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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 3550 words and references 1070 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\textsuperscript{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\textsuperscript{1}. These variations are within the range that could be expected as a result of random variation\textsuperscript{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\textsuperscript{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\textsuperscript{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; 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 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 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

Records identified through database searching (Primary Studies Search n= 10157) (Surgery/Outcomes Search n= 5778) (Citation Searches n = 641) (total n=16,576)

Additional records identified through other sources (Reference Tracking n=116) (Conference Proceedings Search n=27) (Total n=143)

Records after duplicates removed (n=14,343) + (n=143) Total n=14,486

Records screened title and title and abstract (n =14,486)

Records excluded (n = 14038)

Full-text articles assessed for eligibility (n =448)

Full-text articles excluded (n = 417)

Eligible studies (n=31*) AAA (n=14), Carotid (n=11) and lower limb (n=7) vascular procedures

Studies included in AAA review (n =16)

Studies reporting adjusted mortality as an outcome (n=13)

Studies excluded as carotid or lower limb populations (n =17)

Updated searches: June 2016 identified 565 citations – title abstract and full text review

Full text articles meeting AAA review inclusion criteria n=2

*One study reports on the volume outcome relationship in populations of both carotid AAA procedures and AAA repairs

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:

<table>
<thead>
<tr>
<th>Reference</th>
<th>Duration of data collection</th>
<th>country</th>
<th>Study design</th>
<th>Data source</th>
<th>AAA Population(s) studied</th>
<th>Sample size</th>
<th>Average age (years)</th>
<th>outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Powell 2014</td>
<td>2009-13</td>
<td>UK</td>
<td>Post hoc analysis</td>
<td>RCT data (IMPROVE)</td>
<td>Ruptured Open/EVAR</td>
<td>558</td>
<td>76.5</td>
<td>Mortality (30d)</td>
</tr>
<tr>
<td>Sidloff 2014</td>
<td>2008-12</td>
<td>UK</td>
<td>Retrospective analysis</td>
<td>NVD</td>
<td>Elective open/EVAR</td>
<td>21,266</td>
<td>NR</td>
<td>Mortality (IH)</td>
</tr>
<tr>
<td>Karthikesalingam 2016a</td>
<td>2003-12</td>
<td>UK and Sweden</td>
<td>Retrospective analysis</td>
<td>HES SWEDVASC</td>
<td>Ruptured Open /EVAR</td>
<td>15,296</td>
<td>74</td>
<td>Mortality (90d)</td>
</tr>
<tr>
<td>Hafez 2012</td>
<td>2008-10</td>
<td>UK</td>
<td>Retrospective analysis</td>
<td>NVD</td>
<td>Elective open/EVAR</td>
<td>13,068</td>
<td>NR</td>
<td>Mortality (UD), Complications (UD)</td>
</tr>
<tr>
<td>Karthikesalingam 2016b</td>
<td>2005-10</td>
<td>UK</td>
<td>Retrospective analysis</td>
<td>HES</td>
<td>Elective open/EVAR</td>
<td>21,272</td>
<td>74</td>
<td>Mortality (IH)</td>
</tr>
<tr>
<td>Karthikesalingam 2014</td>
<td>2005-10</td>
<td>UK</td>
<td>Retrospective analysis</td>
<td>HES</td>
<td>Ruptured Open /EVAR</td>
<td>6,897</td>
<td>78.2</td>
<td>Mortality (OP/IH)</td>
</tr>
<tr>
<td>Ozdemir 2015</td>
<td>1999-2010</td>
<td>Germany</td>
<td>Retrospective analysis</td>
<td>DGG</td>
<td>Ruptured and non-ruptured Open/EVAR</td>
<td>9,877</td>
<td>78</td>
<td>Mortality (90d)</td>
</tr>
<tr>
<td>Trenner 2016</td>
<td>2003-08</td>
<td>UK</td>
<td>Retrospective analysis</td>
<td>HES</td>
<td>Elective/ Urgent/ruptured Open/EVAR</td>
<td>8,139</td>
<td>NR</td>
<td>Mortality (IH)</td>
</tr>
<tr>
<td>Holt 2010</td>
<td>2007</td>
<td>Germany</td>
<td>Retrospective analysis</td>
<td>DRG</td>
<td>Intact AAA Open/EVAR</td>
<td>7,980</td>
<td>71</td>
<td>Mortality (IH)</td>
</tr>
<tr>
<td>Hentscker 2015</td>
<td>2005-07</td>
<td>UK</td>
<td>Retrospective analysis</td>
<td>HES</td>
<td>Elective Open/EVAR</td>
<td>7,313</td>
<td>72.6</td>
<td>Mortality (IH) LOS</td>
</tr>
<tr>
<td>Holt 2007</td>
<td>2000-05</td>
<td>UK</td>
<td>Retrospective analysis</td>
<td>HES</td>
<td>Elective/ Urgent/ruptured Open/EVAR</td>
<td>26,822</td>
<td>75.8</td>
<td>Mortality (IH) LOS complications</td>
</tr>
<tr>
<td>Holt 2012</td>
<td>1994-2004</td>
<td>Germany</td>
<td>Retrospective analysis</td>
<td>DRG</td>
<td>Elective Open</td>
<td>10,163</td>
<td>67.5</td>
<td>Mortality(PO) BT, LOS, LOS, DD, ITU stay</td>
</tr>
<tr>
<td>Eckstein 2007</td>
<td>2001-02</td>
<td>Norway</td>
<td>Retrospective analysis</td>
<td>Administrative database and voluntary vascular registry</td>
<td>Elective/ Urgent/ruptured Open/EVAR</td>
<td>1,523</td>
<td>NR</td>
<td>Mortality (IH)</td>
</tr>
</tbody>
</table>

*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. 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. (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***

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

**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.

<table>
<thead>
<tr>
<th>Comparison</th>
<th>Population hospital volume measured in</th>
<th>Population mortality measured in</th>
<th>Reference Method of volume stratification</th>
<th>Volume categories</th>
<th>Method of analysis of adjusted data</th>
<th>Confounders adjusted for</th>
<th>Mortality</th>
<th>Statistically significant results</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>C1</td>
<td>Intact AAA repair</td>
<td>Intact AAA repair</td>
<td>Trenner (2015)¹⁶ Quintiles</td>
<td>1-20 21-30 31-49 50-62 63-158 Cases pa</td>
<td>Odds ratio (categorical comparison with low volume as reference)</td>
<td>Age, ASA score, vascular risk factors and treatment modality</td>
<td>IH</td>
<td>Favour high volume: OR 0.48 (95% CI 0.33 - 0.69) for 50-62 vs 1-20 annual cases.</td>
<td>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)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Hentschker (2015)²⁵ Quintiles</td>
<td>3-15 16-25 26-39 40-67 68-209 Cases pa</td>
<td>Odds ratio (categorical comparison with low volume as reference)</td>
<td>Age, sex, Charlson comorbidity index treatment modality and type of hospital, day of procedure and transfer</td>
<td>IH</td>
<td>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</td>
<td>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)</td>
</tr>
<tr>
<td>C2</td>
<td>Elective AAA repair (open or EVAR)</td>
<td>Elective AAA repair (open or EVAR)</td>
<td>Holt (2007)¹⁷ Quintiles</td>
<td>0-0.72 7.3-12.6 12.7-19.4 19.5-32 &gt;32</td>
<td>Odds ratio (multiple logistic regression)</td>
<td>Age, sex</td>
<td>IH</td>
<td>Favour high volume OR 0.92 (95 % CI 0.88 to 0.96; P &lt; 0.001)</td>
<td>An increasing annual hospital volume of AAA repairs was associated with a significant reduction in the in hospital mortality rate</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Holt (2009)²⁸ Quintiles</td>
<td>Average number of cases per trust = 27 per year, low volume quintile 12 ps, high volume 98 pa</td>
<td>Odds ratio expressed per additional case performed</td>
<td>Age, sex and 11 diagnostic risk factors</td>
<td>IH</td>
<td>Favour high volume OR 0.992; (95% CI 0.988 to 0.995; P=0.000) per additional case performed</td>
<td>An increasing hospital volume was associated with a significant reduction in the odds of in hospital mortality.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>IH</td>
<td>Favour high volume OR 0.993; (95% CI 0.989 to 0.997; P=0.010)</td>
<td>This relationship was maintained after including adjustment for the highly significant reduction in mortality described for EVAR.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Holt Quintiles</td>
<td>0.2-12.2 Cox Age, sex and 30 days to Survival data after elective</td>
<td>Age, sex and 11 diagnostic risk factors and effect of EVAR</td>
<td></td>
<td></td>
<td>A statistically significant beneficial effect of</td>
<td></td>
</tr>
<tr>
<td>Study</td>
<td>Type of AAA repair</td>
<td>Unit volume</td>
<td>Cases pa</td>
<td>Proportionality hazard model</td>
<td>Comorbidity</td>
<td>Follow-up</td>
<td>AAA repair for all volume quintiles (Q1–Q5).</td>
<td>P</td>
<td>30-day mortality</td>
</tr>
<tr>
<td>-------</td>
<td>-------------------</td>
<td>-------------</td>
<td>----------</td>
<td>----------------------------</td>
<td>-------------</td>
<td>-----------</td>
<td>-----------------------------------------------</td>
<td>---</td>
<td>------------------</td>
</tr>
<tr>
<td>(2012)</td>
<td>Proportional</td>
<td>12.4-17.8</td>
<td>Proportional hazards model for difference in survival across quintiles</td>
<td>Comorbidity</td>
<td>4 years</td>
<td>AAA repair for all volume quintiles (Q1–Q5).</td>
<td>P&lt; 0.001</td>
<td>30 days</td>
<td>P&lt; 0.001</td>
</tr>
<tr>
<td>Karthikesalan</td>
<td>Tertiles</td>
<td>&lt;13</td>
<td>Logistic regression</td>
<td>Age, gender, social deprivation, and co-morbidity index</td>
<td>IH</td>
<td>Statistically significant relationship</td>
<td>p&lt;0.001</td>
<td>(odds ratio are not given)</td>
<td></td>
</tr>
<tr>
<td>C3</td>
<td>Elective AAA repair (open or EVAR)</td>
<td>Elective open AAA repair</td>
<td>Continuous Quintiles</td>
<td>Average number of cases per trust = 27 per year, low volume quintile 12 pa, high volume 98 pa</td>
<td>Odds ratio expressed per additional case performed</td>
<td>Logistic regression</td>
<td>Age, sex and 11 diagnostic risk factors</td>
<td>IH</td>
<td>Favours high volume OR 0.994 (95% CI 0.991 to 0.998) per additional case performed</td>
</tr>
<tr>
<td>Hafez</td>
<td>UNCLEAR</td>
<td>Not reported</td>
<td>Logistic regression</td>
<td>Gender, ASA and screening status</td>
<td>UD</td>
<td>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)</td>
<td>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’</td>
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<tr>
<td>Karthikesalan</td>
<td>Tertiles</td>
<td>&lt;13</td>
<td>Logistic regression</td>
<td>Age, gender, social deprivation, and co-morbidity index</td>
<td>IH</td>
<td>Statistically significant relationship</td>
<td>p&lt;0.001</td>
<td>(odds ratio are not given)</td>
<td></td>
</tr>
<tr>
<td>C4</td>
<td>Elective open AAA repair</td>
<td>Elective open AAA repair</td>
<td>Quantiles (6)</td>
<td>Odds ratio (categorical comparison with high volume as reference)</td>
<td>Age, ASA, AAA diameter and surgical variables</td>
<td>Logistic regression</td>
<td>Age, ASA, AAA diameter and surgical</td>
<td>PO</td>
<td>Favours high volume OR 1.903 (95% CI 1.124-3.222) for 0-9 vs &gt;50 annual cases</td>
</tr>
<tr>
<td>Eckstein</td>
<td>Continuous</td>
<td>0-9</td>
<td>Stepwise regression</td>
<td>Age, ASA, AAA diameter and surgical</td>
<td>PO</td>
<td>None</td>
<td>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</td>
<td></td>
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<tr>
<td>Case</td>
<td>Type</td>
<td>Author</td>
<td>Year</td>
<td>Method</td>
<td>Trend</td>
<td>Quarters (Cases per year)</td>
<td>Cases per year</td>
<td>Odds ratio expressed per additional case performed</td>
<td>Odds ratio expressed per additional case performed</td>
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<tr>
<td>C5</td>
<td>Elective EVAR</td>
<td>Holt (2009)^a</td>
<td>18</td>
<td>Continuous Quintiles</td>
<td>IH</td>
<td>21</td>
<td>21</td>
<td>0.99 (95% CI, 0.989 to 0.999)</td>
<td>0.99 (95% CI, 0.989 to 0.999)</td>
</tr>
<tr>
<td>C6</td>
<td>Elective AAA repair (open or EVAR)</td>
<td>Holt (2009)^a</td>
<td>18</td>
<td>Continuous Quintiles</td>
<td>IH</td>
<td>27</td>
<td>27</td>
<td>0.989 (95% CI, 0.982 to 0.995, p = 0.0007)</td>
<td>0.989 (95% CI, 0.982 to 0.995, p = 0.0007)</td>
</tr>
<tr>
<td>C6</td>
<td>Elective AAA repair (EVAR)</td>
<td>Hafez (2012)^a</td>
<td>20</td>
<td>Not reported</td>
<td>UD</td>
<td>Not reported</td>
<td>Not reported</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>C6</td>
<td>Elective AAA repair (open or EVAR)</td>
<td>Karthikesaligram (2016b)^a</td>
<td>30</td>
<td>Tertiles</td>
<td>IH</td>
<td>&lt;13</td>
<td>&lt;13</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td></td>
<td>Procedure Type</td>
<td>Procedure Description</td>
<td>Study Reference</td>
<td>Methodology</td>
<td>Odds Ratio (per additional case performed)</td>
<td>Demographics and Comorbidities</td>
<td>OR Favouring High Volume (95% CI)</td>
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<tr>
<td>C7</td>
<td>Elective AAA repair (open or EVAR)</td>
<td>Emergency intact AAA repair (open or EVAR)</td>
<td>Holt (2010)</td>
<td>Continuous</td>
<td>Summary details of volume of elective AAA repairs undertaken not published</td>
<td>Demographics and comorbidities</td>
<td>IH, Favours high volume OR 0.999 (95% CI 0.998 to 0.999, p = 0.015)</td>
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<tr>
<td>C8</td>
<td>Elective AAA repair (open or EVAR)</td>
<td>Repair of ruptured AAA</td>
<td>Holt (2010)</td>
<td>Continuous</td>
<td>Summary details of volume of elective AAA repairs undertaken not published</td>
<td>Demographics and comorbidities</td>
<td>IH, Favours high volume OR 0.998 (95% CI 0.997 to 0.999, p &lt; 0.001)</td>
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<tr>
<td>C9</td>
<td>Elective EVAR</td>
<td>Open repair of ruptured AAA</td>
<td>Holt (2010)</td>
<td>Continuous</td>
<td>Summary details of volume of elective AAA repairs undertaken not published</td>
<td>Demographics and comorbidities</td>
<td>IH, Favours high volume OR 0.982 (95% CI 0.975 to 0.988, p &lt; 0.001)</td>
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<td>C10</td>
<td>Elective EVAR</td>
<td>EVAR of ruptured AAA</td>
<td>Holt (2010)</td>
<td>Quintiles</td>
<td>Summary details of volume of elective AAA repairs undertaken not published</td>
<td>Demographics and comorbidities</td>
<td>IH, Favours high volume OR 0.999 (95% CI 0.997 to 0.999, p &lt; 0.001)</td>
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<tr>
<td>C11</td>
<td>Emergency intact AAA repair</td>
<td>Emergency intact AAA repair</td>
<td>Holt (2007)</td>
<td>Quintiles</td>
<td>0.2 - 2.1, 4.2 - 6.6, 6.7, 12.2</td>
<td>Age and sex</td>
<td>IH, Favours high volume OR 0.94 (95% CI 0.90 to 0.99, p = 0.017)</td>
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<td>Study (Year)</td>
<td>Type of AAA Repairs</td>
<td>Ruptured AAA Repairs</td>
<td>Odds Ratio (Logistic Regression)</td>
<td>Demographics and Comorbidities</td>
<td>IH</td>
<td>Favouring HI Volume OR</td>
<td>95% CI</td>
<td>P Value</td>
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<tr>
<td>Holt (2010)</td>
<td>Continuous Quintiles</td>
<td>1-20 21-34 35-48 49-77 89-149 Cases in 5 years</td>
<td>Odds ratio expressed per additional case performed</td>
<td>Demographics and comorbidities</td>
<td>IH</td>
<td>Favours high volume OR 0.997 (95% CI 0.995 to 0.999 p = 0.004)</td>
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<td>C12 Ruptured AAA Repairs</td>
<td>Quintiles</td>
<td>0.28 2.9-5.6 5.7-9.2 9.3-13.2 &gt;13.2 Cases pa</td>
<td>Odds ratio (multiple logistic regression)</td>
<td>Age and sex</td>
<td>IH</td>
<td>None</td>
<td>Favour high volume OR 0.98 (95% CI 0.95 to 1.02 p = 0.302)</td>
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<tr>
<td>Holt (2010)</td>
<td>Continuous Quintiles</td>
<td>1-26 27-38 39-52 54-72 75-146 Cases in 5 years</td>
<td>Odds ratio expressed per additional case performed</td>
<td>Demographics and comorbidities</td>
<td>IH</td>
<td>Favours high volume OR 0.993 (95% CI 0.991 to 0.995 p&lt; 0.001)</td>
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<tr>
<td>Trenner (2015)</td>
<td>Quartiles</td>
<td>1-3 4-5 6-7 8-15 Cases pa</td>
<td>Odds ratio (categorical comparison with low volume as reference)</td>
<td>Age, ASA score, vascular risk factors and treatment modality</td>
<td>IH</td>
<td>Borderline statistically significant relationship favours highest volume vs lowest volume quartile OR 0.70 (95% CI 0.49-1.00)</td>
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<tr>
<td>Powell (2014)</td>
<td>Continuous</td>
<td>Summary details of volume of ruptured AAA repairs undertaken not published</td>
<td>Logistic regression</td>
<td>Age, sex, Hardman index, randomised group, max aortic diameter, time of randomisation, lowest recorded BP, volume of IV fluids</td>
<td>30 day</td>
<td>None</td>
<td>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</td>
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<tr>
<td>Karthikesalingam (2016a)</td>
<td>Quintiles (UK)</td>
<td>1-4 5-7 8-11 12-16 Cases pa</td>
<td>Logistic regression (of categorical comparisons)</td>
<td>Age, sex, weekend surgery, comorbidity.</td>
<td>90 day</td>
<td>Statistically significant relationship p&lt;0.001 (odds ratio are not given for multiple categorical</td>
<td>Analyses of separate populations were conducted in the UK and Sweden with different volume strata and levels of adjustment used in the different populations.</td>
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<tr>
<td>Quintiles (Sweden)</td>
<td>1-3 4-7 8-11 11-20 &gt;20 Cases pa</td>
<td>Logistic regression (of categorical comparisons)</td>
<td>Age, sex, comorbidity</td>
<td>90 day</td>
<td>Borderline statistically significant relationship p=0.053 (odds ratio are not given for multiple categorical comparisons)</td>
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<tr>
<td><strong>C13</strong> Ruptured AAA repairs (open or EVAR)</td>
<td>Admission with ruptured AAA (corrective and non-corrective treatment)</td>
<td>Odds ratio (categorical comparison with high volume as reference)</td>
<td>Age, sex, comorbidities, deprivation indices, staffing levels and day of admission</td>
<td>90 day</td>
<td>Favour high volume OR 1.31 (95% CI 1.15-1.49, p&lt;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.</td>
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<tr>
<td>C14 Admission with ruptured AAA (corrective and non-corrective treatment)</td>
<td>Ruptured AAA repairs (open or EVAR)</td>
<td>Logistic regression</td>
<td>Age, sex, comorbidity</td>
<td>IH</td>
<td>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&lt;0.001) Odds ratios are not provided in the text or appendices for either analysis.</td>
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Hospital volume and mortality (adjusted) in elective and intact AAA repair

Two analyses\textsuperscript{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\textsuperscript{15,16}.

The volume of elective repair (open or endovascular) was statistically significantly and inversely associated, with short term mortality in four UK studies\textsuperscript{17-19,30} (C2), and this relationship was maintained after adjustment for the effects of EVAR on mortality\textsuperscript{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)\textsuperscript{18,20,30}.

The impact of the volume of elective open AAA repair was investigated in two studies (C4), one (UK) using administrative data\textsuperscript{18} found evidence of a statistically significant effect, while a German study\textsuperscript{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\textsuperscript{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 \textsuperscript{18,20,30} that assessed this relationship
(NNT = 134 associated with each additional 10 procedures performed \textsuperscript{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 \textsuperscript{22} (NNT = 542 associated with each additional 10 procedures performed) (C7)
and ruptured AAA repair by any method\textsuperscript{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 \textsuperscript{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)\textsuperscript{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 \textsuperscript{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\textsuperscript{22,29} and a further two analyses noted borderline statistically significant results favouring high volume\textsuperscript{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\textsuperscript{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\textsuperscript{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\textsuperscript{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\textsuperscript{20} of the outcome of elective EVAR procedures in relation to the same volume grouping there was no evidence of significance. Sidloff et al\textsuperscript{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 is available as an abstract only and the other 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; 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\textsuperscript{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\textsuperscript{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, \textit{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\textsuperscript{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 to 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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The funder had no role in the study design; in data collection, analysis and interpretation of data; in the writing of the report; and in the decision to submit the article for publication.

**Conflicts of interest:** none
References


**Supplementary appendix 1**

**Data Sources**

*Data Sources Scoping Search*

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*Data Sources Primary Studies Search*

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*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:

- BSIR (British Society of Interventional Radiology) [http://www.bsir.org](http://www.bsir.org)
- SVS (Society for Vascular Surgery) [http://www.vascularweb.org/educationandmeetings/2015vam/Pages/home.aspx](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$).mp. (23163)
9  intermittent claudication.mp. (8577)
10  (Aortic aneurysm or triple A or true aneurysm).mp. (43979)
11  Aortic Aneurysm/ (18847)
12  Aortic Aneurysm, Abdominal/ (14281)
13  (carotid disease or carotid angioplasty or carotid surgery).mp. (3114)
14  exp Carotid Artery Diseases/ (38964)
15  exp Carotid arteries/ (51386)
16  (transient isch?emic attack or TIA or stroke).mp. (196320)
17  exp Stroke/ (91854)
18  Cerebrovascular Disorders/ (44229)
exp Brain Ischemia/ (85599)
(venous insufficiency or varicose vein$ or venous leg ulcer$).mp. (20286)
exp Venous Insufficiency/ (6093)
exp Varicose Veins/ (15810)
1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 (485513)
(surgeon volume or case volume or hospital Volume or workload).mp. (30063)
(surgery and (volume or outcome)).ti. (6182)
(surgery adj5 (volume or outcome)).ab. (13415)
exp Physician's Practice Patterns/ (43633)
exp Health services misuse/ (7557)
exp Utilization review/ (10730)
(surgery adj3 (utilisation or utilization)).ti,ab. (252)
24 or 25 or 26 or 27 or 28 or 29 or 30 (106459)
23 and 31 (4107)
Meta-Analysis as Topic/ (14509)
meta analy$.tw. (71100)
metaanaly$.tw. (1422)
Meta-Analysis/ (53861)
(systematic adj (review$1 or overview$1)).tw. (60909)
exp Review Literature as Topic/ (8068)
or/33-38 (136655)
cochrane.ab. (34565)
embase.ab. (33513)
(psychlit or psyclit).ab. (932)
(psychinfo or psycinfo).ab. (14233)
(cinahl or cinhal).ab. (11624)
science citation index.ab. (2193)
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)

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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:

\[
\text{Number fewer per 1000} = 1000 \times \frac{\text{ACR} - \frac{\text{OR} \times \text{ACR}}{1 - \text{ACR} + \text{OR} \times \text{ACR}}}{1}
\]

- 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

\[
\text{Number fewer per 1000} = 1000 \times \left( 0.035 - \frac{0.74 \times 0.035}{0.9909} \right)
\]

Number fewer per 1000 = 1000 x \(0.035 - 0.0259\) = 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.

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

**C5 - elective EVAR – Elective EVAR (Holt 2009)**

Mortality rate in low volume quintile = 6.88, OR 0.993 per additional case performed

\[
0.45 \text{ fewer deaths per 1000 procedures for each additional procedure performed at a higher volume center} \\
\text{NNT} 1/0.0045 = 223
\]

**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

\[
0.75 \text{ fewer deaths per 1000 elective procedures performed for an increase in volume of one procedure (open or EVAR) per institution.}
\]
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