17 September 2010 (updated 9 November 2011)

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1. Title of the project

Systematic review of the diagnostic accuracy and cost-effectiveness of magnetic resonance spectroscopy and enhanced magnetic resonance imaging techniques in aiding the localisation of prostate abnormalities for biopsy

2. Name of TAR team and project 'lead'

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3. Plain English summary

In the UK prostate cancer is the most common cancer in men and the second most common cause of cancer death in men after lung cancer. Cases are rare in men aged under 50 years, but it becomes more common as they grow older. In its early stages prostate cancer usually develops without any symptoms. However, when a tumour causes the prostate gland to become enlarged or cancer spreads beyond the prostate, a range of symptoms can result, including increased frequency of passing urine, problems starting or stopping passing urine, a painful burning sensation or blood in urine.

Techniques commonly used to diagnose prostate cancer include digital rectal examination (DRE), the prostate specific antigen (PSA) blood test, and trans-rectal ultrasound (TRUS)-guided needle biopsy. Although a DRE and the PSA test collectively are able to identify abnormalities that might indicate prostate cancer, a diagnosis can only be confirmed following a prostate biopsy. However, the PSA test can cause false alarms and give false reassurance (15–30% of men with prostate cancer have normal PSA and even in those patients with abnormal PSA results, 7 of 10 men will not have prostate cancer diagnosed in the next two years). Biopsies also have their limitations because prostate cancers cannot be seen during biopsy procedures (so biopsies may miss at least 20–30% of cancers that are present) and biopsy results may not be reliable, underestimating cancer aggressiveness in more than 20–30% of cases. Current diagnostic methods (DRE, TRUS, PSA) are unable to distinguish non-aggressive disease (requiring careful monitoring) from virulent prostate cancer (requiring definitive treatment).

Magnetic resonance imaging (MRI) can be used to assess what stage the prostate cancer is at and in helping to decide whether an operation is needed. MRI relies on identifying tissue changes within the prostate to diagnose the presence and extent of cancer. However, these changes often do not accurately reveal whether cancer is present or its size. MRI can be performed with add-ons including three-dimensional magnetic resonance spectroscopy (MRS), dynamic contrast enhanced MRI (DCE-MRI) and diffusion weighted MRI (DW-MRI). DCE-MRI is sensitive to differences in the amount of blood and the permeability of blood vessels that can be associated with the development of tumours and is performed by obtaining a sequence of images before, during and following the injection of a contrast agent. DW-MRI measures the diffusion of water molecules in tissue and may help to distinguish between cancerous and normal prostate tissue. MRS measures the level of certain chemicals in the prostate. The concentration of these chemicals may be altered in the presence of prostate cancer, and hence this technique may be helpful in identifying this type of cancer.

Many men find themselves with the dilemma of having a raised PSA level and a negative prostate biopsy, and the best way to manage these patients remains uncertain. Sometimes these men undergo many repeated, blind biopsies which can be painful and may provide little additional yield. DCE-MRI, DW-MRI and MRS may be able to provide better information on tumour location, size and aggressiveness. These techniques may also be able to help identify cases where undertaking invasive biopsy may be avoided because the tumours are small, or not aggressive.

This review will assess the diagnostic accuracy of MRS, DCE-MRI and DW-MRI and the clinical effectiveness and cost-effectiveness of strategies involving their use in men with suspected prostate cancer and elevated PSA but previously negative biopsy.

The analysis will also focus on the impact that MRS, DCE-MRI and DW-MRI have for diagnosis, and what the overall impact of introducing these techniques would be on NHS services and patient morbidity and mortality. Cost-effectiveness will be assessed from the perspective of the NHS and personal social services.

Information on the diagnostic accuracy and population subgroups for which the technique is most clinically effective will be derived by systematically reviewing relevant studies. Information on cost-effectiveness will be derived from an economic model which will be developed and which will use the findings of the diagnostic accuracy review to help provide estimates of the relative cost-effectiveness of diagnostic strategies that involve MRS, DCE-MRI or DW-MRI.

4. Decision problem

In the UK prostate cancer is the most common cancer in men and the second most common cause of cancer death in men after lung cancer.[1] Each year around 35,000 men in the UK are diagnosed with prostate cancer and more than 10,000 die from it.[1] The 5-year survival rate is around 77%.[2] Cases are rare in men aged under 50 years, but it becomes more common as they grow older, and almost 60% of cases

are diagnosed in men aged over 70 years.[1] There is evidence of a higher incidence of prostate cancer in men of African or Caribbean origin.[3]

The prostate is located in the pelvis and in a normal young adult male the gland is approximately 3 cm long and weighs around 20 grams.[4] In its early stages prostate cancer usually develops without exhibiting any symptoms. However when a tumour causes the prostate gland to enlarge to a significant degree, or cancer spreads to areas beyond the prostate, a range of symptoms can result, including increased frequency of urination, problems starting or stopping urination, a painful burning sensation or blood in urine.[5]

Four procedures are commonly used to diagnose prostate cancer: digital rectal examination (DRE), the prostate specific antigen (PSA) blood test, trans-rectal ultrasound (TRUS) and needle biopsy.[6] PSA is a protein produced by cells of the prostate gland, and the test measures the level of PSA in the blood. The PSA test is specific to the prostate but not to prostate cancer, and so serum levels may be elevated in the presence of benign prostatic hyperplasia, prostatitis and other non-malignant conditions. TRUS has two potential roles in the diagnosis of prostate cancer: to identify lesions suspected of malignancy (done rarely as the majority of prostate cancers are not visible by TRUS) and to improve the accuracy of prostate biopsy.[7] TRUS is a blind procedure that involves the clinician taking 10–12 biopsies in a manner that attempts to obtain representative tissue within the peripheral zone of the prostate. However, TRUS has limitations in that several parts of the gland are not well sampled using this approach. The anterior part of the gland may be missed as a result of its greater distance from the rectum, tissue in the midline may be missed due to efforts to avoid the urethra, while the apex of the prostate is often inaccessible by the transrectal route. Collectively a DRE and the PSA test are able to identify abnormalities that could be indicators of prostate cancer. However, neither test is conclusive and a diagnosis can only be confirmed following the examination of cells taken from a biopsy of prostate tissue. The aim of prostate biopsy is to detect those prostate cancers with the potential for causing harm. It has been estimated that, of asymptomatic men in whom prostate cancer is detected by prostate biopsy following PSA measurement, around 50% do not require active treatment.(NICE guideline prostate cancer) The use of these tests in the diagnosis of prostate cancer has led to many thousands more patients being identified at increasingly younger ages and earlier (and therefore potentially treatable) stages of disease than occurred previously.[8]

The stage of prostate cancer is classified using the TNM classification of malignant tumours criteria.[9] This describes the extent of the primary tumour (T stage), the absence or presence of spread to nearby lymph nodes (N stage) and the absence or presence of metastasis (M stage). The most commonly used system for grading prostate cancer is the Gleason sum score. The system describes a score between 2 and 10, with 2 being the least aggressive and 10 being the most aggressive,[10] although most pathologists now group scores $1 \leq 6$ as Gleason 6.[11]

Magnetic resonance imaging (MRI) can be used in the local staging of prostate cancer and has acquired a role in pre-operative assessment.[12] Conventional MRI of the prostate relies on abnormal signal intensities that result from morphologic changes within the prostate to define the presence and extent of cancer. However, these changes often do not accurately reflect the presence and extent of active tumour.[13] MRI can be performed with add-ons including three-dimensional magnetic resonance spectroscopy (MRS), dynamic contrast enhanced MRI (DCE-MRI) and diffusion weighted MRI (DW-MRI) in a multifunctional examination that may provide more specific information relating to tumour location, size and aggressiveness. DCE-MRI is sensitive to differences in blood volume and vascular permeability that can be associated with tumour related development of new blood vessels and is performed by obtaining sequential magnetic resonance images before, during and following the injection of a contrast agent.[14] DW-MRI measures the diffusion of water molecules in tissue and may help differentiate between malignant and benign prostatic tissue on the basis of lower apparent diffusion coefficient (ADC) values of prostate cancer compared with normal prostate tissue.[15] MRS measures the level of specific chemicals (including choline, creatine, and citrate) in the targeted tissue. The concentration of these chemicals may be altered in the presence of prostate cancer and this phenomenon may be exploited to identify areas of

tumour activity. MRS may also potentially have a role to play in assessing the aggressiveness of any tumour activity identified.

The management of localised prostate cancer depends on the TNM stage of the disease as well as the PSA level, Gleason score, personal preferences of the patients, their physicians, and other available expertise, equipment and resources. The treatment options for men with localised prostate cancer are: watchful waiting, active surveillance, radical prostatectomy, radical external beam radiotherapy (EBRT), radical brachytherapy, high intensity focused ultrasound (HIFU) and cryotherapy. Treatment of men with localised prostate cancer may be associated with a wide range of significant adverse effects. Adverse effects that are common, long-lasting and that may seriously affect quality of life include rectal problems, sexual dysfunction and urinary incontinence.[16]

Many men find themselves with the dilemma of having an elevated PSA level and a prostatic biopsy with negative findings, and the best way to manage these patients remains uncertain.[17] These men may have enlarged central prostate glands due to benign prostatic hyperplasia, which present sampling problems for TRUS-guided biopsies, or they may have cancer present in locations that are difficult to biopsy.[18] A negative biopsy or biopsies for a persistently raised PSA may have two possible explanations, either a missed cancer (for example through sampling error) or there is no cancer (PSA false positive). The use of MRS and enhanced MRI techniques may help to differentiate between these two situations, thereby avoiding unnecessary further biopsies in the false positives, while at the same time expediting the diagnosis of those men with cancers which are otherwise difficult to diagnose.

Both the National Institute for Health and Clinical Excellence (NICE) and the European Association of Urology (EAU) have issued guidelines on prostate cancer, including diagnosis and staging.[6,7] The NICE guideline states that imaging is not routinely recommended for men in whom no radical treatment is intended. MRS is not recommended for men with prostate cancer except in the context of a clinical trial.[6]

The EAU guidelines state in relation to MRI and MRS for staging prostate cancer:

- Local staging (T-staging of) prostate cancer is based on findings from DRE and possibly MRI.
- In comparison with DRE, TRUS, and CT, MRI demonstrates higher accuracy for the assessment of uni- or bilobar disease (T2), extracapsular extension and seminal vesicle invasion (T3), as well as the invasion of adjacent structures (T4).
- The addition of DCE-MRI can be helpful in equivocal cases.
- The addition of MRS to MRI also increases accuracy and decreases inter-observer variability in the evaluation of extracapsular extension.[7]

This review will assess the diagnostic accuracy of MRS, DCE-MRI and DW-MRI and the clinical effectiveness and cost-effectiveness of strategies involving their use in men with suspected prostate cancer and elevated PSA but previously negative biopsy.

Subsidiary questions to be addressed relating to these techniques include:

- In which patient group are they most clinically effective?
- Can they identify cases where prostate cancer is present but further procedures are unnecessary?
- Does their use lead to changes in patient management?

5. Report methods for synthesis of evidence of clinical effectiveness

Systematic review. A systematic review of the evidence for the diagnostic accuracy of MRS, DCE-MRI and DW-MRI techniques in aiding the localisation of prostate abnormalities for biopsy will be undertaken

following the general principles of the Centre for Reviews and Dissemination (CRD) guidance for undertaking reviews in health care[19] and reported in accordance with the PRISMA statement.[20]

5.1 Population

The population considered will be men with suspected prostate cancer and elevated prostate specific antigen (PSA) up to 20 ng/ml but previously negative biopsy.

The setting is secondary or tertiary care.

5.2 Index tests

The following tests will be considered, alone or in combination:

- Magnetic resonance spectroscopy (MRS) guided biopsy;
- Dynamic contrast enhanced MRI (DCE-MRI) guided biopsy; and
- Diffusion weighted MRI (DW-MRI) guided biopsy.

If sufficient data are available we may undertake sensitivity analysis around when the studies took place, to assess the effects of changes in the technology over time. For example, for MRS, given sufficient data we will consider the different approaches used, including single voxel and 3D-MRSI (chemical shift imaging).

5.3 Comparator tests

The comparator tests considered will be:

- Standard (T2-weighted) MRI;
- Transrectal ultrasound guided prostate biopsy.

5.4 Reference standard

The reference standard considered will be histopathological assessment of biopsied tissue. Tissue samples may be obtained by transrectal needle biopsy, saturation biopsy, transperineal template biopsy or from prostatectomy specimens.

We will incorporate a follow-up time of 12 months as part of the reference standard, to help distinguish between tumours missed by the index/comparator tests (subsequently detected within this 12 month period) and interval tumours that were not missed (and are subsequently detected after the 12-month follow-up time for histology).

5.5 Outcomes

Included studies must report relevant and interpretable data.

The following outcomes will be considered:

- Diagnostic performance of MRS, DCE-MRI and DW-MRI in the localisation of abnormalities of the prostate.

In studies reporting the above outcome, the following outcomes will also be recorded, if reported:

- Altered treatment as a result of the tests;
- Acceptability of the tests;
- Interpretability of the tests;
- Effect of testing on quality of life (disease-specific and generic instruments);
- Adverse effects of testing.

Studies reporting test performance must report the absolute numbers of true positives, false positives, false negatives and true negatives, or provide information allowing their calculation, and report a per-patient analysis.

5.6 Search strategy

Extensive sensitive electronic searches will be conducted to identify reports of published and ongoing studies on the diagnostic accuracy and cost-effectiveness of MRS, DCE-MRI and DW-MRI techniques in aiding the localisation of prostate abnormalities for biopsy. Highly sensitive search strategies will be designed, including appropriate subject headings and text word terms, interventions under consideration and included study designs. Searches will be restricted to years from 1995 onwards, reflecting the introduction of these techniques for the evaluation of prostate cancer, and restricted to the English language. A draft MEDLINE search is reproduced in *Appendix 1*. Databases to be searched will include MEDLINE, MEDLINE in process, Embase, Science Citation Index, Biosis and the Cochrane Controlled Trials Register. Reports of relevant evidence syntheses will also be sought from the Cochrane Database of Systematic Reviews (CDSR), Database of Abstracts of Review of Effects (DARE), the HTA Database and MEDION.

Conference abstracts for the years 2006 onwards from meetings of the European, American and British Urological Associations will be searched. Ongoing studies will be identified through searching the WHO International Clinical Trials Registry, Current Controlled Trials, Clinical Trials, NIHR Portfolio and NIH National Cancer Institute database. Full text searching of key urology journals will also be undertaken. Websites of manufacturers, professional organisations, regulatory bodies and the HTA agencies will be checked to identify unpublished reports.

Reference lists of all included studies will be scanned in order to identify additional potentially relevant reports. We will also ask our clinical advisers to provide details of any additional potentially relevant reports that they are aware of.

5.7 Inclusion criteria

For diagnostic accuracy of MRS, DCE-MRI and DW-MRI the following types of studies will be included:

- Direct (head-to-head) studies in which index test(s), comparator test(s) and reference standard test are done independently in the same group of people.
- Randomised controlled trials (RCTs) in which people are randomised to the index and comparator test(s) and all receive the reference standard test.

If there is insufficient evidence from direct and randomised studies, we will consider indirect (between-study) comparisons by meta-analysing studies that compare each single test or combination of tests with the reference standard test, and making comparisons between meta-analyses of the different tests. However, this type of study design is less reliable than direct studies as differences in diagnostic accuracy are susceptible to confounding factors between studies. The following types of studies will be considered:

- Observational studies, including case series, in which the sample is created by identifying all people presenting at the point of testing (without any reference to the test results).
- Case-control studies in which two groups are created, one known to have the target disease and one known not to have the target disease, where it is reasonable for all included to go through the tests. We may exclude case-control studies comparing severely diseased people with very healthy controls or studies excluding people with other urological disease such that the spectrum of disease and non-disease is unlike that to be encountered in a diagnostic situation.

If the number of studies meeting our inclusion criteria is sufficiently large, we may limit them by type of study design and taking into account the importance of other factors such as study size.

5.8 Exclusion criteria

The following types of report will be excluded:

- Reviews, editorials and opinions;
- Case reports;
- Reports investigating technical aspects of a test;
- Non-English-language reports.

5.9 Data extraction strategy

One reviewer will screen the titles (and abstracts if available) of all reports identified by the search strategy. Full text copies of all studies deemed to be potentially relevant will be obtained and two reviewers will independently assess them for inclusion. Any disagreements will be resolved by consensus or arbitration by a third party.

A data extraction form will be developed and piloted. Two reviewers will independently extract details from full text studies of study design, participants, index, comparator and reference standard tests and outcome data. Any disagreements will be resolved by consensus or arbitration by a third party.

5.10 Quality assessment strategy

Two reviewers will independently assess the quality of all included diagnostic studies using the quality assessment of diagnostic accuracy studies (QUADAS) checklist. The QUADAS checklist was developed for use in systematic reviews of diagnostic studies[21] and is designed to be adapted to make it more applicable to a specific review topic. QUADAS was developed through a formal consensus method and was based on empirical evidence. The QUADAS tool will be adapted to make it more applicable to assessing the quality of studies of tests for detecting prostate cancer.

Two reviewers will independently assess the quality of any diagnostic studies reporting additional effectiveness outcomes (see section 5.5 above) using one of two separate checklists depending on study design. A 14-question checklist will be used to assess the quality of RCTs. An 18-question checklist will be used to assess non-randomised comparative studies, with the same checklist minus four questions used to assess the methodological quality of case series. The checklist for RCTs was adapted from Verhagen *et al.*[22] and the checklist for non-randomised studies and case series was adapted from several sources, including the Centre for Reviews and Dissemination's guidance for undertaking reviews in health care[19] Verhagen *et al.*,[22] Downs and Black[23] and the Generic Appraisal Tool for Epidemiology (GATE).[24] Both checklists were developed through the Review Body for Interventional Procedures (ReBIP). ReBIP is a joint venture between the Health Services Research Unit, University of Aberdeen and Health Services Research at Sheffield University and works under the auspices of the National Institute for Health and Clinical Excellence (NICE) Interventional Procedures programme. The tools rate bias and generalisability, sample definition and selection, description of the intervention, outcome assessment, adequacy of follow up and performance of the analysis.

For both the QUADAS and ReBIP checklists, each question is worded so that a rating of 'Yes' is always optimal in terms of methodological quality. Any disagreements will be resolved by consensus or arbitration by a third party.

5.11 Methods of analysis/synthesis

The results of the individual diagnostic studies will be tabulated and sensitivity, specificity, positive and negative predictive values, positive and negative likelihood ratios and diagnostic odds ratios (DORs) calculated. If reported in a given study, a separate 2×2 table will be derived for patient-level and prostate site-level analyses.

Summary receiver operating characteristic (SROC) curves will be produced for each test where three or more diagnostic studies report sufficient data in RevMan 5. Where studies report 2×2 data for a number

of different cutoff values then the most frequently used cutoff value across studies will be chosen. Meta-analysis models will be fitted using the hierarchical summary receiver operating characteristic (HSROC) model[25] in SAS 9.1. A symmetric SROC model will be used. This model takes proper account of the diseased and non-diseased sample sizes in each study, and allows estimation of random effects for the threshold and accuracy effects. Summary sensitivity, specificity, positive and negative likelihood ratios and diagnostic odds ratios (DORs) for each model will be reported as point estimate and 95% confidence interval (CI).

Sensitivity and specificity will be pooled using the weighted average method[26] if numerical difficulties are encountered with the HSROC model and there is no evidence of a threshold effect. Pooled likelihood ratios and DOR will be calculated using the DerSimonian and Laird random effects method.[27] Where a study has an empty cell, a correction of 0.5 will be added to all four cells. These analyses will be carried out using Metadisc software.[28] Heterogeneity will be assessed using the I^2 statistic, which describes the percentage of the variability in effect estimates that is due to heterogeneity rather than sampling error. A value greater than 50% may be considered to represent substantial heterogeneity.[29] Where data permit we will explore heterogeneity amongst parameter estimates on a variety of characteristics of the primary studies, e.g. PSA threshold.

For additional non-diagnostic outcomes reported (see section 5.5 above), where appropriate, meta-analysis will be employed to estimate a summary measure of effect. Dichotomous outcome data will be combined using the Mantel-Haenszel relative risk (RR) method and continuous outcomes will be combined using the inverse-variance weighted mean difference (WMD) method. For the estimates of RR and WMD 95% CIs and p-values will be calculated. The results will be reported using a fixed-effect model. Chi-squared tests and I-squared statistics will be used to explore statistical heterogeneity across studies. Possible reasons for heterogeneity will be explored using sensitivity analysis. Where there is no obvious reason for heterogeneity, the implications will be explored using a random-effects model. Where a quantitative synthesis is considered to be inappropriate or not feasible, a narrative synthesis of results will be provided.

6. Report methods for synthesising evidence of cost-effectiveness

The economic objectives are:

- To estimate the costs of standard practice (i.e. transrectal ultrasound-guided biopsy) and alternative guided biopsies in the form of MRS, DCE-MRI and DW-MRI techniques in the diagnosis of prostate abnormalities.
- To estimate the cost-effectiveness of MRS, DCE-MRI and DW-MRI in comparison to standard practice in men with suspected prostate cancer.

An economic model will be developed using data from the literature and expert opinion. The model will be populated using results of the systematic review, other focused reviews for key parameters (e.g. utilities) and if necessary study specific estimates (e.g. for some costs). Bibliographic databases that will be searched include MEDLINE, MEDLINE in process, Embase, Science Citation Index, Health Management Information Consortium (HMIC), NIHR Economic Evaluations Database (NEED) and the HTA database. Using this and other routine information such as the cost of treatment, the effectiveness and cost-effectiveness of alternative methods of diagnosis of prostate cancer will be modelled.

6.1 Economic modelling using the results of the systematic reviews to determine the effectiveness and cost-utility of different options

Diagnostic techniques and any subsequent treatment need not only to be effective but also cost-effective. The proposed research will evaluate, using Markov modelling methods, the clinical effectiveness and cost-effectiveness of various diagnostic technologies to aid the localisation of prostate abnormalities

for biopsy. The economic model will describe the pathway of individuals from the point where a choice exists about the form of biopsy that a patient might receive. It will cover the period of diagnosis using the biopsy, subsequent treatment/management and the consequences during that time period. The structure of the model will be based upon detailed care pathways. To formulate the care pathways we will see how previous economic models in this area have been modelled, and recommendations from current clinical guidelines. We will also seek advice from clinical experts involved in this study to identify pathways for all of the options to be included in the economic model.

The economic model represents a further level of evidence synthesis that will integrate information on the relative effectiveness of diagnostic techniques derived from the systematic review along with information on natural history, costs, and utilities of diagnosing and treating prostate cancer. The economic model will compare the alternative diagnostic techniques for a hypothetical cohort of men with suspected prostate cancer or elevated prostate specific antigen. This cohort will reflect the average population of men presenting with these abnormalities. The time horizon of the model will be the patient's lifetime although shorter time horizons will be explored in a sensitivity analysis.

Data on the resource use and costs incurred for the different diagnostic options and their consequences will be derived from consultation with experts, published literature, including of the existing published economic evidence, manufacturers and other suppliers and other routine sources e.g. NHS reference costs. As noted above, study specific costs will be generated if suitable data from other sources are not available and research resources permit. One area we will investigate is the impact of procedure time of the different MRI techniques and whether any differences in procedure time are reflected in existing cost data or whether we need to devise study specific costs to reflect differences in procedure time. The primary perspective of costs will be the NHS and PSS. Cost data will include the direct health service costs associated with each diagnostic option, treatment and subsequent patient management.

Data on utilities associated with prostate cancer and the possible differences in quality of life of the different options will be derived from the published literature, including a structured review of economic evaluations as well as a search of the CEA Registry.[30]

The results of the model will be presented in terms of a cost-consequence analysis (e.g. costs, number of cases detected, etc). Results will also be presented as incremental cost per quality adjusted life-year gained (QALY). The modelling exercise will use a net benefit framework to combine cost and benefit estimates. The results of the analysis will be presented as point estimates of mean incremental costs, effects, and for any cost utility analysis, incremental cost per QALY. Sensitivity analysis will be used to address parameter and other forms of uncertainty. Cost per QALY data will be presented in terms of cost and effect plots and cost-effective acceptability curves (CEACs).

7. Expertise in this TAR team

The TAR team are experienced in conducting reviews of this nature in both the clinical and technical aspects required to address the commissioning brief. Graham Mowatt, Luke Vale and Cynthia Fraser have been involved in a number of similar studies and the remaining TAR team members are also familiar with and experienced in systematic reviews and economic modelling.

7.1 TAR centre

The Aberdeen Technology Assessment Group has a track record of producing these types of focused reports whilst keeping to tight timescales for various policy customers such as the National Institute for Health and Clinical Excellence (NICE), the National Screening Committee and the NHS R&D HTA programme. In recent years the following similar types of systematic reviews have been completed:

- Screening for open angle glaucoma;
- 64-slice computed tomography angiography as an alternative to invasive coronary angiography in the investigation of coronary artery disease;
- Detection and treatment of staphylococcus aureus infection for patients on peritoneal dialysis for end stage renal disease;
- Rapid point of care tests for the detection of genital Chlamydia;
- Photodynamic diagnosis, urine biomarkers and cytology for the detection and follow-up of bladder cancer.

7.2 Team members' contributions

Pawana Sharma, Research Fellow, will be technical lead on this project and will be responsible for the day-to-day running of the review, as well as undertaking the reviews of test performance and effectiveness, and will be supervised by Graham Mowatt, Senior Research Fellow. Graham Scotland, Research Fellow, Health Economics Research Unit will undertake the economic evaluation. Cynthia Fraser, Information Officer, will develop and run the search strategies and will be responsible for obtaining papers and reference management. Charles Boachie, Statistician, will provide statistical advice and support. Thomas Lam, Specialist Registrar, Department of Urology, Aberdeen Royal Infirmary, Justine Royle, Consultant Urologist, Department of Urology, Aberdeen Royal Infirmary, Lutfi Kurban, Consultant Radiologist and Honorary Senior Lecturer, Department of Radiology, University of Aberdeen, Anwar Padhani, Consultant Radiologist and Head of Imaging Research, Mount Vernon Cancer Centre, Northwood, Middlesex, and Tom Scheenen, MR Physicist, Department of Radiology, Radboud University, Nijmegen Medical Center, Netherlands, will provide clinical support and advice to the team.

8. Competing interests of authors

None.

9. Timetable/milestones

2011:

November–December Develop care pathways, screening, data extraction and quality assessment forms, develop and run searches, assess studies for inclusion, start to develop economic model.

2012:

January–February Data extraction and quality assessment, develop economic model.

March–April Data analysis, develop economic model.

May–July Prepare draft report.

End July Submit report.

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Appendix 1: Draft MEDLINE search strategy

1. exp Diffusion Magnetic Resonance Imaging/
2. Magnetic Resonance Imaging/mt [Methods]
3. magnetic resonance spectroscop$.tw. 1
4. dce-mri.tw.
5. (dynamic contrast enhanced adj3 (MRI or magnetic)).tw.
6. dw-mri.tw.
7. (diffusion weight$ adj3 (MRI or magnetic)).tw.

8. or/1-7 6
9. Prostate-Specific Antigen/
10. Prostatic Neoplasms/
11. psa.tw.
12. (prostat$ adj3 (cancer or carcinoma$ or neoplasm$ or malignan$)).tw.
13. or/9-12
14. 8 and 13
15. "sensitivity and specificity"/
16. roc curve/
17. predictive value of tests/
18. false positive reactions/
19. false negative reactions/
20. du.fs. use mesz
21. sensitivity.tw.
22. distinguish$.tw.
23. differentiat$.tw.
24. identif$.tw.
25. detect$.tw.
26. diagnos$.tw.
27. (predictive adj4 value$).tw
28. accura$.tw.
29. comparison.tw.
30. or/15-29
31. 14 and 30
32. limit 31 to english language
33. limit 32 to yr = "1995 -Current"