Cost-effectiveness of open vs endovascular repair of abdominal aortic aneurysm: a systematic review.

Bachelor thesis

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Samenvatting

Inleiding

Sinds in 1990 endovasculaire aneurysma reperatie (EVAR) werd geintroduceerd, ontwikkelde deze techniek zich snel tot één van de twee algemene behandelingen voor aorta aneurysma's. De traditionele behandeling voor aorta aneurysma's is open chirurgie (OS). Om de optimale strategie voor de behandeling van aorta aneurysma's te bepalen, zijn verschillende kosteneffectiviteitsanalyses (KEA) uitgevoerd. Het doel van deze studie was het geven van een overzicht van de KEA's die tot nu toe zijn gepubliceerd over de vergelijking van electieve EVAR met electieve OS.

Methode

Drie databases (Pubmed, Embase, CRD) zijn systematisch doorzocht. Relevante artikelen uit de doorzoeking werden geselecteerd door onafhankelijke reviewers. De dataextractie werd uitgevoerd in vier stappen en de resultaten werden in tabellen gezet, zodat een overzichtelijke vergelijking gemaakt kon worden. Eerst werden de studie karakteristieken geëxtraheerd. Ten tweede werden de invoerparameters geëxtraheerd. Ten derde werden de sensitiviteitsanalyse, de uitkomsten en de conclusies geëxtraheerd. Ten vierde werd een kwaliteits beoordeling gemaakt aan de hand van Drummond checklist. Deze kwaliteitsbeoordeling werd ook gedaan door twee onafhankelijke reviewers.

Resultaten

De systematische doorzoeking en de daar op volgende selectie indentificeerde 13 artikelen die relevant waren voor deze review. De artikelen hadden verschillende studie karakteristieken en invoerparameters. De meeste studies concludeerde dat EVAR niet kosteneffectief was vergeleken met OS. Een minderheid van de studies concludeerde dat EVAR kosteneffectief was. De kwaliteit van de studies verschilde. De algemene kwaliteit van de studies werd beoordeeld als goed.

Conclusie

De gevonden economische evaluaties geven geen duidelijk antwoord op de vraag of EVAR meer kosteneffectief is vergeleken met OS. De kwaliteit van de studies in deze review was over het algemeen goed, maar de kwaliteit varierde wel. De kwaliteit van de studie is mogelijk van invloed op de uitkomsten en conclusies van de studies.

Abstract

Background

Since the introduction of endovascular aortic aneurysm repair (EVAR) in 1990, this techniek rapidly became a common treatment for aortic aneurysms. The conventional treatment for aortic aneurysm was open surgery (OS). In order to determine an optimal strategy for the treatment of aortic aneurysm different cost-effectiveness analyses (CEAs) were untertaken. The aim of this study was to provide an overview of the publications performing a CEA comparing elective EVAR with elective OS.

Methods

A systematic search was performed searching three databases (Pubmed, Embase, CRD). From this search relevant articles were selected by different reviewers. The data extraction was performed in four steps and the results were put into tables so a clear comparison was possible. First, the study characteristics were extracted. Second, the input parameters were extracted. Third, sensitivity analysis, the (incremental) outcomes and conclusions were extracted. Fourth, the methodological quality of the included studies was assessed using the Drummond checklist. The quality assessment was also performed by different reviewers.

Results

The systematic search and the selection identified 13 aricles that were relevant for this review. Articles had different studie characteristics and sources of parameters. Most studies concluded that EVAR was not cost-effective compared with OS. I minority of the studies concluded EVAR to be cost-effective. The quality of the publications was different. The overall quality was found to be reasonably good.

Conclusion

The performed economic evaluations do not provide a clear answer whether elective EVAR is more cost-effective or not compared to elective OS. The overall quality of the studies in this review was reasonably good though quality of the studies also differ. The quality of the studies may be a possible influence on the outcomes of the studies.

Introduction

Abdominal aortic aneurysm (AAA) is a condition in which the aortic wall in the abdomen is dilated and consequently this could lead to a rupture of the aortic wall. The risk that an aneurysm ruptures is associated with its size [1]. Age (>50 years), atherosclerosis, smoking, hypertension, genetic factors and high cholesterol levels are risk factors for AAA, however the exact causes of AAA are unknown [2].

The prevalence of AAA can only be detected by population screening and most population screenings are dated [3]. A research in 1995 in the UK showed a prevalence of 7.6% in men and 1.3% in women [4], in that same year a research in the Netherlands showed a prevalence of 4.1% in men and 0.7% in women [5]. An important factor causing the difference between men and women is smoking; the expectation is that the difference between men and women will decline because more women start smoking and less men start smoking [6].

Nowadays, patients with an AAA larger than 5.0 cm can be treated electively with an open surgery (OS) or an endovascular aneurysm repair (EVAR) [3]. OS is more invasive than EVAR, for example blood loss is higher with OS and a bigger incision must be performed with OS. When a patient is to weak for OS, EVAR will be considered [3]. Patients treated with OS have on average a longer length of stay in the hospital than patients treated with EVAR; 13 days compared with 6 days. Furthermore, patients treated with EVAR have a lower 30-days mortality (1.3%) compared with patients treated with OS (4.7%) [7]. Interestingly, the difference in mortality diminishes over time and seems to have disappeared after two years, since EVAR is associated with higher risk of complications, reinterventions and AAA rupture [7,8]. The risk of rupture during OS was 0.3%, against 2.0% during EVAR and a second intervention was necessary in 28.9% of the patients treated with EVAR, against 25.4% in the OS group [7]. EVAR seems to be more effective than OS in reducing the 30-day mortality, but the initial costs of EVAR are substantially higher compared with the costs of OS [9].

One systematic review has been published in which the cost-effectiveness of elective EVAR is compared with elective OS [10]. This review of Chambers et al. [10] concluded that the studies they included had conflicting results. Some found EVAR to be cost-effective and some EVAR to be non-cost-effective. They stated that the different characteristics and different use of resources may be of influence. After their review they performed a CEA. This review provides a comparison of CEAs, including the CEA performed by Chambers et al. [10]. Chambers et al. [10] included studies that compared EVAR with not only OS but other comparators as well. This study specificly included only publications comparing elective EVAR with elective OS. Chambers et al. [10] performed a quality assessment with the Drummond Checklist [11] as wel, but did not compare the differences in quality between the included studies.

The aim of this study is to give an update of economic evaluations estimating the cost-effectiveness of elective EVAR versus elective OS. A quality assessment of the included studies will be performed as well, using the Drummond checklist [11] and the differences in quality of the studies will be compared. The questions to be answered were: first, what are the conclusions of published studies about the cost-effectiveness of EVAR compared to OSR at patients with AAA? Second, what is the quality of the published studies and does the quality influence the conclusions?

Theoratical background

This systematic review includes economic evaluations that have estimated the cost-effectiveness of EVAR versus OS. When the outcome measure of the economic evaluations is in Quality Adjusted Life Years (QALY) it can be named a cost-utility analysis (CUA). The QALY is an integrated outcome measurement expressing health as a combination of the quantity of life years and the quality of those years [11]. In case of a CEA mostly disease specific of generic measurements are the outcomes, like life years or hospitalization days [11]. Both analyses are used for researches about the expediency of treatments or interventions.

The treatments compared in this study are elective EVAR and elective OS for AAA. When AAA is discovered by a CT-scan or an echo, it is necessary to start a treatment or surveillance programme. The physician has to deside what treatment is best in different situations. Figure 1 shows the management of AAA. When repair through EVAR or OS is necessary, the physician has to decide what type of repair is best for a patient. Patients can be fit or unfit for a type of repair by physical fitness or morphology [3]. Figure 2 shows a decision tree for the management of large AAAs.

Figure 1: Management of AAA depending on size of aneurysm [3]

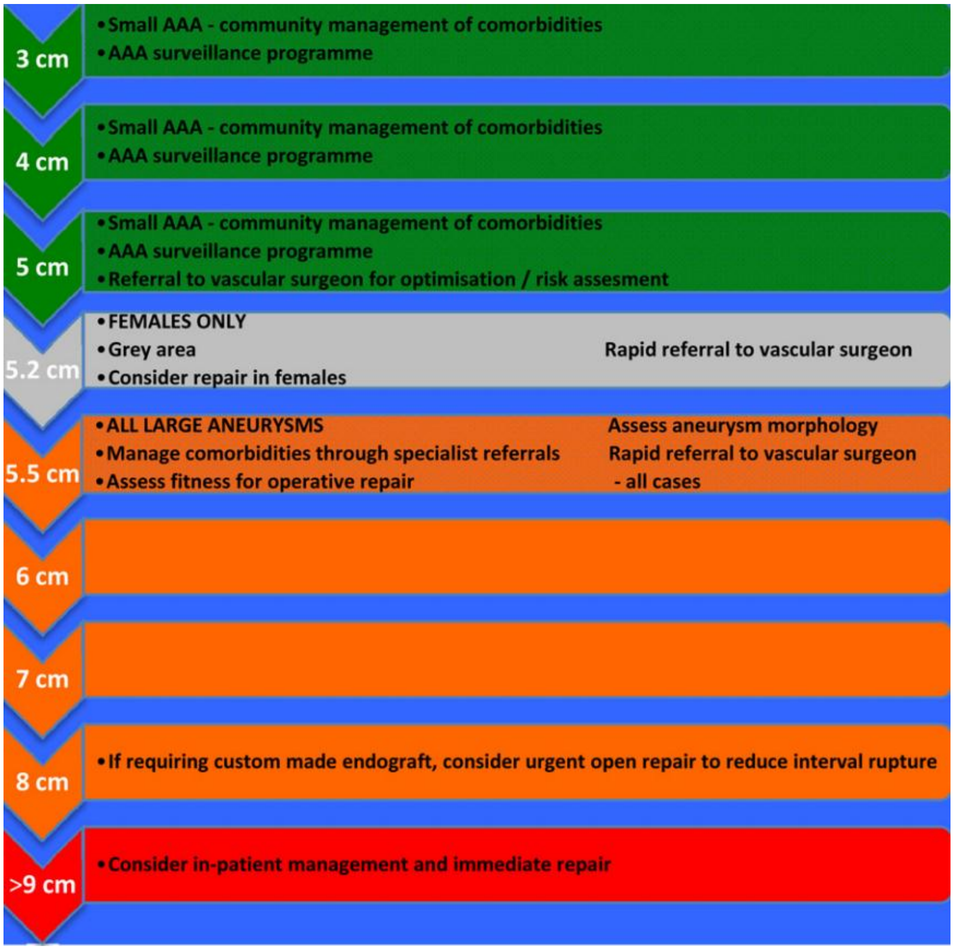
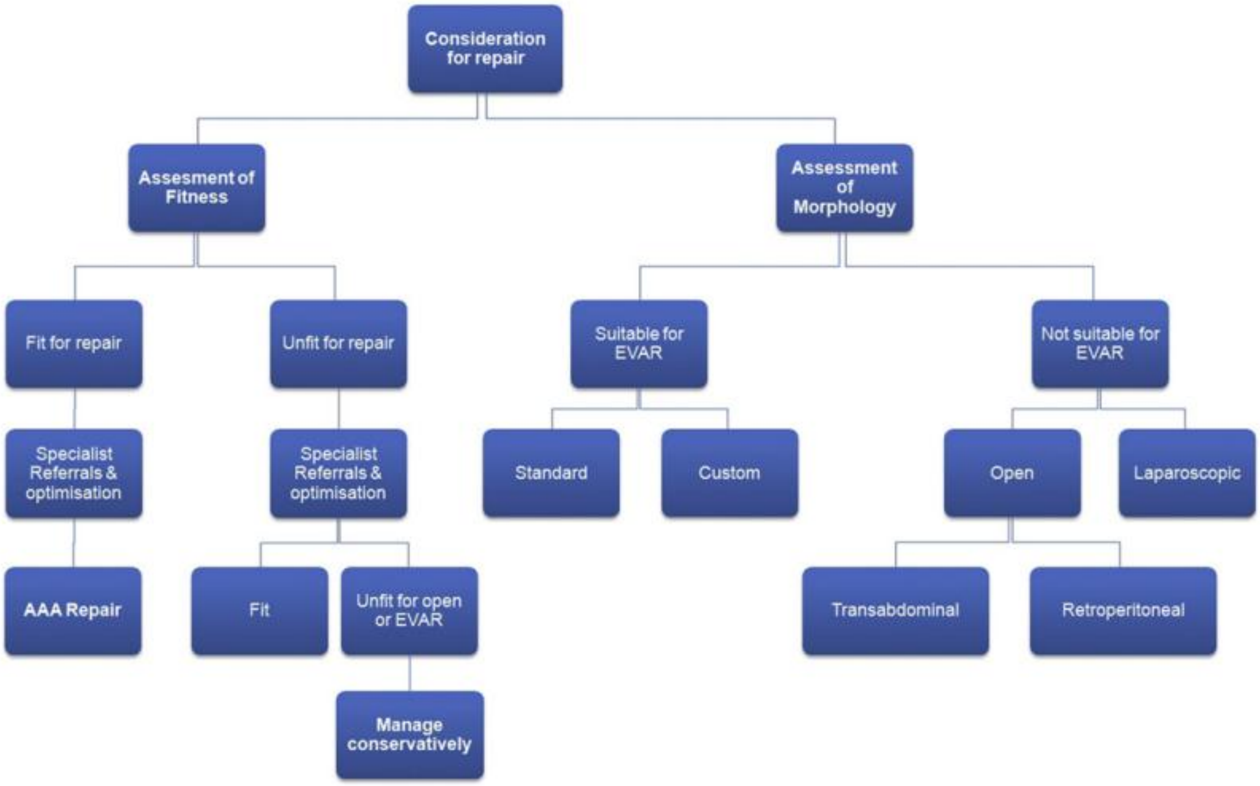


Figure 2: Management of large AAA [3]



Methods:

A systematic literature search was performed to identify all English or Dutch-language publications (until 25-03-2014) of full economic evaluations comparing both the costs and consequences of elective EVAR versus elective OS for patients with an AAA ≥ 5.0 cm. The effectiveness of the studies had to be expressed in quality adjusted life years (QALY) gained or in life years (LY) gained. There was no restriction on the perspective that was used in the economic evaluation. Reviews, editorials and abstracts were not included in this systematic review. Studies were identified using electronic databases (PubMed, Embase, CRD). By scanning reference lists of eligible articles, there was a check to see if all important studies were included. No new publications showed up using this method, all important publications were identified by the electronic databases. A validated NHS search strategy for economic evaluations was used in the Pubmed database [12] and this strategy was also the base for the search strategy for economic evaluations in the Embase database.

Table 1: in- and exclusion criteria (PICO)

PICO	
Research design	Cost-effectiveness analyses and cost utilities analyses
Population	Patients with AAA ≥ 5.0 cm fit for open surgery en EVAR
Intervention	Elective EVAR
Comparator	Elective OS
Outcomes	Incremental costs per QALY gained Incremental costs per life year gained
Language	English or Dutch
Publication date	Publications after 1990 (start of EVAR)

Selection

In order to conduct the selection, the program Refworks has been used. All records conducted from the databases were collected in one database. First, duplicates were removed and then the residual publications were screened on title and abstract. Publications were excluded on study design, intervention, comparator or language. The included study designs are original economic evaluations comparing both costs and effects of EVAR and OS. After this title/abstract selection the residual publications has been read entirely to find publications that fully met in- and exclusion criteria.

Publications were excluded on study design, intervention or comparator. The remaining articles after this last selection have been included in this review.

The first part in the selection of the studies was performed by two independent reviewers (CB & MS). After the title/abstract selection the results were compared, discrepancies were discussed and resolved by consensus or by a third reviewer (LB). The full assessment selection was also performed by two reviewers (CB & LB) and the results were compared and discussed and resolved by consensus.

Data extraction

The data extraction was performed using four steps. First, the study characteristics that were extracted from the publications were year of publication, first author, country of research, population, discounting, time horizon, perspective and outcome measure. Second, the input parameters (effectiveness, resource use and unit costs) and their resources were extracted from the papers. Third, sensitivity analysis, the (incremental) outcomes and conclusions of the included publications were extracted. Fourth, the methodological quality of the included studies was assessed using the Drummond checklist [11]. This checklist contains 10 questions concerning the validity of the results encountered in a study (Table 1). This checklist has also been performed by a second reviewer as well (LB), in order to guarantee the validity of the results of this checklist. The Drummond checklist has been operationalized by two reviewers (CB & MS)

All results from the data extraction and the quality assessment have been compared with each other. Interesting differences or similarities were identified and described.

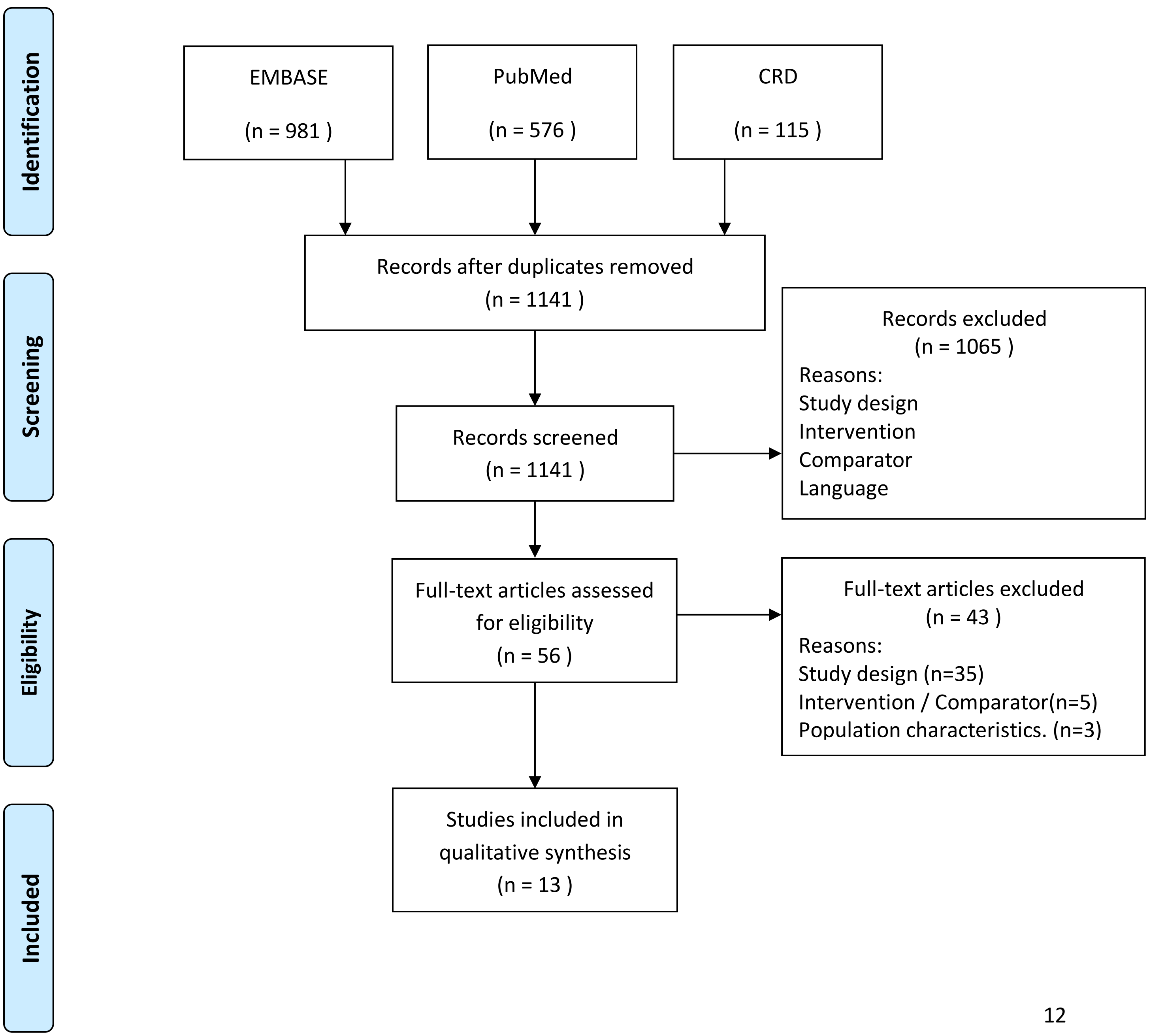
Table 1. Questions for quality assessment of economic evaluations[11]
Was a well-defined question posed in answerable form?
Was a comprehensive description of de competing alternatives given?
Was the effectiveness of the programs or services established?
Were all important & relevant costs & consequences for each alternative identified?
Were costs & consequences measured accurately in appropriate physical units?
Were costs & consequences valued credibly?
Were costs & consequences adjusted for differential timing?
Was an incremental analysis of costs & consequences of alternatives performed?
Was allowance made for uncertainty in the estimates of costs & consequences?
Did the presentation & discussion of study results include all issues of concern to users?

Results:

Search results

Respectively 981, 576 and 115 records were identified in the databases Embase, Pubmed and CRD. After duplicates were removed 1141 records remained for title and abstract selection. 56 records were retrieved and full text assessment was performed leading to 13 articles that met inclusion criteria. All these steps are presented in Figure 1, based on the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines [13].

Figure 1



Study characteristics

The general study characteristics of the included studies are presented in Table 2. All included studies were published in English. Four studies were conducted in Canada [14,16,17,24], four studies in the United Kingdom [9,10,18,19,21], three studies in the United States [15,20,22] and one in the Netherlands [23].

All studies focused on the incremental costs per QALY as primary outcome measure. Three Canadian studies and one study from the US also focused on the incremental costs per life year gained [14,17,20,24].

The populations in all studies were patients with AAA and eligible for elective EVAR and elective OS. The size of the aneurysm differed over the studies. Most studies included aneurysms ≥ 5.5 cm [9,10,14,16,18,21,24], three studies included aneurysms ≥5.0 cm [19,21,22], one study included aneurysms between 5.0 and 6.0 cm [15] and one study had no size criteria [17].

For the base case different ages were selected, although most studies selected a 70 years old patient [14-16,21,22]. Other studies selected a 74 years old patient [20], or patients older than 60 years [9], or had no age condition at all [10,17,20,23,24].

One study estimated the cost-effectiveness for four trials separately and the population was based on the inclusion criteria of those RTCs [19]. Two studies were performed before any results from RCTs were published [15,22].

Most studies applied the perspective of the third-party payer in the different countries; the NHS, medicare of the ministry Ontario [9,10,14,17-19,21]. Two studies took the societal perspective [15,24]. Tarride et al. [24] stated besides a societal perspective a payer perspective as well. All other studies did not state a clear perspective [16,20,22,23].

The time horizon differed between the studies as well. Four studies estimated the cost-effectiveness of EVAR for a time horizon of one year [16,17,23,24], four studies used a lifetime time horizon [10,15,17,22]. The other studies used a time horizon of 2 years [20], ten years [14,21] or 25 years [9,19]. All studies with a time horizon longer than one year, discounted costs and effects. The discount rates differed between 3.0% [14,15,20,22] and 3.5% [9,10,18,19,21].

Sources of parameters

Table 3 presents the sources of input parameters of the included studies. Several studies performed a meta-analysis to obtain estimates for the effectiveness of EVAR and OS [10,14-16], but most studies collected effectiveness data from one [9,17,18,23,24], or several [19,21] RCTs. Patel et al. [22] obtained their data from several single center studies without a comparative study, because no RCT comparing the cost-effectiveness of EVAR and OS was performed at the time. Lederle et al. [20] combined the findings from an RCT (OVER) with national databases.

The sources for the unit costs had the same differences. Some studies used one[14,16,18,24] or more[19] field studies, or (inter)national databases [10,15,20,22,23]. Other studies combined the findings of costs from a field study with databases [9,17]. For the follow- up costs, several publications used other studies for the costs of complications or reintervention due to complications for example [16]. Blackhouse et al. [14] included only follow-up costs for EVAR but not for OS.

Table 2: Study characteristics of the economic evaluations

Author	Publication year	Country of research	Population	Outcome measure	perspective	Time horizon	discounting	Ref.
Blackhouse et al.	2009	Canada	70 year old men with AAA > 5.5 cm. Eligible for both interventions.	Incremental costs per life year gained, Incremental costs per QALY	Third-party payer	10 years	YES (3.0%)	[14]
Bosch et al.	2002	United States	70 year old men with AAA between 5.0 and 6.0 cm. Eligible for both interventions.	Incremental costs per QALY	Societal	Lifetime	YES (3.0%)	[15]
Bowen et al.	2005	Canada	70 year old men with AAA > 5.5 cm. Eligible for both interventions.	Incremental costs per QALY	NS	13 months	NO	[16]
Bowen et al.	2007	Canada	Patients with AAA > 5.5 cm with high risk. Eligible for both interventions.	Incremental costs per life year gained, Incremental costs per QALY	Third-party payer (Ontario Ministry of Health)	12 months	NO	[17]
Brown et al.	2013	United Kingdom	At least 60 years old with AAA >5.5 cm. Eligible for both interventions.	Incremental costs per QALY	Third-party payer (UK NHS)	25 years	YES (3.5%)	[9]
Chambers et al.	2009	United Kingdom	Patients with AAA > 5.5 cm. Eligible for both interventions.	Incremental costs per QALY	Third-party payer (UK NHS)	Lifetime	YES (3.5%)	[10]
Epstein et al.	2007	United Kingdom	74 years old men with AAA > 5.5 cm. Eligible for both interventions.	Incremental costs per QALY	Third-party payer (Collectively funded healthcare system (NHS))	Lifetime	YES (3.5%)	[18]
Epstein et al.	2014	United Kingdom	Four trials: EVAR-1, DREAM, OVER and ACE.	Incremental costs per QALY	Third-party payer (UK NHS)	25 years	YES (3.5%)	[19]
Lederle et al.	2012	United States	Patients with AAA > 5.0 cm. Eligible for both interventions.	Incremental costs per QALY	NS	2 years	YES (3.0%)	[20]
Michaels et al.	2005	United Kingdom	70 year old men with AAA = 5.5 cm. Eligible for both interventions.	Incremental costs per life year gained, Incremental costs per QALY	Third-party payer (UK NHS)	10 years	YES (3.5%)	[21]
Patel et al.	1999	United States	70 year old men with an AAA > 5.0 cm.	Incremental costs per QALY	NS	Lifetime	YES (3.0%)	[22]
Prinssen et al.	2007	The Netherlands	Patients with AAA > 5.0 cm. Eligible for both interventions.	Incremental costs per QALY	NS	1 year	NO	[23]
Tarride et al.	2011	Canada	Patients with AAA > 5.5 cm.	Incremental costs per life year gained, Incremental costs per QALY	Payer and Societal	12 months	NO	[24]

NS; not stated, AAA; abdominal aortic aneurysm, QALY; quality adjusted life year, cm; centimeter

Table 3: Sources of input parameters

Authors (Year)	Source key parameters of effectiveness				Source unit costs and resource use			
	Mortality rate EVAR	**Mortality rate OS**	**Conversion rate**	**Quality of life**	**Cost EVAR**	**Cost OS**	**Cost follow- up**	**Cost reintervention**
Blackhouse et al. (2009) [14]	Meta-analysis: Bowen et al. [17] Harris et al. [25]	Meta-analysis: Bowen et al. [17] Harris et al. [25]	Systematic review (six RCTs and 78 observational studies)	EVAR 1 trial [26]	Bowen et al. (2007) [17]	Bowen et al. (2007) [17]	Bowen et al. [17]*	Forbes et al. (2002) [27] *
Bosch et al. (2002) [15]	Meta-analysis [28-36]	Meta-analysis [28-36]	Meta-analysis [28-36]	Meta-analysis [28-36]	Medicare	Medicare	Medicare	
Bowen et al. (2005) [16]	Meta-analysis: Bowen et al. [17] Harris et al. [25] Rouleau et al [37]., Kapral et al. [38]	Meta-analysis: Bowen et al. [17] Harris et al. [25] Rouleau et al [37]., Kapral et al. [38]	Meta-analysis [14]	Field study [16], Lewis et al. [39], Schleinitz et al. [40], Oldrige et al. [41], Revicki et al [42].	Field study [16]	Field study[16]	Field study[16], Tsuyuki et al.[43], Coyle et al.[44], Kroeker et al.[45], Riviere et al[46].	OCCI, Forbes et al [27].
Bowen et al. (2007) [17]	Field study [15]	Field study [15]	Field study [15]	Field study [15]	Field study [15], Ontario Schedule of Physician Benefits, Statistics Canada			
Brown et al. (2013) [9]	EVAR-1 [47]	EVAR-1 [47]	EVAR-1 [47]	EVAR-1 [47]	EVAR trial survey [47], NICE appraisal [10], NHS reference costs [48], ISD Scotland [49]			
Chambers et al. (2009) [10]	Meta-analysis (*43 studies)*, EUROSTAR	Meta-analysis (*43 studies)*, EUROSTAR	EVAR-1 [47]	EVAR-1 [47]	NHS reference costs [48], ISD Scotland [49]	NHS reference costs [48], ISD Scotland [49]		EVAR trial 1 [47]

***Only EVAR had follow-up costs and reintervention costs**
OS; open surgery, EVAR; endovascular aneurysm repair, RCT; randomized controlled trial

Table 3: Sources of input parameters – *continued*

Authors (Year)	**Source key parameters of effectiveness**				**Source unit costs and resource use**			
	Mortality rate EVAR	**Mortality rate OS**	**Conversion rate**	**Quality of life**	**Cost EVAR**	**Cost OS**	**Cost follow-up**	**Cost reintervention**
Epstein et al. (2007) [18]	EVAR-1 [51]	EVAR-1 [51]	EVAR-1 [51]	Kind et al. [52], EVAR trial 1 [51], Lacey et al. [53]	EVAR-1 [51], Reference costs [54]	EVAR-1 [51], Reference costs [54]		
Epstein et al. (2014) [19]	EVAR-1 [55], DREAM [56], OVER [57] ACE [58]	EVAR-1 [55], DREAM [56], OVER [57] ACE [58].			EVAR-1 [55], DREAM [56], OVER [57] ACE [58]	EVAR-1 [55], DREAM [56], OVER [57] ACE [58].		
Lederle et al. (2012) [20]	OVER study [59]	OVER study [59]		OVER study [59]	VA decision Support System (DSS) [60]			
Michaels et al. (2005) [21]	EVAR-1 [61], DREAM [62]	EVAR-1 [61], DREAM [62]	Review [63]	EVAR-1 [61]	Sheffield teaching Hospitals, NHS reference costs [64]	NHS Reference costs [64]		
Patel et al. (1999) [22]	Blum et al. [65], Goldstone et al. [66], Zarins et al. [67]	Johnston [68]	Blum et al. [65], Mialhe et al. [69], Jacobowitz et al. [70], Zarins et al. [67]	Brewster et al. [71]	Cost accounting system at New York Presbyterian Hospital, Medicare and literature			
Prinssen et al. (2007) [23]	DREAM [72]	DREAM [72]	DREAM [72]	DREAM [72]	DREAM [73], Dutch Costing Manual (National Health Insurance Council) [74]			
Tarride et al. (2011) [24]	Bowen et al. [17]	Bowen et al. [17]	Bowen et al. [17]	Bowen et al. [17]	Bowen et al. [17]	Bowen et al. [17]	Bowen et al. [17]	Bowen et al. [17]

OS; open surgery, EVAR; endovascular aneurysm repair

Costs and effectiveness input parameters

The estimates or the key parameters that were used in the economic evaluations are presented in Table 4. The costs are expressed in different currencies; Canadian dollars [12,15,22], US dollars [13,18,20], UK pounds [9,10,16,19] or Euros [21]. The chosen currency depends on the country the CEA was performed. Because the publications are economic evaluations performed in different countries and different years it is not possible to compare all the costs fairly. Bowen et al. [15] and Tarride et al. [22] made difference in OS high risk (HR) or OS low risk (LR), in both costs and effectiveness results. Bowen et al. [15] presented only the cost-effectiveness of OS HR in their CEA, so this is the only result reported in Table 3. The costs of EVAR are in a wide range. When we take the US for example the costs differ between $ 19,642 [13] - $37,068 [18]. One cause of these differences is included costs in this price. Lederle et al. [18], estimated the overall costs of EVAR, while Bosch et al. [13] only estimated the costs if the operation and the other costs were estimated under the name of reintervention and follow-up.

The mortality rates are very different as presented in Table 3. Some studies presented the 30-days mortality [12,14,15,18]. The range of 30-days mortality rates after EVAR is 0.5 [18] - 2.6 [14] and after OS 3.0 [18] - 4.3 [14]. Other studies presented the over general mortality [9,13,19,20,22]. The range of general mortality after EVAR is 1.2 [20] - 7.1 [15] and after OS 1.6 [16] - 7.7 [15]. It is hard to compare these values, because the time range is different between the studies. Tarride et al. [22] distinguish HR from LR in OS patients, that is why these numbers are not taken into the range. Prinssen et al. [21] did not state the mortality rates. The general included events are AAA rupture, endoleak, myocardial infarction, stroke, congestive heart failure and renal failure. These events are of influence on the costs and effects in the follow-up of EVAR of OS.

Table 4: Input parameters of the economic evaluations

Authors	**Price year**	**Input parameters - cost**				**Input parameters - effectiveness**				
		Costs EVAR	**Costs OS**	**Cost of reintervention**	**Costs of follow-up EVAR**	**Events included**	**Mortality rates EVAR (%)**	**Mortality rates OS (%)**	**Conversion to open surgery (%)**	**Probability of endoleak**
Blackhouse et al. (2009) [14]	Canadian Dollars, price year	$ 31,908	$ 18,552	$17,212 (rupture) $900 (endoleak)	$352	Conversion, stroke, MI, renal failure, CHF, rupture, endoleak	1.47*	4.0*	1.8	2.6
Bosch et al. (2002) [15]	US dollars 2000	$ 19,642	$ 23,484	NS	$ 483 (per visit, including imaging)	Conversion, cardiac, cerebral, renal, pulmonary, rupture	3.0	4.0	3.0	NS
Bowen et al. (2005) [16]	NS****	$ 23.525 (field: $31.986)	$ 13.243 (field: $29.242)	$ 17,122 (rupture) $ 900 (endoleak)	$ 3,266 (OS) $ 7,885 (EVAR)	Conversion, stroke, MI, renal-dialysis, CHF, rupture, endoleak	2.6*	4.3*	1.2* (3.3 following year)	2.2
Bowen et al. (2007) [17]	Canadian Dollars, 2006	$ 34,146	$ 34,170***	NS	EVAR: $5,181 (EVAR medical costs) $835 (EVAR societal costs) OS: $2,171 (medical costs) $818 (societal costs)	MI, CHF, stroke, conversion, rupture, renal failure, graft related complications, treatment related infections.	0.7* (7.1, after 1 year)	3.6* (7.7, after 1 year)	2.0	47.9**
Brown et al. (2013) [9]	UK Pound, 2008-2009	£ 13,019	£ 11,842	£7,536 (EVAR)	£88 (outpatient visit) £108 (CT)	Conversion, non-fatal readmission	2.2 (0-6 months) 0.6 (6 months – 4 years) 0.8 (>4years)	OR 0.35	NS	NS
Chambers et al. (2009) [10]	UK pound, 2007	£ 10,461	£ 9,983	NS	£88 (outpatient visit) £108 (CT)	Conversion, non-fatal readmission	Regression	OR 0.35	0.8	NS

EVAR; endovascular aneurysm repair, OS; open surgery, NS; not stated, MI; myocardial infarction, CHF; congestive heart failure, CT; computer tomogram, OR; odds ratio

Table 4: Input parameters of the economic evaluations - *continued*

Authors	**Price year**	**Input parameters - cost**				**Input parameters - effectiveness**				
		Costs EVAR	**Costs OS**	**Cost of reintervention**	**Costs of follow-up EVAR**	**Events included**	**Mortality rates EVAR (%)**	**Mortality rates OS (%)**	**Conversion to open surgury (%)**	**Probability of endoleak**
Epstein et al. (2007) [18]	UK pound, 2004	£15,823	£12,065	£5,936	NS	Conversion, stroke, MI	5.0	1.6	0.8	NS
Epstein et al. (2014) [19]	UK pound (EVAR), US dollars (OVER), Euro (DREAM) 2008-2009	EVAR-1: £13,019 OVER: $37,068 DREAM: €14,915	EVAR-1: £11,842 OVER: $42,970 DREAM: €11,975	NS	NS	NS	EVAR: 12 of 599 (6months-4years), 10 of 472 (4-8 years) OVER: 8 of 444 DREAM: 1 of 166	EVAR: 8 of 581 (6months-4years), 2 of 461 (4-8 years) OVER: 3 of 437 DREAM: 0 of 169	NS	NS
Lederle et al. (2012) [20]	US dollar, 2008	$37,068	$42,970	NS	NS	NS	0.5*	3.0*	NS	NS
Michaels et al. (2005) [21]	UK pounds, 2003-2004	£ 8,769	£ 4,269	£ 4,790	£ 41,50 (per month)	Endoleak, conversion	1.85	5.80	1.90	17.6 (30 days)
Patel et al. (1999) [22]	US dollars, 1997	$ 20,083	$ 16,016	$6,205/$5,710/ $1,740/$3,210/ $4,005 (different reinterventions)	NS	NS	1.2	4.8	2.0	NS
Prinssen et al. (2007) [23]	Euro, 2003	€ 18,179	€ 13,886	NS	€ 3,618 € 1,651 (OS)	NS	NS	NS	NS	NS
Tarride et al. (2011) [24]	Canadian Dollars, 2006	$28,139	$31,181 (High Risk) $15,494 (Low Risk)	NS	*Hospitalcosts* $5,172 (EVAR) $2,171 (OS HR) $1,890 (OS LR) *Productivity* $835 (EVAR) $818 (OS HR) $1,779 (OS LR)	MI, CHF, stroke, conversion, rupture, renal failure, graft related complications, treatment related infections.	0.7* (7.1 after 1 year)	9.6 (HR)* (17.3 after one year) 1.4 (LR)* (4.2 after one year)	NS	NS

*30-days mortality (*bij de overige geen uitleg),* **Type II endoleak, does not need immediately reintervention, ***Only OS with high risk patients were included
****Probably Canadian Dollars
EVAR; endovascular aneurysm repair, OS; open surgery, NS; not stated, MI; myocardial infarction, CHF; congestive heart failure, HR; high risk, LR; low risk

Table 5: Incremental outcomes

Authors (Year)	Incremental costs	**Incremental LYs gained**	**Incremental QALYs gained**	**Incremental costs per LY gained (ICER)**	**Incremental cost per QALY gained (ICER)**	**Is EVAR cost-effective*?**
Blackhouse et al. (2009) [14]	$ 13,355	0.030	0.050	$444,129	$ 268,337	NO
Bosch et al. (2002) [15]	$ 2,179		0.22		$ 9,905	YES
Bowen et al. (2005) [16]	$ 14,576 (field: $2,744)		0.091 (field: 0.1218)		$ 160,176 (field: $22,528)	NO (field: YES)
Bowen et al. (2007) [17]**	$ -24	0.111	0.025	EVAR dominates	EVAR dominates	YES
Brown et al. (2013) [9]	£3,519 (lifetime: £3521)		-0.032 (lifetime: -0.042)		OS dominates	NO
Chambers et al. (2009) [10]	£ 2,002		0.041		£49,000	NO
Epstein et al. (2007) [18]	£3,758		-0.020		OS dominates	NO
Epstein et al. (2014) [19]	Scenario 1: EVAR-1: £ 4,014 DREAM: £ 3,181 OVER: £-1,852 ACE: £ 2,086 Scenario 2: EVAR-1: £ 3,017 DREAM: £ 2,608 OVER: £ -2,362 ACE: £ 1,485		Scenario 1: EVAR-1: -0.02 DREAM: 0.00 OVER: 0.05 ACE: -0.01 Scenario 2: EVAR-1: 0.04 DREAM: 0.04 OVER: 0.08 ACE: -0.01		Scenario 1: EVAR-1: D- DREAM: £2,845,315 OVER: D+ ACE: D- Scenario 2: EVAR-1: £ 73,035 DREAM: £ 61,462 OVER: D+ ACE: D-	NO (EVAR-1, DREAM, ACE) YES (OVER)
Lederle et al. (2012) [20]	$-5,019	0.04	0.0064	EVAR dominates	EVAR dominates	YES
Michaels et al. (2005) [21]	£ 11,449		0.10		£ 110,000	NO
Patel et al. (1999) [22]	$ 9,587		0.42		$ 22,836	YES
Prinssen et al. (2007) [23]	€4,393		-0.01		OS dominates	NO
Tarride et al. (2011) [24]	$-24 (EVAR vs. OS HR) $14,983 (EVAR vs. OS LR)	0.12 (EVAR vs. OS HR)		EVAR dominates	No QALY gained.	YES (High Risk) / NO (Low Risk)

* Based on authors.

**This publication only used OS in high risk patients for the CEA.

LY; life year, QALY; quality adjusted life year, ICER; incremental cost-effectiveness ratio, D+; EVAR dominates OS, D-; EVAR dominated by OS, HR; high risk, LR; low risk

Main outcome results

Most studies concluded that EVAR was not cost-effective compared with OS using the incremental cost per QALY gained, as presented in table 5. Often the ICER was above their willingness-to-pay threshold [10,14,16,21] or EVAR was dominated by OS [9,18,23]. Adopted willingness-to-pay thresholds in publications concluding EVAR was above the willingness-to-pay were £30,000 [10,21] or $50,000 and $100,000 [14]. Bowen et al [16] did not give a particular willingness to pay. A minority of studies concluded that EVAR to be cost-effective, either because the ICER was below the adopted willingness-to-pay threshold[15,22] or OS dominated EVAR [17,20]. Adopted willingness-to-pay thresholds in publications concluding EVAR was below the willingness to pay were $75,000 [15] and $60,000. The data from Bowen et al. [17] was also used in the publication from Tarride et al. [24], in this study EVAR was more effective and less expensive than OS in high risk patients, but EVAR was less effective and more expensive than OS in low risk patients. Chambers at al. [10] also concluded that eligibility is of influence, although OS is more cost-effective than EVAR, eligibility seemed to be an important factor for the cost-effectiveness of OS. When high risk patients were less suitable for OSR, EVAR seemed to be more cost-effective. Epstein et al. [19] used the input parameters of four RCTs separately, therefore four different ICERs were calculated in this publication. In the EVAR-1, DREAM and ACE trial EVAR resulted to be not cost-effective and in the OVER trial EVAR resulted to be cost-effective. Four publications calculated the incremental costs per life year as well [14,17,20,24]. Bowen et al. [17] and Tarride et al. [24] used the same model to estimate the cost-effectiveness of EVAR, therefore both of these studies resulted the same results; EVAR dominated OS in high risk patients. Blackhouse et al. [14] estimated an incremental life year gain of 0.03 when EVAR is compared with OS and the corresponding ICER was $444,129.

Table 6: Sensitivity analysis used in the literature

Authors (Year)	**Type**	**Time horizons**	**Subgroup analyses**	**Postoperative complication rates**	**Mortality rates**	**Reinter-vention costs**	**Long-term utility values**	**Discount rates**	**Health related QoL**	**Follow-up costs**	**Costs EVAR**	**Cost of hospital-ization**
Blackhouse et al. (2009) [14]	Probabilistic	+	+	+	-	+	+	+	-	-	-	-
Bosch et al. (2002) [15]	Univariate/ Multivariate/ Threshold	-	-	+	+	+	+	+	+	-	-	-
Bowen et al. (2005) [16]*	Not Performed	-	-	-	-	-	-	-	-	-	-	-
Bowen et al. (2007) [17]	Univariate	+	-	-	-	-	-	-	-	-	-	-
Brown et al. (2013) [9]	Probabilistic/ Univariate	+	-	-	+	+	-	-	-	-	-	-
Chambers et al. (2009) [10]	Univariate/Multivariate/Probabilistic	-	+	+	+	+	-	-	-	+	+	-
Epstein et al. (2007) [18]	Univariate/ Probabilistic	-	+	-	+	-	-	+	-	+	+	-
Epstein et al. (2014) [19]	Univariate/ Probabilistic	-	-	-	+	-	-	-	-	-	-	-
Lederle et al. (2012) [20]	Not performed	-	-	-	-	-	-	-	-	-	-	-
Michaels et al. (2005) [21]	Univariate/ Probabilistic	+	+	-	+	+ **	-	+	-	-	+***	-
Patel et al. (1999) [22]	Probabilistic	-	+	+	+	-	-	+	-	-	-	+
Prinssen et al. (2007) [23]	Not performed	-	-	-	-	-	-	-	-	-	-	-
Tarride et al. (2011) [24]	Not performed	-	-	-	-	-	-	-	-	-	-	-

*This is an interim report.
**Not costs, but rates were used in this analysis
***This study spoke of incremental costs EVAR.
+; included, -; not included, QoL; quality of life, EVAR; endovascular aneurysm repair

Consideration of uncertainty

Table 6 presents the parameters that were varied in sensitivity analysis. These parameters might influence whether EVAR is cost-effective or not. When parameters like mortality after EVAR, reintervention costs and follow-up costs are lower, EVAR is more likely to be cost-effective. Four studies did not perform sensitivity analyses [16,20,23,24]. Bowen et al. [16] published an interim report, this publication states that a sensitivity analysis will be performed in the final report. Lederle et al. [20], Prinssen et al. [23] and Tarride et al. [24] did not perform a sensitivity analysis. The studies that did perform a sensitivity analysis include a wide range of different factors. Mortality rates were used most often in sensitivity analyses, seven studies varied this parameter [9,10,15,18,19,21,22]. Both Bowen et al. [17] and Epstein et al. [19] performed a limited sensitivity analysis, by varying the time horizon and mortality rates, respectively. Seven studies also perform a probabilistic sensitivity analysis, to generate a distribution of cost-effectiveness ratio. This method makes it possible to calculate the proportion of patients for which EVAR is cost-effective over OS, given a certain willingness to pay (for example £30.000 per QALY)[75].

Quality of the economic evaluations

Table 7 presents the quality of the economic analysis based on the Drummond checklist [11]. The quality of the publications was different. The overall quality is found te be reasonably good. Six studies did not have a clear description of the competing alternatives [15,18,20,22-24], possible because EVAR and OS are the only elective surgeries for AAA and there is no need of a description of the competing alternatives. But also this was not made clear in the publications.

Discounting for consequences and costs was applied in nine studies [9,10,14,15,18-22]. This adjustment was not needed when the time horizon of a study was one year or less. However, Bowen et al. [17] also reported a discount rate of 5.0%, while the stated time horizon was 12 months. Four studies did not state a perspective [16,20,22,23], so it is not possible to judge if all costs and consequences are identified.

Notable is the fact that only three studies [18-20] had a discussion section containing al required parts according to the Drummond checklist [11], which are . All other studies did not include al issues of concern in their discussion. Studies did not discuss transferability [9,10,14-16,21,22,24], did not reflect on their sensitivity analyses [14,16,21,23,24] or did not compare their conclusions with other publications [10].

Some studies scored less on this quality checklist compared to the other publications in this review. They did not score as many YESs as other studies, as presented in Table 6. Bowen et al. [16] concerns an interim report that could be a reason not every question is answered in their publication. Prinssen et al. [23] scored less as well, the lack of a clear perspective and sensitivity analyses makes it hard to check the validity of this CEA. Tarride et al. [24] also performed a poor quality. Possibly because it is a continuation research with all data from Bowen et al. [17].

Publications of high quality are Blackhouse et al. [14], Brown et al. [9], Chambers et al. [10] and Epstein et al. [18]. Interestingly these four studies concluded EVAR is not likely to be cost-effective compared with OS. But studies like Bowen et al. [17] and Lederle et al. [18] had a slightly less quality according to the Drummond checklist [11] and they concluded EVAR is likely to be cost-effective compared with OS.

Table 7: Quality assessment based on the Drummond checklist [11]

Authors (Year)	**Well defined question posed?**	**Description of competing alternatives given?**	**Effectiveness established?**	**Costs and consequences identified?**	**Costs and consequences measured accurately?**	**Costs and consequences valued credibly?**	**Costs and consequences adjusted?**	**Incremental analysis performed?**	**Allowance made for uncertainty?**	**All issues of concern included?**
Blackhouse et al. (2009) [14]	YES	YES	YES	YES	YES	YES	YES	YES	YES	NO
Bosch et al. (2002) [15]	YES	NO	YES	YES	YES	YES	YES	YES	YES	NO
Bowen et al. (2005) [16]	YES/NO	YES	YES	Can't tell	YES	YES	NO	YES	NO	NO
Bowen et al. (2007) [17]	YES	YES	YES	YES	YES	YES	NO	YES	YES	NO
Brown et al. (2013) [9]	YES	YES	YES	YES	YES	YES	YES	YES	YES	NO
Chambers et al. (2009) [10]	YES	YES	YES	YES	YES	YES	YES	YES	YES	NO
Epstein et al. (2007) [18]	YES	NO	YES	YES	YES	YES	YES	YES	YES	YES
Epstein et al. (2014) [19]	YES	YES	YES	YES	YES	YES	YES	YES	NO	YES
Lederle et al. (2012) [20]	YES?	NO	YES	Can't tell	YES	YES	YES	YES	NO	YES
Michaels et al. (2005) [21]	YES	YES	YES	NO	YES/NO	YES/NO	YES	YES	YES	NO
Patel et al. (1999) [22]	YES	NO	YES	Can't tell	YES	YES	YES	YES	YES	NO
Prinssen et al. (2007) [23]	YES	NO	YES	Can't tell	YES	YES	NO	YES	NO	NO
Tarride et al. (2011) [24]	YES	NO	YES	YES	YES	YES	NO	NO	NO	NO

Discussion

This study contents a review of the publications about the cost-effectiveness of elective EVAR compared to elective OS. There is variation in the outcomes of economic evaluations estimating the cost-effectiveness of EVAR compared with OS. The ICER varied considerably between studies: from EVAR being dominated by OS [9,18,23] to EVAR being dominant [17,20]. Other studies concluded that EVAR resulted in more QALYs gained but also resulted in higher costs. Then EVAR can be cost-effective [15,22] or not [14,16,21], depending on the ICER and the willingness to pay in a country. The same conclusion was made in previous reviews about these treatments [9,10]. The quality of the studies was also assessed by the Drummond checklist [11] and we considered the quality of the studies as reasonably good. Studies of higher quality are associated with no cost-effectiveness of EVAR. This could be important in the discussion whether EVAR is cost-effective or not. But studies of little less quality concluded EVAR was likely to be cost-effective. A closer look at the complete research of these publications could give more insight in the influence of quality on the outcomes of studies.

The studies included in this review used different resources for the costs and consequences of the treatments. This makes it difficult to determine a clear cause of the differences between ICERs across the studies. However, some possible explanations for these differences are described.

Studies differed in patient characteristics (age, gender, size of aneurysm) leading to difference in perioperative mortality rates. These differences influence the outcomes of the studies and consequently it leads to differences in the conclusions. For example an older population could lead to a higher mortality rate, cause patients are less healthy. Another possible cause of the differences between the outcomes of the studies is the difference of included events. Some studies included more events than others and this may have caused differences in the outcomes. Events like endoleaks and conversion can only occur after EVAR, so including these events could raise the costs of EVAR and decline the effects of EVAR in which case the cost-effectiveness of EVAR will be different. Other publications concluded that there are no significant differences in events like myocardial infraction and stroke after EVAR or OS [9,10] and therefore did not include these events in their economic evaluation. This decision is questionable, cause although the differences are not significant they still may influence the outcomes of the cost-effectiveness of EVAR or OS.

It is not made clear in this review what the possible influence of the different included events is on the cost-effectiveness of EVAR or OS. Several studies which included the event conversion concluded EVAR is likely to be cost-effective [15,17,24] but others concluded that is was unlikely that EVAR is cost-effective [9,10,14,16,18,21]. Of the studies which did not include the event conversion several concluded also EVAR is likely to be cost-effective [20,22] and others concluded EVAR is unlikely to be cost-effective[23]. Maybe the inclusion of reintervention makes a difference in cost-effectiveness. Five of the studies including the costs of reintervention concluded EVAR is unlikely to be cost-effective[9,14,16,18,21] and only one study concluded EVAR is unlikely to be cost-effective [22]. And four of the studies which did not included the costs of reintervention concluded EVAR is likely to be cost-effective[15,17,20,24] and only two studies concluded EVAR is unlikely to be cost-effective[10,23]. It looks like studies which did include reintervention costs as event are more likely to say EVAR is unlikely to be cost-effective and studies which did not include the costs of reintervention are more likely to say EVAR is likely to be cost-effective. But it is hard to make a clear comparison, for example; some studies named endoleak under reintervention and other studies made a difference in these events.

Furthermore, the cost-effectiveness of EVAR always depends on data that was used for the economic evaluation. Epstein et al. [19] has estimated the cost-effectiveness of EVAR for four trials separately leading to different conclusions; EVAR dominated OS based on the OVER trial, OS dominated EVAR based on the EVAR-1 trial or ACE trial. EVAR was not cost-effective (ICER £ 2,845,315 in the DREAM trial. Lederle et al. [20] and Brown et al. [9] also concluded that EVAR dominated OS in their studies using OVAR trial data and EVAR-1 trial data, respectively. However, Prinssen et al. [23] concluded that OS dominated EVAR in the DREAM-trial, this conclusion differs from the conclusion of Epstein et al. [19] about the cost-effectiveness in the DREAM trial. Prinssen et al. [23] estimated a not significant 0.01 QALY loss and Epstein et al. [19] estimated a 0.001 difference of QALYs between EVAR and OS.

Other included studies used different resources for their parameters. Two studies were performed before any trial data was available [15,22]. The parameters they used for their economic evaluation were conducted from non-comparative observational data. Because data was not conducted from RCTs there were no matching populations. The data was also conducted from many different studies and therefore different situations. Interestingly both of these studies which found EVAR to be cost-effective but the first publication after an RCT [21] concluded EVAR was not cost-effective. Other studies used trial data for parameters of effectiveness directly from an RCT only [9,17,18,23]. In these studies all results are collected in one country, the population is very specific. All studies are specific for their setting, so the economic evaluations included in this review as well. Differences between countries (e.g. treatment variation) are also an important influence on the economic studies [76] Consequently, the results of studies using data based on an RCT or other studies performed in one country are less transferable than studies that have combined the outcomes of several RCTs, like Epstein et al. [19].

Interesting fact, two of the most recent studies [17,20] using field studies as parameter source conclude EVAR to be cost-effective. Compared to all other studies using field studies as parameter source in which EVAR was not cost-effective. Possible the cost differences or effectiveness differences between EVAR and OS are getting smaller over the years. Because the use of EVAR is becoming more wide spread making EVAR becomes less expensive over the years and more likely to be cost-effective, as shown in sensitivity analyses [20]This phenomenon appears at many economic evaluations [77,78]. Maybe a future research could give more insight in the hypotheses (assumptions) concerning EVAR.

Strength and limitations of this study

This study has several limitations and strengths. For this review three databases were searched. This strengthened the validity of the search outcomes because when only one database was used, it was possible not all CEAs about EVAR were identified in one database. By using more than database we tried to identify all relevant studies evaluating EVAR with OS.

Another strength of this study is the double scoring that has been performed of the title/abstract selection (CB & MS), the full assessment (CB & LB), the data extraction (CB & LB) and the quality assessment (CB & LB). Double scoring of the references is essential since the selection process is subjective.

A limitation of this study is the translation of the validated NHS strategy for Pubmed [12] that was created by two reviewers (CB & MS). This translation is not validated for this database, it is possible the translation had some shortcomings and therefore missed some publications, in that case is possible this systematic review is not complete. However, this is unlikely, since the publications that are included in other systematic reviews [9,10] about the cost-effectiveness of EVAR compared to OS are also included in this this systematic review.

A quality assessment was made using the Drummond checklist [11]. Despite the fact that the quality of models was assessed by one independent reviewer and checked by another reviewer it was difficult to judge the quality due to subjectivity of the questions; this problem has been recognized in the past [79]. Beside the subjectivity the Drummond checklist is performed by checking what is reported in the publications and thus it is possible that studies have fulfilled the requirements but are scored negatively what is the result of lack of transparency.

Recommendations

After performing this review we have some recommendations for future systematic reviews. First we want to emphasize the need of peer reviewers for a systematic review like this study. Especialy the Drummond checklist is a very subjective method to judge the quality of a publication. In this study we have used double scoring however more reviewers could have been used to have a more valid estimate of quality. Furthermorea clear operationalization of the quality checklist as performed in this study leads to less variation between reviewers. This studie also could not make a clear comparison of the costs between all studies, because of the different currencies. We recommend future systematic reviews to convert these different currencies of the included studies to one currency in orde to make a more clear comparison of costs.

Second, in order to make a clear comparison between different publications we recommend to perform a systematic review comparing the outcomes of RTCs compared to observational studies. RCTs use strict in- and exclusion criteria which leads to good estimate of the efficiency of EVAR compared to OS in that specific population which makes it less generalizable to the generalizable to the general population. Observational studies use often less strict in- and exclusion criteria, leading to less comparable populations, however observational studies (e.g. registries) can lead to good estimate of the effectiveness in daily practice after matching. A long follow-up in these studies is preferred since a long time horizon is important to measure all differences between EVAR and OS. For example EVAR has a lower mortality after 30-days, but this difference diminishes over time and seems to have disappeared after two years [7,8]. A long follow-up is necessary to discover developments in mortality like this.It is also preferred to include studies with as much corresponding characteristics as possible.

Furthermore we recommend future systematic reviews comparing publications which estimate the cost-effectiveness of EVAR with OS to examine which parameters for costs and effectiveness are of significant influence. All studies had different included events with possible different influences in the outcomes. These differences between studies makes it hard to make clear whether EVAR is cost-effective or not in this review. It would also be interesting to examine what the influences are of the inclusion of the different events on the cost-effectiveness of EVAR and OS.

Conclusion

The aim of this study was to provide an updated overview of economic evaluations comparing elective EVAR and elective OS and a quality assessment of those economic evaluations. From this review the following conclusion can be drawn: the performed economic evaluations do not provide a clear answer whether elective EVAR is cost-effective or not compared to elective OS because studies had different conclusions. Seven studies concluded EVAR was not cost-effective and four studies concluded EVAR was cost-effective. The overall quality of the studies in this review was reasonably good though quality of the studies also differ. The quality of the studies may be a possible influence on the outcomes of the studies.

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Appendix 1: Search strategies

CRD (date: 25-03-2014):

(evar OR endovascular OR open) AND (abdominal aortic aneurysm AND aaa)

Total hits: 115

Pubmed (date: 25-03-2014):

	Terms	Hits
#1	"Economics"[Mesh:NoExp]	26425
#2	"Costs and Cost Analysis"[Mesh]	19124
#3	"Economics, Dental"[Mesh:NoExp]	1857
#4	"Economics, Hospital"[Mesh]	19124
#5	"Economics, Medical"[Mesh:NoExp]	8553
#6	"Economics, Nursing"[Mesh]	3886
#7	"Economics, Pharmaceutical"[Mesh	2476
#8	((((((((economic*[Title/Abstract]) OR cost[Title/Abstract]) OR costs[Title/Abstract]) OR costly[Title/Abstract]) OR costing[Title/Abstract]) OR price[Title/Abstract]) OR prices[Title/Abstract]) OR pricing[Title/Abstract]) OR pharmacoeconomic*[Title/Abstract]	459392
#9	(expenditure*[Title/Abstract]) NOT energy[Title/Abstract]	18323
#10	value for money[Title/Abstract]	875
#11	budget*[Title/Abstract]	19029
#12	#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11	583740
#13	(energy cost[Title/Abstract]) OR oxygen cost[Title/Abstract]	2863
#14	metabolic cost[Title/Abstract]	833
#15	(energy expenditure[Title/Abstract]) OR oxygen expenditure[Title/Abstract]	16699
#16	#13 OR #14 OR #15	19664
#17	#12 NOT #16	579234

#18	"AAA" OR "Abdominal aneurysm" OR "aortic aneurysm" OR "abdominal aortic aneurysm$" OR "aneurysm" OR AAA endograft$)"	111444
#19	"Open surgery" OR "open" OR "surgery" OR "standard surgery" OR "standard therapy"	2577234
#20	"EVAR" OR "endovascular aneurysm repair" OR "AAA repair" OR "endovascular repair" OR "aneurysm repair" OR "repair" OR "endovascular stent$" OR endovascular surg$ OR endovascular treat$ OR endoluminal repair$ OR endoluminal stent$ OR endoluminal treat$ OR endoluminal surg$"	244242
#21	#18 AND #19 AND #20	18536
#22	#17 AND #21	576

Embase (date: 26-03-2014):

	Terms	Hits
#1	'economics'/de	202668
#2	'cost'/exp	249714
#3	'health economics'/de	33886
#4	'pharmacoeconomics'/de	5845
#5	economic:ab,ti OR cost:ab,ti OR costs:ab,ti OR costly:ab,ti OR costing:ab,ti OR price:ab,ti OR pirces:ab,ti OR pricing:ab,ti OR pharmacoeconomic:ab,ti	541944
#6	expenditure*:ab,ti NOT energy:ab,ti	23411
#7	'value for money':ab,ti	1263
#8	budget*:ab,ti	23829
#9	#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8	839190
#10	((energy OR oxygen) NEAR/3 cost):ab,ti	3790
#11	(metabolic NEAR/3 cost):ab,ti	1030
#12	((energy OR oxygen) NEAR/3 expenditure):ab,ti	20409
#13	#10 OR #11 OR #12	24325
#14	#12 NOT #13	833498
#15	'aaa' OR 'abdominal aneurysm' OR 'aortic aneurysm'/exp OR 'aortic aneurysm' OR 'abdominal aortic aneurysm'/exp OR 'abdominal aortic aneurysm' OR 'aneurysm'/exp OR 'aneurysm' OR 'aaa endograft'	138338
#16	'open' OR 'surgery' OR 'standard surgery' OR 'standard therapy'	4797122
#17	'evar' OR 'endovascular aneurysm repair' OR 'aaa repair' OR 'endovascular repair' OR 'aneurysm repair' OR 'repair' OR (endovascular stent*) OR (endovascular surg*) OR (endovascular treat*) OR (endoluminal repair*) OR (endoluminal stent*) OR (endoluminal treat*) OR (endoluminal surg*)	324640
#18	#15 AND #16 AND #17	29466
#19	#14 AND #18	981