A scoping review protocol for:

The use and analysis of patient-reported outcome measures in randomised controlled trials of the prostate

Version 1.0 (12.07.2021)

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Background

Motivation

Integrating patient reported outcome measures (PROMs) into randomised controlled trials (RCTs) has gained momentum during the past few decades[1]. However, there is little uniformity in the way that these outcomes are handled. Various research groups exist to develop methods of reducing the variation in outcome measures[2] and some have applied this to prostate cancer research[3] but few have then explored how these PROMs are implemented and analysed.

Review question

This scoping review aims to capture (1) which PROMs are being used in prostate research, (2) when they are collected after treatment commencement and (3) how they are then being analysed. The review will focus on statistical analysis techniques used as well as the placement of PROMs in the treatment pathway.

Methods

Data collection

We aim to identify RCT papers, in the PubMed[4] database, that are based on prostate RCTs (e.g. treatments for prostate cancer or lower urinary tract symptoms in men) and include at least one PROM as an outcome. The search for relevant papers is restricted to those published between 1st of January 2011 and 31st December 2020 to capture recent activity, in the use of PROMs, and avoid difficulties in retrieving electronic copies.

The search will be restricted to the top 5 medical journals, the top 5 urology journals and top 5 oncology journals, with highest impact factors in 2015[5], that return at least 1 matching article (Table 1).

Table 1. The journals included, based on impact factors in 2015

InCites Journal Citation Reports (2015)[5], ranked by Impact Factor					
Top "medical" journals	**Ret.**	**Top "urology" journals***	**Ret.**	**Top "oncology" journals**	**Ret.**
New England Journal of Medicine	✓	European Urology	✓	CA-A Cancer Journal for Clinicians	×
The Lancet	✓	Nature Reviews Urology	×	Nature Reviews Cancer	×
Journal of American Medical Association	✓	Journal of Urology	✓	Lancet Oncology	✓
The BMJ	✓	BJU International	✓	Cancer Cell	×
Annals of Internal Medicine	✓	Prostate Cancer and Prostatic Diseases	✓	Journal of Clinical Oncology	✓
		The Prostate	✓	Cancer Discovery	✓
				Nature Reviews Clinical Oncology	×
				Leukemia	×
				Journal of the National Cancer Institute	✓
				Seminars in Cancer Biology	×
				Annals of Oncology	✓

Ret. = Returned at least one matching article from the search, *Within the category Urology & Nephrology

The search will be carried out in PubMed[4] and all articles which match the criteria (Table 2) will be extracted.

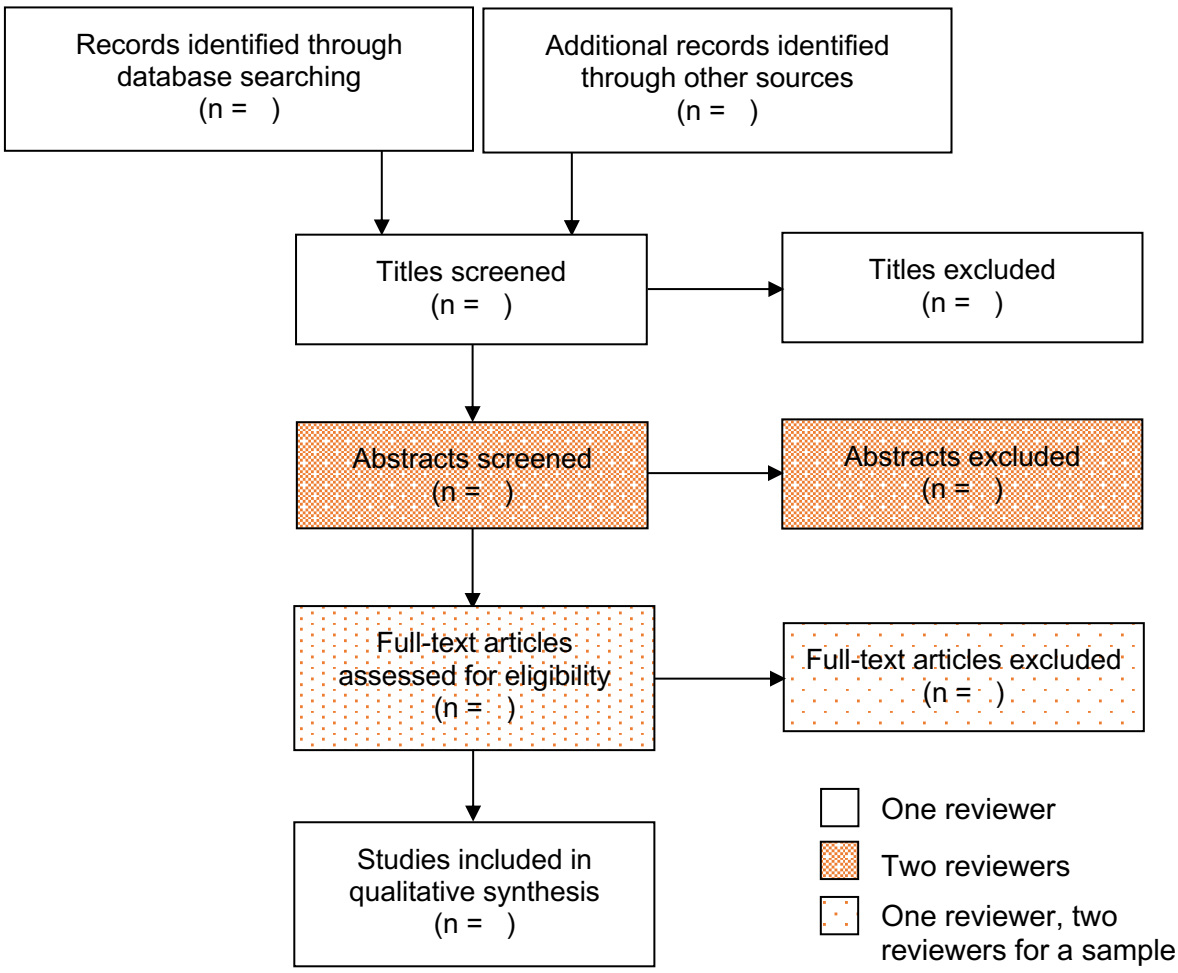
Table 2. The search criteria that will be used for data extraction

Resource (date)	Search terms	Years (incl.)	Papers
PubMed[4] (12/07/21)	((prostat*[Title/Abstract]) OR ((lower urinary tract[Title/Abstract]) AND (men[Title/Abstract]))) AND ((patient-reported[Title/Abstract]) OR (patient reported[Title/Abstract]) OR (quality of life[Title/Abstract]) OR (self-report*[Title/Abstract]) OR (symptom score[Title/Abstract])) AND ((random*[Title/Abstract]) OR (trial[Title/Abstract])) AND (("N Engl J Med"[Journal]) OR ("JAMA"[Journal]) OR ("BMJ"[Journal]) OR ("Lancet"[Journal]) OR ("Annals of internal medicine"[Journal]) OR ("European urology"[Journal]) OR ("The Journal of urology"[Journal]) OR ("BJU international"[Journal]) OR ("Prostate cancer and prostatic diseases"[Journal]) OR ("The Prostate"[Journal]) OR ("The Lancet. Oncology"[Journal]) OR ("Cancer cell"[Journal]) OR ("J Clin Oncol"[Journal]) OR ("Cancer discovery"[Journal]) OR ("Journal of the National Cancer Institute"[Journal]) OR (""annals of oncology official journal of the european society for medical oncology"[Journal])) NOT (review[Publication Type])	≤2000	151
		2001-2010	276
		2011-2020	361
		2021	25

Stages of review

Initially titles will be screened, by the primary researcher, to exclude; protocols, reviews, responses to authors, etc. Abstracts will then be inspected separately, by the primary researcher and an independent reviewer, to exclude any other articles that do not fulfil the inclusion criteria. Full text articles will then be read by the primary researcher to identify the final list of eligible articles. For the first 10 full text reviews, the independent reviewer will also carry out a full text review to ensure that the eligibility criteria is clear and unambiguous. The level of agreement will be reported and the eligibility criteria altered, if required. A proforma, consisting of eligibility criteria will be defined in advance of article extraction.

Stages of review, using the PRISMA flow diagram[6]



Inclusion/exclusion criteria

The inclusion criteria are RCT articles that report PROM findings in men receiving active or placebo/sham treatment, for conditions of the prostate. The minimum number of patients recruited in the trial has to be at least 50 men, randomised to 2-4 arms, in a parallel group design. Where multiple papers have been published, analysing the same dataset, they will all be included at the point of extraction. Longitudinal PROMs are the key items of interest, however, the used of single measure 'static' PROMs will be quantified. Health economic findings, reviews, protocols and methodological papers, including published statistical analysis plans, will be excluded from this extract. However, despite being excluded, they may be referred back to if any of the methodological elements of the main trial results are unclear.

Information collected

The key items, to answer the objectives, are the specific PROM used, where they included it in the treatment pathway and the statistical analysis performed on the PROM. For each article the following items will be identified: the condition which is being treated, the intervention(s) of interest, the number of men, the length of follow up, the specific PROMs used, when they were included in the treatment pathway, whether they were static or transitional and how they were analysed. Analyses will be scrutinised to determine the statistical method used, the handling of missing data, the handling of loss to follow up (e.g. death) and analysis grouping (e.g. intention to treat). If time allows, this review will also assess how adjuvant treatments/therapies were accounted for. There are no plans to carry out a risk of bias review or to carry out a meta-analysis, given that this is a review of trial design and statistical methods, rather than an exhaustive review of a specific outcome. The team aims to publish this review in 2022.

Review team members, their organisation and role in this review

Ms Grace Young, University of Bristol, UK
Primary researcher who will be conducting the review at all stages

Professor Athene Lane, University of Bristol, UK
Overseeing the research; assisting with clinical trial design and PROMs

Mr Hugo Pedder, University of Bristol, UK
Overseeing the research; assisting with the overall review

Ms Eleanor Walsh, University of Bristol, UK
Independent researcher who will be screening the abstracts

Professor Chris Metcalfe, University of Bristol, UK
Overseeing the research; assisting with clinical trial design and statistical techniques

References

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