00 - 1.00	-	-	-	-
B. Surgeon volume and mortality								
<i>Adjusted for most confounders</i>								
Kantonen 1998 ¹¹	<10 vs. >10	Chronic critical leg ischaemia	No association			-	-	-
Biancari 2000 ¹⁶	<40 vs >40 during the entire study period (6 years)	Critical leg ischaemia	No association			-	-	-
<i>Unadjusted</i>								
VSGBI 1995 ¹²	q1(0-10), q2(11-20), q3(21-30), q4(>30)	Critical leg ischaemia	1.1	0.58-2.07	0.76	-	-	-

Notes: FP-femoropopliteal, FD-femorodistal, EL- elective iliac artery angioplasty, Non-EL-non-elective iliac artery angioplasty, VSGBI – The vascular society of Great Britain and Ireland. No association means the authors reported in text that they found no association between volume and outcome but no odds ratios were provided. A dash (-) means data for that statistic was not provided. Volumes were defined as average annual number of procedures conducted by each hospital or surgeon. Bredahl 1997¹⁵ did not provide the exact number of procedures conducted by each hospital. .* means the statistic was significant at $\alpha = 0.05$.

Table 4: Hospital/surgeon volume in lower limb surgery and post-operative amputations

Study	Definition of volume	Indication for surgery	Time of event					
			30 days post-surgery			1 yr post-surgery		
			OR	95% CI	p	OR	95% CI	p
A) Hospital volume and amputations								
<i>Adjusted for most confounders</i>								
Moxey 2012 ⁹	FP q1(<11.2), q2(40.4), q3(50.0), q4(70.4), q5(110.7)	Intermittent claudication 55.0%, gangrene 24%, others not stated	0.96	0.92-1.00	0.06	0.96	0.93-0.98	0.002*
	FD q1(2), q2(6.9), q3(10.0), q4(13.4), q5(19)	Intermittent claudication 54.2%, gangrene 24%, others not stated	No association			0.66	0.52-0.84	< 0.001*
Elfstorm 1996 ¹⁰	q1(<85), q2(83), q3(117), q4(189), q5(175), q6(115)	Ulcer/gangrene (38%), rest pain 36%, Claudication (11%), other (14%)	5.01	2.24 - 3.41	0.01*	2.05	1.24 - 3.42	0.01*
Kantonen 1998 ¹¹	<20 vs. >20	Chronic critical leg ischaemia	1.49	1.00- 2.25	0.05*	-	-	-
B) Surgeon volume and amputations								
<i>Adjusted for most confounders</i>								
Kantonen 1998 ¹¹	<10 vs. >10	Chronic critical leg ischaemia	1.89	1.15 - 2.80	0.01*	-	-	-
Biancari 2000 ¹⁶	<40 vs >40 during the entire study period (6 years)	Critical leg ischaemia	0.40	0.18-0.91	0.03*	-	-	-
<i>Unadjusted</i>								
VSGBA 1995 ¹²	q1(0-10), q2(11-20), q3(21-30) , q4(>30)	Critical leg ischaemia	0.41	0.24-0.69	0.0006*	-	-	-

Notes: FP-femoropopliteal, FD-femorodistal, VSGBI – The vascular society of Great Britain and Ireland. No association means the authors reported in text that they found no association between volume and outcome but no odds ratios were provided. A dash (-) means data for that statistic was not provided. Volumes were defined as average annual number of procedures conducted by each hospital or surgeon.* means the statistic was significant at $\alpha = 0.05$.

Table 5: Hospital volume and repeated surgery/ Surgeon experience and limb salvage rate in lower limb vascular surgery

Study	Definition of volume	Indication for surgery	Time to event					
			30 days post-surgery			1 yr post-surgery		
			OR	95% CI	p	OR	95% CI	p
A) Hospital volume and repeated surgery								
<i>Adjusted for most confounders</i>								
Moxey 2012 ⁹	FP q1(<11.2), q2(40.4), q3(50.0), q4(70.4), q5(110.7)	Intermittent claudication 55%, gangrene 24%, others not stated	1.02	0.97-1.07	0.532	1.03	1.01-1.06	0.018*
	FD q1(2), q2(6.9), q3(10.0), q4(13.4), q5(19)	Intermittent claudication 54.2%, gangrene 24%, others not stated	No association			No association		
B) Surgeon experience and limb salvage rate								
<i>Unadjusted</i>								
Biancari 2000 ¹⁶	<40 vs >40 during the entire study period (6 years)	Critical leg ischaemia	2.36	1.36-4.11	0.002*	-	-	-
VSGBI ¹²	q1(0-10), q2(11-20), q3(21-30), q4(>30)	Critical leg ischaemia	2.93	1.69-5.09	<0,0001*	-	-	-

Notes: FP-femoropopliteal, FD-femorodistal, VSGBI – The vascular society of Great Britain and Ireland No association means the authors reported in text that they found no association between volume and outcome but no odds ratios were provided. A dash (-) means data for that statistic was not provided. Volumes were defined as average annual number of procedures conducted by each hospital or surgeon.* means the statistic was significant at $\alpha = 0.05$.

Table 6: Hospital/surgeon volume and adverse events in lower limb vascular surgery

Study	Definition of volume	Indication for surgery	Time of event						
			30 days post-surgery			1 year post-surgery			
			OR	95% CI	p	OR	95% CI	p	
A) Hospital volume and adverse events									
<i>Adjusted for most confounders</i>									
Moxey 2012 ⁹	FP	q1(<11.2), q2(40.4), q3(50.0), q4(70.4), q5(110.7)	Intermittent claudication 55.0%, gangrene 24%, others not stated	0.97	0.94-1.0	0.034*	0.99	0.97-1.00	0.132
	FD	q1(2), q2(6.9), q3(10.0), q4(13.4), q5(19)	Intermittent claudication 54.2%, gangrene 24%, others not stated	No association			No association		
<i>Adjusted for age and sex</i>									
Goode 2013 ¹³	EL	q1(1-17), q2(18-27), q3(28-41), q4(42-66), q5(67-111)	Conditions that necessitated operation not stated	1	1.0 - 1.0	-	-	-	-
	Non-EL	q1(1-17), q2(18-27), q3(28-41), q4(42-66), q5(67-111)	Conditions that necessitated operation not stated	1	1.0 - 1.0	-	-	-	-
Bredahl 1997 ¹⁵		Continuous annual number of cases	Chronic critical limb ischaemia or intermittent claudication	Increase in volume was associated with fewer adverse events*			-	-	-
B) Surgeon volume and adverse events									
<i>Unadjusted</i>									
Troeg 1992 ¹⁴		S1 (<20), S2 (20-50), S3 (>50)	Chronic critical limb ischaemia	2.1	0.45-3.75	0.15	-	-	-

Notes: FP-femoropopliteal, FD-femorodistal. EL- elective iliac artery angioplasty, Non-EL-non-elective iliac artery angioplasty. No association means the authors reported in text that they found no association between volume and outcome but no odds ratios were provided. A dash (-) means data for that statistic was not provided. Volumes were defined as average annual number of procedures conducted by each hospital or surgeon.* means the statistic was significant at $\alpha = 0.05$.

Table 7: Hospital and surgeon volume of vascular surgery and length of hospitalisation

Study		Definition of volume	Indication for surgery	Procedure	Low volume	High volume	Conclusion
A) Hospital volume and length of hospitalisation							
<i>Adjusted for age and sex</i>							
Goode 2013	EL	q1(1-17), q2(18-27), q3(28-41), q4(42-66) , q5(67-111)	Conditions that necessitated operation not stated	Iliac artery Angioplasty	1.9 days	1.8 days	No association
	Non-EL	q1(1-113), q2(114-163), q3(164-202), q4(202-349) , q5(350-613)	Conditions that necessitated operation not stated	Iliac artery Angioplasty	12.5 days	10.5 days	No association
<i>Unadjusted</i>							
Berridge		Continuous annual number of cases	Critical leg ischaemia	Major amputations	32.4 days	18.3 days	Marked difference
B) Surgeon volume and length of hospitalisation							
<i>Adjusted for most confounders</i>							
Biancari		<40 vs >40 during the entire study period (6 year)	Critical leg ischaemia	Femoropopliteal bypass	-	-	No association

Notes: EL- elective iliac artery angioplasty, Non-EL-non-elective iliac artery angioplasty. Volumes were defined as average annual number of procedures conducted by each hospital or surgeon.

Appendix 1: Search strategy

Data Sources

Data Sources Scoping Search

Medline and Medline in Process via Ovid
Embase via Ovid
The Cochrane library of systematic reviews via Wiley
Database of Abstracts of Effects (DARE) via Wiley

Data Sources Primary Studies Search

Medline and Medline in Process via Ovid
Embase via Ovid
The Cochrane library (all databases) via Wiley
Science Citation Index/ Book Citation Index - Science and Conference Proceedings Citation Index - Science via Thomson Reuters
CINAHL via EBSCO

Data Sources Surgery/Outcomes Search

As for primary studies search

Data Sources Conference Proceedings Search

The websites for the following conferences were scanned for outputs (posters or oral presentations) with any relevance to the topics of volume of vascular surgery and patient outcomes:

UK Vascular Society.

<http://www.vascularsociety.org.uk>

European Vascular Society

<http://www.esvs.org>

BSIR (British Society of Interventional Radiology)

<http://www.bsir.org>,

ISVS (International Society for Vascular Surgery)

(<http://www.isvs.com>)

SVS (Society for Vascular Surgery)

<http://www.vascularweb.org/educationandmeetings/2015vam/Pages/home.aspx>.

Data Sources Citation Search

Science Citation Index (Web of Science) via Thomson Reuters

Scopus via Elsevier (where results not found in WoS)

Search Strategies

Scoping Search

Database: Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations and Ovid MEDLINE(R)
<1946 to Present>

Search Strategy:

-
- 1 exp Vascular Surgical Procedures/ut [Utilization] (1806)
 - 2 vascular surg\$.mp. (33992)
 - 3 exp Endarterectomy/ut (176)
 - 4 Peripheral Arterial Disease/ (2447)
 - 5 exp Peripheral Vascular Diseases/ (45653)
 - 6 Intermittent Claudication/ (7157)
 - 7 Amputation/ (16658)
 - 8 (Peripheral arterial disease\$ or peripheral vascular disease\$).mp. (23163)
 - 9 intermittent claudication.mp. (8577)
 - 10 (Aortic aneurysm or triple A or true aneurysm).mp. (43979)
 - 11 Aortic Aneurysm/ (18847)
 - 12 Aortic Aneurysm, Abdominal/ (14281)
 - 13 (carotid disease or carotid angioplasty or carotid surgery).mp. (3114)
 - 14 exp Carotid Artery Diseases/ (38964)
 - 15 exp Carotid arteries/ (51386)
 - 16 (transient isch?emic attack or TIA or stroke).mp. (196320)
 - 17 exp Stroke/ (91854)
 - 18 Cerebrovascular Disorders/ (44229)
 - 19 exp Brain Ischemia/ (85599)
 - 20 (venous insufficiency or varicose vein\$ or venous leg ulcer\$).mp. (20286)
 - 21 exp Venous Insufficiency/ (6093)
 - 22 exp Varicose Veins/ (15810)
 - 23 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 (485513)
 - 24 (surgeon volume or case volume or hospital Volume or workload).mp. (30063)
 - 25 (surgery and (volume or outcome)).ti. (6182)
 - 26 (surgery adj5 (volume or outcome)).ab. (13415)
 - 27 exp Physician's Practice Patterns/ (43633)
 - 28 exp Health services misuse/ (7557)
 - 29 exp Utilization review/ (10730)
 - 30 (surgery adj3 (utilisation or utilization)).ti,ab. (252)
 - 31 24 or 25 or 26 or 27 or 28 or 29 or 30 (106459)

32 23 and 31 (4107)
33 Meta-Analysis as Topic/ (14509)
34 meta analy\$.tw. (71100)
35 metaanaly\$.tw. (1422)
36 Meta-Analysis/ (53861)
37 (systematic adj (review\$1 or overview\$1)).tw. (60909)
38 exp Review Literature as Topic/ (8068)
39 or/33-38 (136655)
40 cochrane.ab. (34565)
41 embase.ab. (33513)
42 (psychlit or psyclit).ab. (932)
43 (psychinfo or psycinfo).ab. (14233)
44 (cinahl or cinhal).ab. (11624)
45 science citation index.ab. (2193)
46 bids.ab. (388)
47 cancerlit.ab. (606)
48 or/40-47 (59856)
49 reference list\$.ab. (10939)
50 bibliograph\$.ab. (12608)
51 hand-search\$.ab. (4356)
52 relevant journals.ab. (799)
53 manual search\$.ab. (2606)
54 or/49-53 (27997)
55 selection criteria.ab. (21640)
56 data extraction.ab. (11276)
57 55 or 56 (31152)
58 Review/ (1969448)
59 57 and 58 (20616)
60 Comment/ (620891)
61 Letter/ (877156)
62 Editorial/ (373781)
63 animal/ (5531985)
64 human/ (14013133)
65 63 not (63 and 64) (3985649)
66 or/60-62,65 (5328963)
67 39 or 48 or 54 or 59 (171961)
68 67 not 66 (161249)

Primary Studies Search

Database: Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations and Ovid MEDLINE(R)
<1946 to Present>

Search Strategy:

-
- 1 exp Vascular Surgical Procedures/ut [Utilization] (1816)
 - 2 vascular surg\$.mp. (34473)
 - 3 exp Endarterectomy/ (13415)
 - 4 Peripheral Arterial Disease/ (2520)
 - 5 exp Peripheral Vascular Diseases/ (45855)
 - 6 Intermittent Claudication/ (7171)
 - 7 Amputation/ (16863)
 - 8 (Peripheral arterial disease\$ or peripheral vascular disease\$).mp. (23380)
 - 9 intermittent claudication.mp. (8603)
 - 10 (Aortic aneurysm or triple A or true aneurysm).mp. (44255)
 - 11 Aortic Aneurysm/ (18915)
 - 12 Aortic Aneurysm, Abdominal/ (14335)
 - 13 (carotid disease or carotid angioplasty or carotid endarterectomy or carotid surgery).mp. (10408)
 - 14 exp Carotid Artery Diseases/ (39195)
 - 15 carotid stenosis/ (12586)
 - 16 (venous insufficiency or varicose vein\$ or venous leg ulcer\$).mp. (20408)
 - 17 exp Venous Insufficiency/ (6132)
 - 18 exp Varicose Veins/ (15867)
 - 19 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 13 or 14 or 15 or 16 or 17 or 18 (170939)
 - 20 (surgeon volume or case volume or hospital Volume or workload).mp. (30386)
 - 21 ((surgery or surgeon\$ or surgical\$) and (volume or outcome)).ti. (10958)
 - 22 ((surgery or surgeon\$ or surgical\$) adj5 (volume or outcome)).ab. (29362)
 - 23 exp Physician's Practice Patterns/ (44152)
 - 24 exp Health services misuse/ (7624)
 - 25 exp Utilization review/ (10888)
 - 26 (surgery adj3 (utilisation or utilization)).ti,ab. (261)
 - 27 20 or 21 or 22 or 23 or 24 or 25 or 26 (125387)
 - 28 19 and 27 (2535)
 - 29 10 or 11 or 12 (44255)
 - 30 27 and 29 (763)

31 limit 30 to yr="2004 -Current" (487)

32 28 or 31 (2796)

Surgery/Outcomes Search

Database: Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations and Ovid MEDLINE(R)
<1946 to Present>

Search Strategy:

1 (Profundaplasty or carotid endarterectomy or amputation or aortic aneurysm repair or aorto-bifemoral bypass or femoro-popliteal bypass or femoro-distal bypass or endovascular aneurysm repair or EVAR or (carotid adj2 stent\$) or CAS or angioplasty or balloon dilation or revascularisation or ((vascular or endovascular) adj2 (procedure or repair)) or (carotid adj2 (operation\$ or surgery or procedure\$)) or ((lower limb or arterial) adj2 (operation\$ or surgery or procedure\$)) or (arterial adj2 (operation\$ or surgery or procedure\$ or bypass or repair))).ti,ab. (101073)

2 exp *Vascular Surgical Procedures/ (140406)

3 1 or 2 (204334)

4 (re-admission or readmission or re admission or re-do or redo or re do or re-operation or reoperation or re operation or limb salvage or wound heal\$ or length of stay).ti,ab. (104217)

5 (((post-operative or post-operative or postoperative) adj2 complication\$) or mortality rate or hospital mortality or adverse outcome\$ or survival rate or treatment outcome or stroke rate or fatal outcome or case fatality rate or outcome or outcome assessment or process assessment or complication or surgical mortality monitoring or ((clinical or surgical) adj2 performance) or ((amputation or morbidity or infection) adj2 rate)).ti,ab. (978814)

6 *postoperative complications/ or *hospital mortality/ or *survival rate/ or *treatment outcome/ (129746)

7 4 or 5 or 6 (1142018)

8 3 and 7 (52014)

9 (practice pattern\$ or caseload or volume or clinical competence or surgical speciality).ti,ab. (426993)

10 *Physician's Practice Patterns/ or *Specialities, Surgical/ (25900)

11 9 or 10 (450589)

12 8 and 11 (1945)

Appendix 2: Quality assessment tool (Modified ACROBAT-NRSI)

Bias category	Judgement
Bias due to selection	
Was selection of study participants appropriate? (e.g. consecutive patients or a random sample)	yes (low risk), no (high risk, or unclear risk)
Was eligibility criteria administered uniformly across all participants and centres? (use of ICD codes or similar)	yes (low risk), no (high risk, or unclear risk)
Are baseline characteristics provided and are participant characteristics across volume groupings similar at baseline?	yes (low risk), no (high risk)
Bias due to volume measurement	
Was volume presented as continuous data measurement categorised or categorical (quartiles, quintiles etc.)	quantiles yes (high risk), continuous (low risk)
Bias due to Attrition	
Were there complete data for all participants at the end of the study? Were all study participants or cases (e.g. number of procedures) accounted for (or included) in the final analysis of results?	yes (low risk), no (high risk, or unclear risk)
Bias due to outcome measurement	
Is the measurement of outcome objective and administered uniformly throughout the course of the study (between centres and over time)?	yes (low risk), no (high risk)
Were methods of outcome measurements pre-specified and described?	yes (low risk), no (unclear risk)
Bias due to adjustment for confounding	
Was there any adjustment for confounding, no = high risk of bias, yes for any adjustment - then consider extent of adjustment and source of data used in adjustment to reach conclusion on overall risk of bias	adjusted for most confounders (low risk), adjusted for some confounders e.g. age and sex (medium risk), no adjustment (high risk)
Bias due to reporting	
Was the study pre-registered with accessible protocol?	yes (low risk), no (high risk, or unclear)
Is the reported effect estimate unlikely to be selected, on the basis of the results, from multiple analyses of the volume-outcome relationship?	yes (low risk), no (high risk)

Notes: Studies that had used quantiles to define hospital/surgeon volume were considered to have high risk of volume measurement bias, as the accuracy of the applied volume quantiles to correctly predict outcome cannot be ascertained. Studies that had prospectively recorded outcomes were considered to have low risk of bias of outcome measurement especially for mortality, however the measurement of other outcomes, other than mortality could still be biased. Those which had used healthcare administrative database were classified as having high risk of outcome measurement bias, because of the possibility that inter-hospital variation in codes for a similar condition and coding errors might have introduced bias.

Appendix 3: List of studies excluded at full text and reason for exclusion

	Study reference	Study title	Reasons for exclusion
1	Bergqvist et al ²⁵	Auditing surgical outcome. 10 Years with the Swedish Vascular Registry; Swedvasc	No volume outcome relationship investigated
2	Biancari et al ²⁶	Predictive factors for adverse outcome of pedal bypasses	No volume outcome relationship investigated
3	Goode et al ²⁷	Does case volume affect outcome for elective and emergency iliac intervention?	Conference abstract same data as in Goode et al ⁵
4	Holdsworth ²⁸	District Hospital Management and Outcome of Critical Lower Limb Ischaemia: Comparison with National Figures	No volume outcome relationship investigated
5	Huntington et al ²⁹	Lower limb occlusive arterial disease in the North of England: Workload and development of management guidelines	No volume outcome relationship investigated
6	Lepanatalo ³⁰	Should Vascular Surgery be Centralised or Decentralised? A Nordic Point of View	Review article
7	Luther and Lepantalo ³¹	Infrainguinal reconstructions: Influence of surgical experience on outcome	No volume outcome relationship investigated
8	Mao et al ³²	Outcomes and Characteristics of Patients Undergoing Percutaneous Angioplasty Followed by Below-Knee or Above-Knee Amputation for Peripheral Artery Disease	Not European study
9	Michaels et al ³³	Relation between rates of leg amputation and distal arterial reconstructive surgery. Oxford Regional Vascular Audit Group.	No volume outcome relationship investigated
10	Michaels et al ³⁴	Cost and outcome implications of the organisation of vascular services	Review article
11	Moxey et al ³⁵	Establishing a volume-outcome relationship in lower limb bypass surgery using multi-level logistic regression modelling	Conference abstract, full text Moxey et al ¹
12	Moxey et al ³⁶	Trends and outcomes after surgical lower limb revascularization in England	No volume outcome relationship investigated, same data as Moxey et al ¹
13	O'Shaughnessy et al ³⁷	Surgery in the treatment of varicose veins	No volume outcome relationship investigated
14	Prytherch et al ³⁸	A model for national outcome audit in vascular surgery	No volume outcome relationship investigated
15	Troeng et al ³⁹	Incidence and causes of adverse outcomes of operation for chronic ischaemia of the leg	Same data as in Troeng et al ¹⁴
16	VSGBI ⁴⁰	The national vascular database report 2009	No volume outcome relationship investigated
17	VSGBI ⁴¹	UK audit of vascular surgical services and carotid endarterectomy	No volume outcome relationship investigated
18	WVS study group ⁴²	Variations of Rates of Vascular Surgical Procedures for Chronic Critical Limb Ischaemia and Lower Limb Amputation Rates in Western Swedish Counties	No volume outcome relationship investigated

Reference list for studies excluded at full text level

25. Bergqvist et al. Auditing surgical outcome. 10 Years with the Swedish Vascular Registry-Swedvasc. *European Journal of Surgery, Acta Chirurgica, Supplement*. 1998;164(Supp 7):3-32.
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28. Holdsworth J. District hospital management and outcome of critical lower limb ischaemia: comparison with national figures. *Eur J Vasc Endovasc Surg*. 1997;13:159-163.
29. Huntington FP. Lower limb occlusive arterial disease in the North of England: Workload and development of management guidelines. *European Journal of Vascular and Endovascular Surgery*. 2000;20:260-267.
30. Lepantalo M. Should vascular surgery be centralised or decentralised? A Nordic point of view. *Eur J Vasc Surg*. 1994;8:116-118.
31. Luther ML. Infrainguinal reconstructions: Influence of surgical experience on outcome. *Cardiovascular Surgery*. 1998;6:351-357.
32. Mao CT, Tsai ML, Wang CY, Wen MS, Hsieh IC, Hung MJ, et al. Outcomes and Characteristics of Patients Undergoing Percutaneous Angioplasty Followed by Below-Knee or Above-Knee Amputation for Peripheral Artery Disease. *PLoS ONE*. 2014;9(10): doi:10.1371/journal.pone.0111130.

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37. O'Shaughnessy M, Rahall E, Walsh TN, Given HF, O'Shaughnessy M, Rahall E, et al. Surgery in the treatment of varicose veins. *Irish Medical Journal*. 1989;82:54-55.
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41. VSGBI. UK audit of vascular surgical services and carotid endarterectomy. 1-7-2010. Available at:
<http://www.wales.nhs.uk/documents/UK%20Audit%20of%20Vascular%20Surgical%20Services%20and%20carotid%20Endarterectomy.pdf> Accessed on 10th Aug 2015.
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