

REVIEW

## Systematic Review and Meta-analysis of Long-term survival After Elective Infrarenal Abdominal Aortic Aneurysm Repair 1969–2011: 5 Year Survival Remains Poor Despite Advances in Medical Care and Treatment Strategies

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### WHAT THIS PAPER ADDS

The key findings of this study are that 5 year survival after elective infrarenal AAA repair is 69% and that this value has not improved over the period 1969–2011. A larger aneurysm diameter at the time of surgery was associated with poorer 5 year survival. This 5 year survival figure is disappointingly poor; patients diagnosed with a Dukes B colorectal cancer can expect better 5 year survival. More needs to be done to address the shortfall in survival to ensure that patients who can now reasonably expect to survive major aortic surgery live long enough to justify what remains a significant intervention.

**Background:** Improved critical care, pre-operative optimization, and the advent of endovascular surgery (EVAR) have improved 30 day mortality for elective abdominal aortic aneurysm (AAA) repair. It remains unknown whether this has translated into improvements in long-term survival, particularly because these factors have also encouraged the treatment of older patients with greater comorbidity. The aim of this study was to quantify how 5 year survival after elective AAA repair has changed over time.

**Methods:** A systematic review was performed identifying studies reporting 5 year survival after elective infrarenal AAA repair. An electronic search of the Embase and Medline databases was conducted to January 2014. Thirty-six studies, 60 study arms, and 107,814 patients were identified. Meta-analyses were conducted to determine 5 year survival and to report whether 5 year survival changed over time.

**Results:** Five-year survival was 69% (95% CI 67 to 71%,  $I^2 = 87\%$ ). Meta-regression on study midpoint showed no improvement in 5 year survival over the period 1969–2011 (log OR  $-0.001$ , 95% CI  $-0.014$ – $0.012$ ). Larger average aneurysm diameter was associated with poorer 5 year survival (adjusted log OR  $-0.058$ , 95% CI  $-0.095$  to  $-0.021$ ,  $I^2 = 85\%$ ). Older average patient age at surgery was associated with poorer 5 year survival (adjusted log OR  $-0.118$ , 95% CI  $-0.142$  to  $-0.094$ ,  $I^2 = 70\%$ ). After adjusting for average patient age, an improvement in 5 year survival over the period that these data spanned was obtained (adjusted log OR  $0.027$ , 95% CI  $0.012$  to  $0.042$ ).

**Conclusion:** Five-year survival remains poor after elective AAA repair despite advances in short-term outcomes and is associated with AAA diameter and patient age at the time of surgery. Age-adjusted survival appears to have improved; however, this cohort as a whole continues to have poor long-term survival. Research in this field should attempt to improve the life expectancy of patients with repaired AAA and to optimise patient selection.

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**INTRODUCTION**

Over recent decades, there has been a consistent improvement in the short-term mortality associated with elective repair of infrarenal aortic aneurysms (AAA). These improvements have followed general developments in surgical technique and peri-operative procedures,<sup>1</sup> the advent of endovascular surgery,<sup>2-7</sup> improvements in critical care and vascular anaesthesia, and the centralization of aortic surgery to specialist teams with high operative caseload.

The decision to repair an AAA requires consideration of the risk of rupture without surgery, the peri-operative risk of death, and the patient’s overall life expectancy; balanced with the patient’s own preference. As the aim of AAA repair is to prolong life through the prevention of rupture, surgery should only be performed if the risk of rupture without surgery outweighs the peri-operative risk of surgery itself, in patients whose life expectancy is long enough to result in long-term benefit. It is therefore perhaps unsurprising that short-term operative mortality has been the primary focus of most outcomes research reporting the results of AAA repair. However, longer-term mortality continues to be concerning in the years that follow surgery,<sup>8</sup> as patients

with AAA have considerable cardiovascular risk factors compared with the wider population.<sup>9,10</sup>

It remains unknown whether improvements in the peri-operative safety of AAA repair have translated to improved 5 year survival following surgery. Long-term survival critically influences the cost-effectiveness of AAA repair,<sup>2</sup> and is a key measure to justify surgical intervention at a population level. Understanding trends in published results will clarify whether long-term survival is an appropriate therapeutic target for further research. The aim of this study was to quantitatively summarise the evidence for 5 year survival after elective infrarenal AAA repair to assess whether improvements in peri-operative practice have translated into better long-term mortality over time.

**METHODS**

An electronic search of all English-language literature was performed using the Embase and Medline databases, covering the years 1950–2013, in accordance with Preferred Items for Reporting of Systematic Reviews and Meta Analyses (PRISMA) guidelines (Fig. 1). The free-text search terms “abdom\*,” “aortic aneurysm,” “abdom\*aort\*,” “AAA,” “surger\*,” “surgical\*,” “repair\*,” “surviv\*,”

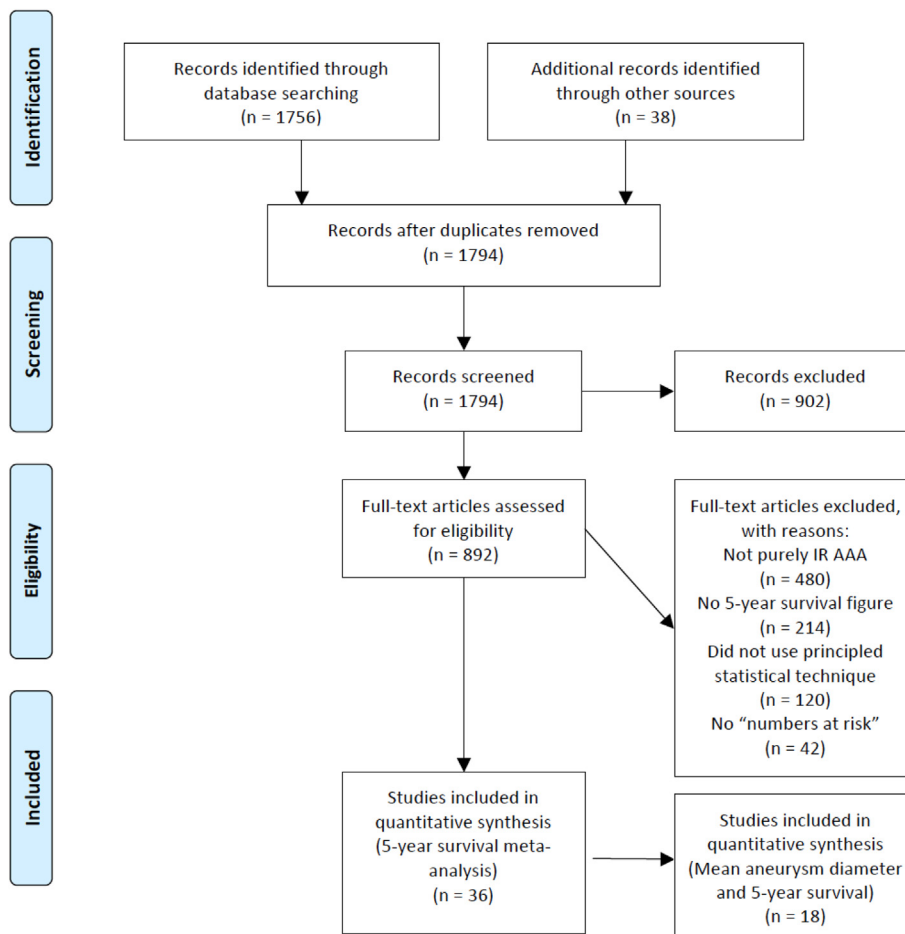


Figure 1. PRISMA diagram.

“mortal\*,” “electiv\*,” “elect\*,” “emergenc\*,” and MeSH/Emtree terms “aortic aneurysm, abdominal, surgical procedures, operative, mortality, survival rate, disease-free survival, surgical procedures, elective,” [MeSH] and “abdominal aorta aneurysm, surgery, aorta surgery, abdominal surgery, aneurysm surgery, survival, disease free survival, failure free survival, long term survival, post treatment survival, survival rate, survival time, mortality, surgical mortality, elective surgery,” [Emtree] were used in combination with the Boolean operators AND or OR and NOT (Appendix I). RefWorks software (RefWorks, Bethesda, MD, USA) was used to de-duplicate the electronic search results.

Grey literature and reference lists from relevant papers were reviewed to identify other studies that may have contained relevant data. The inclusion criteria for this meta-analysis comprised studies reporting 4 year, 5 year, or 6 year survival after elective repair of an infrarenal aortic aneurysm, using a principled statistical technique to account for loss to follow up, other censoring of data, or varying recruitment over time. Studies were excluded if they did not report the “numbers at risk” at 5 years or at both 4 and 6 years. Abstracts of citations identified from the literature search were reviewed by two of the authors (SSB and BOP), who then independently extracted all relevant data. Any disagreements were resolved by consensus agreement; this was overseen and arbitrated when necessary by another of the authors (AK).

Studies were also excluded where data for patients with AAA were not separable from data for patients with other aneurysm morphologies (juxtarenal, suprarenal, thoraco-abdominal) or occlusive aortic disease, if no date range for the study was given, if emergent and elective survival was not reported separately, and if specific age or comorbidity patient subgroups were reported without survival data for the patient group as a whole.

Data were extracted regarding each study’s country of origin, study timeframe and midpoint, medical therapies such as antiplatelet and statin therapy and comorbidity data such as known ischaemic heart disease, diabetes mellitus, or smoking status. The mean/median aneurysm diameter for patients undergoing surgery was extracted where described.

A random effects meta-analysis was conducted to quantify the 5 year survival of patients undergoing elective AAA repair. Meta-regression was performed to assess whether 5 year survival was associated with study midpoint or aneurysm diameter at the time of surgery.

### Statistical analyses

The meta-analysis to quantify 5 year survival was performed using a random effects model (dictated by the large degree of heterogeneity among the studies included in the analysis) as per DerSimonian and Laird on the log odds of survival outcome scale.<sup>11</sup> All meta-analyses and meta-regressions treated the arm level data as independent

and so any correlation resulting from arms from the same study was ignored in analysis. This was an acknowledged limitation of the statistical modelling. Within-study variances were calculated using a conservative sample size (number at risk at 5 years/survival probability) to produce large within study variances such that censoring had the most effect in increasing the uncertainty of the study arm estimates. For studies that only provided 4 year and 6 year survival values, and number of patients at risk, averaging the 4 year and 6 year values derived the 5 year survival value.

A random effects meta-regression analysis was carried out to assess the change, if any, over the timescale that these studies covered using moments estimator methodology. This analysis used the same outcome data as in the meta-analysis for survival; and study mid-date (in years) was used as the only covariate. This analysis resulted in a log-odds ratio of survival associated with a 1 year change in study mid-date, where a positive log-odds ratio indicated that the probability of 5 year survival after AAA repair increased over time.

A second random effects meta-regression analysis was conducted to evaluate the effect of aneurysm diameter on 5 year survival, while adjusting for the effect of time. This analysis used study mid-date and the mean diameter (in mm) as covariates, so that an adjusted (for time) log-odds ratio associated with a 1 mm increase in mean diameter was obtained. Here a positive log-odds ratio indicated that the survival probability increased as mean diameter increased. Finally, a third random effects meta-regression was conducted using mid-date and average patient age (in years), so that an adjusted (for time) log-odds ratio associated with a 1 year increase in age was obtained. Here a positive log-odds ratio indicated that the survival probability increased as age increased. All analyses were performed in “R” using the metafor package.

## RESULTS

Thirty-six studies reported 107,814 patients from 14 different countries between 1969 and 2011 and contributed to survival meta-analysis and a meta-regression of the relationship between 5 year survival and study mid-point (PRISMA diagram and Table 1). Of these, 18 studies consisting of 13,281 patients contributed to the meta-regression of the relationship between aneurysm diameter at the time of surgery and subsequent 5 year survival (Table 2).

Information to describe comorbid conditions and medication was limited; eight studies reported the proportion of patients prescribed statin or antiplatelet agents but with limited data on dose regimens. Twenty-nine of 36 studies reported relevant comorbidity but with poor precision in classification (Table 3). There was a wide range of prevalence of diabetes (5.4–22.7%), dyslipidaemia (11.0–56.2%), ischaemic heart disease (25.0–82.7%), and

**Table 1.** Studies contributing to overall 5 year survival.

Country providing data	Number of studies	Number of patients	First author or study name
US	11	92,957	Bernstein, <sup>14</sup> Brewster, <sup>18</sup> Conrad, <sup>21</sup> De Martino, <sup>45</sup> Egorova, <sup>24</sup> Evans, <sup>25</sup> Hallett, <sup>28</sup> Lederle, <sup>5,31</sup> Lifeline Registry, <sup>32</sup> Whittemore <sup>43</sup>
UK	6	2853	Bryce, <sup>19</sup> Stonebridge, <sup>38</sup> Taylor, <sup>39</sup> UK SAT, <sup>40</sup> UK EVAR-1, <sup>26</sup> UK EVAR-2 <sup>27</sup>
France	3	1581	Bartoli, <sup>12</sup> Koskas, <sup>30</sup> Steinmetz, <sup>37</sup>
Holland	3	950	Bos, <sup>16</sup> De Bruin, <sup>3</sup> Verhoeven, <sup>41</sup>
Australia	2	1264	Boult, <sup>17</sup> May <sup>33</sup>
Japan	2	730	Mukai, <sup>35</sup> Yasuhara <sup>44</sup>
Italy	2	1169	Cao, <sup>20</sup> Coppi <sup>22</sup>
Austria	1	895	Sahal <sup>36</sup>
Belgium	1	143	Mertens <sup>34</sup>
Finland	1	358	Biancari <sup>15</sup>
Germany	1	205	Hinterseher <sup>29</sup>
Turkey	1	167	Bayazit <sup>13</sup>
Sweden	1	3831	Wahlgren <sup>42</sup>
Switzerland	1	711	Diehm <sup>23</sup>
<b>TOTAL</b>	<b>36</b>	<b>107,814</b>	

hypertension (24.0–83.7%) between studies, reflecting considerable variation in reporting standards. The distribution between Type 1 and Type 2 diabetes was not reported. Fifteen of these 29 studies reported the percentage of active smokers (16.0–82.9%), with six of the 29 studies reporting the percentage of ex-smokers (48.0–77.2%).

Of the eight studies reporting concomitant medication, the range of patients on antiplatelet agents was 40.5–72.6% and 14.8–69.1% were reported as taking a statin. Dosage ranges and specific drug names were not provided. There was very limited reporting on cause of death. Mean age and study characteristics for all studies included in these analyses are also reported (Tables 4 and 5).

**Table 2.** Studies contributing to aneurysm diameter analysis.

First author or study name	Year of publication	Number of patients	Mean aneurysm diameter (mm)
Bernstein <sup>14</sup>	1988	123	58
Biancari <sup>15</sup>	2003	358	50
Bos <sup>16</sup>	2008	234	60.9
Brewster <sup>18</sup>	2006	873	56.8
Cao <sup>20</sup>	2004	1119	54.1
Conrad <sup>21</sup>	2007	540	58.9
Coppi <sup>22</sup>	2008	50	58
De Martino <sup>45</sup>	2013	2367	53.6
Diehm <sup>23</sup>	2007	711	58.2
EVAR-1 <sup>26</sup>	2010	1252	64.5
EVAR-2 <sup>27</sup>	2010	197	68
Lederle <sup>5</sup>	2012	881	57
Lifeline Registry <sup>32</sup>	2005	2577	55.8
May <sup>33</sup>	1998	303	54.9
Mertens <sup>34</sup>	2011	143	57.5
Steinmetz <sup>37</sup>	2010	625	57.2
UK SAT <sup>40</sup>	2002	563	46.3
Verhoeven <sup>41</sup>	2011	365	61
<b>TOTAL</b>		<b>13,281</b>	<b>Range 46.3–68</b>

### Five-year survival after elective AAA repair

Thirty-six studies consisting of 60 study arms and a total of 107,814 patients,<sup>3,5,12–45</sup> covering the period 1969 to 2011 (Table 1) contributed to the meta-analysis of 5 year survival after AAA repair.

Of the patients, 80.3% (86,475/107,691) were male and 49.9% (53,490/107,251) underwent open repair. The pooled estimate for 5 year survival after elective AAA repair was 69% (95% CI 67 to 71%,  $I^2 = 87\%$ ; Fig. 2).

### Trend over time for 5 year survival after AAA repair

Meta-regression conducted to evaluate the survival trend over time demonstrated that there was no significant improvement (or deterioration) in 5 year survival over the period that these data span (log OR  $-0.001$ , 95% CI  $-0.014$  to  $0.012$ ,  $I^2 = 87\%$ ; Fig. 3).

### Aneurysm diameter and 5 year survival after AAA repair

Eighteen studies, consisting of 29 study arms, provided mean aneurysm diameter data and were included in this analysis.<sup>5,14–16,18,20–23,26,27,32–34,37,40,41,45</sup> This comprised 13,281 patients with a mean aneurysm diameter range of 46.3 mm to 68 mm, from data covering the period 1978–2011 (Table 2).

Meta-regression demonstrated that larger aneurysm diameter at the time of surgery was associated with poorer 5 year survival (adjusted log OR  $-0.058$ , 95% CI  $-0.095$  to  $-0.021$ ,  $I^2 = 85\%$ ). There was no evidence of significant improvement (or deterioration) in 5 year survival (adjusted log OR  $0.015$ , 95% CI  $-0.020$  to  $0.050$ ).

Visualizing regression analyses for more than a single covariate is difficult, and here the effect of time was small and statistically insignificant, so in Fig. 4 a plot is shown for a meta-regression where the only covariate is the mean diameter. The resulting unadjusted log OR ( $-0.052$ , 95%

**Table 3.** Comorbidity and medication.

Study	N at start	Diab (%)	Dyslipid. (%)	IHD <sup>a</sup> (%)	HTN (%)	Ex-smoker (%)	Smoker (%)	AntiPLT (%)	Statin (%)
Lederle et al. (OVER) <sup>5</sup>	881	22.7	—	40.7	76.9	54.2	41.2	59.2	—
Conrad et al. <sup>21</sup>	540	8.0	—	25.0	68.0	48.0	16.0	—	—
EVAR-1 <sup>26</sup>	1252	10.4	—	42.4	—	69.0	21.6	53.0	35.5
De Bruin et al. <sup>3</sup>	351	11.4	49.8	43.8	56.7	—	59.6	40.5	39.6
Brewster et al. <sup>18</sup>	873	12.4	43.5	57.2	73.4	—	65.1	—	—
Lederle et al. <sup>31</sup>	569	9.7	—	43.6	57.8	52.8	41.4	—	—
Wahlgren et al. <sup>42</sup>	3831	9.3	41.7	54.6	56.9	—	46.1	—	14.8
EVAR-2 <sup>27</sup>	197	15.4	—	67.0	—	77.2	16.8	58.2	41.8
Bartoli et al. <sup>12</sup>	162	80.8	48.8	37.0	73.0	—	75.9	—	—
Bayazit et al. <sup>13</sup>	167	5.4	—	50.7	65.0	—	—	—	—
Bos et al. <sup>16</sup>	234	14.5	35.0	48.7	57.3	—	—	—	—
Bryce et al. <sup>19</sup>	106	8.0	14.0	24.0	67.0	52.0	33.0	59.0	62.0
Cao et al. <sup>20</sup>	1119	8.0	32.5	41.5	66.0	—	—	—	—
Coppi et al. <sup>22</sup>	50	10.0	14.0	40.0	46.0	—	26.0	—	—
De Martino et al. <sup>45</sup>	2367	18.7	—	33.8	83.7	—	—	72.6	69.1
Diehm et al. <sup>23</sup>	711	15.0	51.3	45.0	80.6	—	—	45.6	42.6
Koskas et al. <sup>30</sup>	794	9.2	37.3	42.8	47.6	—	—	—	—
Hallett et al. <sup>28</sup>	130	8.0	—	42.0	47.0	—	44.0	—	—
May et al. <sup>33</sup>	303	8.0	—	51.4	31.4	—	—	—	—
Sahal et al. <sup>36</sup>	895	15.8	—	—	73.3	—	—	—	—
Steinmetz et al. <sup>37</sup>	626	14.1	56.2	49.3	72.8	—	—	—	—
Evans et al. <sup>25</sup>	147	11.0	—	38.0	44.0	—	48.0	—	—
Whittemore et al. <sup>43</sup>	110	6.0	—	44.0	24.0	—	—	—	—
Yasuhara et al. <sup>44</sup>	338	8.6	—	23.3	55.0	—	—	—	—
Lifeline Registry <sup>32</sup>	2577	12.4	—	82.7	64.0	—	—	—	—
Biancari et al. <sup>15</sup>	358	9.7	14.4	50.1	39.0	—	31.5	—	—
Egorova et al. <sup>24</sup>	84,640	15.1	39.3	52.0	71.8	—	—	—	—
Bernstein et al. <sup>14</sup>	123	8.1	—	—	45.9	—	82.9	—	—
Mukai et al. <sup>35</sup>	392	11.0	11.0	35.0	69.0	—	—	—	—
<b>Range</b>		5.4–22.7	11.0–56.2	25.0–82.7	24.0–83.7	48.0–77.2	16.0–82.9	40.5–72.6	14.8–69.1

<sup>a</sup> Ischaemic heart disease was reported variously from “previous myocardial infarction” to “previous coronary artery intervention” to “known ischaemic heart disease.”

CI  $-0.088$  to  $-0.017$ ,  $I^2 = 86\%$ ) is very similar to the adjusted one.

### Patient age and 5 year survival after AAA repair

Twenty-four studies, consisting of 40 study arms, provided mean age data and were included in this analysis.<sup>3,5,12,13,15–17,21,23,24,26,27,29,31,32,35,37–42,44,45</sup> This comprised 103,021 patients with a mean age range of 63 years to 78.5 years, from data covering the period 1978–2011 (Table 5).

Meta-regression demonstrated that older patient age at the time of surgery was associated with poorer 5 year survival (adjusted log OR  $-0.118$ , 95% CI  $-0.142$  to  $-0.094$ ,  $I^2 = 70\%$ ). Having adjusted for mean patient age in this meta-regression, there was evidence of significant improvement in 5 year survival over the period that these data span (adjusted log OR 0.027, 95% CI 0.012 to 0.042). As both estimated effects in this meta-regression are quite large and statistically significant it is difficult to visualize this regression model using two dimensions. This meta-regression model predicts 5 year survival probabilities in 1970 of around 72%, 58%, and 44% in patients aged 65, 70, and 75 respectively; in 2010 the meta-regression model predicts 5 year survival probabilities of around

88%, 81%, and 70% at these three patient ages, respectively.

### DISCUSSION

Early survival after elective AAA repair has improved dramatically over the last 50 years; the advent and rapid uptake of EVAR has played a part, as have improved pre-operative optimisation strategies, and peri- and post-operative critical care management. This study, however, demonstrates that there has been no measurable improvement in the overall long-term survival of patients undergoing elective infrarenal AAA repair, because increasingly elderly cohorts have been treated over the time period examined. After adjustment for the increasing age of patients undergoing AAA repair, long-term survival improved over time.

Five year survival after elective infrarenal AAA repair was 69% (67–71%). The pooled survival estimate reported is identical to registry data reported from the Swedvasc prospectively maintained registry covering the periods 1987–2005.<sup>46</sup> Although there was an improvement in age adjusted survival, long-term mortality remains concerning for this cohort despite improvements in cardiovascular risk

**Table 4.** Study characteristics.

First author or study name	Study type 1 = Admin Dataset 2 = Prospective RCT 3 = Cohort Study 4 = Case Series 5 = Registry	Study start	Study mid-point	Study end	Median F/U	Mean F/U	Min F/U	Max F/U
Bartoli	3	1998	2003	2007	—	—	—	—
Bayazit	4	1990	1993	1996	—	34.5	2	87
Bernstein	3	1978	1982	1985	—	—	—	—
Biancari	1	1979	1991	2002	54	—	19.2	103.2
Bos	5	1999	2003	2006	26.9	—	—	—
Boult	3	2002	2004	2008	—	—	—	—
Brewster	1	1994	2000	2005	—	—	—	—
Bryce	3	2005	2006	2007	—	—	—	—
Cao	4	1997	2000	2003	—	—	—	—
Conrad	1	1994	1996	1998	—	87	1	138
Coppi	3	1997	1999	2001	—	—	—	—
De Bruin	2	2000	2002	2003	76.8	—	61.2	98.4
De Martino	1	2003	2007	2011	22.8	28.8	—	—
Diehm	5	1994	2000	2006	—	—	—	—
Egorova	1	1995	2001	2006	—	—	—	—
Evans	4	1969	1977	1985	—	52	2	168
EVAR-1	2	1999	2002	2004	—	—	—	—
EVAR-2	2	1999	2002	2004	—	—	—	—
Hallett	1	1971	1979	1987	—	—	—	—
Hinterseher	3	1995	2000	2005	—	—	—	—
Koskas	1	1989	1992	1994	—	—	—	—
Lederle — OVER	2	2002	2004	2008	—	62.4	—	—
Lederle	2	1992	1997	2001	—	58.8	—	—
Lifeline Registry	5	1998	2001	2004	—	—	—	—
May	4	1992	1994	1996	—	—	—	—
Mertens	5	1998	2001	2003	—	—	—	—
Mukai	4	1974	1987	2000	—	66	2	254.4
Sahal	4	1995	2001	2006	—	—	—	—
Steinmetz	5	1999	2003	2006	—	—	—	—
Stonebridge	1	1980	1985	1989	—	—	—	—
Taylor	1	1990	1994	1998	—	—	60	—
UK SAT	2	1991	1993	1995	—	96	72	120
Verhoeven	3	2000	2004	2007	—	40	1	106
Wahlgren	5	2000	2003	2006	—	—	—	—
Whittemore	4	1972	1975	1979	—	—	—	—
Yasuhara	3	1980	1989	1997	—	30.2	—	—

F/U = follow up, in months.

prevention strategies, peri-operative and post-operative management of aortic surgery, and vastly improved peri-operative mortality rates, especially since the advent and implementation of EVAR. A Western Australia study that retrospectively reviewed long-term survival in survivors of elective AAA surgery reported that 57.9% of deaths after 30 days in this patient group were attributable to cardiovascular causes.<sup>9</sup> Existing evidence demonstrates that patients with AAA have at least a twofold increase in 5 year mortality compared with matched controls, and that this increases with aorta diameter despite surgical repair.<sup>47</sup> Studies have also reported that patients with aneurysmal aortas have an unusually pronounced burden of widespread cardiovascular disease,<sup>9</sup> and that patients with AAA suffer

from significant multisystem atherosclerosis, causing higher rates of heart attacks, strokes, and major amputation.<sup>48</sup>

Where comorbidity was reported, the patients included in this study had a characteristically high burden of multi-system atherosclerosis. However, the relative paucity of data to describe comorbidity also demonstrates the lack of clear reporting standards and definitions in the existing literature documenting long-term outcome for AAA repair. Ischaemic heart disease was reported variously from “previous myocardial infarction” to “previous coronary artery intervention” to “known ischaemic heart disease.” Similarly the definition of abnormal lipids ranged from dyslipidaemia to hypercholesterolemia. Reporting of concomitant preventative medication such as antiplatelet agents and statins



**Table 5.** Studies contributing to mean age analysis.

First author or study name	Year of publication (study period)	Number of patients	Mean age (years)
Bartoli	2012 (1998–2007)	162	74.69
Bayazit	1999 (1990–1996)	167	64.01
Biancari	2003 (1979–2002)	358	67.30
Bos	2008 (1999–2006)	234	72.10
Boult	2007 (1999–2001)	961	75.00
Conrad	2007 (1994–1998)	540	73.00
De Bruin	2010 (2000–2003)	351	70.14
De Martino	2013 (2003–2011)	2367	72.16
Diehm	2007 (1994–2006)	711	75.80
Egorova	2011 (1995–2006)	84,640	75.73
EVAR-1	2010 (1999–2004)	1252	74.05
EVAR-2	2010 (1999–2004)	197	77.20
Hinterseher	2012 (1995–2005)	205	69.87
Lederle (OVER)	2012 (2002–2008)	881	70.05
Lederle	2002 (1992–2001)	569	68.40
Lifeline Registry	2005 (1998–2004)	2577	73.10
Mukai	2002 (1974–2000)	392	69.80
Steinmetz	2010 (1999–2006)	625	74.08
Stonebridge	1993 (1980–1989)	311	68.00
Taylor	2004 (1990–1998)	424	69.45
UK SAT	2002 (1991–1995)	563	69.30
Verhoeven	2011 (2000–2007)	365	74.00
Wahlgren	2008 (2000–2006)	3831	71.78
Yasuhara	1999 (1980–1997)	338	72.00

was also very limited (Table 3), with little information on dosage regimens or the particular details of individual drugs that were used.

The link between larger aneurysm diameter and poorer outcome has been described extensively in the past. The UK Small Aneurysm Trial reported that baseline AAA diameter was associated with increasing risks of non-aneurysm related mortality and of cardiovascular mortality before/after surgery; even after adjustment for other known risk factors.<sup>40,49</sup> The interaction between AAA diameter and factors such as gender, age, smoking, hypertension, hypercholesterolemia, and underlying genetic predisposition is likely to play an important role for this association, but remains incompletely understood.

Studies to modify cardiovascular risk in patients with similar cardiovascular profile to those with AAA have demonstrated that multifactorial goal directed strategies can significantly reduce mid-term mortality.<sup>50</sup> The same is true for smoking cessation interventions, proactive prescribing of risk modifying drugs, supervised exercise programmes, and the management of other contributory risk factors such as hypertension. Focused research is required to assess whether such efforts could modify long-term survival in patients undergoing elective AAA repair and, perhaps more importantly, whether patient selection needs addressing to ensure only those likely to enjoy a survival benefit are offered intervention.

#### Limitations of this work

This study was limited by the changes in clinical practice over a long included timescale. Given the range of studies

analysed, time period covered, and varied numbers of contributing patients from each study, the pooled analysis was associated with considerable statistical and methodological heterogeneity. The associations derived are observational rather than causal and should be interpreted with caution. Meta-regression techniques are susceptible to aggregation bias or ecological fallacy. In the absence of individual patient data, associations identified from between-study relationships should be interpreted with caution. This study does not take into account potential variability of life expectancy in the different countries that have contributed to the overall analyses.

#### Further research

It is clear that focused research is needed to further improve the long-term survival of patients undergoing elective AAA repair. Most mortality for AAA patients is attributable to cardiovascular disease. Goal directed medical therapy and behavioural interventions have a well established role in patients surviving coronary intervention; and require focused appraisal in patients with AAA. Research should also address the objectivity of patient selection, as it may be possible to identify a cohort with AAA whose long-term survival is not modifiable regardless of AAA repair.

#### CONCLUSION

Survivors of elective AAA repair continue to have poor life expectancy despite surgery, although age adjusted survival has improved. Focused research is needed to improve long-term outcomes and case selection.

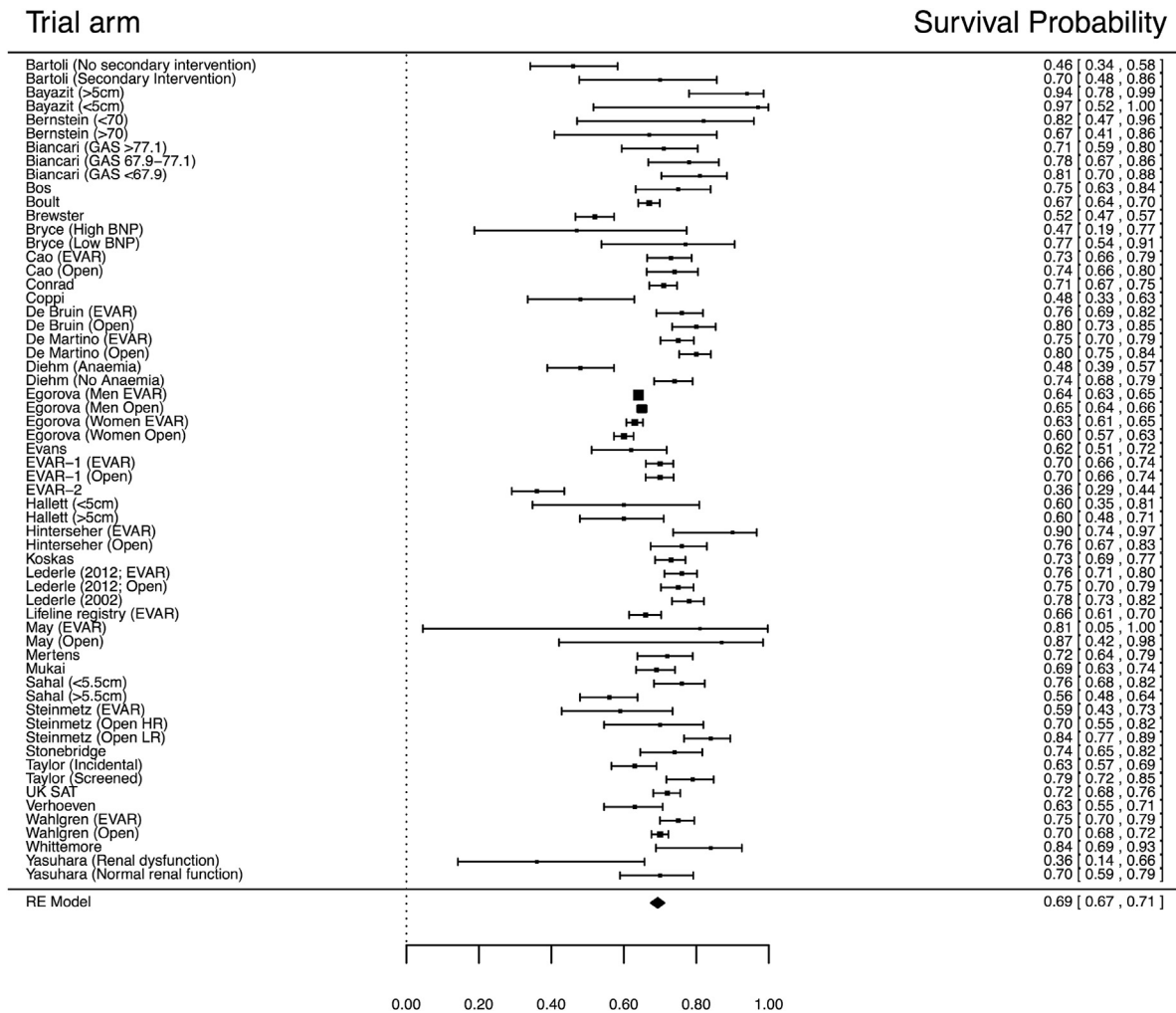


Figure 2. Pooled 5 year survival after elective IR AAA.

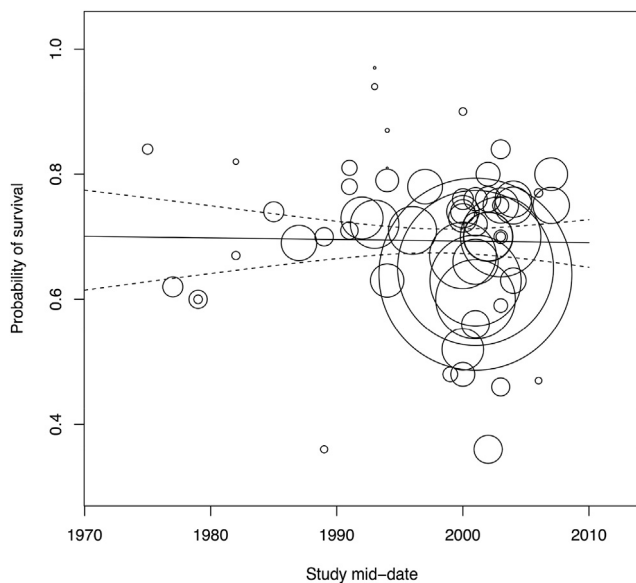


Figure 3. Survival probability (5 year) vs. study mid-date. The solid curve shows the meta-regression model fit, transformed to the probability of survival scale. The dashed curves show point wise confidence intervals and the areas of the circles are inversely proportional to the within study variances.

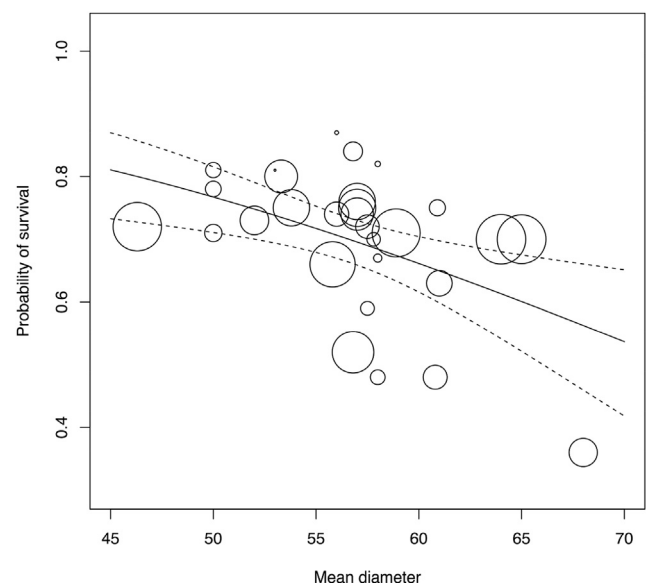


Figure 4. Survival probability (5 year) vs. study mean diameter. The solid curve shows an unadjusted meta-regression model fit, transformed to the probability of survival scale. The dashed curves show point wise confidence intervals and the areas of the circles are inversely proportional to the within study variances.



## CONFLICT OF INTEREST

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## FUNDING

None.

## APPENDIX I. DATABASE SEARCH STRATEGIES

### Medline

1. MEDLINE; AORTIC ANEURYSM, ABDOMINAL/; 12672 results.
2. MEDLINE; (abdom\* adj5 "aortic aneurysm\*").ti,ab; 11980 results.
3. MEDLINE; ("abdom\* aort\*" adj5 aneurysm\*).ti,ab; 13277 results.
4. MEDLINE; AAA.ti,ab; 7955 results.
5. MEDLINE; 1 OR 2 OR 3 OR 4; 20771 results.
6. MEDLINE; (surger\* OR surgical\* OR repair\*).ti,ab; 1326166 results.
7. MEDLINE; exp SURGICAL PROCEDURES, OPERATIVE/; 2260545 results.
8. MEDLINE; 6 OR 7; 2949023 results.
9. MEDLINE; 5 AND 8; 12080 results.
10. MEDLINE; SURVIVAL/; 3690 results.
11. MEDLINE; exp MORTALITY/OR SURVIVAL RATE/; 262329 results.
12. MEDLINE; DISEASE-FREE SURVIVAL/; 37912 results.
13. MEDLINE; (surviv\* OR mortal\*).ti,ab; 1005533 results.
14. MEDLINE; 10 OR 11 OR 12 OR 13; 1127177 results.
15. MEDLINE; 9 AND 14; 4098 results.
16. MEDLINE; SURGICAL PROCEDURES, ELECTIVE/; 7330 results.
17. MEDLINE; electiv\*.ti,ab; 51612 results.
18. MEDLINE; (elect\* OR choice\* OR choos\*).ti,ab; 1571983 results.
19. MEDLINE; ((non OR "not") adj5 emergenc\*).ti,ab; 5992 results.
20. MEDLINE; 16 OR 17 OR 18 OR 19; 1578904 results.
21. MEDLINE; 15 AND 20; 1473 results.
22. MEDLINE; 21 [Limit to: English Language]; 1286 results.
23. MEDLINE; 16 OR 17 OR 19; 59123 results.
24. MEDLINE; 15 AND 23; 1303 results.
25. MEDLINE; 24 [Limit to: English Language]; 1145 results.

### Embase

1. abdominal aorta aneurysm/
2. (abdom\* adj5 "aortic aneurysm\*").ti,ab.
3. ("abdom\* aort\*" adj5 aneurysm\*).ti,ab.
4. AAA.ti,ab.

5. 1 or 2 or 3 or 4
6. (surger\* or surgical\* or repair\*).ti,ab.
7. surgery/or exp aorta surgery/or exp abdominal surgery/or exp aneurysm surgery/
8. 6 or 7
9. (surviv\* or mortal\*).ti,ab.
10. survival/or disease free survival/or exp failure free survival/or long term survival/or post treatment survival/or survival rate/or survival time/
11. mortality/or surgical mortality/
12. 9 or 10 or 11
13. 5 and 8 and 12
14. (elect\* or choice\* or choos\*).ti,ab.
15. ((non or "not") adj5 emergenc\*).ti,ab.
16. elective surgery/
17. 14 or 15 or 16
18. 13 and 17
19. limit 18 to english language

## REFERENCES

- 1 Sinha S, Karthikesalingam A, Poloniecki JD, Thompson MM, Holt PJ. Inter relationship of procedural mortality rates in vascular surgery in England: retrospective analysis of hospital episode statistics from 2005 to 2010. *Circ Cardiovasc Qual Outcomes* 2014;**7**:131–41.
- 2 Brown LC, Powell JT, Thompson SG, Epstein DM, Sculpher MJ, Greenhalgh RM. The UK endovascular aneurysm repair (evar) trials: randomised trials of evar versus standard therapy. *Health Technol Assess* 2012;**16**:1–218.
- 3 De Bruin JL, Baas AF, Buth J, Prinssen M, Verhoeven EL, Cuypers PW, et al. Long-term outcome of open or endovascular repair of abdominal aortic aneurysm. *N Engl J Med* 2010;**362**: 1881–9.
- 4 Becquemin JP, Pillet JC, Lescalie F, Sapoval M, Goueffic Y, Lermusiaux P, et al. A randomized controlled trial of endovascular aneurysm repair versus open surgery for abdominal aortic aneurysms in low- to moderate-risk patients. *J Vasc Surg* 2011;**53**: 1167–73 e1161.
- 5 Lederle FA, Freischlag JA, Kyriakides TC, Matsumura JS, Padberg Jr FT, Kohler TR, et al. Long-term comparison of endovascular and open repair of abdominal aortic aneurysm. *N Engl J Med* 2012;**367**:1988–97.
- 6 Bahia SS, Karthikesalingam A, Thompson MM. Abdominal aortic aneurysms: endovascular options and outcomes — proliferating therapy, but effective? *Prog Cardiovasc Dis* 2013;**56**:19–25.
- 7 Karthikesalingam A, Thompson MM. Vascular disease: repair of infrarenal aortic aneurysm—the debate is over. *Nat Rev Cardiol* 2013;**10**:122–4.
- 8 Karthikesalingam A, Bahia SS, Patterson BO, Peach G, Vidal-Diez A, Ray KK, et al. The shortfall in long-term survival of patients with repaired thoracic or abdominal aortic aneurysms: retrospective case-control analysis of hospital episode statistics. *Eur J Vasc Endovasc Surg* 2013;**46**:533–41.
- 9 Norman PE, Semmens JB, Lawrence-Brown MM, Holman CD. Long term relative survival after surgery for abdominal aortic aneurysm in Western Australia: population based study. *BMJ* 1998;**317**:852–6.
- 10 Norman PE, Semmens JB, Lawrence-Brown MM. Long-term relative survival following surgery for abdominal aortic aneurysm: a review. *Cardiovasc Surg* 2001;**9**:219–24.

- 11 Jackson D, White IR, Thompson SG. Extending Dersimonian and Laird's methodology to perform multivariate random effects meta-analyses. *Stat Med* 2010;**29**:1282–97.
- 12 Bartoli MA, Thevenin B, Sarlon G, Giorgi R, Albertini JN, Lerussi G, et al. Secondary procedures after infrarenal abdominal aortic aneurysms endovascular repair with second-generation endografts. *Ann Vasc Surg* 2012;**26**:166–74.
- 13 Bayazit M, Kamil Göl M, Zafer Işcan H, Ulus T, Taşdemir O, Bayazit K. Is surgery justifiable for treatment of small abdominal aortic aneurysms? *Asian Cardiovasc Thorac Ann* 1999;**7**:200–3.
- 14 Bernstein EF, Dilley RB, Randolph 3rd HF. The improving long-term outlook for patients over 70 years of age with abdominal aortic aneurysms. *Ann Surg* 1988;**207**:318–22.
- 15 Biancari F, Leo E, Ylonen K, Vaarala MH, Rainio P, Juvonen T. Value of the glasgow aneurysm score in predicting the immediate and long-term outcome after elective open repair of infrarenal abdominal aortic aneurysm. *Br J Surg* 2003;**90**:838–44.
- 16 Bos WT, Tielliu IF, Zeebregts CJ, Prins TR, van den Dungen JJ, Verhoeven EL. Results of endovascular abdominal aortic aneurysm repair with the zenith stent graft. *Eur J Vasc Endovasc Surg* 2008;**36**:653–60.
- 17 Boulton M, Maddern G, Barnes M, Fitridge R. Factors affecting survival after endovascular aneurysm repair: results from a population based audit. *Eur J Vasc Endovasc Surg* 2007;**34**:156–62.
- 18 Brewster DC, Jones JE, Chung TK, Lamuraglia GM, Kwolek CJ, Watkins MT, et al. Long-term outcomes after endovascular abdominal aortic aneurysm repair: the first decade. *Ann Surg* 2006;**244**:426–38.
- 19 Bryce GJ, Payne C, Gibson SC, Byrne DS, Delles C, McClure J, et al. B-type natriuretic peptide predicts post-operative cardiac events and mortality after elective open abdominal aortic aneurysm repair. *J Vasc Surg* 2013;**57**:345–53.
- 20 Cao P, Verzini F, Parlani G, Romano L, De Rango P, Pagliuca V, et al. Clinical effect of abdominal aortic aneurysm endografting: 7-year concurrent comparison with open repair. *J Vasc Surg* 2004;**40**:841–8.
- 21 Conrad MF, Crawford RS, Pedraza JD, Brewster DC, Lamuraglia GM, Corey M, et al. Long-term durability of open abdominal aortic aneurysm repair. *J Vasc Surg* 2007;**46**:669–75.
- 22 Coppi G, Silingardi R, Saitta G, Gennai S. Single center experience with the Talent Ips endograft in patients with at least 5 years of follow up. *J Endovasc Ther* 2008;**15**:23–32.
- 23 Diehm N, Benenati JF, Becker GJ, Quesada R, Tsoukas AI, Katzen BT, et al. Anemia is associated with abdominal aortic aneurysm (aaa) size and decreased long-term survival after endovascular aaa repair. *J Vasc Surg* 2007;**46**:676–81.
- 24 Egorova NN, Vouyouka AG, McKinsey JF, Faries PL, Kent KC, Moskowitz AJ, et al. Effect of gender on long-term survival after abdominal aortic aneurysm repair based on results from the medicare national database. *J Vasc Surg* 2011;**54**: 1–12 e16; discussion 11–12.
- 25 Evans WE, Hayes JP. Tube graft replacement of abdominal aortic aneurysm. *Am J Surg* 1988;**156**:119–21.
- 26 United Kingdom EVAR Trial Investigators, Greenhalgh RM, Brown LC, Powell JT, Thompson SG, Epstein D, Sculpher MJ. Endovascular versus open repair of abdominal aortic aneurysm. *N Engl J Med* 2010;**362**:1863–71.
- 27 United Kingdom EVAR Trial Investigators, Greenhalgh RM, Brown LC, Powell JT, Thompson SG, Epstein D. Endovascular repair of aortic aneurysm in patients physically ineligible for open repair. *N Engl J Med* 2010;**362**:1872–80.
- 28 Hallett Jr JW, Naessens JM, Ballard DJ. Early and late outcome of surgical repair for small abdominal aortic aneurysms: a population-based analysis. *J Vasc Surg* 1993;**18**:684–91.
- 29 Hinterseher I, Kuffner H, Koch R, Gabel G, Saeger HD, Smelser D. Comparison of survival rates for abdominal aortic aneurysm treatment methods. *World J Surg* 2012;**36**: 917–22.
- 30 Koskas F, Kieffer E. Long-term survival after elective repair of infrarenal abdominal aortic aneurysm: results of a prospective multicentric study. Association for academic research in vascular surgery (aurc). *Ann Vasc Surg* 1997;**11**:473–81.
- 31 Lederle FA, Wilson SE, Johnson GR, Reinke DB, Littooy FN, Acher CW, et al. Immediate repair compared with surveillance of small abdominal aortic aneurysms. *N Engl J Med* 2002;**346**: 1437–44.
- 32 Lifeline Registry of EPC. Lifeline registry of endovascular aneurysm repair: long-term primary outcome measures. *J Vasc Surg* 2005;**42**:1–10.
- 33 May J, White GH, Yu W, Ly CN, Waugh R, Stephen MS, et al. Concurrent comparison of endoluminal versus open repair in the treatment of abdominal aortic aneurysms: analysis of 303 patients by life table method. *J Vasc Surg* 1998;**27**:213–20. discussion 220–21.
- 34 Mertens J, Houthoofd S, Daenens K, Fourneau I, Maleux G, Lerut P, et al. Long-term results after endovascular abdominal aortic aneurysm repair using the cook zenith endograft. *J Vasc Surg* 2011;**54**: 48–57 e42.
- 35 Mukai S, Yao H, Miyamoto T, Yamamura M, Nakagawa T, Ryomoto M. The long-term follow up results of elective surgical treatment for abdominal aortic aneurysms. *Ann Thorac Cardiovasc Surg* 2002;**8**:38–41.
- 36 Sahal M, Prusa AM, Wibmer A, Wolff KS, Lammer J, Polterauer P, et al. Elective abdominal aortic aneurysm repair: does the aneurysm diameter influence long-term survival? *Eur J Vasc Endovasc Surg* 2008;**35**:288–94.
- 37 Steinmetz E, Abello N, Kretz B, Gauthier E, Bouchot O, Brenot R. Analysis of outcome after using high risk criteria selection to surgery versus endovascular repair in the modern era of abdominal aortic aneurysm treatment. *Eur J Vasc Endovasc Surg* 2010;**39**:403–9.
- 38 Stonebridge PA, Callam MJ, Bradbury AW, Murie JA, Jenkins AM, Ruckley CV. Comparison of long-term survival after successful repair of ruptured and non-ruptured abdominal aortic aneurysm. *Br J Surg* 1993;**80**:585–6.
- 39 Taylor JC, Shaw E, Whyman MR, Poskitt KR, Heather BP, Earnshaw JJ. Late survival after elective repair of aortic aneurysms detected by screening. *Eur J Vasc Endovasc Surg* 2004;**28**:270–3.
- 40 United Kingdom Small Aneurysm Trial Participants. Long-term outcomes of immediate repair compared with surveillance of small abdominal aortic aneurysms. *N Engl J Med* 2002;**346**: 1445–52.
- 41 Verhoeven BA, Waasdorp EJ, Gorrepati ML, van Herwaarden JA, Vos JA, Wille J, et al. Long-term results of Talent endografts for endovascular abdominal aortic aneurysm repair. *J Vasc Surg* 2011;**53**:293–8.
- 42 Wahlgren CM, Malmstedt J. Swedish Vascular Registry. Outcomes of endovascular abdominal aortic aneurysm repair compared with open surgical repair in high risk patients: results from the Swedish Vascular Registry. *J Vasc Surg* 2008;**48**: 1382–8. discussion 1388–9.

- 43 Whittemore AD, Clowes AW, Hechtman HB, Mannick JA. Aortic aneurysm repair. Reduced operative mortality associated with maintenance of optimal cardiac performance. *Ann Surg* 1980;**192**:414–21.
- 44 Yasuhara H, Ishiguro T, Muto T. Factors affecting late survival after elective abdominal aortic aneurysm repair. *Br J Surg* 1999;**86**:1047–52.
- 45 De Martino RR, Goodney PP, Nolan BW, Robinson WP, Farber A, Patel VI, et al. Optimal selection of patients for elective abdominal aortic aneurysm repair based on life expectancy. *J Vasc Surg* 2013;**58**:589–95.
- 46 Mani K, Bjorck M, Lundkvist J, Wanhainen A. Improved long-term survival after abdominal aortic aneurysm repair. *Circulation* 2009;**120**:201–11.
- 47 Forsdahl SH, Solberg S, Singh K, Jacobsen BK. Abdominal aortic aneurysms, or a relatively large diameter of non-aneurysmal aortas, increase total and cardiovascular mortality: the Tromso Study. *Int J Epidemiol* 2010;**39**:225–32.
- 48 Brown OW, Hollier LH, Pairolero PC, Kazmier FJ, McCready RA. Abdominal aortic aneurysm and coronary artery disease. *Arch Surg* 1981;**116**:1484–8.
- 49 Brady AR, Fowkes FG, Thompson SG, Powell JT. Aortic aneurysm diameter and risk of cardiovascular mortality. *Arterioscler Thromb Vasc Biol* 2001;**21**:1203–7.
- 50 Gaede P, Lund-Andersen H, Parving HH, Pedersen O. Effect of a multifactorial intervention on mortality in type 2 diabetes. *N Engl J Med* 2008;**358**:580–91.