



Original article

Comparative analysis of the outcomes of elective abdominal aortic aneurysm repair in England and Sweden

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Background: There is substantial international variation in mortality after abdominal aortic aneurysm (AAA) repair; many non-operative factors influence risk-adjusted outcomes. This study compared 90-day and 5-year mortality for patients undergoing elective AAA repair in England and Sweden.

Methods: Patients were identified from English Hospital Episode Statistics and the Swedish Vascular Registry between 2003 and 2012. Ninety-day mortality and 5-year survival were compared after adjustment for age and sex. Separate within-country analyses were performed to examine the impact of co-morbidity, hospital teaching status and hospital annual caseload.

Results: The study included 36 249 patients who had AAA treatment in England, with a median age of 74 (i.q.r. 69–79) years, of whom 87.2 per cent were men. There were 7806 patients treated for AAA in Sweden, with a median of age 73 (68–78) years, of whom 82.9 per cent were men. Ninety-day mortality rates were poorer in England than in Sweden (5.0 versus 3.9 per cent respectively; $P < 0.001$), but were not significantly different after 2007. Five-year survival was poorer in England (70.5 versus 72.8 per cent; $P < 0.001$). Use of EVAR was initially lower in England, but surpassed that in Sweden after 2010. In both countries, poor outcome was associated with increased age. In England, institutions with higher operative annual volume had lower mortality rates.

Conclusion: Mortality for elective AAA repair was initially poorer in England than Sweden, but improved over time alongside greater uptake of EVAR, and now there is no difference. Centres performing a greater proportion of EVAR procedures achieved better results in England.

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Introduction

Perioperative mortality remains the key benchmark for patients offered elective abdominal aortic aneurysm (AAA) repair. There is substantial international variation in mortality from AAA¹, and many non-operative factors may influence risk-adjusted outcomes. Endovascular aneurysm repair (EVAR) provides safer short-term results than open surgery^{2–5}, but the availability of this technology varies. Both the use of EVAR and the outcomes of vascular surgery are known to vary between hospitals and countries^{6,7}, and benchmarking of institutional and national data is required to provide perspective for the increasing trend to publish mortality results in the public domain. Comparative

analysis of international data can highlight factors that are associated with best practice and aid the formulation of strategies to improve patient care or the equity of service provision. Existing international comparisons have reported in-hospital mortality⁸. Multiple studies have shown that there is an increased mortality risk approximately 90 days after aortic surgery, which is a reason to evaluate 90-day rather than 30-day or in-hospital mortality for short-term results⁹. From the patient's perspective, however, the durability of repair and long-term survival are of greater importance^{10,11}.

The objective of this work was to study differences and time trends in short-term (90 days) and long-term (5 years)

Table 1 Descriptive results for elective abdominal aortic aneurysm repair in England and Sweden

	England (n = 36 249)	Sweden (n = 7806)	P*
No. of patients undergoing EVAR	14 226 (39.3)	3705 (47.5)	< 0.001
30-day mortality	1237 (3.4)	183 (2.3)	< 0.001
Open repair	1042 of 22 023 (4.7)	129 of 4101 (3.1)	< 0.001
EVAR	195 of 14 226 (1.4)	54 of 3705 (1.5)	0.747
90-day mortality	1812 (5.0)	304 (3.9)	< 0.001
Open repair	1423 of 22 023 (6.5)	195 of 4101 (4.8)	< 0.001
EVAR	389 of 14 226 (2.7)	109 of 3705 (2.9)	0.530
5-year survival (%)	70.5	72.8	< 0.001
Teaching hospitals in analysis	31 of 157 (19.7)	9 of 37 (24)	0.694
No. of AAAs treated in teaching hospital	8511 (23.4)	3797 of 7754 (49.0)	< 0.001

Values in parentheses are percentages. EVAR, endovascular aneurysm repair; AAA, abdominal aortic aneurysm. * χ^2 test.

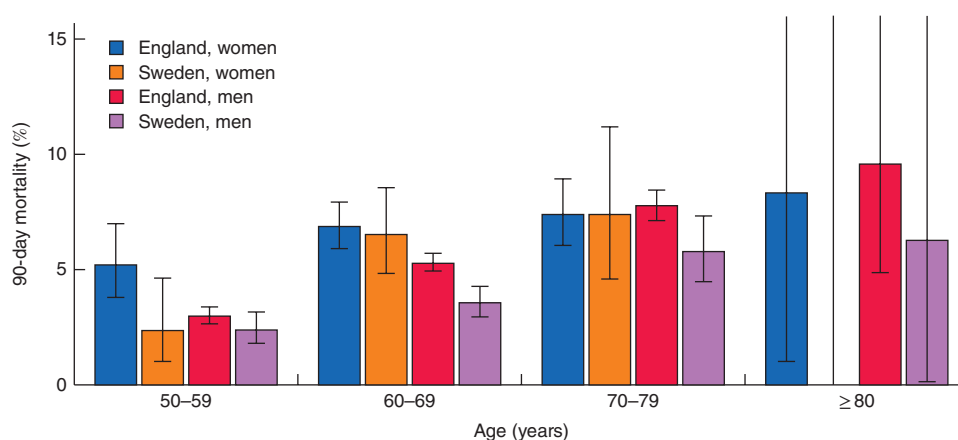


Fig. 1 Ninety-day mortality after elective abdominal aortic aneurysm repair in England and Sweden. Values are means with 95 per cent confidence intervals

mortality after elective AAA repair in two European countries, with special focus on the importance of uptake of EVAR and centralization to high-volume centres. There are few similar international comparative studies^{6,12}.

Methods

Demographic and in-hospital outcome data were extracted from Hospital Episode Statistics (HES) in England, and the Swedish Vascular Registry (Swedvasc) for all patients undergoing elective infrarenal AAA repair between 1 January 2003 and 31 December 2012. HES is the administrative data set for the English National Health Service (NHS) and describes every admission to an English hospital. Swedvasc is based on prospectively collected data, with nationwide coverage. Both data sets have been subject to extensive internal and external studies of data quality^{9,13-15}, and shown excellent validity. Accurate long-term survival data were available through the linkage of both countries' data sets to the national (government)

population registry, obviating the problem with loss to follow-up in the analysis of long-term survival.

The inclusion criteria comprised: patients undergoing elective infrarenal AAA repair, defined by an elective mode of admission and ICD-10 or OPCS-4 codes in HES; and according to predefined variables in the Swedvasc database. EVAR and open AAA repairs were identified according to previously published methodology for HES and Swedvasc. The primary outcome measures were 90-day and 5-year mortality after open or endovascular repair, with outcomes considered separately for three age groups (less than 70 years, 70-79 years and 80 years or more). Secondary outcome measures included the proportion of patients managed by EVAR, outcomes in teaching *versus* non-teaching hospitals, and outcomes for hospitals with varying annual caseload (volume) for AAA repair.

Patient- and hospital-level factors were extracted to enable comparable risk adjustment in both HES and Swedvasc data. Pre-existing co-morbidity was defined separately for Sweden and England, with techniques validated

Elective abdominal aortic aneurysm repair outcomes in England and Sweden

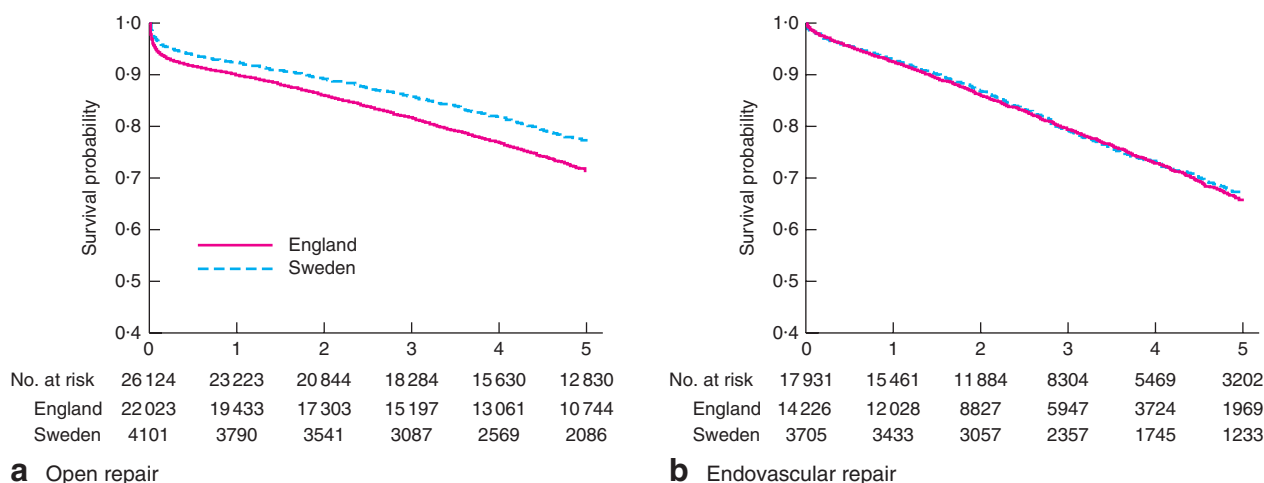


Fig. 2 Five-year survival after elective abdominal aortic aneurysm repair in England and Sweden, adjusted for age and sex in both countries: **a** open repair and **b** endovascular repair

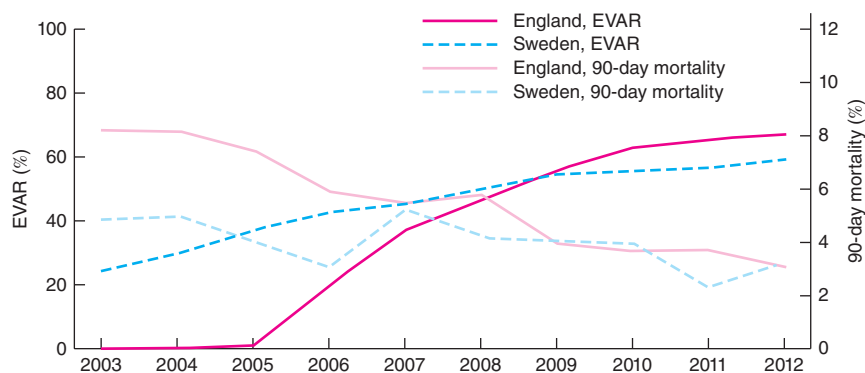


Fig. 3 Use of endovascular aneurysm repair (EVAR) and 90-day mortality in England and Sweden during the study

independently for each country, using the variables available within the Swedvasc data set, and separate components of the Royal College of Surgeons' modified Charlson Index for HES¹⁶. Hospital factors included bed capacity, teaching status and institutional annual volume (caseload) for AAA repair. Hospital teaching status and bed capacity were classified for English hospitals from publicly available data. Institutional volume (caseload) for AAA repair was represented using previously defined methodology for quintile analysis¹⁷. The quintiles comprised five groups of institutions in each country, arranged by the number of AAA repairs undertaken per year; each quintile contained a similar number of patients. They were created to ensure that all hospitals of a particular annual operative caseload were grouped together, rather than splitting hospitals of the same annual volume to create exactly the same number of patients in each quintile. A sensitivity analysis was carried out by merging both data sets and calculating the

mean number of operations per hospital per year, with classification of the quintiles based on the overall volume per hospital in both countries. Owing to potentially systematic differences in diagnostic coding between England and Sweden, risk adjustment for co-morbidity was used only for within-country analysis, rather than for comparative analysis between countries.

Statistical analysis

Primary and secondary outcomes were modelled separately for HES and Swedvasc data. Binary logistic regression was used for within-country analysis of 90-day mortality, whereas Cox regression analysis was used to assess the 5-year mortality. Backward selection procedures were used with comparison of models by means of the likelihood ratio test to ascertain whether individual co-variables improved goodness of fit. The selection process was based on models that included all potential predictor variables

Table 2 Multivariable logistic regression analysis of predictors of 90-day mortality in England

	Odds ratio	P
Age		< 0.001
Sex (F versus M)	1.14 (1.00, 1.30)	0.045
Year of operation*		< 0.001
2003–2004 versus 2005–2008	1.20 (1.07, 1.36)	
2005–2008 versus 2009–2012	1.38 (1.23, 1.56)	
Hospital volume (quintiles 1–4 versus 5)*†	1.54 (1.39, 1.71)	< 0.001
Teaching hospital (no versus yes)	0.99 (1.11, 0.88)	0.892§
No. of co-morbidities‡		< 0.001
> 3 versus 3	1.83 (1.40, 2.41)	
3 versus 2	1.21 (1.02, 1.44)	
2 versus 0–1	1.41 (1.27, 1.57)	
Type of repair		< 0.001
Type of repair by age (open repair versus EVAR)*		0.004
Age < 70 years	1.69 (1.37, 2.24)	
Age 70–79 years	2.73 (2.41, 3.14)	
Age ≥ 80 years	2.99 (2.57, 3.49)	

Values in parentheses are 95 per cent confidence intervals. *Orthogonal contrasts were calculated where possible to establish the differences between categories. †Hospital volume was analysed in quintiles based on annual number of intact abdominal aortic aneurysm repairs; quintile 5 had the highest volume. ‡Assessed according to Royal College of Surgeons' modified Charlson Index. EVAR, endovascular aneurysm repair. §P value before being out of the model.

Table 3 Multivariable logistic regression analysis of predictors of 90-day mortality in Sweden

	Odds ratio	P
Age		< 0.001
Sex (F versus M)	1.37 (0.99, 1.89)	0.054
Year of operation*		< 0.001
2003–2005 versus 2006–2007	1.33 (1.14, 1.56)	
2006–2007 versus 2008–2009	0.75 (0.64, 0.89)	
2008–2009 versus 2010–2012	1.29 (1.10, 1.51)	
Hospital volume (quintiles)*†		< 0.001
1–2 versus 4–5	0.60 (0.38, 0.95)	
1–2 versus 3	1.81 (1.08, 3.03)	
Teaching hospital (no versus yes)	1.66 (1.11, 2.50)	0.015
Type of repair		< 0.001
Type of repair by age (open repair versus EVAR)*		0.019
Age < 70 years	0.98 (0.60, 1.83)	
Age 70–79 years	2.18 (1.51, 3.03)	
Age ≥ 80 years	3.17 (0.90, 4.77)	

Values in parentheses are 95 per cent confidence intervals. *Orthogonal contrasts were calculated when possible to establish the differences between categories. †Hospital volume was analysed in quintiles based on annual number of intact abdominal aortic aneurysm repairs; quintile 5 had the highest volume. EVAR, endovascular aneurysm repair.

without univariable preselection, followed by backward selection. Co-variables considered for modelling included endovascular repair, age, sex, co-morbidity, hospital procedural volume (caseload), hospital bed capacity and

Table 4 Cox regression analysis of factors influencing 5-year survival in England

	Hazard ratio	P
Age (per year)		< 0.001
Sex (F versus M)	1.09 (0.95, 1.25)	0.209§
Year of operation*		< 0.001
2003–2005 versus 2006–2008	1.11 (1.05, 1.18)	
2006–2008 versus 2009–2010	1.19 (1.12, 1.26)	
2009–2010 versus 2011	1.14 (1.03, 1.25)	
2011 versus 2012	1.20 (1.04, 1.39)	
Hospital volume (quintiles 1–4 versus 5)*†	1.10 (1.05, 1.16)	0.003
Teaching hospital (no versus yes)	0.94 (0.89, 0.99)	0.037
No. of co-morbidities‡		< 0.001
> 3 versus 3	1.29 (1.14, 1.47)	
3 versus 2	1.28 (1.19, 1.38)	
2 versus 0–1	2.62 (1.49, 4.62)	
Type of repair by age (open repair versus EVAR)*		0.009
Age < 70 years	0.85 (0.77, 0.94)	
Age 70–79 years	1.01 (0.95, 1.07)	
Age ≥ 80 years	0.99 (0.93, 1.05)	

Values in parentheses are 95 per cent confidence intervals. *Orthogonal contrasts were calculated when possible to establish the differences between categories. †Hospital volume was analysed in quintiles based on annual number of intact abdominal aortic aneurysm repairs; quintile 5 had the highest volume. ‡Assessed according to Royal College of Surgeons' modified Charlson Index. EVAR, endovascular aneurysm repair. §P value before being out of the model.

Table 5 Cox regression analysis of factors influencing 5-year survival in Sweden

	Hazard ratio	P
Age		< 0.001
Sex (F versus M)	1.09 (0.95, 1.25)	0.209‡
Year of operation*		0.001
2003–2005 versus 2006–2007	1.33 (1.14, 1.56)	
2006–2007 versus 2008–2009	0.75 (0.64, 0.89)	
2008–2009 versus 2010–2012	1.29 (1.10, 1.51)	
Hospital volume (quintiles 1–3 versus 4–5)*†	0.84 (0.74, 0.95)	0.006
Teaching hospital (no versus yes)	1.66 (1.11, 2.50)	0.015
Type of repair by age (open repair versus EVAR)*		0.004
Age < 70 years	0.55 (0.46, 0.65)	
Age 70–79 years	0.74 (0.66, 0.82)	
Age ≥ 80 years	0.92 (0.77, 1.12)	
Current smoker (yes versus no)	1.26 (0.95, 1.69)	0.114‡
Pulmonary disease (yes versus no)	1.79 (1.34, 2.39)	< 0.001
Diabetes mellitus (yes versus no)	1.33 (0.89, 1.99)	0.165‡
Hypertension (yes versus no)	1.31 (0.99, 1.74)	0.535‡
Cardiovascular disease (yes versus no)	1.20 (0.83, 1.74)	0.328‡
Myocardial infarction (yes versus no)	1.31 (0.99, 1.73)	0.059‡
Renal disease (yes versus no)	2.47 (1.73, 3.52)	< 0.001

Values in parentheses are 95 per cent confidence intervals. *Orthogonal contrasts were calculated when possible to establish the differences between categories. †Hospital volume was analysed in quintiles based on annual number of intact abdominal aortic aneurysm repairs; quintile 5 had the highest volume. EVAR, endovascular aneurysm repair. ‡P value before being out of the model.

teaching status, geographical region and year of surgery. These risk factors were included in the models as they were reported to be important in the literature^{18–20}.

It is acknowledged that estimates of the association between type of operation performed (open repair or EVAR) and mortality can be biased owing to confounding by other co-variables in observational data. To adjust for the propensity of patients to undergo open repair or EVAR, the g-formula technique (a causal inference analysis)^{17,21} was employed for estimation of the odds ratio (OR) for the association between type of surgery (open repair or EVAR) and 90-day mortality. The g-formula is a standard application of a propensity weighting technique that reduces the impact of selection bias between EVAR and open repair.

Confidence limits were estimated using bootstrapping with 1000 samples in each country. Age- and sex-matched analyses were undertaken to compare English and Swedish outcomes for 90-day or 5-year mortality after both EVAR and open repair, with focused analysis for patients aged 80 years or older and those younger than 80 years. HES and Swedvasc data sets were linked using common variables, and stratified for sex and 5-year age groups. A conditional logistic regression analysis was performed incorporating the strata as a blocking variable, to report the adjusted difference between England and Sweden.

$P < 0.050$ was regarded as statistically significant. All analyses were carried out using SAS[®] version 9.3 (SAS Institute, Cary, North Carolina, USA) and R software (R Foundation for Statistical Computing, Vienna, Austria).

Results

Elective AAA repair was done in 36 249 patients in England and 7806 in Sweden during the study interval. In England, the median age was 74 (i.q.r. 69–79) years and 87.2 per cent were men. In Sweden, the median age was 73 (68–78) years and 82.9 per cent were men. During the study, the rate of elective AAA repair recorded in England was 26.68 per 100 000 population in 2003 and 33.08 per 100 000 in 2012. For Sweden, the rate of elective AAA repair was 28.81 and 36.97 per 100 000 population in 2003 and 2012 respectively. Further information on the annual rates of elective AAA repair is provided in *Table S1* (supporting information).

Comparative 90-day mortality and 5-year survival

The crude 90-day mortality rate was greater after AAA repair in England compared with Sweden (5.0 *versus* 3.9 per cent respectively; $P < 0.001$) (*Table 1*). Overall age and sex-adjusted 90-day mortality was greater in England (OR

1.36, 95 per cent c.i. 1.20 to 1.54; $P < 0.001$) (*Fig. 1*). Ninety-day mortality was worse in England than Sweden for open repair (OR 1.40, 1.20 to 1.63; $P < 0.001$), but similar after EVAR (OR 0.93, 0.75 to 1.16; $P = 0.530$) (*Table 1*).

Five-year survival rates were worse in England than in Sweden: 70.5 (95 per cent c.i. 70.0 to 71.1) *versus* 72.8 (71.7 to 73.9) per cent ($P < 0.001$). This difference persisted after matching for age and sex (hazard ratio (HR) 1.08, 95 per cent c.i. 1.03 to 1.14; $P = 0.002$). Subgroup analysis demonstrated a difference in life expectancy for patients undergoing open repair in England compared with Sweden (HR 1.22, 1.13 to 1.31; $P < 0.001$) but not for those undergoing EVAR (HR 1.01, 0.94 to 1.08; $P = 0.899$) (*Fig. 2*; *Fig. S1*, supporting information).

Increased use of EVAR in England over time coincided with a reduced difference in 90-day mortality, such that a sensitivity analysis for 90-day mortality in England compared with Sweden by year (adjusted in accordance with previous logistic models for 90-day mortality) demonstrated no significant difference between the countries from 2007 to 2012 (*Fig. 3*; *Fig. S2*, supporting information).

Secondary outcomes

The overall use of EVAR was greater in Sweden (47.5 per cent *versus* 39.1 per cent in England) but increased considerably in England during the study (*Fig. 3*), and even surpassed that in Sweden between 2010 and 2012. EVAR was used in the majority of AAA repairs in both countries after 2009.

In both England and Sweden, factors associated with 90-day mortality were increasing age, female sex and use of open repair (*Tables 2 and 3*). Five-year survival was associated with age at surgery and year of surgery in both countries (*Tables 4 and 5*).

In both countries, quintiles of hospital volume were distributed at similar intervals, with low-volume hospitals in England performing 14 or fewer AAA repairs per annum and those in Sweden undertaking ten or fewer AAA repairs per annum, and high-volume hospitals carrying out at least 67 and at least 55 AAA repairs annually respectively (*Table S2*, supporting information). Thirty-day mortality by hospital caseload for each country is shown in *Table S3* (supporting information). In England, institutions with a high annual volume had lower 90-day and 5-year mortality. The sensitivity analysis, with definition of quintiles based on overall volumes in both countries, resulted in an increased number of high-volume centres in England, as the threshold for highest-volume centres was set at 60 procedures (*Table S4*, supporting information). This analysis

confirmed the association between volume and outcome in England for both 90-day mortality ($P < 0.001$) and 5-year mortality ($P = 0.017$), but did not find a significant association in Sweden (Tables S5 and S6, supporting information).

Analysis of outcomes by age revealed that 90-day mortality was worse in England than Sweden both for patients aged less than 80 years (OR 1.33, 95 per cent c.i. 1.14 to 1.54; $P < 0.001$) and those aged 80 years or more (OR 1.30, 1.03 to 1.64; $P = 0.028$) (Table S7, supporting information). There was no difference in outcome after EVAR between England and Sweden in these age groups ($P = 0.640$ and $P = 0.828$ respectively). In patients younger than 80 years, open repair was associated with higher mortality in England than in Sweden (OR 1.61, 1.29 to 2.01; $P < 0.001$), but there was no difference in outcome after open repair between the two countries in those aged 80 years or more ($P = 0.533$). Five-year survival after open surgery was worse in England than Sweden for patients younger than 80 years (HR 1.23, 1.13 to 1.34; $P < 0.001$).

There was a statistically significant interaction between age and type of surgery: EVAR or open AAA repair. Ninety-day mortality in England was significantly better for EVAR than open repair in all age groups. In Sweden, 90-day mortality after EVAR was significantly better than open repair in the 70–79-year age group. Five-year survival was significantly worse after EVAR than open repair among patients younger than 70 years in England and those aged less than 80 years in Sweden (Tables 2–5).

Discussion

In this study, the short- and long-term outcomes of AAA repair were analysed for a 10-year national cohort of patients in two European countries with similar health-care systems. The main finding was that 90-day and 5-year outcomes for elective AAA repair were significantly better in Sweden than in England. This appeared partially attributable to the poor outcome of open repair in England, where introduction of EVAR occurred later than in Sweden. In both countries, better results were seen each year. In England, institutions performing greater numbers of AAAs repair per annum had lower mortality rates. In recent years, the use of EVAR has increased dramatically in England, where up to 60 per cent of repairs currently are performed with the endovascular technique. This is most likely the main explanation for the observed reduction in mortality over time, with abolition of any difference between England and Sweden after 2007.

Increased perioperative mortality after AAA repair in England compared with other countries has been

documented previously in registry-based analyses using data from the UK National Vascular Database^{6,22}. However, this finding has been criticized owing to potential case selection in early iterations of the database, which was previously based on voluntary registration. The present report confirms the previous finding using HES data for England with linked data for long-term mortality, allowing long-term comparison of two full national cohorts of patients. Additionally, this report shows that the perioperative mortality difference between England and Sweden is sustained up to 5 years after repair. The fact that long-term survival curves are virtually parallel (Fig. 2), contradicts the suggestion that eventual differences in case-mix can explain the difference in short-term outcomes.

Although it was not possible to analyse the mean AAA diameter in each country, previous publications^{23,24} showed that the mean diameter of treated AAA between 2005 and 2013 was 6.2 cm in Sweden, whereas it was 6.6 cm in the UK. In Sweden 20.5 per cent of patients had AAA repair at a diameter less than 5.5 cm, compared with only 9.2 per cent in the UK. Part of this difference could be explained by the fact that Swedvasc did not differentiate between treatment for iliac or aortic aneurysm. The higher rate of small AAA repair in Sweden could partly explain the better overall 90-day mortality and 5-year survival. However, as this was not analysed, causality cannot be inferred. Even though the overall results (after adjustment for age and sex) showed a difference in mortality, the AAA diameter size does not explain why there was no difference in 90-day mortality between England and Sweden for the years 2007–2012. This suggests that difference in size of AAA diameter at repair is not the main reason for the discrepancy between the two countries.

A potential confounder in long-term survival is differences in expected survival between countries. According to Organisation for Economic Co-operation and Development data²⁵, the life expectancy of a 65-year-old is 18.6 years in the UK, compared with 18.8 years in Sweden for men, and 20.9 versus 21.3 years for women²⁵. Based on this small difference, it is unlikely that general life expectancy explains the differences between countries.

Another potential confounder is the way vascular surgery services were arranged in each country. During the study, vascular surgery in Sweden was already carried out by vascular specialist centres. However, in England, pressures to centralize vascular surgery started around 2007, with initial processes starting around 2009^{26,27} and further remodelling around 2013²⁸. The present study showed that, through increased use of EVAR in England between 2007 and 2012, the difference in 90-day mortality between the two countries was abolished. High-volume centres in

England had better 90-day mortality and 5-year survival results, in line with previous studies^{29–31}. Thus, centralization, while improving service provision in England, could have increased the rate of EVAR, abolishing the difference in the 90-day mortality between the two countries after 2010. This effect was similarly demonstrated in a previous study³² of mortality after ruptured AAA between the two countries.

This study showed that 90-day mortality in women was higher than among men in both countries. However, this sex difference was not noted at 5 years. Although previous studies^{33,34} highlighted the higher initial perioperative mortality in women, the 5-year mortality did not confirm this^{34,35}. This is possibly due to other competing factors, including increasing age, co-morbidities and type of repair, in line with other studies³⁶.

Although short- and long-term mortality after intact AAA repair was higher in England than in Sweden after open repair, there was no difference after EVAR. Even though young patients (aged under 70 years) had a survival benefit from EVAR in the early postoperative period, these patients had an increased long-term risk of death compared with those in the same age cohort treated by open surgery. There are several potential explanations for this finding, including an effect of case selection, with younger patients at higher operative risk being offered EVAR.

Perioperative and long-term outcomes were both affected by hospital volume and teaching status. A recent analysis of ruptured AAA mortality in Sweden and England confirmed the same trend in terms of hospital volume and outcome during the same time interval (2003–2012)³².

Limitations of this study include its retrospective nature, and differences in the national databases included in the report. The English HES is exposed to risks of coding variations. However, previous validations have underlined the robustness of this database for analysis of AAA mortality³². The Swedvasc database has been validated internally and externally, with excellent results^{13,15}. A further limitation is the lack of standardized co-morbidity data, including smoking habits. However, population-based data on smoking status published by Eurostat³⁷ in 2014 do not show any difference between the two countries (Table S8, supporting information). Lack of data on AAA diameter and morphology, as well as cause of death, is another limitation. These data are not available within nationally comprehensive administrative data sets. Thus, comparison of patient selection, anatomical suitability for EVAR and long-term aortic-related death rate could not be carried out.

In both countries, better results from AAA repair were seen each year, and in England institutions performing greater numbers of AAA repair per annum had lower

90-day and 5-year mortality rates. These findings may justify central funding for EVAR programmes to ensure equity of access to endovascular technology. In younger patients, long-term outcome was, however, inferior after EVAR despite a short-term survival benefit, which may question use of EVAR in treatment of patients with long life expectancy.

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Supporting information

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