NETSCC, HTA

3rd June 2011

DETAILED PROJECT DESCRIPTION

1. The Project Title: To develop an algorithm to calculate for individual patients with abdominal aortic aneurysm (AAA) when repair is indicated to improve survival.

2. Planned Investigation

Research Objectives

We plan to develop algorithms to calculate when elective AAA repair should be performed to optimise survival for patients with AAA. This proposal is primarily focussed on open surgical AAA repair. We will however now include EVARs in our analysis of risk factors associated with short and long term mortality. The inclusion of EVAR would be ideal as it broadens the clinical relevance of this study. The concern is that the number of EVAR patients available for analysis is still inadequate. Currently, in Vascular Governance North West (VGNW) there is data on 753 elective EVAR patients of whom 17 have died. The follow up data for EVAR patients is also shorter than for open AAA repair. The analysis of outcome following EVAR is also complicated by the frequent need for secondary interventions, and occasional late ruptures which are rare with open AAA repair.

The number of EVAR procedures available for analysis is however rising rapidly in both the VGNW and National Vascular Databases (NVD). Collaboration with other groups and registries that hold data on EVAR procedures will be explored. The inclusion of EVARs remains a "work in progress" and that it is unlikely that the development of a reliable algorithm on long-term outcomes following EVAR will be possible within 2 years. The research methodology developed in this project will allow the development of an algorithm on EVAR as reliable data becomes available.

AAA is common, affecting 5-10 % of men aged 65-79[1]. AAA rupture causes 7,000 deaths/year in the UK; 2.1% of all deaths in men over the age of 65[2]. Most patients suffering AAA rupture die immediately and even in those that reach hospital alive the operative mortality approaches 50%[3]. Mortality for elective AAA repair is much lower at approximately 5%[4] for open surgical repair and approximately 1% for EVAR [5 6]. Emergency repair is also twice the cost of elective repair at over £11K[7]. The incidence of AAA is increasing as the population gets older[8]; the introduction of the UK National AAA Screening Programme will identify many more men aged 65 with asymptomatic AAA's. We aim to identify the ideal timing for AAA repair for each individual patient ensuring the most efficient use of resources and optimising clinical care. The AAAQIP has been established to reduce mortality following elective open AAA repair to 3.5%. This research will help achieve this objective by identifying for each patient when surgery is indicated to improve survival.

Currently, based on randomised controlled trials such as the UK Small Aneurysm Trial (UKSAT), elective repair is indicated for men when the AAA diameter reaches 5.5 cm[9]. Intuitively this can not be correct for all patients. Older patients, especially those with cardiovascular or pulmonary co-morbidities, have a high risk of perioperative mortality. The risk of rupture may not outweigh the risk of surgery in these patients and surgery may both shorten life expectancy and impair quality of life.

There is some evidence for this in the sub-group analysis of the UKSAT (Table 1). Annual death rates in older patients under surveillance tend to be lower than in those offered early surgery. Whereas younger men undergoing early surgery appear to have a survival benefit. Across all age ranges death rates during surveillance rise with AAA size and early surgery may reduce death rates if offered for AAA sizes as low as 5.0cm.

Table 1 - Analysis of AAAs 4.0-5.5cm from UKSAT [(4)]

age	deaths 100-person years Surveillance	deaths 100-person years Early surgery
60-66	5.8	4.7
67-71	8.9	6.8
72-76	7.6	9.5

AAA diameter (cm)	deaths 100-person years surveillance	deaths 100-person years early surgery
4.0-4.4	6.5	7.4
4.5-4.8	6.8	6.3
4.9-5.5	9.5	7.4

As AAA symptoms are themselves an indication for surgery, the main purpose of AAA repair for asymptomatic patients is to improve survival by preventing death due to rupture. Simple calculations based on life expectancy in our feasibility study (page 7), suggest that earlier surgery (in smaller AAA's) is likely to improve survival in younger patients. For those aged >80 years, where operative mortality is higher and life expectancy shorter, surgery should be delayed to AAA diameters of >5.5 or possibly >6.0 cm. A recent study in patients undergoing elective AAA repair reported 30-day mortality as high as 20% in men and 25% in women aged 80-84[10]. The effect of major surgery on the quality of life for these elderly patients may be devastating and at a year following surgery 32% of men and 34% of women had died[10]

The current indication to operate when the AAA reaches 5.5 cm in men ignores age, life expectancy and all the risk factors that influence operative mortality. Our objective is to establish the evidence-base required to calculate when AAA repair improves survival. For each individual patient, the indication for surgery should be influenced by age, AAA growth rate and risk of rupture and patient risk factors that influence either life expectancy or operative mortality. Our aim is to develop an algorithm which calculates how open surgical repair influences health-adjusted life expectancy of men with asymptomatic AAA.

This proposal utilises research already commissioned by NIHR HTA at the MRC Biostatistics Unit in Cambridge to determine AAA growth rates and risk of rupture in patients with small asymptomatic AAA. The Cambridge team will identify the factors influencing AAA growth and risk of rupture by analysing individual participant data from previous studies.

The Manchester team have access to the VGNW database on outcome following AAA repair in over 3,600 patients. This group has already begun to develop algorithms for predicting mortality following elective AAA repair. A recent systematic review of the available risk prediction models found none to be entirely satisfactory[11]. We have been able to accurately identify high risk patients in which the predicted mortality is over 10%. To improve these algorithms the quality of data will need to be improved by reviewing medical records for missing data and risk factors not initially recorded in all cases. The model will also improve as more data is added. The proposed algorithm is intended to evolve continuously as new risk-predictors are shown to be significantly associated with outcome. Recently, data relating to pre-operative cardio pulmonary exercise testing (CPEX) has been incorporated into VGNW and it is possible that this data may, in the future, improve the accuracy by which we can predict outcome. The ability to recognise and predict frailty, using either the information already collected in VGNW or additional data fields, has the potential to improve the accuracy of our algorithm.

We will extend data collection to include those predictors of frailty thought to be appropriate and easily collectable following discussions with experts in frailty research. Initially we will begin collecting data using the CSHA Clinical Frailty Scale which has been shown to perform better than measures of cognition, function or co-morbidity in assessing risk for death. This process of additional data collection regarding frailty will occur alongside the current extension of VGNW to include data from CPEX. This data may potentially influence the proposed algorithm on risk of perioperative mortality within three years. The National Vascular Database (NVD) will be used to validate the developed risk prediction models.

Once suitable algorithms for 30-day operative mortality have been created and validated, the long term survival of the patients in VGNW will be analysed. This information will allow the impact of surgery on the life expectancy to be calculated for each individual patient. When we have completed algorithms to calculate: 1) AAA growth and risk of rupture from the Cambridge team and 2) Operative mortality for each individual patient, we will combine these to reach our objective: An algorithm to calculate at which AAA diameter each individual patient should undergo open surgical repair in order to improve survival.

The resulting information on both the risk of surgery and the risk of continued surveillance will be of immense value to patients trying to decide on the merits of surgery and to clinicians involved in providing information to patients as part of the consent process. It should also reduce AAA related mortality. It will provide a clear indication when to operate and when not to operate for each patient.
Our proposal also includes research to calculate the cost to the NHS of implementing this algorithm. We aim to show whether this approach is cost effective as surgery will only be offered if it improves survival. The NHS and NICE will then have the information needed to best allocate resources for elective AAA surgery.

Existing Research

An AAA is a focal dilatation of the infra-renal aorta with an increase in diameter of at least 50% over the expected normal diameter. AAAs are found in 5-10% of men aged 65–79[2]. Advancing age, male sex, smoking and a family history of AAA are all significant risk factors[12-15]. AAA growth rates accelerate as the diameter increases, particularly as AAAs grow to >5 cm[16]. The rate of growth of AAAs is influenced by risk factors such as smoking, hypertension and diabetes[17] and is the subject of a systematic review being conducted by Professor Thompson and his team at the MRC Biostatistics Unit in Cambridge which will be done through a re-analysis of individual participant data from all relevant studies.

The annual rupture rate for patients with AAAs <5cm during ultrasound surveillance was under 1% in two large studies[9 18] but increases with AAA diameter[16]. There is increasing evidence that the risk of rupture at an equivalent size of AAA is higher in women than in men. Ultrasound reliably detects AAA and is used to measure AAA diameters during aneurysm surveillance[19]. In four large control trials randomizing 127,891 men, ultrasound screening reduced AAA related mortality and the frequency of rupture[2 15 20 21]. The MASS trial estimated the life-time costs effectiveness of AAA screening at only £2970/QALY[22]. A pooled analysis based on these trials also reported a significant reduction in overall mortality and in the number of emergency operations[1] and as a result the UK National AAA Screening Programme has been introduced.

Open surgical repair is indicated currently when the AAA diameter reaches 5.5 cm in men (5.0 cm in women) based on two randomised control trials comparing early surgery with surveillance[9 18]. This indication for surgery is partly predetermined as patients with AAAs only in the size range 4.0 – 5.5 cm were randomised to either surgery or surveillance. These trials were not designed to explore any indication for surgery other than the extremes of this "grey area". Both these trials average results for patients aged 60-90 years even though the life expectancy of a man aged 60 is for a further 22 years; almost four times that for man aged 85.

The Vascular Society has recently introduced the AAAQIP which is aiming to reduce the mortality rate following open elective AAA repair to 3.5%. This work will facilitate this as it will help identify the patients who have the most to gain from surgery and reduce the number of high risk patients who undergo AAA surgery.

Feasibility Study

Our feasibility calculations are necessarily simple as they do not include the detailed analysis of factors influencing AAA growth and risk of rupture being undertaken by the Department of Biostatistics in Cambridge. Nor are they be influenced by the risk factors for peri-operative mortality that will be determined as the result of the analysis of the factors influencing mortality we proposed to undertake in Manchester (the research planned in this application). Our feasibility study is simply designed to demonstrate that the indication for elective AAA should not be based on a single standard size of AAA, but should vary according to the patient's age, risk of rupture and risk of peri-operative mortality.

This feasibility study is based on the average life expectancy of men aged 65 and 85. We have also assumed a constant AAA growth rate and risk of rupture over time based on the initial AAA size. We have used values from the literature for AAA growth rate and risk of rupture (table 2) [4 16], which will be provided for the final algorithm by the Cambridge group.

Table 2 Aneurysm growth rate and risk of rupture

AAA size(cm)	mean growth rate mm/year	predicted % AAA to rupture/ year
4.0-4.4	2.0	0.8
4.5-4.9	2.5	1.4
5.0-5.4	3.5	2.5

We have assumed the AAA growth rate for aneurysms measuring 4.5cm is 2.5mm/year and for those measuring 5.5cm is 3.5mm/year with an annual risk of rupture of 1.4% and 2.5% respectively. We have also assumed that if a patient aged 85 does not have surgery initially, elective surgery will not be offered in that patient's remaining life time. The peri-operative mortality by age group has been calculated using the elective open AAA repairs in the VGNW. This clearly showing markedly lower expected mortality for 60-69 year old men than for the same elective surgery in patients aged 80-89 years (Table 3). A further assumption that peri-operative mortality remains the same throughout each 10 year age band has been made.

Table 3 Operative mortality (Source VGNW)

Age	Operative mortality (%)
60-69	3.8
70-79	5.2
80-89	12.8

For men aged 80-89 the operative mortality is 12.8% (and is immediate), more than 3x the peri-operative mortality risk in 60-69 year olds which is only 3.8% and overwhelms the yearly risk of rupture of a 5.5cm AAA during the average life expectancy for such men (5.6 years). These crude calculations are based on crude life expectancy rather than health – adjusted life expectancy which will be used in the final algorithm. Nevertheless Table 4 clearly shows that life expectancy is likely to be optimised in healthy younger men aged 65 by operating on AAAs of 4.5cm or perhaps even smaller. We have also shown in this simple illustration that the risks of surgery in an 85 year old overwhelm any potential benefit at 5.5cm and possibly up to >6.0cm. It is obvious that co-morbidities that reduce life expectancy and increase operative mortality in the elderly will adjust our model away from early surgery.

Table 4 Life expectancy adjusted for AAA treatment at presentation

AAA size 4.5cm

age	healthy life expectancy (years)	treatment plan	time to elective repair (years)	risk of rupture before repair (%)	peri-operative mortality (%)	AAA adjusted life expectancy
65	82.3	Surveillance	4	5.6	3.8	80.8
		Early surgery	N/A	N/A	3.8	81.7
85	90.6	Surveillance	N/A	7.8	N/A	90.3
		Early surgery	N/A	N/A	13.8	89.9

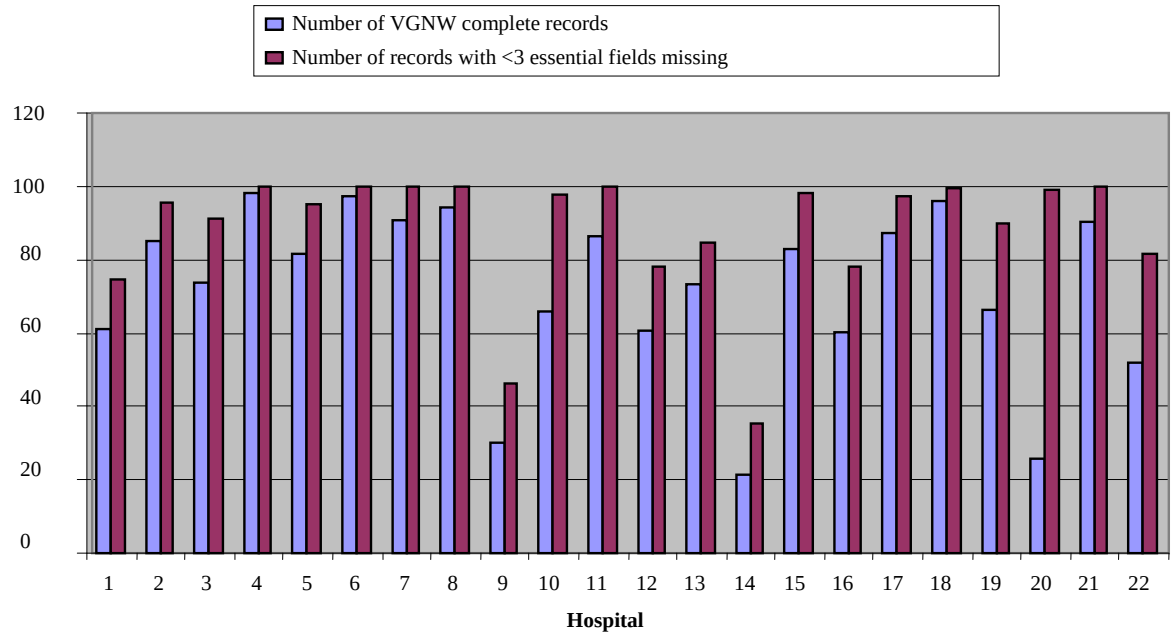
			AAA size 5.5cm				
85	90.6	No surgery	N/A	14%	N/A	90.0
		Early surgery	N/A	N/A	13.8	89.9

Feasibility of additional data extraction

How complete is the VGNW database?

The number of complete records held in the database for each hospital in VGNW is shown in figure 1. This graph demonstrates that additional data extraction can be targeted at certain hospitals with a higher percentage of poorly completed records.

Figure 1. The percentage of VGNW datasets complete for each hospital.



Pilot study of data completion

Over a period of three weeks the VGNW team visited three hospitals selected for high levels of missing data. At each hospital they aimed to complete 25 records per visit for the essential risk factors listed above. Each visit lasts approximately three hours and the completion rate for each visit was over 90%.

Research Methods

This collaborative study combines evidence synthesis with primary research. Our collaboration utilizes research already commissioned by NIHR HTA at the MRC Biostatistics Unit in Cambridge to complete a systematic review and develop an algorithm on AAA growth rates and risk of rupture in patients with small

asymptomatic AAA. Having identified the available studies they plan to obtain individual participant data (IPD) as outlined in their application. This application supports the Cambridge research by providing funding for the collection of data on over 1,210 patients with small AAA in the size range 3.0 – 5.4cm that have been in the University Hospital of South Manchester (UHSM) surveillance programme for up to 11 years. The Manchester team (funded by this application) will ensure the complete collection of all data required by Cambridge to assist in the development and validation of an algorithm to calculate growth rates and risk of rupture for different AAA size ranges (4.0-4.4, 4.5-4.9cm etc).

With the exception of the inclusion of our Manchester surveillance programme data, the design and research methods being used by the MRC Biostatistics Unit in Cambridge have already been described in detail in their HTA application "The growth and rupture rate of small abdominal aortic aneurysms: implications for population re-screening intervals" awarded in 2008. This project started in April 2009, Professor Thompson advises the algorithm on AAA growth rates and risk or rupture will be available by November 2010.

Design

Although the planned algorithm will incorporate information on AAA growth rates and risk of rupture from the Cambridge programme, this application focuses on the research design and methods planned for the Manchester team who are responsible for developing the algorithm predicting risk of peri-operative mortality for individual men undergoing elective open surgery for asymptomatic AAA. This will initially be done for 30-day mortality, however this proposal has been further developed to include information on long term survival following AAA repair.

Statistical Plan

VGNW data will be used to calculate for each individual patient the risk of 30-day mortality following open elective AAA repair. VGNW currently has pre-operative patient data on over 3,600 patients following AAA repair (with 240 who died post-operatively) and is accumulating over 300 new patients a year. A multiple logistic regression model, incorporating patient-specific risk factors, will be derived to predict 30-day mortality. Potential risk factors will be identified using simple logistic regression models. Those having a significant relationship with mortality, measured by $p<0.20$, or thought to be of high clinical importance and have been included in predictive models in previous published studies, will be considered as candidates for the multiple logistic regression model. This model will be constructed using the backward stepwise method. The optimal parametric relationship of the continuous variables with mortality will be investigated. Interactions between risk factors will also be considered. Multiple imputation methods will be employed to take account of

missing patient information. A number of different regression models, relating to groups of risk factors with varying degrees of missing information, will also be constructed. Goodness of fit tests (including Homer-Lemershow) and residual diagnostic procedures will be used to assess the fit of the various regression models.

Power of the study

This study will have over 90% power to detect odds ratios of 1.3 or more for a risk factor added to the regression model after adjustment for prior factors. This assumes its multiple correlation with these prior factors is 0.1 and that the mortality rate is approximately 7%.

Validation of model

An internal validation of the regression models will be determined using bootstrap methods (drawing 200 random bootstrap samples from the VGNWE database with replacement). Predictive accuracy will be assessed by discrimination techniques (ROC curve analysis, c-index, sensitivity, specificity). The perioperative risk prediction model will then be validated externally using the NVD database which includes data on over 4,900 AAA repairs (excluding the VGNW data). The predictive accuracy of the model will be evaluated as described above.

Estimates of longer-term survival

Data on the long-term follow-up of VGNW patients will be used to construct Cox proportional hazard models to assess the impact of risk factors on survival. Patient-specific risk factors will be identified using a similar procedure to that described for the multiple logistic regression analysis. The regression models will be tested for violation of the proportional hazard assumption using graphical methods.

Life expectancy estimates

Published life tables produced by the Office for National Statistics will provide estimates, by age and sex, of expected annual mortality rates and expected life-expectancy for the general population. Adjusted mortality rates and life-expectancy rates to take account of important co-morbidities such as history of smoking, hypertension or diabetes will be derived by applying published relative risk estimates for mortality associated with these morbidities to the annual mortality rates in the life table calculations.

The combined algorithm

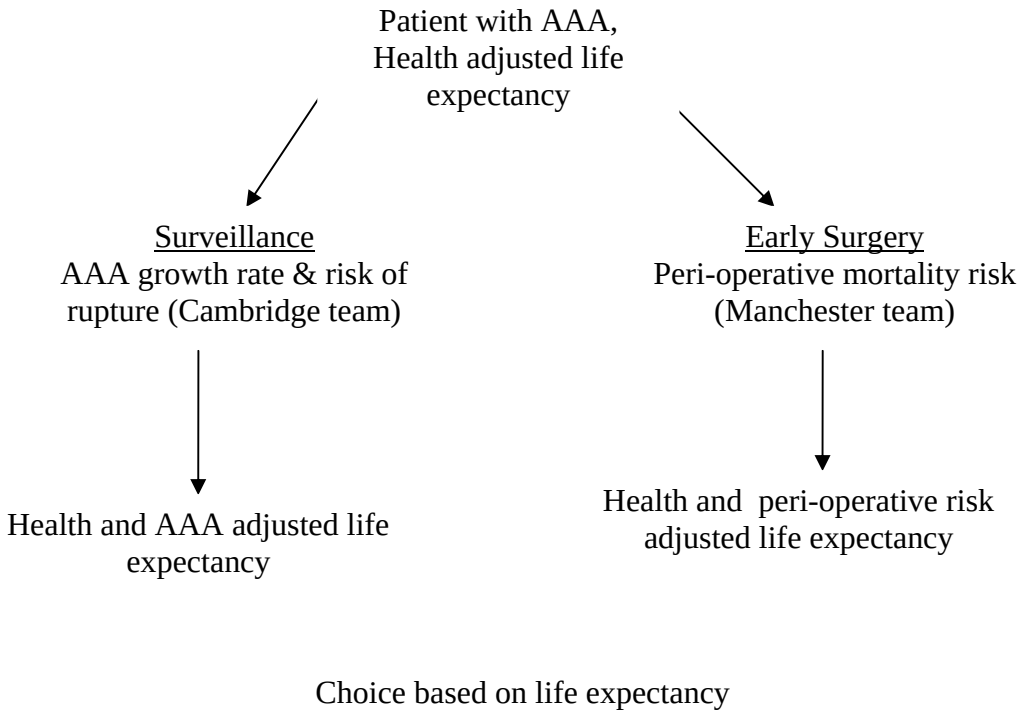
A Markov decision model, evaluated as cohort simulation, will be constructed to provide a prognostic tool to assess the mortality risk of patients with an AAA, incorporating information on AAA growth rates, AAA rupture rates, operative mortality following open repair, and life-expectancy data. The Markov process

characterises the transitions of a cohort of patients between different health states, with transition probabilities, allowed to vary with time, estimated from the predictions determined from the previous derived regression models and the information gained from the life-expectancy calculations. Each state will be assigned an appropriate incremental utility related to quality-adjusted life-years. The algorithm shown in figure 2 will produce estimates of quality-adjusted life years for the two scenarios, immediate surgery and delayed/no surgery.

Statistical software

SPSS and STATA will be used to derive regression models and adjusted annual mortality rates.

Figure 2. Development of final algorithm



Target Population

The algorithm will be applicable to all patients found to have an asymptomatic AAA.

Health Technologies Being Assessed

The new technology is usual care (AAA surveillance) plus the use of an algorithm to calculate in individual patients with AAA when repair is indicated to improve survival. This will be compared with current standard care, which is AAA surveillance with repair at 5.5cm in men. This technology will formalise assessment of individual patient risk factors as well as the risk of rupture associated with AAA size and other factors identified by the Cambridge team. The comparator is usual

care; surveillance to monitor the growth and size of the AAA with repair at 5.5cm in men (5.0cm in women).

Economic evaluation

Aims and objectives

The key aim of the economic evaluation is to inform clinical policy and practice about the relative cost effectiveness of selecting individuals for AAA repair using the algorithm to calculate health-adjusted life expectancy (developed as part of the clinical component of this study), compared with the current indication based on the diameter of the AAA alone (5.5cm in men and 5.0cm in women).

Key objectives of the economic evaluation will be to consider

i. the cost effectiveness of the algorithm to improve health-adjusted life expectancy compared to usual care as it is specified in national guidelines
ii. the cost effectiveness of a clinical algorithm to maximise life expectancy and quality adjusted life years (QALYs) and
iii. estimate the life expectancy and QALYs gained from an algorithm to minimise the incremental cost per QALY gained from changing clinical practice guidelines.

Approach

The economic analyses will use the perspective of the NHS, (the key funder and provider of care for AAA) and patients. These comprise the key components of a societal perspective. The time horizon for the primary analysis will be from diagnosis of the AAA to death, for a one year incidence cohort of people diagnosed with AAA not requiring immediate surgical repair, stratified by age. The impact of alternative time horizons will be tested in one way sensitivity analysis.

The measure of outcome for the primary analysis will be QALYs. The costs of events will include the direct costs of screening, surveillance and elective repair of the AAA. The direct costs of surveillance will include the NHS AAA Screening Programme service costs to screen and monitor the patient (or hospital costs if appropriate), primary/community or secondary based care services for cardiovascular risk management during surveillance and the use of services for emergency care (including emergency repair) during surveillance. The direct costs of elective and emergency repairs will include the use of hospital inpatient and outpatient services and primary/community based follow up. Future costs and QALYs will be discounted at the recommended rates at the time of analysis (currently 3.5%).

The economic evaluation will extend the Markov model planned for the clinical algorithm to include the costs and utilities or QALYs of the events and states included in the model. This means that clinical and economic Markov model will be jointly

developed and designed by all members of the project team to ensure appropriate events and states from an economics perspective are included. The Markov model will include events relevant to effectiveness and safety (patient outcomes, side effects and adverse events), and resource use and costs of the alternative surveillance strategies. Any additional events/health states required for the economic evaluation will be identified from a review of current guidelines, previous economic models and systematic reviews of health economic models in the field [23-25] and discussion with clinical experts and the service users in the project team. The model structure will be validated with experts in AAA surveillance and surgery to ensure it incorporates an accurate and feasible representation of practice.

Data sources

Data to populate the expanded economic model will be collected from a range of sources. The data on risk factors for rupture and mortality will be collected as part of the systematic reviews and re-analysis of individual patient data conducted as part of the Cambridge study by Thompson et al. Analysis of the VGNW and NVD data collected as part of this Manchester based study will be used to calculate the perioperative and long term mortality risk following AAA repair. Health and AAA adjusted life expectancy and health and perioperative risk adjusted life expectancy will be estimated by the clinical model.

The data to estimate the NHS services used for events in the model will also be derived from the VGNW and NVD databases and a systematic review of the trial and model based economic evaluations of screening, surveillance and repair. The service use data will be combined with published unit costs [23-25] to estimate the direct NHS costs of events. Where appropriate, the costs of events included in published trial and model based evaluations will be updated and used in the model for this study. The unit costs and direct costs used will be tested in one way sensitivity analysis.

Utility values will be generated from a systematic review of the published literature for each of the events included in the model, to adjust the measures of life expectancy generated by the model and estimate QALYs. Using the approach followed in the Cambridge study for the base case analysis, it will be assumed that (i) utility values for patients will follow age adjusted population norms for people during surveillance and after post surgery, (ii) there will be a temporary decline in utility for the duration of the hospital admission and post-surgical recovery period. This impact of this assumption and the impact of alternative utility values will be tested in one way sensitivity analysis (see below).

Analysis

Incremental cost effectiveness ratios will be estimated for the following cases:

- Comparing the algorithm on health adjusted life-expectancy with standard practice (repair when the AAA reaches 5.5cm in men and 5.0cm in women).

- Comparing an algorithm to maximize both survival and QALYs with standard practice
- Comparing an algorithm to minimize cost/QALY to standard care.

Cost-effectiveness acceptability curves (CEACs) will be plotted and the probability that the algorithm is cost effective will be estimated for the primary and sensitivity analyses for each of these cases. Probabilistic sensitivity analysis will used for the primary and one way sensitivity analyses.
One way sensitivity analysis will be used to explore the impact of structural factors inherent in the model or data (e.g. target AAA size for elective repair, shorter time horizons, utility values attached to events, unit costs and direct costs of events) and to explore in more detail the impact of using the algorithm in different age groups of patients. In addition, it is recognised that in usual care, clinicians and patients will reach a decision to operate or not based on additional factors to the diameter of the AAA. This means that the actual surgery rate may differ from that indicated by the guidelines. The rate of surgery in the usual care arm will be adjusted in a sensitivity analysis to assess the uncertainty this may introduce. The simulation software will be WINBUGS.

3. Project timetable and milestones
Assuming the grant is awarded in September 2010, the Manchester start date will be 3rd January 2011. As the Cambridge Team have started their systematic review, the algorithm on AAA growth rates and risk of rupture will be ready by November 2010. Although we already have extensive data on all 1,210 patients in the AAA surveillance programme, three months is needed to review these patients and their medical records to complete and verify the data required by the Cambridge team to validate their algorithm.

Completing the VGNW data will require examination of the medical records in most of the 3600 AAA patients which will take approximately six months. We have allowed a further three months to analyse this data and develop algorithms to predict 30 day mortality. Preparation in Manchester starts as soon as this grant is awarded: Start date 3/01/2011. The literature review and data validation for 1210 AAA surveillance patients completed by June 2011. Validation of data (incorporating risk factors from the literature review) on the VGNW database and subsequent analysis will be completed by December 2011. The results of this analysis will then be validated against NVD data. The systematic review of health costs will be commenced in January 2012. The final Markov algorithm incorporating health-adjusted life expectancy, the Cambridge algorithm and the Manchester and health costs will be developed May – October 2012.

4. Sites and expertise

The Aneursym Surveillance Clinic (ASC) at UHSM has data on 1210 patients with AAA (3.0-5.4 cm) under surveillance for up to 10 years. Gtr Manchester is an early implementer in the National AAA Screening Programme; the population to be screened in 2010 is around 2.7 million and 580 new AAA patients will enter surveillance in the first year alone. UHSM is also the base for the VGNW database. Professor McCollum has been the PI in several national clinical trials, founded VGNW and is the director of AAA Screening in Gtr Manchester.

Prof Dunn's Biostatistics Group has extensive collaborations with clinical scientists, are co-investigators on several current MRC trials and NIHR Applied Research Programmes and lead three current MRC-funded methodology projects. Professor Dunn has long-standing expertise in the evaluation of clinical measurements and diagnostic tests. He is a co-investigator on the current HTA-funded MAVARIC trial and is supervisor of an MRC training fellow working on systematic reviews of diagnostic test performance.

Professor Thompson is Director of the MRC biostatistics unit and has methodological research interests in meta-analysis, health economic modelling and clinical trials. He has had statistical responsibility for all the major UK trials on screening and treatment for AAA, including the UK Small Aneurysm Trial (UKSAT), the Multicentre Aneurysm Screening Study (MASS) trial and the UK EVAR trials . He is principal investigator for the recently funded HTA research on growth and rupture rates for small AAA, designed to inform screening intervals in the National AAA Screening Programme.

David Mitchell is the chair of Vascular Society Research and Audit Committee and also project director of the AAA Quality Improvement Programme. Julie Morris has expertise in multivariate analysis of risk factors. Prof Linda Davies has expertise in health economics, design and analysis of systemic reviews and Markov models.

5. Service Users

Lay members have been involved in the design of this project since its inception; the Chair of our AAA Service User Group is a co-applicant on the proposal and attends our Steering Committee meetings. The Service User Group will be supported by opinions from the AAA Quality Improvement Programme (AAAQIP) service user group who advise the Vascular Society on this programme to reduce mortality in elective AAA surgery. Our service user group includes a ruptured AAA survivor, two patients under surveillance and a relative of a patient who died from rupture.

Members of the Service User Group have been involved in

i) The development and analysis of surveys of patients opinions on AAA screening and surveillance
ii) Gathering patient opinions regarding the development and implementation of the proposed algorithm and the design of patient information leaflets
iii) The publication of reports resulting from the above screening research
iv) The design of presentations to the general public on AAA screening and the treatment options available for patients with AAA.

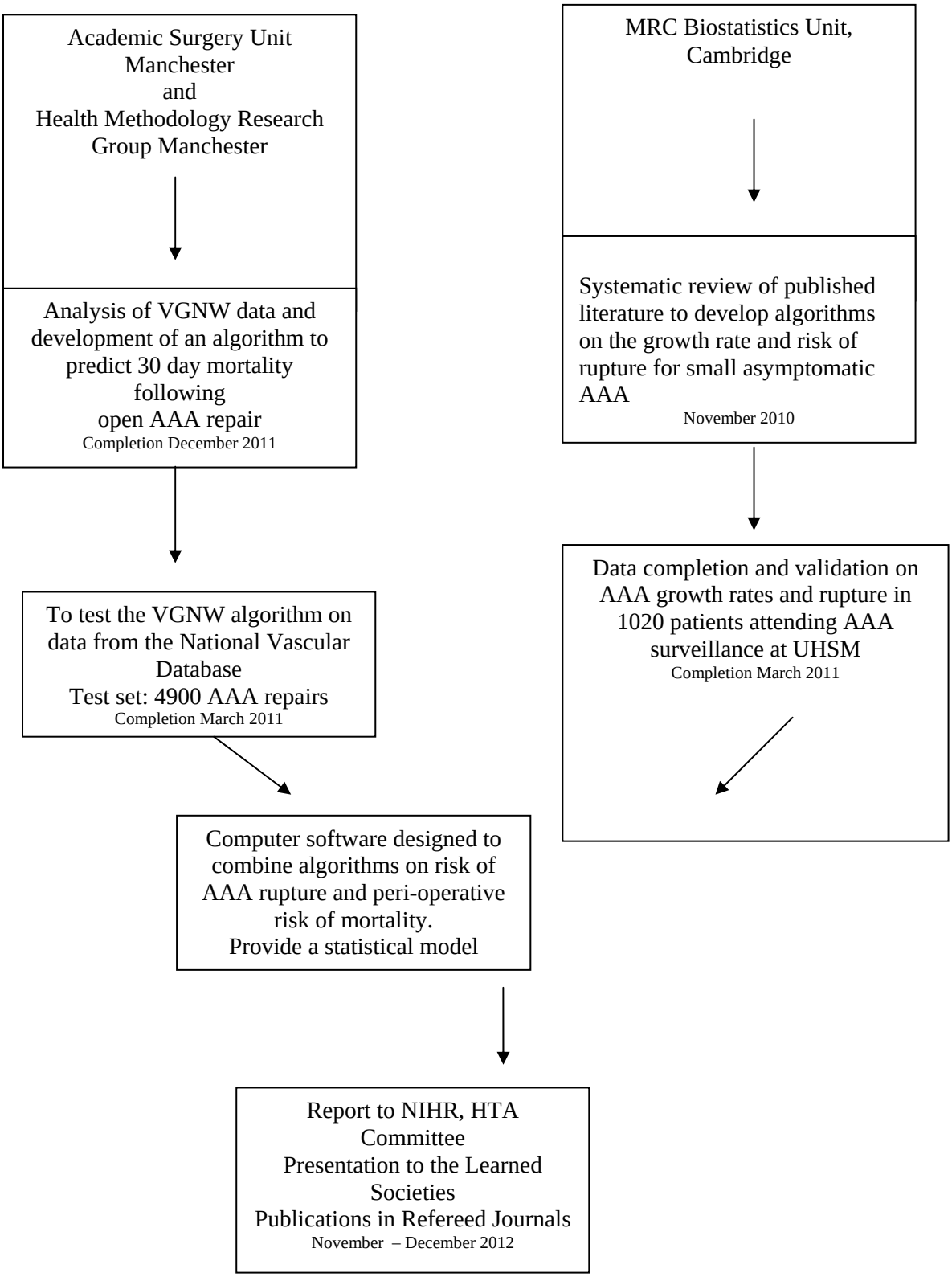
In the future we plan that the group contribute to the design of our database on quality of life in patients continuing AAA surveillance and following either EVAR or open AAA repair. The Chairman of the AAA Service User Group, Mr Claydon, will attend our monthly Management Committee meetings.

6. Dissemination of results

The results of this research will be sent as interim reports to NIHR HTA at six monthly intervals. On completion in December 2012 they will be presented at relevant national and international learned societies (The Vascular Society and Association of Surgeons in the UK and Vascular Surgery meetings internationally). The support of the Vascular Society of Great Britain and Ireland will understandably help in the rapid dissemination of the results and adoption of our conclusions. They will be published in appropriate refereed journals and disseminated to relevant Strategic Health Authorities, the Department of Health and to the National Institute of Clinical Excellence.

7. Flow Diagram

To Develop an Algorithm to Calculate for Individual Patients with Abdominal Aortic Aneurysm (AAA) When Repair is Indicated to Improve Survival



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