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1. Title of the project

The clinical and cost-effectiveness of protocols using contrast-enhanced ultrasound and/or colour duplex ultrasound in the long-term surveillance of endovascular abdominal aortic aneurysm repair

2. Name of External Assessment Group (EAG) and project lead

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3. Plain English Summary

An abdominal aortic aneurysm is a swelling or bulge that causes the wall of the main blood vessel (aorta) to weaken and become pouched or sac-shaped. Large aneurysms can burst, causing massive internal bleeding, which can lead to death. Endovascular aneurysm repair (EVAR) of the aneurysm is minimally invasive but it is associated with potential complications. The most common complication is the occurrence of an endoleak (blood flow in the aneurysm sac). Consequently, patients who receive EVAR treatment must be followed-up for the rest of their life.

Computed tomography angiography (CTA) is an imaging modality widely used for the surveillance after EVAR. CTA is considered to be very accurate but it is not very good at detecting the direction of blood flow from an endoleak. It also carries the risk of repeated exposure to radiation and to a toxic contrast agent. Colour duplex ultrasound (CDU) and contrast enhanced ultrasound (CEU) have been suggested as possible, safer, imaging alternatives to CTA but have not been widely adopted. The optimal surveillance strategy with regard to the choice of imaging modalities and the frequency of testing has not been established yet.

The purpose of this appraisal is to perform a literature search to assess the current evidence for the clinical effectiveness and cost-effectiveness of surveillance strategies using colour duplex and contrast-enhanced ultrasound compared with CTA in the surveillance after EVAR. Where possible we will include data from national and international clinical registries and databases. The results of the project will be used by the National Institute for Health and Care Excellence (NICE) to issue clinical guidance in England and Wales on the optimal surveillance strategy after EVAR.

4 Decision problem

4.1 Purpose of the decision to be made

Endovascular aneurysm repair (EVAR) has become the preferred treatment option for abdominal aortic aneurysm.[1] Even though less invasive than open surgery, EVAR is associated with potential complications, including graft migration, kinking and fracture, endoleaks, limb outflow impairment and aneurysm rupture.[2-5] It is, therefore, necessary that patients receive life-long surveillance following EVAR. The main purpose of surveillance is to detect clinically significant complications, which are often asymptomatic, and prevent aneurysm rupture.[6]

Endoleak, defined as persistent blood flow in the aneurysm sac outside the graft, represents the most frequent complication after EVAR, and affects approximately 20% of patients at a certain point during follow up. Endoleaks vary in size, direction and rate of flow and have variable origins.[7] Five categories of endoleaks have been described in the literature according to the source of blood flow (see Table 1).

Table 1 Classification of endoleaks [5 8]

Endoleak		**Origin of blood flow**
Type I		***Attachment site leaks***
	A	Proximal
	B	Distal
	C	Iliac occluder
Type II		***Branch leaks***
	A	Simple (1 patent branch)
	B	Complex (2 or more patient branches)
Type III		***Graft defect***
	A	Junctional leak or modular defect
	B	Fabric disruption (midgraft hole)
Type IV		***Fabric porosity (within 30 days of procedure)***
Type V		***Endotension***
	A	With no endoleak
	B	With sealed endoleak
	C	With type 1 or 3 endoleak discovered at the time of open redo surgery
	D	With type 2 endoleak discovered at the time of open redo surgery

Treatment and prognosis depends on the type of endoleak. **Type I** endoleaks, which have been reported to occur in as many as 10% of patients after EVAR,[9] have blood flow from the stent-graft attachment site as a result of sealing failure and are associated with increased pressure in the aneurysm sac. Type I endoleaks are usually treated at the time of the index operation and require urgent treatment if they present later. Incidence of type I endoleaks appears to increase when there are anatomically difficult situations and with time. **Type II** endoleaks, which are characterised by retrograde blood flow into the aneurysm sac, are the most common type of endoleaks after abdominal EVAR and account for 20-30% of cases at 30 days, 18.9% at 1 year and 10% after 1 year.[9] Usually, a "wait and see" follow-up approach is adopted for Type II endoleaks and surveillance monitoring may be increased. Treatment is required if the aneurysm sac increases in size; often a >5mm increase is deemed clinically significant, although there is no an agreed definition[7 10].[10] **Type III** endoleaks, which arise due to structural graft defects, always require treatment. Graft failure is more likely to happen over time as arterial pulsations and other factors cause repetitive stress on the device. Tears or holes in the fabric of the graft can be hard to detect but modular disconnections are usually well seen with computed tomography angiography (CTA). Incidence of type III endoleaks is usually low (4% incidence beyond 1 year). **Type IV** endoleaks occur peri-operatively (<30 days following EVAR) due to graft fabric porosity. However, with the advent of low-porosity graft fabrics they are observed less frequently than in the past, although incidence may increase in the future as these grafts age. Treatment is not usually required [7 10]but care should be taken to exclude other types of endoleaks at the point of diagnosis, as they can mimic Type IV leaks. The definition of **Type V** endoleaks includes the persistent or recurrent pressurisation or expansion of the aneurysm sac, or endotension in the absence of an identifiable type I-IV leak. Causes of endotension may include an existing endoleak that is not visible on imaging, other complications or graft design. Type V endoleaks are usually treated on an individual basis. [7 10]

Post-EVAR surveillance should include: measurement of the aortic aneurysm, identification and classification of endoleaks and detection of stent-graft deformation[11 12]. The ideal frequency of surveillance is not empirically defined[7 13] and heterogeneous strategies exist between centres.[5], A UK survey of current surveillance practice amongst the members of the British Society of Interventional Radiologists (BSIR) indicated that, usually, imaging protocols comprise routine CTA imaging at 1 month, 6 months, 12 months and annually thereafter[13]. CTA scanning has however limited ability to determine the direction of blood flow associated with an endoleak and its frequent use has the disadvantage of exposing the patient to cumulative doses of ionizing radiation with potential lifetime cancer risk as well as to contrast medium-induced nephrotoxicity.[14-16] The risks associated with the repeated use of

CTA have led some investigators to consider revising current surveillance protocols in order to minimise radiation dose and eliminating unnecessary CTA examinations.[17-19] Moreover, it has been observed that only 1.4-9% of patients require reintervention due to surveillance-detected abnormalities, while the majority of reinterventions occur in symptomatic patients with previously normal surveillance assessments[6 20-22]. Colour duplex ultrasound (CDU) and, more recently, contrast enhanced ultrasound (CEU) have been proposed as possible safer alternatives to CTA but have not been widely adopted. Thus, the optimal surveillance strategy with regard to the choice of imaging modalities and the frequency of testing has yet to be established.

The purpose of this appraisal is to assess the current evidence for the clinical effectiveness and cost-effectiveness of imaging strategies using either colour duplex or contrast-enhanced ultrasound alone or in conjunction with plain film X-ray compared with CTA for the surveillance of EVAR.

4.2 Clear definition of the intervention

- *Plain film X-ray*

Despite the availability of advanced imaging modalities plan film X-ray is still used in many centres in Europe and North America for a general assessment of stent-graft position and integrity[19 23] as well as for evaluating device migration, wire frame fracture, kinking or distortion.[24 25] The European Society for Vascular Surgery recommends using plain film X-ray in conjunction with CTA for the first 12 months of surveillance and, if no endoleaks are detected, in conjunction with CDU or CEU thereafter.[15] The BSIR survey showed that 20 out of 37 respondents (54%) performed plain films in addition to CTA at the 1 year post-operative follow-up.[13] Contrary to CTA, CDU and CEU, plan film X-ray has little if no role in the surveillance for sac enlargement and endoleaks detection[19]. For this reason plain film X-ray must be used in conjunction with other imaging modalities and cannot be used as sole surveillance modality after EVAR.[6]

- *Colour duplex ultrasound*

Colour duplex ultrasound (CDU) offers high levels of endoleak characterisation by delivering information regarding the direction/bi-direction of endoleaks and velocity of blood flow, not provided by CTA. CDU can also be used to guide endovascular treatment of endoleaks, is inexpensive, portable and avoids exposing the patient to radiation and potentially nephrotoxic contrast agents. The imaging quality of CDU is, however, operator-dependent and scanning protocols can vary considerably between institutions.[26] CDU imaging is also affected by

patient habitus and bowel gas and is less able to detect graft defects or migration compared with CTA.

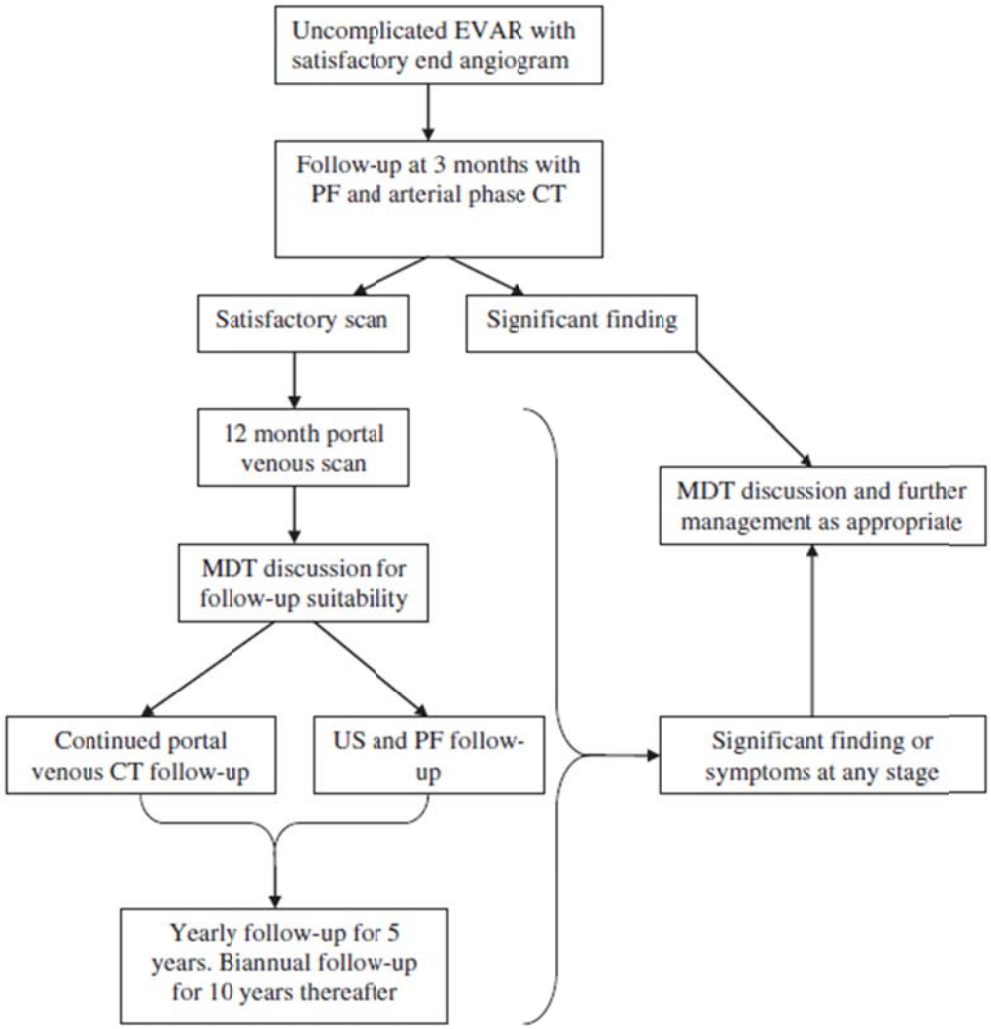
- *Contrast-enhanced ultrasound*

Contrast-enhanced ultrasound (CEU) provides dynamic examination through the administration of an intravenous contrast agent, which can be followed in real-time as it appears within the graft, with endoleaks appearing as contrast outside the graft within the aneurysmal sac.[6] Unlike CTA, CEU is safe to use in patients with renal difficulty. Possible advantages of CEU over CDU include better detection of aneurysm sac enlargement. Like CDU, CEU imaging is highly operator-dependent and the sonographer/operator requires additional training, both for operating the technology and administering the contrast agent. CEU is more expensive than CDU, due to the additional cost of the contrast agent, but is less expensive than CTA. In the UK, CEU is not as widely available as CDU.[13]

Neither CDU nor CEU can currently replace CTA in the immediate post-EVAR surveillance period, as complications are more likely in the post-operative period, and CTA provides more precise evaluation of aneurysm morphologic changes, sac diameter, graft anchorage and integrity.[10] Nevertheless, some investigators have suggested that CDU/CEU might have a role as a problem-solving tool in situations when CTA is unequivocal or when endotension is suspected.[27] It has also been suggested that CDU/CEU could replace CTA for annual surveillance for patients who have not experienced endoleaks or an increase in aneurysmal sac size in the first year after EVAR.[28-31] However, CTA is still recommended when a significant increase in the aneurysm size or a new endoleak is detected.[1 32] Both CDU and CEU should be conducted by specialist sonographers trained in detecting vascular abnormalities (especially CEU), rather than general sonographers, due to the highly skilled technique required.

A systematic review published by Karthikesalingam and colleagues in 2012[33] compared the performance of CEU and duplex ultrasound (DUS) versus CT for identification of endoleaks. Both CEUS and DUS appeared to be specific for detection of types I and III endoeak. Estimates of sensitivity were uncertain but there was no clear evidence of a clinically significant difference. When all endoleaks were considered, CEU demonstrated a greater sensitivity but lower specificity then DUS. These findings are similar to those of the systematic review published previously by Mirza and colleagues.[34] In both reviews, however, analyses were limited by the heterogeneity between included studies and no recommendations in terms of the role of DUS and/or CEUS for the surveillance after EVAR could be drawn.

While there is currently no clear consensus on the best place of CDU/CEU in the care pathway of surveillance post EVAR, some clinical guidelines have contemplated a possible role of CDU/CEU within the existing CT imaging care pathway. In the USA, the Society for Vascular Surgery practice guidelines published in 2009 recommend contrast enhanced CT imaging one month and 12 months during the first year after EVAR. If at one month, the CT imaging identifies an endoleak or other abnormalities of concern, post-operative imaging at six months should be considered to further evaluate the proper exclusion of an aneurysm. If neither an endoleak nor an aneurysm enlargement is detected during the first year surveillance after EVAR, colour duplex ultrasonography may be regarded as a reasonable alternative to CT imaging for post-operative surveillance. The presence of a Type II endoleak should initially prompt continued CT surveillance to ascertain whether the aneurysm is increasing in size. However, if the aneurysm is shrinking in size or is stable follow up with CDU may be an option. Similarly, Gartnavel General Hospital in the UK has developed clinical guidelines for surveillance after uncomplicated EVAR based on their local experience (see Figure 1).[13]



PF= plain film, CT=computed tomography, MDT = multidisciplinary team, US=ultrasound

Figure 1 Post-EVAR follow-up algorithm, Glasgow (source: Gartnavel Hospital, UK clinical guidelines**)**

4.3 Populations and relevant subgroups

The populations considered are adult men and women who require surveillance following endovascular abdominal aortic aneurysm repair.

4.4 Relevant comparators

Computed tomography angiography

CTA is the most widely used imaging modality for surveillance after EVAR and is considered to be the reference standard imaging test.[6] Multiphasic CTA is recommended initially due to the variable flow rates of endoleaks. With multiphasic CTA, imaging is conducted before the administration of an intravenous (IV) iodinated contrast medium after administration and in the post-contrast delayed phase[7]. CTA is quick, widely available and is not operator-

dependent. CTA offers clear vascular and non-vascular imaging, and enables differentiation between true endoleaks and areas of calcification or high attenuation that may mimic an endoleak. Disadvantages include the cost of CTA follow-up, radiation exposure (15-31 mSv per study[6] compared with 0.014mSv for a chest X-ray)[35] and allergic complications due to the nephrotoxic properties of the contrast medium. Incidence of contrast-induced nephropathy is estimated to range from 7% to 12%.[16 28 36 37] CTA imaging is therefore unsuitable for use in patients with, or at risk of, renal disease. CTA is also limited by streak artifacts that restrict the ability to determine blood flow direction, which is critical for endoleak classification.[38]

5 Report methods for assessing the outcomes arising from the use of the interventions

We will conduct a systematic review of the clinical effectiveness of CDU and/or CEU alone or in conjunction with plain film X-ray compared with CTA in the long-term surveillance of endovascular abdominal aortic aneurysm repair. We will also extract high quality and appropriate diagnostic test accuracy data from relevant, recently published, systematic reviews. Furthermore, we will conduct an analysis of registry data (e.g. the recently published EUROSTAR)[39] and other clinical databases. Parameter estimates derived from these methods will be used to develop an economic model to represent possible alternative surveillance strategies modelled at varying surveillance intervals. If data from the registry analysis are not forthcoming, we will extract data concerning incidence of endoleaks and other complications from published secondary sources.

5.1 Inclusion and Exclusion criteria

- *Population*

  Patients undergoing surveillance following endovascular abdominal repair (EVAR) for abdominal aortic aneurysm.

- *Setting*

  Secondary and tertiary care

- *Interventions*

  Contrast-enhanced ultrasound (CEU) or

  Colour-duplex ultrasound (CD) used alone or in conjunction with plain film X-ray

- *Comparator*

  Computed tomography angiography

- *Outcomes*

The following EVAR outcomes will be considered:

a) Incidence and type of complications (e.g. significant and non-significant endoleaks, migration, kinking and fracture) as defined by the authors of the relevant selected studies
b) Re-intervention rate
c) Incidence and type of secondary interventions

Adverse effects and harms associated with the specific mode of surveillance (imaging modalities) will also be taken into consideration (e.g. contrast related nephropathy).

- *Study design*

  We will consider randomised controlled trials (RCTs) of different surveillance imaging modalities, regimens and follow-up strategies. In the absence of RCT evidence, we will consider non-randomised comparative studies and/or prospective and retrospective cohort studies of different surveillance imaging regimes and follow up strategies.

We will exclude the following types of report:

- Preclinical and biological studies
- Case reports
- Reports investigating technical aspects of imaging modalities
- Editorials
- Letters

Non-English language reports may be excluded if the evidence base containing English language reports is sufficiently large.

5.2 Search strategy

Extensive electronic searches will be conducted to identify reports of published, unpublished and ongoing studies. The search strategies will be designed to be highly sensitive, including both appropriate subject heading and text word terms to capture the concepts of surveillance strategies using contrast-enhanced ultrasound; colour-duplex ultrasound or computed tomography in the post-EVAR population. The searches will be conducted from 1997 to the present, without any language restriction, in order to reflect the introduction of contrast enhanced ultrasound in clinical practice. The proposed MEDLINE strategy is documented in Appendix 1 and will be adapted for other databases. For primary studies we will search the following databases: MEDLINE, MEDLINE In-Process, EMBASE, Science Citation Index (SCI), Scopus and Cochrane Central Register of Controlled Trials (CENTRAL). These

searches will be supplemented by consulting EVAR registry and manufacturers' websites for additional analyses. Reports of ongoing and recently completed trials will be sought from the WHO International Clinical Trials Registry Platform (ICTRP), Current Controlled Trials (CCT), Clinical Trials.gov. Reference lists of all selected studies will be perused and experts in the field contacted for details of additional reports.

We will also search the Database of Abstracts of Reviews of Effects (DARE) HTA Database, MEDION, MEDLINE, MEDLINE In-Process, EMBASE and CDSR as well as scrutinising the websites of key HTA organisations for systematic reviews of clinical effectiveness and diagnostic test accuracy.

5.3 Study selection and data extraction strategies

One reviewer will independently screen the titles and, when available, abstracts of all reports identified by the search strategies using a screening form that will be developed for the purpose of this assessment. A second reviewer will conduct a 10% random screening check and provide an additional check for any reports where eligibility is uncertain. Full text versions of reports deemed to be potentially relevant will be obtained, and independently assessed by two reviewers for inclusion using a study eligibility screening form based on the pre-specified inclusion criteria. Any disagreements between the two reviewers will be resolved by consensus or, where necessary, by a third reviewer. A data extraction form will be designed and piloted for the purpose of this assessment. One reviewer will extract information on study design, characteristics of participants (age, sex, ethnicity, severity of disease), technical characteristics of EVAR (type of grafts), characteristics of the intervention (mode of surveillance, technical characteristics of imaging modalities, expertise and competence of the clinician/technician performing the scanning and interpreting imaging results) and outcome measures. A second reviewer will validate the information extracted by the first reviewer.

5.4 Quality assessment strategy

Two reviewers will independently assess the risk of bias of all included studies using the tool developed by Cochrane for assessing RCTs.[40]Non-randomised studies (NRS) as well as cohort studies will be assessed using ACROBAT, the newly developed Cochrane risk of bias tool for NRS.[41] Any disagreements will be resolved by consensus or arbitration by a third reviewer. Studies will not be included or excluded on the basis of the results of the risk of bias assessment.

5.5 Methods of analysis/synthesis

Summary results and baseline characteristics from eligible studies will be tabulated and graphed using methods appropriate for the types of measurements encountered. Outcome data

will be combined in a quantitative synthesis, where possible. The outcomes proposed are binary and the meta-analytic techniques to analyse the data will reflect this, we will report results as pooled odds ratios and 95% confidence intervals. We will assume between study heterogeneity exists and use a conservative random effects meta-analysis for all outcomes. We shall also describe potential sources of heterogeneity and if data allow explore any variation in effect size due to these sources of heterogeneity using meta-regression. We will rely on published data and no attempt will be made to obtain individual patients data. For non-RCT comparative studies we will critically appraise the characteristics and methods of included studies to describe heterogeneity and assess the risk of bias. Meta-regression analyses will explore determinants of heterogeneity. Only non-RCTs judged at low risk of bias will be considered for inclusion in quantitative syntheses of results.

If available, data on adverse events and quality of life (QoL) will be collected and combined. However, a decision of how to combine the QoL outcomes will made depending on if and how this information was collected in each trial. Ideally we will us the Cochrane's standardised mean difference to compare QoL.

No attempt will be made to quantitatively synthesise the economic outcomes data. Data from the included studies will be summarised in order to identify common results, variations and weaknesses between studies. If a study only reported average cost-effectiveness ratios (ACERs) then, where possible, the data will be reanalysed to provide estimates of incremental cost-effectiveness. Where possible the data extracted from the included studies will be used to provide estimates of the secondary outcomes described above.

Sub-group analyses

Where data permit, a sub-group analysis will be conducted to assess the effect of significant versus non-significant endoleaks (as defined by the Advisory Group for this assessment).

6. Report methods for synthesising evidence of cost-effectiveness

6.1 Systematic review of economic evaluations

We will assess efficiency in the first instance by systematically searching for and reviewing the literature. Sensitive electronic searches for economic evaluations will be undertaken in the Health Management Information Consortium Database, NHS Economic Evaluations Database (NEED) and the HTA Database as well as general health care databases (MEDLINE, EMBASE and SCI) from 1997 onwards. The proposed MEDLINE strategy is documented in Appendix 1 and will be adapted for other databases. Reference lists of all included studies will be scrutinised and experts in the field contacted for details of additional reports. Studies

that compare, in terms of cost and outcomes, strategies that include contrast-enhanced ultrasound and/or colour duplex ultrasound in the long-term surveillance of EVAR will be included. Studies will be included even if no formal attempt to relate cost to outcome data in a cost-effectiveness or cost-utility analyses is available. One reviewer will assess all titles and abstracts for relevance and full-text papers will be obtained for all reports deemed potentially relevant. One economist will assess included studies following the NHS-EED guidelines for reviewers.[42 43] These guidelines address all the important issues that should be reported when conducting an economic evaluation in health care. No attempt will be made to synthesise quantitatively the primary studies. Data from included studies will be summarised and appraised in order to identify common results, variations and weaknesses between studies. If a study does not report incremental cost effectiveness ratios (ICERs) but provides sufficient data then, where possible, these will be reanalysed to provide estimates of ICERs.

6.2 Evaluation of cost-effectiveness

An economic evaluation will also be conducted as part of this assessment.[44] The decision analytic modelling will be used to assess the cost effectiveness of alternative surveillance strategies using contrast-enhanced ultrasound and/or colour duplex ultrasound compared with standard practice / strategies that do not include these modalities. The economic model will include a Markov model structure to capture the consequences of correct and incorrect diagnoses and follow up[1]. The structure of the economic model will describe different care pathways for EVAR patients from the moment of the initial intervention. These care pathways and hence model structure, while informed by existing evidence, will also be determined in consultation with the project steering and advisory committee that will comprise methodological and clinical experts as well as patient representatives. If data permit alternative monitoring intervals will be considered within the model. The perspective of the analyses will be that of the UK NHS. Data to populate these models will be obtained from the review of clinical effectiveness and from other relevant sources in the literature. Two recent Health Technology Assessment studies provide important insights and potentially relevant data for the economic model.[45 46] However, as the research question of the current assessment is substantially different from that addressed by these previous HTAs, a new economic model will be developed ad hoc. The main outputs of the model will be total NHS costs (modelled up to the lifetime of patients), QALYs, and incremental cost per QALY. In addition to

[1] It should be noted that, while a simple cohort Markov model is the preferred approach, the complexities of the condition and alternative possible clinical decision-making could result in several care pathways. If these could not be modelled by defining cohort sub-groups and a sensible number of Markov health states, a microsimulation with a Markov structure will be considered. On the other hand, if from the review of clinical effectiveness there is strong evidence of very similar effectiveness between surveillance strategies, a simpler cost-minimisation analysis will be taken into consideration.

diagnostic performance, data will be required on the natural history of EVAR patients, subsequent events, resource used, costs and health state utilities. These data will be assembled from structured reviews of UK relevant literature as well as retrieved from relevant registries (see section 5) whenever possible. Unit costs will be obtained from typical public sources (e.g. Personal Social Services Research Unit (PSSRU) for staff unit costs,[47] British National Formulary (BNF)[48] for cost of medicines, Scottish Health Care Costs (SHSC)[49] or National Schedule for Reference Costs[50] for health interventions. Results will be reported in terms of incremental cost-effectiveness ratios using a suitable measure of effectiveness (e.g. number of endoleaks detected, number of complications avoided, QALYs). Uncertainty in the model will be dealt by conducting sensitivity analyses[43 44 51] Parameter uncertainty will be addressed by conducting deterministic and probabilistic sensitivity analyses.[52] For the latter, probability distributions will be attached to model parameters and Monte Carlo simulations will be performed. Whenever possible, heterogeneity will be tackled by running models for different sub-groups. Other potential sources of uncertainty, which may be the result of assumptions made within the models (e.g. structural uncertainty), will be explored when necessary. Probabilistic results will be presented using scatter plots and/or cost-effectiveness acceptability curves (CEACs).

7. TAR team expertise

The TAR team at the University of Aberdeen are experienced in conducting reviews of this nature, in both the clinical and technical aspects required to address the commissioning brief. Miriam Brazzelli, Craig Ramsay, Marion Campbell, and Cynthia Fraser have been involved in a number of similar appraisals and the remaining TAR team members are familiar with the methods of systematic reviewing and health technology assessments.

7.1 Team members' contribution

Miriam Brazzelli, Senior Research Fellow at the HSRU, and Craig Ramsay, lead of the Aberdeen Health Technology Assessment Group will oversee and co-ordinate all aspects of the appraisal and be the guarantors of the complete work. Marion Campbell, Director of the HSRU, University of Aberdeen, will provide methodological expertise and guidance. Clare Robertson, Research Fellow at the Health Services Research Unit (HSRU), University of Aberdeen, will be responsible for the day-to-day running of the appraisal and will undertake the review of clinical effectiveness with advice and guidance from Miriam Brazzelli. Rodolfo Hernandez, Research Fellow, Health Economics Research Unit, University of Aberdeen, will undertake the economic evaluation and conduct quality assurance of the model structure and outputs. Cynthia Fraser, Senior Information Specialist at the HSRU, will develop and run the search strategies and will be responsible for obtaining papers and managing references.

Graeme MacLennan, Senior Statistician at the Health Services Research Unit (HSRU), University of Aberdeen, will conduct statistical analyses. Russell Jamieson, Consultant Vascular Surgeon, NHS Grampian, Aberdeen, and Christopher Burton, Senior Clinical Lecturer, Centre of Academic Primary Care, University of Aberdeen, will provide expert advice on relevant clinical aspects.

7.2 Advisory Group

In addition to the members of the TAR team, an Advisory Group comprising of vascular surgeons, interventional radiologists, general practitioners and lay members will be set up to provide guidance on the care pathways, advise on important outcomes, and assist in the interpretation of the clinical effectiveness findings. The Advisory Group will be convened at least twice during the duration of the appraisal.

8. Handling information from the companies

Following a request for information, any 'commercial in confidence' data provided by a manufacturer and specified as such will be highlighted in blue and underlined in the assessment report (followed by an indication of the relevant company name e.g. in brackets).

9. Competing interests of authors

None.

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11. APPENDICES

Appendix 1 MEDLINE Search Strategy

Clinical Effectiveness of Post-EVAR Surveillance

Database: Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations and Ovid MEDLINE(R) <1946 to Present>
Search Strategy:

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1 Endoleak/di [Diagnosis] (126)
2 endoleak/ or endoleak?.tw,kw. (3268)
3 evar.tw,kw. (2357)
4 (endovascular adj5 repair? adj5 abdominal).tw,kw. (2201)
5 or/2-4 (5571)
6 Ultrasonography/ (65123)
7 (duplex adj2 (ultrasound or ultrasono$)).tw. (5708)
8 Ultrasonography, Doppler, Duplex/ (5522)
9 (contrast enhanced adj2 (ultrasound or ultrasono$)).tw. (3092)
10 Tomography, X-Ray Computed/ (314366)
11 Multidetector Computed Tomography/ (3662)
12 (computed adj3 tomograph$).tw. (187914)
13 Endoleak/us [Ultrasonography] (30)
14 5 and (6 or 7 or 8 or 9 or 10 or 11 or 12) (2467)
15 1 or 13 or 14 (2514)
16 Aortic Aneurysm, Abdominal/ (15012)
17 endovascular procedures/ (7840)
18 evar.tw,kw. (2357)
19 (endovasc$ adj5 repair?).tw. (7990)
20 16 and (17 or 18 or 19) (4319)
21 exp Epidemiological Monitoring/ (4667)
22 surveillance.tw,kw. (120978)
23 monitor$.tw,kw. (585143)
24 20 and (21 or 22 or 23) (437)
25 15 or 24 (2737)
26 randomized controlled trial.pt. (416560)
27 controlled clinical trial.pt. (92193)
28 randomi?ed.ab. (406677)
29 placebo.ab. (169932)
30 drug therapy.fs. (1858104)
31 randomly.ab. (244496)
32 trial.ab. (352733)
33 groups.ab. (1521640)
34 or/26-33 (3714530)
35 (chang$ or evaluat$ or reviewed or baseline).tw. (4970483)
36 comparative study/ (1750531)
37 follow-up studies/ (540405)
38 time factors/ (1064137)
39 (prospective$ or retrospective$).tw. (922946)
40 (cohort$ or case series).tw. (383738)
41 (compare$ or compara$).tw. (3219485)
42 or/34-41 (10351029)
43 25 and 42 (2058)
44 43 not (editorial or letter or comment or case reports).pt. (1825)

Cost Effectiveness of Post-EVAR Surveillance

Database: Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations and Ovid MEDLINE(R) <1946 to Present>
Search Strategy:

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1 Endoleak/di [Diagnosis] (126)
2 Endoleak/us [Ultrasonography] (30)
3 Aortic Aneurysm, Abdominal/ (15012)
4 endoleak/ or endoleak?.tw,kw. (3268)
5 evar.tw,kw. (2357)
6 (endovascular adj5 repair? adj5 abdominal).tw,kw. (2201)
7 or/3-6 (17022)
8 Ultrasonography/ (65123)
9 (duplex adj2 (ultrasound or ultrasono$)).tw. (5708)
10 Ultrasonography, Doppler, Duplex/ (5522)
11 (contrast enhanced adj2 (ultrasound or ultrasono$)).tw. (3092)
12 Tomography, X-Ray Computed/ (314366)
13 Multidetector Computed Tomography/ (3662)
14 (computed adj3 tomograph$).tw. (187953)
15 Endoleak/us [Ultrasonography] (30)
16 exp Epidemiological Monitoring/ (4667)
17 surveillance.tw,kw. (120992)
18 monitor$.tw,kw. (585205)
19 or/8-18 (1150526)
20 7 and 19 (5703)
21 1 or 2 or 20 (5733)
22 exp "costs and cost analysis"/ (195528)
23 economics/ (27220)
24 exp models, economic/ (11282)
25 exp decision theory/ (10287)
26 monte carlo method/ (22270)
27 markov chains/ (11096)
28 exp technology assessment, biomedical/ (9592)
29 (cost$ adj2 (effective$ or utilit$ or benefit$ or minimis$)).ab. (97769)
30 economics model$.tw. (30)
31 (economic$ or pharmacoeconomic$).tw. (179371)
32 (price or prices or pricing).tw. (27274)
33 budget$.tw. (21283)
34 (value adj1 money).tw. (28)
35 (expenditure$ not energy).tw. (20980)
36 markov$.tw. (16078)
37 monte carlo.tw. (33264)
38 (decision$ adj2 (tree? or analy$ or model$)).tw. (14952)
39 or/22-38 (530178)
40 21 and 39 (131)