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Optimising the Diagnosis of Prostate Cancer in the Era of Multiparametric Magnetic Resonance Imaging: A Cost-effectiveness Analysis Based on the Prostate MR Imaging Study (PROMIS)

Rita Faria [a,*], *Marta O. Soares* [a], *Eldon Spackman* [b], *Hashim U. Ahmed* [c,g], *Louise C. Brown* [d,**], *Richard Kaplan* [d], *Mark Emberton* [e,f], *Mark J. Sculpher* [a]

[a] *Centre for Health Economics, University of York, York, UK;* [b] *University of Calgary, Alberta, Canada;* [c] *Imperial Urology—Division of Surgery, Imperial College London, London, UK;* [d] *Medical Research Council Clinical Trials Unit at University College London, London, UK;* [e] *Division of Surgery and Interventional Science, Faculty of Medical Sciences, University College London, London, UK;* [f] *Department of Urology, University College London Hospitals NHS Foundation Trust, London, UK;* [g] *Imperial Urology, Imperial College Healthcare NHS Trust*

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Abstract

Background: The current recommendation of using transrectal ultrasound-guided biopsy (TRUSB) to diagnose prostate cancer misses clinically significant (CS) cancers. More sensitive biopsies (eg, template prostate mapping biopsy [TPMB]) are too resource intensive for routine use, and there is little evidence on multiparametric magnetic resonance imaging (MPMRI).
Objective: To identify the most effective and cost-effective way of using these tests to detect CS prostate cancer.
Design, setting, and participants: Cost-effectiveness modelling of health outcomes and costs of men referred to secondary care with a suspicion of prostate cancer prior to any biopsy in the UK National Health Service using information from the diagnostic Prostate MR Imaging Study (PROMIS).
Intervention: Combinations of MPMRI, TRUSB, and TPMB, using different definitions and diagnostic cut-offs for CS cancer.
Outcome measurements and statistical analysis: Strategies that detect the most CS cancers given testing costs, and incremental cost-effectiveness ratios (ICERs) in quality-adjusted life years (QALYs) given long-term costs.
Results and limitations: The use of MPMRI first and then up to two MRI-targeted TRUSBs detects more CS cancers per pound spent than a strategy using TRUSB first (sensitivity = 0.95 [95% confidence interval {CI} 0.92–0.98] vs 0.91 [95% CI 0.86–0.94]) and is cost effective (ICER = £7,076 [€8350/QALY gained]). The limitations stem from the evidence base in the accuracy of MRI-targeted biopsy and the long-term outcomes of men with CS prostate cancer.
Conclusions: An MPMRI-first strategy is effective and cost effective for the diagnosis of CS prostate cancer. These findings are sensitive to the test costs, sensitivity of MRI-targeted TRUSB, and long-term outcomes of men with cancer, which warrant more empirical research. This analysis can inform the development of clinical guidelines.

* Corresponding author. Centre for Health Economics, University of York, Heslington, York YO10 5DD, UK. Tel. +44 (0)1904 32 14 35; Fax: +44 1904 321402.
E-mail address: rita.nevesdefaria@york.ac.uk (R. Faria).
** Corresponding author.
E-mail address: l.brown@ucl.ac.uk (L.C. Brown).

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Patient summary: We found that, under certain assumptions, the use of multiparametric magnetic resonance imaging first and then up to two transrectal ultrasound-guided biopsy is better than the current clinical standard and is good value for money.

1. Introduction

Multiparametric magnetic resonance imaging (MPMRI) is increasingly being recommended for the diagnosis of clinically significant (CS) prostate cancer, if the initial biopsy proves negative [1,2]. An alternative approach is to begin with MPMRI imaging to inform who needs a biopsy and, in those who need it, how it might be best conducted [3]. Recent studies have reported encouraging results on the performance of MPMRI in detecting CS prostate cancer [3–5]. The Prostate MR Imaging Study (PROMIS) was the largest accuracy study on the use of MPMRI and transrectal ultrasound-guided biopsy (TRUSB) in the diagnosis of prostate cancer [4]. Using template mapping biopsy (TPMB) as the reference standard, it was found that MPMRI had better sensitivity for CS prostate cancer compared with TRUSB but worse specificity [4]. It is therefore necessary to explore how best to combine these tests and the consequences of incorrect diagnosis on health outcomes. This study aims to identify the combinations of tests—diagnostic strategies—that detect the most CS cancers per pound spent in testing and achieve the maximum health given their cost to the healthcare service.

2. Patients and methods

The target population was men at risk of prostate cancer referred to secondary care for further investigation [4,6]. The perspective was the UK National Health Service (NHS). Costs were expressed in pound sterling from a 2015 price base. The time horizon is the population's predicted lifetime. Costs incurred and health outcomes attained in the future were discounted to present values at 3.5% per annum [7].

2.1. Diagnostic strategies

The diagnostic strategies consisted of clinically feasible combinations of MPMRI, TRUSB, and TPMB, in addition to the use of TRUSB and TPMB in isolation (Table 1; details in the Supplementary material, section 1.1). These included strategies using MPMRI to decide whether a TRUSB or TPMB is necessary and target the TRUSB, and strategies starting with TRUSB and using MPMRI to decide whether a repeat biopsy is warranted. A diagnosis of CS cancer requires a biopsy, hence strategies were defined to always end with a confirmatory biopsy. Within each test combination, there are alternative ways each test can be used, following the definitions used in PROMIS (see Tables 2 and 3). Each of the 32 test combinations were tested for the alternative classifications and cut-offs, returning a total of 383 strategies.

2.2. Model structure

The model had a diagnosis and a long-term component (Supplementary Fig. 1). For diagnosis, a decision tree combined the information on diagnostic accuracy of the tests to determine the accuracy of the test combinations (Fig. 1). The long-term outcome component calculated the long-term health outcomes and costs of men with CS cancer, non-CS cancer, and no cancer, by whether they were correctly diagnosed or missed. Their diagnosis determined their clinical management, as either immediate radical treatment if CS cancer is diagnosed or surveillance if not. The long-term outcome component was a cohort Markov, with two health states for men with no cancer (alive and dead) and three states for men with cancer: localised cancer, metastatic cancer, and death. The decision model was developed in Microsoft Excel.

2.3. Diagnostic performance

The model explicitly reflects the sensitivity and specificity of TRUSB and MPMRI in detecting prostate cancer. Tables 2 and 3 show the diagnostic performance of the tests, calculated from the individual level data collected in the PROMIS [4] (details in the Supplementary material, section 2). The men's true disease status was classified in four subgroups, according to the TPMB results and their serum prostate-specific antigen (PSA) level [1]:

1. No cancer
2. Low risk: PSA ≤10 ng/ml and Gleason score ≤6, who should be classified as having non-CS cancer
3.

Table 1 – Diagnostic strategies

Test	Strategies
MPMRI	
First test	M1–M7; N1–N7
Second test after TRUSB	T5–T9; P5–P9
TRUSB	
First test	T1–T9; P2–P9
Repeat TRUSB in men with no cancer detected	T2, T4
Repeat TRUSB in men with non-CS cancer detected	T3, T4
Second test after MPMRI: MRI-targeted TRUSB, in men with lesions visible at the MPMRI	M1–M7
Repeat MRI-targeted TRUSB in men with no previous cancer or non-CS cancer at first MRI-targeted TRUSB, but with lesions visible at MRI	M3–M7; T5–T9; N3–N7
TPMB	
First test	P1
Second test	P2–P4; N1–N4
Third test	P5–P9; N3–N7

MPMRI = multiparametric magnetic resonance imaging; TRUSB = transrectal ultrasound-guided biopsy; TPMB = template prostate mapping biopsy; CS = clinically significant. MRI-targeted TRUSB is a TRUSB informed by a prior MPMRI. All TRUSB post-MPMRI are assumed to be MRI-targeted TRUSB. Diagnostic strategies were labelled according to their test combination first (M1–M7, N1–N7, T1–T9, P1–P9), and then their biopsy TRUSB definition (1 or 2), MPMRI definition (1 or 2), and cut-off (2 to 5). T strategies start with TRUSB, M strategies start with MPMRI, P strategies are the same as T strategies, and N strategies are the same as M strategies but have TPMB as the last biopsy. For example, strategy M1 125 refers to test combination M1, in which all men were first assessed using MPMRI definition 2 and cut-off 5 and then followed up with biopsy definition 1 for those with a suspicion of CS cancer. See the Supplementary material, section 1, for full details on the test sequences for each diagnostic strategy.

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