



# eunetha

EUROPEAN NETWORK FOR HEALTH TECHNOLOGY ASSESSMENT

EUnetHTA Joint Action 3 WP4

**Rapid assessment of other technologies using the HTA Core Model®  
for Rapid Relative Effectiveness Assessment**

**PROPHYLACTIC OR THERAPEUTIC USE OF ENDOANCHORING SYSTEMS  
IN ENDOVASCULAR AORTIC ANEURYSM REPAIR (EVAR/TEVAR)**

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### Assessment team

Author(s)	Agencia de Evaluación de Tecnologías Sanitarias-Instituto de Salud Carlos III (AETS-ISCIII), Spain Juan Pablo Chalco, María del Carmen Sánchez, Esther García-Carpintero, Jesús González and Iñaki Imaz
Co-Author(s)	Republika Slovenija Ministrstvo za Zdravje (MoH Slovenia), Slovenia Doroteja Novak-Gosarič and Natalija Tripković
Dedicated Reviewer(s)	Università Cattolica del Sacro Cuore (UCSC Gemelli), Italy Rossella Di Bidino and Carmen Furno Swiss Network for Health Technology Assessment (SNHTA), Switzerland Heike Raatz

### Consultation of the draft Rapid Assessment

External experts	Dr Mercedes Guerra, Hospital Universitario de Guadalajara (Spain) and President of the Chapter of Endovascular Surgery of the Spanish Society of Angiology and Vascular Surgery Dr Andrew Tambyraja, Consultant Vascular Surgeon at the Royal Infirmary of Edinburgh (Scotland) and Honorary Clinical Senior Lecturer at the University of Edinburgh
Manufacturer [v1.2] (factual accuracy check)	Medtronic, Minneapolis, MN, USA
Edition [v1.3]	Joseph A. Moore, USA

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All authors, co-authors, dedicated reviewers, external experts and patients or patient representatives involved in the production of this assessment have declared that they have no conflicts of interest in relation to the technology and comparator assessed according to the EUnetHTA Declaration of Interest and Confidentiality Undertaking (DOICU) statement form. One external expert, Dr. Guerra, is President of the Chapter of Endovascular Surgery of the Spanish Society of Angiology and Vascular Surgery. According to EUnetHTA guidelines, her involvement as an external expert is acceptable in terms of commenting on the draft project plan and draft assessment; however, all decisions and conclusions pertaining to the report remain under the sole purview of the authoring team.

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## TABLE OF CONTENTS

<b>DOCUMENT HISTORY AND CONTRIBUTORS .....</b>	<b>2</b>
<b>TABLE OF CONTENTS.....</b>	<b>4</b>
<b>LIST OF TABLES AND FIGURES .....</b>	<b>5</b>
<b>LIST OF ABBREVIATIONS.....</b>	<b>6</b>
<b>SUMMARY OF RELATIVE EFFECTIVENESS OF ENDOANCHORING SYSTEMS IN ENDOVASCULAR AORTIC ANEURYSM REPAIR.....</b>	<b>8</b>
SCOPE.....	8
INTRODUCTION .....	8
RESULTS.....	10
DISCUSSION.....	18
CONCLUSION.....	19
<b>1 SCOPE.....</b>	<b>20</b>
<b>2 METHODS AND EVIDENCE INCLUDED .....</b>	<b>23</b>
2.1 AUTHORIZING TEAM.....	23
2.2 SOURCE OF ASSESSMENT ELEMENTS .....	23
2.3 SEARCH.....	23
2.4 STUDY SELECTION.....	25
2.5 DATA EXTRACTION AND ANALYSES .....	26
2.6 QUALITY RATING .....	26
2.7 PATIENT INVOLVEMENT (IF APPLICABLE).....	27
2.8 DESCRIPTION OF THE EVIDENCE USED.....	27
2.9 DEVIATIONS FROM PROJECT PLAN .....	29
<b>3 DESCRIPTION AND TECHNICAL CHARACTERISTICS OF TECHNOLOGY (TEC) .....</b>	<b>30</b>
3.1 RESEARCH QUESTIONS.....	30
3.2 RESULTS .....	30
<b>4 HEALTH PROBLEM AND CURRENT USE OF THE TECHNOLOGY (CUR) .....</b>	<b>35</b>
4.1 RESEARCH QUESTIONS.....	35
4.2 RESULTS .....	35
<b>5 CLINICAL EFFECTIVENESS (EFF) .....</b>	<b>47</b>
5.1 RESEARCH QUESTIONS.....	47
5.2 RESULTS .....	47
<b>6 SAFETY (SAF) .....</b>	<b>56</b>
6.1 RESEARCH QUESTIONS.....	56
6.2 RESULTS .....	56
<b>7 POTENTIAL ETHICAL, ORGANISATIONAL, PATIENT AND SOCIAL, AND LEGAL ASPECTS (ETH, ORG, SOC, LEG).....</b>	<b>59</b>
7.1 RESEARCH QUESTIONS.....	59
<b>8 PATIENT INVOLVEMENT .....</b>	<b>61</b>
<b>9 DISCUSSION .....</b>	<b>62</b>
9.1 DISCUSSION OF THE METHODOLOGY.....	62
9.2 DISCUSSION OF EFFECTIVENESS AND SAFETY .....	65
<b>11 REFERENCES.....</b>	<b>70</b>

## LIST OF TABLES AND FIGURES

### Tables

Table 1: Summary of findings table for Heli-FX <sup>TM</sup> EndoAnchor <sup>TM</sup> (critical outcomes).....	13
Table 2: Main characteristics of the studies included .....	27
Table 3: Treatment options for post-EVAR procedures: .....	42
Table 4: Summary of events and quality of the evidence for critical outcomes on effectiveness:..	53
Table 5: Summary of events and quality of the evidence for critical outcomes on safety: .....	58

### Figures

Figure 1: Flow chart.....	25
Figure 2: 2018 EVAR Heli-Fx EndoAnchor sales .....	45
Figure 3: 2018 TEVAR Heli-Fx EndoAnchor sales .....	45

### Appendix

Table A1: Overview of guidelines.....	81
Table A2: Characteristics of relevant studies.....	88
Table A3: Characteristics of relevant studies (continued).....	91
Table A4: List of ongoing studies with endoanchors.....	93
Table A5: Risk of bias – study level .....	95
Table A6: GRADE quality assessment on effectiveness .....	99
Table A7: GRADE quality assessment on safety.....	119
Table A8: Summary table characterising the applicability of a body of studies .....	129

**LIST OF ABBREVIATIONS**

AAA	Abdominal Aortic Aneurysm
ASA	American Society of Anesthesiologists
CI	Confidence Interval
CT	Computed Tomography
CUR	Current use of technology domain
DOICU	Declaration of Interest and Confidentiality Undertaking
DRG	Diagnosis-Related Group
DSA	Digital Subtraction Angiography
ESAR	Endovascular Sutured Aneurysm Repair
EVAR	Endovascular Aortic Repair
FDA	U.S. Food and Drug Administration
GRADE	Grading of Recommendations, Assessment, Development and Evaluation
HCD	High-Cost Devices
HTAi	Health Technology Assessment International
HRQoL	Health-Related Quality of Life
ICD	International Classification of Diseases
IDE	Investigational Device Exemption
IFU	Indications for Use
IHE	Institute of Health Economics
JRAAA	Juxtarenal Abdominal Aortic Aneurysm
MA	Meta-analysis
MAH	Marketing Authorisation Holder
MeSH	Medical Subject Headings
MRI	Magnetic Resonance Imaging
NUB	<i>Neue untersuchungs und behandlungsmethoden</i> (acronym, from the German, meaning <i>New examination and treatment methods</i> ) (Market Access & Reimbursement for Inpatient Medical Devices in Germany, Reimbursement Institute)
OR	Odds Ratio
OSR	Open Surgical Repair
PET/CT	Positron Emission Tomography/Computed Tomography
PICO	Population-Intervention-Control-Outcome (scheme)
PROM	Patient-Reported Outcome Measures
RCT	Randomised Controlled Trial

REA	Relative Effectiveness Assessment
RR	Relative Risk
SR	Systematic Review
TAA	Thoracic Aortic Aneurysm
T/A AA	Thoracoabdominal Aortic Aneurysm
TEC	Technical Characteristics of Technology Domain
TEVAR	Thoracic Endovascular Aortic Repair

## **SUMMARY OF RELATIVE EFFECTIVENESS OF ENDOANCHORING SYSTEMS IN ENDOVASCULAR AORTIC ANEURYSM REPAIR**

### ***Scope***

The objective of this rapid assessment was to evaluate relative effectiveness and safety of The Heli-FX™ EndoAnchor™ system as an anchoring system in addition to the standard endoprostheses used in Endovascular Aortic Repair (EVAR) and Thoracic Endovascular Aortic Repair (TEVAR) procedures.

The scope can be found here: [Scope](#).

### ***Introduction***

#### **Description of technology and comparators**

The Heli-FX™ EndoAnchor™ system (Medtronic, Minneapolis, MN, USA) consists of the Heli-FX™ applicator with the EndoAnchor™ cassette and the Heli-FX™ guide catheter with an obturator. The comparators consist of commercially available endografts including newly introduced ones (debranching, chimneys, fenestrations and branches) ([B0001](#)).

Their use is indicated in patients whose anatomical features may predispose them to suboptimal positioning of the endoprosthesis and consequent endovascular losses (endoleaks) and/or migration of the endoprosthesis itself (unfavourable anatomy or hostile neck-related issues). The Heli-FX™ EndoAnchor™ can be used at the time of the initial positioning of the endoprosthesis or during subsequent procedures (i.e., a repair) [1] ([A0020](#)).

The device has been proposed as an anchoring system in addition to the standard endoprostheses used in EVAR or TEVAR for abdominal, thoracoabdominal aortic aneurysm repair as a means of increasing adhesion and fixation of the vascular endoprosthesis to the aortic wall, recreating the durability of a sutures anastomosis [2, 3] ([B0002](#)).

Use of the device, as well as the Endovascular Aortic Repair (EVAR) and Thoracic Endovascular Aortic Repair (TEVAR) procedures, requires highly specialized personnel and suitable facilities to support it [4, 5] ([B0004](#)).

#### **Health problem**

The main restriction limiting EVAR procedures for Abdominal Aortic Aneurysm (AAA) disease is the unfavourable morphology of the aneurysm, as well as the adverse anatomical characteristics of the infrarenal aortic neck in particular [6]. The latter can include marked angulation, short length, complex shape, wide diameter or the presence of calcification or thrombus [7]. The term “hostile neck” has often been used when the aortic neck anatomy in AAA, fell outside the eligibility criteria for approved stent endograft indications and their clinical trials [8, 9]. Currently, the broader term “complex” (or unsuitable necks) encompasses short or absent necks, angulated necks, conical necks, or large necks exceeding the size applicability of current stent grafts, all of which have been linked to an increased risk of type I endoleaks and/or stent/endograft migrations [6, 10].

In Thoracic Aortic Aneurysm (TAA) patients, endoleak occurrences are associated with many factors besides the anatomic characteristic of short proximal or distal neck (landing zone). In general, larger and more extensive TAAs, as well as the position of the landing zone for endografts



in the thoracic aorta, meet the definition of high-risk TAA for developing type I endoleak and migration [11, 12] (A0002).

Due to the technical problems constraining endovascular procedures in unsuitable necks, the incidence of complications such as aneurysmal ruptures, which have been linked to type I endoleaks (HR 0= 7.6; 90%IC: 2.1 to 27.6) and stent/endograft migrations (HR= 4.5; 90%IC: 1.2 to 16.7) is higher [13, 14].

Endoleaks are indicative of a failure to completely exclude the aneurysm. A type I endoleak occurs due to an incompetent seal at the proximal (type Ia) or distal (type Ib) endograft attachment site [15]. Endograft or stent migration involves a displacement of more than 5–10 mm from its original position, movement of the stent graft > 10 mm, or any migration resulting in symptoms or requiring re-intervention [5, 15] (A0002).

Female gender is a known risk factor for presenting unsuitable or hostile necks in infrarenal AAA, according to the Characterisation of Aortic Aneurysm Project. Female gender was also found to be a risk factor for intraoperative type I endoleaks in patients undergoing EVAR procedures. The role of age as a known risk factor for unsuitable or hostile necks in infrarenal AAA, or an increased presence of type I endoleaks or migrations is less described. No clear role of gender or age as a risk factor for type I endoleaks or stent/endograft migrations in TAA patients has been found [16] (A0003).

The known risks for AAA patients suffering type I endoleaks or stent/endograft migrations after an EVAR/TEVAR procedure include an unfavourable aortic neck anatomy (4-fold increased risk of developing a type I endoleak (Odds Ratio (OR) = 4.56; 95% Confidence Interval (CI), 1.43 to 14.56) compared with patients presenting friendly neck AAA anatomy [6]. Regarding intraoperative type I endoleaks, aortic neck calcification and aortic curvature have been identified as independent predictors of intraoperative type Ia endoleaks (EVAR patients) [17] (A0003).

For endograft migration, the angulation, extension, and diameter of the neck and transversal size of the aneurysmatic sac are important morphological aspects related to migration in AAA. In terms of this technique, endoprosthesis implantation in cases of excessive oversizing (> 30%) is not recommended [18] (A0003).

In TAA patients, landing zones 0-2 have higher numbers of type I endoleaks compared to those in zone 4. In addition, proximal neck diameters  $\geq 38$  mm (OR= 3.6; 95% CI 1.2 to 10.8) are among the anatomical features that must be taken into account in such patients [12]. Regarding endograft migration, the only reported risk factors independent of type I endoleak are aortic elongation and changes in the curvature of TEVAR stent grafts [19, 20] (A0003).

Patients who have undergone EVAR/TEVAR require lifelong surveillance because endoleak type I and stent migration can lead to aneurysm expansion and rupture [13, 14] (A0004).

That most patients with AAA will be asymptomatic at the time of diagnosis is well known. There are no specific symptoms that AAA patients at high risk for type I endoleaks or stent migrations typically present [21, 22]. Most asymptomatic thoracoabdominal aortic aneurysm (T/A AA) cases are discovered incidentally, while symptomatic patients usually present more fully developed complications. As with AAA, there is no typical clinical manifestation in patients at high risk of type I endoleaks or migrations in TAA [22, 23]. Type I endoleaks and stent migrations are radiologic signs associated with a high risk for aortic rupture, however there are no recognised or associated symptoms for these conditions [22-24] (A0005).

## Results

### Available evidence

Two prospective single-arm trials are the studies with the largest number of patients, the STAPLE - I and II (FDA-sanctioned Phase I Investigational Device Exemption (IDE) Study and the Pivotal Study of the Aptus Endovascular AAA Repair System, both completed) - and the ANCHOR trial (Aneurysm Treatment Using the Heli-FX™ EndoAnchor™ System Global Registry, currently ongoing).

Overall, eleven studies have been included in this analysis, totalling 684 patients with a follow-up range of 2 to 72 months [25-35]. All studies have been included in the effectiveness analysis and eight studies were included in the safety analysis (Table 2). However, two ANCHOR publications were excluded due to overlapping safety results with other two ANCHOR studies. Only one study had a control group, an abdominal aneurysm observational study with a propensity matched control group. This study presented results on abdominal aneurysms in a patient subset of the Anchor registry [32]. Four studies involved prospective cohorts derived from a registry from the marketing authorization holder (MAH), -ANCHOR registry- [26, 29, 30, 35] and two cohorts from the STAPLE-1 and STAPLE-2 registries [27, 31]. Two retrospective series were found, one on abdominal aneurysms requiring a primary intervention [28], and one with patients who underwent an intervention for a thoracic aneurysm [33].

Two prospective series [25, 34], and two retrospective series [28, 33], were not directly related to the MAH registries.

The available evidence permitted an analysis by different groups, based on the type of intervention: primary intervention and secondary or revision intervention. In cases involving primary intervention, we differentiated the patients into three subgroups based on the indications pertaining to the relevant procedure: one when the intervention was prophylactic in nature (e.g., due to risk, such as a hostile neck) and the other two when the patients presented type I endoleak during the procedure (immediate type I endoleak) or maldeployment of the graft. In secondary interventions, we analysed the available evidence according to the indications of the repair requirements (migration, endoleak or both).

### Clinical effectiveness

#### Mortality (D0001)

One patient in the prophylaxis subgroup (4 studies, 392 patients) (1/392) ( $0.25\% \pm 0.32$  weighted by sample size) died of aneurysm-related causes within 30 days. However, this outcome did not occur in the other subgroups that required a primary intervention. In the studies containing data on secondary interventions (2 studies, 88 patients) no deaths were attributed to aneurysm. In the retrospective series, 2 patients of 51 died (3.9%, 1 study). For thoracic aneurysms, the aneurysm-related mortality rate at 30 days was 2/54, 3.7% of the retrospective cohort [33].

Aneurysm-related mortality at one year (abdominal aneurysm) was  $0.26\% \pm 0.32$  (1 patient from a sample of 379 prophylactic patients from 3 studies, weighted by sample size) [27, 29, 31].

No deaths related to aneurysm were recorded in cases requiring a secondary intervention (2 studies, 88 patients) [25, 26]. In the retrospective series, primary interventions (including prophylaxis, immediate type I endoleaks and maldeployment) in a series of 51 patients revealed a

mortality rate of 5.88% [28]. Aneurysm-related mortality in thoracic aneurysm at one year was 9.3% (5 patients in a retrospective series of 54).

### *Morbidity (D0005)*

Regarding ruptured aneurysms (abdominal aneurysms), measured as the proportion of patients who experienced an aneurysm rupture, four observational studies (prospective cohorts) presented data on the outcomes for primary interventions (only prophylaxis patients subset). No patients presented a ruptured aneurysm during the 48-month follow-up period. This outcome was not reported by the studies that analysed patients requiring primary intervention due to an immediate type I endoleak or graft maldeployment, except for the retrospective series, in which 1 patient of 51 presented this outcome (1.96%). In the only study with data on patients who underwent a secondary intervention with this outcome, no aneurysm ruptures were reported.

The aneurysm rupture rate for thoracic aneurysms was 1.9% (1/54) in the only study available.

Regarding the reintervention rate (abdominal aneurysm), 4 observational studies (prospective cohorts) presented data on the outcomes for primary interventions. This consisted of a subgroup of prophylaxis patients, measured as the proportion of those treated patients who required a reintervention. Of the 392 patients included, 38 underwent a reintervention (9.7%±7), weighted according to sample size [27, 29, 31, 34]. The follow-up period ranged from 0 to 48 months. A retrospective case series found that 25.5% of the patients needed a reintervention (13/51; these 13 patients required a total of 17 reinterventions) with a mean follow-up period of 23.9 months (IQR 13.4, 35.6 months) [28].

The literature search yielded only one study that reported the reintervention rate for thoracic aneurysm, a retrospective cohort study of 54 patients, in which the reintervention rate was 16.7% (9/54). Follow-up was not reported [33]. In the patient subgroup that underwent a primary intervention due to an immediate type I endoleak, one study involving 60 patients reported a reintervention rate of 5% (3/60). The only sample involving a primary intervention due to graft maldeployment (4 patients from a subgroup within a larger registry) did not necessitate any reinterventions [26].

In the case of one type of secondary intervention, subset migration, 2 studies reported that 3 of 12 patients suffered a reintervention (25%±7.87). This number decreased in the type I endoleak subset, falling to 16.3%±10.14 (8/49), and to 7.4%±4.03 (2/27) in the subset of patients who required both types of complication repairs [25, 26].

The rate of occurrence or recurrence of complications (abdominal aneurysms) was assessed based on the proportion of patients who suffered a graft migration or type I endoleak. In the prophylaxis subgroup (4 prospective cohorts, with a follow-up range up to 72 months, 392 patients) the rate was 2.5%±2.80 (10/392). In the retrospective series, the rate of occurrence or recurrence of complications (abdominal aneurysm) was 17.64% (9/51), and for thoracic aneurysm 9.3% (5 of 54 patients from a retrospective study). The only study containing comparative data involving EVAR without Heli-FX™ EndoAnchor™ reported a rate of 2% in the intervention group and 4% in the control group, over a 2-year period, with no significant differences in the Kaplan-Meier analysis [32].

The rate of occurrence or recurrence of complications (abdominal aneurysms) in the immediate type I endoleak subgroup was 28.3% (17 from a 60-patient prospective cohort with complications, with a mean follow-up period of 16 months) [26]. One of the four patients in the subgroup with maldeployment also suffered a recurrence of complications, specifically a type I endoleak at the

end of the procedure. Regarding secondary interventions, 2 studies showed that 12 of 88 patients suffered some type of complication (13.63%±1.73).

Health-related quality of life (HRQoL) data was not reported by any of the studies, and no Patient Reported Outcome Measures (PROMs) were found or planned in any of the retrieved cohorts or case-series ([D0012](#), [D0013](#), [D0017](#)).

## Safety

Procedure-related mortality was the only safety outcome rated as critical. One possible overlapping scenario concerns all-cause mortality at 30 days due to the heterogeneity of the outcomes standardisation among the studies. A weighted mean of 0.2% ± 0.13% (1/517) from five observational studies at 30 days after the EVAR procedure was determined [25-27, 31, 34]. In the case of thoracic aneurysm repair, the procedure-related mortality rate at 30 days was 3.7% (2/54); this was based on one retrospective study of patients who had undergone a TEVAR procedure [33] ([C0008](#)).

No studies reported patient groups that were more susceptible to harm from the use of Heli-FX™ EndoAnchor™ ([C0005](#)).

**Table 1** shows a summary of findings regarding the clinical effectiveness and safety of Heli-FX™ EndoAnchor™ on critical outcomes. Important and not important outcomes are presented and discussed later in the report.

## Upcoming evidence

The only study currently in progress is the ANCHOR study (NCT01534819), a multicenter prospective registry that collects efficacy, safety and technical performance data on the Heli-FX™ EndoAnchor™ system, both in prophylaxis and in treatment regimens that include EVAR and TEVAR procedures. However, no controlled nor randomised trials are currently underway.

## Reimbursement

Reimbursement policies are variable throughout the EU. Whereas some countries have specific reimbursement for the device, other countries do not provide separate and/or distinct reimbursement plans for the Heli-FX™ EndoAnchor™ (covered as part of the procedure or a more general grouping) ([A0021](#)).

**Table 1: Summary of findings table for Heli-FX™ EndoAnchor™ (critical outcomes)**

Outcome (Subset of patients)	Patients with event	Number of participants (studies)	Certainty of the evidence (GRADE)	Comments
<b>Reintervention rate</b>				
<b>Abdominal Aneurysm</b>				
<b>Reintervention rate (prophylaxis)</b>	38/392 (9.7%±7)	392 (4 observational studies)	Very low	In a retrospective series of primary interventions (prophylaxis, immediate type I endoleak and maldeployment without distinct results) the percentage of events collected was 33.3% (17/51)
<b>Reintervention rate (immediate type I endoleak)</b>	3/60 (5%)	60 (1 observational study)	Very low	Primary interventions due to immediate type I endoleak
<b>Reintervention rate (maldeployment)</b>	0	4 (1 observational study)	Very low	Subset of patients in a larger study; no information on this kind of patients in other studies. Primary intervention due to maldeployment.
<b>Reintervention rate (secondary-revision migration)</b>	3/12 (25%±7.87)	12 (2 observational studies)	Very low	Subset of patients with secondary interventions due to migration.
<b>Reintervention rate (secondary-revision type I endoleak)</b>	8/49 (16.32%±10.14)	49 (2 observational studies)	Very low	Subset of patients with secondary interventions due to a type I endoleak
<b>Reintervention rate (secondary-revision type I endoleak and migration)</b>	2/27 (7.4%±4.03)	27 (2 observational studies)	Very low	Subset of patients with secondary intervention due to a type I endoleak and migration
<b>Thoracic Aneurysm</b>				
<b>Reintervention rate</b>	9/54 (16.7%)	54 (2 observational studies)	Very low	All patients (primary and secondary interventions) included in a retrospective study
<b>Aneurysm rupture</b>				
<b>Abdominal Aneurysm</b>				

<b>Aneurysm rupture (prophylaxis)</b>	0	392 (4 observational studies)	Very low	Aneurysm rupture in primary intervention due to an immediate endoleak type I or maldeployment was not measured/ reported. The final report from the trial registry webpage informs one aneurysm rupture at five years (end of the trial), not included in the analysis.  In a retrospective series of primary intervention (prophylaxis, immediate type I endoleak and/or maldeployment without separated results) the percentage of events collected was 2% (1/51)
<b>Aneurysm rupture (secondary-revision Migration)</b>	0	1 (1 observational study)	Very low	Secondary intervention due to migration.
<b>Aneurysm rupture (secondary-revision type I endoleak)</b>	0	4 (1 observational study)	Very low	Secondary intervention due to a type I endoleak
<b>Aneurysm rupture (secondary-revision type I endoleak and migration)</b>	0	6 (1 observational study)	Very low	Secondary intervention due to a type I endoleak and migration.
<b>Thoracic Aneurysm</b>				
<b>Aneurysm rupture</b>	1/54 (1.9%)	54 (1 observational study)	Very low	All patients (primary and secondary intervention) included in a retrospective study
<b>Aneurysm-related mortality 30 days</b>				
<b>Abdominal Aneurysm</b>				
<b>Aneurysm-related mortality 30 days (prophylaxis)</b>	1/392 (0.25%±0,32)	392 (4 observational studies)	Very low	Aneurysm-related mortality in primary intervention due to an immediate type I endoleak or maldeployment was not measured / reported.  In a retrospective series of primary interventions (prophylaxis, immediate type I endoleak and maldeployment without distinct results) the percentage of events collected was 3.9% (2/51)
<b>Aneurysm-related mortality 30 days (secondary-revision migration)</b>	0	12 (2 observational studies)	Very low	Subset of patients with a secondary intervention due to a migration.
<b>Aneurysm-related mortality 30 days (secondary-revision type I endoleak)</b>	0	49 (2 observational studies)	Very low	Subset of patients with secondary intervention due to a type I endoleak

<b>Aneurysm-related mortality 30 days (secondary-revision type I endoleak and migration)</b>	0	27 (2 observational studies)	Very low	Subset of patients with secondary intervention due to a type I endoleak and migration
<b>Thoracic Aneurysm</b>				
<b>Aneurysm-related mortality 30 days</b>	2/54 (3.7%)	54 (1 observational study)	Very low	All patients (primary and secondary interventions) included in a retrospective study
<b>Aneurysm-related mortality 1 year</b>				
<b>Abdominal Aneurysm</b>				
<b>Aneurysm-related mortality 1 year (prophylaxis)</b>	1/379 (0.26%±0,32)	379 (3 observational studies)	Very low	Aneurysm-related mortality in primary intervention due to an immediate type I endoleak or maldeployment was not measured / reported. In a retrospective series of primary interventions with all kind of patients (prophylaxis, immediate type I endoleak and maldeployment) the percentage of events collected was 5.9% (3/51)
<b>Aneurysm-related mortality 1 year (secondary-revision migration)</b>	0	12 (2 observational studies)	Very low	Subset of patients with secondary interventions due to migration.
<b>Aneurysm-related mortality 1 year (secondary-revision type I endoleak)</b>	0	49 (2 observational studies)	Very low	Subset of patients with secondary intervention due to a type I endoleak.
<b>Aneurysm-related mortality 1 year (secondary-revision type I endoleak I and migration)</b>	0	27 (2 observational studies)	Very low	Subset of patients with secondary intervention due to a type I endoleak and migration.
<b>Thoracic Aneurysm</b>				
<b>Aneurysm-related mortality 1 year</b>	5/54 (9.3%)	54 (1 observational study)	Very low	All patients (primary and secondary interventions) included in a retrospective study.
<b>Rate of occurrence or recurrence of complications (graft migration or endoleak type I)</b>				
<b>Abdominal Aneurysm</b>				

Rate of occurrence or recurrence of complications (prophylaxis)	10/392 (2.5%±2,80)		392 (4 observational studies)	Very low	In a retrospective series of primary intervention (prophylaxis, immediate type I endoleak and maldeployment without distinct results) the percentage of events collected was 17.6% (9/51).
Rate of occurrence or recurrence of complications (Immediate type I endoleak)	17/60 (28.3%)		60 (1 observational study)	Very low	Primary intervention due to an immediate type I endoleak.
Rate of occurrence or recurrence of complications (maldeployment)	1/4 (25%)		4 (1 observational study)	Very low	Subset of patients in a larger study, no information on this subgroup of patients in other studies. Primary intervention due to maldeployment.
Rate of occurrence or recurrence of complications (secondary-revision migration/ type I endoleak / type I endoleak and migration)	12/88 (13.63%±1.73)		88 (2 observational studies)	Very low	Overall patients in the 2 studies, results not separated by subgroups.
Rate of occurrence or recurrence of complications (primary intervention/ no subgroups)	Anticipated absolute effects (95% CI)	Relative effect (95% CI)	99 (1 observational study)	Very low	Propensity matched cohort with primary intervention patients (not separated by subgroups) controlled by a matched cohort of 99 patients.
	20 fewer per 1000 (from 37 fewer to 67 more)	RR 0.50 (0.09 to 2.67)			
Thoracic aneurysm					
Rate of occurrence or recurrence of complications	4/54 (7.4%)		54 (1 observational study)	Very low	All patients (primary and secondary interventions) included in a retrospective study
Safety Outcomes (All primary and secondary/revision intervention arms)					
Abdominal aneurysm					



<b>Procedure-related mortality follow-up: 30 days</b>	1/517 (0.2% $\pm$ 1.41%)	517 (5 observational studies)	Very low	Reports of safety outcomes include primary and secondary/revision arms in most of the studies with two clinical scenarios.
<b>Thoracic aneurysm</b>				
<b>Procedure-related mortality follow-up: 30 days</b>	2/54 (3.7%)	54 (1 observational study)	Very low	Report of safety outcomes includes primary and secondary/revision arms from a retrospective study.

## **Discussion**

In the assessment, the quality of evidence for the outcomes largely depended on the risk of bias and the lack of control groups. These two issues diminished the quality, with the lowest quality of critical outcomes ranking very low. This was also the result for important and not important outcomes. All outcomes—critical, important and not important—were rated with this quality, and none could be increased (large effect, plausible confounder that would change the effect or dose-response gradient cases).

The variability of the follow-up (from less than a year to 48 months) for most of the outcomes, and not always well specified time points of the events, limited the analysis. We presented results with a broad range of follow-up periods due to this heterogeneity, with a median of 12 months in the prospective series. Only one study presented some results at 72 months, encompassing both endoleaks, and adverse events, though it included very few patients with longer-term data [31]. One retrospective series had a median follow-up period of 24 months, and the only study that addressed thoracic aneurysm, a retrospective case series, had a median follow-up time of 9.6 months. In the studies, patients with long-term data were low in number, and not all had CT imaging results in their follow-up records. Sample sizes were small for those patients with secondary interventions and with TEVAR. Patients who underwent a primary intervention due to prophylaxis were the most studied group, although this sample, when pooled, numbered less than 400 patients, and not all had at least one year of follow-up. This may cause that late outcomes were not yet occurring; e.g., reinterventions due to complications. The risk of endograft complications at the proximal neck increased over time, with endoleaks and migration more commonly arising as a longer-term problem. Thus, medium-term follow-up periods should be extended for greater numbers of patients.

Overall mortality (an outcome rated as important) appeared to be lower in the prophylactic group, most likely because the intervention was not necessitated by complications. It was also low in the secondary intervention groups, however, this may be a reflection of the small sample size and brief follow-up period. Nevertheless, in the latter case, those patients whose interventions were due to type I endoleaks had the highest rate of mortality at one year within the secondary setting (7%). The highest mortality rates at one year was recorded by the thoracic study and the retrospective series on primary patients (all kinds) (11% and 13%, respectively) [28, 33].

The only registered trial (ANCHOR) ongoing in 2018 involved a symposium that reported the following comparative 1-, 2- and 3-year results for the occurrence of type 1a endoleaks: 0.6%, 1.1% and 1.7%, respectively, for the primary arm, and 7.9%, 5.9% and 2.4%, respectively, for the revision arm. No cases of endograft migration were reported in the primary intervention or in the revision arm (secondary intervention) in AAA patients [36].

These results should be compared with the treatment regimens lacking endoanchors in randomised controlled trials. The only control data involved a cohort of 99 patients yielded by a propensity match in one study, although data on only 3 outcomes (rate of migration or endoleaks, sac regression and sac enlargement) was retrievable. The only outcome rated as critical among these is the rate of complications (migration or endoleaks), and here there were no significant differences with the intervention-free control group [32].

The lack of larger cohorts, control groups, as well as the short follow-up ranges for most of the outcomes makes the drawing of reliable conclusions difficult.

## **Conclusion**

Based on the results from observational studies, and within the limitations of the low-quality evidence available, the data suggest that the use of Heli-FX™ EndoAnchor™ in EVAR patients (prophylactically or as part of endograft migration or type I endoleak treatment) would be safe in the midterm follow-up for those presenting unfavourable neck anatomy and probably safe over long-term follow-up for those with friendly neck anatomies. However, comparative data on standard endovascular therapy are not currently available. We cannot form any conclusions regarding the safety of Heli-FX™ EndoAnchor™ in TEVAR patients.

In terms of effectiveness, again the evidence precludes any firm conclusions as to whether the use of endoanchors in EVAR/TEVAR procedures results in better outcomes. Globally, the information compiled on critical outcomes (rate of type I endoleaks or migration, rate of reintervention, rate of aneurysm rupture or rate of aneurysm-related mortality), although of very low quality, would suggest effectiveness of the device. Nonetheless, evidence from high-quality comparative studies remains lacking. Results should be compared with treatment regimens without the Heli-FX™ EndoAnchor™ system in randomised controlled trials for most of the critical and important outcomes.

# 1 SCOPE

Description	Project scope
Population	<p><b><u>Clinical Scenario 1 or Primary Intervention:</u></b></p> <p><b><i>Patients with abdominal or thoracic aortic aneurysm undergoing endovascular repair with a high risk of complications* (migration or type I endoleak).</i></b></p> <ul style="list-style-type: none"> <li><b><u>International Classification of Diseases (ICD)10:</u></b> I71.1 Thoracic aortic aneurysm, ruptured. I71.2 Thoracic aortic aneurysm, without mention of rupture. I71.3 Abdominal aortic aneurysm, ruptured. I71.4 Abdominal aortic aneurysm, without mention of rupture. I71.5 Thoracoabdominal aortic aneurysm, ruptured. I71.6 Thoracoabdominal aortic aneurysm, without mention of rupture. I71.8 Aortic aneurysm of unspecified site, ruptured. Incl.: Rupture of aorta NOS. I71.9 Aortic aneurysm of unspecified site, without mention of rupture. Incl.: Aortic Aneurysm, Dilatation or Hyaline Necrosis. S25.09 Other specified injury of thoracic aorta. S35.09 Other injury of abdominal aorta.</li> </ul> <p><b><u>Medical Subject Headings (MeSH terms):</u></b> Aortic Aneurysm, Thoracic C14.907.055.239.125, and C14.907.109.139.125. Aortic Aneurysm, Abdominal C14.907.055.239.075, C14.907.109.139.075. Aortic Rupture C14.907.055.185.125, C14.907.055.239.175, C14.907.109.139.175, C26.761.125</p> <p><i>*High-risk migration/endoleak (i.e., hostile neck in abdominal aortic aneurysm). "Hostile neck" is one with marked angulation, short length, complex shape, wide diameter or the presence of calcification or thrombus) [7]</i></p> <p><b><u>Clinical Scenario 2 or Secondary Intervention:</u></b></p> <p><b><i>Patients with failure of previous endovascular repair of an aortic aneurysm (migration or endoleak type I) that need secondary aortic repair.</i></b></p> <ul style="list-style-type: none"> <li><b><u>ICD10:</u></b> T82.8 Other specified complications of cardiac and vascular prosthetic devices, implants and grafts. (Embolism, Fibrosis, Hemorrhage, Pain, Stenosis. and Thrombosis). T82.9 Unspecified complication of cardiac and vascular prosthetic device, implant and graft</li> </ul> <p><b><u>MeSH terms:</u></b> Endoleak C14.907.055.501, C23.550.414.941.500, C23.550.767.850.500. Prosthesis Failure C23.550.767.865, E05.325.771.</p>
Intervention	<p>Fixation with endoanchoring systems, like Heli-FX™ of Aortic aneurysm graft/stents in EVAR/TEVAR.</p> <p>Other Names:</p> <ul style="list-style-type: none"> <li>EndoAnchors</li> <li>Endosuturing</li> <li>Endostaples</li> <li>Heli-FX</li> <li>Enhanced fixation devices</li> <li>Endovascular sutured aneurysm repair (ESAR)</li> </ul>

Description	Project scope
	Products/manufacturers: Aptus™ Heli-FX™ & Heli-FX™ Thoracic EndoAnchor™ Systems/Medtronic, Minneapolis, MN, USA.
<b>Comparison</b>	<p><b><u>Clinical Scenario 1 or Primary Intervention:</u></b></p> <p>Primary endovascular aortic aneurysm repair with a high risk of complications** (migration or type I endoleak) without the use of endoanchoring systems (all EVAR/TEVAR stents/endografts).</p> <p><i>**High-risk migration/endoleak (i.e., hostile neck in abdominal aortic aneurysm). "Hostile neck" is one with marked angulation, short length, complex shape, wide diameter or the presence of calcification or thrombus [7].</i></p> <p><b><u>Clinical Scenario 2 or Secondary Intervention:</u></b></p> <p>Secondary repair of EVAR/TEVAR complications (type I endoleak or endograft migration): embolisation, extensions of proximal / distal grafts, balloon angioplasty, metallic stents) or open surgical repair (OSR).</p> <ul style="list-style-type: none"> <li>MeSH terms: Endovascular Procedures E04.100.814.529, E04.502.382 Blood Vessel Prosthesis Implantation E04.100.814.868.500, E04.650.200.</li> </ul> <p>Rationale: The standard endovascular approach with endografts/stents in aortic aneurysm does not explicitly require the use of external anchoring systems [21, 37] except for the Endurant II/Endurant IIs Stent Graft System in short neck abdominal aortic aneurysms [38]. Almost all new generation aortic endografts/stents include active fixation mechanisms to avoid migration [10]. There is no standard treatment for type I endoleaks or for the migration of aortic endografts/stents [39].</p>
<b>Outcomes</b>	<p><b><u>Effectiveness</u></b></p> <ul style="list-style-type: none"> <li>Rate of occurrence or recurrence of complications (freedom from graft migration or type I endoleaks). (Critical)</li> <li>Reintervention rate. (Critical)</li> <li>Aneurysm rupture. (Critical)</li> <li>Aneurysm-related mortality (30days-≥1y). (Critical)</li> <li>All-cause mortality (early=30days/late≥1y). (Important)</li> <li>Conversion to open surgical repair. (Important)</li> <li>Technical and procedural success. (Important)</li> <li>Health-related quality of life (HRQoL). (Important)</li> <li>Rate of neck dilation or sac enlargement. (not important)</li> <li>Rate of sac regression. (not important)</li> </ul> <p><b><u>Safety</u></b></p> <p>All adverse events and serious adverse events (related or unrelated to the device or intervention):</p> <ul style="list-style-type: none"> <li>Procedure-related mortality. (Critical)</li> <li>Vessel damage (including dissection, perforation, and spasm). (Important)</li> <li>EndoAnchor implant embolisation. (Important)</li> <li>Endoleaks (types II-V). (Important)</li> <li>Stroke. (Important)</li> </ul>

Description	Project scope
	<ul style="list-style-type: none"> <li>• Vascular access complications (including infection, pain, hematoma, pseudoaneurysm and arteriovenous fistula). (Important)</li> <li>• Renal complications (renal artery occlusion/dissection or contrast-induced acute kidney injury). (Important)</li> <li>• Cardiac complications. (Important)</li> <li>• Respiratory failure. (Important)</li> <li>• Other ischemic complications. (Important)</li> <li>• Others: pneumonia, fever, urologic and gastrointestinal complications. (Important)</li> </ul> <p>Rationale: Included main outcomes already described in the Instructions for Use and the pivotal trial ANCHOR of Aptus™ Heli-FX™ and Heli-FX Thoracic EndoAnchor™ Systems by Medtronic (Minneapolis, MN, USA), a preliminary search of literature and their objective selection [1, 40, 41]</p>
<b>Study design</b>	<p><u>Effectiveness</u>: Randomized clinical trials (RCTs), prospective non-randomized controlled studies, other observational comparative studies.</p> <p><u>Safety</u>: Randomized clinical trials, prospective non-randomized controlled studies, other observational comparative and non-comparative studies, single arm studies with &gt;10 patients.</p>

## **2 METHODS AND EVIDENCE INCLUDED**

### **2.1 *Authoring Team***

Distribution of the responsibilities and workload between authors and co-authors was as follows:

AETS-ISCI:

- Developed the first draft of EUnetHTA project plan, amend the draft if necessary
- Performed the literature search.
- Carried out the assessment: answered assessment elements (Production of current use of technology (CUR), technical characteristics of technology (TEC), effectiveness (EFF) and safety (SAF) domains), completed checklist regarding potential “ethical, organisational, patient / social and legal aspects” of the HTA Core Model R for rapid Relative Effectiveness Assessment (REA).
- Sent “draft versions” to reviewers, compile feedback from same and perform changes based on their comments.
- Prepared final assessment and wrote a final summary of the assessment.

MoH Slovenia:

- Reviewed the project plan draft.
- Supported the production of all domains (Focus on CUR and TEC domains), and quality checked all steps of their production (data, information, sources).
- Contributed to answer questions related to potential ethical, organisational, patient / social, and legal aspects if needed.
- Approved/endorsed conclusions drawn, including all draft versions and the final assessment, as well as the executive summary.

### **2.2 *Source of assessment elements***

The selection of assessment elements is based on the HTA) Core Model Application for Rapid REA Assessments (4.2) [42]. The selected issues (generic questions) were translated into actual research questions (answerable questions).

Please note that in some instances multiple research questions were answered in summary fashion; that is, these questions might be listed below one another, with a single answer subsequently addressing them all.

### **2.3 *Search***

For Effectiveness (EFF) and Safety (SAF) domains, we performed a systematic literature search in the following bibliographic databases: PubMed, MEDLINE, EMBASE, the Cochrane Central Register of Controlled Trials, and the Cochrane Database for Systematic Reviews, according to a predefined search strategy. Furthermore, a search of the clinical trials registries ClinicalTrials.gov, EU Clinical Trials Registry and the International Clinical Trials Registry Platform (ICTRP) was carried out for those studies still ongoing. In addition to these electronic searches, a hand search

(reference lists of the relevant studies), as well as an internet search, including HTA agency websites, was performed. Moreover, a search of regulatory documents was also carried out at the U.S. Food and Drug Administration (FDA) website.

In order to identify the various studies, different search strategies for each database were designed. These were then combined with controlled terms (MeSH and EMTREE) and free text for indications (Aortic Aneurysm, Thoracic Aortic Aneurysm, Abdominal Aortic Rupture Aneurysm, Dissecting, Endoleak, Prosthesis Failure) and interventions (EndoAnchors, Endostaples, Heli-FX, Endosuturing, Enhanced fixation devices and Endovascular sutures aneurysm repair or ESAR). There were no language restrictions.

Inclusion criteria: human subjects, without language restrictions, and according to Population-Intervention-Comparison-Outcome (PICO) criteria. Exclusion criteria: publication date before 2001.01.01 (date of the first animal research publication on the EndoAnchor system's predecessor) and any norms governed by PICO criteria.

First search: 20/02/2019. Second search: 23/04/2019.

Medline Elsevier: First search, 121 results; Second search, 9 new results.

EMBASE: First search, 410 results; Second search, 13 new results.

CENTRAL (Cochrane): First search, 21 results; Second search, no new results.

A two-step process for validating the search strategies used for Medline and EMBASE was followed, including validation sets and the PRESS Peer review tool [43].

Information to more fully describe the technical characteristics of the technology (TEC) and current use (CUR) domains were obtained from the relevant literature identified in the systematic reviews (SRs), clinical guideline sites, and hand searches, including searches of manufacturer websites.

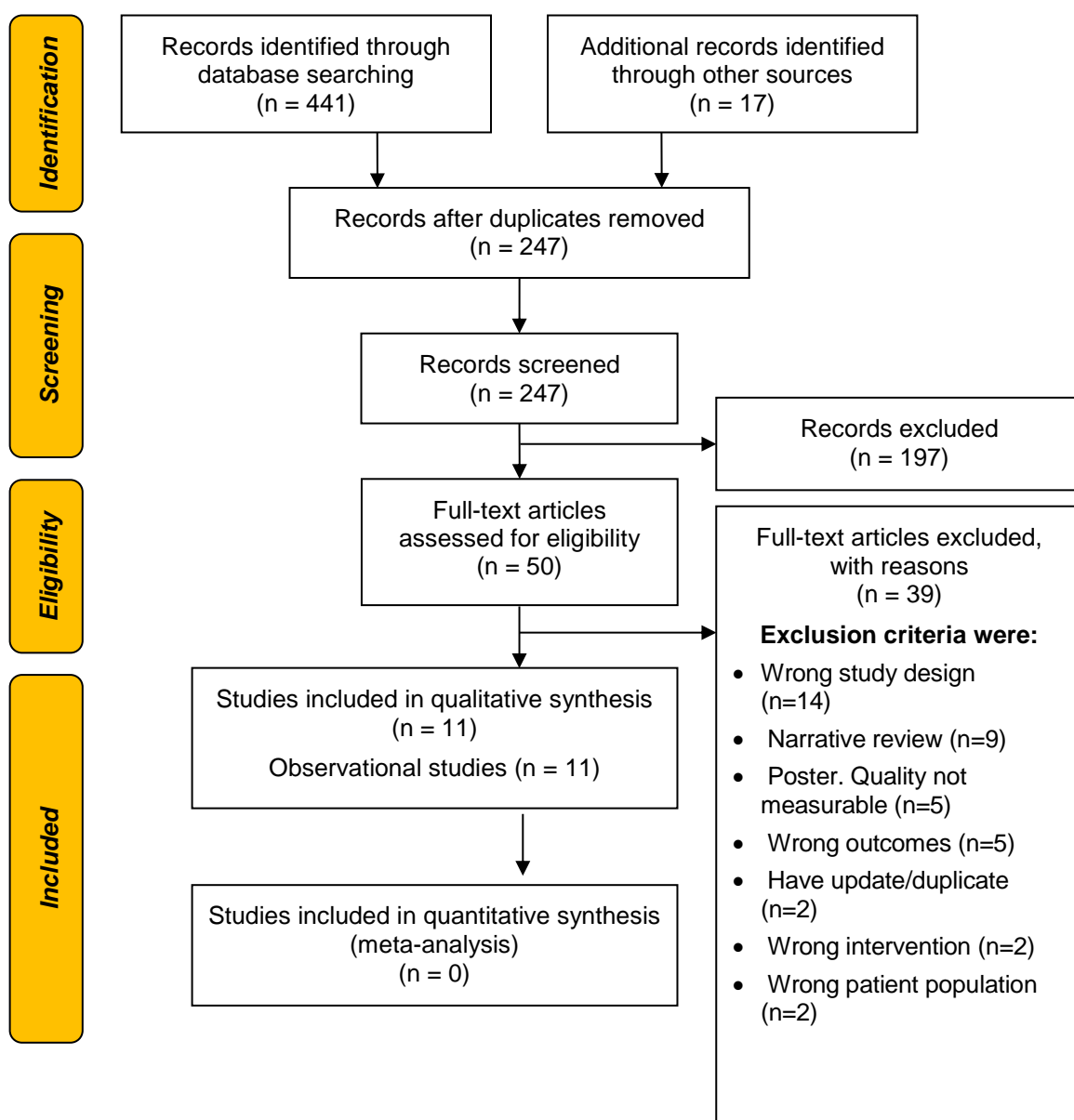
We also used information submitted by the manufacturer for the TEC and CUR domains. Some of the information regarding the EFF & SAF domains is only referred to in the Results section due to the impossibility of assessing the quality on the abstracts, press reports and meeting presentations.

A survey of EUnetHTA partners was carried out from December 2018 to February 2019 to obtain information not only on the use of Heli-FX<sup>™</sup> EndoAnchor<sup>™</sup>, but also on reimbursement issues related to the CUR domain.

Detailed tables on the search strategies can be found in [Appendix 1](#).



## 2.4 Study selection



**Figure 1: Flow chart**

Systematic literature searches of bibliographic databases yielded 441 citations after the first and second (updated) searches. Seventeen additional references were identified through the search of study registries. After removing all duplicates, 247 references remained. Two researchers independently screened the 247 citations for eligibility. In cases of disagreement, a third researcher was involved to resolve the situation. In the first step, 197 citations were excluded based on their titles and abstracts; in the second step, 39 of the remaining 50 articles were excluded after reviewing the full texts. This left 11 articles that met the inclusion criteria, of which only one was a retrospective comparative study, the rest being case series that could be included. Hand searches of the reference lists of the included studies, topic-related systematic and non-systematic reviews, and queries to the device manufacturer resulted in no additional relevant studies. Five posters/abstracts were reviewed for published articles (or in-press manuscripts), and queries to the first or the last author were sent with minimal or no response [Appendix 1](#) [44-48]. Two studies, in the forms of

abstracts, comparing Heli-FX™ EndoAnchor™ and other EVAR procedures, were also found [45, 48].

## **2.5 Data extraction and analyses**

Two review authors independently reviewed the extracted data using prepared data extraction sheets. The authors resolved any discrepancies through discussion with a third author. Data extracted from the studies included the following: information about the study (authors, year of publication, setting/country, funding, study design, clinical trial identification number/registry identifier and funding source). Participant/patient characteristics (diagnosis, number of participants in the trial, ages, clinical stage, and any relevant risk categories or risk factors). Intervention and control characteristics (description of procedure, emergency/elective setting, comparator, name/type of the device, frequency of intervention per patient, length of follow-up and loss of follow-up). Outcomes for EFF and SAF domains were classified (critical, important, non-important) according to a previously used GRADE rating process shared among the Assessment Team (author(s), co-author team, dedicated reviewers) and the clinical experts [49]. A separate process to identify overlapping or repetitive data for any outcome from those trials with more than one publication was conducted. Queries to Medtronic (Minneapolis, MN, USA) and to the Principal Investigator of the ANCHOR trial were sent to determine the existence of unpublished or in-press articles and results on TEVAR patients who participated in the ANCHOR trial. No clinical results or publications concerning TEVAR patients included in the ANCHOR trial were sent to the Authoring Team.

Effect measures of variables extracted as dichotomous data were expressed as a relative risk (RR) with 95% CIs, or as the number of events or percentages. When results could not be pooled, they were presented qualitatively or mean-weighted by sample size. For the effectiveness outcomes analysis, abdominal and thoracic results were separated. This was also accomplished by using a subset of patients (prophylaxis group, immediate type I endoleak and maldeployment in primary interventions, and repaired migration, type I endoleak or both in secondary interventions). Differences in the study designs were also considered for the analyses. For safety outcomes, the data were analysed and grouped into different follow-up periods (e.g., 30 days, 1 year, 2 years, 3 years) due to the impossibility, in most studies, of extracting adverse events data from the various subgroups (primary or secondary/revision arm). Most of the safety results are derived from EVAR (AAA) studies; only one study reports a single safety outcome involving TEVAR (TAA) patients. Most of the included patients had undergone elective endovascular procedures. Six of the eleven selected studies did not include urgent procedures or patients with a ruptured aneurysm [25, 27, 29, 31, 32]. Five studies reported a minor number of urgent procedures, albeit without a separate analysis for this subgroup [26, 28, 30, 33, 35]. Finally, we could not make a separate efficacy or safety analysis based on the outcomes of elective and/or urgent procedures subgroups.

## **2.6 Quality rating**

For the Description and Technical Characteristics of Technology (TEC) and Health Problems and Current Use of the Technology (CUR) domains, no quality assessment tool was used. However, multiple sources were utilized to validate various individual, possibly biased, sources. Descriptive analysis of the different information sources was performed.

For the Effectiveness (EFF) and the Safety (SAF) domains, we applied EUnetHTA guidelines in selecting quality-rating tools. The risk of bias at the study level was assessed using the Institute of Health Economics (IHE-20) checklist for single-arm studies (case series) [50].

The quality of the body of evidence was assessed using Grading of Recommendations, Assessment, Development and Evaluation (GRADE). The Authoring Team carried out risk-of-bias assessments independently and the author conducted the GRADE assessment. Disagreements were resolved by consensus.

## 2.7 Patient involvement (if applicable)

Patient involvement was planned, and European patient organisations, as well as national patient organisations from Spain, were contacted to provide input on the preliminary PICO and via the Health Technology Assessment International (HTAi) patient input form. We also invited individual patients through a local hospital. However, it was not possible to identify these patients or enlist their participation.

## 2.8 Description of the evidence used

**Table 2: Main characteristics of the studies included**

Author and year or study name	Study type	Number of patients	Intervention	Main endpoints	Included in clinical effectiveness and/or safety domain
Avci 2012 [25]	Single prospective cohort	11 AAA (Revision arm)	Aptus Heli-FX <sup>™</sup> EndoAnchor <sup>™</sup> System	Initial technical success (implantation of endoanchors) & clinical success (absence of graft-related complications or type Ia)	EFF & SAF
Deaton 2009 [27] (STAPLE I)	Single prospective cohort	21 AAA (Primary arm)	Aptus AAA Endovascular Repair System	Feasibility (successful deployment of all endograft components) & major device-related adverse events at 30 days	EFF & SAF
de Vries 2014 [26] (ANCHOR)	Single prospective cohort	319 AAA (242 Primary arm, 77 revision arm)	Aptus Heli-FX EndoAnchor System in conjunction with commercially available non-Aptus Endografts	Technical and procedural success; AE as Aneurysm & EndoAnchor-related reinterventions	EFF & SAF
Goudekettering 2019 [28]	Single prospective cohort	51 AAA (31 Primary arm, 20 revision arm)	Aptus Heli-FX EndoAnchor System in conjunction with commercially available non-Aptus Endografts	Procedure success (successful deployment of the endograft and the endoanchors)	EFF & SAF

Author and year or study name	Study type	Number of patients	Intervention	Main endpoints	Included in clinical effectiveness and/or safety domain
Jordan Jr 2014 [30] (ANCHOR)	Single prospective cohort	319 AAA (242 primary arm, 77 revision arm)	Aptus Heli-FX EndoAnchor System in conjunction with commercially available non-Aptus Endografts	Composite primary efficacy endpoints & composite primary safety endpoints	EFF
Jordan Jr 2015 [29] (ANCHOR)	Single prospective cohort	208 (ANCHOR primary arm patients with unfavourable neck anatomy according to site investigator)	Aptus Heli-FX EndoAnchor System in conjunction with commercially available non-Aptus Endografts	Technical success & primary safety endpoints	EFF
Jordan Jr 2016 [35] (ANCHOR)	Single prospective cohort	100 AAA (73 primary arm+27 revision arm).	Aptus Heli-FX EndoAnchor System in conjunction with commercially available non-Aptus Endografts	Composite primary efficacy endpoints & composite primary safety endpoints	EFF & SAF
Mehta 2014 [31] (STAPLE 2)	Single prospective cohort	153 AAA primary arm	Aptus AAA Endovascular Repair System	Primary safety endpoint: freedom from major adverse events at 30 days; primary effectiveness endpoint: successful aneurysm treatment at 12 months	EFF & SAF
Muhs 2018 [32]	Prospective cohort with propensity-matched retrospective controls	198 AAA (99 primary arm and 99 controls)	<u>Intervention group:</u> Aptus Heli-FX EndoAnchor System in conjunction with commercially available non-Aptus Endografts; <u>Control group:</u> endografts without use of Aptus Heli-FX EndoAnchor System	Freedom from migration, freedom from post-operative types I or III endoleaks, freedom from sac enlargement & estimated cumulative incidence of sac regression	EFF
Ongstad 2016 [33]	Single retrospective cohort	54 TAA (40 TAA+ 14 T/A AA) 27 primary arm and 27 revision arms	EndoAnchor System in conjunction with commercially available TEVAR endografts	Freedom from migration, freedom from aortic-related intervention & freedom from post-operative type I or III endoleaks	EFF & SAF

Author and year or study name	Study type	Number of patients	Intervention	Main endpoints	Included in clinical effectiveness and/or safety domain
Perdikides 2012 [34]	Single prospective cohort	13 AAA (primary arm)	EndoAnchor System in conjunction with commercially available EVAR endografts	Primary technical success & assisted primary technical success.	EFF & SAF

**Abbreviations:** AAA: abdominal aortic aneurysm; EFF: effectiveness; EVAR: endovascular aortic repair; SAF: safety; T/A AA: thoracoabdominal aortic aneurysm; TAA: thoracic aortic aneurysm; TEVAR: thoracic endovascular aortic repair.

## 2.9 Deviations from project plan

It was not possible to conduct an effectiveness or safety analysis vis-à-vis elective vs urgent endovascular procedures. In addition, safety analyses based on primary or revision arms were similarly impossible due to the difficulty of extracting adverse events data for these subgroup analyses.

### 3 DESCRIPTION AND TECHNICAL CHARACTERISTICS OF TECHNOLOGY (TEC)

#### 3.1 Research questions

Element ID	Research question
B0001	<p>What is Heli-FX™ EndoAnchor™ fixation system in EVAR/TEVAR procedures?</p> <p>What is Heli-FX™ EndoAnchor™ fixation system in the management of a type I endoleak or a stent/endograft migration in patients previously treated with EVAR/TEVAR?</p> <p>What are EVAR /TEVAR procedures conducted without the use of the Heli-FX™ EndoAnchor™ system?</p> <p>What are embolisation, extensions of grafts-proximal/distal, balloon angioplasty, metallic stents or open surgical repair (OSR) of endoleaks type I or stent/endografts migration in patients treated previously with EVAR/TEVAR?</p>
A0020	For which indications have Aptus™ Heli-FX™ & Heli-FX™ Thoracic EndoAnchor™ Systems from Medtronic (Minneapolis, MN, USA) received marketing authorisation or CE marking?
B0002	<p>What is the claimed benefit of Heli-FX™ EndoAnchor™ in patients at high risk of type I endoleaks or migration in relation to the comparator(s)?</p> <p>What is the claimed benefit of Heli-FX™ EndoAnchor™ in the management of type I endoleaks or stent/endograft migration in patients previously treated with EVAR/TEVAR in relation to the comparator(s)?</p>
B0004	<p>Who administers the Heli-FX™ EndoAnchor™ system during EVAR/TEVAR procedures, embolisation, and extensions of proximal/distal grafts, balloon angioplasties, metallic stents or open surgeries?</p> <p>In what context and level of care are Heli-FX™ EndoAnchor™ EVAR/TEVAR procedures, embolisation, extensions of proximal/distal grafts, balloon angioplasties, metallic stents or open surgical repairs provided?</p>
B0009	What equipment and supplies are needed to use Heli-FX™ EndoAnchor™ during EVAR/TEVAR procedures, embolisation, and extensions of proximal/distal grafts, balloon angioplasties, metallic stents or open surgical repairs?
A0021	What is the reimbursement status of the Aptus™ Heli-FX™ & Heli-FX™ Thoracic EndoAnchor™ Systems (Medtronic (Minneapolis, MN, USA))?

#### 3.2 Results

##### [B0001] – What is Heli-FX™ EndoAnchor™ fixation system in EVAR/TEVAR procedures?

The EndoAnchor is a helical-shaped intravascular-applied implant designed to aid the endovascular attachment of an endograft to the vessel wall; i.e., to engage the tissue and secure attachment of the endograft, in the form of a suture, to the vessel wall. The EndoAnchor is manufactured from 0.5 mm diameter medical-grade wire (nickel-cobalt) wire and meets the requirements of ISO 10993 (in accordance with the relevant FDA G95-1 guidance). Its total length is approximately 4.5 mm and it measures approximately 3 mm in diameter.

The Heli-FX EndoAnchor System is comprised of three components: an implant cassette (containing 10 endoanchors), a delivery mechanism (the Heli-FX Guide with obturator) and a deployment device (the Heli-FX Applier). The Heli-FX Guide (a deflectable sheath) with obturator

is a sterile, single-patient use, disposable device that directs the Heli-FX Applier to the desired location in order to fix the EndoAnchor implants. The obturator, which is compatible with a 0.89 mm (0.035") guidewire, allows the Heli-FX Guide to be advanced over the wire through the patient's vasculature. The Heli-FX Applier (catheter-based) is a sterile, single-patient-use disposable device designed to embed one EndoAnchor implant at a time. The Heli-FX Applier can be reloaded and deployed multiple times for the same patient. EndoAnchor implants are loaded into the Applier from the EndoAnchor Cassette by placing the distal end of the Applier into an unused EndoAnchor implant port, each one of which holds a single EndoAnchor implant. The EndoAnchor is implanted in a two-stage process, allowing the physician to retract the EndoAnchor and re-position it before final deployment. Audible tones and visible lights during the procedure indicate the endoanchors' position and the available directions of motion.

The EndoAnchor™ is intended to provide both fixation and sealing between the endovascular aortic endo-grafts and the native artery during the procedures to treat AAA or TAA. It may be implanted at the time of the initial endograft placement, in either a hostile or complex neck (AAA), and/or in cases presenting a high risk of type I endoleaks or migration [1].

**[B0001]- What is EndoAnchor fixation system in the management of type I endoleaks or stent/endograft migrations in patients previously treated with EVAR/TEVAR?**

Endoleaks are defined as persistent blood flow perfusing the residual aneurysm sac, thus indicating a failure to completely exclude the aneurysm. A type I endoleak stems from an incompetent seal at the proximal (type IA) or distal (type IB) endograft attachment site [15]. Endoleaks can also be classified based on the time of their first detection: perioperative (within 24 hours), early (1-90 days after EVAR) and late (after 90 days) [11]. Endograft or stent migration is defined as a displacement of more than 5–10 mm from its original position [15].

Fixation with EndoAnchor is an endovascular procedure for repairing an intraoperative, early or late type I endoleak or endograft migration, with the deployment of endoanchors evenly distributed across the circumference of the endograft's main body [2].

**[B0001]- What are EVAR /TEVAR procedures conducted without the use of the EndoAnchor system?**

The conventional treatment for abdominal aortic aneurysms consists of placing a polyester tube graft, the ends of which are sutured to the arterial wall, both proximally and distally to the aneurysmal dilatation, thereby preventing blood flow from straining the wall of the aneurysm. [18] The introduction of EVAR by Parodi et al. in 1991 [51] revolutionised the treatment of aortic aneurysms [8].

Endovascular repair (EVAR/TEVAR) is based on the insertion of an endoprosthetic device through the femoral or iliac artery. The device is then deployed within the lumen of the aorta, so its ends are anchored to the normal artery, both proximally and distally, to the aneurysm. After the sheath is released, the elasticity of the stent graft provides radial strength, which keeps the device fixed to the neck of the aneurysm. Some stents have hooks or barbs to improve fixation to the arterial wall.

In general, standard criteria for EVAR procedures in AAA patients include: proximal aortic neck (normal aortic segment between the lowest renal artery and the most cephalad dimensions of the aneurysm) between 10-15 mm; a diameter not greater than 32 mm and an angulation below 60 degrees [22].

The United Kingdom's NHS, in their draft guidelines, defines these complex EVAR procedures as any endovascular strategy that falls outside the 'instructions for use' for aortic stent grafts, typically adopted because of an AAA's anatomical complexity (i.e., hostile or unsuitable neck). This includes using unmodified endografts outside their 'instructions for use', physician-modified endografts, customised fenestrated endografts, and 'snorkel' or 'chimney' approaches with parallel covered stents. [10, 52] In general, these advanced procedures are less frequently used and more expensive [53].

In asymptomatic TAA patients, TEVAR is often indicated when the maximum diameter of the aneurysm exceeds 5.5 cm or if rapid expansion (0.5 mm in 6 months) occurs. In certain morphologic situations considered prone to rupture (e.g., saccular aneurysms), TEVAR may be justified at a diameter of less than the above-referenced 5.5 cm. [4].

More advanced TEVAR procedures are needed in the management of a proximal or distal short neck in TAA patients. Management of the proximal landing zone remains challenging in cases of short proximal necks or severe angulations of the arch. In such instances, if coverage of the left subclavian cannot sufficiently tolerate a compromised proximal sealing, then the development of alternative techniques, such as hybrid repair with debranching, chimneys, fenestrations and branches, or scallops should be considered [54].

New generations of endografts and stents require a variety of strategies to avoid endoleaks or device migration or both, including placing hooks on the endografts, using outward radial forces to attach self-expanding stent-grafts to the inner surface of the aortic neck and generally trying to avoid complications and reinterventions. However, emerging endovascular technologies focusing on intrasac sealing instead of fixation comprise a new research field, as the hemodynamic basis of medium- and long-term sealing is not fully understood [55].

**[B0001] – What are embolisation, extensions of grafts-proximal/distal, balloon angioplasty, metallic stents or open surgical repair (OSR) of endoleaks type I or stent/endografts migration in patients treated previously with EVAR/TEVAR?**

The objective of these treatments is to seal a type I endoleak. Some of these techniques are often used in combination. Microcatheter embolisation involves agents like N-Butyl cyanoacrylate, glue, dimethyl sulfoxideethylene vinyl alcohol solution and coils, or a combination of coils and liquid embolic agents. Embolisation can be performed using a transarterial approach or by direct percutaneous puncture of the aneurysm sac via a transabdominal, trans-lumbar (left side), or trans-caval (right side) approach. Transluminal balloon angioplasty moulds the endograft to the aortic wall and decreases the infolding of an oversized graft. It is sometimes used with a Palmaz graft extension. Endograft cuffs or additional stent-graft placement are "extensions" to the initial endograft deployment. They include the use of metallic, fenestrated or branched stents. Conversion to an open procedure may be the only option when a type I endoleak becomes uncontrollable. The traditional approach for late surgical conversion entails complete endograft removal, followed by aortic replacement with a standard surgical prosthetic graft [56, 57].

**[A0020] – For which indications have Aptus™ Heli-FX™ & Heli-FX™ Thoracic EndoAnchor™ Systems from Medtronic (Minneapolis, MN, USA) received marketing authorisation or CE marking?**

The Heli-FX EndoAnchor System is intended to provide fixation and sealing between endovascular aortic endografts and the native artery. The Heli-FX EndoAnchor System is indicated for use in patients whose endovascular endografts have exhibited a migration or endoleak, or who are at risk



of such complications, and in whom augmented radial fixation and/or sealing is required to regain or maintain adequate aneurysm exclusion. The EndoAnchor may be implanted at the time of the initial endograft placement, or during a secondary (i.e., repair) procedure [1].

From the Indications for Use (IFU) and from the manufacturer's website [Medtronic, Minneapolis, MN, USA], it appears that the Heli-FX™ EndoAnchor™ system has been evaluated and is compatible with the following endografts used for abdominal aortic aneurysm treatment: Medtronic Endurant, Medtronic Talent™, Medtronic AneuRX™, Cook Zenith™, Gore Excluder™, Jotec E-vita™; its use in combination with the Endologix Powerlink® endoprosthesis is contraindicated.

In addition, both the IFU and the manufacturer's website report that the Heli-FX™ EndoAnchor™ thoracic system has been evaluated and is compatible with the following prostheses used for the treatment of thoracic aortic aneurysm: Medtronic Valiant™ with Captivia™ release system, Medtronic Talent™, Cook Zenith TX2™, Gore TAG™ and E-Vita™ [1].

Detailed tables on CE certification can be found in **Appendix 1**

**[B0002] – What is the claimed benefit of Heli-FX™ EndoAnchor™ in patients at high risk of type I endoleaks or migration in relation to the comparator(s). What is the claimed benefit of Heli-FX™ EndoAnchor™ in the management of type I endoleaks or stent/endograft migrations in patients previously treated with EVAR/TEVAR in relation to the comparator(s)?**

No direct comparison was reported. ANCHOR includes post-clearance use of the Heli-FX™ system with primarily grafts from Medtronic (Minneapolis, MN, USA), Gore Excluder™\* grafts, Cook Zenith™\* grafts and Jotec E™\* -vita grafts.

By recreating the durability of a sutured anastomosis, the EndoAnchor System protects AAA patients against neck dilatation and promotes sac regression, which have been shown to be better predictors of long-term survival [3]. The marketing authorization holder (MAH) website showed no claimed benefits deriving from the use of the EndoAnchor System in TAA patients.

**[B0004] – Who administers the endoanchors during EVAR/TEVAR procedures, embolisation, and extensions of proximal/distal grafts, balloon angioplasties, metallic stents or open surgical repairs?**

The system must be used exclusively by specially trained teams and physicians (vascular surgeons, interventionist radiologists, heart surgeons or cardiologists). It is intended for use in vascular intervention techniques, including endovascular repair of aneurysms and in tandem with the anchoring system. A Hybrid operating room is preferred in cases requiring conversion to open surgical repair [4, 5]. Although regular operating rooms have been used, some authors propose a Hybrid operating room as preferred in case of conversion to open surgical repair.

**[B0004] – In what context and level of care are endoanchors EVAR/TEVAR procedures, embolisation, and extensions of proximal/distal grafts, balloon angioplasties, metallic stents or open surgical repairs provided?**

The literature suggests that endoanchors, EVAR/TEVAR procedures, embolisation, extensions of proximal/distal endografts, balloon angioplasties, metallic stents or open surgical repairs should take place at a tertiary referral hospital in a hybrid operating room [4, 5].

**[B0009] – What equipment and supplies are needed to use the Heli-FX™ EndoAnchor™ during EVAR/TEVAR procedures, embolisation, and extensions of proximal/distal grafts, balloon angioplasties, metallic stents or open surgical repairs?**

Besides the device itself (endografts, extensions of proximal/distal grafts, balloon angioplasties, metallic stents) and the embolisation solutions, a complete endovascular laboratory (with endovascular equipment and guide wires) and a hybrid operating room are preferable.

The equipment used by the multidisciplinary team must include the following capabilities:

- Vascular access and management of any related complications,
- Non-selective and selective guide wire and catheter techniques,
- Fluoroscopic and angiographic image interpretation,
- Snare techniques,
- Appropriate use of radiographic contrast material and techniques to minimise radiation exposure [1, 58].

**[A0021] – What is the reimbursement status of the Aptus™ Heli-FX™ & Heli-FX™ Thoracic EndoAnchor™ Systems (Medtronic (Minneapolis, MN, USA))?**

Reimbursement policies are variable throughout the EU. In England, the Heli-FX™ EndoAnchor™ system is categorised as an “endovascular fixation device” under the “endovascular stent grafts” category of the High-Cost Devices (HCD) list; thus, the NHS reimburses hospitals when a Heli-FX is used. In Germany, Heli-FX has a specific OPS code (5-98c.4) and is currently classified as NUB status 1 for repairs (hospitals are reimbursed at a negotiated rate).

This is similar to some US healthcare insurance systems, although this codification does not impact the reimbursement of endovascular (EVAR/TEVAR) surgical procedures in Germany as it does in the USA healthcare system [59]. In the UK, the Heli-FX™ EndoAnchor™ has recently been added to the HCD list, which affords hospitals the opportunity to apply for additional reimbursement from the NHS to offset the cost of Heli-FX at a negotiated rate [60]. In Spain, the device is reimbursed separately. Other countries do not provide specific reimbursement for the Heli-FX™ EndoAnchor™ system. In many other European countries, Heli-FX™ EndoAnchor™ is covered as part of the main procedure (e.g., EVAR or TEVAR) or even under a more general grouping such as hybrid cardiac surgery.

## 4 HEALTH PROBLEM AND CURRENT USE OF THE TECHNOLOGY (CUR)

### 4.1 Research questions

Element ID	Research question
A0002	How is “high risk” defined for type I endoleaks or stents/endograft migrations in aortic aneurysm disease? How is type I endoleaks or migrations defined in patients who have previously undergone EVAR/TEVAR procedures?
A0003	What are the known risk factors for those at high risk of type I endoleaks or stents/endograft migrations in aortic aneurysm disease? What are the known risks for type I endoleaks or stents/endograft migrations following EVAR/TEVAR procedures?
A0004	What is the natural course in aortic aneurysm disease for those at high risk of type I endoleaks or migrations? What is the natural course of type I endoleaks stents/endograft migrations after EVAR/TEVAR procedures?
A0005	What are the symptoms and disease burden of patients at high risk of type I endoleaks or migrations who are suffering aortic aneurysm disease? What are the symptoms and the burden associated with type I endoleaks or stent/endograft migrations after EVAR/TEVAR procedures?
A0024	How is high risk of type I endoleaks or stent/endograft migrations in aortic aneurysm disease currently diagnosed according to published guidelines and in practice? How are type I endoleaks or stent/endograft migrations currently diagnosed according to published guidelines and in practice?
A0025	How is high risk of type I endoleaks or stent/endograft migration in aortic aneurysm disease currently managed according to published guidelines and in practice? How are type I endoleaks and stent/endograft migrations currently managed according to published guidelines and in practice?
A0007	What is the target population in this assessment?
A0023	How many people belong to the target population?
A0011	How often is the Heli-FX <sup>TM</sup> EndoAnchor <sup>TM</sup> system utilised?

### 4.2 Results

#### Overview of the disease or health condition

**[A0002] – How is high risk defined for type 1 endoleaks or stents/endograft migrations in aortic aneurysm disease?**

AAA patients:

The principal challenge confronting EVAR procedures for AAA disease is the unfavourable morphology of the aneurysm, as well as the potentially adverse anatomic characteristics of the infrarenal aortic neck in particular. These issues have long restricted the widespread applicability of EVAR [6].

The term “hostile neck” in AAA was first used by Dillavou in 2003 to characterise EVAR outcome in patients with unfavourable aortic neck anatomies (marked angulation, short length, complex shape, wide diameter or the presence of calcification or thrombus) [7, 61]. Subsequently this term was more widely adopted when the aortic neck anatomy of AAA cases fell outside the eligibility criteria for approved stent endograft indications and their clinical trials [8, 62]. Currently, the broader term “complex” or “unsuitable” neck encompasses short or absent necks, angulated necks, conical necks, or large necks exceeding the size availability of current stent grafts, all of which have been linked to an increased risk of type I endoleaks or stent/endograft migrations [6, 10]. Some authors are now using the term “Juxtarenal AAA (JRAAA)” as a way of extended definition, though this does not involve the renal arteries, this newly expanded definition does take in those cases necessitating suprarenal aortic clamping for open surgical repair, including AAA patients who present a short neck (< 10 mm) [5, 63]. The NICE (UK) guidelines, still in progress, have adopted the more general term “Complex EVAR” to encompass all EVAR procedures (stents used out of IFU, physician-modified endografts, customised fenestrated endografts, parallel covered stents) that are typically adopted due to an AAA’s anatomical complexity (i.e., hostile necks) [52].

#### TAA patients:

In TAA patients, the endoleak occurrences are associated with many factors besides the anatomic characteristics of short, proximal or distal necks (landing zones). The specific proximal landing zone of the aortic arc (described by Ishimaru as zones 0-4) has been well studied. Zones 0-2-1 have been identified as being prone to higher occurrences of type 1 endoleaks than zone 4. In general, larger and more extensive TAAs and the position of the landing zone for endografts in the thoracic aorta constitute the definition of high-risk TAA for type 1 endoleaks and migrations [11, 64].

Due to the technical problems that unsuitable necks pose to endovascular procedures, the incidence of complications such as aneurysmal rupture, which has been linked to type 1 endoleaks (HR 0= 7.6; 90%IC: 2.1 to 27.6) and migration (HR= 4.5; 90%IC: 1.2 to 16.7) is higher [13, 14].

#### **[A0002] – How is type I endoleaks or migrations defined in patients who have previously undergone EVAR/TEVAR procedures?**

Endoleaks are defined as persistent blood flow perfusing the residual aneurysm sac, and are indicative of a failure to exclude the aneurysm completely. A type I endoleak typically occurs because of an incompetent seal at the proximal (type Ia) or distal (type Ib) endograft attachment site [15]. Based on the time of their first detection, endoleaks can also be classified as perioperative (within 24 hours), early (1-90 days after EVAR/TEVAR) or late (after 90 days) [11].

Endograft or stent migration is a displacement of more than 5–10 mm from its original position, or a movement of the stent graft > 10 mm compared to fixed anatomical landmarks verified using flow centreline CT reconstructions, or any migration resulting in symptoms or re-intervention [5, 15].

#### **[A0003] – What are the known risk factors for those at high risk of type I endoleaks or stents/endograft migrations in aortic aneurysm disease?**

Female gender is the most common risk factor for presenting unsuitable or hostile necks in infrarenal AAA, according to the Characterisation of Aortic Aneurysm Project. The authors of this

project identified a gender difference, with women tending to present shorter neck lengths and a neck angulation exceeding 60 degrees more often compared to men [65]. Women are more likely than men to have a neck length of < 4 mm and a neck angulation > 45 degrees [66]. A recent systematic review (SR) on gender differences vis-à-vis the suitability of EVAR procedures for elective AAA found an overall pooled proportion of women eligible (34%) for EVAR, which was lower than the rate in men (54%) (OR = 0.44, 95% CI 0.32 to 0.62) [67]. Female gender was also found to be a risk factor for intraoperative type I endoleaks in patients who underwent EVAR procedures [68].

There was no gender-based difference in the proportion of TAA cases with hostile proximal necks, hostile distal necks, or both, according to Jackson et al [69].

The role of age as a known risk for unsuitable or hostile necks in cases of infrarenal AAA or for type I endoleaks or migrations is less described. Png et al. found an increased prevalence of type I endoleaks with a ratio (incidence ratio: person-years) of 1.89 (CI95%:1.19 to 3.00) in those patients >70 years old patients after undergoing EVAR [70].

The generally accepted EVAR device IFU criteria for a suitable aortic neck are an infrarenal neck diameter of 18-32 mm, an infrarenal neck length of at least 15 mm, an infrarenal neck angulation of <60 degrees, and an iliac access lumen of at least 6 mm. In the older patients with AAA, Sweet et al. estimated an adjusted OR = 0.84 per decade and an adjusted OR=0.4 for female gender as a “protector factor or prevention” of having a suitable neck. Therefore, age and female gender appear to increase the likelihood of having a hostile neck [65]. No clear role of age as a risk factor for type I endoleaks or endograft migrations in TAA patients was found.

#### **[A0003] – What are the known risks for type I endoleaks or stents/endograft migrations following EVAR/TEVAR procedures?**

##### AAA patients:

##### *Type I endoleaks:*

A SR and a meta-analysis (MA) found that unfavourable aortic neck anatomy (hostile neck anatomy: neck length <15 mm and neck angulation >60) equated to a 4-fold increased risk of developing a type I endoleak (OR = 4.56; 95% CI, 1.43 to 14.56) compared with patients who presented a friendly AAA neck anatomy [6].

Tan et al also identified an increased risk of type I endoleaks in < 70-year-old patients (OR = 2.0; 95%CI, 1.1 to 3.8) and those of female gender (OR = 2.2; 95%CI, 1.3 to 3.7) [71].

##### Intraoperative type I endoleaks:

Aortic neck calcification and aortic curvature have been found to be independent predictors of intraoperative type I endoleaks in EVAR patients, with a final regression model AUC = 0.77 95% CI; 0.70 to 0.85 [17].

##### Early type I endoleaks:

AbuRahma et al. only identified reverse taper (as a gradual neck dilatation of >2 mm occurring within the first 10 mm distant from the most caudal renal artery) as an anatomical neck feature in post-EVAR patients (second generation devices) as being related to early type I endoleaks (OR = 5.25; 95% CI 2.4 to 11.46) [72].

### *Endograft migrations:*

The angulation, extension, and diameter of the neck and transversal measure of the aneurysmatic sac are important morphological aspects related to migration in AAA. In terms of technique, endoprosthesis implantation in cases of excessive oversizing (> 30%) is not recommended as it can lead to aortic neck dilatation, folds and proximal leakage, which can also contribute to migration [18]. Shuurmann et al. described maximum curvature over the length of the aneurysm sac (>47 m<sup>-1</sup>), the widest aneurysm sac diameter (>56 mm), and mural neck thrombus (>11° circumference) as predictors of late type I endoleaks and migrations in EVAR patients (AUC = 0.80; 95%CI: 0.72 to 0.89) [73].

### TAA patients:

#### *Type I endoleaks:*

The Ishimaru landing zones are used to describe the aortic anatomy during endovascular repair. Zone 0 includes the ascending aorta and the origin of the brachiocephalic artery. Zone 1 includes the origin of the left common carotid artery, and Zone 2 the left subclavian artery origin. Zone 3 is longer, extending to an imaginary border at the end of the arch curvature, where Zone 4 begins [74]. Kanoaka et al. described significantly higher numbers of type I endoleaks in zones 0–2 compared to those in zone 4 (OR = 10.9; 95% CI 2.6 to 46.3). They also described a proximal neck diameter ≥38 mm (OR= 3.6; 95% CI 1.2 to 10.8) among the anatomical features associated with TAA [64]. Ueda et al. described the increased risk of type I endoleaks with the bird-beak configuration, which signifies the radiologic detection of a wedge-shaped gap between the under-surface of the stent graft and the aortic wall (OR= 14.73; 95%; CI 2.95 to 73.55) [75].

### *Endograft migrations:*

The only reported risk factors for endograft migration, independent of a type I endoleak, are aortic elongation and changes in the curvature of the TEVAR stent graft [19, 20].

### **[A0004] – What is the natural course in aortic aneurysm disease for those at high risk of type I endoleaks or migrations?**

A study by Tassiopoulos et al. reported that 13% of patients after EVAR had significant aneurysm neck dilatation. If aneurysms are left untreated, the natural history of the proximal aneurysmal neck is progressive dilatation in diameter and shortening of length [56]. Continuing aortic neck dilatation is reported to occur in up to 43% of patients after open repair, whereas the incidence of false-aneurysm formation is 1.3–3% during long-term follow-up. However, neck dilatation has been reported in up to 28% of patients at 2 years and in 59% at 4 years and is associated with adverse mid-term outcomes after EVAR [76].

### **[A0004] – What is the natural course of type I endoleaks stents/endograft migrations after EVAR/TEVAR procedures?**

Patients who undergo EVAR/TEVAR require lifelong surveillance because type I endoleaks and stent migrations can lead to both aneurysm expansion and rupture [13, 77].

### AAA patients:

#### *Type I endoleaks and endograft migrations*

In a 5-year follow-up study by Parent et al., type I endoleaks were detected in 2% of post-EVAR patients at 36 months [78]. One SR reported increased rates in 30-day type I endoleaks (OR 2.92, 95% CI 1.61 to 5.30; p, 0.001) and late type I (OR 1.71, 95% CI 1.31 to 2.23) in hostile neck. Thus, the natural course of post-EVAR is a worsening rate of type I endoleaks, both at 30 days and at 1 year post-EVAR when comparing friendly necks to hostile necks [79].

Graft migration without a loss of proximal fixation length has a benign natural history, eliminating the need for reinterventions. However, in cases where the increased infrarenal aortic neck diameter involves oversizing, infrarenal aortic neck shortening or loss of proximal fixation length, there are more clinically relevant predictors of proximal stent graft failure, usually requiring a reintervention [80].

#### TAA patients:

##### *Type I endoleaks and endografts migration*

Adams et al. reported type I endoleaks in 21% (27/129) of patients post-TEVAR after 25 months of follow-up. Fifty-nine percent (16/27) closed spontaneously, 30% (8/27) required secondary endovascular intervention, and 11% (3/27) persisted with no increase in maximum aortic diameter. No patients died or required open surgical conversion as a result of their type I endoleak [81]. Melissano et al. reported a persistent prevalence of type I endoleaks and stent migrations as cause of late open surgical repairs in post-TEVAR patients [82].

#### **Effects of the disease or health condition**

**[A0005] – What are the symptoms and disease burden of patients at high risk of type I endoleaks or migrations who are suffering aortic aneurysm disease? What are the symptoms and the burden associated with type I endoleaks or stent/endograft migrations after EVAR/TEVAR procedures?**

It is well known that most patients with AAA will be asymptomatic at the time of diagnosis. Less frequently, the first presentation of an unrecognised AAA may involve a symptomatic aneurysm manifested by abdominal or back pain, a pulsatile abdominal mass or even rupture. However, there are no specific symptoms for AAA patients at high risk of type I endoleaks or stent migrations [21, 22].

Most asymptomatic T/A AA cases are discovered incidentally, while symptomatic patients usually present complications. A new onset of hoarseness or dysphagia may indicate a developing aneurysm in the distal aortic arch and proximal descending aorta. Chest pain, back pain and signs of malperfusion are often missed due to a lack of diagnostic accuracy. As with AAA, there is no typical clinical manifestation in patients at high risk of type I endoleaks or stent migrations in TAA [22, 23].

Type I endoleaks and stent migrations are radiologic signs linked to a high risk of aortic rupture, although there are no recognised or associated symptoms for these conditions [22, 23, 57].

#### **Current clinical management of the disease or health condition**

**[A0024] – How is high risk of type I endoleaks or stent/endograft migrations in aortic aneurysm disease currently diagnosed according to published guidelines and in practice?**

#### AAA patients:

According to most of the guidelines—and independently of an established national screening program to detect AAA (ultrasound evaluation)—assessments of the progress and anatomic characteristics of AAA are preferably done by CT angiography, although other options include Magnetic Resonance Imaging (MRI), Digital Subtraction Angiography (DSA) and Positron Emission Tomography/Computed Tomography (PET/CT) [22, 83-85].

#### TAA patients:

For TAA patients, CT angiography (CTA) is the method of choice for diagnosing and planning treatment. Magnetic resonance imaging (MRI), transoesophageal echocardiography and PET/CT may also be used. Conventional angiography is no longer recommended as a routine diagnostic procedure [4, 23].

### **[A0024] – How are type I endoleaks or stent/endograft migrations currently diagnosed according to published guidelines and in practice?**

#### AAA patients

In the follow up for post-EVAR patients, the preferred imaging technique is contrast-enhanced CT angiography (to detect postoperative complications and further aneurysm expansion). If contrast-enhanced CT angiography is contraindicated, contrast-enhanced ultrasound can be utilised to detect endoleaks and further aneurysm expansion [22, 23, 27]. In practice, CT remains the standard for surveilling patients post-EVAR [86].

#### TAA patients:

In two European guidelines from 2012 and 2017, CT or MRI was recommended for follow-up evaluations of post-TEVAR procedures; further follow-ups at 6 and 12 months can be made using CT angiography and annually thereafter MRI/CT angiography [4, 23]. In practice, CT is the main technique used for follow-up evaluations in post-TEVAR procedures [87].

### **[A0025] – How is high risk of type I endoleaks or stent/endograft migrations in aortic aneurysm disease currently managed according to published guidelines and in practice?**

#### AAA patients:

According to most European guidelines, including two published in recent years and one in draft, the first option for unsuitable, complex or short necks in AAA patients is open surgical repair [22, 52, 83]. A 2016 Spanish guidelines recommend EVAR procedures with fenestrated stents, while a European guidelines recommend both treatments: open surgical repair or complex endovascular repair (fenestrated, or parallel endografts) [5, 84]. Regarding complex EVAR procedures, most European guidelines first recommend a fenestrated (versus parallel) endograft (Chimney or snorkel) approach [5, 83, 84]. Only one guideline, that from the UK's National Institute for Health and Care Excellence (NICE), advises against complex EVAR procedures in these patients. This is true even in cases considered unsuitable for open surgical repair in un-ruptured AAA, or as part of randomised controlled trials comparing complex EVAR with open surgical repair in ruptured AAA patients. Nevertheless, these guidelines remain under review and a draft with preliminary conclusions is referenced. [52]. Only the European Society for Vascular Surgery (ESVS) recommends the newly introduced technique, the Heli-FX™ EndoAnchor™ system, in cases involving an endovascular aneurysm seal and in situ laser fenestration [5].

#### TAA patients:



In patients with descending TAA, open surgical repair is the first option in unsuitable anatomies or in the absence of landing zones for TEVAR procedures [23]. A recently updated medical technologies guidance from NICE recommends a hybrid one-stage approach (E-vita open plus) for treating complex aneurysms such as ascending, arch or descending aortic aneurysms [88].

Patients presenting a thoracoabdominal aneurysm and unsuitable anatomy are not the best candidates for TEVAR procedures in ruptured or non-ruptured T/A AA. A hybrid procedure is an option for most such cases [23].

**[A0025] – How are type I endoleaks and stent/endograft migrations currently managed according to published guidelines and in practice?**

The management of type I endoleaks and stent migrations as complications from EVAR or TEVAR procedures are included in more general guidelines addressing the endovascular management of AAA or TAA, although there are fewer regarding the latter than the former.

Management of type I endoleaks in post-EVAR procedures:

In general, most guidelines recommend an endovascular approach for treating early or late type I endoleaks with no distinction made as to the preferred option and with different levels of evidence (see Table A1) [5, 22, 83]. Only NICE guidelines recommend open, endovascular or percutaneous management of type I endoleaks (draft guidelines) [52].

In practice, first-line approaches consist of standard endovascular strategies such as cuff extensions or open repair [89]. When these prove insufficient, other endovascular or open strategies are available, including fenestrated or parallel (chimney/snorkel) stents, embolisation, endostaples, iliac branch devices, or conversion to open surgical repair [2, 11, 22, 90, 91].

Management of stent migration post-EVAR:

In general, most AAA or TAA management guidelines did not include specific recommendations on treating stent migration; only a German set of guidelines advised an endovascular approach with no further distinctions among the different options [83].

In practice, migration becomes clinically significant only when it results in a loss of proximal fixation length, which is the case when the aortic neck shortens. Only these patients must be treated with a cuff; those without loss of proximal fixation length require no therapy [83]. Treatment for caudal device migration depends on anatomic considerations, including the quality of the aortic seal zone, as well as the distance between the renal arteries and the flow divider of the original endograft. Options include conversion to an aorto-unilateral iliac bypass with crossover femoral-femoral bypass and iliac occlusion or placement of an aortic extension cuff, although some guidelines only recommend aortic extension to treat migration. Alternatives include proximal extensions with branched or fenestrated endografts or endostaples (in conjunction with aortic cuff extensions) [7, 15, 21]. A SR from 2000 to 2014, which encompassed all stent types used in EVAR procedures (except fenestrated or chimney procedures) and stent migrations evident during follow-up, found that the most widely used option for managing stent migration was aortic cuff extension, followed by open repair and an aorto-uni-iliac device [92].

**Table 3: Treatment options for post-EVAR procedures:**

<b>Common device-related and systemic complications post-EVAR and recommended management approaches [2, 11, 15, 21, 90]</b>	
<b>Complications</b>	<b>Management</b>
<b>Device-related complications</b>	
Type I endoleaks	Use of balloon angioplasty (First/Common option); Endograft extension(s): Palmaz, fenestrated or parallel (chimney/snorkel) stents; embolisation (glue or coil); endostaples; Iliac branch devices (in type IB endoleaks); Conversion to open surgical repair.
Stent migration	Use of large balloon-expandable stents; Aortic/proximal extensions; Aorto-uni-iliac devices; Fenestrated or parallel (chimney/snorkel) stents; endostaples; Conversion to open surgical repair.

**Management of type I endoleaks post-TEVAR:**

Although two sets of European guidelines recommend the prompt treatment of type I endoleaks, neither indicated a preferred option, and only one described coil embolisation, plug occlusion or surgical ligation as indistinct options [4, 23]. Some experts recommend balloon angioplasty as a first option, followed by a Palmaz stent or other cuff extension; and, less frequently, coil embolisation or fenestrated/parallel stents and open surgery [57].

In practice, the most commonly used treatments are extension cuffs, embolisation or open surgery [75, 82, 93].

**Management of stent migration post-TEVAR:**

Only one of the European guidelines mentions makes the general recommendation of “prompt intervention” when evidence of stent migration appears during follow-up, albeit with no distinction made as to the preferred management option or level of evidence criteria [23].

In practice, the preferred options for stent migration are endovascular procedures, with the occasional conversion to open surgical repair [82, 94].

**Target population****[A0007] – What is the target population in this assessment?**

AAA in men of European origin can be defined as an abdominal aortic diameter of 3.0 cm in either the anteroposterior or transverse planes. A lower threshold might be more appropriate in women and some Asian populations. AAA also can be defined when the maximum diameter is > 50% greater than the suprarenal diameter [5]. Many patients at the time of diagnosis present a small

aneurysm, particularly with screening programs, and are thus not suitable for surgical reparation. The presence of an abdominal aortic diameter  $\geq 3.0$  cm, based on external ultrasound diameters, had a sensitivity of 67.86% (CI 95% 54.04% to 79.71%) and a specificity of 97% (CI 95% 96.25% to 97.28%) in predicting the need for AAA repair within 10 years (Diagnostic Odds Ratio 63.73 95% CI: 35.54 to 114.27) [95].

The increased selection of EVAR procedures for the elective treatment or for ruptured AAA in non-suitable or hostile necks represents a target population for the Heli-FX™ EndoAnchor™ system, even in cases falling outside IFU regarding endografts [96]. Endografts compatible with the Heli-FX EndoAnchor system include the following: Cook Zenith™, Cook Zenith TX2™, Gore Excluder™, Gore TAG™, Jotec E™-vita abdominal, Jotec E™-vita thoracic, Medtronic AneuRx™, Medtronic Endurant™, Medtronic Talent™ AAA, Medtronic Talent™ TAA, and Medtronic Valiant™ [1]. The US FDA expanded their indications of use for the Endurant II/IIIs Stent Graft System to include treatment of infrarenal abdominal aortic aneurysms with neck lengths  $> 4$  mm and  $< 10$  mm (“short necks”) when used in conjunction with the Heli-FX EndoAnchor System [97].

Type I endoleak and/or endograft migration management in post-EVAR patients represents another target population for the Heli-FX EndoAnchor system, with or without the use of other endovascular treatments [1].

TAA is defined as a permanent localised dilatation of an artery, exhibiting at least a 50% increase in diameter compared to the expected normal diameter of the evaluated artery [23, 98].

Type I endoleak and/or endograft migration management in post-TEVAR patients constitutes yet another target population for the Heli-FX EndoAnchor system, with or without the use of endovascular treatments [57].

### **[A0023] – How many people belong to the target population?**

#### AAA patients:

The estimated incidence of clinical AAA in persons aged 45-64 years in the United States was 3.17 per 1,000 person-years in men and 0.95 per 1,000 person-years in women, according to the retrospective population-based Atherosclerosis Risk in Communities (ARIC) cohort study involving 15,703 persons aged 45-64 years; median follow-up was 22.5 years [99].

Endovascular abdominal aortic aneurysm (AAA) repair accounted for 41% of all elective aortic aneurysm repairs and 10.6% of all ruptured aortic aneurysm repairs performed in the U.S in 2003 [100]. In a 10-year retrospective German cohort, the percentage of patients who received endovascular treatment rose from 29% to 75% in those with non-ruptured AAA, and from 8% to 36% in those with ruptured AAA [101].

#### *Type I endoleaks and migrations in EVAR*

An HTA comparing open surgical repair vs EVAR treatment for AAA identified ten studies (n=2,617) that reported an occurrence rate of 4.2% for type I endoleaks within 30 days. The overall incidence was 3.5% (range 0–14 %) after one year in the 13 studies (n=2,544) included. The incidence of type I endoleaks beyond 1 year was 6.7 % (range 0 to 21.5 %) for the 18 studies included (n=7,848) [102]. A recent cohort of EVAR-treated AAA patients also found a global type I endoleak incidence of 3.3% [71]. Some authors reported a range of intraoperative type I endoleaks of 0%-30% (mean 7.5%) [103].

Mehta et al. reported a late stent migration rate of 2.6% in EVAR patients [104]. A SR from Spanos et al. estimated a frequency of 8.6% based on 22 retrospective studies (200-2014). In addition, 87/389 of the patients with a migration also presented a concomitant type I endoleak (22.4%) [92]. A recent review estimates a stent migration frequency of 1% in EVAR patients after 5 years of follow-up [5]. While stent/graft migration was a common event with first-generation stent grafts, the development of active supra- or infrarenal fixation in newer stent grafts has reduced the prevalence of this complication [5].

#### TAA patients:

The overall incidence rate of TAA is about 10 per 100,000 person-years, according to a Canadian HTA. The descending aorta was involved in about 30% to 40% of these cases [105].

#### *Type I endoleaks and migrations in TEVAR*

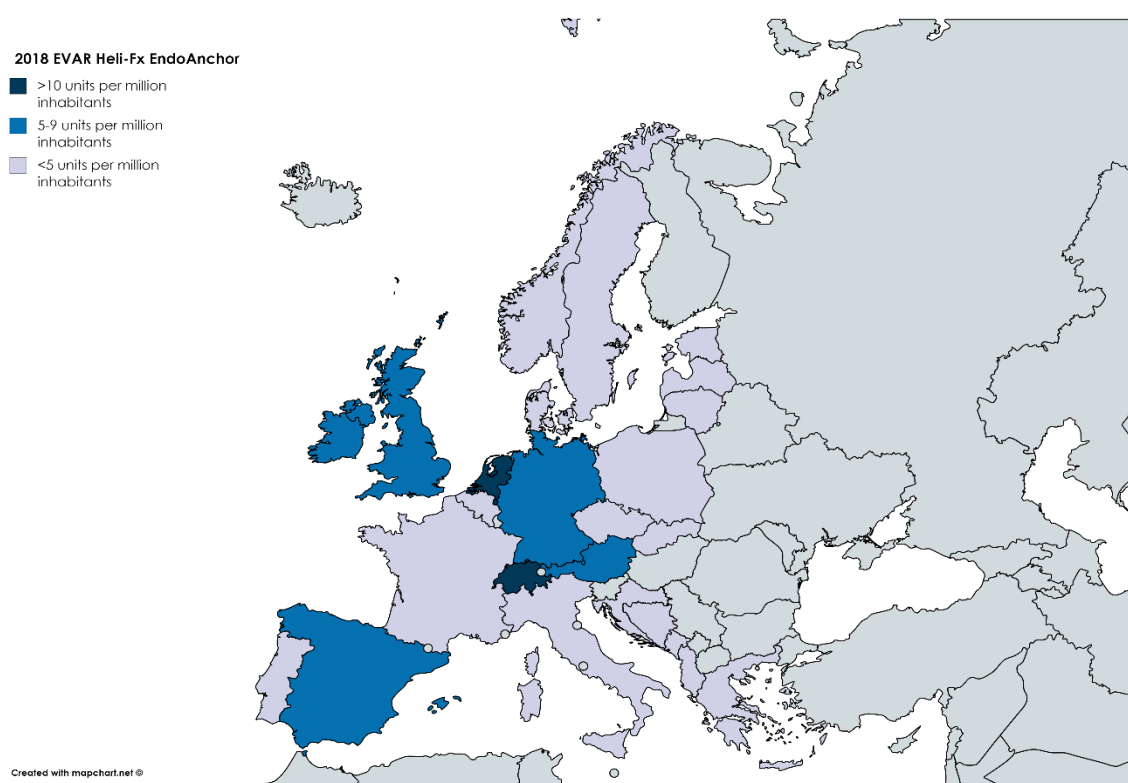
A Canadian HTA (drawing on data from articles published during the years 2000 to 2005) found an overall incidence of graft migration of 2.6% across 8 studies (363 patients, range of follow-up: 12 m-38 m) in TEVAR patients who suffered descendent TAA. In this HTA report data from EUROSTAR, the United Kingdom Thoracic Endograft Registries (1997 to 2003) and some case-series is presented, finding an incidence of early type I endoleaks in TEVAR patients of 7.6%- 8.8% and of 4.2%, respectively, at 1 year [105]. Parmer et al. (data from 1999 to 2006) reported a type I endoleak rate of 11.6% in a series of 69 patients treated for TAA, Piffaretti et al. (data from 2000-2008) reported a type I endoleak rate of 11.5% among 61 TEVAR patients, while Ueda et al. reported a rate of 23.43% in 64 patients [75, 93, 106]. A non-SR from Ricotta estimated an average frequency of 8.4% for type I endoleaks across 19 studies (2003-2008) [107].

#### **[A0011] – How often is the Heli-FX™ EndoAnchor™ system utilised?**

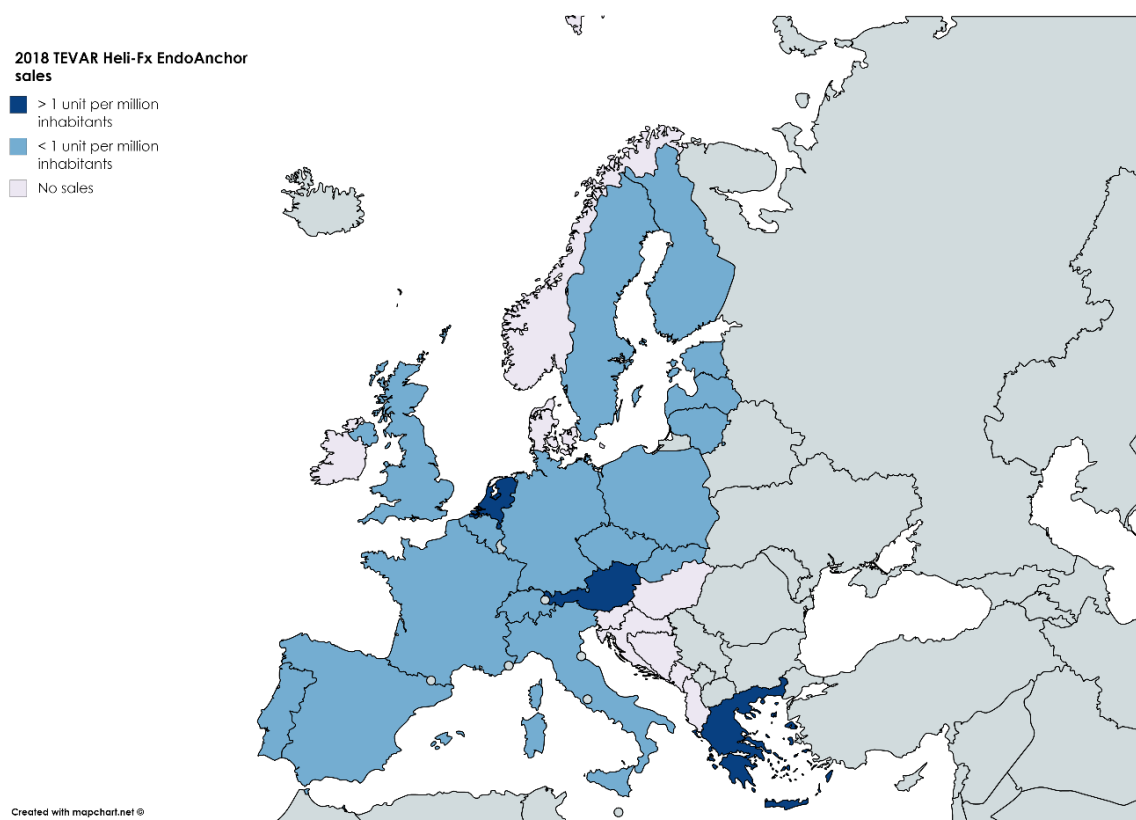
Data on the clinical use of the Heli-FX™ EndoAnchor™ system in EU countries is not available, in part because it is used in tandem with EVAR and TEVAR procedures. The sales data from 2018 (provided by MAH), divided by the estimated 2018 population of European countries, could indirectly reflect the demand for use of the Heli-FX™ EndoAnchor™ in the EU [108].

In the last two years (2017-2018), the number of EVAR Heli FX AAA units sold in the EU has increased. Sales in the United Kingdom grew during these same years, followed by Germany, Spain, The Netherlands, Italy and France. If we compare by country the number of Heli-FX™ units sold per million of inhabitants in 2018 (see [Figure 2](#)), first place is occupied by The Netherlands (13 units per million inhabitants) followed by Switzerland (10.4), Austria (6.2), Spain (5.7), Germany (5.4), Ireland (5.4) and the United Kingdom (5.4).

**Figure 2: 2018 EVAR Heli-Fx EndoAnchor sales**



**Figure 3: 2018 TEVAR Heli-Fx EndoAnchor sales**



These data could also confirm the lower use rates of Heli-FX™ in TEVAR procedures compared to EVAR procedures in European countries. In [Figure 3](#) one can see those countries with more than one TEVAR Heli-FX™ unit sold per million inhabitants (The Netherlands, Austria and Greece) followed by the remaining countries (less than 1 unit per million inhabitants). Note the countries reporting any sales in 2018 for use in TEVAR procedures (Norway, Denmark, Ireland, Hungary and the Adriatic nations) compared to the sales for the device's use in EVAR procedures in these same countries.

These differences in the demand or Heli-FX™ or use in EVAR vs. TEVAR procedures can be attributed to different market factors (investment, benefits, etc.), in addition to epidemiological, clinical and safety issues. In 2015, abdominal aortic endografts generated \$1.4 billion and accounted for 79% of the market, while thoracic aortic endografts generated \$300 million and accounted for only 18% of the market [109].

## 5 CLINICAL EFFECTIVENESS (EFF)

### 5.1 Research questions

A summary of the critical outcomes can be found at the end of this section.

Element ID	Research question
D0001	What is the expected beneficial effect of Heli-FX <sup>TM</sup> EndoAnchor <sup>TM</sup> on mortality?
D0005	How does use of the EndoaAchor system affect the symptoms and findings (severity, frequency) of those patients at high risk of type I endoleaks or stent/endograft migrations and who are suffering from aortic aneurysm disease?  How does the Heli-FX <sup>TM</sup> EndoAnchor <sup>TM</sup> system affect the symptoms and findings (severity, frequency) of type I endoleaks or stent/endograft migrations in post-EVAR/TEVAR procedures?
D0006	How does Heli-FX <sup>TM</sup> EndoAnchor <sup>TM</sup> affect the progression (or recurrence) of type I endoleaks or stent/endograft migrations in those patients at high risk with aortic aneurysm disease?  How does Heli-FX <sup>TM</sup> EndoAnchor <sup>TM</sup> affect the progression (or recurrence) of type I endografts or stent/endograft migrations in patients with aortic aneurysm disease?
D0011	What is the effect of Heli-FX <sup>TM</sup> EndoAnchor <sup>TM</sup> on patients' body functions?
D0016	How does the use of Heli-FX <sup>TM</sup> EndoAnchor <sup>TM</sup> affect activities of daily living?
D0012	What is the effect of Heli-FX <sup>TM</sup> EndoAnchor <sup>TM</sup> on generic health-related quality of life?
D0013	What is the effect of Heli-FX <sup>TM</sup> EndoAnchor <sup>TM</sup> on disease-specific quality of life?
D0017	Were patients satisfied with the Heli-FX <sup>TM</sup> EndoAnchor <sup>TM</sup> system?

### 5.2 Results

Effectiveness outcomes were rated by the Assessment Team and the clinical experts. As before, the critical outcomes consisted of the reintervention rate, aneurysm ruptures, aneurysm-related mortality at 30 and 365 days, and the rate of occurrence or recurrence of complications, including graft migrations and/or type I endoleaks. All-cause mortality at 30 days and 365 days, conversion to open surgical repair, technical and procedural success and health-related quality of life (HRQoL) measures were the outcomes considered important. The two outcomes rated as not important were the rate of neck dilation or sac enlargement and the rate of sac regression.

The tables in [Appendix 1](#) summarise the GRADE quality assessment, the effect and its importance, with a quality rating for each outcome. Calculations are weighted by study size. Outcomes are presented in three sections according to the GRADE rating. Within each section, abdominal and thoracic results are separated; they are also stratified by patient subsets (prophylaxis group, immediate type I endoleaks and maldeployment in primary interventions; repair of migrations, type

I endoleaks or both in secondary interventions). The design of the studies has also been considered for separate analysis.

## Included studies

Eleven studies were included in the effectiveness analysis. Only one study had a control group, an abdominal aneurysm observational study with a propensity matched control group [32]. This study showed the results of abdominal aneurysms in a subset of the Anchor registry. Four studies [26, 29, 30, 35] were prospective cohorts derived from a MAH registry, the ANCHOR registry and two from the STAPLE-1 and STAPLE-2 registries [27, 31]. Two retrospective series were also found, one on abdominal aneurysms requiring a primary intervention [28] and one on thoracic aneurysms requiring intervention [33]. Two prospective series [25, 34] and two retrospective series [28, 33] were not directly related to the MAH registries.

## Mortality

### [D0001] – What is the expected beneficial effect of Heli-FX™ EndoAnchor™ on mortality?

#### *Outcomes rated as critical*

Mortality outcomes rated as critical were the aneurysm-related mortality rates at 30 and 365 days.

**Aneurysm-related mortality at 30 days (abdominal aneurysm)** was assessed based on the proportion of aneurysm-related deaths at 30 days. One patient in the prophylaxis subgroup (4 studies, 392 patients: 1/392; 0.25%±0.32 weighted by sample size) died. This type of outcome was not reported in the other subgroups that required a primary intervention. In the studies containing data about secondary interventions (2 studies, 88 patients) [25, 26], none of the deaths were attributed to the aneurysm. In the retrospective series, 2 patients of 51 died (3.9%, 1 study).

For thoracic aneurysms, the aneurysm-related mortality rate at 30 days was 3.7% (2/54 of the retrospective cohort).

**The aneurysm-related mortality at one year (abdominal aneurysm)** was 0.26%±0.32 (1 from a sample of 379 prophylaxis patients across 3 studies, weighted by sample size) [27, 29, 31]. No deaths related to aneurysm were registered in cases requiring a secondary intervention (2 studies, 88 patients). For retrospective series, primary interventions (including prophylaxis, immediate type I endoleaks and maldeployment) in a series of 51 patients resulted in a mortality rate of 5.88%. **The aneurysm-related mortality rate at one year in thoracic aneurysm** was 9.3% (5 patients from a retrospective series of 54).

#### *Outcomes rated as important*

Overall mortality was rated as important.

**All-cause mortality at 30 days (abdominal aneurysm)** was calculated as the proportion of deaths that occurred within 30 days of the procedure. In the subgroup of patients with a prophylaxis indication, 4 studies recorded a mortality rate of 1.27%±0.71 (5 of 392 patients, weighted by study size). In the case of primary interventions due to an immediate type I endoleak or maldeployment no such outcome was reported in the only cohort containing data about these groups. This also occurred in the retrospective series with data on patients who required primary interventions. No deaths were reported in the secondary intervention subsets in two of the studies. Regarding **thoracic intervention**, the only study available, a retrospective series, reported a mortality rate within the 30 days following the index procedure of 3.7% (2 patients from a series of 54).



When all-cause mortality was measured **at 365 days (abdominal aneurysm)**, the results for the prophylaxis group measured  $2.9\% \pm 0.67$  (11 of 379 patients across 3 studies). In the case of primary interventions due to immediate endoleaks, this number increased, reaching 5% in a unique study involving 60 patients (3 patients, prospective cohort). In the maldeployment series, 1 patient of 4 died. The subgroup of patients that required a secondary intervention due to endoleaks had a mortality rate of  $6.12\% \pm 1.84$  (3 patients of 49 across 2 studies, weighted by size) and  $3.7\% \pm 2.02$  in the subset of patients requiring intervention due to migrations and type I endoleaks (1 patient of 27 across 2 studies, weighted by series size). The retrospective series recorded 7 deaths among 51 patients (13.72%), while for all-cause mortality (**thoracic aneurysm**) 11.1% of the series died (6 patients of 54).

## Morbidity

**[D0005] – How does use of the EndoaAchor system affect the symptoms and findings (severity, frequency) of those patients at high risk of type I endoleaks or stent/endograft migrations and who are suffering from aortic aneurysm disease?**

### *Outcomes rated as critical*

Regarding **aneurysm rupture (abdominal aneurysm)**, 4 observational studies (prospective cohorts) presented data on the outcomes resulting from primary interventions in a subgroup of prophylaxis patients, based on the proportion of patients who suffered an aneurysm rupture. No patients presented a ruptured aneurysm during the 48-month follow-up period.

The **aneurysm rupture rate (thoracic aneurysm)** was 1.9% (1/54) in the only study available.

Regarding the **reintervention rate (abdominal aneurysm)**, 4 observational studies (prospective cohorts) reported data on the outcomes resulting from primary interventions in a subgroup of prophylaxis patients, based on the proportion of reinterventions in the treated patients. Of the 392 included patients, 38 required a reintervention ( $9.7\% \pm 7$ ), weighted by sample size) [27, 29, 31, 34]. The follow-up period ranged from 0 to 48 months. A retrospective case series found that 25.5% of the patients needed a reintervention (13/51; these 13 patients required a total of 17 reinterventions) with a mean follow-up period of 23.9 months (IQR 13.4, 35.6 months) [28].

The **reintervention rate for thoracic aneurysms** is shown for the only study identified during the literature search: a retrospective cohort study of 54 patients, in which the reintervention rate was 16.7% (9/54). Follow-up was not reported [33].

### *Outcomes rated as important*

**Conversion to open surgical repair (abdominal aneurysm)** in the prophylaxis subgroup (primary intervention) occurred in 6 patients ( $1.5\% \pm 1.91$ , 392 patients across 4 studies, weighted by sample size). For **thoracic aneurysms**, none of the 54 patients in the retrospective series underwent an open surgical repair.

**Technical and procedural success (abdominal aneurysm)** in the prophylaxis subgroup was achieved in 389 of 392 patients ( $98.45\% \pm 2.74$ , 4 studies, weighted by sample size). Regarding the **thoracic aneurysm** series (1 study, 54 patients; retrospective cohort) the success rate was 98.1% (53 of 54 patients).

**[D0005] – How does Heli-FX™ EndoAnchor™ affect the progression (or recurrence) of type I endografts or stent/endograft migrations in patients with aortic aneurysm disease?**

*Outcomes rated as critical*

Regarding **aneurysm ruptures (abdominal aneurysm)**, this outcome was not reported by those studies that analysed patients requiring primary interventions due to immediate type I endoleaks or graft maldeployment except for the retrospective series, in which 1 of 51 patients presented this outcome (1.96%). In the only study containing data about patients who required secondary interventions, no aneurysm ruptures were reported [25].

The **aneurysm rupture rate (thoracic aneurysm)** was 1.9% (1/54) in the only study available.

Regarding the **reintervention rate (abdominal aneurysm)**, in the subgroup of patients requiring primary intervention due to an immediate type I endoleak, one study involving 60 patients reported a reintervention rate of 5% (3/60) [26]. The only sample featuring primary interventions due to graft maldeployment (a 4-patient subgroup within a larger registry) had no reinterventions [26]. The follow-up period ranged from 0 to 48 months.

For secondary interventions (migration subset), 2 studies reported that 3 of 12 patients required a reintervention (25%±7.87). This number decreased in the type I endoleak subset to 16.3%±10.14 (8/49), and occurred even less in the subset of patients who required both repairs: 7.4%±4.03 (2/27) [25, 26].

*Outcomes rated as important*

In the patient subset involving immediate type I endoleaks and maldeployment, **conversion to open surgical repair (abdominal aneurysm)** was not reported, and in the retrospective series, which encompassed all types of primary interventions, none of the patients required an open repair. In secondary interventions, 1 of 88 patients underwent a conversion to OSR (1.13%±0.43, 2 studies, weighted by size).

**Technical and procedural success (abdominal aneurysm)** in primary interventions due to prophylaxis measured 98.45% ± 2.74. In the subgroup that underwent a primary intervention due to an immediate endoleak, the success rate was lower than that in prophylaxis: 71.7% (43 from a patient series of 60) and in only 2 of 4 patients with a maldeployment was the procedure deemed to have been successful. In the retrospective collection of data on primary intervention patients (1 study, 51 patients), this data was not reported. In the secondary intervention groups, the migration patient had a successful procedure rate of 75%±7.87 (9/12 patients). For the endoleak subset the success rate was 75.51%±7.68 (37/49 patients). For the endoleak and migration subset the success was 92.6%±4.03 (25/27 patients).

**[D0006] – How does Heli-FX™ EndoAnchor™ affect the progression (or recurrence) of type I endoleaks or stent/endograft migrations in those patients at high risk with aortic aneurysm disease?**

*Outcomes rated as critical*

The **rate of occurrence or recurrence of complications (abdominal aneurysm)** was assessed based on the proportion of patients with a graft migration or type I endoleak. In the prophylaxis subgroup (392 patients, 4 prospective cohorts, with a follow-up range extending up to 72 months) the rate was 2.5%±2.80 (10/392). In the retrospective series, the rate of occurrence or recurrence

of complications associated with an abdominal aneurysm was 17.64% (9/51), and for **thoracic aneurysm**, the rate of complications was 9.3% (5 of 54 patients from a retrospective study). The only study with comparative data on EVAR not involving the Heli-FX™ EndoAnchor™ system showed a rate of 2% in the intervention group and 4% in the control group, over a 2-year period, without significant differences in the Kaplan-Meier analysis [32].

**[D0006] – How does Heli-FX™ EndoAnchor™ affect the progression (or recurrence) of type I endografts or stent/endograft migrations in patients with aortic aneurysm disease?**

The **rate of occurrence or recurrence of complications (abdominal aneurysm)** in the immediate type I endoleak subgroup measured 28.3% (17 from a prospective cohort of 60 patients, with a mean follow-up of 16 months) [26]. One of the four patients in the subgroup with maldeployment suffered recurrent complications as well, specifically a type I endoleak at the end of the procedure. Regarding secondary interventions, 2 studies showed that 12 of 88 patients suffered a complication (13.63%±1.73).

*Outcomes rated as not important*

Two outcomes were rated as not important, the **rate of neck dilation or sac enlargement** and the **rate of sac regression**. In the prophylaxis subgroup) the rate of patients who presented a neck dilation was 1.78%±1.21 (7 of 392 patients across 4 studies, weighted by sample size, range of follow-up extending to 48 months). No cases were reported involving immediate type I endoleaks or maldeployment subsets of patients (mean of follow-up of 16 months). For secondary interventions, the rate measured 1.3% (1 of 77 patients in a prospective cohort) [26]. The retrospective series with the primary intervention reported 1 case among its 51 patients (1.9%). The thoracic series had no such outcomes. The propensity matched study (99 patients) found no differences between the intervention and control groups over a 2-year period based on a Kaplan-Meier analysis (5.1% vs 12.1%, respectively) (see GRADE tables).

Regarding the **rate of sac regression**, 3 studies with data on the prophylaxis subgroup reported sac regression in 143 of 379 patients (37.7%±12.47, weighted by sample size, range of follow-up extending to 48 months). In the immediate type I endoleak subgroup, the rate was 3.3% (2/60), and in the maldeployment subgroup, no sac regression was recorded. The secondary intervention group had a rate of 9.1% (8 of 88 patients, with a follow-up range of up to 18 months). The retrospective series involving primary interventions (51 patients) did not measure this outcome, nor did the **thoracic aneurysm retrospective series** (54 patients). The comparative study on primary interventions (a control group obtained through propensity matching) showed significant differences at 1 and 2 years (p 0.03 and p 0.01, respectively) between the intervention group and the control group: 35.4% (CI 26.6%-45.2%) vs 36.4% (CI 27.5%-46.2%), respectively (see GRADE tables).

**[D0011] – What is the effect of Heli-FX™ EndoAnchor™ on patients' body functions?**

**[D0016] – How does the use of Heli-FX™ EndoAnchor™ affect activities of daily living?**

No evidence was found that might answer these research questions.

## **Health-related quality of life**

**[D0012] – What is the effect of Heli-FX™ EndoAnchor™ on generic health-related quality of life?**

**[D0013] – What is the effect of Heli-FX™ EndoAnchor™ on disease-specific quality of life?**

Health-related quality of life (HRQoL) data was not included in any of the cohort or case-series reports.

## **Satisfaction**

**[D0017] – Were patients satisfied with the Heli-FX™ EndoAnchor™ system?**

No Patient-Reported Outcome Measures (PROMs) were found or planned in any of the retrieved cohort or case-series reports.

**Table 4: Summary of events and quality of the evidence for critical outcomes on effectiveness:**

Outcome (Subset of patients)	Patients with an event	Number of participants (studies)	Certainty of the evidence (GRADE)
<b>Reintervention rate</b>			
<i><b>Abdominal Aneurysm</b></i>			
Reintervention rate (prophylaxis)	38/392 (9.7%±7)	392 (4 observational studies)	Very low
Reintervention rate (immediate type I endoleak)	3/60 (5%)	60 (1 observational study)	Very low
Reintervention rate (maldeployment)	0	4 (1 observational study)	Very low
Reintervention rate (secondary-revision migration)	3/12 (25%±7.87)	12 (2 observational studies)	Very low
Reintervention rate (secondary-revision type I endoleak)	8/49 (16.32%±10.14)	49 (2 observational studies)	Very low
Reintervention rate (secondary-revision type I endoleak and migration)	2/27 (7.4%±4.03)	27 (2 observational studies)	Very low
<i><b>Thoracic Aneurysm</b></i>			
Reintervention rate	9/54 (16.7%)	54 (2 observational studies)	Very low
<b>Aneurysm rupture</b>			
<i><b>Abdominal Aneurysm</b></i>			
Aneurysm rupture (prophylaxis)	0	392 (4 observational studies)	Very low
Aneurysm rupture (secondary-revision migration)	0	1 (1 observational study)	Very low
Aneurysm rupture (secondary-revision type I endoleak)	0	4 (1 observational study)	Very low
Aneurysm rupture (secondary-revision type I endoleak and migration)	0	6 (1 observational study)	Very low
<i><b>Thoracic Aneurysm</b></i>			
Aneurysm rupture	1/54 (1.9%)	54 (1 observational study)	Very low
<b>Aneurysm-related mortality at 30 days</b>			
<i><b>Abdominal Aneurysm</b></i>			
Aneurysm-related mortality at 30 days (prophylaxis)	1/392 (0.25%±0.32)	392 (4 observational studies)	Very low
Aneurysm-related mortality at 30 days	0	12 (2 observational studies)	Very low

Outcome (Subset of patients)	Patients with an event	Number of participants (studies)	Certainty of the evidence (GRADE)
(secondary-revision migration)			
Aneurysm-related mortality at 30 days (secondary-revision type I endoleak)	0	49 (2 observational studies)	Very low
Aneurysm-related mortality at 30 days (secondary-revision type I endoleak and migration)	0	27 (2 observational studies)	Very low
<b>Thoracic Aneurysm</b>			
Aneurysm-related mortality at 30 days	2/54 (3.7%)	54 (1 observational study)	Very low
<b>Aneurysm-related mortality 1 year</b>			
<b>Abdominal Aneurysm</b>			
Aneurysm-related mortality at 1 year (prophylaxis)	1/379 (0.26%±0.32)	379 (3 observational studies)	Very low
Aneurysm-related mortality at 1 year (secondary-revision migration)	0	12 (2 observational studies)	Very low
Aneurysm-related mortality at 1 year (secondary-revision type I endoleak)	0	49 (2 observational studies)	Very low
Aneurysm-related mortality at 1 year (secondary-revision type I endoleak and migration)	0	27 (2 observational studies)	Very low
<b>Thoracic Aneurysm</b>			
Aneurysm-related mortality 1 year	5/54 (9.3%)	54 (1 observational study)	Very low
<b>Rate of occurrence or recurrence of complications (graft migrations or type I endoleaks)</b>			
<b>Abdominal Aneurysm</b>			
Rate of occurrence or recurrence of complications (prophylaxis)	10/392 (2.5%±2.80)	392 (4 observational studies)	Very low
Rate of occurrence or recurrence of complications (immediate type I endoleak)	17/60 (28.3%)	60 (1 observational study)	Very low
Rate of occurrence or recurrence of	1/4 (25%)	4 (1 observational study)	Very low

Outcome (Subset of patients)	Patients with an event		Number of participants (studies)	Certainty of the evidence (GRADE)
complications (maldeployment)				
Rate of occurrence or recurrence of complications (secondary-revision migration/type I endoleak; type I endoleak and migration)	12/88 (13.63%±1.73)		88 (2 observational studies)	Very low
Rate of occurrence or recurrence of complications (primary intervention / no subgroups)	Anticipated absolute effects (95% CI)	Relative effect (95% CI)	99 (1 observational study)	Very low
	20 fewer per 1000 (from 37 fewer to 67 more)	RR 0.50 (0.09 to 2.67)		
Thoracic aneurysm				
Rate of occurrence or recurrence of complications	4/54 (7.4%)		54 (1 observational study)	Very low

## 6 SAFETY (SAF)

### 6.1 Research questions

A summary of the critical outcomes can be found at the end of this section.

Element ID	Research question
C0008	How safe is the use of Heli-FX <sup>TM</sup> EndoAnchor <sup>TM</sup> in relation to the comparator(s)?
C0004	How does the frequency or severity of harmful effects change over time or in different settings?
C0005	What are the susceptible patient groups that are more likely to be harmed through the use of Heli-FX <sup>TM</sup> EndoAnchor <sup>TM</sup> ?
C0007	Is the use of Heli-FX <sup>TM</sup> EndoAnchor <sup>TM</sup> associated with any user-dependent harmful effects?
B0010	What kind of data/records and/or registry is needed to monitor the use of the Heli-FX <sup>TM</sup> EndoAnchor <sup>TM</sup> system and the comparator(s)?

### 6.2 Results

Safety outcomes were also rated by the Assessment Team and the clinical experts. The only critical outcome was procedure-related mortality. Vessel damage (including dissection, perforation, and spasm), EndoAnchor implant embolisation, endoleaks (Types II-V), stroke, vascular access complications (including infection, pain, hematoma, pseudoaneurysm and arteriovenous fistula), renal complications (renal artery occlusion/dissection or contrast-induced acute kidney injury), cardiac complications, respiratory failure, other ischemic complications and others (pneumonia, fever, urologic- and gastrointestinal-related) were the outcomes considered important.

The tables in [Appendix 1](#) summarise the GRADE quality assessment, as well as the effect and importance, with a quality rating for each outcome. Calculations were weighted by study size. Outcomes are presented in 2 sections by GRADE rating and EVAR or TEVAR results. Within the EVAR section, all safety outcomes are summarised for the relevant follow-up periods: 30 days, 1 year, 2 years, 3 years and other as indicated. Within the TEVAR section, we present only the rates for types II-IV endoleaks. Due to the absent or negligible results reported for most of the safety outcomes, we did not present the results by study design (i.e., retrospective vs prospective). As most of the studies did not report or discuss safety outcomes for primary or revision arms, we have presented results only for the total sample (one or both arms).

#### Included studies

Eight studies were included in the safety analysis. Four of these studies were associated with MAH, two [26, 35] were prospective cohorts from the ANCHOR registry and two were from the STAPLE-1 and STAPLE-2 registries [27, 31]. For the safety analyses, we excluded two of the ANCHOR publications [29, 30] due to overlapping safety results with two other ANCHOR studies that had been included. Two retrospective series were found, one on abdominal aneurysms requiring a primary intervention [28] and one with patients who required an intervention for a thoracic aneurysm [33]. Two prospective series [25, 34] and two retrospective series [28, 33] were not directly related to the MAH registries.



## Patient safety

### [C0008] – How safe is the use of Heli-FX™ EndoAnchor™ in relation to the comparator(s)?

No data from comparative studies for analyses of safety outcomes was found. Only data from single-arm cohorts (prospective or retrospective) is presented.

#### *Outcomes rated as critical*

Procedure-related mortality was the only safety outcome rated as critical. Possible overlapping with all-cause mortality at 30 days exists due to the incorrect use of standardised outcomes. In AAA patients, a weighted mean of  $0.2\% \pm 0.13\%$  (1/517) from five observational studies at 30 days following the EVAR procedures was calculated. A rate of 3.7% (2/54) from one retrospective study at 30 days after a TEVAR procedure was reported [33].

#### *Outcomes rated as important*

Vessel damage (including dissection, perforation, and spasm) were rated as important. The following rates (all in AAA patients) were reported: 14.3% (3/21) in one observational study at 30 days after EVAR procedures; No vessel damage reported in two observational studies at 1 year (167 patients); and none of 153 in one observational study at 2 years of follow-up [27, 31].

EndoAnchor implant embolisation. A rate of 20.9% (32/50) at 1 year of follow-up and 36.6% (56/153) at 3 years of follow-up in one observational study with AAA patients was reported [31].

Endoleaks (types II-V). Recorded were the following: a weighted mean of  $28.4\% \pm 13.52\%$  (55/194) from 4 observational studies at 30 days after the EVAR procedure;  $14.8\% \pm 8\%$  (38/256) across 4 studies at 1-year of follow-up;  $7.7\% \pm 6.1\%$  (12/155) from 2 observational studies at 2 years; 12.8% (10/78) in one study at 3 years of follow-up [25-28, 31, 34, 35]. In TAA patients, a rate of 15.8% (3/19) from one retrospective study at 1-year of follow-up was reported [33].

Stroke. No strokes were reported in 174 patients at 30 days; in two observational studies, the rate at one year was  $1.8\% \pm 1.3\%$  (3/167); in one observational study the rate was 3.9% (6/153) at 3 years [27, 31]. No data was found in relation to the TEVAR study subgroup.

Vascular access complications (including infection, pain, hematomas, pseudoaneurysms and arteriovenous fistulae). The following rates were recorded: 0 patients of 21 patients at 30 days after the EVAR procedure; 0/14 at 1 year of follow-up in one study; 5.9% (3/51) at 2 years of follow-up in another study [27, 28]. No data was found in relation to the TEVAR study subgroup.

Renal complications (including renal artery occlusion/dissection or contrast-induced acute kidney injury). No events were recorded in 187 patients from 3 observational studies at 30 days after EVAR procedure; two observational studies reported a rate of  $1.23\% \pm 0.92\%$  (2/167) at 1 year of follow-up; one study recorded a rate of 3.1% (10/319) at 16 months; another study reported a rate of 3.9% (2/51) at 2 years; and a study reported 3.9% (6/153) at 3 years of follow-up [26-28, 31, 34]. No data was found in relation to the TEVAR study subgroup.

Cardiac complications. A weighted mean of  $1.33\% \pm 1\%$  (3/255) from 3 observational studies at 30 days after EVAR procedure was reported. Three studies recorded a rate of  $4.5\% \pm 1.67\%$  (12/267) from 3 studies at 1 year of follow-up, while another study reported a rate of 6.5% (10/153) at 3 years of follow-up [27, 28, 31, 35]. No data was found in relation to the TEVAR study subgroup.

Respiratory failure. No respiratory failures were reported in 174 patients from two observational studies at 30 days after EVAR procedure. Three observational studies reported a rate of  $0.7\% \pm 0.51\%$  (2/226) at 1 year of follow-up. Another observational study recorded a rate of 2.0% (3/153) at 3 years of follow-up [27, 31, 35]. No data was found in relation to the TEVAR study subgroup.

Other ischemic complications. A weighted mean of  $5.9\% \pm 6.73\%$  (2/34) from two observational studies at 30 days after EVAR procedure was reported. Two observational studies recorded a rate of  $4.4\% \pm 1.57\%$  (5/114) at 1 year of follow-up. A third study recorded a rate of 3.9% (2/51) at 2 years of follow-up [27, 28, 34, 35]. No data was found in relation to the TEVAR study subgroup.

Others: pneumonia, fever, urologic- and gastrointestinal-related complications. Such outcomes are difficult to analyse as they fall into a general "other" category of safety outcomes not reported in the previous classification. A weighted mean of  $12.5\% \pm 17\%$  (9/72) from two observational studies at 30 days after an EVAR procedure was recorded. In one study, these outcomes did not happen (14 patients) at 1 year of follow-up, while another reported a rate of 2.0% (1/51) at 2 years of follow-up [27, 28]. No data was found in relation to the TEVAR study subgroup.

**[C0004] – How does the frequency or severity of harmful effects change over time or in different settings?**

No evidence was found to answer this research question.

**[C0005] – What are the susceptible patient groups that are more likely to be harmed through the use of the Heli-FX™ EndoAnchor™?**

No studies were retrieved that reported on patient groups that were more susceptible to harmful effects stemming from the use of the Heli-FX™ EndoAnchor™ system.

**[C0007] – Is the use of the Heli-FX™ EndoAnchor™ associated with any user-dependent harmful effects?**

No evidence was found that might answer this research question.

**[B0010] – What kind of data/records and/or registry is needed to monitor the use of the Heli-FX™ EndoAnchor™ system and the comparator(s)?**

No studies were retrieved that reported on specific data records or registries that should be used to monitor the use of Heli-FX™ EndoAnchor™.

**Table 5: Summary of events and quality of the evidence for critical outcomes on safety:**

Outcome	Patients with event	Number of participants (studies)	Certainty of the evidence (GRADE)
<b>Safety Outcomes (All primary and secondary/revision intervention arms)</b>			
<b>Abdominal aneurysm</b>			
<b>Procedure-related mortality follow-up: 30 days</b>	1/517 (0.2% $\pm$ 1.41%)	517 (5 observational studies)	Very low
<b>Thoracic aneurysm</b>			
<b>Procedure-related mortality follow-up: 30 days</b>	2/54 (3.7%)	54 (1 observational study)	Very low

## 7 POTENTIAL ETHICAL, ORGANISATIONAL, PATIENT AND SOCIAL, AND LEGAL ASPECTS (ETH, ORG, SOC, LEG)

To answer the checklist, we used information drawn from the literature search and the Assessment Team's opinion. The checklist summarizes our judgment that there might be ethical, organisational and legal aspects that the users of this report may wish to consider further. It was not our objective to undertake an extensive search of the literature to provide a comprehensive overview for each aspect relating to the use of the Heli-FX™ EndoAnchor™ system.

### 7.1 Research questions

<b>7.1.1 Ethical</b>
<b>Does the Heli-FX™ EndoAnchor™ system and its potential use/non-use instead of the defined, existing comparator(s) give rise to any new ethical issues?</b>
We could not find any specific reports that address device-specific ethical issues for the Heli-FX™ EndoAnchor™. As with any new technology, the Heli-FX™ EndoAnchor™ could involve ethical issues related to equal access to treatment, especially if the intervention is not available to every patient in need of it. Some authors have deemed late mortality and informed consent specifications as relevant ethical aspects related to the associated intervention [EVAR] [110].
<b>7.1.2 Organisational</b>
<b>Does comparing Heli-FX™ EndoAnchor™ to the defined, existing comparator(s) point to any differences that may be organisationally relevant?</b>
Although no specific literature could be found regarding the specific device, it is reasonable to assume there might exist implementation issues related to learning curves and requisite skills for conducting EVAR/TEVAR with an additional technology [111]. The use of Heli-FX™ EndoAnchor™ might require specific training, especially in challenging cases. Some authors have concluded that virtual training with specific software could improve the outcomes of patients undergoing EVAR/TEVAR [112, 113]. Some authors have suggested that in the case of EVAR, elective repair of AAA the perioperative mortality would be associated to hospital volume (higher survival rates in high-volume hospitals), although not specifically to surgeon-related volume of interventions [114]. In any case, clinical practice guidelines from the Society for Vascular Surgery suggest that elective EVAR should be performed at centers with a volume of at least 10 EVAR cases per year and a documented perioperative mortality and conversion rate to OSR of 2% or less [21].
<b>7.1.3 Legal</b>
<b>Does the introduction of Heli-FX™ EndoAnchor™ and its potential use/non-use instead of the defined, existing comparator(s) give rise to any legal issues?</b>
Legal requirements for providing the patient with sufficient information about treatment (benefits and potential harms) must be met. Informed consent should be implemented in health care institutions, especially if the use of Heli-FX™ EndoAnchor™ is planned. Other potential legal aspects are associated with coverage and reimbursement decisions.
<b>Does comparing Heli-FX™ EndoAnchor™ to the defined, existing comparator(s) point to any differences that may be legally relevant?</b>

The use of Heli-FX<sup>™</sup> EndoAnchor<sup>™</sup> can be recommended in selected patients at high risk of complications from EVAR/TEVAR procedures. The selection of these high-risk patients must be carefully done. Endoleaks and other late complications related to EVAR/TEVAR are particularly prevalent in patients with hostile neck anatomy, thus validating the narrow anatomic spectrum indicated in EVAR device instructions for use. However, these stringent anatomic guidelines have led to widespread off-label use. Heli-FX<sup>™</sup> EndoAnchor<sup>™</sup> use could expand the indications for EVAR/TEVAR procedures.

## **8 PATIENT INVOLVEMENT**

Patient involvement was planned and European patient organisations (the European Heart Network and the European Patient forum), as well as national patient organisations from Spain (Cardio Alliance Spanish Patient's Forum, Patient's Alliance and Patient's Platform), were contacted to provide input on the preliminary PICO and through the HTAi patient input form. We also invited individual patients under the auspices of a local Hospital. However, it was not possible to identify any patients and enlist their participation.

## 9 DISCUSSION

### 9.1 *Discussion of the methodology*

#### **Discussion of the search strategy**

As stated in the project plan, a predefined search strategy with controlled terms and free text in the main databases was followed. Hand searching complemented this strategy, in order to avoid missing any study relevant to the inclusion criteria. An updated search was carried out 2 months after the first, yielding 22 additional studies for classification. None were selected in the end. No specific search strategy was developed for the CUR or TEC domains.

#### **Discussion of the inclusion and exclusion criteria**

Due to the lack of clinical trials with a control group, observational studies were accepted for inclusion in the analyses. Those studies with data on more than 10 patients were included.

A specific software (Covidence) was utilised by two independent reviewers to classify the studies obtained during the search [115]. Those studies that could not be evaluated based only their abstracts were retrieved in full text to reach a final decision. When a conflict occurred between the two reviewers, a third reviewer took part in the discussions for final classification. Editorials, letters and congress communications in which an analysis of the quality of evidence or additional follow-up data was not possible were excluded. We tried to contact authors in those cases where additional data was deemed necessary. When no answer was forthcoming, this was noted and the study discarded. When a study had been updated, the most recent publication was included in the analysis. Two comparative studies of the Heli-FX™ EndoAnchor™ vs other EVAR procedures were located. However, as these were abstracts, they were discarded because no additional data could be obtained from the authors [45, 48].

No systematic reviews were updated due to differences in inclusion criteria, objectives and/or non-use of the GRADE methodology.

#### **Discussion of the quality of evidence**

Rating of the outcomes using GRADE methodology was done only by the Assessment Team (authors, co-authors, dedicated reviewers) and clinical experts during the scoping phase. Patients were not available. Discrepancies between the rating and the clinical relevance could occasionally arise due to variabilities between methodologists and clinicians (e.g., this affected such variables as all-cause mortality, which was rated important and not critical).

We included the analysis of the effectiveness outcomes, which was rated as not important; i.e., the rate of neck dilation or sac enlargement and the rate of sac regression. These outcomes could have been excluded from the analysis due to this rating, and based on the fact that these were regarded as surrogate outcomes. Endoleaks were also presented as a surrogate outcome in the literature, due to the difficulty of ascertaining whether the absence of an endoleak signified the absence of aneurysm rupture [116]. The risk of indirectness due to surrogate outcomes was noted in the GRADE assessment, which resulted in a downgrading of the quality of the outcomes as well.

Of all the adverse events and serious adverse events (related or unrelated to the device or intervention) that were included in the safety analyses, only procedure-related mortality was deemed as critical. All others were classified as important. We analysed each adverse event independently. As explained later in the limitations section, no groups of adverse events were made due to the differences in how various reports presented adverse events.

The global quality of available evidence would be based on the lowest quality rate of the critical outcomes. In the assessment, the quality of evidence of the outcomes depended mainly on the risk of bias and the lack of control groups. These two aspects of the quality assessment downgraded the overall quality, resulting in the lowest of the critical outcomes ranking *very low*. This was also the result concerning important and not important outcomes. All outcomes—critical, important and not important—were rated very low, and none could be increased (i.e. due to a large effect, a plausible confounder that might alter the effect, or a dose-response gradient).

These factors are noted in the GRADE tables. Data from all but four studies were drawn from MAH registries [25, 28, 33, 34]. Conflicts of interest, resources and funding information is detailed in most of the studies. Publication bias could also be present; e.g., data on thoracic aneurysm procedures is lacking in comparison with data on abdominal aneurysms, and information requests made to MAHs proved unsuccessful.

The scoring of the risk of bias in the IHE checklist for individual studies had a mode of 15 (9-18). Details on the quality evaluation are shown in [Table A5](#).

### Limitations of the studies

There are some limitations to the analyses of the data. The fact that the different studies contain data from the same registry increases the likelihood that some overlapping of patient data occurred. Although some follow-up periods are reflected, others were mixed; thus, it was not possible to confirm whether some of the same patients were being followed-up in other studies. However, this limitation is somewhat compensated by the differences in the subgroups of populations. This will be explained later in the section *Discussion of the analyses and results presentation*. Longer follow-up periods were also absent, although some results (e.g., the STAPLE-2 trial) involved follow-ups period of up to 5 years [117]. However, these results stem from a clinical trial registry, with no explicit information available to adequately assess their quality. At a 2018 symposium, the ANCHOR trial team also presented their 3-year data, but did not respond to requests for additional information. Thus, it was impossible to assess the quality of the information presented [3]. Another limitation was the variability of the follow-up periods (from less than a year to 48 months) vis-à-vis most of the outcomes, and the time-point of events was not always well specified. Another relevant limitation is that female gender is underrepresented in the studies, despite it being a known factor in cases involving unsuitable or hostile necks in infrarenal AAA [65].

Subgroups of patients are also defined in different ways across the various studies, particularly in regards to most safety outcomes. This could influence the analysis due to patient misclassifications. Inclusion of these different subgroups was also sometimes subject to change while studies were underway, as was the case with one study [31] in which some patients with unfavourable necks were included despite the existence of a protocol precluding this kind of patient.

One subgroup of patients (primary intervention: maldeployment), although included in the analysis, could have been excluded due to the small number of patients involved (4). The sample size was so low that any analysis of it could have been discarded. The decision to include this group of patients is discussed in the following sections. In the case of patients who required a secondary intervention, data from 3 patient subsets were analysed, based on the indication for said intervention (type I endoleak, graft migration or both). The presentation of results as percentages also affected some calculations due to the impossibility of obtaining denominators. Percentages (where no numerators or denominators were indicated) limited the addition of such data to the analyses. How variables were defined could also affect the analyses. In one study [25], two different techniques were used according to the graft migration degree, depending on whether the sealing to the infrarenal neck was done properly. If the sealing was insufficient (<1 cm), an extender cuff

was placed in addition to the endoanchors. This was not described in the other studies. Technical and procedural success was evaluated separately in most of the studies. For our purposes, in order to simplify the analysis, the outcome “technical and successful procedure” was chosen. However, it could be argued that this might result in an underestimation of the technical success alone. Another limitation is the overlapping use between all-cause mortality and procedure-related mortality at 30 days, despite the recommendations of the Ad Hoc Committee for Standardized Reporting Practices in Vascular Surgery (Society for Vascular Surgery/American Association for Vascular Surgery) [118].

A limitation of the safety analysis, in which we itemised the possible complications (as per project plan), is the lack of consensus and the differences among the studies in characterizing adverse events; e.g., the use of composite variables (as major adverse events) without defining the breakdown of the different adverse events included, or the use of partial lists of major adverse events. This could have lowered the power of the analysis to detect harmful effects. This heterogeneity in the studies made answering questions related to safety difficult. Another limitation was that one study did not detail safety events using the most commonly reportedly periods of other studies (30 days, 1, 2, 3 years), thus hindering its classification and analysis [28]. This could result in an over- or under-estimation of effects.

Lastly, we could not analyse the effectiveness or safety in the urgent procedures subgroup, due to the lack of inclusion of these patients in the studies. Only five studies included such a subgroup, and the number of urgent procedures conducted was low; moreover, the results for this subgroup were not analysed separately [28, 30, 33-35].

## **Discussion of the analyses and results presentation**

GRADE tables on effectiveness and safety outcomes were constructed. As per project plan, the primary and secondary (or revision) interventions were separated due to the differences in these groups. A comparative analysis between the groups has not been done. In the case of primary interventions, we differentiated three subgroups based on the indications used for a given procedure. The first group consisted of prophylactic interventions carried out because of certain risks involved (e.g., hostile neck) while the second and third groups corresponded to those patients who presented a type I endoleak during the procedure (immediate type I endoleak) or a maldeployment of the graft, respectively. This separation decreased the number of patients that could be included for analysis. However, due to inconsistencies among the different patient groups, pooling all types of primary intervention patients together could result in an overestimation or underestimation of the effects. In the case of maldeployment the results could have been excluded because the number of patients was less than ten, but the Authoring Team decided to present at least some of the results for this specific group of patients. No other data related to them was found in the literature, and no other studies that met the set limit of 10 patients were included in the analysis. This was also the case when the results from secondary interventions were separated by indications of the repair type (migration, endoleak or both). The analysis was also conducted in keeping with the design of the studies, separating out only one study found in the literature that had an adequate control group [32]. This observational study had a control group obtained by propensity matching. No other comparative data was found, with one exception, an FDA-approved historical control for all EVAR trials, which was not included in the analysis for this very reason – i.e., lack of a contemporary control group and the nature of the intervention in said control group (open surgical repair group) [119].



Abdominal aneurysms and thoracic aneurysms were also separated in the analysis due to the prognostic differences between the two locations [15]. Possible differences between the first uses of the technology and the current device were not considered in the analysis.

We presented results with a broad range of follow-up periods due to the heterogeneity of the included studies. The prospective series reported a median follow-up period of 12 months (from a range of 2 to 72 months). Only one study presented some results at 72 months, encompassing both endoleaks, and adverse events, though it included very few patients with longer-term data [31]. A retrospective series had a median of 24 months of follow-up [28], and the only study available on thoracic aneurysms, a retrospective case series, had a median of follow-up of 9.6 months [33]. The number of patients with long-term data was low in these studies, and not all patients had a CT imaging result ordered during their follow-up. Sample sizes were low for those patients with secondary interventions [25, 26] and with TEVAR [33]. Patients who underwent a primary intervention due to prophylaxis were the most studied group, although this sample, when pooled, numbered less than 400 patients, and not all had at least one year of follow-up. This can signify that late outcomes were not yet occurring; e.g., reinterventions due to complications.

## **9.2 Discussion of effectiveness and safety**

### **Discussion of Effectiveness**

Despite beneficial results of EVAR and TEVAR, procedures, complications such as type I endoleaks and graft migrations occur, sometimes causing a failure of the endograft. These complications frequently occur in those with a so-called “hostile neck” (i.e., short, angulated, calcified, conical) as is often observed in AAA patients [120]. Endograft indications would exclude patients with these anatomic characteristics. Therefore, several options have been developed: fenestrated and branched devices, albeit with a potentially increased risk of renal artery complications and secondary interventions; cuffs, balloon stents, and staples [29, 120, 121].

The largest group of patients with data available was comprised of those who underwent a prophylactic primary intervention due to high risk (hostile neck). A study found that outcomes such as serious adverse events, technical failure, type I endoleaks and sac enlargements appeared to be worst in those patients with shorter aortic neck lengths (<10mm) compared to those with lengths ≥10 mm, although these differences did not reach statistical significance [29].

Some results on variables classified as critical by the Assessment Team proved similar to those in a series of patients whose interventions did not involve endoanchors, although a robust analysis with control groups was absent and thus could not be confirmed. For example, the reintervention rate (9.7%; follow-up period of up to 48 months) appeared higher in the prophylactic group compared to those presented in a metaanalysis of EVAR procedures that compared hostile and friendly neck patients (5% of both groups), although this metaanalysis examined results at one year of follow-up [6]. In the study where this outcome is clearly differentiated based on the period of follow-up, reintervention at one year was similar (5.1%) to that calculated in the metaanalysis, increasing over time, the highest proportion occurring between 12 and 48 months [31]. The rate for type I endoleaks (2.5%) and mortality due to aneurysms (0.25%) appeared to be lower in the patients analysed in our report than in the hostile neck series in the aforementioned metaanalysis (10% and 4% respectively), although the latter included an older series [6]. The retrospective series had more similar numbers, although this could be because the results for the different subgroups requiring a primary intervention (prophylaxis, immediate type I endoleak, maldeployment) were not presented separately [28]. In the case of thoracic interventions, rates for type I endoleaks (7.4%)

and death related to aneurysm rupture (3.7%) were similar to those reported in a systematic review of TEVAR alone (without the use of endoanchors) (7.4% and 3.2%, respectively) [122].

Overall mortality was rated as important, the highest mortality rates at one year being recorded in the thoracic study and the retrospective series on primary patients (all types), 11% and 13%, respectively [28, 33]. Mortality was lower in the prophylactic group [27, 29, 31, 34], probably because the intervention was not done due to complications and in the secondary intervention settings, possibly due to their smaller sample size and shorter follow-up periods. Nevertheless, in the latter case, those patients who required an intervention due to a type I endoleak suffered the highest rate of mortality at one year within the secondary setting (7%) [25, 26]. The lack of larger-sized cohorts, control groups and the short follow-up ranges for most of the outcomes makes it difficult to draw more definitive conclusions.

The risk of endograft complications at the proximal neck increases over time, with endoleaks and migration the most commonly encountered problem in the longer term. As such, intermediate-term follow-up periods needs to be extended for more patients [26, 120]. No subgroup analyses comparing patients who underwent a prophylactic intervention with other subgroups that required a primary intervention (immediate type I endoleak, maldeployment) or secondary intervention could be performed, as the required data were not available due to the small sample sizes found in these subgroups. Moreover, it is unlikely that the quality of the evidence would be sufficiently high to draw reliable conclusions. This is more pronounced in primary interventions due to maldeployment and secondary interventions for migration repair, probably due to their incidence. The only ongoing registered trial (ANCHOR) presented in 2018 their comparative 1-, 2- and 3-year results for occurrences of type Ia endoleaks: 0.6%, 1.1% and 1.7% respectively, for the primary arm; and 7.9%, 5.9% and 2.4%, respectively, for the revision arm. No cases of endograft migration were reported in the primary intervention or in the revision arm (secondary intervention) series in AAA patients [36].

These results should be compared with those for treatment without endoanchors in randomised controlled trials. The only control data included was a set of 99 patients yielded by a propensity matched study, although data on only three outcomes (rate of migration or endoleak, sac regression and sac enlargement) were retrieved [32]. The only outcome rated as critical among these was the rate of complications (migration or endoleak), which did not reach statistical significance. Regarding the other two, which were rated as not important, the only with differences in the survival analysis concerned sac regression at 1 and 2 years. According to the authors this outcome, although often considered a surrogate—in fact, it was rated as not important by the clinical experts who participated in the assessment—is associated with a lower risk for later complications [32].

Some comparative data on an historical control from another study [31] was not used, due to the nature of the control. This was a pooled open surgical AAA repair group, the data drawn from four controlled investigational device exemption (IDE) clinical trials of the Lifeline Registry for EVAR [119]. As a comparison with open surgery in our assessment would not be relevant based on our research questions, this historical control was excluded from the analysis. Comparisons with historical controls are not without a risk of bias, and such comparisons could not confirm any relevant differences between using, versus not using, the device.

Possible prognostic differences between the patient subgroups should be considered; e.g., in the case of the primary interventions, in addition to the prophylactic subgroup of patients, the device has been utilised in patients presenting some type of complication (immediate type I endoleak or maldeployment) [26]. Differences between these indications would be expected. Those studies reporting comparisons between indications observed that the results were better in the prophylactic

group [26, 35]. These differences could be higher when comparing the results of patients who have undergone a primary prophylactic intervention to those who have undergone a secondary intervention [35].

The lack of results on thoracic patients, whose prognostic basis would be different from that of abdominal patients [15], must be remarked upon. Data on thoracic aneurysms is exiguous compared to abdominal aneurysm repair and queries to authors and MAHs for additional data on thoracic patients were unsuccessful. This issue could represent a publication bias. The only available series was a small retrospective cohort in which indications for prophylactic Heli-FX™ EndoAnchor™ use were not protocolised [33].

The lack of data on quality of life is also noteworthy. HRQoL was rated as an important outcome by the Assessment Team. We did not find any data on this outcome in the studies. As patient participation in the assessment was unsuccessful, there was no input to compliment this outcome for comparisons. Although no specific data related to the device was found, some condition-specific AAA PROs measures have been proposed in the literature. Measures such as the AneurysmDQoL and AneurysmSRQ are both condition-specific measures of health developed from qualitative studies of AAA patient experiences, including those patients who are undergoing conservative, OR, or EVAR treatments [123]. Some authors believe that there is an urgent need for identifying condition-specific AAA PRO measures, given the increasing need for EVAR repairs. These authors propose the previous questionnaires and the AneurysmTSQ to assess the impact of symptoms and the treatment satisfaction of AAA patients both before and after repair [124]. However, no PROM includes questions addressing fear of rupture, death or ability to forget about the condition, despite the fact that these are key issues for patients in the qualitative studies thus far conducted [123, 124].

## Discussion of Safety

The same issues and limitations of the available evidence regarding effectiveness data apply to the evidence on the safety of the intervention. The lack of available results (published or unpublished) on TEVAR in the ANCHOR trial is an important publication bias in terms of this assessment. At difference with the efficacy outcomes analysed and discussed is that most of the adverse events were presented and analysed as a pooled total (not per subgroup) due to the difficulty of extracting and/or calculating by subgroups in most of the studies included in the SAF domain. No subgroup analysis by type of indication of use (primary vs secondary or revision arm), nor of urgent vs elective endovascular procedure, has been conducted. Another limitation was the partial report of complications such as the use of “severe adverse events” as a classification, instead of a more highly detailed stratification of complications and/or adverse events. No comparative studies with comparators (for primary or revision arms) were found that addressed safety outcomes. Thus, assessing safety profiles based only on case series, with very low-quality evaluations for all included outcomes, is less reliable. It is relatively difficult to separate the adverse effects attributable exclusively to Heli-FX™ EndoAnchor™ from those related to the endovascular procedure and/or the other medical devices used.

One of the known long-term data points in EVAR patients, compared to open surgical repair, is that there is no difference in mortality rates beyond 3 years of follow-up. In fact, there is an increased rate of reinterventions in the EVAR group [125]. The only long-term available data (5 years) for EVAR + Heli-FX™ EndoAnchor™ use comes from the STAPLE-2 finalised trial (only elective EVAR procedures and with a lower incidence of unfavourable neck anatomy). There was no apparent significant increase in the rate of safety outcomes at 5 years when comparing the 1-, 2-

and 3-year published results from the same trial [31, 117]. There is no long-term (>3 years) data published on safety outcomes from the ongoing ANCHOR trial [40].

Procedure-related mortality (a critical outcome) in EVAR patients was one of the most reported safety outcomes in the eight included studies, with a rate close to 0% at 30 days follow-up. This rate measured 3.7% in the only TEVAR study included. The rate of stroke, low in these case series, is more commonly associated with TEVAR procedures (specifically to left subclavian artery revascularisation) and with EVAR procedures, as procedure-related morbidity, than in OSR in short- or mid-term follow-up periods [126].

Worth noting are the dissimilarities found in the retrieved studies compared to the voluntary notifications present in such databases as FDA's MAUDE (Manufacturer and User Facility Device Experience), where device dislodgement and embolization remain the most common adverse events, followed by applicator malfunction [127].

The frequency of critical, as well as of most of the important, safety outcomes are very low in EVAR plus Heli-FX™ EndoAnchor™ patients over mid-term follow-up periods. However, there is a critical gap in the safety data of TEVAR plus Heli-FX™ EndoAnchor™ patients, due to the small size of the cohort in the only relevant study, one with a short follow-up period [33].

## 10 CONCLUSION

The rationale underlying the use of the Heli-FX™ EndoAnchor™ system appears logical as it reportedly increases the adherence of the endoprosthesis to the aortic wall in order to prolong the duration of the endovascular aortic aneurysm repairs.

Based on the results from observational studies, and within the limitations of the low-quality evidence available, the data suggest that the use of Heli-FX™ EndoAnchor™ in EVAR patients (prophylactically or as treatment for endograft migrations or type I endoleaks) would be safe in the mid-term follow-up for patients presenting unfavourable neck anatomy, and probably safe over long-term follow-up for those with friendly neck anatomies. However, comparative data on standard endovascular therapy are not currently available. In the case of TEVAR, safety data also remains very scarce.

Regarding effectiveness, the evidence does not allow for any definitive conclusions on whether the use of endoanchors represents an improvement in EVAR/TEVAR procedures outcomes. Globally, the information gathered on critical outcomes in terms of effectiveness, (rate of type I endoleaks or migrations, rate of reinterventions, rate of aneurysm ruptures or rate of aneurysm-related mortality) although of very low quality, would suggest effectiveness of the device, however, there is a lack of evidence from high-quality comparative studies. Results should be compared with treatments not involving the Heli-FX™ EndoAnchor™ system in randomised controlled trials for most of the critical and important outcomes.

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**APPENDIX 1: METHODS AND DESCRIPTION OF THE EVIDENCE USED****DOCUMENTATION OF THE SEARCH STRATEGIES****Database: Ovid Medline ® 1946 to present****Search date: 2019-02-20 (update 2019-04-23: 9 new results)**

#	Search	Hits
1	Aortic Aneurysm/	20687
2	Aortic Aneurysm, Thoracic/	11149
3	Aortic Aneurysm, Abdominal/	17735
4	Aortic Rupture/	9259
5	Endoleak/	1216
6	Prosthesis Failure/	26942
7	(ascend* adj2 aort* adj3 aneurysm*).ti,ab,kw.	2172
8	(descend* adj2 aort* adj3 aneurysm*).ti,ab,kw.	1257
9	(aort* adj4 aneurysm*).ti,ab,kw.	37114
10	(abdominal adj1 aort* adj3 aneurysm*).ti,ab,kw.	18325
11	(thoracic* adj1 aort* adj3 aneurysm*).ti,ab,kw.	3846
12	(thoracoabdominal adj1 aort* adj3 aneurysm*).ti,ab,kw.	1482
13	AAA.ti,ab,kw.	12278
14	endoleak.ti,ab,kw.	3471
15	(prosthesis adj3 (failure or migration)).ti,ab,kw.	687
16	(graft adj2 failure).ti,ab,kw.	10226
17	(rupture adj3 aneurysm*).ti,ab,kw.	6922
18	(rupture adj3 aort*).ti,ab,kw.	4257
19	1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18	106460
20	endoanchor.ti,ab,kw.	26
21	Heli-FX.ti,ab,kw.	11
22	Aptus.ti,ab,kw.	54
23	(Helical adj3 Anchor*).ti,ab,kw.	47
24	vascular stapler.ti,ab,kw.	94
25	fixation device*.ti,ab,kw.	2900
26	endostapl*.ti,ab,kw.	237
27	endosuturing.ti,ab,kw.	9
28	(endovascular adj4 sutur* adj4 aneurysm* adj4 repair).ti,ab,kw.	3
29	20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28	3357
30	19 and 29	121
31	limit 30 to (comparative study or controlled clinical trial or observational study or randomized controlled trial)	22

**Database: EMBASE Elsevier 1947 to present****Search date: 2019-02-20 (update 23/04/2018: 13 new results)**

#	Search	Hits
1	'aortic aneurysm'/exp	57440
2	'aneurysm rupture'/exp	13650
3	'endoleak'/exp	6409
4	'thoracoabdominal aorta aneurysm'/exp	1167
5	'thoracic aorta aneurysm'/exp	7534
6	'abdominal aortic aneurysm'/exp	26401
7	((('abdominal' OR 'thoracic' OR 'thoracoabdominal') NEAR/1 aort* NEAR/3 aneurysm*):ti,ab,kw	29856
8	(aort* NEAR/3 aneurysm*):ti,ab,kw	45550
9	(descend* NEAR/2 aort* NEAR/3 aneurysm):ti,ab,kw	1077
10	(aort* NEAR/3 rupture*):ti,ab,kw	9262
11	endoleak*:ti,ab,kw	6290
12	((prosthesis OR graft) NEAR/2 (failure OR migration)):ti,ab,kw	18983
13	(ascend* NEAR/2 aort* NEAR/3 aneurysm):ti,ab,kw	2273
14	#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13	98254
15	endoanchor:ti,ab,kw	33
16	'heli-fx':ti,ab,kw	19
17	aptus:ti,ab,kw	62
18	endostapl*:ti,ab,kw	424
19	'endosuturing':ti,ab,kw	32
20	vascular:ti,ab,kw AND stapler:ti,ab,kw	538
21	(endovascular NEAR/4 sutur* NEAR/4 aneurysm* NEAR/4 repair):ti,ab,kw	4
22	fixation:ti,ab,kw AND device*:ti,ab,kw	10641
23	#15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 #22	11709
24	#14 AND #23	410
25	#24 AND ('clinical trial'/de OR 'cohort analysis'/de OR 'comparative study'/de OR 'controlled clinical trial'/de OR 'controlled study'/de OR 'multicenter study'/de OR 'prospective study'/de OR 'randomized controlled trial'/de OR 'observational study'/de)	145

**Database: Cochrane Library databases collection (Wiley) 1992 to present****Search date: 2019-02-20 (update 2019-04-23: no new results)**

#	Search	Hits
#1	MeSH descriptor: [Aortic Aneurysm] explode all trees	734
#2	MeSH descriptor: [Aortic Aneurysm, Abdominal] explode all trees	540
#3	MeSH descriptor: [Aortic Aneurysm, Thoracic] explode all trees	78
#4	MeSH descriptor: [Aortic Rupture] explode all trees	69
#5	MeSH descriptor: [Endoleak] explode all trees	13
#6	MeSH descriptor: [Prosthesis Failure] explode all trees	675
#7	(#1 OR #2 OR #3 OR #4 #5 OR #6)	1383

#8	(aort* NEAR4 aneurysm*):ti,ab,kw	11473
#9	(ascend* NEAR2 aort* NEAR3 aneurysm*):ti,ab,kw	15439
#10	(descend* NEAR2 aort* NEAR3 aneurysm*):ti,ab,kw	13343
#11	(abdominal NEAR1 aort* NEAR3 aneurysm*):ti,ab,kw	38685
#12	(thoracic NEAR1 aort* NEAR3 aneurysm*):ti,ab,kw	20674
#13	(thoracoabdominal NEAR1 aort* NEAR3 aneurysm*):ti,ab,kw	11667
#14	(endoleak*):ti,ab,kw	147
#15	((prosthesis OR graft) AND (failure OR migration)):ti,ab,kw	5752
#16	((rupture NEAR3 aneurysm*) OR (ruptura NEAR3 aort*)):ti,ab,kw	14949
#17	(#8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 #15 OR #16)	55933
#18	(endoanchor*):ti,ab,kw	3
#19	(Heli-FX):ti,ab,kw	1
#20	Aptus:ti,ab,kw	8
#21	endostapl*:ti,ab,kw	20
#22	endosutur*:ti,ab,kw	1
#23	(endovascular NEAR/4 sutur* NEAR/4 aneurysm* NEAR/4 repair):ti,ab,kw	1
#24	(fixation NEAR/3 devices):ti,ab,kw	157
#25	(vascular NEAR/3 stapler):ti,ab,kw	3
#26	(#18 OR #19 OR #20 #21 OR #22 OR #23 OR #24 OR #25)	171
#27	#7 OR #17	56535
#28	#27 AND #26 in Cochrane Reviews, Trials	21

**Database: ClinicalTrial.gov**

**Provider: U.S. National Institutes of Health**

URL: <http://www.clinicaltrials.gov>

Input interface: Advance Search

**Search date: 2019-02-20 (update 2019-04-23)**

Search	Hits
endoanchor OR "Heli FX" OR "aptus" OR endostapler* or endosuturing or (endovascular sutur* aneurysm* repair)	6

**Database: International Clinical Trials Registry Platform**

**Provider: World Health Organization**

URL: <https://www.who.int/ictrp/en/>

Input interface: Advance Search

**Search date: 2019-02-20 (update 2019-04-23)**

Search strategy	Hits
endoanchor OR "Heli FX" OR "aptus" OR endostapler* or endosuturing or (endovascular sutur* aneurysm* repair)	11



## DESCRIPTION OF THE EVIDENCE USED

### Guidelines for diagnosis and management

**Table A1: Overview of guidelines**

Name of society/organisation issuing guidance	Date of issue	Country/ies to which applicable	Summary of recommendation	Quality appraisal tool and Level of evidence
AAA				
European Society of Cardiology [22]	2014		<p>Once aortic dilation is suspected, based on echocardiography and/or chest X-ray, CT or MRI (with or without contrast) it is required to adequately visualise the entire aorta and identify the affected parts.</p> <p>In patients with more complex aortic anatomy, who are unsuitable for EVAR—<b>open repair remains the standard</b>. Endovascular treatment strategies exist to address such aneurysms, for instance, branched or fenestrated endografts, but comparisons with open repair in RCTs are still awaited.</p> <p>CT is recommended as the first-choice imaging technique for follow-up after TEVAR or EVAR.</p> <p>Type I and Type III endoleaks demand correction (<b>proximal cuff or extension</b>).</p> <p>No recommendation about stent migration management.</p>	<p>Grading system based on the European Society of Cardiology (ESC) guidelines methodology. (A,B,C)/ <i>class of recommendation (I, IIa, IIb, III)</i>. No critical appraisal of individual studies reported.</p> <p>None</p> <p>None</p> <p>Class 1: Level C None</p> <p>None</p>



<p>Spanish Society of Arteriosclerosis (SEA) and the Spanish Society of Angiology and Vascular Surgery (SEACV) [84]</p>	<p>2016</p>	<p>Spain</p>	<p>It recommends the application of a population screening program of AAA in men between 65 and 75 years to reduce the mortality due to aneurysm. Abdominal ultrasound is recommended as a method of initial diagnosis, screening and subsequent surveillance. It does not recommend Arteriography as a diagnostic method in patients with suspected AAA.</p> <p>Computed tomography (CT) is the diagnostic technique of choice for the decision and planning of treatment in patients with AAA. To detect the development of anastomotic pseudoaneurysm or para-anastomotic aneurysm or endoleak during the follow-up of patients undergoing AAA repair, it is necessary to carry out complementary imaging tests, such as Doppler ultrasound or CT. If CT scanning is not possible, magnetic resonance imaging (MRI) is the procedure of choice for diagnosis in these patients.</p> <p>Fenestrated stenting is the preferred choice in cases with <b>short or pathological aortic necks</b>, in reference centres and with extensive experience in EVAR procedures.</p> <p>No special recommendation about endoleak type I and stent migration management options.</p>	<p>Strength of the recommendation: strong. Quality of the evidence: high</p> <p>Strength of the recommendation: strong. Quality of the evidence: high</p> <p>Strength of the recommendation: strong. Quality of the evidence: low</p> <p>Strength of the recommendation: strong. Quality of the evidence: moderate</p> <p>Strength of the recommendation: strong. Quality of the evidence: low</p> <p>Strength of the recommendation: strong. Quality of the evidence: low</p> <p>Strength of the recommendation: weak. Quality of the evidence: low</p>
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Name of society/organisation issuing guidance	Date of issue	Country/ies to which applicable	Summary of recommendation	Quality appraisal tool and Level of evidence
European Society for Vascular Surgery (ESVS) [5]	2018		<p><u>Recommendation 9:</u> in patients with abdominal aortic aneurysms computed tomography angiography it is recommended for therapeutic decision making and treatment planning, and for the diagnosis of rupture.</p> <p><u>Recommendation 95:</u> In patients with juxtarenal abdominal aortic aneurysm*, <b>open repair or complex endovascular repair</b> should be considered based on patient status, anatomy, local routines, team experience, and patient preference.</p> <p><u>Recommendation 96:</u> In complex endovascular repair of juxtarenal abdominal aortic aneurysm, <b>endovascular repair with fenestrated stent grafts</b> should be considered the preferred treatment option when feasible.</p> <p><u>Recommendation 97:</u> In complex endovascular repair for juxtarenal abdominal aortic aneurysm, using <b>parallel graft techniques</b> may be considered as an alternative in the emergency setting or when fenestrated stent grafts are not indicated or available, or as a bailout, ideally restricted to &gt; 2 chimneys.</p> <p><u>Recommendation 98:</u> In patients with juxtarenal abdominal aortic aneurysm, <b>new techniques/ concepts, including endovascular aneurysm seal, endostaples, and in situ laser fenestration</b>, are not recommended as first line</p>	<p>Grading system based on the European Society of Cardiology (ESC) guidelines methodology. (A,B,C)/ class of recommendation (I, IIa, IIb, III). No critical appraisal of individual studies reported.</p> <p>Class I Level C</p> <p>Class IIa Level C</p> <p>Class IIa Level C</p> <p>Class IIb Level Class III Level C</p> <p>Class IIb Level C</p>

Name of society/organisation issuing guidance	Date of issue	Country/ies to which applicable	Summary of recommendation	Quality appraisal tool and Level of evidence
			<p>treatment, but should be limited to studies approved by research ethics committees, until adequately evaluated.</p> <p><b>Recommendation 99:</b> In patients with ruptured juxta/pararenal abdominal aortic aneurysm <b>open repair or complex endovascular repair (with a physician modified fenestrated stent graft, off the shelf branched stent graft, or parallel graft)</b> may be considered based on patient status, anatomy, local routines, team experience, and patient preference.</p> <p><b>Recommendation 86:</b> In patients with type I endoleak after endovascular abdominal aortic aneurysm repair, <b>re-intervention to achieve a seal, primarily by endovascular means</b>, is recommended.</p> <p>* Juxtarenal AAA (JRAAA) is defined as an aneurysm extending up to but not involving the renal arteries, necessitating suprarenal aortic clamping for OSR, i.e. a short neck ( &lt; 10 mm)</p>	<p>Class IIb Level C</p> <p>Class I Level B</p>
German Society of Vascular Surgery and Vascular Medicine (DGG) plus: German Society of Anaesthesiology and Intensive Care Medicine (DGAI); German Society for Angiology / Society for Vascular Medicine (DGA); German Society of Surgery (DGCH); German Society for Interventional Radiology (DEGIR); German Society of Thoracic and Cardiovascular Surgery (DGTHG); German Society for Ultrasound in Medicine (DEGUM); German Vascular League e.V.; German Interdisciplinary Association for Intensive and Emergency Medicine (DIVI) and German Roentgen Society (DRG) [83]	2018	Germany	<p>Patients with AAA should receive diagnostic imaging, including CT, prior to invasive care.</p> <p>Evidence level 2b / recommendation grade A, strong consensus</p> <p>For the endovascular treatment of AAA with a short neck, <b>if the open procedure is not chosen, fenestrated/dented prostheses and - if this is not anatomically feasible - the Chimney technique is an option.</b></p> <p>Endoleaks are primarily be treated <b>endovascularly</b>. Type I endoleaks, whose</p>	<p>Centre of evidence-based Medicine (CEBM) tools. University of Oxford.</p> <p>Evidence level 2b / recommendation grade A, strong consensus</p> <p>Evidence level 3a, strong consensus.</p>



Name of society/organisation issuing guidance	Date of issue	Country/ies to which applicable	Summary of recommendation	Quality appraisal tool and Level of evidence
			<p>elimination is not possible by endovascular procedures, should be carefully monitored in the absence of aneurysm growth. If the size is increased, it should be treated.</p> <p>Stent migration &gt; 10 mm with aneurysm diameter increase and/or endoleak detection requires <b>endovascular therapy</b>.</p>	<p>Evidence level 4 / recommendation grade A, strong consensus</p> <p>Evidence level 4 / recommendation grade 0, strong consensus</p>
The National Institute for Health and Care Excellence (NICE) [52]	<p>Accessed in 2019.</p> <p>Draft, in progress: (Note as per 20 June 2019: The timelines for this guideline have been extended although Committee work has been completed)</p>	UK	<p>The committee recommended thin-slice contrast-enhanced arterial-phase CT angiography for imaging in people being evaluated for elective surgery, as it is widely recognised as the gold standard technique for measuring aneurysm size and anatomy before repair.</p> <p>Use contrast-enhanced CT angiography to detect postoperative complications and further aneurysm expansion. If contrast-enhanced CT angiography is contraindicated, consider contrast-enhanced ultrasound to detect endoleaks and further aneurysm expansion. Do not use colour duplex ultrasound as the main imaging technique to detect endoleaks in people who have had an EVAR.</p> <p>Do not offer <b>complex EVAR*</b> to people with an unruptured AAA <b>if open surgical repair is a suitable option</b>, except as part of a randomised controlled trial comparing complex EVAR with open surgical repair. Do not offer <b>complex EVAR</b> to people with an unruptured AAA <b>if open surgical repair is unsuitable</b> because of their anaesthetic and medical condition. Do not offer <b>complex EVAR</b> to people with a ruptured AAA <b>if open surgical repair is suitable</b>, except as part of a randomised controlled trial comparing complex EVAR with open surgical repair.</p>	<p><b>GRADE</b></p> <p>Consensus</p> <p>Consensus, expert opinion.</p> <p>Consensus, expert opinion</p> <p>No evidence. Expert opinion</p> <p>Practice established or no consensus.</p>

Name of society/organisation issuing guidance	Date of issue	Country/ies to which applicable	Summary of recommendation	Quality appraisal tool and Level of evidence
			<p>Consider <b>open, endovascular or percutaneous intervention for type I and type III endoleaks</b> following endovascular aneurysm repair (EVAR)</p> <p>No recommendation about stent migration management.</p> <p>*Any endovascular strategy that is outside the 'instructions for use' of aortic stent grafts, typically adopted because of an <b>AAA's anatomical complexity</b>. This includes using unmodified endografts outside their 'instructions for use', physician-modified endografts, customised fenestrated endografts, and 'snorkel' or 'chimney' approaches with parallel covered stents.</p>	
TAA				
European Association for Cardio-Thoracic Surgery (EACTS), European Society of Cardiology (ESC), European Association of Percutaneous Cardiovascular Interventions (EAPCI) [4]	2012		<p>For TAA patients CT angiography (CTA) is the method of choice for diagnosis and planning treatment</p> <p>Currently, CTA is recommended prior to discharge. Further follow-ups at 6 and 12 months are based on CTA, thereafter MRI/CTA.</p> <p>Coil embolisation, plug occlusion or surgical ligation should be performed during or early after the TEVAR procedure for Endoleak type I or III.</p> <p>No recommendation about stent migration management with TEVAR procedures.</p>	<p>Quality tool not reported.</p> <p>None</p> <p>None</p> <p>None</p>
European Society for Vascular Surgery (ESVS) [23]	2017		<p><u>Recommendation 1:</u> All patients with clinical suspicion of thoracic aortic disease and abnormal chest radiograph should undergo computed</p>	<p>Grading system based on the European Society of Cardiology (ESC) guidelines methodology. (A,B,C)/ class of recommendation (I, IIa, IIb, III). No critical appraisal of individual studies reported.</p> <p>Class I Level B</p>

Name of society/organisation issuing guidance	Date of issue	Country/ies to which applicable	Summary of recommendation	Quality appraisal tool and Level of evidence
			<p>tomographic angiography for diagnosis confirmation.</p> <p><u>Recommendation 23:</u> In patients with ruptured descending thoracic aortic aneurysm, endovascular repair should be the first treatment option when the anatomy is appropriate.</p> <p><u>Recommendation 46a:</u> <b>In fit and unfit patients with favourable anatomy</b>, endovascular repair may be considered for descending thoracic aorta aneurysms between 56 - 59 mm diameter.</p> <p><u>Recommendation 46b:</u> <b>In fit and unfit patients with favourable anatomy</b>, endovascular repair should be considered for descending thoracic aorta aneurysms &gt;60 mm diameter</p> <p><u>Recommendation 79:</u> Any <b>early or late type I</b> or <b>III</b> endoleak after an endovascular repair of the descending thoracic aorta should undergo prompt intervention.</p> <p>No distinction between open repair vs endovascular repair for Endoleak type I or stent migration.</p>	<p>Class 1 Level C</p> <p>Class IIb Level B</p> <p>Class IIa Level B</p> <p>Class I Level C</p> <p>Class I Level C</p>
The National Institute for Health and Care Excellence (NICE). Medical technologies guidance [88]	2018	UK	<p>The case for adopting the E-vita open plus for treating <b>complex aneurysms and dissections of the thoracic aorta</b>, in a carefully selected group of people, is supported by the evidence.</p> <p>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:</p> <ul style="list-style-type: none"> <li>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.</li> </ul>	Not specified.

Name of society/organisation issuing guidance	Date of issue	Country/ies to which applicable	Summary of recommendation	Quality appraisal tool and Level of evidence
			No recommendations about complications such as stent migration or endoleaks	

- Evidence tables of individual studies included for clinical effectiveness and safety**

**Table A2: Characteristics of relevant studies**

Studies	Study Type	Number of patients	Population	Intervention (s)	Endograft
Avci 2012 [25]	Single Prospective Cohort	11 (Secondary intervention)	AAA; Mean age 77 years (59-88). Male 8 (73%). ASA physical status class 3: 9 (82%)	Aptus Heli-FX EndoAnchor System for treatment of migration (with or without other endovascular treatments and Endoleak Ia)	Gore Excluder, Medtronic AneuRx & Talent
Deaton 2009 [27] (STAPLE 1)	Single Prospective Cohort	21 (Primary intervention)	AAA; Median age (min, max) 75 (64-90). Male 20 (95%) Female 1 (5%)	Aptus AAA Endovascular Repair System (Fortevo predecessor + EndoAnchor)	Aptus AAA Endovascular
deVries 2014 [26] (ANCHOR)	Single Prospective Cohort	319 (Primary intervention 242, Secondary intervention 77) Prevention in 186 cases with hostile proximal aortic neck anatomy (76.9%), treatment of endoleak type Ia after endograft deployment in 52 cases (21.5%), and treatment of misdeployed endografts in four cases (1.7%). Treatment of endoleak type Ia in 45 cases (58%), treatment of endograft migration with endoleak type Ia in 21 cases (27%), and treatment of migration without endoleak type Ia in 11 cases (14%)	AAA; Mean age of 74.1 ± 8.2 years. 238 Men (74.6%) ASA physical status class 3 (71.5%) or class 4 (18.5%).	Aptus Heli-FX EndoAnchor System in conjunction with commercially available non-Aptus Endografts prophylactically or Aptus Heli-FX EndoAnchor System for treatment of Endoleak Ia or migration (with or without other endovascular treatments)	Gore Excluder, Cook Zenith, Medtronic Endurant, AneuRx & Talent





Studies	Study Type	Number of patients	Population	Intervention (s)	Endograft
Goudekettig 2019 [28]	Single Retrospective Cohort	51 (31 Primary intervention, 20 Secondary intervention)	AAA. Mean age 75 (70, 78) range 53–88. Men 38 (75%). American Society of ASA physical status class 2 (37%) class 3 (63%) or class 4 (2%).	Aptus Heli-FX EndoAnchor System in conjunction with commercially available non-Aptus Endografts prophylactically (EVAR or ch-EVAR) or Aptus Heli-FX EndoAnchor System for treatment of Endoleak Ia or migration (with or without other endovascular treatments)	Gore Excluder, Cook Zenith, Medtronic Endurant, Valiant & Talent
JordanJr 2014 [30] (ANCHOR)	Single Prospective Cohort	319(242 Primary intervention-77 Secondary intervention) Prevention in 186 cases with hostile proximal aortic neck anatomy (76.9%), treatment of endoleak type Ia after endograft deployment in 52 cases (21.5%), and treatment of misdeployed endografts in four cases (1.7%). Treatment of endoleak type Ia in 45 cases (58%), treatment of endograft migration with endoleak type Ia in 21 cases (27%), and treatment of migration without endoleak type Ia in 11 cases (14%).	AAA: Mean age of 74.1 ± 8.2 y. Gender 238 male (74.6%). American Society of ASA physical status class 3 (71.5%) or class 4 (18.5%).	Aptus Heli-FX EndoAnchor System in conjunction with commercially available non-Aptus Endografts prophylactically or Aptus Heli-FX EndoAnchor System for treatment of Endoleak Ia or migration (with or without other endovascular treatments)	Gore Excluder, Cook Zenith, Medtronic Endurant, AneuRx & Talent
JordanJr 2015 [29] (ANCHOR)	Single Prospective Cohort	208 (ANCHOR Primary intervention patients with unfavourable neck anatomy according to site investigator). 157 at baseline and 130 at follow up with complete core lab evaluation.	AAA: Age 72 ± 8 years. Men 159 (76.4%). ASA physical status class 2 (6.7%) 3 (70.7%) or class 4 (21.2%).	Aptus Heli-FX EndoAnchor System in conjunction with commercially available non-Aptus Endografts prophylactically or Aptus Heli-FX EndoAnchor System for treatment of Endoleak Ia or migration (with or without other endovascular treatments)	Gore Excluder, Cook Zenith, Medtronic Endurant & Talent



Studies	Study Type	Number of patients	Population	Intervention (s)	Endograft
JordanJr 2016 [35] (ANCHOR)	Single Prospective Cohort	100 (73 Primary intervention + 27 Secondary intervention). Prevent type Ia endoleak or endograft migration (62), primary cases with endoleak type Ia (10) or endograft distal misdeployment (1); and secondary cases performed for endoleak alone (11), endoleak with endograft migration (8), or migration alone (8)	AAA Mean Age 73 years ( $\pm$ 8) years. Men 80 (80%).	Aptus Heli-FX EndoAnchor System in conjunction with commercially available non-Aptus Endografts prophylactically or Aptus Heli-FX EndoAnchor System for treatment of Endoleak Ia or migration (with or without other endovascular treatments)	Gore Excluder, Cook Zenith, Medtronic Endurant, AneuRx & Talent
Mehta 2014 [31] (STAPLE 2)	Single Prospective Cohort with historical control group	208 (328 primary intervention). 157 at baseline and 130 at follow up with complete core lab evaluation.	AAA: Mean age 73 $\pm$ 8 y (range, 57-91 years), and 145 (93.5%) men	Aptus AAA Endovascular Repair System (Fortevo predecessor+EndoAnchor)	Aptus AAA Endovascular
Muhs 2018 [32]	Prospective cohort with propensity-matched and retrospective controls	198 (99 primary intervention and 99 controls)	AAA: No reported Age, sex and other characteristics.	Intervention group: Aptus Heli-FX EndoAnchor System in conjunction with commercially available non-Aptus Endografts: Control group: endografts without use of Aptus Heli-FX EndoAnchor System	Gore Excluder, Cook Zenith, Lombard Aor fi x, Endologix AFX or Powerlink, TriVascular Ovation and Medtronic Endurant, & Talent
Ongstad 2016 [33]	Single retrospective cohort	54 (27 Primary intervention and 27 Secondary intervention)	TAA (40 TAA+ 14 T/A AA) Average age 69.4 $\pm$ 13.3 years (range 33-88) Men 36/54 (64.8%)	EndoAnchor System in conjunction with commercially available TEVAR Endografts	No reported
Perdikides 2012 [34]	Single Prospective Cohort	13 (Primary intervention)	AAA: Median age 73 (range 62-82). Men 13/13 (100%). None at high risk for surgical repair.	Aptus Heli-FX EndoAnchor System in conjunction with commercially available non-Aptus Endografts prophylactically or Aptus Heli-FX EndoAnchor System for treatment of Endoleak Ia or migration (with or without other endovascular treatments)	Medtronic Endurant, Cook Zenith

**Table A3: Characteristics of relevant studies (continued)**

Studies	Main endpoints	Included in clinical effectiveness and/or safety domain	Location (N)	Funding	Short or Complex or Hostile Neck	Mean follow up
Avci 2012 [25]	Initial technical success (defined as successful implantation of the endoanchors and removal of the HeliFx Applier and Endoguid). Clinical success (defined as absence of graft-related complications or endoleak type Ia at completion angiography).	EFF & SAF	EU	No reported	No reported	10 months (range, 3-18 months)
Deaton 2009 [27] (STAPLE 1)	Major device-related adverse events at 30 days and feasibility (successful deployment of all endograft components)	EFF & SAF	USA (6)	Aptus	No	10m ± 2.9months
deVries 2014 [26] (ANCHOR)	Technical and Procedural success, AE as Aneurysm and EndoAnchor related reinterventions.	EFF & SAF	USA+EU(43)	Aptus/ Medtronic, Minneapolis, MN, USA	Yes, hostile neck 209/249 (83,94%); Primary arm 160/89 (84,66%), Revision arm 79/160 (81,7%)	16months ± 5months (Imaging follow up ± 7,1months ± 5,6months)
Goudekettig 2019 [28]	Procedure success (successful deployment of the endograft and the EndoAnchor™ without endoleak type Ia or III at completion angiography)	EFF & SAF	EU(1)	Medtronic, Minneapolis, MN, USA	Yes, 48/51 (94%); Primary 30/31 (97%) and Revision 18/20 (90%)	23.9 months (IQR 13.4, 35.6 months)
JordanJr 2014 [30] (ANCHOR)	Composite Primary Efficacy Endpoint (successful implantation of the minimum number of EndoAnchor™ and freedom from migration). Composite Primary safety Endpoint (freedom from serious adverse device-related events or procedure-related adverse events during 12-months)	EFF	USA+EU(43)	Medtronic, Minneapolis, MN, USA	Yes, Short Neck <15 mm in length in 58.8% and <10 mm in length in 42.7% all arms.	9.3 m ± 4.7 m
JordanJr 2015 [29] (ANCHOR)	Technical success (successful implantation of EndoAnchor™ with adequate penetration of the aortic wall and absence of endoleak type Ia at	EFF	USA+EU(43)	Medtronic, Minneapolis, MN, USA	Yes, hostile neck 123/157 (78.3%)	14±7 months (range 0–29)



Studies	Main endpoints	Included in clinical effectiveness and/or safety domain	Location (N)	Funding	Short or Complex or Hostile Neck	Mean follow up
	completion angiography). Primary safety Endpoints (aneurysm-related mortality, serious device events, or procedure-related events followed to 12 months)					
JordanJr 2016 [35] (ANCHOR)	Composite Primary Efficacy Endpoint (successful implantation of the minimum number of EndoAnchor™ and freedom from migration). Composite Primary safety Endpoint (freedom from serious adverse device-related events or procedure-related adverse events during 12-months)	EFF & SAF	USA+EU(43)	Aptus/Medtronic, Minneapolis, MN, USA	Yes, hostile neck in 84/100 (84%), Primary arm 63/73 (86%) and Revision arm 21/27 (78%)	18 ± 4months
Mehta 2014 [31] (STAPLE 2)	Composite Primary Efficacy Endpoints (successful implantation of the minimum number of EndoAnchor™, freedom from migration)	EFF & SAF	USA (25)	Aptus/Medtronic, Minneapolis, MN, USA	18/153 (12%), included despite Inclusion criteria.	3.4 years (IQR 3.1 to 3.8 years)
Muhs 2018 [32]	Freedom from migration, freedom from post-operative endoleak type I or type III, freedom from sac enlargement and estimated cumulative incidence of sac regression	EFF	USA (21)+ 4 (EU)	No reported, although four of five authors was related to Medtronic (Minneapolis, MN, USA) (advisor/grants)	Yes, hostile neck 74/99 (74.7%) of Intervention group and 55/99 (55.6%) of control group.	24 months
Ongstad 2016 [33]	Freedom from migration, freedom from aortic-related intervention, and freedom from post-operative endoleak type I or type III	EFF & SAF	USA(1)	No reported, although one author was advisor for Medtronic, (Minneapolis, MN, USA)	No reported	9.6 ± 8.8 months
Perdikides 2012 [34]	Primary technical success (successful endograft and EndoAnchor™)	EFF & SAF	EU(2)	No reported, although two	Yes, hostile neck: 13/13 (100%)	7 months (range 2-17)



Studies	Main endpoints	Included in clinical effectiveness and/or safety domain	Location (N)	Funding	Short or Complex or Hostile Neck	Mean follow up
	deployment to exclude the aneurysm and achieve a patent graft without the need for additional intervention). & Assisted primary technical success (aneurysm exclusion and a patent graft after an adjunctive intraoperative manoeuvre, such as cuff deployment)			principal authors participated in STAPLE trial (sponsored by APTUS)		

- List of ongoing and planned studies

Table A4: List of ongoing studies with endoanchors

Study Identifier	Estimated completion date	Study type	Number of patients	Intervention	Comparator	Patient population	Endpoints
NCT01534819	April 2028 (first primary outcomes April 2022)	Single arm cohort	1200 (2000 originally)	Heli-FX™ EndoAnchor™ System in conjunction with commercially available abdominal and thoracic Endografts,	No	Subjects with AAA, TAA, or advanced aortic aneurysmal disease and who meet the inclusion/exclusion criteria	<p>Primary safety endpoint is defined by: I. freedom from device-related serious adverse events at 12 months and II. Freedom from procedure-related serious adverse events at 12 months III. Freedom from aneurysm-related mortality defined as: I. Death within 30 days of the index procedure II. Death within 30 days of a secondary procedure to address the aneurysm III. Death from rupture of the treated aneurysm.</p> <p>Primary effectiveness endpoint requires all of the following: I. Successful implantation of the minimum number of EndoAnchor™ and II. Freedom from migration at 12 months and iii freedom from</p>

Study Identifier	Estimated completion date	Study type	Number of patients	Intervention	Comparator	Patient population	Endpoints
							endoleak type I at the targeted attachment site(s) at 12 months

**Abbreviations:** AAA: abdominal aortic aneurysm; TAA: thoracic aortic aneurysm; Sources: ClinicalTrials.gov

**Risk of bias tables**
**Table A5: Risk of bias – study level**

Study	18/19 criteria checklist: critical appraisal single-group studies									
	1. Was the hypothesis/aim/objective of the study clearly stated?	2. Was the study conducted prospectively?	3. Were the cases collected in more than one centre?	4. Were patients recruited consecutively?	5. Were the characteristics of the patients included in the study described?	6. Were the eligibility criteria (i.e. inclusion and exclusion criteria) for entry into the study clearly stated?	7. Did patients enter the study at a similar point in the disease?	8. Was the intervention of interest clearly described?	9. Were additional interventions (co-interventions) clearly described?	10. Were relevant outcome measures established a priori?
Avci 2012 [25]	YES	YES	UNCLEAR	YES	YES	PARTIAL	YES	YES	YES	PARTIAL
Deaton 2009 [27] (STAPLE 1)	YES	YES	YES	YES	YES	YES	YES	YES	YES	YES
deVries 2014 [26] (ANCHOR)	YES	YES	YES	YES	PARTIAL	PARTIAL	YES	YES	YES	YES
Goudekettig 2019 [28]	YES	NO	NO	YES	YES	PARTIAL	YES	YES	YES	YES
JordanJr 2014 [30] (ANCHOR)	YES	YES	YES	YES	YES	YES	YES	YES	YES	YES
JordanJr 2015 [29] (ANCHOR)	YES	YES	YES	YES	YES	YES	YES	YES	YES	YES
JordanJr 2016 [35] (ANCHOR)	YES	YES	YES	YES	YES	YES	YES	YES	YES	YES

Study	18/19 criteria checklist: critical appraisal single-group studies									
	1. Was the hypothesis/aim/objective of the study clearly stated?	2. Was the study conducted prospectively?	3. Were the cases collected in more than one centre?	4. Were patients recruited consecutively?	5. Were the characteristics of the patients included in the study described?	6. Were the eligibility criteria (i.e. inclusion and exclusion criteria) for entry into the study clearly stated?	7. Did patients enter the study at a similar point in the disease?	8. Was the intervention of interest clearly described?	9. Were additional interventions (co-interventions) clearly described?	10. Were relevant outcome measures established a priori?
Mehta 2014 [31] (STAPLE 2)	YES	YES	YES	YES	YES	YES	YES	YES	YES	YES
Ongstad 2016 [33]	YES	NO	NO	NO	YES	PARTIAL	YES	YES	NO	YES
Perdikides 2012 [34]	YES	YES	YES	YES	PARTIAL	YES	YES	YES	YES	YES
Muhs 2018 [32]	YES	PARTIAL	YES	UNCLEAR	NO	YES	YES	YES	YES	YES



Study	18/19 criteria checklist: critical appraisal single-group studies									
	11. Were the relevant outcomes measured using appropriate objective/subjective methods?	12. Were the relevant outcome measures made before and after the intervention?	13. Were the statistical tests used to assess the relevant outcomes appropriate?	14. Was follow-up long enough for important events and outcomes to occur?	15. Were losses to follow-up reported?	16. Did the study provide estimates of random variability in the data analysis of relevant outcomes?	17. Were the adverse events reported?	18. Were the conclusions of the study supported by the results?	19. Were both competing interests and sources of support for the study reported?	TOTAL AFFIRMATIVE
Avci 2012 [25]	YES	YES	UNCLEAR	NO	YES	PARTIAL	PARTIAL	YES	NO	10/19
Deaton 2009 [27] (STAPLE 1)	YES	YES	UNCLEAR	NO	NO	PARTIAL	YES	YES	PARTIAL	13/19
deVries 2014 [26] (ANCHOR)	YES	YES	YES	YES	YES	YES	YES	YES	YES	16/19
Goudekettig 2019 [28]	YES	YES	YES	YES	YES	YES	YES	YES	YES	15/19
JordanJr 2014 [30] (ANCHOR)	YES	YES	YES	NO	YES	PARTIAL	YES	YES	PARTIAL	15/19
JordanJr 2015 [29] (ANCHOR)	YES	YES	YES	NO	YES	PARTIAL	YES	YES	YES	17/19
JordanJr 2016 [35] (ANCHOR)	YES	YES	YES	NO	YES	PARTIAL	YES	YES	YES	17/19
Mehta 2014 [31] (STAPLE 2)	YES	YES	YES	YES	YES	PARTIAL	YES	YES	YES	18/19
Ongstad 2016 [33]	YES	YES	YES	NO	NO	PARTIAL	PARTIAL	YES	NO	9/19
Perdikides 2012 [34]	YES	YES	YES	NO	NO	NO	PARTIAL	YES	PARTIAL	13/19

Study	18/19 criteria checklist: critical appraisal single-group studies									
	11. Were the relevant outcomes measured using appropriate objective/subjective methods?	12. Were the relevant outcome measures made before and after the intervention?	13. Were the statistical tests used to assess the relevant outcomes appropriate?	14. Was follow-up long enough for important events and outcomes to occur?	15. Were losses to follow-up reported?	16. Did the study provide estimates of random variability in the data analysis of relevant outcomes?	17. Were the adverse events reported?	18. Were the conclusions of the study supported by the results?	19. Were both competing interests and sources of support for the study reported?	TOTAL AFFIRMATIVE
Muhs 2018 [32]	YES	YES	YES	NO	YES	YES	NO	YES	YES	15/19

**Table A6: GRADE quality assessment on effectiveness****Outcomes from primary intervention prophylaxis subset of patients****Question:** Should EVAR WITH ENDOANCHORS be used for AORTIC ANEURISM?**Intervention:** PRIMARY INTERVENTION<sup>1</sup>**Bibliography:** [27, 29, 31, 34]

Certainty assessment							No of patients		Effect		Certainty	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	EVAR with EndoAnchor™ 5	Control	Relative (95% CI)	Absolute		
Reintervention rate (Prophylaxis) (follow-up up to 48 months; assessed with: Proportion of reintervention on patients treated)												
4	observational studies <sup>3</sup>	serious <sup>4</sup>	no serious	no serious	serious <sup>5</sup>	none	38/392 (9.7%±7)	-	not pooled <sup>2</sup>	not pooled <sup>2</sup>	⊕000 VERY LOW	CRITICAL
Aneurysm rupture (Prophylaxis) <sup>2</sup> assessed with: Proportion of aneurysm ruptures on treated patients)												
4	observational studies <sup>3</sup>	serious <sup>4</sup>	no serious	no serious	no serious	none	0/392 (0%)	0%	not pooled <sup>2</sup>	not pooled <sup>2</sup>	⊕000 VERY LOW	CRITICAL
Aneurysm-related mortality 30 days (Prophylaxis) <sup>2</sup> assessed with: Proportion of aneurysm-related deaths at 30 days)												
4	observational studies <sup>3</sup>	serious <sup>4</sup>	no serious	no serious	no serious	none	1/392 (0.25%±0,32)	-	not pooled <sup>2</sup>	not pooled <sup>2</sup>	⊕000 VERY LOW	CRITICAL
Aneurysm-related mortality 1year (Prophylaxis) <sup>2</sup> assessed with: Proportion of aneurysm-related deaths at 365 days)												
3	observational studies <sup>3</sup>	serious <sup>4</sup>	no serious	no serious	no serious	none	1/379 (0.26%±0,32)	-	not pooled <sup>2</sup>	not pooled <sup>2</sup>	⊕000 VERY LOW	CRITICAL

Certainty assessment							No of patients		Effect		Certainty	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	EVAR with EndoAnchor™ 5	Control	Relative (95% CI)	Absolute		
Rate of occurrence or recurrence of complications (Prophylaxis) <sup>2</sup> (follow-up up to 72 months; assessed with: Proportion of patients with graft migration or endoleak type I)												
4	observational studies <sup>3</sup>	serious <sup>4</sup>	no serious	no serious	no serious	none	10/392 (2.5%±2,80)	-	not pooled <sup>2</sup>	not pooled <sup>2</sup>	⊕000 VERY LOW	CRITICAL
All-cause mortality early 30d (Prophylaxis) (assessed with: Proportion of deaths of any cause at 30 days)												
4	observational studies <sup>3</sup>	serious <sup>4</sup>	no serious	no serious	no serious	none	5/392 (1,27%±0,71)	-	-	-	⊕000 VERY LOW	IMPORTANT
All-cause mortality 1 year (Prophylaxis) <sup>2</sup> (assessed with: Proportion of deaths by any cause at 365 days)												
3	observational studies <sup>3</sup>	serious <sup>4</sup>	no serious	no serious	no serious	none	11/379 (2.9%±0,67)	-	not pooled <sup>2</sup>	not pooled <sup>2</sup>	⊕000 VERY LOW	IMPORTANT
Conversion to open surgical repair (Prophylaxis) (follow-up up to 48 months; assessed with: Proportion of conversions to open surgical repair)												
4	observational studies <sup>3</sup>	serious <sup>4</sup>	no serious	no serious	no serious	none	6/392 (1.5%±1,91)	-	not pooled <sup>2</sup>	not pooled <sup>2</sup>	⊕000 VERY LOW	IMPORTANT
Technical and Procedural Success (Prophylaxis) (assessed with: Proportion of interventions with deployment without endoleak)												
4	observational studies <sup>3</sup>	serious <sup>4</sup>	no serious	no serious	no serious	none	389/392 (98,45% ± 2,74)	-	not pooled <sup>2</sup>	not pooled <sup>2</sup>	⊕000 VERY LOW	IMPORTANT
Health-related quality of life (HRQoL)(Prophylaxis) - not reported												
Rate of neck dilation or sac enlargement (Prophylaxis) (follow-up up to 48 months; assessed with: Proportion of patients with neck dilation or sac enlargement (>5 mm))												

Certainty assessment							No of patients		Effect		Certainty	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	EVAR with EndoAnchor™ <sup>5</sup>	Control	Relative (95% CI)	Absolute		
4	observational studies <sup>3</sup>	serious <sup>4</sup>	no serious	serious <sup>8</sup>	no serious	none	7/392 (1.78%±1,21)	-	not pooled <sup>2</sup>	not pooled <sup>2</sup>	⊕000 VERY LOW	NOT IMPORTANT
<b>Rate of sac regression (Prophylaxis)<sup>2</sup> (follow-up up to 48 months; assessed with: Proportion of patients with sac regression (&gt;5 mm))</b>												
3	observational studies <sup>3</sup>	serious <sup>4</sup>	no serious	serious <sup>8</sup>	no serious	none	143/379 (37.7%±12,47)	-	not pooled <sup>2</sup>	not pooled <sup>2</sup>	⊕000 VERY LOW	NOT IMPORTANT

<sup>1</sup> Primary endovascular aortic aneurysm repair with high risk of complications (high-risk migration/endoleak (i.e. hostile neck in abdominal aortic length, complex shape, wide diameter or the presence of calcification or thrombus) — subgroup of a larger register.

<sup>2</sup> No metaanalysis was done; weighted calculation by study size

<sup>3</sup> Prospective single-arm to follow outcomes

<sup>4</sup> Conflict of interest & funding: some authors related to the MAH. No control group. Follow-up mid-term. See Table A5 IHE Quality Appraisal Checklist for Case Series Studies.

<sup>5</sup> Large differences between studies.

<sup>6</sup> Complications measured: graft migration, endoleak type I.

<sup>7</sup> It includes index intervention and reintervention due to any cause.

<sup>8</sup> Surrogate outcome

**Outcomes from primary intervention due to immediate endoleak I subset of patients****Question:** Should EVAR WITH ENDOANCHORS be used for AORTIC ANEURISM?**Intervention:** PRIMARY INTERVENTION<sup>3</sup>**Bibliography:** [26]

Certainty assessment							No of patients		Effect		Certainty	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	EVAR with EndoAnchor™	Control	Relative (95% CI)	Absolute		
Reintervention rate <sup>7</sup> (ImmediateEndoleak type I) (follow-up mean 16 months; assessed with: Proportion of reintervention on patients treated)												
1	observational studies <sup>1</sup>	serious <sup>2</sup>	no serious	no serious	serious <sup>4</sup>	none	3/60 (5%)	-	-	-	⊕000 VERY LOW	CRITICAL
Aneurysm rupture (ImmediateEndoleak type I) - not reported												
Aneurysm-related mortality 30 days (ImmediateEndoleak type I) - not reported												
Aneurysm-related mortality 1year (ImmediateEndoleak type I) - not reported												
Rate of occurrence or recurrence of complications <sup>6</sup> (ImmediateEndoleak type I) (follow-up mean 16 months; assessed with: Proportion of patients with graft migration or endoleak type I)												
1	observational studies <sup>1</sup>	serious <sup>2</sup>	no serious	serious <sup>2</sup>	serious <sup>4</sup>	none	17/60 (28.3%)	-	-	-	⊕000 VERY LOW	CRITICAL
All-cause mortality early 30d (ImmediateEndoleak type I) - not reported												
All-cause mortality early 1 year (ImmediateEndoleak type I) (assessed with: Proportion of deaths by any cause at 365 days)												
1	observational studies <sup>1</sup>	serious <sup>2</sup>	no serious	no serious	serious <sup>4</sup>	none	3/60 (5%)	-	not pooled	not pooled	⊕000 VERY LOW	IMPORTANT
Conversion to open surgical repair (ImmediateEndoleak type I) - not reported												
Technical and Procedural Success (ImmediateEndoleak type I) (assessed with: Proportion of interventions with deployment without endoleak)												

Certainty assessment							No of patients		Effect		Certainty	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	EVAR with EndoAnchor™	Control	Relative (95% CI)	Absolute		
1	observational studies <sup>1</sup>	serious <sup>2</sup>	no serious	no serious	serious <sup>4</sup>	none	43/60 (71.7%)	-	-	-	⊕000 VERY LOW	IMPORTANT
<b>Health-related quality of life (HRQoL) (ImmediateEndoleak type I) - not reported</b>												
<b>Rate of neck dilation or sac enlargement (ImmediateEndoleak type I) (follow-up mean 16 months; assessed with: Proportion of patients with neck dilation or sac enlargement (&gt;5 mm))</b>												
1	observational studies <sup>1</sup>	serious <sup>2</sup>	no serious	serious <sup>8</sup>	serious <sup>4</sup>	none	0/60 (0%)	-	-	-	⊕000 VERY LOW	NOT IMPORTANT
<b>Rate of sac regression (ImmediateEndoleak type I) (follow-up mean 16 months; assessed with: Proportion of patients with sac regression (&gt;5 mm))</b>												
1	observational studies <sup>1</sup>	serious <sup>2</sup>	no serious	serious <sup>8</sup>	serious <sup>4</sup>	none	2/60 (3.3%)	-	-	-	⊕000 VERY LOW	NOT IMPORTANT

<sup>1</sup> Prospective single-arm to follow outcomes.<sup>2</sup> Conflict of interest & funding: some authors related to the MAH. No control group. Follow-up mid-term. IHE 16/19.<sup>3</sup> Primary endovascular aortic aneurysm repair with high risk of complications (high-risk migration/endoleak (i.e. hostile neck in abdominal aortic length, complex shape, wide diameter or the presence of calcification or thrombus). Patients with immediate endoleak I. Subgroup of patients from a larger register.<sup>4</sup> Small size.<sup>5</sup> Number total of patients: available for analysis.<sup>6</sup> Complications measured: graft migration, endoleak type I.<sup>7</sup> It includes index intervention and reintervention due to any cause.<sup>8</sup> Surrogate outcome

**Outcomes from primary intervention due to maldeployment subset of patients****Question:** Should EVAR WITH ENDOANCHORS be used for AORTIC ANEURYSM?**Intervention:** PRIMARY INTERVENTION<sup>4</sup>**Bibliography:** [26]

Certainty assessment							No of patients		Effect		Certainty	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	EVAR with EndoAnchor™	Control	Relative (95% CI)	Absolute		
Reintervention rate <sup>6</sup> (Maldeployment) (follow-up mean 16 months; assessed with: Proportion of reintervention)												
1	observational studies <sup>1</sup>	serious <sup>2</sup>	not serious	serious <sup>2</sup>	serious <sup>3</sup>	none	0/4 (0%) <sup>3</sup>	-	-	-	⊕000 VERY LOW	CRITICAL
Aneurysm rupture (Maldeployment) - not reported												
Aneurysm-related mortality 30 days (Maldeployment) - not reported												
Aneurysm-related mortality 1year (Maldeployment) - not reported												
Rate of occurrence or recurrence of complications <sup>5</sup> (Maldeployment) (follow-up mean 16 months; assessed with: Proportion of patients with graft migration or endoleak type I)												
1	observational studies <sup>1</sup>	serious <sup>2</sup>	not serious	not serious	serious <sup>3</sup>	none	1/4 (25%)	-	-	-	⊕000 VERY LOW	CRITICAL
All-cause mortality early 30d (Maldeployment) - not reported												
All-cause mortality early 1year (Maldeployment) <sup>3</sup> (assessed with: Proportion of deaths by any cause at 365 days)												
1	observational studies <sup>1</sup>	serious <sup>2</sup>	not serious	not serious	serious <sup>3</sup>	none	1/4 (25%)	-	-	-	⊕000 VERY LOW	IMPORTANT
Conversion to open surgical repair (Maldeployment) - not reported												
Technical and Procedural Success (Maldeployment) <sup>3</sup> (assessed with: Proportion of interventions with deployment without endoleak)												



Certainty assessment							No of patients		Effect		Certainty	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	EVAR with EndoAnchor™	Control	Relative (95% CI)	Absolute		
1	observational studies <sup>1</sup>	serious <sup>2</sup>	not serious	not serious	serious <sup>3</sup>	none	2/4 (50%)	-	-	-	⊕000 VERY LOW	IMPORTANT
<b>Health-related quality of life (HRQoL)(Maldeployment) - not reported</b>												
<b>Rate of neck dilation or sac enlargement (Maldeployment) (follow-up mean 16 months; assessed with: Proportion of patients with neck dilation or sac enlargement (&gt;5 mm))</b>												
1	observational studies <sup>1</sup>	serious <sup>2</sup>	not serious	serious <sup>7</sup>	serious <sup>3</sup>	none	0/4 (0%) <sup>3</sup>	-	-	-	⊕000 VERY LOW	NOT IMPORTANT
<b>Rate of sac regression (Maldeployment) (follow-up mean 16 months; assessed with: Proportion of patients with sac regression (&gt;5 mm))</b>												
1	observational studies <sup>1</sup>	serious <sup>2</sup>	not serious	serious <sup>7</sup>	serious <sup>3</sup>	none	0/4 (0%) <sup>3</sup>	-	-	-	⊕000 VERY LOW	NOT IMPORTANT

<sup>1</sup> Prospective single-arm to follow outcomes.<sup>2</sup> Conflict of interest & funding: some authors related to the MAH. No control group. Follow-up mid-term. IHE 16/19.<sup>3</sup> Number total of patients: available for analysis. Only 4 patients in a larger study. Small size.<sup>4</sup> Primary endovascular aortic aneurysm repair with high risk of complications (high-risk migration/endoleak (i.e. hostile neck in abdominal aortic length, complex shape, wide diameter or the presence of calcification or thrombus). Patients with maldeployment in the intervention. Subgroup of patients of a larger register.<sup>5</sup> Complications measured: graft migration, endoleak type I.<sup>6</sup> It includes index intervention and reintervention due to any cause.<sup>7</sup> Surrogate outcome.

**Outcomes from secondary intervention due to migration subset of patients****Question:** Should EVAR WITH ENDOANCHORS be used for AORTIC ANEURYSM?**Intervention:** SECONDARY INTERVENTION MIGRATION<sup>4</sup>**Bibliography:** [25, 26]

Certainty assessment							No of patients		Effect		Certainty	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	EVAR with EndoAnchor™	Control	Relative (95% CI)	Absolute		
Reintervention rate <sup>7</sup> (Secondary-Revision Migration) (follow-up up to 18 months; assessed with: Proportion of reintervention)												
2	observational studies <sup>2</sup>	serious <sup>3</sup>	not serious	not serious	serious <sup>8</sup>	none	3/12 (25%±7.87)	-	not pooled <sup>1</sup>	not pooled <sup>1</sup>	⊕000 VERY LOW	CRITICAL
Aneurysm rupture (Secondary-Revision Migration) (follow-up mean 10 months; assessed with: Proportion of aneurysm ruptures)												
1	observational studies <sup>2</sup>	very serious <sup>3</sup>	not serious	not serious	serious <sup>8</sup>	none	0/1 (0%)	-	-	-	⊕000 VERY LOW	CRITICAL
Aneurysm-related mortality 30 days (Secondary-Revision Migration) (assessed with: Proportion of aneurysm-related deaths at 30 days)												
2	observational studies <sup>2</sup>	serious <sup>3</sup>	not serious	not serious	serious <sup>8</sup>	none	0/12 (0%)	-	not pooled <sup>1</sup>	not pooled <sup>1</sup>	⊕000 VERY LOW	CRITICAL
Aneurysm-related mortality 1 year (Secondary-Revision Migration) (assessed with: Proportion of aneurysm-related deaths at 365 days)												
2	observational studies <sup>2</sup>	serious <sup>3</sup>	not serious	not serious	serious <sup>8</sup>	none	0/12 (0%)	-	not pooled <sup>1</sup>	not pooled <sup>1</sup>	⊕000 VERY LOW	CRITICAL
Rate of occurrence or recurrence of complications <sup>6</sup> (All groups Secondary-Revision) <sup>9</sup> (follow-up up to 18 months; assessed with: Proportion of patients with graft migration or endoleak type I)												
2	observational studies <sup>2</sup>	serious <sup>3</sup>	not serious	not serious	serious <sup>8</sup>	none	12/88 (13.63%±1.73) <sup>5,9</sup>	-	-	-	⊕000 VERY LOW	CRITICAL

Certainty assessment							No of patients		Effect		Certainty	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	EVAR with EndoAnchor™	Control	Relative (95% CI)	Absolute		
All-cause mortality early 30d (Secondary-Revision Migration) (assessed with: Proportion of deaths of any cause at 30 days)												
2	observational studies <sup>2</sup>	serious <sup>3</sup>	not serious	not serious	serious <sup>8</sup>	none	0/12 (0%)	-	not pooled <sup>1</sup>	not pooled <sup>1</sup>	⊕000 VERY LOW	IMPORTANT
All-cause mortality early 1 year (Secondary-Revision Migration) (assessed with: Proportion of deaths by any cause at 365 days)												
2	observational studies <sup>2</sup>	serious <sup>3</sup>	not serious	not serious	serious <sup>8</sup>	none	0/12 (0%)	-	not pooled <sup>1</sup>	not pooled <sup>1</sup>	⊕000 VERY LOW	IMPORTANT
Conversion to open surgical repair (All groups Secondary-Revision) <sup>9</sup> (follow-up mean up to 18 months; assessed with: Proportion of conversions to open surgical repair)												
2	observational studies <sup>2</sup>	serious <sup>3</sup>	not serious	not serious	serious <sup>8</sup>	none	1/88 (1.13%±0.43) <sup>9</sup>	-	not pooled <sup>1</sup>	not pooled <sup>1</sup>	⊕000 VERY LOW	IMPORTANT
Technical and Procedural Success (Secondary-Revision Migration) (assessed with: Proportion of interventions with deployment without endoleak)												
2	observational studies <sup>2</sup>	serious <sup>3</sup>	not serious	not serious	serious <sup>8</sup>	none	9/12 (75%±7.87)	-	-	-	⊕000 VERY LOW	IMPORTANT
Health-related quality of life (HRQoL) (All groups Secondary-Revision) - not reported												
Rate of neck dilation or sac enlargement (Secondary-Revision) <sup>9</sup> (follow-up mean 16 months; assessed with: Proportion of patients with neck dilation or sac enlargement (>5mm))												
1	observational studies <sup>2</sup>	serious <sup>3</sup>	not serious	serious <sup>10</sup>	serious <sup>8</sup>	none	1/77 (1.3%) <sup>9</sup>	-	-	-	⊕000 VERY LOW	NOT IMPORTANT

Certainty assessment							No of patients		Effect		Certainty	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	EVAR with EndoAnchor™	Control	Relative (95% CI)	Absolute		
Rate of sac regression (All groups Secondary-Revision) <sup>9</sup> (follow-up up to 18 months; assessed with: Proportion of patients with sac regression (>5 mm))												
2	observational studies <sup>2</sup>	serious <sup>3</sup>	not serious	serious <sup>10</sup>	serious <sup>8</sup>	none	8/88 (9.1%±1.03) <sup>9</sup>	-	not pooled <sup>1</sup>	not pooled <sup>1</sup>	⊕○○○ VERY LOW	NOT IMPORTANT

<sup>1</sup> No meta-analysis was done; weighted calculations by study size.

<sup>2</sup> Prospective single-arm to follow outcomes.

<sup>3</sup> Conflict of interest & funding: some authors related to the MAH. No control group. Follow-up mid-term. See Table A5 IHE Quality Appraisal Checklist for Case Series Studies

<sup>4</sup> Secondary repair of EVAR/TEVAR complications (endograft migration).

<sup>5</sup> Data is from patients with intervention due to previous endoleak type I. The other 2 groups have insufficient information. If it is only considered the denominator of patients with endoleak, the estimation would be 24.48%±7.70.

<sup>6</sup> Complications measured: graft migration, endoleak type I.

<sup>7</sup> It includes index intervention and reintervention due to any cause.

<sup>8</sup> Small size.

<sup>9</sup> Overall patients in the studies (migration, endoleak, and migration and endoleak).

<sup>10</sup> Surrogate outcome.

**Outcomes from secondary intervention due to endoleak I subset of patients****Question:** Should EVAR WITH ENDOANCHORS be used for AORTIC ANEURYSM?**Intervention:** SECONDARY INTERVENTION ENDOLEAK<sup>4</sup>**Bibliography:** [25, 26]

Certainty assessment							No of patients		Effect		Certainty	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	EVAR with EndoAnchor™	Control	Relative (95% CI)	Absolute		
Reintervention rate <sup>7</sup> (Secondary-Revision Endoleak type I) (follow-up up to 18 months; assessed with: Proportion of reintervention on patients treated)												
2	observational studies <sup>2</sup>	serious <sup>3</sup>	not serious	not serious	serious <sup>8</sup>	none	8/49 (16.32%±10.14)	-	not pooled <sup>1</sup>	not pooled <sup>1</sup>	⊕○○○ VERY LOW	CRITICAL
Aneurysm rupture (Secondary-Revision Endoleak) (follow-up mean 10 months; assessed with: Proportion of aneurysm ruptures on treated patients)												
1	observational studies <sup>2</sup>	very serious <sup>3</sup>	not serious	not serious	serious <sup>8</sup>	none	0/4 (0%)	-	-	-	⊕○○○ VERY LOW	CRITICAL
Aneurysm-related mortality 30 days (Secondary-Revision Endoleak type I) <sup>1</sup> (assessed with: Proportion of aneurysm-related deaths at 30 days)												
2	observational studies <sup>2</sup>	serious <sup>3</sup>	not serious	not serious	serious <sup>8</sup>	none	0/49 (0%)	-	not pooled <sup>1</sup>	not pooled <sup>1</sup>	⊕○○○ VERY LOW	CRITICAL
Aneurysm-related mortality 1 year (Secondary-Revision Endoleak type I) <sup>1</sup> (assessed with: Proportion of aneurysm-related deaths at 365 days)												
2	observational studies <sup>2</sup>	serious <sup>3</sup>	not serious	not serious	serious <sup>8</sup>	none	0/49 (0%)	-	not pooled <sup>1</sup>	not pooled <sup>1</sup>	⊕○○○ VERY LOW	CRITICAL
All-cause mortality early 30d (Secondary-Revision Endoleak type I) <sup>1</sup> (assessed with: Proportion of deaths of any cause at 30 days)												
2	observational studies <sup>2</sup>	serious <sup>3</sup>	not serious	not serious	serious <sup>8</sup>	none	0/49 (0%)	-	not pooled <sup>1</sup>	not pooled <sup>1</sup>	⊕○○○ VERY LOW	IMPORTANT

Certainty assessment							No of patients		Effect		Certainty	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	EVAR with EndoAnchor™	Control	Relative (95% CI)	Absolute		
All-cause mortality early 1year (Secondary-Revision Endoleak type I (assessed with: Proportion of deaths by any cause at 365 days)												
2	observational studies <sup>2</sup>	serious <sup>3</sup>	not serious	not serious	serious <sup>8</sup>	none	3/49 (6.12%±1.84)	-	not pooled <sup>1</sup>	not pooled <sup>1</sup>	⊕○○○ VERY LOW	IMPORTANT
Technical and Procedural Success (Secondary-Revision Endoleak type I) (assessed with: Proportion of interventions with deployment without endoleak)												
2	observational studies <sup>2</sup>	serious <sup>3</sup>	not serious	not serious	serious <sup>8</sup>	none	37/49 (75.51%±7.68)	-	not pooled <sup>1</sup>	not pooled <sup>1</sup>	⊕○○○ VERY LOW	IMPORTANT

<sup>1</sup> No meta-analysis was done; weighted mean by study size.

<sup>2</sup> Prospective single-arm to follow outcomes.

<sup>3</sup> Conflict of interest & funding: some authors related to the MAH. No control group. Follow-up mid-term. See Table A5 IHE Quality Appraisal Checklist for Case Series Studies

<sup>4</sup> Secondary repair of EVAR/TEVAR complications (endoleak type I).

<sup>5</sup> Data proceed from patients with intervention due to previous endoleak type I. The other 2 groups with insufficient information.

<sup>6</sup> Complications measured: graft migration, endoleak type I.

<sup>7</sup> It includes index intervention and reintervention due to any cause.

<sup>8</sup> Small size.

**Outcomes from secondary intervention due to endoleak type I and migration subset of patients****Question:** Should EVAR WITH ENDOANCHORS be used for AORTIC ANEURYSM?**Intervention:** SECONDARY INTERVENTION MIGRATION AND ENDOLEAK<sup>4</sup>**Bibliography:** [25, 26]

Certainty assessment							No of patients		Effect		Certainty	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	EVAR with EndoAnchor™	Control	Relative (95% CI)	Absolute		
Reintervention rate <sup>7</sup> (Revision-Secondary Endoleak type I AND Migration) <sup>1</sup> (follow-up up to 18 months; assessed with: Proportion of reintervention)												
2	observational studies <sup>2</sup>	serious <sup>3</sup>	not serious	not serious	serious <sup>8</sup>	none	2/27 (7.4%±4.03)	-	not pooled <sup>1</sup>	not pooled <sup>1</sup>	⊕○○○ VERY LOW	CRITICAL
Aneurysm rupture (Revision-Secondary Endoleak type I AND Migration) (follow-up mean 10 months; assessed with: Proportion of aneurysm ruptures)												
1	observational studies <sup>2</sup>	very serious <sup>3</sup>	not serious	not serious	serious <sup>8</sup>	none	0/6 (0%)	-	-	-	⊕○○○ VERY LOW	CRITICAL
Aneurysm-related mortality 30 days (Secondary-Revision Endoleak type I AND Migration) <sup>1</sup> (assessed with: Proportion of aneurysm-related deaths at 30 days)												
2	observational studies <sup>2</sup>	serious <sup>3</sup>	not serious	not serious	serious <sup>8</sup>	none	0/27 (0%)	-	not pooled <sup>1</sup>	not pooled <sup>1</sup>	⊕○○○ VERY LOW	CRITICAL
Aneurysm-related mortality 1year (Secondary-Revision Endoleak type I AND Migration) <sup>1</sup> (assessed with: Proportion of aneurysm-related deaths at 365 days)												
2	observational studies <sup>2</sup>	serious <sup>3</sup>	not serious	not serious	serious <sup>8</sup>	none	0/27 (0%)	-	not pooled <sup>1</sup>	not pooled <sup>1</sup>	⊕○○○ VERY LOW	CRITICAL
All-cause mortality early 30d (Secondary-Revision Endoleak type I AND Migration) <sup>1</sup> (assessed with: Proportion of deaths of any cause at 30 days)												
2	observational studies <sup>2</sup>	serious <sup>3</sup>	not serious	not serious	serious <sup>8</sup>	none	0/27 (0%)	-	not pooled <sup>1</sup>	not pooled <sup>1</sup>	⊕○○○ VERY LOW	IMPORTANT

Certainty assessment							No of patients		Effect		Certainty	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	EVAR with EndoAnchor™	Control	Relative (95% CI)	Absolute		
All-cause mortality early 1 year (Secondary-Revision Endoleak type I AND Migration (assessed with: Proportion of deaths by any cause at 365 days)												
2	observational studies <sup>2</sup>	serious <sup>3</sup>	not serious	not serious	serious <sup>8</sup>	none	1/27 (3.7%±2.02)	-	not pooled	not pooled	⊕000 VERY LOW	IMPORTANT
Technical and Procedural Success (Secondary-Revision Endoleak type I AND Migration) <sup>1</sup> (assessed with: Proportion of interventions with deployment without endoleak type I)												
2	observational studies <sup>2</sup>	serious <sup>3</sup>	not serious	not serious	serious <sup>8</sup>	none	25/27 (92.6%±4.03)	-	not pooled <sup>1</sup>	not pooled <sup>1</sup>	⊕000 VERY LOW	IMPORTANT
Health-related quality of life (HRQoL) (All groups Secondary-Revision) - not reported												
Rate of neck dilation or sac enlargement (Secondary-Revision) (follow-up mean 16 months; assessed with: Proportion of patients with neck dilation or sac enlargement (>5mm))												
1	observational studies <sup>2</sup>	serious <sup>3</sup>	not serious	serious <sup>9</sup>	serious <sup>8</sup>	none	1/77 (1.3%)	-	-	-	⊕000 VERY LOW	NOT IMPORTANT

<sup>1</sup> No meta-analysis was done; weighted calculations by study size.

<sup>2</sup> Prospective single-arm to follow outcomes.

<sup>3</sup> Conflict of interest & funding: some authors related to the MAH. No control group. Follow-up mid-term. See Table A5 IHE Quality Appraisal Checklist for Case Series Studies

<sup>4</sup> Secondary repair of EVAR/TEVAR complications (endoleak type I AND endograft migration).

<sup>5</sup> Data is from patients with intervention due to previous endoleak type I. The other 2 groups with insufficient information.

<sup>6</sup> Complications measured: graft migration, endoleak type I.

<sup>7</sup> It includes index intervention and reintervention due to any cause.

<sup>8</sup> Small size.

<sup>9</sup> Surrogate outcome.



**Outcomes from primary intervention (not separated data on subgroups, 1 retrospective series)****Question:** Should EVAR WITH ENDOANCHORS be used for AORTIC ANEURISM?**Intervention:** PRIMARY INTERVENTION RETROSPECTIVE SERIES<sup>4</sup>**Bibliography:** [28]

Certainty assessment							No of patients		Effect		Certainty	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	EVAR with En-doAnchor™ 4	Control	Relative (95% CI)	Absolute		
Reintervention rate (assessed with: Proportion of reintervention)												
1	observational studies <sup>1</sup>	very serious <sup>2</sup>	not serious	not serious	serious <sup>3</sup>	none	13/51 (25.5%)	-	-	-	⊕000 VERY LOW	CRITICAL
Aneurysm rupture <sup>5</sup> (assessed with: Proportion of aneurysm ruptures )												
1	observational studies <sup>1</sup>	very serious <sup>2</sup>	not serious	not serious	serious <sup>3</sup>	none	1/51 (2%)	0%	-	-	⊕000 VERY LOW	CRITICAL
Aneurysm-related mortality 30 days (assessed with: Proportion of aneurysm-related deaths at 30 days)												
1	observational studies <sup>1</sup>	very serious <sup>2</sup>	not serious	not serious	serious <sup>3</sup>	none	2/51 (3.9%)	-	not pooled <sup>5</sup>	not pooled <sup>5</sup>	⊕000 VERY LOW	CRITICAL
Aneurysm-related mortality 1year (assessed with: Proportion of aneurysm-related deaths at 365 days)												
1	observational studies <sup>1</sup>	very serious <sup>2</sup>	not serious	not serious	serious <sup>3</sup>	none	3/51 (5.9%)	-	-	-	⊕000 VERY LOW	CRITICAL
Rate of occurrence or recurrence of complications <sup>6</sup> (assessed with: Proportion of patients with graft migration or endoleak type I)												
1	observational studies <sup>1</sup>	very serious <sup>2</sup>	not serious	not serious	serious <sup>3</sup>	none	9/51 (17.6%)	-	-	-	⊕000 VERY LOW	CRITICAL

Certainty assessment							No of patients		Effect		Certainty	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	EVAR with En-doAnchor™ 4	Control	Relative (95% CI)	Absolute		
All-cause mortality early 30d												
1	observational studies <sup>1</sup>	very serious <sup>2</sup>	not serious	not serious	serious <sup>3</sup>	none	2/51 (3.9%)	-	-	-	⊕000 VERY LOW	IMPORTANT
All-cause mortality early 1 year (assessed with: Proportion of deaths by any cause at 365 days)												
1	observational studies <sup>1</sup>	very serious <sup>2</sup>	not serious	not serious	serious <sup>3</sup>	none	7/51 (13.7%)	-	-	-	⊕000 VERY LOW	IMPORTANT
Conversion to open surgical repair - not reported												
Technical and Procedural Success - not reported												
Health-related quality of life (HRQoL) - not reported												
Rate of neck dilation or sac enlargement (assessed with: Proportion of patients with neck dilation or sac enlargement (>5 mm))												
1	observational studies <sup>1</sup>	very serious <sup>2</sup>	not serious	serious <sup>9</sup>	serious <sup>3</sup>	none	1/51 (2%)	-	-	-	⊕000 VERY LOW	NOT IMPORTANT
Rate of sac regression - not reported												

<sup>1</sup> Retrospective series.<sup>2</sup> Conflict of interest & funding: some authors related to the MAH. Retrospective case series review. No control group. Follow-up mid-term. IHE 15/19.<sup>3</sup> Small size.<sup>4</sup> Primary endovascular aortic aneurysm repair with high risk of complications (high-risk migration/endoleak (i.e. hostile neck in abdominal aortic length, complex shape, wide diameter or the presence of calcification or thrombus).<sup>5</sup> No meta-analysis was done; weighted calculations by study size.<sup>6</sup> Complications measured: graft migration, endoleak type I.<sup>7</sup> It includes index intervention and reintervention due to any cause.<sup>8</sup> Prospective single-arm to follow outcomes.<sup>9</sup> Surrogate outcome.

**Outcomes from primary intervention (not separated) in thoracic aneurysm****Question:** Should TEVAR WITH ENDOANCHORS be used for THORACIC ANEURYSMS?**Intervention:** PRIMARY INTERVENTION<sup>5</sup>**Bibliography:** [33]

Certainty assessment							No of patients		Effect		Certainty	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	TEVAR with EndoAnchor™	Control	Relative (95% CI)	Absolute		
Reintervention rate <sup>7</sup> (all patients: primary and secondary-revision) (assessed with: Proportion of reintervention)												
1	observational studies <sup>1</sup>	very serious <sup>3</sup>	not serious	not serious	not serious	reporting bias <sup>2</sup>	9/54 (16.7%)	-	-	-	⊕000 VERY LOW	CRITICAL
Aneurysm rupture (all patients: primary and secondary-revision) (assessed with: Proportion of aneurysm ruptures)												
1	observational studies <sup>1</sup>	very serious <sup>3</sup>	not serious	not serious	not serious	reporting bias <sup>2</sup>	1/54 (1.9%)	-	-	-	⊕000 VERY LOW	CRITICAL
Aneurysm-related mortality 30 days (all patients: primary and secondary-revision) (assessed with: Proportion of aneurysm-related deaths at 30 days)												
1	observational studies <sup>1</sup>	very serious <sup>3</sup>	not serious	not serious	not serious	reporting bias <sup>2</sup>	2/54 (3.7%)	-	-	-	⊕000 VERY LOW	CRITICAL
Aneurysm-related mortality 1 year (all patients: primary and secondary-revision) (assessed with: Proportion of aneurysm-related deaths at 365 days)												
1	observational studies <sup>1</sup>	very serious <sup>3</sup>	not serious	not serious	not serious	reporting bias <sup>2</sup>	5/54 (9.3%)	-	-	-	⊕000 VERY LOW	CRITICAL
Rate of occurrence or recurrence of complications <sup>6</sup> (all patients: primary and secondary-revision) (assessed with: Proportion of patients with graft migration or endoleak type I)												
1	observational studies <sup>1</sup>	very serious <sup>3</sup>	not serious	not serious	not serious	reporting bias <sup>2</sup>	4/54 (7.4%)	-	-	-	⊕000 VERY LOW	CRITICAL

Certainty assessment							No of patients		Effect		Certainty	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	TEVAR with EndoAnchor™	Control	Relative (95% CI)	Absolute		
All-cause mortality early 30d (all patients: primary and secondary-revision) (assessed with: Proportion of deaths of any cause at 30 days)												
1	observational studies <sup>1</sup>	very serious <sup>3</sup>	not serious	not serious	not serious	reporting bias <sup>2</sup>	2/54 (3.7%) <sup>4</sup>	-	-	-	⊕○○○ VERY LOW	IMPORTANT
All-cause mortality early 1 year (all patients: primary and secondary-revision) (assessed with: Proportion of deaths by any cause at 365 days)												
1	observational studies <sup>1</sup>	very serious <sup>3</sup>	not serious	not serious	not serious	reporting bias <sup>2</sup>	6/54 (11.1%)	-	-	-	□□□□ VERY LOW	IMPORTANT
Conversion to open surgical repair (all patients: primary and secondary-revision) (assessed with: Proportion of conversions to open surgical repair)												
1	observational studies <sup>1</sup>	very serious <sup>3</sup>	not serious	not serious	not serious	reporting bias <sup>2</sup>	0/54 (0%)	-	-	-	⊕○○○ VERY LOW	IMPORTANT
Technical and Procedural Success (all patients: primary and secondary-revision) (assessed with: Proportion of interventions with deployment without endoleak)												
1	observational studies <sup>1</sup>	very serious <sup>3</sup>	not serious	not serious	not serious	reporting bias <sup>2</sup>	53/54 (98.1%)	-	-	-	⊕○○○ VERY LOW	IMPORTANT
Health-related quality of life (HRQoL) (all patients: primary and secondary-revision) - not reported												
Rate of neck dilation or sac enlargement (all patients: primary and secondary-revision) - not reported												
Rate of sac regression (all patients: primary and secondary-revision) - not reported												

<sup>1</sup> Retrospective case series.<sup>2</sup> Outcomes of patients in the original registry not reported in other studies.<sup>3</sup> No conflict of interest stated. Retrospective case series review. No control group. Short follow-up. Low power. IHE 9/19.<sup>4</sup> 2 deaths related to Aneurysm included.<sup>5</sup> Primary endovascular aortic aneurysm repair with high risk of complications (high-risk migration/endoleak (i.e. hostile neck in abdominal aortic length, complex shape, wide diameter or the presence of calcification or thrombus).

<sup>6</sup> Complications measured: graft migration, endoleak type I.

<sup>7</sup> It includes index intervention and reintervention due to any cause.

#### Outcomes from primary intervention (not separated, comparative studies)

**Question:** Should EVAR/TEVAR WITH ENDOANCHORS be used for AORTIC ANEURISM VS EVAR/TEVAR WITHOUT?

**Intervention:** PRIMARY INTERVENTION<sup>5</sup>

**Bibliography:** [32]

Certainty assessment								No of patients		Effect		Certainty	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations		EVAR with EndoAnchor™	Control	Relative (95% CI)	Absolute		
Rate of occurrence or recurrence of complications <sup>6</sup> (follow-up 12-24 months; assessed with: Proportion of patients with graft migration or endoleak type I)													
1	observational studies <sup>1</sup>	serious <sup>2</sup>	not serious	not serious	serious <sup>8</sup>	none		2/99 (2%) <sup>3</sup>	4/99 (4%) <sup>4</sup>	OR 0.49 (0.09 to 2.73)	20 fewer per 1.000 (from 37 fewer to 63 more)	⊕000 VERY LOW	CRITICAL
Rate of neck dilation or sac enlargement (Prophylaxis) (follow-up 12-24 months; assessed with: Proportion of patients with neck dilation or sac enlargement (>5 mm))													
1	observational studies <sup>1</sup>	serious <sup>2</sup>	not serious	serious <sup>10</sup>	serious <sup>8</sup>	none		5/99 (5.1%)	12/99 (12.1%) <sup>4</sup>	OR 0.39 (0.15 to 1.14)	71 fewer per 1.000 (from 104 fewer to 15 more)	⊕000 VERY LOW	NOT IMPORTANT
Rate of sac regression <sup>9</sup> (Prophylaxis) (follow-up 12-24 months; assessed with: Proportion of patients with sac regression (>5 mm))													
1	observational studies <sup>1</sup>	serious <sup>2</sup>	not serious	serious <sup>10</sup>	serious <sup>8</sup>	none		35/99 (35.4%)	36/99 (36.4%)	OR 0.96 (0.54 to 1.71)	10 fewer per 1.000 (from 12 fewer to 14 more)	⊕000 VERY LOW	NOT IMPORTANT

<sup>1</sup> Propensity Match Cohort.

<sup>2</sup> Conflict of interest & funding: some authors related to the MAH. Lack of baseline demographic data and procedural data for control subjects, matching performed on anatomic criteria alone. Midterm follow-up. IHE 15/19

<sup>3</sup> All complications were endoleaks. No migrations > 10 mm through 24 months follow-up.

<sup>4</sup> No differences in Kaplan-Meier analysis at 1 and 2 years.

<sup>5</sup> Primary endovascular aortic aneurysm repair with high-risk of complications (high-risk migration/endoleak (i.e. hostile neck in abdominal aortic length, complex shape, wide diameter or the presence of calcification or thrombus).

<sup>6</sup> Complications measured: graft migration, endoleak type I.

<sup>7</sup> Neck dilation  $\geq 4$  mm and sac enlargement  $> 5$  mm data pooled.

<sup>8</sup> Small size.

<sup>9</sup> 29 patients in intervention arm and 25 in control arm at 1 year, and 6 and 11 more at 2 years. With differences in Kaplan-Meier analysis (p 0.03 and p 0.01).

<sup>10</sup> Surrogate outcome.

**Table A7: GRADE quality assessment on safety**

**Question:** Are the primary or secondary use of endoanchoring systems in patients with EVAR/ safer (or at least as safe) than primary or secondary endovascular aortic aneurysm repair without use of endoanchoring system?

**Setting:** EVAR/ high risk for Endoleak type I/endograft migration or treatment of Endoleak type I/endograft migration

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	EVAR with EndoAnchor™	Control	Relative (95% CI)	Absolute (95% CI)		
Procedure-related mortality (follow up: 30 days); assessed with; Proportion of patients with Procedure-related mortality at 30 days												
Bibliography: [25-27, 31, 34]												
5	observational studies	serious <sup>1</sup>	not serious	not serious	serious <sup>2</sup>	none	1/517 (0.2% ± 0.13%)	not pooled <sup>6</sup>	not pooled <sup>6</sup>	see comment	⊕○○○ VERY LOW	CRITICAL
Vessel damage (including dissection, perforation, and spasm) (follow up: 30 days); assessed with; Proportion of patients with Vessel damage at 30 days												
Bibliography: [27]												
1	observational studies	serious <sup>1</sup>	not serious	not serious	very serious <sup>3</sup>	none	3/21 (14.3%)	-	-	-	⊕○○○ VERY LOW	IMPORTANT
Vessel damage (including dissection, perforation, and spasm) (follow up: 1 year); assessed with; Proportion of patients with Vessel damage at 1 year												
Bibliography: [27, 31]												
2	observational studies	serious <sup>1</sup>	not serious	not serious	serious <sup>3</sup>	none	0/167 (0.0%)	not pooled <sup>6</sup>	not pooled <sup>6</sup>	see comment	⊕○○○ VERY LOW	IMPORTANT
Vessel damage (including dissection, perforation, and spasm) (follow up: 2 years); assessed with; Proportion of patients with Vessel damage at 2 years												
Bibliography: [31]												
1	observational studies	serious <sup>1</sup>	not serious	not serious	serious <sup>3</sup>	none	0/153 (0.0%)	-	-	-	⊕○○○ VERY LOW	IMPORTANT

CI: Confidence interval; 1. Prospective single-arm to follow outcomes. No control group. 2. Very few events and 3 studies with small sample size. 3. No or few events in small sample studies. 4. Small sample. 5. Retrospective case series study. 6. No meta-analysis was done; weighted mean by study size.

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	EVAR with EndoAnchor™	Control	Relative (95% CI)	Absolute (95% CI)		
EndoAnchor™ implant embolisation (follow up: 1 year); assessed with; Proportion of patients with EndoAnchor™ implant embolisation at 1 year Bibliography [31]												
1	observational studies	serious <sup>1</sup>	not serious	not serious	serious <sup>2</sup>	none	32/153 (20.9%)	-	-	-	⊕○○○ VERY LOW	IMPORTANT
EndoAnchor™ implant embolisation (follow up: 3 years); assessed with; Proportion of patients with EndoAnchor™ implant embolisation at 3 years Bibliography [31]												
1	observational studies	serious <sup>1</sup>	not serious	not serious	serious <sup>4</sup>	none	56/153 (36.6%)	-	-	-	⊕○○○ VERY LOW	IMPORTANT
Endoleak type II-V (follow up: 30 days); assessed with; Proportion of patients with Endoleak type II-V at 30 days Bibliography [25, 27, 31, 34]												
4	observational studies	serious <sup>1</sup>	not serious	not serious	serious <sup>3</sup>	none	55/194 (28.4% ± 13.52%)	not pooled <sup>6</sup>	not pooled <sup>6</sup>	see comment	⊕○○○ VERY LOW	IMPORTANT
Endoleak type II-V (follow up: 1 year); assessed with; Proportion of patients with Endoleak type II-V at 1 year Bibliography [25, 27, 31, 35]												
4	observational studies	very serious <sup>1,5</sup>	not serious	not serious	serious <sup>3</sup>	none	38/256 (14.8% ± 8%)	not pooled <sup>6</sup>	not pooled <sup>6</sup>	see comment	⊕○○○ VERY LOW	IMPORTANT

CI: Confidence interval; 1. Prospective single-arm to follow outcomes. No control group. 2. Very few events and 3 studies with small sample size. 3. No or few events in small sample studies. 4. Small sample. 5. Retrospective case series study. 6. No meta-analysis was done; weighted mean by study size.



Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	EVAR with EndoAnchor™	Control	Relative (95% CI)	Absolute (95% CI)		
Endoleak type II-V (follow up: 2 years); assessed with; Proportion of patients with Endoleak type II-V at 2 years Bibliography [28, 31]												
2	observational studies	very serious <sup>1,3</sup>	not serious	not serious	serious <sup>3</sup>	none	12/155 (7.7% ± 6.1%)	not pooled <sup>6</sup>	not pooled <sup>6</sup>	see comment	⊕○○○ VERY LOW	IMPORTANT
Endoleak type II-V (follow up: 3 years); assessed with; Proportion of patients with Endoleak type II-V at 3 years Bibliography [31]												
1	observational studies	serious <sup>1</sup>	not serious	not serious	serious <sup>3</sup>	none	10/78 (12.8%)	-	-	-	⊕○○○ VERY LOW	IMPORTANT
Stroke (follow up: 30 days); assessed with; Proportion of patients with Stroke at 30 days Bibliography [27, 31]												
2	observational studies	serious <sup>1</sup>	not serious	not serious	serious <sup>4</sup>	none	0/174 (0.0%)	not pooled <sup>6</sup>	not pooled <sup>6</sup>	see comment	⊕○○○ VERY LOW	IMPORTANT
Stroke (follow up: 1 year); assessed with; Proportion of patients with Stroke at 1 year Bibliography [27, 31]												
2	observational studies	serious <sup>1</sup>	not serious	not serious	serious <sup>4</sup>	none	3/167 (1.8%± 1.3 %%)	not pooled <sup>6</sup>	not pooled <sup>6</sup>	see comment	⊕○○○ VERY LOW	IMPORTANT

CI: Confidence interval; 1. Prospective single-arm to follow outcomes. No control group. 2. Very few events and 3 studies with small sample size. 3. No or few events in small sample studies. 4. Small sample. 5. Retrospective case series study. 6. No meta-analysis was done; weighted mean by study size.

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	EVAR with EndoAnchor™	Control	Relative (95% CI)	Absolute (95% CI)		
Stroke (follow up: 3 years); assessed with; Proportion of patients with Stroke at 3 years												
Bibliography [31]												
1	observational studies	serious <sup>1</sup>	not serious	not serious	serious <sup>4</sup>	none	6/153 (3.9%)	-	-	-	⊕○○○ VERY LOW	IMPORTANT
Vascular access complications (including infection, pain, hematoma, pseudoaneurysm and arteriovenous fistula) (follow up: 30 days); assessed with; Proportion of patients with Vascular access complications at 30 days												
Bibliography [27]												
1	observational studies	serious <sup>1</sup>	not serious	not serious	serious <sup>4</sup>	none	0/21 (0.0%)	-	-	-	⊕○○○ VERY LOW	IMPORTANT
Vascular access complications (including infection, pain, hematoma, pseudoaneurysm and arteriovenous fistula) (follow up: 1 year); assessed with; Proportion of patients with Vascular access complications at 1 year												
Bibliography [27]												
1	observational studies	serious <sup>1</sup>	not serious	not serious	serious <sup>4</sup>	none	0/14 (0.0%)	-	-	-	⊕○○○ VERY LOW	IMPORTANT
Vascular access complications (including infection, pain, hematoma, pseudoaneurysm and arteriovenous fistula) (follow up: 2 years); assessed with; Proportion of patients with Vascular access complications at 2 years												
Bibliography [28]												
1	observational studies	very serious <sup>1,5</sup>	not serious	not serious	serious <sup>4</sup>	none	3/51 (5.9%)	-	-	-	⊕○○○ VERY LOW	IMPORTANT

CI: Confidence interval; 1. Prospective single-arm to follow outcomes. No control group. 2. Very few events and 3 studies with small sample size. 3. No or few events in small sample studies. 4. Small sample. 5. Retrospective case series study. 6. No meta-analysis was done; weighted mean by study size.

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	EVAR with EndoAnchor™	Control	Relative (95% CI)	Absolute (95% CI)		
Renal complications (renal artery occlusion/dissection or contrast-induced acute kidney injury) (follow up: 30 days); assessed with; Proportion of patients with Renal complications at 30 days												
Bibliography [27, 31, 34]												
3	observational studies	serious <sup>1</sup>	not serious	not serious	serious <sup>4</sup>	none	0/187 (0.0%)	not pooled <sup>6</sup>	not pooled <sup>6</sup>	see comment	⊕○○○ VERY LOW	IMPORTANT
Renal complications (renal artery occlusion/dissection or contrast-induced acute kidney injury) (follow up: 1 year); assessed with; Proportion of patients with Renal complications at 1 year												
Bibliography [27, 31]												
2	observational studies	serious <sup>1</sup>	not serious	not serious	serious <sup>4</sup>	none	2/167 (1.2% ± 0.92%)	not pooled <sup>6</sup>	not pooled <sup>6</sup>	see comment	⊕○○○ VERY LOW	IMPORTANT
Renal complications (renal artery occlusion/dissection or contrast-induced acute kidney injury) (follow up: 16 months); assessed with; Proportion of patients with Renal complications at 16 months												
Bibliography [26]												
1	observational studies	serious <sup>1</sup>	not serious	not serious	serious <sup>4</sup>	none	10/319 (3.1%)	-	-	-	⊕○○○ VERY LOW	IMPORTANT

CI: Confidence interval; 1. Prospective single-arm to follow outcomes. No control group. 2. Very few events and 3 studies with small sample size. 3. No or few events in small sample studies. 4. Small sample. 5. Retrospective case series study. 6. No meta-analysis was done; weighted mean by study size.

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	EVAR with EndoAnchor™	Control	Relative (95% CI)	Absolute (95% CI)		
Renal complications (renal artery occlusion/dissection or contrast-induced acute kidney injury) (follow up: 2 years); assessed with; Proportion of patients with Renal complications at 2 years												
Bibliography [28]												
1	observational studies	very serious <sup>1,5</sup>	not serious	not serious	serious <sup>3</sup>	none	2/51 (3.9%)	-	-	-	⊕○○○ VERY LOW	IMPORTANT
Renal complications (renal artery occlusion/dissection or contrast-induced acute kidney injury) (follow up: 3 years); assessed with; Proportion of patients with Renal complications at 3 years												
Bibliography [31]												
1	observational studies	serious <sup>1</sup>	not serious	not serious	serious <sup>3</sup>	none	6/153 (3.9%)	-	-	-	⊕○○○ VERY LOW	IMPORTANT
Cardiac complications (follow up: 30 days); assessed with; Proportion of patients with Cardiac complications at 30 days												
Bibliography [27, 28, 31]												
3	observational studies	very serious <sup>1,5</sup>	not serious	not serious	serious <sup>3</sup>	none	3/225 (1.33 % ±1% )	not pooled <sup>6</sup>	not pooled <sup>6</sup>	see comment	⊕○○○ VERY LOW	IMPORTANT
Cardiac complications (follow up: 1 year); assessed with; Proportion of patients with Cardiac complications at 1 year												
Bibliography [27, 31, 35]												
3	observational studies	serious <sup>1</sup>	not serious	not serious	serious <sup>3</sup>	none	12/267 (4.5% ± 1.67%)	not pooled <sup>6</sup>	not pooled <sup>6</sup>	see comment	⊕○○○ VERY LOW	IMPORTANT

CI: Confidence interval; 1. Prospective single-arm to follow outcomes. No control group. 2. Very few events and 3 studies with small sample size. 3. No or few events in small sample studies. 4. Small sample. 5. Retrospective case series study. 6. No meta-analysis was done; weighted mean by study size.

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	EVAR with EndoAnchor™	Control	Relative (95% CI)	Absolute (95% CI)		
Cardiac complications (follow up: 3 years); assessed with; Proportion of patients with Cardiac complications at 3 years												
Bibliography [31]												
1	observational studies	serious <sup>1</sup>	not serious	not serious	serious <sup>3</sup>	none	10/153 (6.5%)	-	-	-	⊕○○○ VERY LOW	IMPORTANT
Respiratory failure (follow up: 30 days); assessed with; Proportion of patients with Respiratory failure at 30 days												
Bibliography [27, 31]												
2	observational studies	serious <sup>1</sup>	not serious	not serious	serious <sup>3</sup>	none	0/174 (0.0%)	not pooled <sup>6</sup>	not pooled <sup>6</sup>	see comment	⊕○○○ VERY LOW	IMPORTANT
Respiratory failure (follow up: 1 year); assessed with; Proportion of patients with Respiratory failure at 1 year												
Bibliography [27, 31, 35]												
3	observational studies	serious <sup>1</sup>	not serious	not serious	serious <sup>3</sup>	none	2/267 (0.7% ±0.51%)	not pooled <sup>6</sup>	not pooled <sup>6</sup>	see comment	⊕○○○ VERY LOW	IMPORTANT
Respiratory failure (follow up: 3 years); assessed with; Proportion of patients with Respiratory failure at 3 years												
Bibliography [31]												
1	observational studies	serious <sup>1</sup>	not serious	not serious	serious <sup>3</sup>	none	3/153 (2.0%)	-	-	-	⊕○○○ VERY LOW	IMPORTANT

CI: Confidence interval; 1. Prospective single-arm to follow outcomes. No control group. 2. Very few events and 3 studies with small sample size. 3. No or few events in small sample studies. 4. Small sample. 5. Retrospective case series study. 6. No meta-analysis was done; weighted mean by study size.

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	EVAR with EndoAnchor™	Control	Relative (95% CI)	Absolute (95% CI)		
Other ischemic complication (follow up: 30 days); assessed with; Proportion of patients with Other ischemic complication at 30 days												
Bibliography [27, 34]												
2	observational studies	serious <sup>1</sup>	not serious	not serious	serious <sup>3</sup>	none	2/34 (5.9% ± 6.73%)	not pooled <sup>6</sup>	not pooled <sup>6</sup>	see comment	⊕○○○ VERY LOW	IMPORTANT
Other ischemic complication (follow up: 1 year); assessed with; Proportion of patients with Other ischemic complication at 1 year												
Bibliography [27, 35]												
2	observational studies	serious <sup>1</sup>	not serious	not serious	serious <sup>c</sup>	none	5/114 (4.4%±1.57%)	not pooled <sup>6</sup>	not pooled <sup>6</sup>	see comment	⊕○○○ VERY LOW	IMPORTANT
Other ischemic complication (follow up: 2 years); assessed with; Proportion of patients with Other ischemic complication at 2 years												
Bibliography [28]												
1	observational studies	very serious <sup>1,5</sup>	not serious	not serious	serious <sup>3</sup>	none	2/51 (3.9%)	-	-	-	⊕○○○ VERY LOW	IMPORTANT
Others: pneumonia, fever, Urologic & Gastrointestinal (follow up: 30 days); assessed with; Proportion of patients with Others: pneumonia, fever, Urologic & Gastrointestinal at 30 days												
Bibliography [27, 28]												
2	observational studies	very serious <sup>1,5</sup>	not serious	not serious	serious <sup>3</sup>	none	9/72 (12.5%±17%)	not pooled <sup>6</sup>	not pooled <sup>6</sup>	see comment	⊕○○○ VERY LOW	IMPORTANT

CI: Confidence interval; 1. Prospective single-arm to follow outcomes. No control group. 2. Very few events and 3 studies with small sample size. 3. No or few events in small sample studies. 4. Small sample. 5 Retrospective case series study. 6. No meta-analysis was done; weighted mean by study size.

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	EVAR with EndoAnchor™	Control	Relative (95% CI)	Absolute (95% CI)		
Others: pneumonia, fever, Urologic & Gastrointestinal (follow up: 1 year); assessed with; Proportion of patients with Others: pneumonia, fever, Urologic & Gastrointestinal at 1 year												
Bibliography [27]												
1	observational studies	serious <sup>1</sup>	not serious	not serious	serious <sup>3</sup>	none	0/14 (0.0%)	-	-	-	⊕○○○ VERY LOW	IMPORTANT
Others: pneumonia, fever, Urologic & Gastrointestinal (follow up: 2 years); assessed with; Proportion of patients with Others: pneumonia, fever, Urologic & Gastrointestinal at 2 years												
Bibliography [28]												
1	observational studies	very serious <sup>1,5</sup>	not serious	not serious	serious <sup>3</sup>	none	1/51 (2.0%)	-	-	-	⊕○○○ VERY LOW	IMPORTANT

CI: Confidence interval; 1. Prospective single-arm to follow outcomes. No control group. 2. Very few events and 3 studies with small sample size. 3. No or few events in small sample studies. 4. Small sample. 5. Retrospective case series study. 6. No meta-analysis was done; weighted mean by study size.

**Question: Are the primary or secondary use of endoanchoring systems in patients with TEVAR/ safer (or at least as safe) than primary or secondary endovascular aortic aneurysm repair without use of endoanchoring system?**

**Setting: TEVAR/ high risk for Endoleak type I/endograft migration or treatment of Endoleak type I/endograft migration**

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	[intervention]	[comparison]	Relative (95% CI)	Absolute (95% CI)		
Procedure-related mortality (follow up: 30 days); assessed with; Proportion of patients with Procedure-related mortality at 30 days												
Bibliography [33]												
1	observational studies	very serious <sup>1,2</sup>	not serious	not serious	serious <sup>1,3</sup>	none	2/54 (3.7%)	-	-	-	⊕○○○ VERY LOW	CRITICAL
Endoleak type II-V (follow up: 1 year); assessed with; Proportion of patients with Endoleak type II-V at 1 year												
Bibliography [33]												
1	observational studies	very serious <sup>1,2</sup>	not serious	not serious	serious <sup>1,3</sup>	none	3/19 (15.8%)	-	-	-	⊕○○○ VERY LOW	IMPORTANT

CI: Confidence interval. 1. Small sample 2. Retrospective case series study. No control group. 3. Very few events



**Table A8: Summary table characterising the applicability of a body of studies**

Domain	Description of the applicability of the evidence
Population	<p>The target population for this assessment were adults (&gt;18yrs) in 3 MAH-registered trials (STAPLE1, STAPLE-2 and ANCHOR). STAPLE-1 included, according to its inclusion criteria, only friendly or favourable necks. STAPLE-2 included 18/153 (12%) hostile necks despite its inclusion criteria.</p> <p>ANCHOR trials [26, 29, 30, 35] included patients with hostile necks (any criteria) over a range of 58% to 84% of the sample. Three studies [28, 32, 34] reported patients with hostile necks (any criteria) ranging from 47%-100%. Two studies [25, 33] did not report the proportion of patients with a hostile neck in their samples.</p> <p>Patients who underwent a primary intervention for AAA were the most studied group, numbering approximately 400 patients, whereas the patients requiring a secondary intervention represented a small sample in these same studies, only 88 patients in total. [25, 26] Results for T/A AA patients are scarce, with only a small retrospective series of 54 patients currently available [33].</p> <p>The average age ranged from 69 years to 77 years, the male gender being predominant, with a range of 64% to 100%. Female representation measured 0%-35.2% of patients, despite their higher risk for hostile necks or complications. The ASA physical status class was reported in five studies [25, 26, 28-30] with a range of 63% to 82% for Class 3 patients.</p> <p>The characteristics of the patients in the included studies closely matched only the targeted male AAA population, who underwent primary interventions (prophylaxis, immediate type I endoleaks or maldeployment).</p>
Intervention	<p>The studies included in the analyses did align with our questions. Small differences were to be expected from the system used in earlier studies (APTUS) and that of more recent studies (Heli-FX). The Aptus / Heli-FX EndoAnchor™ system was used with different commercially available endografts or in conjunction with other procedures in EVAR; e.g., cuffs when treating migration, type I endoleaks or as a supporting device in patients presenting shorter necks.</p>
Comparators	<p>Only one study (Muhs 2018) used propensity-matched controls, and compared the use of EVAR procedures vs EVAR procedures plus EndoAnchor™ in AAA patients. No other studies included a comparison with EVAR alone (without the evaluated device). In one study [31], some comparative results were found that included a historical control, but this consisted of a cohort of open surgery patients.</p>
Outcomes	<p>All outcomes considered by the Assessment Team are reported in the pool of studies, except for the health-related quality of life measurements. This outcome was not reported in any of the studies. The most reported outcomes during the first 30 days were reintervention and procedure-related mortality (critical), as well as technical success and procedural success (rated as not important). Conversion to open surgery (important) was not clearly reported in the studies. All studies except for one reported some safety outcomes during the first 24 months [32].</p> <p>There was overlapping between all-cause mortality and procedure-related mortality at 30 days, despite the recommendations of the Committee for Standardized Reporting Practices in Vascular Surgery.</p> <p>Follow-up was heterogeneous and encompassed a broad range (a median of 12 months in the prospective series, and from 2 to 72 months in another study), with longer term data available in only a very few patients. The only available study on thoracic aneurysms, a retrospective case series, had a median follow-up of 9.6 months [27]. The mid-term follow-up can signify that late outcomes were not yet occurring; e.g., reinterventions due to complications. Only one study presented clear data on the reintervention time points [31], with most of the cases occurring after 12 months of follow-up.</p>