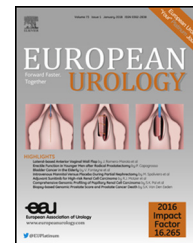


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Platinum Priority – Review – Prostate Cancer

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## Factors Influencing Men's Choice of and Adherence to Active Surveillance for Low-risk Prostate Cancer: A Mixed-method Systematic Review

Netty Kinsella<sup>a,b,\*</sup>, Pär Stattin<sup>c</sup>, Declan Cahill<sup>b</sup>, Christian Brown<sup>d</sup>, Anna Bill-Axelson<sup>c</sup>, Ola Bratt<sup>e</sup>, Sigrid Carlsson<sup>e,f,g,†</sup>, Mieke Van Hemelrijck<sup>a,h,†</sup>

<sup>a</sup> Translational Oncology & Urology Research (TOUR), School of Cancer and Pharmaceutical Sciences, King's College London, London, UK; <sup>b</sup> Department of Urology, The Royal Marsden Hospital, London, UK; <sup>c</sup> Department of Surgical Sciences, Uppsala University, Uppsala, Sweden; <sup>d</sup> Department of Urology, Kings College Hospital, London, UK; <sup>e</sup> Department of Urology, Institute of Clinical Sciences, Sahlgrenska Academy at Gothenburg University, Sweden; <sup>f</sup> Department of Surgery, Memorial Sloan Kettering Cancer Center, New York, NY, USA; <sup>g</sup> Department of Epidemiology and Biostatistics, Memorial Sloan Kettering Cancer Center, New York, NY, USA; <sup>h</sup> Institute of Environmental Medicine, Karolinska Institute, Stockholm, Sweden

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### Abstract

**Context:** Despite support for active surveillance (AS) as a first treatment choice for men with low-risk prostate cancer (PC), this strategy is largely underutilised.

**Objective:** To systematically review barriers and facilitators to selecting and adhering to AS for low-risk PC.

**Evidence acquisition:** We searched PsychINFO, PubMed, Medline 2000–now, Embase, CINAHL, and Cochrane Central databases between 2002 and 2017 using the Preferred Reporting Items for Systematic Review and Meta-analysis (PRISMA) statement. The Purpose, Respondents, Explanation, Findings and Significance (PREFS) and Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) quality criteria were applied. Forty-seven studies were identified.

**Evidence synthesis:** Key themes emerged as factors influencing both choice and adherence to AS: (1) patient and tumour factors (age, comorbidities, knowledge, education, socioeconomic status, family history, grade, tumour volume, and fear of progression/side effects); (2) family and social support; (3) provider (speciality, communication, and attitudes); (4) healthcare organisation (geography and type of practice); and (5) health policy (guidelines, year, and awareness).

**Conclusions:** Many factors influence men's choice and adherence to AS on multiple levels. It is important to learn from the experience of other chronic health conditions as well as from institutions/countries that are making significant headway in appropriately recruiting men to AS protocols, through standardised patient information, clinician education, and nationally agreed guidelines, to ultimately decrease heterogeneity in AS practice.

**Patient summary:** We reviewed the scientific literature for factors affecting men's choice and adherence to active surveillance (AS) for low-risk prostate cancer. Our findings suggest that the use of AS could be increased by addressing a variety of factors such as information, psychosocial support, clinician education, and standardised guidelines.

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† Both authors contributed equally as senior authors.

\* Corresponding author. Translational Oncology & Urology Research, Kings College London, Guy's Hospital, 3rd Floor Bermondsey Wing, London SE1 9RT, UK.

E-mail addresses: [Netty.kinsella@rmh.nhs.uk](mailto:Netty.kinsella@rmh.nhs.uk), [Janette.e.kinsella@kcl.ac.uk](mailto:Janette.e.kinsella@kcl.ac.uk) (N. Kinsella).

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## 1. Introduction

Prostate cancer (PC) accounts for 400 000 new cancer cases in Europe [1] and 160 000 in the USA [2] annually. Rapid uptake of prostate-specific antigen (PSA) testing and better diagnostic procedures have led to a significant stage migration with earlier diagnosis of localised, low-risk PC (LRPC), ranging from 10% to 80% of all men diagnosed with PC worldwide [3–5]. A large proportion of these men do not require immediate radical treatment, but can be monitored using blood tests, digital rectal examination, prostate biopsy and/or multiparametric magnetic resonance imaging (MRI)— an approach known as active surveillance (AS) [5].

While there are no universally agreed upon selection criteria for AS, the authors of a recent review of currently used guidelines worldwide agreed on the following criteria, consistent with the definition of very LRPC: clinical stage T1c–T2a, PSA <10 ng/ml, biopsy Gleason score 6, maximum 1 or 2 positive biopsy cores, and/or maximum 50% of cores with cancer [6].

Large cohort studies (Supplementary material, Overview of large cohort active surveillance studies) reporting over the last 5 yr have shown little physical morbidity and low PC-specific mortality while on AS: 0.1–5.7% over 10–15 yr [7,8], observations that have recently contributed to an increased uptake of this management strategy [5,9].

AS uptake continues to vary across countries and practices, and among physicians [10]. This was most noticeable in the US Cancer of the Prostate Strategic Urologic Research Endeavour (CaPSURE) database, which reported a sharp rise in the uptake of AS, from 10% over the past 2 decades to 40% in 2010–2013 [5], and the Swedish National Prostate Cancer Register (NPCR), which noted a rise from 40% to 74% between 2009 and 2014 [11]. In Australia, where the healthcare culture is fairly evenly split between private and public systems, a 25% overall recruitment to AS was recorded by the Victorian PC Registry during the period 2008–2012 [12]. However, in Sweden, where healthcare is delivered largely by the public sector, the proportion of men selecting AS was significantly higher (80–90% of eligible men) [11]. Understanding the drivers for this variation in practice is essential.

In cohort studies reporting on AS adherence, a large proportion of men continue to drop out of AS, despite no evidence of disease progression (Supplementary material, Overview of large cohort active surveillance studies). Much research has focused on the influence of anxiety and depression on adherence. Cancer Research UK describes depression as an established response to a diagnosis of cancer, unrelated to stage or severity [13]. However, in PC the risk of moderate to severe depression (requiring treatment) has been reported as relatively low in comparison with other tumour groups, at 5% [14].

There is thus a need to identify and understand the barriers and facilitators to AS. This would then provide means for future research themes to study interventions aimed at increasing both uptake of and adherence to AS. The purpose of this paper is, therefore, to systematically evaluate the literature for factors affecting choice and adherence to AS as a PC management strategy for LRPC.

## 2. Evidence acquisition

This systematic review followed the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines [15].

### 2.1. Search strategy

Studies published between 2002 (when AS was first described in the literature [16]) and December 2017 were identified through a systematic search of electronic databases (PsychINFO, PubMed, Medline 2000–now, Embase, CINAHL, and Cochrane Library; Fig. 1). The search strategy focused on the use of keyword search terms to identify studies based on PC AS: prostate cancer OR prostatic neoplasm, active surveillance OR watchful waiting, facilitators OR barriers, treatment adherence OR treatment compliance, treatment OR therapy OR therapeutics, and decision making. The full search strategy is identified in Figure 2. References were also searched for eligible publications.

### 2.2. Study eligibility and selection

Eligible studies for inclusion in the final analysis were those that evaluated choice and/or adherence to AS rather than watchful waiting (WW). Although there are similarities between choice of AS and WW, they are conceptually different management strategies (AS is a strategy employed to monitor a patient where there is intention to offer radical treatment with curative intent when/if required; WW implies no intention to offer curative treatment). Hence, studies where AS and WW subgroups were combined were excluded to reduce bias.

We considered studies eligible if they were original articles with a qualitative or quantitative design generating data on decision making in LRPC when AS was considered a primary treatment option. Eleven studies were excluded on the basis of poor study quality or mixed WW/AS subgroup [17], as were qualitative studies that failed to state that saturation of information had been reached (usually  $\geq 20$  participants). Inclusion of at least 20 participants in a study is a general guideline in qualitative research to reach data saturation [18]. One study that fell beneath this threshold was included as information saturation was demonstrated.

Cohort/registry studies were included when they were multi-institutional and included >500 patients to reduce the associated risk of bias in small sample sizes and increase the external validity and generalisability. Studies reporting on AS adherence also included  $\geq 2$  yr of follow-up.

### 2.3. Data quality

Qualitative and mixed-methodology studies were evaluated for quality using the Purpose, Respondents, Explanation, Findings and Significance (PREFS) quality checklist. This checklist was developed by Joy and Bridges [17] for assessing quality of reports in systematic reviews of literature on patient preferences and comprises questions

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