Review report of MTG16: The E-vita Open Plus for treating complex aneurysms and dissections of the thoracic aorta

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1.0	29/06/2018	T Macmillan T Langford	for review by MTEP technical lead
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3.0	16/07/2018	T Macmillan T Langford	final version
3.2	24/08/2018	T Langford	Updated version

This medical technology guidance was published in December 2013.

All medical technology guidance is reviewed 3 years after publication.

This review report summarises new evidence and information that has become available since this medical technology guidance was published, and that has been identified as relevant for the purposes of this report. This report will be used to inform NICE's decision on whether this guidance needs to be updated at this time.

Produced by:

King's Technology Evaluation Centre (KiTEC), King's College London (KCL).

Authors:

Anastasia Chalkidou, Senior Health Technology Assessor, KiTEC, KCL.

Huajie Jin, Senior Health Economist, KiTEC, KCL.

Tom Langford, Health Technology Assessor, KiTEC, KCL.

Tom Macmillan, Information Specialist, KiTEC, KCL.

Stephen Keevil, Director, KiTEC, KCL.

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Mr Pedro Catarino, Consultant surgeon, Royal Papworth Hospital

Mr Andrew Goodwin, Consultant Cardiac Surgeon, Middlesbrough Hospital

Mr Stephen Large, Consultant surgeon, Royal Papworth Hospital

Mr Jorge Mascaro, Consultant Cardiac Surgeon, Director of Heart and Lung Transplantation and Mechanical Circulatory Support, Lead of Major Aortic Surgery, University Hospitals Birmingham NHS Foundation Trust

Mr Robert A Morgan, Consultant Interventional and Diagnostic Radiologist (Honorary Senior Lecturer), President - Cardiovascular and Interventional Radiological Society of Europe, St George's University Hospitals NHS Foundation Trust

1. Original objective of guidance

To assess the clinical and cost effectiveness of E-vita Open Plus for treating complex aneurysms and dissections of the thoracic aorta.

2. Current guidance recommendations

1.1 The case for adopting the E-vita Open Plus for treating complex aneurysms and dissections of the thoracic aorta, in a carefully selected group of people, is supported by the evidence.

1.2 Using the E-vita Open Plus could remove the need for a second procedure and the associated risk of serious complications, and it should therefore be considered for people:

- who would otherwise need a 2-stage repair procedure because their aortic disease extends into or beyond the distal part of their aortic arch (into the proximal descending aorta), but
- who would not need additional intervention (such as stent grafting) in the descending aorta.

1.3 The E-vita Open Plus is estimated to generate cost savings compared with current 2-stage repair from about 2 years after the procedure. The estimated cost saving per patient at 5 years after the procedure is around £13,800 when compared with 2-stage repair involving open insertion of a vascular graft, £9850 when compared with 2-stage repair involving

endovascular stent grafting and £12,000 when compared with open surgical debranching followed by endoluminal stent grafting. At 10 years after the procedure, the estimated cost savings range from around £21,850 to £28,160 across the 3 comparators.

3. Methods of review

The date ranges for all databases were updated to “2013 to present”, or more precise date ranges where possible, in order to avoid overlap with the original report. The EAC manually excluded any studies from the original report that appeared in the updated search. All search strategies conducted by the EAC are listed in Appendix C including the gIS search strategy.

Once the individual databases had been searched, the returns were collated using EndNote X8 (Thomson Reuters) and then de-duplicated. Abstracts and titles of the search results were reviewed by 2 reviewers using the inclusion and exclusion criteria outlined in the original report. The literature update provided by the manufacturer was cross-matched with the results of the systematic review. Only one reference was provided by the manufacturer. This paper (Jakob et al. 2017) was also identified in the search strategy. This reference was collated along with the 77 references which were sifted from the 1368 de-duplicated references found by the database searches, leaving 78 references for full text assessment.

At the full text assessment eligibility stage (as per PRISMA guidelines), all publications were reviewed by 2 reviewers and any disagreements about the relevance of a study were resolved by discussion and consensus. In total 7 studies were reviewed and summarised (see Appendix B for study details).

4. New evidence

4.1. Changes in technology

A year after the initial guidance was published in 2013, a suture collar was added to the design in order to facilitate anastomosis between the stent graft and the aortic wall. The intended use and function of the medical device have not been changed. Evita Open Plus Stent Graft is available with and without the suture collar. The Design Examination Certificate has been updated to include both versions of the technology. The E-vita Open Plus Stent Graft with added suture collar was CE marked on June 5, 2014.

One expert advisor commented that “implantation has become easier with the later generation E-vita (due to the newer nose cone – although even this can get stuck post deployment, but is a lot better than previously)”.

A search of FDA-MAUDE and MHRA found no adverse events associated with E-vita Open Plus.

4.2. Changes in care pathways

Since the publication of the original guidance, there have been no changes to NICE interventional procedure guidance on endovascular stent–graft placement in thoracic aortic aneurysms and dissections.

The EAC conducted a search for relevant NICE guidance on the topic and no new guidance was discovered.

In 2014, the European Society of Cardiology published guidelines on the diagnosis and treatment of aortic diseases.

Relevant guidance is listed in Appendix A.

4.3. Results from MTEP MTG review

Not applicable.

4.4. New studies

The EAC included 7 studies in this report, all of which are summarised in this section. All studies included E-vita Open Plus as an intervention. Details for all studies are tabulated in Appendix B.

Erkanli et al. (2017) presented a study of 9 patients who underwent surgical treatment using E-vita Open Plus and the frozen elephant trunk (FET) technique for treating thoracic aorta disease involving the descending aorta. The study design was retrospective and non-comparative. Five patients were operated on for an aneurysm; 3 patients for dissection; and 1 patient for a dissecting aneurysm. No deaths were observed during the intraoperative period. One patient died of gastrointestinal haemorrhage. No neurological complications were observed during the postoperative period, and no revision surgeries were required.

Hoffman et al. (2013) reported a single centre, retrospective, non-comparative study into the safety of E-vita Open Plus that took place in Turkey. The study involved 32 patients with acute type A aortic dissection involving the descending thoracic aorta who underwent FET repair with the E-vita Open Plus. At 30 days post-operation, the survival rate was 100%. The all-cause mortality at 17 +/- 4 months follow-up was 3.1% (1/32). No aortic events or revision surgeries occurred during the follow-up period. Postoperative complications included 5 cases of pneumonia, 3 pulmonary embolisms, 1 case of sepsis and 1 patient suffering permanent recurrent laryngeal nerve damage. No brain or spinal cord injuries were observed. No endoleaks or false lumen patency occurred either. The authors concluded that the

implantation of E-vita Open Plus is safe to use with low mid-term mortality and morbidity rates.

Iafrancesco et al. (2017) reported on a multicentre, retrospective, registry study that took place in 5 countries in Europe. The study investigated clinical efficacy and safety of E-vita Open Plus. The study identified 137 patients with aortic dissection (65 acute and 72 chronic) who had survived a 1-year follow-up period. All patients were implanted with E-vita Open Plus. The hybrid stent graft was successfully implanted in all cases. The rate of false lumen thrombosis was higher in the mid-descending thoracic aorta (99.3%) than the distal abdominal aorta (13.9%); but similar between acute and chronic cases. The incidence of stroke, spinal cord ischaemia, renal failure, mechanical ventilator support longer than 72h and type Ib endoleak was 2.2%, 3.6%, 19.7%, 24.1% and 5.1% respectively. Ten patients died during the follow-up period (median follow-up period was 32 months), all deaths were in the chronic group. One-, 3- and 5-year estimates of survival in the chronic group were 100%, 92.3% and 82.3%, respectively with a statically significant difference (P=0.03). 5-year estimates of survival for the acute group was 100% as no death occurred. One-, 3- and 5-year estimates of freedom from distal reintervention in the acute and chronic groups were 100%, 100% and 96.3%, and 84.7%, 79.7% and 64.3%, respectively with a statically significant difference (P<0.001).

Jakob et al. (2017) conducted a single centre, prospective, non-comparative study in Germany investigated clinical efficacy and safety of the E-vita Open Plus. This study recruited 178 consecutive adult patients with aortic dissection and complex aneurysm; 96 acute, 43 chronic and 39 complex. The interventions used were the E-vita Open and E-vita Open Plus (though they were not compared). Overall 30-day mortality was 10%; 13% for complex thoracic aortic aneurysms (TAA). After 7 years, estimated survival was 73% for TAA patients. Freedom from aorta-related late death was 97% in TAA. Positive remodelling occurred in 88% of TAA patients. Freedom from endovascular intervention downstream was 74% in TAA patients. Freedom from thoraco-abdominal surgery was 93%. The authors concluded that E-vita hybrid stent grafts offer durable long-term performance without significant risk of proximal endoleakage or graft failure over time.

Kozlov et al. (2018) reported a single centre, retrospective, non-comparative study from Russia investigating the risk of spinal cord injuries in repair of acute aortic dissection. The study population was 37 consecutive patients who underwent total aortic arch surgery using the FET technique and E-vita Open Plus hybrid stent grafts. No permanent spinal cord injuries were observed. The incidence of permanent neurological deficit and temporary neurological deficit was 2.4% and 4.8% respectively. The 30-day mortality

rate was 4.8%. The in-hospital mortality rate was 10.8%. The causes of death were abdominal aortic rupture (n=1), profuse intraoperative bleeding due to disseminated intravascular coagulation (n=1) and multiorgan failure (n=2). Preoperatively, the mean number of intercostal arteries was 10±1 on the left side and 10±2 on the right side (P=0.59). Postoperatively, the mean number of open segmental arteries was 3±2 on the left and 4±1 on the right (P=0.003). The authors concluded that a low risk of spinal cord injury for the FET technique with E-vita Open Plus is achievable provided strict adherence to accepted surgical management protocols is followed. However, this implantation leads to extensive occlusion of intercoastal arteries; a potential cause of spinal cord injury.

Verhoye et al. (2014) reported on a single centre, retrospective, non-comparative study investigating the mid-term surgical outcomes of treating extensive thoracic aortic disease with E-vita Open Plus. This study collected data on 16 patients who underwent the FET procedure. There were no cases of operative mortality, cerebral stroke or postoperative paraplegia. Two cases of transient paraparesis and one case of Brown-Séquard syndrome occurred. At follow-up (12 months), no cases of endoleak or endotension had occurred. One patient was reoperated for thoracoabdominal aortic replacement. All patients survived the follow-up period. No adverse neurological events were observed.

Verhoye et al. (2017) reported on a French multicentre, retrospective registry study investigating the safety of E-vita Open Plus. The registry analysis identified 94 patients (including the 16 patients in the above study) with extensive thoracic aortic disease who underwent total aortic arch surgery using E-vita Open Plus. The perioperative mortality rate was 11.7%. Spinal cord ischaemia and stroke rates were 4% and 9.6%, respectively. Concomitant procedures were observed in 15% of patients. Among the 83 surviving patients at the 1-year follow-up, the survival rate was 98%. 11% of patients underwent endovascular completion, whereas 4% of patients required aortic reintervention at 1 year. The authors concluded that the E-Vita Open Plus hybrid device maintains the favourable short- and mid-term outcomes offered by its predecessor in FET procedures in patients with chronic aortic arch disease.

4.5. Ongoing trials

Only one relevant ongoing clinical trial was identified by an expert advisor. No other relevant ongoing trials were identified by the EAC's ongoing trial search strategy.

The Effective Treatments for Thoracic Aortic Aneurysms (ETTAA Study): A Prospective Cohort Study (NCT02010892) aims to investigate the clinical outcomes and risks of different interventions (endovascular stent grafting, open surgical repair, best medical therapy or watchful waiting) in patients being referred to a specialist centre for diagnosis and treatment of their aneurysm in a prospective observational cohort study. The estimated completion date is July 2019. The primary outcome measures are listed as;

- Aneurysm Growth
- Quality of life
- Freedom from reintervention
- Freedom from death or permanent neurological injury
- Costs to the NHS
- Incremental cost per quality adjusted life year gained

4.6. Changes in costs

The EAC updated the cost model analysis and have concluded that the pathway is still relevant. The original model was used with updated costs. Further details are available in the E-vita Open Plus cost model report (see Appendix E). The result of the updated analysis is reported in Table 1 below.

Table 1. Base case result per patient

Expected cost per patient	E-vita open plus	Two stage with vascular graft	Two stage with endovascular stent graft	Open debranching with endoluminal stent graft
1 year (Short-term)	£32,666	£31,799	£27,634	£24,905
5 years	£45,721	£59,055	£55,946	£58,257
10 years	£56,445	£81,446	£79,149	£85,655
20 years (Long-term)	£72,125	£114,182	£113,118	£125,712

In the short-term (1-year), E-vita Open Plus was the most expensive intervention, and incurred £7,761 additional cost compared to the least expensive strategy. The short-term cost difference was mainly driven by the high technology costs and longer length of stay for patients receiving E-vita Open Plus. However, from 5 years onwards, E-vita Open Plus becomes the least expensive intervention. This is because E-vita is a single-stage procedure, and is therefore less likely to cause surgery-related adverse events (i.e. bleeding, stroke, paraplegia and renal failure) than the two-stage procedures. The long-term (20-year) cost-saving associated with E-vita Open Plus over the comparators ranged between £40,993 and £53,587. This conclusion is robust to all scenarios tested. The results of the updated model are consistent with the findings of the original model.

From the economic literature search, other than the original NICE MTG16 on E-vita Open Plus, no published evidence on the resource consequences of adopting E-vita Open Plus was found (including economic evaluations or costing studies).

4.7. Other relevant information

None

5. Conclusion

The clinical evidence has not changed significantly since the original guidance was published in 2013. The evidence that has been produced since this time broadly supports the recommendations from the original guidance. The results of the included evidence were compared to the pooled estimates from the EAC's meta-analysis in the original assessment report for E-vita Open Plus. The outcomes included in the meta-analysis were in-hospital mortality, 30 day mortality, incidences of bleeding, stroke, paraplegia and renal failure. The results of the new studies largely fell within the 95% confidence levels of the EAC's meta-analysis. An exception being Iafrancesco et al. (2017) which had a significantly higher incidence of renal failure (19.7% versus 3.6% in the meta-analysis). This is not discussed in the paper, however, incidence of renal failure at baseline was higher than the pooled estimate at 8%.

All of the included papers concluded the E-vita Open Plus was safe and effective for use in treating complex aneurysms and dissections of the thoracic aorta. Verhoye et al. (2017) concluded that the E-vita Open Plus had comparable outcomes to the E-vita Open hybrid stent graft. None of the papers reported significant adverse negative outcomes for patients undergoing treatment with E-vita Open Plus, except Kozlov et al. (2018) which reported significant occlusion of intercoastal arteries as a result of the surgical implantation. However, this study also found low incidences of spinal cord injuries and no permanent injuries. The other included studies also found low incidences of spinal cord injury. It should be noted that none of the studies were comparative and population sizes were small; ranging from 9 to 178 participants. Jakob et al. (2017) had the longest follow-up period (7 years), they found that E-vita Open Plus has good long-term clinical effectiveness and safety, with low incidences of stent failure and reintervention. They referred to the FET procedure with E-vita Open Plus as the current 'gold standard' for treating multisegmental thoracic aortic disease.

Regarding the cost-effectiveness of E-vita Open Plus, the current evidence supports the recommendations from the original report. No new published evidence was uncovered in the EAC's economic literature search and the

results of the updated cost model was consistent with the findings of the original model that E-vita Open Plus is cost-saving in the long term compared with current 2-stage repair comparators .

Appendix A – Relevant guidance

NICE guidance – published

Aortic aneurysms (2014) NICE Pathway

Endovascular stent–graft placement in thoracic aortic aneurysms and dissections (2005) Interventional procedures guidance IPG127

NICE guidance – in development

None identified.

Guidance from other professional bodies

Aortic diseases: Clinical Practice Guidelines (2014) European Society of Cardiology

Appendix B – Details of studies and ongoing trials

Completed Studies

STUDY	STUDY DESIGN	POPULATION	INTERVENTION	COMPARATOR	OUTCOMES
Erkanli et al. 2017	Single centre, retrospective, non-comparative study, Turkey	9 adult patients with thoracic aorta disease involving the descending aorta	E-vita Open Plus	None	No deaths were observed during the intraoperative period. One patient died of gastrointestinal hemorrhage. No neurological complications were observed during the postoperative period, and no revision surgeries were required.
Hoffman et al. 2013	Single centre, retrospective, non-comparative study, Turkey	32 patients with acute type A aortic dissection	E-vita Open Plus	None	30-day survival rate was 100% with 3.1% (1/32) all-cause mortality at 17 +/- 4 months follow-up. No aortic events or revision surgeries occurred during the follow-up period. Postoperative complications included 5 cases of pneumonia, 3 pulmonary embolisms, 1 case of sepsis and 1 patient suffering permenant recurrent laryngeal nerve damage. No brain or spinal cord injuries were observed. No endoleaks or false lumen patency occurred either.

Iafranc esco et al. 2017	Multicen tre, internati onal, retrospe ctive, registry study, (Austria, Finland Germany, Italy and the UK)	137 patients with aortic dissection (65 acute and 72 chronic) who had survived at a 1-year follow-up period.	E-vita Open Plus	none	The stent graft was successfully implanted in all cases. The incidence of stroke, spinal cord ischaemia, renal failure, mechanical ventilator support longer than 72h and type Ib endoleak was 2.2%, 3.6%, 19.7%, 24.1% and 5.1% respectively. Ten patients died during the follow-up period (median follow-up period was 32 months), all deaths were in the chronic dissections group. One-, 3- and 5-year estimates of survival in the acute and chronic groups were 100%, 100% and 100% and 100%, 92.3% and 82.3%, respectively with a statically significant difference (P=0.03). One-, 3- and 5-year estimates of freedom from distal reintervention in the acute and chronic groups were 100%, 100% and 96.3%, and 84.7%, 79.7% and 64.3%, respectively with a statically significant difference (P<0.001).

Jakob et al. 2017	single centre, prospective non-comparative study, Germany	178 consecutive adult patients with aortic dissection and complex aneurysm; 96 acute, 43 chronic and 39 complex.	E-vita Open and E-vita Open Plus	None	Overall 30-day mortality was 10%; 13% for complex thoracic aortic aneurysms (TAA). After 7 years, estimated survival was 73% for TAA patients. Freedom from aorta-related late death was 97% in TAA. Positive remodelling occurred in 88% of TAA patients. Freedom from endovascular intervention downstream was 74% in TAA patients. Freedom from thoraco-abdominal surgery was 93%.
Kozlov et al. 2018	Single centre, retrospective, non-comparative study, Russia	37 consecutive patients undergoing total aortic arch surgery	E-vita Open Plus	None	No permanent spinal cord injuries occurred. Preoperatively, the mean number of intercostal arteries was 10±1 on the left side and 10±2 on the right side (P=0.59). Postoperatively, the mean number of open segmental arteries was 3±2 on the left and 4±1 on the right (P=0.003). The incidence of permanent neurological deficit and temporary neurological deficit

					was 2.4% (n=1) and 4.8% (n=2), respectively. The 30-day mortality rate was 4.8% (n=2). The in-hospital mortality rate was 10.8% (n=4). The causes of death were abdominal aortic rupture (n=1), profuse intraoperative bleeding due to disseminated intravascular coagulation (n=1) and multiorgan failure (n=2).
Verhoye et al. 2014	Single centre, retrospective, non-comparative study	16 patients undergoing frozen elephant trunk procedure for either post-dissection aneurysm (50%), true aneurysm (31%) or other etiologies (19%	E-vita Open Plus	None	There were no cases of operative mortality, nor cases of cerebral stroke nor postoperative paraplegia. Two cases of transient paraparesis and one case of Brown-Séquard syndrome occurred. At follow-up (12 months), there were no cases of endoleak or endotension. One patient was reoperated for distal completion (thoracoabdominal aortic replacement). All patients survived the follow-up period. No adverse neurological events were observed.
Verhoye et al. 2017	Multicentre, retrospe	94 patients with extensive	E-vita Open Plus	None	The perioperative mortality rate was 11.7%. Spinal cord

	ctive registry study, France	thoracic aortic disease undergoing total aortic arch surgery			ischaemia and stroke rates were 4% and 9.6%, respectively. Concomitant procedures were observed in 15% of patients. Among the 83 surviving patients, the survival rate after the 1-year follow-up was 98%. 11% of patients underwent endovascular completion, whereas 4% of patients required aortic reintervention at 1 year.

Ongoing Trials

NCT02010892	Effective Treatments for Thoracic Aortic Aneurysms (ETTAA Study): A Prospective Cohort Study	https://clinicaltrials.gov/ct2/show/NCT02010892

Appendix C – Literature search strategy

For the clinical evidence the original searches were re-run with some adaptations in Ovid Medline, Medline In-Process, Embase and the Cochrane Database of Systematic Reviews. These searches retrieved 1490 records. The EAC decided additionally to search CENTRAL, DARE, HTA, NHSEE (via the Cochrane platform), PubMed and Web of Science, which retrieved 737 records. The NICE gIS search retrieved 116 records. In total there were 2343 records which was reduced to 1368 following de-duplication.

For the economics search the adapted searches were run in Ovid Medline, Medline In-Process, Embase, Cochrane (CDSR, CENTRAL, DARE, HTA, NHSEED), EconLit, PubMed and Web of Science. These searches retrieved 140 records which was reduced to 107 following de-duplication.

NICE gIS searches

Database: Medline
Strategy used: Database: Ovid MEDLINE(R) <1946 to Present with Daily Update> Search Strategy: --- 1 (e-vita or evita).tw. (157) 2 Stents/ or Blood Vessel Prosthesis Implantation/ or Endovascular Procedures/ (78133) 3 ((blood adj4 vessel* adj4 prosthe* adj4 implant*) or (vascular adj4 prosthe* adj4 implant*)).tw. (215) 4 ((endovascular or intravascular) adj4 (procedure* or technique*)).tw. (6415) 5 (stent* or graft*).tw. (329033) 6 (thoracic* or TAA).tw. (114076) 7 "elephant trunk".tw. (614) 8 Aneurysm, Dissecting/ (15587) 9 exp Aortic Aneurysm/ (49265) 10 ((aortic* or "acute type A" or "chronic type A" or degenerat*) adj4 (aneurysm* or dissect* or dissecan*)).tw. (37118) 11 (aortic* adj4 arch).tw. (13737) 12 (open adj4 surgical adj4 debranch).tw. (0) 13 ((ascending or descending) adj4 aorta).tw. (17489) 14 or/2-13 (506219)

15 1 and 14 (46)

16 animals/ not humans/ (4408192)

17 15 not 16 (46)

18 limit 17 to english language (41)

19 limit 18 to ed=20130501-20180411 (18)

Database: Medline in Process

Strategy used:

Database: Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations <April 10, 2018>

Search Strategy:

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1 (e-vita or evita).tw. (32)

2 Stents/ or Blood Vessel Prosthesis Implantation/ or Endovascular Procedures/ (0)

3 ((blood adj4 vessel* adj4 prosthe* adj4 implant*) or (vascular adj4 prosthe* adj4 implant*)).tw. (6)

4 ((endovascular or intravascular) adj4 (procedure* or technique*)).tw. (974)

5 (stent* or graft*).tw. (34782)

6 (thoracic* or TAA).tw. (11751)

7 "elephant trunk".tw. (111)

8 Aneurysm, Dissecting/ (0)

9 exp Aortic Aneurysm/ (0)

10 ((aortic* or "acute type A" or "chronic type A" or degenerat*) adj4 (aneurysm* or dissect* or dissecan*)).tw. (3649)

11 (aortic* adj4 arch).tw. (1139)

12 (open adj4 surgical adj4 debranch).tw. (0)

13 ((ascending or descending) adj4 aorta).tw. (1304)

14 or/2-13 (49612)

15 1 and 14 (14)

16 animals/ not humans/ (0)

17 15 not 16 (14)

18 limit 17 to english language (14)

Database: Embase

Strategy used:

Database: Embase <1974 to 2018 April 10>

Search Strategy:

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1 (e-vita or evita).tw. (334)

2 jotec.dm. (138)

3 evita.dv. (213)

4 e-vita.dv. (99)

5 or/1-4 (625)

6 stent/ or stent graft/ (83223)

7 blood vessel transplantation/ (3057)

8 exp endovascular surgery/ (29947)

9 (stent* or graft*).tw. (512438)

10 (thoracic* or TAA).tw. (190067)

11 "elephant trunk".tw. (887)

12 dissecting aneurysm/ (5430)

13 exp aortic aneurysm/ (10349)

14 ((aortic* or "acute type A" or "chronic type A" or degenerat*) adj4 (aneurysm* or dissect* or dissecan*)).tw. (52510)

15 (aortic* adj4 arch).tw. (19731)

16 (open adj4 surgical adj4 debranch).tw. (0)

17 ((ascending or descending) adj4 aorta).tw. (25807)

18 or/6-17 (765598)

19 5 and 18 (236)

20 nonhuman/ not human/ (4131881)

21 19 not 20 (232)

22 limit 21 to english language (226)

23 limit 22 to (conference abstract or conference paper or "conference review") (59)

24 22 not 23 (167)

25 limit 24 to dc=20130501-20180411 (100)

26 limit 23 to dc=20130501-20180411

Database: Cochrane

Strategy used:

Search Name: MTG16 - E-Vita_11th April 2018

Date Run: 11/04/18 13:46:23.799

Description:

ID	Search	Hits
#1	(e-vita or evita):ti,ab,kw (Word variations have been searched)	47
#2	MeSH descriptor: [Stents] this term only	3555
#3	MeSH descriptor: [Blood Vessel Prosthesis Implantation] this term only	621
#4	MeSH descriptor: [Endovascular Procedures] this term only	465
#5	((blood near/4 vessel* near/4 prosthe* near/4 implant*) or (vascular near/4 prosthe* near/4 implant*)):ti,ab,kw (Word variations have been searched)	637
#6	((endovascular or intravascular) near/4 (procedure* or technique*)):ti,ab,kw (Word variations have been searched)	749
#7	(stent* or graft*):ti,ab,kw (Word variations have been searched)	31502
#8	(thoracic* or TAA):ti,ab,kw (Word variations have been searched)	10085
#9	"elephant trunk":ti,ab,kw (Word variations have been searched)	6
#10	MeSH descriptor: [Aneurysm, Dissecting] this term only	98
#11	MeSH descriptor: [Aortic Aneurysm] explode all trees	954
#12	((aortic* or "acute type A" or "chronic type A" or degenerat*) near/4 (aneurysm* or dissect* or dissecan*)):ti,ab,kw (Word variations have been searched)	1699

#13 (aortic* near/4 arch):ti,ab,kw (Word variations have been searched) 242

#14 (open near/4 surgical near/4 debranch):ti,ab,kw (Word variations have been searched) 0

#15 ((ascending or descending) near/4 aorta):ti,ab,kw (Word variations have been searched) 421

#16 (Setacci, Galzerano, Donato, et al. -#15) 42901

#17 #1 and #16 Publication Year from 2013 to 2018 4

Database: PubMed

Strategy used:

History

Search	Add to builder	Query
#12	Add	Search **(#10 or #11)**
#11	Add	Search **(#9 AND "2018/04/08"[Entrez Date]: "3000"[Entrez Date])**
#10	Add	Search **(#9 AND publisher [sb])**
#9	Add	Search **(#1 and #8)**
#8	Add	Search **(#2 or #3 or #4 or #5 or #6 or #7)**
#7	Add	Search **((ascending[Title/Abstract] OR descending[Title/Abstract]**
#6	Add	Search **((aortic*[Title/Abstract] AND arch[Title/Abstract])) OR (ope [Title/Abstract] AND debranch[Title/Abstract])**
#5	Add	Search **((aortic*[Title/Abstract] OR "acute type A"[Title/Abstract] (OR degenerat*[Title/Abstract])) AND (aneurysm*[Title/Abstract] O dissecan*[Title/Abstract])**
#4	Add	Search **((stent*[Title/Abstract] OR graft*[Title/Abstract] OR thorac [Title/Abstract])) OR "elephant trunk"[Title/Abstract]**
#3	Add	Search **((endovascular[Title/Abstract] OR intravascular[Title/Abst [Title/Abstract] OR technique*[Title/Abstract])**
#2	Add	Search **((blood[Title/Abstract] AND vessel*[Title/Abstract] AND pr [Title/Abstract])) OR (vascular[Title/Abstract] AND prosthe*[Title/ [Title/Abstract])**
#1	Add	Search **(e-vita[Title/Abstract] OR evita[Title/Abstract])**

Database: Econlit

Strategy used:

Database: Econlit <1886 to April 05, 2018>

Search Strategy:

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1 (e-vita or evita).tw. (7)

2 [Stents/ or Blood Vessel Prosthesis Implantation/ or Endovascular Procedures/] (0)

3 ((blood adj4 vessel* adj4 prosthe* adj4 implant*) or (vascular adj4 prosthe* adj4 implant*)).tw. (0)

4 ((endovascular or intravascular) adj4 (procedure* or technique*)).tw. (0)

5 (stent* or graft*).tw. (210)

6 (thoracic* or TAA).tw. (35)

7 "elephant trunk".tw. (0)

8 [Aneurysm, Dissecting/] (0)

9 [exp Aortic Aneurysm/] (0)

10 ((aortic* or "acute type A" or "chronic type A" or degenerat*) adj4 (aneurysm* or dissect* or dissecan*)).tw. (11)

11 (aortic* adj4 arch).tw. (0)

12 (open adj4 surgical adj4 debranch).tw. (0)

13 ((ascending or descending) adj4 aorta).tw. (0)

14 or/2-13 (254)

15 1 and 14 (1)

16 [animals/ not humans/] (0)

17 15 not 16 (1)

Clinical Evidence

- Ovid MEDLINE(R) Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present
- Embase 1974 to 2018 Week 26
- Search date: 26th June 2018
- Changes to the original search: The search terms were restructured so that terms for E-Vita are searched without combination with the other elements. A number of redundant terms were removed (for example "**hybrid stent graft$.mp**" which would be found by "**(hybrid adj3 stent adj3 graft$).mp**"). Some wildcard terms have been added or amended to increase the sensitivity of the search. Although the original search was carried out in 2013 this search is limited to 2013-present; any duplicates from the original have been manually removed.

1	exp Aortic Aneurysm/ or exp Aorta, Thoracic/ or exp Aortic Aneurysm, Thoracic/ or degenerative aneurysm.mp. or exp Aneurysm, Dissecting/	81296
2	chronic type A dissection.mp.	37
3	acute type A dissection.mp.	417
4	or/1-3	81366
5	(hybrid adj3 stent adj3 graft$).mp.	68
6	(elephant adj3 trunk).mp.	791
7	(aortic adj3 arch adj3 replac*).mp.	1017
8	(aortic adj3 arch adj3 repair*).mp.	1021
9	hybrid stent*.mp.	97
10	(thoracic adj3 stent adj3 graft$).mp.	623
11	thoracic stent*.mp.	390
12	(open adj3 stent adj3 graft$).mp.	188
13	(open adj3 surgical adj3 debranch$).mp.	5
14	branched graft$.mp.	135
15	(endovascular adj3 stent adj3 graft$).mp.	1900
16	endovascular stent*.mp.	3269
17	or/5-16	6630
18	mortality.mp. or exp Hospital Mortality/ or exp Mortality/	1106603

19	exp Stroke/ or stroke.mp.	270533
20	exp Paraplegia/ or paraplegia.mp.	19368
21	Renal Failure$.mp. or exp Renal Insufficiency/	193015
22	endoleak*.mp. or exp Endoleak/	4372
23	exp Long-Term Care/ or long term.mp.	709963
24	exp Survival Analysis/ or exp Survival/ or exp Survival Rate/ or survival.mp.	1116343
25	or/18-24	2750882
26	4 and 17 and 25	2157
27	(E-vita or evita).mp.	226
28	26 or 27	2357
29	limit 28 to yr="2013-Current"	663
	Re-run in EMBASE	764

- Cochrane (CDSR, CENTRAL, DARE, HTA, NHSEED)
- Search date: 26th June 2018
- Changes to original search: The original search was altered to reflect the search strategy used in Medline, with terms translated for the Cochrane platform using the Polyglot Search Syntax Translator (http://crebp-sra.com/#/polyglot). All of the databases searchable via Cochrane were included in the new search, not just the CDSR.

ID	Search	Hits
#1	[mh "Aortic Aneurysm"] or [mh "Aorta, Thoracic"] or [mh "Aortic Aneurysm, Thoracic"] or "degenerative aneurysm" or [mh "Aneurysm, Dissecting"]	1229
#2	(chronic type A dissection)	320
#3	(acute type A dissection)	423
#4	(Montelione, Pecoraro, Puippe, et al. -#3)	1691
#5	hybrid near/3 stent near/3 graft*	1
#6	elephant near/3 trunk	9
#7	aortic near/3 arch near/3 replac*	19
#8	aortic near/3 arch near/3 repair*	26
#9	(hybrid stent*)	100
#10	thoracic near/3 stent near/3 graft*	19
#11	(thoracic stent*)	326
#12	open near/3 stent near/3 graft*	14

#13	open near/3 surgical near/3 debranch*	0
#14	(branched graft*)	47
#15	endovascular near/3 stent near/3 graft*	69
#16	(endovascular stent*)	1017
#17	(Moz, Misfeld, Leontyev, et al. -#16)	1351
#18	mortality or [mh "Hospital Mortality"] or [mh Mortality]	80684
#19	[mh Stroke] or stroke	55766
#20	[mh Paraplegia] or paraplegia	590
#21	Renal Failure* or [mh "Renal Insufficiency"]	12466
#22	endoleak* or [mh Endoleak]	205
#23	[mh "Long-Term Care"] or "long term"	82868
#24	[mh "Survival Analysis"] or [mh Survival] or [mh "Survival Rate"] or survival	84334
#25	{or #18-#24}	245690
#26	#4 and #17 and #25	180
#27	(E-vita or evita)	81
#28	#26 or #27 Publication Year from 2013	133

- PubMed
- Search date: 27th June 2018
- PubMed was not used in the original search.

Search	Query	Items found
#38	Search (#35 or #36) Filters: Publication date from 2013/01/01 Sort by: [pubsolr12]	555
#37	Search (#35 or #36)	1896
#36	Search ((E-vita or evita))	228
#35	Search (#13 and #26 and #34)	1694
#34	Search (#27 OR #28 OR #29 OR #30 OR #31 OR #32 OR #33)	2469614
#33	Search (Survival Analysis[mh] or Survival[mh] or Survival Rate[mh] or survival[tiab])	965055
#32	Search (Long-Term Care[mh] or long term[tiab])	706089
#31	Search (endoleak*[tiab] or endoleak[mh])	4357
#30	Search (Renal Failure*[tiab] or Renal Insufficiency[mh])	193033
#29	Search (Paraplegia[mh] or paraplegia[tiab])	19113
#28	Search (Stroke[mh] or stroke[tiab])	240738
#27	Search (mortality[tiab] or Hospital Mortality[mh] or Mortality[mh])	870155
#26	Search (#14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24 OR #25)	5378
#25	Search endovascular stent*[tiab]	3233
#24	Search endovascular stent graft*[tiab]	1587
#23	Search branched graft*[tiab]	131

#22	Search thoracic surgical debranch*[tiab]	17
#21	Search open stent graft*[tiab]	79
#20	Search thoracic stent*[tiab]	387
#19	Search thoracic stent graft*[tiab]	372
#18	Search hybrid stent*[tiab]	93
#17	Search aortic arch repair*[tiab]	433
#16	Search aortic arch replac*[tiab]	662
#15	Search elephant trunk*[tiab]	780
#14	Search hybrid stent graft*[tiab]	35
#13	Search (#10 OR #11 OR #12)	81467
#12	Search acute type A dissection[tiab]	416
#11	Search chronic type A dissection[tiab]	171
#10	Search (Aortic Aneurysm[mh] or Aorta, Thoracic[mh] or Aortic Aneurysm, Thoracic[mh] or Aneurysm, Dissecting[mh] or degenerative aneurysm[tiab])	81386

- Web of Science
- Search date: 27th June 2018
- Web of Science was not used in the original search.

#1	TS=(evita OR e-vita) Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI Timespan=2013-2018	113

Economic evidence

- Ovid MEDLINE(R) Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present
- Embase 1974 to 2018 Week 26
- Search date: 26th June 2018

Evidence selection

Total Abstracts: 107
Abstracts Reviewed: 107
Full papers reviewed: 0

1	exp Aortic Aneurysm/ or exp Aorta, Thoracic/ or exp Aortic Aneurysm, Thoracic/ or degenerative aneurysm.mp. or exp Aneurysm, Dissecting/	81296
2	chronic type A dissection.mp.	37
3	acute type A dissection.mp.	417
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5	(hybrid adj3 stent adj3 graft$).mp.	68

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17	or/5-16	6630
18	mortality.mp. or exp Hospital Mortality/ or exp Mortality/	1106603
19	exp Stroke/ or stroke.mp.	270533
20	exp Paraplegia/ or paraplegia.mp.	19368
21	Renal Failure$.mp. or exp Renal Insufficiency/	193015
22	endoleak*.mp. or exp Endoleak/	4372
23	exp Long-Term Care/ or long term.mp.	709963
24	exp Survival Analysis/ or exp Survival/ or exp Survival Rate/ or survival.mp.	1116343
25	or/18-24	2750882
26	4 and 17 and 25	2157
27	(E-vita or evita).mp.	226
28	26 or 27	2357
29	limit 28 to yr="2013-Current"	663

30	quality-adjusted life years/ or exp economics/ or exp economic aspect/ or (cost* or econ* or reimburs* or payment* or copayment* or icer or icers or qaly* or quality adjusted life year* or payer* or fee or fees or price or prices or pricing or technology assessment* or hcfa or health care finance administration*).mp.	1226237
31	29 and 30	20
	Re-run in EMBASE	27

- Cochrane (CDSR, CENTRAL, DARE, HTA, NHSEED)
- Search date: 26th June 2018

ID	Search	Hits
#1	[mh "Aortic Aneurysm"] or [mh "Aorta, Thoracic"] or [mh "Aortic Aneurysm, Thoracic"] or "degenerative aneurysm" or [mh "Aneurysm, Dissecting"]	1229
#2	(chronic type A dissection)	320
#3	(acute type A dissection)	423
#4	(Montelione, Pecoraro, Puippe, Chaykovska, Rancic, Pfammatter, Mayer, Amann-Vesti, Husmann, Veith, Mangialardi and Lachat -#3)	1691
#5	hybrid near/3 stent near/3 graft*	1
#6	elephant near/3 trunk	9
#7	aortic near/3 arch near/3 replac*	19
#8	aortic near/3 arch near/3 repair*	26
#9	(hybrid stent*)	100
#10	thoracic near/3 stent near/3 graft*	19
#11	(thoracic stent*)	326
#12	open near/3 stent near/3 graft*	14
#13	open near/3 surgical near/3 debranch*	0
#14	(branched graft*)	47
#15	endovascular near/3 stent near/3 graft*	69
#16	(endovascular stent*)	1017
#17	(Moz, Misfeld, Leontyev, Borger, Davierwala and Mohr -#16)	1351
#18	mortality or [mh "Hospital Mortality"] or [mh Mortality]	80684
#19	[mh Stroke] or stroke	55766
#20	[mh Paraplegia] or paraplegia	590
#21	Renal Failure* or [mh "Renal Insufficiency"]	12466
#22	endoleak* or [mh Endoleak]	205
#23	[mh "Long-Term Care"] or "long term"	82868
#24	[mh "Survival Analysis"] or [mh Survival] or [mh "Survival Rate"] or survival	84334
#25	{or #18-#24}	245690
#26	#4 and #17 and #25	180
#27	(E-vita or evita)	81

#28	#26 or #27 Publication Year from 2013	133
#29	(cost* or econ* or reimburs* or payment* or copayment* or icer or icers or qaly* or quality adjusted life year* or payer* or fee or fees or price or prices or pricing or technology assessment* or hcfa or health care finance administration*)	120149
#30	#28 and #29	61

- EconLit (via Proquest)
- Search date: 27th June 2018
- The original search was adapted for the Proquest platform. The filter (cost$ OR economic$) was removed from every line and the free text terms "Evita" and "E-vita" were included as extra lines.

Set#	Searched for	Databases	Results
S2	(E-vita N/3 open) AND ("aortic aneurysm" OR "type a aortic dissection")	EconLit	0
S3	(elephant N/3 trunk) AND (aortic aneurysm OR type a aortic dissection)	EconLit	0
S4	((branched graft*) OR (open surgi cal debranch*)) AND (aortic aneurysm OR type a aortic dissection)	EconLit	0
S5	((endovascular stent graft*) or (endovascular stent)) AND (aortic aneurysm OR type a aortic dissection)	EconLit	0
S6	evita	EconLit	12
S7	e-vita	EconLit	5

- PubMed
- Search date: 27th June 2018

Search	Query	Items found
#44	Search (#38 and #43) Filters: Publication date from 2013/01/01	6
#43	Search ((quality-adjusted life years[mh] or economics[mh])) OR ((cost*[Title/Abstract] OR econ*[Title/Abstract] OR reimburs*[Title/Abstract] OR payment*[Title/Abstract] OR copayment*[Title/Abstract] OR icer[Title/Abstract] OR icers[Title/Abstract] OR qaly*[Title/Abstract] OR quality adjusted life year*[Title/Abstract] OR payer*[Title/Abstract] OR fee[Title/Abstract] OR fees[Title/Abstract] OR price[Title/Abstract] OR prices[Title/Abstract] OR	89598

	pricing[Title/Abstract] OR technology assessment*[Title/Abstract] OR hcfa[Title/Abstract] OR health care finance administration*)[Title/Abstract]) Filters: Publication date from 2013/01/01	
#38	Search (#35 or #36) Filters: Publication date from 2013/01/01 Sort by: [pubsolr12]	555
#37	Search (#35 or #36)	1896
#36	Search ((E-vita or evita))	228
#35	Search (#13 and #26 and #34)	1694
#34	Search (#27 OR #28 OR #29 OR #30 OR #31 OR #32 OR #33)	2469614
#33	Search (Survival Analysis[mh] or Survival[mh] or Survival Rate[mh] or survival[tiab])	965055
#32	Search (Long-Term Care[mh] or long term[tiab])	706089
#31	Search (endoleak*[tiab] or endoleak[mh])	4357
#30	Search (Renal Failure*[tiab] or Renal Insufficiency[mh])	193033
#29	Search (Paraplegia[mh] or paraplegia[tiab])	19113
#28	Search (Stroke[mh] or stroke[tiab])	240738
#27	Search (mortality[tiab] or Hospital Mortality[mh] or Mortality[mh])	870155
#26	Search (#14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24 OR #25)	5378
#25	Search endovascular stent*[tiab]	3233
#24	Search endovascular stent graft*[tiab]	1587
#23	Search branched graft*[tiab]	131
#22	Search thoracic surgical debranch*[tiab]	17
#21	Search open stent graft*[tiab]	79
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#19	Search thoracic stent graft*[tiab]	372
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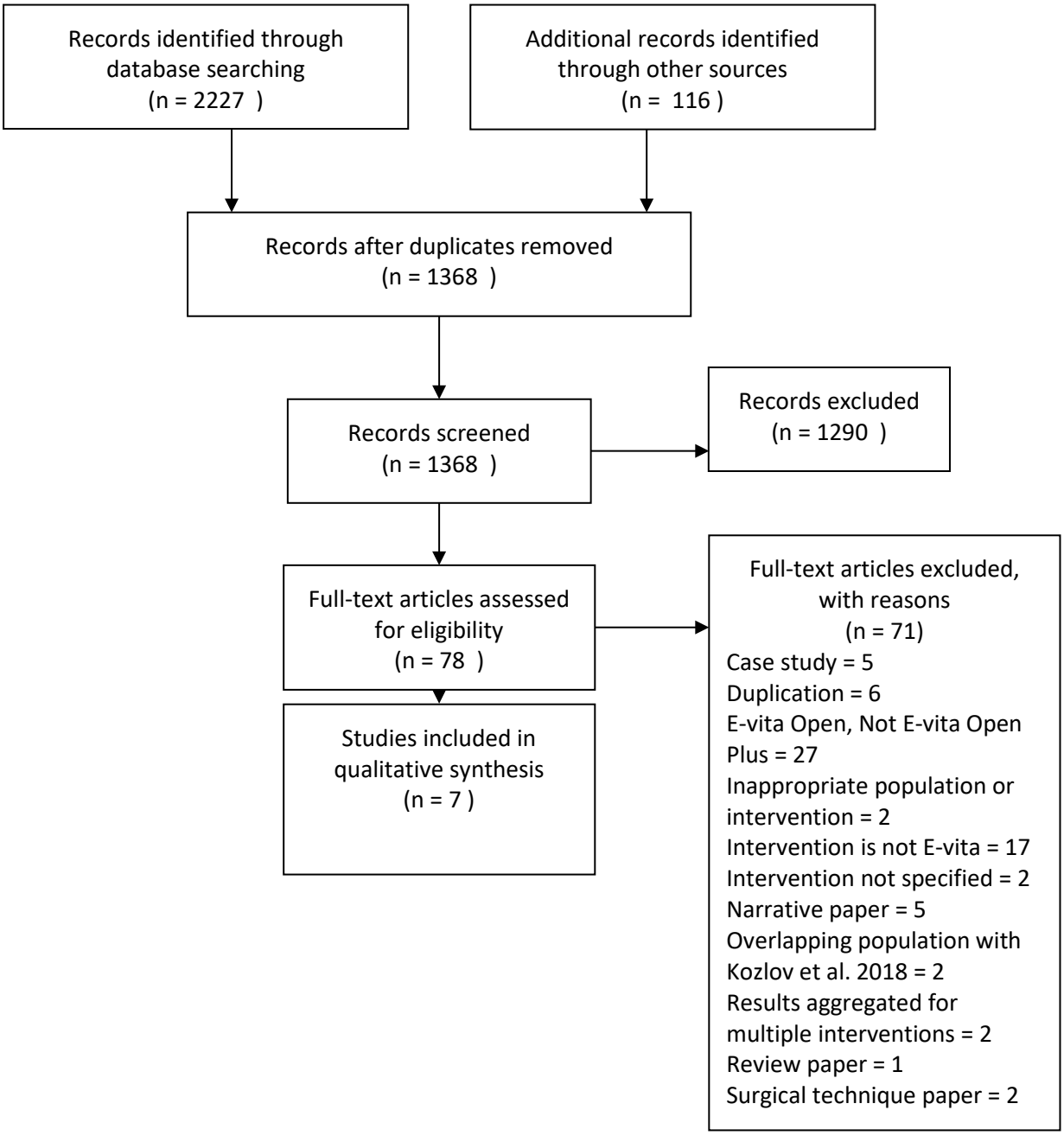
#11	Search chronic type A dissection[tiab]	171
#10	Search (Aortic Aneurysm[mh] or Aorta, Thoracic[mh] or Aortic Aneurysm, Thoracic[mh] or Aneurysm, Dissecting[mh] or degenerative aneurysm[tiab])	81386

- Web of Science
- Search date: 27th June 2018

#3	#2 AND #1 Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI Timespan=2013-2018	10

#2	TS=(cost* or econ* or reimburs* or payment* or copayment* or icer or icers or qaly* or quality adjusted life year* or payer* or fee or fees or price or prices or pricing or technology assessment* or hcfa or health care finance administration*) Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI Timespan=2013-2018	1,037,050
#1	TS=(evita OR e-vita) Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI Timespan=2013-2018	113

EAC PRISMA 2009 Flow Diagram (Clinical evidence)



Ongoing studies

Total records found: 52
Total following de-duplication: 40

- ClinicalTrials.gov
- Search date: 28th June 2018

(e-vita OR evita) – 31 results

- WHO ICTRP
- Search date: 28th June 2018

e-vita OR evita – 21 results

Appendix D – References

K. Erkanli, E. Kadirogullari, U. Aydin, et al. (2017) "Elephant trunk technique: A less-invasive, single-staged approach to complex thoracic aorta diseases." Innovations: Technology and Techniques in Cardiothoracic and Vascular Surgery 12 (Supplement 1)(S3

Hoffman, A. L. Damberg, G. Schalte, et al. (2013) "Thoracic stent graft sizing for frozen elephant trunk repair in acute type A dissection." Journal of Thoracic & Cardiovascular Surgery 145(4): 964-9

M. Iafrancesco, N. Goebel, J. Mascaro, et al. (2017) "Aortic diameter remodelling after the frozen elephant trunk technique in aortic dissection: results from an international multicentre registry." European Journal of Cardio-Thoracic Surgery 52(2): 310-318

H. Jakob, D. Dohle, J. Benedik, et al. (2017) "Long-term experience with the E-vita Open hybrid graft in complex thoracic aortic disease." European Journal of Cardio-thoracic Surgery 51(2): 329-338

B. N. Kozlov, D. S. Panfilov, I. V. Ponomarenko, et al. (2018) "The risk of spinal cord injury during the frozen elephant trunk procedure in acute aortic dissection." Interactive Cardiovascular and Thoracic Surgery 26(6): 972-976

J.-P. Verhoye, A. Anselmi, A. Kaladji, et al. (2014) "Mid-term results of elective repair of extensive thoracic aortic pathology by the Evita Open Plus hybrid endoprosthesis only." European journal of cardio-thoracic surgery : official journal of the European Association for Cardio-thoracic Surgery 45(5): 812-7

J. P. Verhoye, R. B. Soulami, O. Fouquet, et al. (2017) "Elective frozen elephant trunk procedure using the E-Vita Open Plus prosthesis in 94 patients: A multicentre French registry." European Journal of Cardio-thoracic Surgery 52(4): 733-739

Appendix E – E-vita Open Plus Cost Model Update

1. Background

The E-vita open plus (JOTEC GmbH) is an endoluminal stent graft system designed for treating aneurysms and dissections of the thoracic aorta. The technology was evaluated by NICE, with assessments completed by one of the external assessment centre (EAC), KITEC in 2013. The assessment result is published as a NICE medical technology guidance (MTG16). An update of this assessment is planned and as part of the assessment review process NICE has requested an update to the cost analysis for the base-case scenario.

The management of thoracic aortic aneurysms and dissections is determined by the location, severity and rate of change of the disease, as well as the clinical circumstances. Thoracic aortic aneurysms result from a weakening of the aortic wall, leading to localised dilation. People with thoracic aneurysms are often observed with clinical and imaging surveillance. Invasive treatment may be offered depending upon the size and rate of enlargement of the aneurysm. Aortic dissections result from a tear in the inner layer of the aorta. Blood flows through the tear, separating the layers of the wall. Acute aortic dissections are less than 2 weeks old, and chronic dissections have been present for longer than 2 weeks. Management of aortic dissections depends primarily on their location. Emergency surgery is usually offered for a Stanford type A aortic dissection, which affects the ascending thoracic aorta and often also the arch and descending aorta. Stanford type B dissections, typically involving the descending thoracic aorta, are often managed with conservative medical treatment. Elective surgical repair is sometimes undertaken, but endovascular repair with stent grafts is more commonly used. There are 3 main current methods of surgically treating complex aneurysms and dissections of the thoracic aorta, 2 of which involve a two-stage 'elephant trunk' procedure. Both approaches are similar in their first stage but use alternative repair techniques to complete the second stage. During the first stage, the ascending aorta and arch are repaired with a vascular graft through a median sternotomy. During this procedure a free-floating extension of the arch graft prosthesis (the 'elephant trunk') is left unattached in the descending aorta. Attaching it (and extending it as necessary) may be done by an endovascular procedure during which a stent graft is inserted into the descending aorta with access via the femoral artery (thoracic endovascular aortic repair – TEVAR). Alternatively the descending aorta may be repaired in a second surgical procedure some weeks or months later, by extending the 'elephant trunk' as necessary, through a lateral thoracotomy approach. The

third method involves 'debranching' of the head and neck vessels from the aortic arch by creating a surgical anastomosis between the ascending aorta and the head and neck vessels using a vascular graft. This then allows an endoluminal stent graft to be inserted into the aortic arch and descending aorta either as a hybrid procedure (during the same operation) or at a second-stage operation.
The E-vita open plus is used in a single-stage procedure known as a 'frozen elephant trunk'. The thoracic aorta is surgically opened with access through a median sternotomy approach. The distal stent graft portion of the device is self-expanding, containing nitinol springs, and is used to treat the upper part of the descending aorta. The vascular graft part of the device (for repair of the arch and ascending aorta) is invaginated in the distal stent graft portion. The stent graft, in its delivery system, is inserted into the descending aorta and deployed by retracting a retaining sheath. Once the stent graft is in place, the delivery system is removed and the proximal vascular graft component is drawn out a short distance (5–10 mm). The stent graft is then surgically anastomosed to the distal aorta. The vascular graft portion of the device is then drawn out fully and used to repair the ascending aorta and arch in a standard surgical fashion. The aortic branch vessels are attached to the vascular graft using a patch and the graft is anastomosed to the ascending aorta. Comparing to the conventional two-stage treatments as described above, the use of E-vita open plus (single-stage procedure) may reduce need for procedures, reduce the probability of developing surgery-related adverse events, and thus lead to resource savings to the NHS.

A de novo cost model was submitted by the sponsor as a part of the assessment. This model compared the per-patient costs for the E-vita open plus and the 3 comparators: vascular graft, endovascular stent graft, and open debranching with endoluminal stent graft. The population was a cohort of 3500 people with aneurysms, dissections and other specified lesions of the thoracic aorta. The time horizon of the economic model was one year. The EAC considered that the sponsor's de novo cost model was flawed because firstly, the cost model did not include the short-term or long-term costs of adverse events of E-vita open plus and its comparators; secondly, some of the costs and clinical parameters were inaccurate or inappropriate. To address these issues, the EAC carried out additional modelling work to estimate the short- term (1-year) and long-term (20-year) cost of E-vita open plus and its comparators. The costs of four adverse events were considered: bleeding, stroke, paraplegia and renal failure. The short-term analysis showed that E-vita open plus was £4760 more expensive than the two-stage repair with endovascular stent graft, £7663 more expensive than the open

debranching with endoluminal stent graft, and £280 cheaper than the two-stage repair with vascular graft. The long-term analysis showed that E-vita open generate significant cost savings when compared with all three comparators: the estimated saving per patient 20 years after the procedure was £41,213 when compared against two-stage repair with vascular graft, £39,392 when compared against two-stage repair with endovascular stent graft and £51,778 when compared against open debranching with endoluminal stent graft. The results of the cost model informed recommendation development by NICE.

2. Analysis

KiTEC reviewed the cost model and updated all cost parameters. The original unit costs were taken from the 2012 NHS reference costs and the unit Costs published by the Personal Social Services Research Unit (PSSRU) 2012; while the updated costs were taken from the 2016-17 NHS reference costs, and the unit Costs published by PSSRU 2017. Where updated unit costs were not readily available, the original cost was inflated to 2017 prices using the Hospital and community health service (HCHS) Index. The major changes in the update relate to cost of adverse events and cost of staff cost. In the original model, the cost of managing any adverse events was calculated as the difference between the HRG code QZ01A (Aortic or Abdominal Surgery, with CC) (£8292) and the HRG code QZ01B (Aortic or Abdominal Surgery, without CC) (£6137), as reported in the 2012 NHS reference costs. This means for all patients who experienced serious adverse events of surgery, a uniform treatment cost of £2,155 was applied, regardless of which adverse event the patient has experienced. In the updated model, the cost of each individual adverse event was identified, including bleeding, stroke, paraplegia, renal failure and in-hospital death. Another major change was related to staff cost. When counting staff cost, both PSSRU 2012 and PSSRU 2017 have included staff salary, salary oncosts, overheads, capital overheads etc. However the staff salaries used in PSSRU 2017 are much lower than the staff salaries used in PSSRU 2012. For example, the salary of a surgical consultant is £128,800 per year as reported by PSSRU 2012, but is only £89,708 as reported by PSSRU 2017. As a result, the staff cost used in the updated model is lower than the cost used in the original model. The PSSRU 2017 didn't report the reason why the staff salary cost they used are much lower than the previous PSSRU.

The updated unit costs and source of the costs are presented in Table 1.

Table 1. Updated unit costs

Cost Parameter	Cost parameters		Source for updated cost parameters
	Value used in the original model	Updated value	
Intervention cost			
Cost of E-vita open plus	£10,500	£11,235	The manufacturer reported that the cost of E-vita open plus has not changed significantly since the original report published in 2013. Therefore the cost of E-vita open plus was uplifted from the original report
Cost of woven graft	£200	£214	Uplifted from the original report
Cost of branched graft	£1,000	£1,070	Uplifted from the original report
Cost of endovascular stent graft	£5,000	£5,350	Uplifted from the original report
Other consumables	£130	£139	Uplifted from the original report
Staff cost (per hour)			
Consultant surgeon	£172	£107	PSSRU 2017 Hospital based doctors: Consultant (surgical)
Consultant anaesthetist	£172	£107	PSSRU 2017 Hospital based doctors: Consultant (surgical)
Associate specialist	£131	£101	PSSRU 2017 Hospital based doctors: Associate specialist
Perfusionist at registrar's rate	£86	£43	PSSRU 2017 Hospital based doctors: Registrar
Specialist nurse	£100	£62	PSSRU 2017 Hospital-based nurse, band 8a (nurse consultant)
Consultant radiologist (medical)	£157	£106	PSSRU 2017 Hospital based doctors: Consultant (medical)
Cost of ward (per day)			
Cost of ICU	1,410	£1,594	NHS Reference Cost 2016-17

			HRG Code XC04Z (Adult Critical Care, 3 Organs Supported). A range of £948 (HRG code XC06Z, Adult Critical Care, 1 Organ Supported) to £2,153 (HRG code XC01Z, Adult Critical Care, 6 or more Organs Supported) was tested in sensitivity analysis.
Cost of surgical ward	£383	£285	NHS Reference Cost 2016-17 The cost of surgical ward was calculated based on the weighted cost* of elective inpatient excess bed day for: • HRG Data for HRG code YQ01A (Multiple or Revisional, Open Repair of, Abdominal or Thoracoabdominal Aortic Aneurysm, with CC Score 6+') (£243) • HRG code YQ01B (Multiple or Revisional, Open Repair of, Abdominal or Thoracoabdominal Aortic Aneurysm, with CC Score 0-5) (£534) A range of £243 (HRG code YQ01A) to £534 (HRG code YQ01B) was tested in sensitivity analysis.
Acute treatment cost of adverse events			
Bleeding	£2,155	£498	NHS Reference Cost 2016-17 HRG code SA44A (Single Plasma Exchange or Other Intravenous Blood Transfusion, 19 years and over)
Stroke	£2,155	10,957	Uplifted from NICE Clinical Guidance on Atrial fibrillation, 2014 The reported cost for stroke patients over acute period with

			unknown stroke type (£4,426) and ischaemic stroke (£11,410) was tested in sensitivity analysis.
Paraplegia	£2,155	£11,663	NHS Reference Cost 2016-17 The acute treatment cost of treating paraplegia was calculated based on the weighted cost* of: • HRG code HC21E (Spinal Cord Injury with CC Score 0-1) (£3,974) • HRG code HC21D (Spinal Cord Injury with CC Score 2+) (£13,969) A range of £3,974 (HRG code HC21E) to £13,969 (HRG code HC21D) was tested in sensitivity analysis.
Renal failure	£2,155	£4,711	NHS Reference Cost 2016-17 The acute treatment cost of treating renal failure was calculated based on the weighted cost* of: • HRG code LA07K (Acute Kidney Injury with Interventions, with CC Score 0-5) (£3,698) • HRG code LA07J (Acute Kidney Injury with Interventions, with CC Score 6-10) (£4,781) • HRG code LA07H (Acute Kidney Injury with Interventions, with CC Score 11+) (£7,044) A range of £3,698 (HRG code LA07K) to £7,044 (HRG code LA07H) was tested in sensitivity analysis.
End of life care for patients died in hospital	£2,155	£3,377	Uplifted from National End of Life Care Programme, 2012 The reported minimum cost (£2,709) and maximum cost

			(£4,044) was tested in sensitivity analysis.
Long-term cost of adverse events			
Annual cost of stroke care	£9,597	£8,085	Uplifted from NICE Clinical Guidance on Atrial fibrillation, 2014 The reported cost for stroke patients with no disability (£1,393) and severe disability (£25,626) was tested in sensitivity analysis.
Annual cost of paraplegia	£14,580	£15,341	Converted and uplifted from French et al 2007 The reported minimum cost (£11,911) and maximum cost (£20,261) was tested in sensitivity analysis.
Annual cost of renal failure care	£32,961	£34,682	Uplifted from NICE guideline of Peritoneal Dialysis 2011 The reported minimum cost (£26,015) and maximum cost (£43,362) was tested in sensitivity analysis.

Note:
*: Cost was weight by number of activities as reported by NHS Reference Cost 2016-17

The results of the updated base case scenario are reported in Table 2. In the short-term (1-year) analysis, E-vita open plus was the most expensive intervention, and incurred £7,761 additional cost comparing to the least expensive strategy (open debranching with endoluminal stent graft). The short-term cost difference was mainly driven by the high technology costs and longer length of stay for patients received E-vita open plus. However, at year 5, E-vita open plus already became the least expensive intervention. As time horizon for model increases, the cost savings of E-vita open plus become more significant. In the long-term (20-year) analysis, the saving of E-vita open plus was £42,057 when compared to two-stage with vascular graft, £40,993 when compared to two-stage with endovascular stent graft and £53,587 when compared to open debranching with endoluminal stent graft. This is because E-vita is a single-stage procedure, and is therefore less likely to cause surgery-related adverse events (i.e. bleeding, stroke, paraplegia and renal failure), when compared to the other two-stage procedures.

Table 2. Base case result per patient

Expected cost per patient	E-vita open plus	Two stage with vascular graft	Two stage with endovascular stent graft	Open debranching with endoluminal stent graft
1-year	£32,666	£31,799	£27,634	£24,905
5-year	£45,721	£59,055	£55,946	£58,257
10-year	£56,445	£81,446	£79,149	£85,655
20-year	£72,125	£114,182	£113,118	£125,712

In the deterministic sensitivity analysis, a number of variables with uncertainty were varied. The variables included in the sensitivity analysis included In-hospital mortality and paraplegia probability of E-vita open plus, proportion of ICU stay, cost of ICU, cost of surgical ward, cost of acute and long-term care of adverse events (stroke, paraplegia and renal failure), and cost of end of life care. The conclusions of the base-case analysis were robust to all variables tested: in the short-term, open debranching with endoluminal stent graft has always been the least expensive intervention, while in the long-term, E-vita open plus has always been the least expensive intervention. The detailed results of sensitivity analysis for short-term and long-term analyses are presented in Table 3 and 4, respectively.

Table 3. Short-term (1-year) results of sensitivity analysis

Analysis	Value	E-vita open plus	Two stage with vascular graft	Two stage with endovascular stent graft	Open debranching with endoluminal stent graft	Optimal intervention (least expensive)
Baseline result	N/A	£32,666	£31,799	£27,634	£24,905	Open debranching with endoluminal stent graft
Probability of In-hospital mortality of E-vita open plus	10%	£32,498	£31,799	£27,634	£24,905	Open debranching with endoluminal stent graft
	20%	£32,835	£31,799	£27,634	£24,905	Open debranching with endoluminal stent graft
Probability of paraplegia of E-vita open plus	3%	£32,083	£31,799	£27,634	£24,905	Open debranching with endoluminal stent graft
	10%	£32,900	£31,799	£27,634	£24,905	Open debranching with endoluminal stent graft
Proportion of ICU stay	20%	£27,692	£24,254	£22,393	£20,334	Open debranching with endoluminal stent graft
	60%	£37,641	£39,344	£32,876	£29,477	Open debranching with endoluminal stent graft
Cost of ICU	£948	£27,757	£24,352	£22,461	£20,393	Open debranching with endoluminal stent graft
	£2,153	£36,915	£38,243	£32,111	£28,810	Open debranching with endoluminal stent graft
Cost of surgical ward	£243	£32,188	£31,073	£27,130	£24,465	Open debranching with endoluminal stent graft
	£534	£35,505	£36,104	£30,625	£27,514	Open debranching with endoluminal stent graft
Acute treatment cost of stroke	£4,426	£32,288	£31,385	£27,151	£24,237	Open debranching with endoluminal stent graft

	£11,410	£32,693	£31,828	£27,668	£24,952	Open debranching with endoluminal stent graft
Acute treatment cost of paraplegia	£3,974	£32,051	£31,238	£26,910	£24,713	Open debranching with endoluminal stent graft
	£13,969	£32,851	£31,967	£27,852	£24,963	Open debranching with endoluminal stent graft
Acute treatment cost of renal failure	£3,698	£32,630	£31,667	£27,508	£24,721	Open debranching with endoluminal stent graft
	£7,044	£32,750	£32,103	£27,926	£25,330	Open debranching with endoluminal stent graft
End of life care for patients died in hospital	£2,709	£32,566	£31,702	£27,532	£24,801	Open debranching with endoluminal stent graft
	£4,044	£32,766	£31,896	£27,737	£25,010	Open debranching with endoluminal stent graft

Table 4. Long-term (20-year) results of sensitivity analysis

Analysis	Value	E-vita open plus	Two stage with vascular graft	Two stage with endovascular stent graft	Open debranching with endoluminal stent graft	Optimal intervention (least expensive)
Baseline result	N/A	£72,125	£114,182	£113,118	£125,712	E-vita open plus
Probability of In-hospital mortality of E-vita open plus	10%	£71,956	£114,182	£113,118	£125,712	E-vita open plus
	20%	£72,294	£114,182	£113,118	£125,712	E-vita open plus
Probability of paraplegia of E-vita open plus	3%	£61,264	£114,182	£113,118	£125,712	E-vita open plus
	10%	£76,470	£114,182	£113,118	£125,712	E-vita open plus
Proportion of ICU stay	20%	£67,151	£106,638	£107,877	£121,141	E-vita open plus
	60%	£77,099	£121,727	£118,359	£130,284	E-vita open plus
Cost of ICU	£948	£67,215	£106,736	£107,945	£121,200	E-vita open plus
	£2,153	£76,373	£120,626	£117,594	£129,617	E-vita open plus
Cost of surgical ward	£243	£71,646	£113,456	£112,614	£125,272	E-vita open plus
	£534	£74,964	£118,488	£116,109	£128,321	E-vita open plus
Acute treatment cost of stroke	£4,426	£71,746	£113,768	£112,635	£125,044	E-vita open plus

	£11,410	£72,151	£114,211	£113,152	£125,759	E-vita open plus
Acute treatment cost of paraplegia	£3,974	£71,510	£113,622	£112,393	£125,520	E-vita open plus
	£13,969	£72,309	£114,350	£113,335	£125,770	E-vita open plus
Acute treatment cost of renal failure	£3,698	£72,089	£114,050	£112,991	£125,528	E-vita open plus
	£7,044	£72,209	£114,486	£113,410	£126,137	E-vita open plus
End of life care for patients died in hospital	£2,709	£72,025	£114,085	£113,016	£125,608	E-vita open plus
	£4,044	£72,225	£114,279	£113,220	£125,817	E-vita open plus
Long-term annual cost of stroke	£1,393	£66,924	£108,497	£106,482	£116,535	E-vita open plus
	£25,626	£85,757	£129,085	£130,511	£149,769	E-vita open plus
Long-term annual cost of paraplegia	£11,911	£68,448	£110,831	£108,786	£124,563	E-vita open plus
	£20,261	£77,399	£118,989	£119,332	£127,360	E-vita open plus
Long-term annual cost of renal failure	£26,015	£67,944	£99,057	£98,601	£104,576	E-vita open plus
	£43,362	£76,312	£129,330	£127,657	£146,880	E-vita open plus

3. Conclusions

The new base-case analysis with updated unit costs shows that E-vita open plus incurs additional cost in the short-term (1-year), but is cost-saving in the long-term (20 years). This conclusion is robust to all scenarios tested. The results of the updated model are consistent with the findings of the original model.