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Enhancements to angioplasty for peripheral arterial occlusive disease (PAOD): systematic review, cost-effectiveness assessment and expected value of information analysis.

Background

Peripheral arterial occlusive disease (PAOD) is a cause of major morbidity in the UK. Disease in the arteries to the legs causes reduction in the circulation and can present clinically as intermittent claudication (pain on walking) which can severely impair life style. More severe disease may present as critical ischaemia with rest pain, ulceration or gangrene in the lower extremities. In recent years there has been a rapid increase in the use of endovascular treatment, particularly percutaneous transluminal balloon angioplasty. In this procedure a device is inserted through a small puncture under local anaesthetic and a narrowed or blocked area of artery is opened up by the inflation of balloons.

The use of these techniques has expanded rapidly with about a 50% increase in the last few years to approximately 23,000 procedures per year in England and Wales.[1]

There have also been rapid technological developments aimed at improving the short and long term results of this treatment. Such developments include the use of stents[2], drug eluting stents[3], drug eluting balloons[4], cryotherapy[5], atherectomy[6] and drug treatments.[7] Many of these techniques have been developed for use in the coronary circulation and extended to the peripheral circulation or may be evaluated in the peripheral circulation with a view to using similar methods in the coronary circulation.

The purpose of the proposed research would be to evaluate the range of additional technologies that are available and identify those technologies and clinical situations where they are most likely to be of benefit, or where further research studies are justified.

Decision problem

Purpose of assessment

The planned assessment is to answer the following research questions.

- What is the clinical and cost effectiveness of additional techniques designed to improve the results of endovascular treatment (standard transluminal balloon angioplasty) for peripheral arterial disease?
- In which of these techniques is further primary research likely to lead to information that will improve the effectiveness and cost effectiveness of care in this condition?

Definition of interventions

This assessment is of new endovascular techniques that may be used to either supplement or replace existing endovascular procedures to improve the circulation of the lower limb in cases of PAOD. The following is a summary of various known techniques but others may be identified during the initial review.

Bare metal stents

There are a number of different designs and materials used for producing bare metal stents that can be inserted in a narrowed or occluded artery in order to try and improve flow and maintain patency. These are made from a variety of metals and have different designs. These can be divided into particular subgroups based upon those that require expansion with a balloon or those that are self-expanding.[8] These are extensively used in the coronary vessels and quite commonly in the iliac vessels, but use within the infra-inguinal circulation is less well established.

Drug eluting stents

There are a number of designs of metal stents that are coated with drugs that are gradually released and may reduce the rate of re-stenosis. These include stents that release cytotoxic or immunosuppressant drugs such as Paclitaxel[9] and Sirolimus.[10] These have been quite widely used in the coronary circulation and various configurations are now available that are suitable for use in the peripheral circulation.

Stent-grafts

Stents may be covered with graft material, usually ePTFE, to produce stent-grafts. Large stent-grafts are now commonly used for treating aneurysms and smaller diameter versions are available for use in the peripheral arteries. Such devices may be inserted by a percutaneous route[11] or may be used as a part of surgical procedures[12].

Atherectomy

Whereas conventional balloon angioplasty or stenting does not remove the occluding material but opens up and stretches the lumen of the vessel, atherectomy is a technique which attempts to remove some of the occluding material. There are a number of proprietary devices for this technique including the Simpson catheter[13], the Rotablator[14] and Silverhawk atherectomy device.[15] Again, these may be divided into subgroups depending upon the mechanism of action, with available devices being either “rotational” in nature[16], removing material in a concentric fashion or “directional”.[17] removing material from one aspect of the arterial wall.

Cryoplasty

This is a method which combines transluminal angioplasty using a balloon with the cryotherapy by cooling the vessel wall.[5] The technique uses inflation of the balloon with a cooling mixture rather than the standard use of contrast medium.

Therapies using radiation sources

Radiation therapy has been used to try and reduce re-stenosis following angioplasty. This may be carried out through different techniques. Randomised controlled trials have been reported with external beam radiotherapy[18] and brachytherapy using small radioactive probes that can be inserted through an endovascular route.[19]

Cutting balloon

The cutting balloon is a device that combines a conventional angioplasty balloon with small blades that cut the atheroma at the time of dilatation.[20]

Drug eluting balloon

A recent development has been the use of balloons coated in drugs similar to those used for drug eluting stents in order to deliver the agent at the time of angioplasty. Paclitaxel coated balloons have been used elsewhere and have recently become available in the UK.

Laser angioplasty

There was a considerable body of research in the late 1980's regarding the use of lasers to unblock arteries. The majority of devices that were used at that time have subsequently been withdrawn. However there are some devices still available that use Excimer lasers as part of an atherectomy procedure to ablate occluding material.[21]

Excluded interventions

In order for the review to be practicable some limitations will be placed on the interventions and devices that will be considered.

Pharmacological interventions

The separate effects of pharmacological measures aimed at altering patency will not be specifically considered, except where the use of a particular agent is required as an integral part of a new endovascular technique.

Combined surgical procedures

Some new techniques, such as remote femoral endartarectomy, require a combined surgical and endovascular approach. Many of the others may also be combined with surgical procedures and, in some cases, may be used for different indications in patients who would not necessarily be amenable to conventional endovascular techniques. Inclusion would considerably extend the scope of the proposed reviews and require additional modelling. These will therefore be excluded from the current review.

Other techniques

There are a number of other new endovascular techniques that may be used as an adjunct to angioplasty. These include closure devices, devices to protect from embolisation and techniques for thrombolysis or thrombectomy. These will only be considered where they are a component of one of the other techniques referred to above.

Place of the intervention in the treatment pathway

The techniques under consideration in this assessment will be those that are either used as a replacement for, or in conjunction with, conventional balloon angioplasty. These cover a variety of different clinical settings and subgroups (see below). In general, treatments will be considered that occupy the same place as balloon angioplasty in the treatment pathway for PAOD. There are however several different potential situations that may need to be considered separately, particularly in relation to the assumptions of an economic model.

- A technique intended to be used as a replacement or adjunct in all primary procedures.
- A procedure or device that is intended to be used selectively in a subgroup of patients based upon anatomical or radiological features or an inadequate response to the initial balloon procedure.
- Those procedures intended to be used in cases of re-stenosis or failure of the primary procedure.

The specific place in the pathway will therefore need to be considered individually for each of the technologies, depending upon their intended use and the available evidence.

Relevant comparators

There are a large number of potential new technologies, many of which are mutually exclusive alternatives for the endovascular treatment of PAOD. The starting point for the evaluation will be direct comparisons with balloon angioplasty but where several treatments are appropriate to the same clinical subgroups mixed treatment comparisons will be carried out to compare all relevant technologies.

If technologies are identified that are primarily intended for use in patients who would be unsuitable for conventional endovascular techniques then comparison with other methods for managing PAOD will be considered. These may include best medical treatment, exercise therapy and surgical treatment. The decision on the extension of studies to include these comparators will be driven by initial review of the evidence and expert advice.

Population and subgroups

There are a number of different subgroups of population that may need to be considered separately within the review and modelling as they may have different clinical and economic implications. Subgroups will be identified where possible, within the published literature. Modelling will include a consideration of appropriate subgroups as regards clinical presentation, anatomical site, demographic features and co-morbidities. Several of these represent potentially important issues that will need to be addressed within the review.

Symptomatic presentation

Patients with PAOD may present either with intermittent claudication (pain on exercise) or with critical ischaemia which includes ulceration, gangrene and ischaemic rest pain. The Trans-Atlantic Inter-Society Consensus (TASC) has standardised the anatomical and symptomatic definitions of vascular disease, including the use of the Rutherford classification[22], which is often used to categorise the severity of ischaemia. The symptomatic classification has significant implications both for the appropriate treatment modalities and comparators and the likely outcome of treated and untreated disease. It is also closely related to the utilities associated with the relevant health states. It will therefore be necessary to consider separate subgroups within the review, and economic analysis will be based upon these factors.

Anatomical features

The outcome of endovascular treatment is also known to be heavily influenced by the site and distribution of arterial occlusive disease. Aorto-iliac disease affects the larger vessels above the inguinal ligament. Conventional angioplasty, with or without the use of stents, has been common practice in this area for some years and clinical results are generally good with a lower rates of re-stenosis or re-occlusion.[23] In view of this, the potential advantages of new techniques to improve outcomes are likely to be very much smaller in absolute terms, with very large clinical studies being required to demonstrate significant clinical benefit. The current assessment will therefore focus on disease below the inguinal ligament.

The assessment will include all infra-inguinal disease, but it is recognised that some technologies are used or designed specifically for certain areas within this and, where the evidence allows, subgroups will be considered separately for femoral, popliteal and infra-geniculate disease.

In addition to the anatomical site of treatment other anatomical features may be used to identify appropriate subgroups where these are relevant to a specific technology or clinical evidence indicates that this would be appropriate. Such anatomical features include.

- Proximity to bifurcations
- Stenosis versus complete occlusion

- Length of occlusion
- Degree of calcification
- Multi-level disease with disease in inflow or outflow vessels
- Eccentric disease

Other features

Other features that may identify relevant subgroups include co-existing disease such as diabetes or renal disease, smoking habits, age and ethnicity. Subgroups based upon these characteristics will be considered where the available evidence, or clinical advice, makes this appropriate.

Key factors to be addressed

The specific objectives of the review are:-

1. To investigate by systematic review the effectiveness and cost effectiveness of endovascular techniques to supplement or replace balloon angioplasty in the infra-inguinal arterial circulation (Review 1).
2. To investigate by systematic review the utilities associated with health states relating to the natural history of treated and untreated PAOD (Review 2).
3. To estimate the incremental cost effectiveness of the new technologies identified in Review 1.
4. To assess the potential value and optimum design for further research studies to collect data on areas of uncertainty identified by the above reviews.

Methods for synthesis of evidence

Description of reviews

Review stage 1: A comprehensive search will be undertaken to systematically identify clinical and cost effectiveness literature concerning endovascular techniques to supplement or replace balloon angioplasty in the infra-inguinal arterial circulation.

Review stage 2: Where utility data are unavailable from studies identified in review stage 1, literature reviews will be conducted to provide data to populate the economic model. This will comprise data on the utilities associated with health states relating to the natural history of treated and untreated PAOD. This is likely to be necessary as it is expected that most published clinical research in this area will provide surrogate endpoints such as vessel patency or symptomatic and disease specific endpoints such as exercise tolerance, symptomatic state or amputation rates.

Identifying and systematic reviewing of clinical effectiveness evidence

Population

The population will be patients with symptomatic PAOD undergoing endovascular treatment for disease distal to the inguinal ligament.

Interventions

Clinical studies that evaluate techniques used as an adjunct to, or as a replacement for balloon angioplasty in the peripheral circulation. The identified procedures include but are not limited to those procedures identified in the inclusion criteria below.

Search strategy

The search strategy for both reviews will comprise the following main elements: searching of electronic databases; contact with experts in the field; scrutiny of bibliographies of retrieved papers. The electronic databases to be searched from inception will include MEDLINE; Medline in Process (for latest publications); EMBASE; Cochrane Database of Systematic Reviews; Cochrane Controlled Trials Register; CINAHL; NHS EED, DARE, and HTA databases; NIHR Clinical Research Network Portfolio database; NRR (National Research Register) Archive; Web of Science Proceedings; Science Citation Index; Current Controlled Trials; Clinical Trials.gov; FDA website; EMEA website; and relevant conference proceedings. These will include the proceedings of the Vascular Society of Great Britain and Ireland, The European Society of Vascular and Endovascular Surgery, The British Society of Interventional Radiology, Cardiovascular and Interventional Radiological Society of Europe, The Society for Interventional Radiology and the Society for Vascular Surgery.

Searches will not be restricted by publication type, study design, date or language. In addition citations within relevant papers will be checked and hand searching of relevant journals, using the search strategy described by the Cochrane Peripheral Vascular Diseases Group, will be performed (Cochrane Collaboration 2006).

An initial draft search strategy based upon the identified technologies and relevant anatomical sites identified over 5,000 references. Standard methodological filters will be used to limit this to systematic reviews, randomised and controlled trials and cost effectiveness analyses. This is still expected to identify a large number of potentially relevant papers. Further limitation may be required to exclude papers referring to angioplasty at other sites. Limitation by publication date may also be necessary, but is likely to be different for individual technologies based upon expert advice regarding technological developments (see below).

Study selection

In both stages of the review citations will be imported into reference management software and screened for inclusion, based on inclusion/exclusion criteria below. Titles and abstracts will be examined for inclusion by one reviewer. Two reviewers will independently make decisions on inclusion of studies at full text stage and any discrepancies resolved by discussion.

Inclusion criteria

Interventions

Transluminal balloon angioplasty, self-expanding and balloon expandable stent, drug eluting stent, drug eluting balloon angioplasty, percutaneous stent-graft insertion, laser angioplasty, atherectomy, cryoplasty, cutting balloon angioplasty, brachytherapy and external beam radiotherapy and other techniques used as an adjunct to, or replacement for, balloon angioplasty in the peripheral circulation.

Population

Adult patients with symptomatic PAOD suitable for endovascular treatment for disease distal to the inguinal ligament. Patients with critical ischaemia will be considered as a separate group to those with only claudication. Other important subgroups will be identified from the included studies.

Comparator

Conventional balloon angioplasty. Other comparators will be considered if included interventions are specifically designed as alternatives to angioplasty for patients in whom

conventional angioplasty has failed or is contraindicated, in which case the comparator will be current standard care as determined by the clinical evidence and expert advice.

Setting

Secondary care

Outcomes

Outcome measures will include: Disease-specific and generic measures of quality of life, exercise tolerance, pain (patient reported pain scores and analgesic use), limb salvage (for patients with critical ischaemia), walking distance (for patients with claudication), patency measures, re-occurrence and need for re-intervention, mortality and complications/adverse events.

Study types

According to the accepted hierarchy of evidence, randomised controlled trials and meta-analyses from systematic reviews will be searched initially, as they provide the most authoritative forms of evidence. If data are not available from these, other study types will be included.

Exclusion criteria

Interventions: Pharmacological interventions, combined surgical procedures, devices that have been withdrawn, such as older laser angioplasty devices.

Publication types: Studies which are only published in languages other than English; studies based on animal models; preclinical and biological studies; narrative reviews, editorials, opinions; and reports published as meeting abstracts only where insufficient details are reported to allow inclusion.

Data extraction and critical appraisal

Data will be extracted with no blinding to authors or journal. Data will be extracted by one reviewer using a standardised form. A standard proforma will be used and the data checked by a second reviewer. Discrepancies will be resolved by discussion, with involvement of a third reviewer when necessary.

Quality assessment will be subject to the types of studies identified but will be undertaken using appropriate and established tools, for example randomised controlled trials will be assessed according to criteria based on NHS CRD Report No.4[24] (http://www.york.ac.uk/inst/crd/report4.htm). The purpose of such quality assessment is to provide a narrative account of trial quality for the reader and, where meta-analysis is appropriate, inform potential exclusions from any sensitivity analysis.

Data synthesis

Pre-specified outcomes will be tabulated and discussed within a descriptive synthesis. Where statistical synthesis is appropriate, meta-analysis will be conducted using fixed or random effect models, using RevMan software[25]. If sufficient trials are available, a sensitivity analysis will be undertaken to see if the removal of poor quality trials affects the results.

Mixed treatment comparisons

If it is deemed appropriate a mixed treatment comparison (MTC)[26] will be undertaken to synthesise the direct and indirect evidence in a single network, and to provide an indirect comparison where head-to-head trials are not available. This would be undertaken in the modelling software WinBugs.[27] Current MTC methods draw on Bayesian rather than classical statistics and can make quantitative statements about the uncertainty around

parameters such as relative risk. This allows for the calculation of 95% (or any other percentage) credible intervals.

A 95% credible interval is a range that we are 95% sure the relative risk lies in, furthermore, the Bayesian method allows for estimation of intuitively appealing values such as the probability that the relative risk is 1 or higher. Where there are trials comparing interventions both to no treatment and to other interventions, a mixed treatment comparison synthesises all the trials into a single consistent network that uses the evidence from all the trials to estimate a relative risk for each comparison.[28] This internal consistent approach eliminates the possibility that contradictory evidence is provided from isolated head-to-head trials. Such discrepancies can occur in standard analyses, for example, direct trial evidence may show that treatment A is more efficacious than treatment B; treatment B more efficacious than treatment C, whilst treatment C was assumed to be more efficacious than treatment A, which cannot be correct.

Expert advisory panel

An expert advisory panel will be established to provide clarification on clinical issues. The panel will be based upon an existing group of experts in Yorkshire who have worked together on previous research related to vascular disease. The group will include representative of all relevant disciplines and professions, including interventional radiologist, vascular surgeons, physicians, vascular nurse specialists. Experts who have already agreed to participate are based upon the Sheffield Vascular Institute (including Prof Beard and Prof Gaines) and the Leeds Vascular Institute in (including Prof Gough, Prof Scott and Dr Kessel).

Additional experts will specifically be sought with experience of each of the techniques identified in the systematic review. A variety of methods will be used to seek the views of the expert panel, including electronic communication, direct discussions, interviews by members of the research team and focus groups if required.

Issues to be addressed by the expert advisory panel will include:-

- Identification of relevant technologies
- Identification of potential subgroups and inclusion/exclusion criteria for specific techniques
- Expert views about criteria for technique selection
- Assistance with defining resource use implications of specific techniques
- Consideration of face validity of modelling assumptions
- Consideration of feasibility of potential research proposals

Specific issues relating to new and emerging technologies

There are a number of specific issues relating to the assessment of new and emerging technologies that will need to be addressed. Unlike drugs, which are in their final version when they are marketed, it is common for new devices and technologies to undergo a period of continuing development. This creates some difficulties in reviewing the evidence and assessing the appropriate data for populating economic models. There are a number of specific issues that need to be addressed;-

- Devices that are used in clinical trials may be withdrawn or modified within the course of the research, or studies may have been carried out at different stages of device development[29].
- In an area of rapid technological development new devices may be introduced during the study or there may be a large number of ongoing trials.

- There may be a "learning curve" effect, both for individual clinicians using such devices and for the collective experience, in defining contra-indications to a new technology and the situations in which it is most appropriate[30, 31].

A number of steps will be taken to deal with these issues;-

- The expert advisory panel will be specifically asked to consider each technology under review to identify specific device design, patient selection and methodological changes that may be relevant. If necessary they will be asked to identify a date before which the device or mode of use may be considered to be sufficiently different to current models for there to be concerns about combining the results of clinical trials.
- The expert advisory panel will also be asked to identify specific issues regarding skills and training requirements for individual techniques.
- In carrying out the systematic review, data extraction will specifically include information regarding devices used, modifications, recruitment period and prior experience of participating centres. Where this information is available it will be used to identify subgroups within the meta-analysis.
- Where sufficient data exist, meta-regression techniques will be applied to consider the effect of time trends, case mix and device characteristics.
- During the course of the project (month 12) the searches will be repeated, particularly focussing on conference proceedings to identify newly emerging evidence.
- The economic model and expected value of information analysis will be used to generate conclusions that can be generalised to consider the hypothetical situation of a new technology of given cost and treatment effect based upon relevant clinical scenarios.

Methods for synthesising cost effectiveness evidence

Identifying and reviewing published cost effectiveness studies

The review above will be used to identify studies of cost effectiveness of balloon angioplasty and the new technologies. An economic search filter will be incorporated into the search strategy to identify relevant studies. Identified economic literature will be critically appraised and quality assessed using the critical appraisal checklist for economic evaluations proposed by Drummond *et al* (2005).[32] Existing cost effectiveness analyses will also be used to identify sources of evidence to inform structural modelling assumptions and parameter values for the *de novo* economic model.

Development of a health economic model

A new economic evaluation of the cost effectiveness of technologies for the management of PAOD will be developed. Cost effectiveness modelling will take account of potential benefits and harms of the new treatment and will identify subgroups of patients based upon the anatomical, radiological, symptomatic and other features discussed above where the data allows this.

The primary outcome from the model will be an estimate of the incremental cost per additional quality-adjusted life year (QALY) gained associated with the use of new technologies to improve outcomes, used alongside or as alternatives for conventional balloon angioplasty of the infra-inguinal arteries. A lifetime time horizon will be used in order to reflect the chronic effects of arterial disease and the ongoing risk of vessel re-occlusion, symptomatic deterioration, amputation and potential mortality. The perspective used will be that of the National Health Services and Personal Social Services. Costs and QALYS will be discounted at 3.5% as recommended in current guidelines [33]. Modelling assumptions will be taken from the literature, supplemented by clinical expert opinion where required.

The ScHARR modelling team have published papers using different modelling techniques (such as discrete event simulation [34-36], transition state modelling [37] and meta-modelling [38]).

The model structure and software used to construct the model will be determined following data collection in order that the most appropriate technique is used for this particular assessment. The expert advisory group will be consulted at the conceptual stage to ensure that the structure of the model is appropriate to clinical practice.

Ideally, health related quality of life evidence will be available directly from the review of the literature. In the absence of such evidence, the mathematical model may use indirect evidence on quality of life from alternative sources. Quality of life data will be reviewed and used to generate the quality adjustment weights required for the model. In addition to the reviewed literature, national sources (eg. NHS reference costs [39], national unit costs [40], British National Formulary (http://bnf.org)) and manufacturers' list prices will be used to estimate unit costs for use in the economic model. Where data on resource use associated with the new technologies are not available from the literature, advice will be sought from the expert advisory panel in the first instance. If uncertainty remains regarding the resources required for specific procedures, arrangements will be made for a member of the research team to observe and record the resource use associated with the procedures.

It is anticipated that there may be limited evidence for some of the parameters that will be included in the economic model. Therefore, the uncertainty around the parameter estimates will be modelled to take this into account. The uncertainty in the central value for each required parameter will be represented by a distribution, enabling probabilistic sensitivity analysis to be undertaken. This will allow an assessment of the uncertainty to be made [41].

Value of information techniques will be undertaken within the work. The expected value of perfect information (EVPI) [42] will be explicitly calculated. EVPI is defined as the maximum investment a decision maker would be willing to pay to eliminate all uncertainty from the decision problem. It is initially calculated in terms of a defined unit (typically per patient) and then multiplied by the number of people expected to benefit from eliminating all uncertainty to form an estimate of total EVPI. EVPI per person is relatively high where there is large uncertainty in the adoption decision; conversely where there is only a small probability of error and the impact of an incorrect decision is small the EVPI per person will be relatively low.

Depending upon the resources required more complex methodologies (the expected value of partial perfect information (EVPPI) [42] and the expected value of sample information (EVSI))[43] may be undertaken. EVPPI differs from EVPI as it evaluates the maximum value of removing all uncertainty in one, or a subset of parameters, but it is more computationally expensive as it requires two nested Monte Carlo sampling levels.[44]

EVSI is more advanced methodology for determining the value of information, which explicitly takes into account that uncertainty will not be removed even with large sample sizes. The EVSI methodology simulates the results from the proposed research and synthesises the simulated data with prior knowledge to form a posterior distribution: the larger the trial size the more the posterior distribution resembles the simulated data which is then used in probabilistic sensitivity analyses. The optimal trial size from the options evaluated can then be estimated based on the costs of conducting the trial and the expected net benefit of the sampled information. The application of EVSI is becoming more widespread and case studies employing this methodology have been published.[35, 36]

Expected outputs

The expected outputs are:-

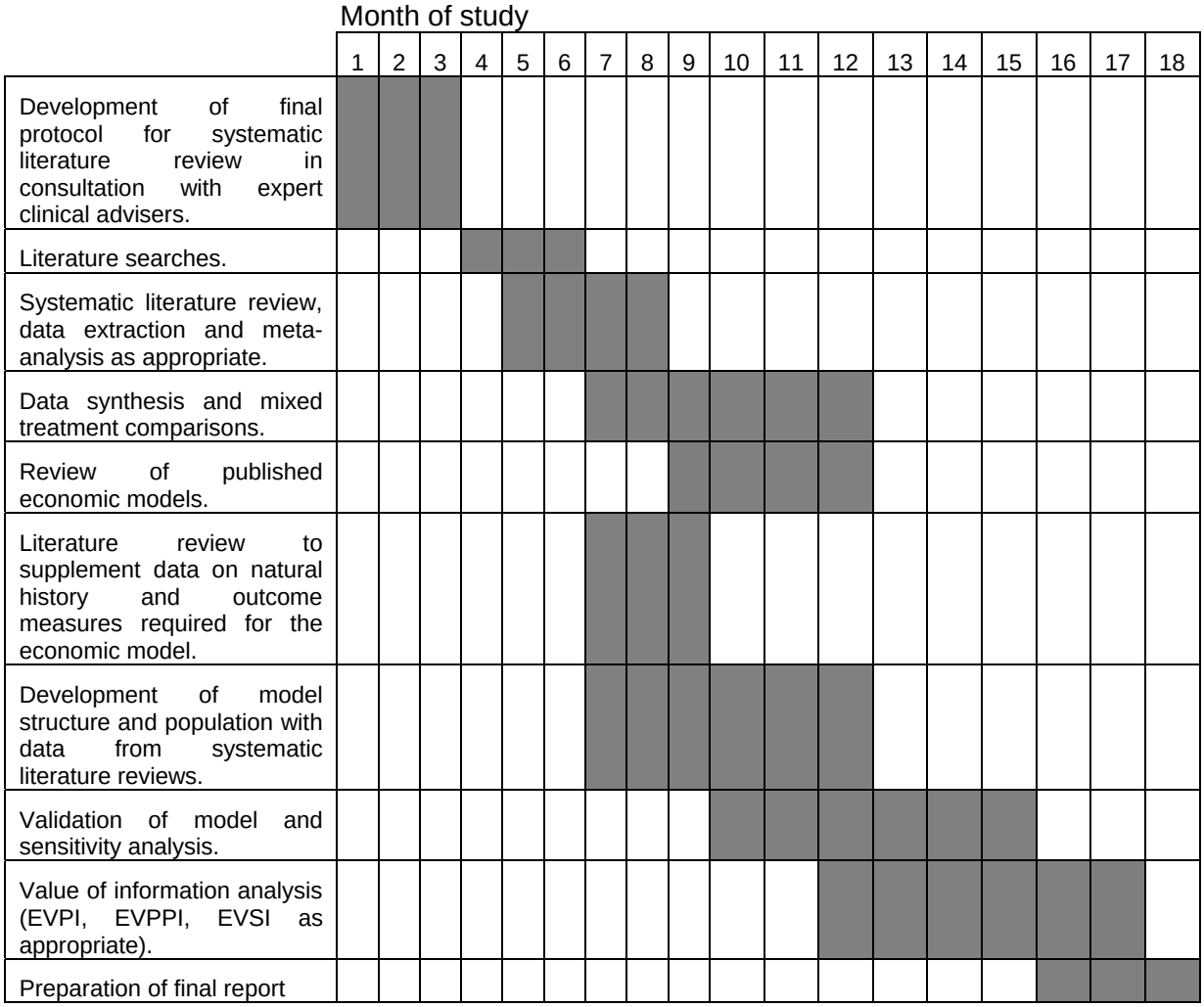
- A systematic literature review compiling the existing evidence for the clinical effectiveness of the various techniques under consideration.
- A review of existing cost effectiveness analyses of the relevant technologies.
- Data synthesis using mixed treatment comparisons, where appropriate.

- A summary of estimated utility values associated with health states relating to PAOD and its treatment.
- Cost effectiveness analysis detailing the cost effectiveness frontier for the full range of competing technologies, dealing with specific subgroups and clinical situations as appropriate.
- An analysis of EVPI/EVPPI/EVSI giving an indication of those areas in which further research is likely to be most productive.

Timetable and milestones

The timetable for the project is shown in the diagram below. Specific milestones are:-

1. Development of final protocol for systematic literature review. Month 3
2. Completion of initial literature searches and data extraction. Month 8
3. Completion of data synthesis/mixed treatment comparisons. Month 12
4. Review of published economic models. Month 12
5. Model completion and validation. Month 15
6. Completion of final report. Month 18



Expertise

The project team is based upon a group at ScHARR with considerable experience in using similar techniques in other fields [35, 37, 38, 45]. The team also has extensive experience in the field of evidence review data synthesis and cost effectiveness analysis relating to vascular disease and its treatment.[34, 46-55]

The team is also currently part of the Technology Assessment Group that has been commissioned by the HTA to prepare a multiple technology assessment of drug treatments for intermittent claudication, an area in which there will be considerable overlap in subject knowledge and similarities in model structure.

The expert advisory group will provide expertise in all the relevant clinical areas and procedures and will advise on details of procedures, issues around training and device usage and resource use and costs.

User involvement

The Sheffield Vascular Institute has a long history of user involvement in previous research. In the past, patient and public involvement has largely been arranged through the patient partnership team at Sheffield Teaching Hospital NHS Trust. The Sheffield Vascular Institute is currently in the process of establishing a specific vascular user group, consisting of a panel of patients with a variety of vascular conditions, those who have undergone previous vascular procedures and carers and relatives of previous service users. This group is being established jointly between the University department and the clinical unit and will provide advice on both clinical issues and all stages of research from initial project development through to analysis and dissemination results.

Whilst this project is secondary research and, therefore, has less scope for public and patient involvement, it is expected that there may be issues relating to the processes of care involved with particular devices, modelling assumptions, health state valuations and the interpretation and dissemination of advice for which a user perspective would be valuable. It is expected that the user advisory panel will be fully established by the time that the research is commenced.

Justification of support

The co-applicants will require a contribution for their time in supervising the various aspects of the project including overall project management (JM/ST), provision of clinical expertise and identification of other clinical experts (JM/ST), development of systematic review search strategy and critical appraisal (SP/ES/PS), development of economic model (MS/YM), literature appraisal (ES/SP/PS), systematic review, meta analysis and mixed treatment comparison (MS/PS) and overseeing general health economic aspects of the work (PS).

A full time research salary for a senior researcher has been included to undertake the overall project management and co-ordination, to ensure timely production of interim and final reports, and assist in the systematic literature review and modelling. One of the co-applicants (SP) currently has other grant applications in progress. He has recently undertaken project management for another HTA project and, depending upon this availability, some of the full-time salary may be used to enable him to act as project manager. The remainder of the full time salary will be used for one or more existing researchers or new appointments at ScHARR depending on the skill mix and personnel availability at the time that the various tasks are undertaken.

Additional funding is required for:-

- reprints of journal articles

- an additional computer for the research assistant
- computer modelling software
- expenses related to obtaining views of relevant clinical experts through the clinical advisory group
- dissemination of study results.

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