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Procedure volume and the association with short-term mortality following abdominal aortic aneurysm repair in European populations: a systematic review

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Review article
Volume of abdominal aortic aneurysm repairs and mortality

Word Count: 4911 words (abstract 291 words, text 3 550 words and references 1 070 words)

What this paper adds: This review addresses the volume outcome relationship from a modern European perspective and includes studies from the past ten years. Previous reviews are relatively old, dominated by data from the USA and lack a rigorous quality assessment of included studies. The results represent the best available evidence on this topic.

Key Words (MESH):

Aortic aneurysm, abdominal; Hospitals, low volume; Hospitals, high volume; Workload;

Review: Surgical Procedures, Operative

Procedure volume and the association with short-term mortality following abdominal aortic aneurysm repair in European populations: a systematic review

Abstract

Objective: To evaluate the relationship between the volume of abdominal aortic aneurysm (AAA) procedures undertaken and the primary outcome of mortality in Europe. Previous systematic reviews of this relationship are out-dated and are overwhelmingly based on US data.

Data sources: Comprehensive searching within MEDLINE and other bibliographic databases supplemented by citation searching and hand-searching of journals was undertaken to identify studies that reported the effect of hospital or clinician volume on any reported outcomes in adult, European populations, undergoing AAA repair and published in the last ten years.

Methods: two reviewers conducted study selection with independent, duplicate data extraction and quality assessment. A planned meta-analysis was not conducted due to the high risk of bias, the likelihood of individual study subjects being included in more than one study and diversity in the clinical populations studied and methods used.

Results: Sixteen studies (n = 237 074 participants) from the UK (n=11 studies), Germany (n=3 studies), Norway (n=1 study) and one from the UK and Sweden were included. Data in included studies came from administrative databases and clinical registries incorporating a variety of clinical and procedural groups; the study quality was limited by the use of observational study designs.

Overall, the evidence favoured the existence of an inverse volume outcome relationship between hospital volume and mortality. Insufficient evidence was available to reach conclusions on the relationship between clinician volume and outcome and between hospital, or clinician, volume and secondary outcomes including complications and length of hospital stay.

Conclusions: The evidence from this review suggests a relationship between the hospital volume of AAA procedures conducted and short-term mortality, however as volume typically represents a complex amalgamation of factors further research will be useful to identify the core characteristics of volume that influence improved outcomes.

Procedure volume and the association with short-term mortality following abdominal aortic aneurysm repair in European populations: a systematic review

Abdominal aortic aneurysms (AAA) are a major cause of death and disability. Despite reduced rates of in hospital mortality over the last decade[1] variations in outcomes between hospitals, and between surgeons, persist. Adjusted in hospital mortality rates following AAA repair in the UK vary between zero to 5.9% and zero to over 13% for hospitals and vascular surgeons' respectively[1]. These variations are within the range that could be expected as a result of random variation[1, 2], though factors other than chance could explain some of the differences. Volume has been identified as one possible explanatory variable and also as a proxy for quality[3] which has been accepted and used to justify the centralisation of vascular services, though differences in case mix, characteristics of the surgeon or structural and procedural characteristics of the hospital or local healthcare infrastructure might also explain some of this variation either independently or as components of volume.

Preliminary searches identified eight relevant systematic reviews [4-11] which generally supported the existence of an inverse relationship between the volume of AAA repair and mortality. The most recent was published in 2010, these reviews predominantly included evidence originating in the USA, thereby having limited relevance to the current European context. Additionally, a number of new studies from Europe that reflected recent technological advances in technique and delivery of vascular services (increased use of EVAR and centralisation of services) were identified. As a result, a new review was considered to be appropriate.

The aim of this study was to systematically review the evidence to evaluate the relationship between the volume of AAA surgery, undertaken by individual clinicians or hospitals in European populations, and mortality.

Methods

This systematic review is reported using the Preferred Reporting Outcomes for Systematic Reviews and Meta-analysis (PRISMA) statement[12]; it was conducted according to a publicly available and pre-registered protocol:

http://www.crd.york.ac.uk/PROSPERO/display_record.asp?ID=CRD42014014850

Search strategy

Electronic databases including MEDLINE, EMBASE, the Cochrane Library, Science Citation Index and CINAHL were searched in two stages between December 2014 and March 2015; searches were updated in June 2016. Search strategies were developed in consultation with a multi-disciplinary team including experts in information retrieval; an initial search combined free text and subject headings for terms based on volume and vascular conditions using database specific syntax; a second search was conducted using similar methods comprising terms for specific vascular surgical procedures and patient outcomes to increase sensitivity. Additionally conference proceedings, citation and reference list searches (of included studies and relevant systematic reviews) were conducted. (See supplementary appendix 1 for details of the search strategy).

Study Selection

We included studies published in the last ten years (based on clinical advice) of European populations of adults undergoing elective or emergency abdominal AAA repair, where the effect of hospital or operator volume on outcomes is reported and the paper was published in English (the primary outcome was mortality but we did not limit inclusion/ exclusion to the review by specific outcomes).

Data extraction and quality assessment

Two reviewers using a study specific and piloted data extraction form independently conducted data extraction and quality assessment of papers that met the inclusion criteria. The title and abstract of all studies identified by the searches were sifted by a single reviewer and checked by a second reviewer. All potential full text papers were retrieved and read independently by two reviewers. Data extracted included details of the clinical and procedural populations included, types of analysis, volume measurement, study design and results. Quality assessment was conducted using ACROBAT NRSI [13] a tool developed by the Cochrane collaboration for use with non-randomised studies, which is based on the premise that quality of non-randomised trials can be assessed in relation to a target or exemplar trial. This tool was revised to include headings for specific domains of bias that were considered to be relevant to a volume outcome context. The adapted tool was subsequently piloted with a selection of studies to ensure fitness for purpose.

Data Analysis

Analysis was planned to include meta-analysis where appropriate, however the extent of clinical and methodological heterogeneity coupled with the risk of selection, reporting and confounding bias made this inappropriate in accordance with the accepted recommendations of the Cochrane Collaboration:

- *Meta-analyses of studies that are at risk of bias may be seriously misleading. If bias is present in each (or some) of the individual studies, meta-analysis will simply compound the errors, and produce a 'wrong' result that may be interpreted as having more credibility.*
- *Finally, meta-analyses in the presence of serious publication and/or reporting biases are likely to produce an inappropriate summary* [14]

Therefore a narrative synthesis was conducted with tabulation of results according to the clinical subgroupings presented in individual studies. Subgroups were organised based on level of urgency and technique used. The majority of studies reporting on the relationship between hospital volume and mortality included either adjusted or both adjusted and unadjusted mortality rates. As adjusted mortality rates represented higher quality evidence the primary results of the syntheses are based on this adjusted data.

Results

Of a total of 17 284 citations, 16 studies [15-30] (237 074 patients) were eligible for inclusion in this review of the volume outcome relationship in patients undergoing AAA repair. A summary of the study selection is shown in the PRISMA flow chart (Figure 1).

Studies were excluded if they were conducted outside of Europe, did not report a volume outcome relationship or were of the wrong clinical population. Details of excluded studies are available from the author.

The majority of the included studies (n=11) [17-20, 22-26, 28,30] were from the UK with an additional three from Germany [15, 16, 21], one from Norway [27] and a study that reported UK and Swedish data separately[29]. Nine of the studies used data from administrative databases [15, 17-19, 22, 24, 25, 28, 30] with the remaining studies using other sources including clinical registries (n=4) [16, 20, 21, 26], databases and registries (n=2) [27, 30] and a single study used data collected as part of a randomised controlled trial [23]. Details of included studies are supplied (Table I).

Figure 1: PRISMA Flow Diagram

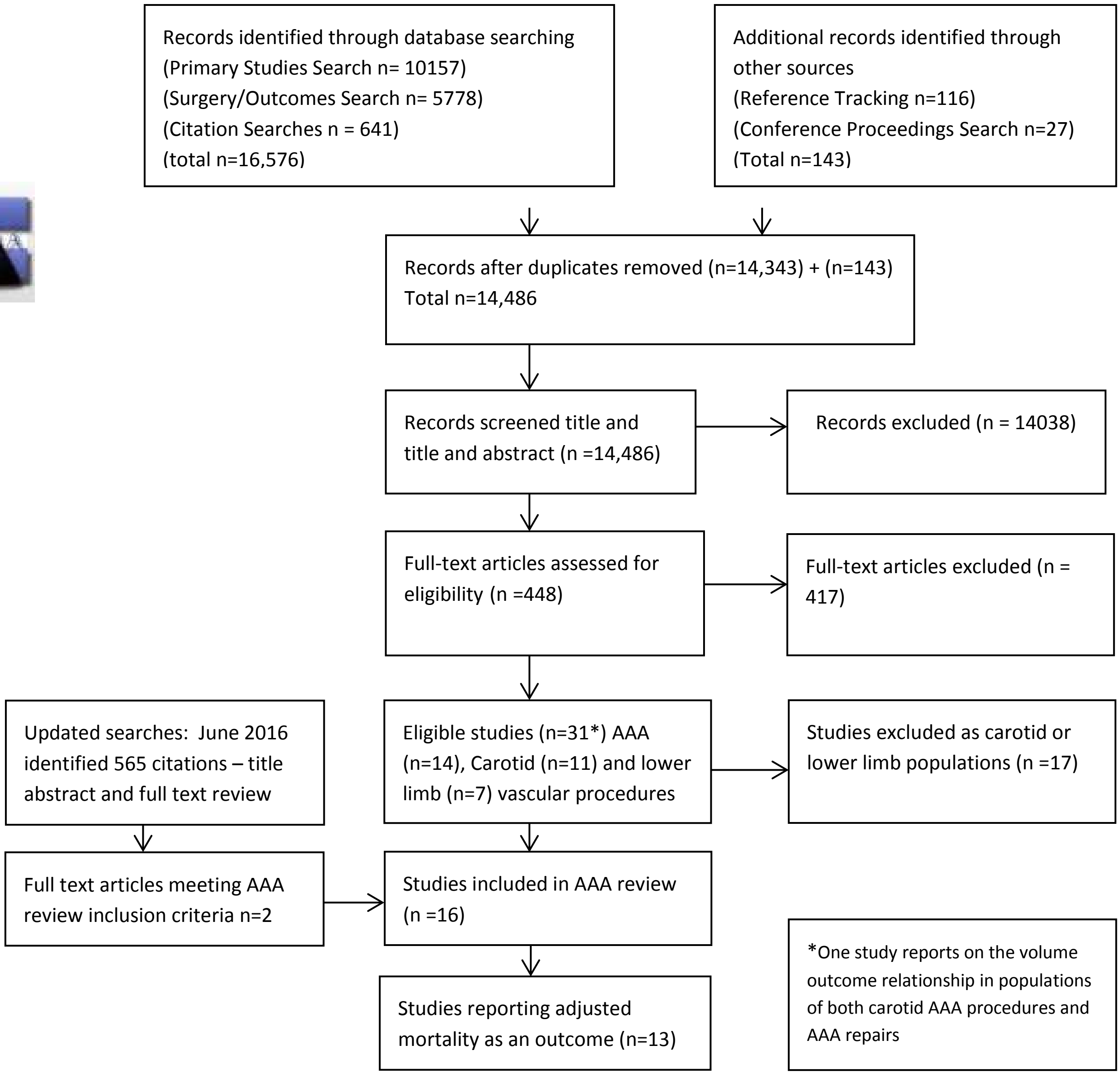

Figure 1: PRISMA diagram of search results and study selection

Notes: The initial search included terms for other conditions (carotid procedures and lower limb vascular procedures) separate reviews are planned for these populations.

Table I. table of included studies:

Reference	Duration of data collection	country	Study design	Data source	AAA Population(s) studied	Sample size	Average age (years)	outcomes
Powell 2014 [23]	2009-13	UK	Post hoc analysis	RCT data (IMPROVE)	Ruptured Open/EVAR	558	76.5	Mortality (30d)
Sidloff 2014 [26]	2008-12	UK	Retrospective analysis	NVD	Elective open/EVAR	21 266	NR	Mortality (IH)
Karthikesalingam 2016a [29]	2003-12	UK and Sweden	Retrospective analysis	HES SWEDVASC	Ruptured Open /EVAR	15296	74	Mortality (90d)
Hafez 2012 [20]	2008-10	UK	Retrospective analysis	NVD	Elective open/EVAR	13 068	NR	Mortality (UD) Complications (UD)
Karthikesalingam 2016b [30]	2005-10	UK	Retrospective analysis	HES	Elective open/EVAR	21 272	74	Mortality (IH)
Karthikesalingam 2014 [24]	2005-10	UK	Retrospective analysis	HES	Ruptured Open /EVAR	6 897	78.2	Mortality (OP/IH)
Ozdemir 2015 [25]	2005-10	UK	Retrospective analysis	HES	Ruptured Open /EVAR	9 877	78	Mortality (90d)
Trenner 2016 [16]	1999-2010	Germany	Retrospective analysis	DGG	Ruptured and non-ruptured Open/EVAR	41453	73.8	Mortality (IH)
Holt 2010[22]	2003-08	UK	Retrospective analysis	HES	Elective/ Urgent/ruptured Open/EVAR	8 139	NR	Mortality (IH)
Hentscker 2015 [15]	2007	Germany	Retrospective analysis	DRG	Intact AAA Open/EVAR	7 980	71	Mortality (IH)
Holt 2009 [18]	2005-07	UK	Retrospective analysis	HES	Elective Open/EVAR	7 313	72.6	Mortality (IH) LOS
Holt 2007 [17]	2000-05	UK	Retrospective analysis	HES	Elective/ Urgent/ruptured Open/EVAR	26 822	75.8	Mortality (IH) LOS complications
Holt 2012[19]	2000-05	UK	Retrospective analysis	HES	Elective Open/EVAR	14 396	72	Mortality 30d to 4 years
Eckstein 2007 [21]	1994-2004	Germany	Retrospective analysis	DRG	Elective Open	10 163	67.5	Mortality(PO) BT, LOP, LOS, DD, ITU stay
Haug 2005 [27]*	2001-02	Norway	Retrospective analysis	Administrative database and voluntary vascular registry	Elective/ Urgent/ruptured Open/EVAR	1 523	NR	Mortality (IH)
Jibawi 2006 [28]*	1997-2002	UK	Retrospective analysis	HES	Elective/ Urgent/ruptured Open/EVAR	31 078	72	Mortality (IH)

*Met review inclusion criteria but contained only raw data or conducted unadjusted analysis on mortality, with no other outcome reported. BT – blood transfusion; DD – discharge destination; DGG – German Quality Assurance Register (vascular register); DRG – Diagnosis related groups (administrative data); HES – Hospital Episode Statistics; IH- in hospital; ITU – intensive care unit; LOP – length of procedure; LOS – length of stay; NVD – National Vascular Database: OP – operative; PO – peri-operative; RCT – Randomised Controlled Trial; UD – undefined; 30d- 30 day; 90d – 90 day;

All 16 studies reported the relationship between hospital volume and outcome, of these two studies also reported on clinician volume and outcomes [20, 26]. The main outcome reported was short-term mortality with the majority of studies (n=13) conducting some adjustment for confounders. Measures of effect are predominantly presented as odds ratios in included studies; selected odds ratios have been converted to absolute measures to illustrate the estimated effect size and aid interpretation. These calculations have been conducted in accordance with the guidance of the Cochrane Collaboration [31]. (See supplementary appendix 2 for details and sample calculations).

The quality assessment of the 13 studies that present mortality with some level of adjustment for confounding is presented in Table II.

Table II summary of risk of bias*

Study reference	Selection	Volume measurement	Attrition	Outcome	Confounding	Reporting
Powell 2014 [(23)]	H	L	L	L	M	H
Kartikesalingam 2016a [(29)]	H	H	L	L	M	H
Hafez 2012 [(20)]	H	UC	UC	UC	UC	H
Kartikesalingam 2016b [(30)]	H	H	L	L	M	H
Kartikesalingam 2014 [(24)]	H	H	L	L	M	H
Ozdemir 2015 [(25)]	H	H	L	L	M	H
Trenner 2015 [(16)]	H	H	UC	L	M	H
Holt 2010 [(22)]	H	L	L	L	M	H
Hentschker 2015 [(15)]	H	H	L	L	M	H
Holt 2009 [(18)]	H	L	L	L	M	H
Holt 2007 [(17)]	H	UC	L	L	M	H
Holt 2012 [(19)]	H	UC	L	L	M	H
Eckstein 2007 [(21)]	H	L/H**	UC	L	M	H

Notes: H-high, L- low, M- medium, UC- unclear risk of bias. Risk of bias was assessed using a modified version of ACROBAT-NRSI and is detailed here in relation to the risk of bias in analyses of adjusted mortality.
*This table includes the 13 studies that report analyses of the volume outcome relationship and short term mortality adjusted for confounding
**Study conducts analyses of both of both continuous (low risk) and categorical (high risk) volume measurements.

All included studies were judged as high risk for selection bias based on the likelihood of 'selection' to 'low' or 'high' volume resulting from the impossibility of randomisation. A low risk of volume measurement bias was assigned when volume data had been analysed as continuous data. Where categorisation, in the absence of any empirical justification, was used this was classified as a high risk of bias; this assessment was made on the basis that the categories could have been selected following multiple analyses. Included studies that used categorisation did not justify the decisions made to use particular quantiles either *a priori*, or in the published text. A low risk of bias due to attrition was attributed to studies using population based administrative data as there seemed little likelihood that there was a differential loss to follow up. The likely influence of attrition bias was less clear in the case of the voluntary vascular databases. The low risk of outcome bias attributed to the majority of the included studies is a result of the use of mortality as an outcome; the exception is a paper available as an abstract only. Studies that used some form of adjustment for some confounders were judged as medium risk of bias. If all possible confounders were adjusted for, a low risk of bias would be assigned. However none of the included studies achieved this. A wide range of confounders identified (see Table III) and adjusted for within studies included; demographics, comorbidities, vascular risk factors, treatment modality, day of the week, transfer between hospitals and health professional staffing levels. Due to a lack of *a priori* statements of planned outcomes and analyses, all studies were judged as high risk of reporting bias.

Hospital volume and mortality

The results of the analyses conducted on the relationships between hospital volume and adjusted short-term mortality are presented, according to the clinical and procedural groups reported in individual studies, in Table III and discussed below.

Table III: results of analyses, from individual studies, of the relationship between the hospital volume of procedures that are undertaken and adjusted mortality in various clinical and procedural groupings.

Comparison	Population hospital volume measured in	Population mortality measured in	Reference	Method of volume stratification	Volume categories	Method of analysis of adjusted data	Confounders adjusted for	Mortality	Statistically significant results	Comments
C1	Intact AAA repair	Intact AAA repair	Trenner (2015) [16]	Quintiles	1-20 21-30 31-49 50-62 63-158 Cases pa	Odds ratio (categorical comparison with low volume as reference)	Age, ASA score, vascular risk factors and treatment modality	IH	Favour high volume: OR 0.48 (95% CI 0.33-0.69) for 50-62 vs 1-20 annual cases.	One of 4 comparisons is statistically significant, though all the analyses suggest favourable results for high volume hospitals when compared to the lowest volume quintile (OR range 0.48 - 0.82)
			Hentschker (2015)[15]	Quintiles	3-15 16-25 26-39 40-67 68-209 Cases pa	Odds ratio (categorical comparison with low volume as reference)	Age, sex, Charlson comorbidity index treatment modality and type of hospital, day of procedure and transfer	IH	Favour high volume: OR 0.605 (95% CI 0.3876 - 0.9446) for 26-39 vs 3-15 annual cases OR 0.5466 (95% CI 0.302 - 0.8533) for 40-67 vs 3-15 annual cases	Two of the 4 comparisons are statistically significant, though all the analyses suggest favourable results for high volume hospitals when compared to the lowest volume quintile, (OR range 0.55 – 0.93)
C2	Elective AAA repair (open or EVAR)	Elective AAA repair (open or EVAR)	Holt (2007)[17]	Quintiles	0-0.72 7.3-12.6 12.7-19.4 19.5-32 >32	Odds ratio (multiple logistic regression)	Age, sex	IH	Favours high volume OR 0·92 (95 % CI 0·88 to 0·96; P < 0·001)	An increasing annual hospital volume of AAA repairs was associated with a significant reduction in the in hospital mortality rate
			Holt (2009)[18]	Continuous Quintiles	Average number of cases per trust = 27 per year, low volume quintile 12 pa, high volume 98 pa	Odds ratio expressed per additional case performed	Age, sex and 11 diagnostic risk factors	IH	Favours high volume OR 0.992; (95% CI, 0.988 to 0.995; P=0.000) per additional case performed	An increasing hospital volume was associated with a significant reduction in the odds of in hospital mortality.
							Age, sex and 11 diagnostic risk factors and effect of EVAR	IH	Favours high volume OR 0.993; 95% CI, 0.989 to 0.997; P=0.010)	This relationship was maintained after including adjustment for the highly significant reduction in mortality described for EVAR
			Holt	Quintiles	0.2-12.2	Cox	Age, sex and	30 days to	Survival data after elective	A statistically significant beneficial effect of

			(2012)[19]		12.4-17.8 18-27.4 27.6-41.6 44.4-67.2 Cases pa	proportional hazards model for difference in survival across quintiles	comorbidity	4 years	AAA repair for all volume quintiles (Q1–Q5). P< 0.001at 30 days P< 0.001 at 1 year P = 0.013 at 2 years P = 0.009 at 3 years with data remodelled data to exclude 30-day mortality	volume was found on 30 day, and 1 and 2 year survival but not at 3 and 4 years. Analyses based on remodelled data to exclude 30 day mortality showed no significant effect at 1 and 2 years but found a statistically significant effect at 3 years and a trend at 4 years.
			Karthikesalingam (2016b)[(30)]	Tertiles	<13 13-31 >31 Cases pa	Logistic regression	Age, gender, social deprivation, and co-morbidity index	IH	Statistically significant relationship p<0.0001 (odds ratio are not given)	
C3	Elective AAA repair (open or EVAR)	Elective open AAA repair	Holt (2009)[18]	Continuous Quintiles	Average number of cases per trust = 27 per year, low volume quintile 12 pa, high volume 98 pa	Odds ratio expressed per additional case performed	Age, sex and 11 diagnostic risk factors	IH	Favours high volume OR 0.994 (95% CI, 0.991 to 0.998 P=0.0008) per additional case performed	A statistically significant beneficial effect of volume on in hospital mortality was found
			Hafez (2012)[20]	Unclear	Not reported	Logistic regression	Gender, ASA and screening status	UD	Unit volume of 41-50 cases per year was associated with a reduced risk OR 0.57 (95% CI 0.38-0.87; p=0.008)	This study is reported as a conference abstract only with scant detail. The authors conclude that: '*This analysis demonstrates that the relationship between AAA repair volume and outcome is not linear*'
			Karthikesalingam (2016b)[(30)]	Tertiles	<13 13-31 >31 Cases pa	Logistic regression	Age, gender, social deprivation, and co-morbidity index	IH	Statistically significant relationship p<0.001 (odds ratio are not given)	
C4	Elective open AAA repair	Elective open AAA repair	Eckstein (2007) [21]	Quantiles (6)	0-9 10-19 20-29 30-39 40-49 > 50 Cases pa	Odds ratio (categorical comparison with high volume as reference)	Age, ASA, AAA diameter and surgical variables	PO	Favours high volume OR 1.903, (95% CI 1.124-3.222) for 0-9 vs >50 annual cases	A statistically significant relationship wasn't evident in the other analyses of quantiles though there appeared to be a trend with higher volume hospitals achieving better results (OR range 1.092 - 1.375)
			Eckstein (2007) [21]	Continuous	0-9 10-19 20-29	Stepwise regression	Age, ASA, AAA diameter and surgical	PO	None	A moderate but statistically non-significant effect of volume on perioperative mortality (OR 1.003 95% CI 1-1.006 p=0.07) was found

					30-39 40-49 > 50 Cases pa		variables			
			Holt (2009)[18]	Continuous Quintiles	Average number of cases per trust = 21 per year, low volume quintile 9 pa, high volume 56 Cases pa	Odds ratio expressed per additional case performed	Age, sex and 11 diagnostic risk factors	IH	Favours high volume OR 0.99 (95% CI, 0.989 to 0.999 p0.0216)	
C5	Elective EVAR	Elective EVAR	Holt (2009)[18]	Continuous Quintiles	Average number of cases per trust = 9 per year, low volume quintile 2.5 pa, high volume 104 Cases pa	Odds ratio expressed per additional case performed	Age, sex and 11 diagnostic risk factors	IH	Borderline statistically significant relationship favours high volume OR, 0.993; (95% CI, 0.987 to 1.000 p=0.0572)	
C6	Elective AAA repair (open or EVAR)	Elective EVAR	Holt (2009)[18]	Continuous Quintiles	Average number of cases per trust = 27 per year, low volume quintile 12 pa, high volume 98 Cases pa	Odds ratio expressed per additional case performed	Age, sex and 11 diagnostic risk factors	IH	Favours high volume OR 0.989; (95% CI, 0.982 to 0.995, p = 0.0007)	
			Hafez (2012)[20]	Unclear	Not reported	Logistic regression	Gender, ASA and screening status	UD	None	Mortality was not associated with risk reduction at any level
			Karthikesalingam (2016b)[(30)]	Tertiles	<13 13-31 >31	Logistic regression	Age, gender, social deprivation, and co-morbidity index	IH	None	No statistically significant relationship p=0.6202 (odds ratio are not given)

					Cases pa						
C7	Elective AAA repair (open or EVAR)	Emergency intact AAA repair (open or EVAR)	Holt (2010)[22]	Continuous	Summary details of volume of elective AAA repairs undertaken not published	Odds ratio expressed per additional case performed	Demographics and comorbidities	IH	Favours high volume OR 0·999 (95% CI 0·998 to 0·999 p = 0·015)		
C8	Elective AAA repair (open or EVAR)	Repair of ruptured AAA	Holt (2010)[22]	Continuous	Summary details of volume of elective AAA repairs undertaken not published	Odds ratio expressed per additional case performed	Demographics and comorbidities	IH	Favours high volume OR 0·998, (95 % CI 0·997 to 0·999 p < 0·001)		
C9	Elective EVAR	Open repair of ruptured AAA	Holt (2010)[22]	Continuous	Summary details of volume of elective AAA repairs undertaken not published	Odds ratio expressed per additional case performed	Demographics and comorbidities	IH	Favours high volume OR 0·982 (95% CI 0·975 to 0·988 p < 0·001)		
C10	Elective EVAR	EVAR of ruptured AAA	Holt (2010)[22]	Continuous Quintiles	Summary details of volume of elective AAA repairs undertaken not published	Odds ratio expressed per additional case performed	Demographics and comorbidities	IH	Favours high volume OR 0·999 (95% CI 0·997 to 0·999 p< 0·001)		
C11	Emergency intact AAA repair	Emergency intact AAA repair	Holt (2007)[17]	Quintiles	0-2 2.1-4.2 4.3-6.6 6.712.2	Odds ratio (multiple logistic regression)	Age and sex	IH	Favours high volume OR 0·94 (95% CI 0·90 to 0·99 p= 0·017)		

					>12.2 Cases pa					
			Holt (2010)[22]	Continuous Quintiles	1-20 21-34 35-48 49-77 89-149 Cases in 5 years	Odds ratio expressed per additional case performed	Demographics and comorbidities	IH	Favours high volume OR 0·997 (95% CI 0·995 to 0·999 p = 0·004)	
C12	Ruptured AAA repairs	Ruptured AAA repairs	Holt (2007)[17]	Quintiles	0-2.8 2.9-5.6 5.7-9.2 9.3-13.2 >13.2 Cases pa	Odds ratio (multiple logistic regression)	Age and sex	IH	None	Favours high volume OR 0·98 (95% CI 0·95 to 1·02 p = 0·302)
			Holt (2010)[22]	Continuous Quintiles	1-26 27-38 39-52 54-72 75-146 Cases in 5 years	Odds ratio expressed per additional case performed	Demographics and comorbidities	IH	Favours high volume OR 0·993 (95 % CI 0·991 to 0·995 p< 0·001)	
			Trenner (2015)[16]	Quartiles	1-3 4-5 6-7 8-15 Cases pa	Odds ratio (categorical comparison with low volume as reference)	Age, ASA score, vascular risk factors and treatment modality	IH	Borderline statistically significant relationship favours highest volume vs lowest volume quartile OR 0.70 (95% CI 0.49-1.00)	No statistically significant evidence of an effect of volume on in-hospital mortality (OR range = 0.89 - 0.70)
			Powell (2014)[23]	Continuous	Summary details of volume of ruptured AAA repairs undertaken not published	Logistic regression	Age, sex, Hardman index, randomised group, max aortic diameter, time of randomisation, lowest recorded BP, volume of IV fluids	30 day	None	No statistically significant was found in a primary analysis adjusted for; age, sex, Hardman index, randomised group and max aortic diameter, or in the subsequent analysis adjusting for additional factors OR 0.93 95% CI 0.65, 1.32 P value=0.674 additionally adjusting for; time of randomisation, lowest recorded BP, total volume of IV fluids were also included in the adjustment
			Karthikesalingam (2016a)[(29)]	Quintiles (UK)	1-4 5-7 8-11 12-16	Logistic regression (of categorical comparisons)	Age, sex, weekend surgery, comorbidity,	90 day	Statistically significant relationship p<0.001 (odds ratio are not given for multiple categorical	Analyses of separate populations were conducted in the UK and Sweden with different volume strata and levels of adjustment used in the different populations.

					>16 Cases pa		and inter hospital transfer before surgery		comparisons	Data came from an administrative data base in the UK (HES) and a clinical vascular registry in Sweden (SWEDVASC).
				Quintiles (Sweden)	1-3 4-7 8-11 11-20 >20 Cases pa	Logistic regression (of categorical comparisons)	Age, sex, comorbidity	90 day	Borderline statistically significant relationship p=0.053 (odds ratio are not given for multiple categorical comparisons)	
C13	Ruptured AAA repairs (open or EVAR)	Admission with ruptured AAA (corrective and non-corrective treatment)	Ozdemir (2015)[25]	Tertiles	Summary details of volume of ruptured AAA repairs undertaken not published	Odds ratio (categorical comparison with high volume as reference)	Age, sex, comorbidities, deprivation indices, staffing levels and day of admission	90 day	Favours high volume OR1.31 (95% CI 1.15-1.49, p<0.001 lowest vs highest tertile) OR 1.13 (95% CI 1.00-1.27, p=0.05, medium vs highest tertile)	The effect was evident between both low and medium volume groups vs the high volume group when age, sex, comorbidities and deprivation were included in the adjustment. The effect persisted when additional adjustment was included for nurse and doctor staffing and day of admission.
C14	Admission with ruptured AAA (corrective and non-corrective treatment)	Ruptured AAA repairs (open or EVAR)	Karthikesalingam (2013) [24]	Quintiles	Summary details of volume of admission with ruptured AAA not published	Logistic regression	Age, sex, comorbidity	IH	A statistically significant effect on mortality in those undergoing operative treatment for ruptured AAA was identified (p=0.0371),	An statistically significant effect was also evident when the outcome was analysed in all patients admitted whether they underwent an operation or not (p<0.001) Odds ratios are not provided in the text or appendices for either analysis.

Hospital volume and mortality (adjusted) in elective and intact AAA repair

Two analyses [15, 16] suggest an association between a higher hospital volume of procedures undertaken for intact AAA and improved short term mortality in patients undergoing repair of intact AAA in Germany (comparison 1**(C1)**). These are the most comprehensive and inclusive of the analyses undertaken in terms of clinical and procedural groups excluding only patients undergoing repair of ruptured AAA. Categorical analyses were conducted using quintiles in both studies; three of eight analyses reached statistical significance while the remaining five favoured the high volume group but did not reach statistical significance. The odds ratios (OR) appear consistent across the two studies and there are no significant differences in the quality of the studies included. Conversion of odds ratio to absolute risk reduction suggests there could be as many as 22.87 fewer deaths per 1000 procedures conducted (numbers needed to treat (NNT) 44) when procedures are carried out at higher volume institutions [15, 16].

The volume of elective repair (open or endovascular) was statistically significantly and inversely associated, with short term mortality in four UK studies[17-19, 30] **(C2),** and this relationship was maintained after adjustment for the effects of EVAR on mortality[18] with an estimated decrease of in hospital mortality of 4.8 per thousand procedures associated with each additional 10 procedures performed at a given hospital (NNT 209). The volume of elective AAA repair (open or endovascular) was also statistically significantly associated with lower mortality in patients undergoing elective open AAA repair **(C3)** [18, 20, 30.]

The impact of the volume of elective open AAA repair was investigated in two studies **(C4)**, one (UK) using administrative data[18] found evidence of a statistically significant effect, while a German study [21] using registry data conducted two different analyses and found a statistically significant difference between high and low volume quantiles. However when an alternative analysis was conducted using volume as a continuous variable statistical significance was not reached ($p = 0.07$).

One study found evidence of a borderline statistically significant beneficial effect of volume of elective EVAR on mortality in elective EVAR[18] (NNT = 223 associated with each additional 10 procedures performed) **(C5)**. There was also some evidence of a relationship between the volume of elective AAA repair (open or EVAR) and elective EVAR, with a statistically significant effect in one of the three studies [18, 20, 30] that assessed this relationship (NNT = 134 associated with each additional 10 procedures performed [18]) **(C6)**.

Hospital volume and mortality (adjusted) in emergency and ruptured AAA repair

Two analyses by Holt et al found a statistically significant effect between the volume of elective AAA repair, regardless of method, and in hospital mortality for emergency intact AAA repair [22] (NNT = 542 associated with each additional 10 procedures performed) **(C7)** and ruptured AAA repair by any method[22] (NNT = 271 associated with each additional 10 procedures performed) **(C8).** The relationship between the volume of elective EVAR conducted and in hospital mortality in patients undergoing open repair of ruptured AAA **(C9)** and EVAR of ruptured AAA **(C10)** was also statistically significant [22] (NNT = 400 associated with each additional 10 procedures performed).

A relationship between the volume of emergency procedures and mortality was observed. Evidence from two UK studies of administrative data **(C11)** shows a statistically significant effect of volume on short-term mortality in the same clinical and procedural grouping, (emergency intact AAA repair) [17, 22].

Four out of seven studies **(C12-14)** reported evidence of a statistically significant relationship based on the volume of ruptured AAA undertaken. These four results are based on UK administrative data. Five studies [16,17,22,23, 29] **(C 12)** reported outcomes in patients undergoing ruptured AAA repair in relation to the volume of patients in the same clinical and procedural group. Two of these studies presented evidence of a statistically significant relationship[22, 29] and a further two analyses noted borderline statistically significant results favouring high volume[16, 29], with numbers needed to treat as low as 13 for a comparison of outcomes between a low volume centre (1-3 procedures per year) and relatively high volume (8-15 cases per year). Two studies [24, 25] also include the numbers of admissions for non-corrective treatment in their analyses, either in the group in which volume is measured **(C13)** or in the group that outcome is measured **(C14),** both studies finding evidence of statistically significant effects of volume on mortality (in hospital and 90 day).

Mortality (adjusted) - longer-term outcomes

Further analyses **(C2)** performed by Holt and colleagues [19] included long term mortality between the combined volume of elective open and endovascular repairs conducted by hospitals and mortality in the same population from 30 days to four years. They found evidence of a significant effect at: 30 days ($p<0.001$), one year ($p<0.001$) and 2 years ($p<0.13$), but not at 3 and 4 years ($p=0.324$ and $p=0.225$ respectively). Remodelling the data to exclude 30-day mortality demonstrated no significant effect of volume after 1 and 2 years. On the other hand a late significant effect of hospital volume at 3 years ($p = 0.009$) and a trend in favour of an inverse relationship at 4 years ($p = 0.088$) was detected.

Mortality - surgeon volume

One study [20] reported an adjusted analysis of mortality in relation to the volume of surgery undertaken by individual clinicians, finding a statistically significant association between the combined volume of open and endovascular procedures and mortality for elective open repair, surgeon volume of 11–20 cases/year was associated with a reduced risk (OR 0·70 (95% CI, 0·92–0·52); p = 0·013). This analysis was adjusted for gender, ASA score and screening status. In a second analysis [(20)] of the outcome of elective EVAR procedures in relation to the same volume grouping there was no evidence of significance. Sidloff et al [26] reported a significant association between the number of elective AAA repairs by any method and in hospital mortality using data from a national vascular database, but this was unadjusted for any potential confounders.

Other outcomes

A wide variety of pre, peri and post-operative variables were reported in the included studies, when considering these variables as outcomes there is some ambiguity over the difference between predictive (independent) variables and outcome variables. For instance Eckstein et al[21] analysed factors such as length of procedure, use of blood transfusion and length of intensive therapy unit (ITU) stay and reported statistically significant associations with volume though the position of such factors on the causal pathway is open to debate. The lack of explicit statements regarding the theoretical relationship that are being tested in some of these studies coupled with the lack of pre-registered study protocols suggests that there is a high risk of reporting bias in these outcomes and many of these secondary outcomes were reported without details of the analysis such that there are concerns about the influence of multiple analyses and selective reporting for the majority of these outcomes.

Complications Hafez et al [20] reported an association between surgeon volume and complications for open and endovascular AAA repair. However no corresponding evidence of significance was found for hospital volume and complications were not defined. Holt[17] and Eckstein[21] found no evidence of an effect of hospital volume on a comprehensive range of post-operative complications including renal, respiratory, cardiovascular, infection, bleeding and thrombosis/embolism.

Length of hospital stay - Holt et al[17] found an increased length of stay at low volume hospitals for elective AAA repair a result that was duplicated by Holt[18] for EVAR. Conversely the authors noted an increased length of stay at high volume hospitals following urgent AAA repair, this may be a result of the difficulties associated with the multifaceted and complex care required by patients who have survived in these hospitals. This issue further highlighting the potential ambiguity of the use of length of stay and similar variables as outcome measures.

Discussion

The evidence from this review suggests that there is an inverse relationship between the volume of AAA procedures undertaken in individual hospitals and short-term mortality in Europe. This correlation appears to be robust across all clinical and procedural groups and is maintained despite differences in the methods and levels of adjustment used in included studies. There is a lack of robust evidence of a surgeon volume outcome effect, the two studies that report this are of lower quality; one[20] is available as an abstract only and the other [26] does not include any adjustment in the analysis. Further data on the relationship between surgeon volume and outcomes including adjusted mortality and length of stay is available on databases, notably in the UK [2]; such data could form the basis of useful analyses. However this evidence was not available in a form that met the inclusion criteria for the current review.

The findings of this review are in agreement with the earlier reviews that analysed predominantly US data, suggesting that the hospital volume and mortality relationship is consistent irrespective of differences in models of health service delivery. For instance, it could be argued that selective referral, as a result of professional or patient choice, might affect the volume outcome relationship differently where there is a market driven model of health care delivery, as in the USA, in comparison to the European context where a ‘socialised’ model is the norm, this appears not to be the case.

The restriction of the review to studies published in the last ten years also suggests that the relationship is maintained:

- In the context of increased use of endovascular techniques. This is evident across analyses; where EVAR has been considered in combination with open repair, where EVAR has been considered in isolation, across various levels of urgency and where adjustment has been included for the use of EVAR[18].
- In the context of ongoing centralisation of complex arterial endovascular and surgical interventions in the UK organised on the basis of existing evidence of a volume outcome relationship[32].

Investigation of the volume outcome relationship by comparing concurrent outcomes between centralised and devolved models of care and/or by conducting before and after studies in areas that currently or will soon undergo re-organisation would be useful in further confirming the volume outcome relationship. This could also be used to help explain the relationship in terms of the factors for which volume is a proxy. Such analyses are planned using UK HES data as part of the on-going vascular services programme grant of which this review is a part.

The use of clinical and administrative databases ensures that large populations can be included in studies more efficiently than in an RCT, though conversely study populations cannot be manipulated or randomly allocated leading to a higher risk of selection bias. The influence of selection bias is attenuated by attempts at adjustment for confounding in included studies, but the effects of these adjustments are always going to be imperfect due to the wide range of potential confounders and the impossibility of identifying and adjusting for the full range of physiological, demographic, organisational and technical variables for which volume is a proxy. These problems are unavoidable; however the quality of the evidence is further weakened by the potential for selective reporting, *a priori* registration, detailing planned analyses and volume groupings might increase confidence that effects of estimate were not selected on the basis of the significance of the results. This is an area needing further research, with suggestions that variation in results could be related to inconsistencies in categorisation, definitions of volume quantiles and statistical approaches[33]. Additionally further work is needed to identify the individual factors that contribute to the volume effect so that effective and accessible services can be designed the suit the local context and are acceptable to service users.

Conclusion

This review represents the best available evidence of the relationship between volume and outcome in AAA repair in Europe and while it suggests that a relationship exists, between higher hospital volume and lower short term mortality, there is insufficient evidence to reach conclusions for other outcomes or for the relationship between clinician volume and outcomes. The quality of the evidence included in this review is low; this reflects the necessary use of observational methods and the quality of the available data sources rather than any deficiencies in the conduct of the research. This requires that decisions made on the strength of it are cautious and more research is needed to identify the specific variables that contribute to the volume outcome effect.

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Conflicts of interest: none

References

1. Waton S, Johal A, Hekkila K, Cromwell D, Loftus I. National Vascular registry 2015 Annual Report. London; 2015.
2. Vascular Surgeons Quality Improvement Programme [Internet]. London: Surgeons outcomes. 2015 [cited 2016 Jan 14]. Available from: https://www.vsqip.org.uk/surgeon-outcomes/
3. Luft HS, Hunt SS, Maerki SC. The volume-outcome relationship: practice-makes-perfect or selective-referral patterns? *Health Serv Res.* 1987;22(2):157–82.
4. Hoornweg LL, Storm-Versloot MN, Ubbink DT, Koelemay MJW, Legemate D A, Balm R. Meta Analysis on Mortality of Ruptured Abdominal Aortic Aneurysms. *Eur J Vasc Endovasc Surg*. 2008 May; 35(5):558–70.
5. Gandjour A, Bannenberg A, Lauterbach KWK. Threshold volumes associated with higher survival in health care: a systematic review. *Med Care*. 2003;41(10):1129–41.
6. Henebiens M, van den Broek T , Vahl AC, Koelemay MJW. Relation between hospital volume and outcome of elective surgery for abdominal aortic aneurysm: a systematic review. *Eur J Vasc Endovasc Surg*. 2007 Mar;33(3):285–92.
7. Holt PJE, Poloniecki JD, Gerrard D, Loftus IM, Thompson MM. Meta-analysis and systematic review of the relationship between volume and outcome in abdominal aortic aneurysm surgery. *Br J Surg.* 2007 Apr;94(4):395–403.
8. Killeen SD, Andrews EJ, Redmond HP, Fulton GJ. Provider volume and outcomes for abdominal aortic aneurysm repair, carotid endarterectomy, and lower extremity revascularization procedures. *J Vasc Surg*. 2007 Mar; 45(3):615–26.
9. Wilt TJ, Lederle FA, MacDonald R. Comparison of Endovascular and Open Surgical Repairs for Abdominal Aortic Aneurysm. Agency for Healthcare Research and Quality (US); 2006 Aug. (Evidence Reports/Technology Assessments), No. 144.

10. Marlow NE, Barraclough B, Collier NA, Dickinson IC, Fawcett J, Graham JC, et al. Effect of hospital and surgeon volume on patient outcomes following treatment of abdominal aortic aneurysms: a systematic review. *Eur J Vasc Endovasc Surg.* Elsevier Ltd; 2010 Nov; 40(5):572–9.

11. Young EL, Holt PJE, Poloniecki JD, Loftus IM, Thompson MM. Meta-analysis and systematic review of the relationship between surgeon annual caseload and mortality for elective open abdominal aortic aneurysm repairs. *J Vasc Surg*. 2007 Dec;46(6):1287–94.

12. Moher D, Liberati A, Tetzlaff J, Altman DG. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *PLoS Med [Internet]*. 2009 Jul 21 [cited 2014 Jul 9];6(7):e1000097. Available from: http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=2707599&tool=pmcentrez&rendertype=abstract

13. Sterne JAC, Higgins JPT RB. on behalf of the development group for ACROBAT-NRSI. A Cochrane Risk Of Bias Assessment Tool: for Non- Randomized Studies of Interventions (ACROBAT-NRSI) Version 1.0.0. 2014 September 2014. Available from: http://www.riskofbias.info (accessed14/01/2016)

14. Deeks JJ, Higgins JPT, Altman DG (editors). Chapter 9: Analysing data and undertaking meta-analyses. In: Higgins JPT, Green S (editors). Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0 (updated March 2011). The Cochrane Collaboration, 2011. Available from www.handbook.cochrane.org

15. Hentschker CRM, Mennicken R. The Volume outcome relationship and minimum volume standards-empirical evidence for Germany. *Health Econ*. 2015;24:644–58.

16. Trenner M, Haller B, Sollner H, Storck M, Umscheid T, Niedermeier H et al. Twelve years of the quality assurance registry abdominal aortic aneurysm of the German

Vascular Society (DGG): Part 3: Predictors of the perioperative outcome with focus on annual caseload. *Gefasschirurgie*. 2015;(supplement 1)20:32 - 44

17. Holt PJE, Poloniecki JD, Loftus IM, Michaels JA, Thompson MM. Epidemiological study of the relationship between volume and outcome after abdominal aortic aneurysm surgery in the UK from 2000 to 2005. *Br J Surg.* 2007 Apr;94(4):441–8.
18. Holt PJE, Poloniecki JD, Khalid U, Hinchliffe RJ, Loftus IM, Thompson MM. Effect of Endovascular Aneurysm Repair on the Volume-Outcome Relationship in Aneurysm Repair. *Circ Cardiovasc Qual Outcomes*. 2009;2(6):624–32.
19. Holt PJE, Karthikesalingam A, Hofman D, Poloniecki JD, Hinchliffe RJ, Loftus IM, et al. Provider volume and long-term outcome after elective abdominal aortic aneurysm repair. *Br J Surg*. 2012 May;99(5):666–72.
20. Hafez. National Vascular Database analysis: the relationship between AAA repair volume and outcome. *Br J Surg.* 2012;99(supplement 3):4.
21. Eckstein HH, Bruckner T, Heider P, Wolf O, Hanke M, Niedermeier HP, et al. The Relationship Between Volume and Outcome Following Elective Open Repair of Abdominal Aortic Aneurysms (AAA) in 131 German Hospitals. *Eur J Vasc Endovasc Surg*. 2007;34(3):260–6.
22. Holt PJE, Karthikesalingam A, Poloniecki JD, Hinchliffe RJ, Loftus IM, Thompson MM. Propensity scored analysis of outcomes after ruptured abdominal aortic aneurysm. *Br J Surg*. 2010 Apr (97):496-503.
23. Powell JT, Surgery V. Observations from the IMPROVE trial concerning the clinical care of patients with ruptured abdominal aortic aneurysm. *Br J Surg*. 2014;101(3):216–24.
24. Karthikesalingam A, Holt PJ, Vidal-Diez A, Ozdemir BA, Poloniecki JD, Hinchliffe RJ, et al. Mortality from ruptured abdominal aortic aneurysms: Clinical lessons from a

comparison of outcomes in England and the USA. *Lancet*. 2014;383(9921):963–9.

25. Ozdemir BA, Karthikesalingam A, Sinha S, Poloniecki JD, Vidal-Diez A, Hinchliffe RJ, et al. Association of hospital structures with mortality from ruptured abdominal aortic aneurysm. *Br J Surg.* 2015;102(5):516–24.

26. Sidloff DA, Gokani VJ, Stather PW, Choke E, Bown MJ, Sayers RD. National Vascular Registry Report on surgical outcomes and implications for vascular centres. *Br J Surg*. 2014;101(6):637–42.

27. Haug ES, Romundstad P, Saether OD, Jørgenvåg R, Myhre HO. Quality of data reported on abdominal aortic aneurysm repair--a comparison between a national vascular and a national administrative registry. *Eur J Vasc Endovasc Surg*. 2005 Jun;29(6):571–8.

28. Jibawi A, Hanafy M, Guy A, Is there a Minimum Caseload that Achieves Acceptable Operative Mortality in Abdominal Aortic Aneurysm Operations? *Eur J Vasc Endovasc Surg*. 2006;32(3):273–6.

29. Karthikesalingam A, Wanhainen A, Holt PJ, Vidal-Diez A, Brownrigg JR, Shpitser I, et al, Comparison of long-term mortality after ruptured abdominal aortic aneurysm in England and Sweden. *Br J Surg* 2016a;103(3): 199-206.

30. Karthikesalingam A, Holt PJ, Vidal-Diez A, Bahia SS, Patterson BO, Hinchliffe RJ, et al. The impact of endovascular aneurysm repair on mortality for elective abdominal aortic aneurysm repair in England and the United States. *J Vasc Surg*. 2016b; article in press

31. Schünemann HJ, Oxman AD, Vist GE, Higgins JPT, Deeks JJ, Glasziou P, Guyatt GH. Chapter 12: Interpreting results and drawing conclusions. In: Higgins JPT, Green S (editors), Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0 (updated March 2011). The Cochrane Collaboration, 2011. Available from

www.handbook.cochrane.org.

32. Vascular Society of Great Britain and Ireland. The Provision of Services for Patients with Vascular Disease. Vascular Society of Great Britain and Ireland. London, 2015; 1–40

33. Yu TH, Tung YC and Chung KP. Does Categorization Method Matter in Exploring Volume-Outcome Relation? A Multiple Categorization Methods Comparison in Coronary Artery Bypass Graft Surgery Surgical Site Infection. *Surgical infections.* 2015; 16(4):466-472

Supplementary appendix 1

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:

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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)

69 32 and 68 (100)

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Primary Studies Search

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

Search Strategy:

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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)

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Surgery/Outcomes Search

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

Search Strategy:

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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)

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Appendix 2 - Calculations

Calculations performed based on the Cochrane handbook for systematic reviews of interventions (section 12.5.4.3) computing absolute risk reduction or NNT from an odds ratio.

Formula for calculating absolute risk reduction:

$$\text{Number fewer per 1000} = 1000 \text{ X } \left(ACR - \frac{OR \text{ x } ACR}{1 - ACR + OR \text{ x } ACR} \right)$$

- OR – odds ratio
- ACR assumed control risk

We have used the event rate for the lowest quantile from each study as the assumed control risk.

Trenner - adjusted calculations – C1

- The adjusted odds ratio for in hospital mortality (high volume quantile vs low volume quantile with low volume as reference) is 0.74 (95% CI 0.48-1.14)
- The mortality rate in the lowest volume quantile is 3.5%, therefore the ACR = 0.035

$$\text{Number fewer per 1000} = 1000 \text{ x } \left(0.035 - \frac{0.74 \text{ x } 0.035}{1 - 0.035 + 0.74 \text{ x } 0.035} \right)$$

$$\text{Number fewer per 1000} = 1000 \text{ x } \left(0.035 - \frac{0.0259}{0.9909} \right)$$

Number fewer per 1000 =1000 (0.035-0.026) = 8.86

That is approximately 9 fewer deaths per 1000 operations conducted – however it must be borne in mind that this is based on an odds ratio that is non-significant. Numbers needed to treat (NNT) can also be calculated, NNT = 113, suggesting that for every 113 patients treated at the high volume hospitals there will be one less in hospital death.

These calculations can be duplicated using the overall in hospital mortality rate (2.7%) as the ACR where the absolute risk is reduction is 6.87 fewer deaths per 1000 procedures when high volume hospitals are compared with the lowest volume German hospitals (NNT 146). This is a more conservative estimate based on a lower assumed control rate, but is still based on an odds ratio that is non significant.

The odds ratio for adjusted in hospital mortality in the lowest volume quantile versus quantile 4, the second highest volume quantile is statistically significant OR 0.48 (95% CI 0.33-0.69). When the conversion calculation is conducted, using an ACR of 0.035, it suggests that there are 17.89 fewer deaths per 1000 (NNT 56) un-ruptured AAA repairs (open or EVAR) when the procedures are carried out at the higher volume institutions.

Hentscker – adjusted calculations – C1

Hentscker et al calculated odds ratios again in quantiles (quintiles) for non-ruptured AAA repair with the low volume group as the reference. The in hospital mortality rate was 5.2% in the low volume group and so 0.052 will be used as the ACR. Age, sex, type and urgency of procedure, Charlson comorbidity index, transfer between hospitals or departments, weekday/ weekend, and hospital type were adjusted for and the odds ratios between low and high volume hospitals were in the range 0.547 to 0.927 with two of the four estimates suggesting statistical significance. When the odds ratios (0.547 to 0.927) are converted to absolute risk this suggests a range of 3.61 to 22.87 fewer deaths per 1000 procedures (in hospital mortality) if procedures were carried out at the higher volume hospitals (NNT = 1/0.0287 = 44).

Holt 2009 - adjusted calculation – C2

Holt et al calculate the odds ratio for in hospital mortality per additional case performed – odds ratio 0.993 (95% CI 0.989- 0.997) adjusted for age, sex and 11 diagnostic risk factors and additionally adjusting for effects on mortality of EVAR. Using the in hospital mortality rate for the low volume quintile as the ACR (7.34%) and basing the calculation on the OR as above there will be 0.48 fewer deaths (per 1000 procedures performed) associated with an increase of one in the volume of procedures performed per hospital. In other words, assuming a linear relationship and all other factors being equal we could expect a decrease of in hospital mortality of 4.8 per thousand procedures performed for every additional 10 procedures performed at a given hospital.

0.48 fewer deaths per 1000 = 0.048 fewer deaths per 100
Therefore ARR = 0.00048
NNT = 1/0.00048 = 2083.3 – thus for each 2083 patients treated at a higher volume hospital (increments of one extra procedure per year) there will be one less death
Or multiply by 10 to give NNT per increment in volume of 10 procedures per year - NNT = 1/0.0048 = 208.33 = 209

C5 - elective EVAR – Elective EVAR (Holt 2009)
Mortality rate in low volume quintile = 6.88, OR 0.993 per additional case performed

0.45 fewer deaths per 1000 procedures for each additional procedure performed at a higher volume center

NNT 1/0.0045 = 223

C6 Elective AAA repair (open or EVAR – Elective EVAR)(Holt 2009)
Mortality rate in lower volume quantile of combined open or EVAR patients 7.34% (used this as ACR in preference to the mortality rate in the low volume quantile of patients undergoing EVAR alone which was 6.88%).

Odds ratio of 0.989 for in hospital mortality per additional case performed

0.75 fewer deaths per 1000 elective procedures performed for an increase in volume of one procedure (open or EVAR) per institution.

NNT per increment in volume of 10 procedures per year – NNT = 1/0.0075 = 133.33 = NNT 134

C7 Influence of volume of elective AAA repair (open or EVAR) on repair of emergency (intact) AAA repair (open or EVAR)(Holt 2010)

OR 0.999, mortality rate in low volume quantile 24.4% (open or EVAR repair of urgent AAA)
Number fewer per 1000=0.184509
0.185 fewer deaths per 1000 elective procedures performed for an increase in volume of one procedure
NNT per increment in volume of 10 procedures per year – NNT = 1/0.00185 = 540.54 = NNT 542

C8 Influence of volume of elective AAA repair (open or EVAR) on repair of ruptured AAA repair (open or EVAR)(Holt 2010)

OR 0.998, ACR 24.4% (0.244) in low volume quantile (open or EVAR repair of urgent AAA)

0.369109 = 0.37 fewer deaths per 1000 procedures performed for each increase of volume of one procedure per year

NNT = 1/0.0037 = 270.27 = 271 = NNT per volume increase of 10 cases per year

C10 Influence of volume of elective EVAR on repair of ruptured AAA repair (EVAR)(Holt 2010)

OR 0.999, ACR 0.44, taken from mortality rate in the low volume quantile of patients undergoing EVAR of ruptured AAA – 44%

0.24650899 =0.25 fewer deaths per 1000 procedures performed for each increase of volume of one procedure per year

NNT = 1/0.0025 = 400 = NNT per volume increase of 10 cases per year

C12 volume of ruptured AAA repairs conducted and outcomes in those undergoing ruptured AAA repair

Holt 2010 OR 0.993 mortality rate in low volume quintile of 53.9% for ruptured AAA repair (open or EVAR)
1.74594=1.7 fewer deaths per 1000 procedures performed for each increase of volume of one procedure per year
NNT= 1/0.017 = 58.82 = NNT 59 per volume increase of 10 cases per year

Trenner OR high volume Vs low volume 0.7, mortality rate in low value reference group 41.4%
0.083102535 = 83 fewer deaths per 1000 procedures treated if procedures performed at the high volume centers (8-15 cases per year) vs low volume centres (1-3 per year)

NNT =1/0.083 = 12.05 = 13. Thus for each 13 patients treated at the high volume hospital we would expect one fewer death.

Reference

Schünemann HJ, Oxman AD, Vist GE, Higgins JPT, Deeks JJ, Glasziou P, Guyatt GH. Chapter 12: Interpreting results and drawing conclusions. In: Higgins JPT, Green S (editors), Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0 (updated March 2011). The Cochrane Collaboration, 2011. Available from: www.handbook.cochrane.org.