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European Association of Urology

## Best Current Practice and Research Priorities in Active Surveillance for Prostate Cancer—A Report of a Movember International Consensus Meeting

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## Abstract

**Background:** Active surveillance (AS) is recommended for low-risk and some intermediate-risk prostate cancer. Uptake and practice of AS vary significantly across different settings, as does the experience of surveillance—from which tests are offered, and to the levels of psychological support.

**Objective:** To explore the current best practice and determine the most important research priorities in AS for prostate cancer.

**Design, setting, and participants:** A formal consensus process was followed, with an international expert panel of purposively sampled participants across a range of health care professionals and researchers, and those with lived experience of prostate cancer. Statements regarding the practice of AS and potential research priorities spanning the patient journey from surveillance to initiating treatment were developed.

**Outcome measurements and statistical analysis:** Panel members scored each statement on a Likert scale. The group median score and measure of consensus were presented to participants prior to discussion and rescoring at panel meetings. Current best practice and future research priorities were identified, agreed upon, and finally ranked by panel members.

**Results and limitations:** There was consensus agreement that best practice includes the use of high-quality magnetic resonance imaging (MRI), which allows digital rectal examination (DRE) to be omitted, that repeat standard biopsy can be omitted when MRI and prostate-specific antigen (PSA) kinetics are stable, and that changes in PSA or DRE should prompt MRI ± biopsy rather than immediate active treatment. The highest ranked research priority was a dynamic, risk-adjusted AS approach, reducing testing for those at the least risk of progression. Improving the tests used in surveillance, ensuring equity of access and experience across different patients and settings, and improving information and communication between and within clinicians and patients were also high priorities. Limitations include the use of a limited number of panel members for practical reasons.

**Conclusions:** The current best practice in AS includes the use of high-quality MRI to avoid DRE and as the first assessment for changes in PSA, with omission of repeat standard biopsy when PSA and MRI are stable. Development of a robust, dynamic, risk-adapted approach to surveillance is the highest research priority in AS for prostate cancer.

**Patient summary:** A diverse group of experts in active surveillance, including a broad range of health care professionals and researchers and those with lived experience of prostate cancer, agreed that best practice includes the use of high-quality magnetic resonance imaging, which can allow digital rectal examination and some biopsies to be omitted. The highest research priority in active surveillance research was identified as the development of a dynamic, risk-adjusted approach.

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## 1. Introduction

Active surveillance (AS) for localised prostate cancer aims to defer or avoid treatment and its side effects, using repeat testing to detect disease that would benefit from treatment. The uptake and practice of surveillance vary significantly between different countries [1] and settings [2,3].

This variation starts with differences in the approach to prostate cancer detection, which impacts the number and proportion of men diagnosed with lower-risk prostate cancer who could be considered for AS. In the UK, where prostate-specific antigen (PSA) testing can be requested by patients but is not offered routinely, magnetic resonance imaging (MRI) before biopsy was performed in 80% of men in 2016/2017 [4], and biopsy is often omitted in men with negative MRI and low PSA density. The 2018–2019 National Prostate Cancer Audit data show that low-risk prostate can-

cer comprises 6% of new diagnoses [5]. However, in the USA, where PSA testing is much more widespread, low-risk disease comprises one-third of new diagnoses, and Gleason 6 disease accounts for more than half of the diagnoses of localised prostate cancer in a series assessing the risk profile of prostate cancer at diagnosis over 10 years [6]. The United States Preventative Services Taskforce recommendations in 2008 [7] led to a reduction in the proportion of men seen with low-risk disease, according to the National Cancer Database, with a reduction from 38% in 2004 to 27% in 2014.

The biopsy and PSA thresholds for entry to AS vary, and there is also significant variation between published protocols and usual practice, particularly in the uptake of routine biopsies after the 1st year or 2nd year of AS. Although all established guidelines include the use of clinical staging by digital rectal examination (DRE), it is common in some centres for MRI to be used for staging, with DRE not done where

MRI is used. We know that there is significant variation in adherence to different protocols [8].

The use of MRI, and subsequent MRI-targeted biopsies, before enrolment and during follow-up differs significantly between different settings. Even for those who regularly use MRI, there are no agreed MRI features that denote magnetic resonance characteristics unsuitable for surveillance.

Movember is a global men's health charity that has invested in prostate cancer research since 2005. Movember's investment in AS to date has largely focussed on the Global Action Plan (GAP3) Prostate Cancer Active Surveillance consortium and database [9–13].

Movember commissioned this work to identify best practice and research priorities in AS, using a recognised structured consensus framework.

## 2. Patients and methods

The aim was to explore consensus for best practice in AS and then identify the highest research priorities. We used expert experience to explore the gap between published guidelines and common practice.

The intention was to respectfully build on rather than duplicate other excellent collaborative efforts, including the following:

1. Movember GAP3 [9–13]
2. European Association of Urology (EAU) DETECTIVE [14,15]
3. The Lancet Prostate Cancer Commission [16]
4. PIONEER data collaborative [17–20]
5. University of Maryland initiative [21]

Some of these focus on the whole prostate cancer pathway (Lancet prostate cancer commission [16] and PIONEER [17–20]), whilst others focus purely on AS (GAP3 and EAU DETECTIVE). Both GAP3 and PIONEER focus on using real-world data. EAU DETECTIVE focussed on recommendations for biomedical aspects of current AS practice, based on evidence review and consensus methods.

The University of Maryland initiative [21] focussed on designing novel research studies relevant to AS, using a Population, Intervention, Comparator, Outcome, and Timeline framework.

In order to build on these initiatives, key participants from each panel were invited to this consensus group (Supplementary Table 1). The unique approach of this project was to identify research priorities, for future investment by Movember, and the research community more widely.

### 2.1. Study design

The RAND-UCLA appropriateness method for assessing the agreement in areas of uncertainty [22] was used (Fig. 1). This includes the following:

1. An evidence review comprising an overview of recent systematic reviews in AS
2. Formation of an expert panel of health care and research professionals (HCP panel) and one of those with lived experience of prostate cancer (LE panel)

3. Iterative development of discussion statements informed by the evidence review and modified by the panels
4. Independent scoring of statements for the strength of agreement from 1 (strongly disagree) to 9 (strongly agree)
5. An analysis of group median scores (where 1–3 show disagreement, 4–6 uncertainty, and 7–9 agreement)
6. Calculation of group consensus (yes, no, or uncertain) based on the interpercentile range adjusted for symmetry [22]

After scoring, panellists received a summary of their own results, group median scores and consensus status, and distribution of anonymised scores. Online discussions were held, where statements could be removed, added, or modified, prior to rescoreing. Weighted summed scores were used to analyse these data.

Given the importance of hearing the distinct voice of those with lived experience, dedicated meetings were held for each panel, with an iterative process of sharing outcomes between the two panels (Fig. 1).

An initial list of potential research priorities was identified from the literature. These were then discussed at each panel, following the scoring of the statements across patient journey. A revised list of ten research priority areas was developed, and all panel participants were asked to rank their top five priorities from these ten areas.

### 2.2. Setting and participants

The health care professional expert panel included expertise across urology, oncology, radiology, pathology, translational science, population health, psycho-oncology (including behavioural science), general practice, nursing, clinical trials, health care, and health services research. First, potential participants were purposively sampled via author listings on papers identified in the evidence review. We also aimed to include diversity of thought, gender, profession, and race. Additional participants were invited based on track record in AS research in areas complementary to the other panellists. Urologists represented a spectrum of those working within a more general practice with prostate cancer, to those with a specialist academic practice in prostate cancer, with a range of surgical options offered across the group including radical prostatectomy and focal treatment for prostate cancer (Fig. 2 and Supplementary Table 1).

The lived experience expert panel was purposively sampled to include participants across a range of experience of AS (new to AS, established on AS, previously on AS, and now had active treatment) and international representation. Many of the lived experience panellists participated as representatives of patient advocacy organisations and so could represent a broad range of views.

## 3. Results

The initial HCP survey contained 234 statements, formulated from the evidence review, with 117 of these sent to the LE panel.

The two panels removed a total of seven statements, added 74 statements, and rephrased 31 statements prior to final scoring. The additions were to address the panels' per-

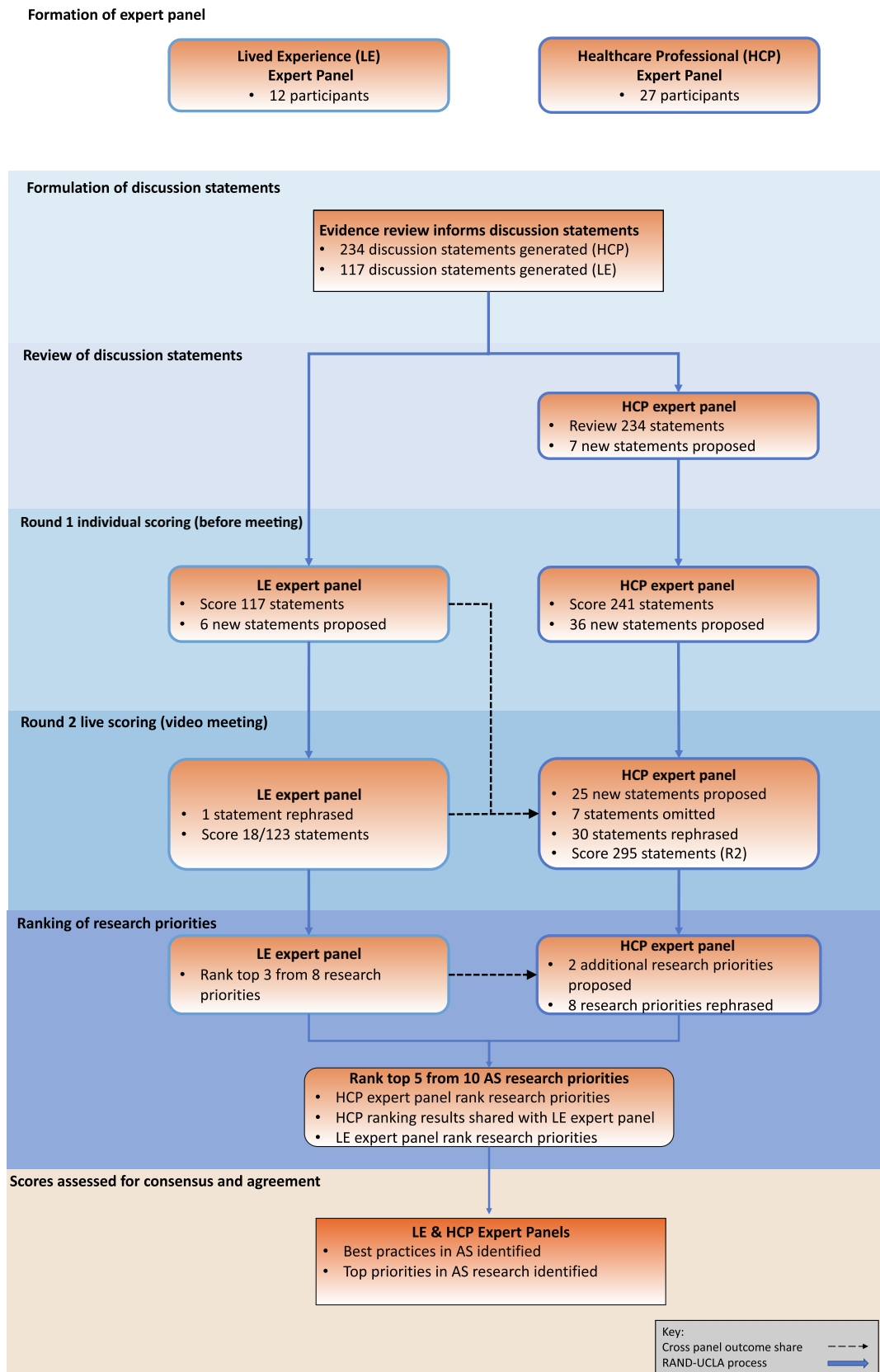


Fig. 1 – RAND-UCLA consensus pathway. AS = active surveillance.

ceived gaps in the statements derived from the narrative review, and the rephrasing was necessary to clarify mean-

ing. A total of 307 statements underwent final scoring and analysis across both panels.

## Global effort to identify the top priorities in AS

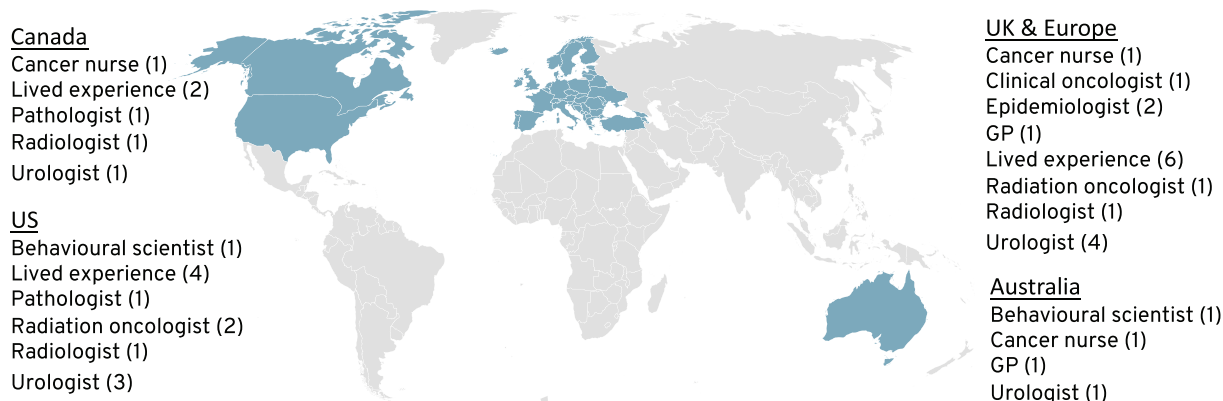


Fig. 2 – Expert panel participants. GP = general practitioner.

The statements were discussed and are reported according to the patient journey from diagnosis to active treatment. The statements and panel scores are shown in Table 1.

### 3.1. Who should be offered AS?

There was consensus and agreement across the two panels that a number of factors, including clinical factors, comorbidities, and patient preferences, should be used to determine whether someone should be offered AS.

Gleason grade and MRI findings were the most important criteria, with PSA density and PSA being the next most important ones (Fig. 3A). There was much discussion on the use of other parameters, including cancer core length (in millimetres), tumour visibility, and tumour volume on MRI, none of which are recognised in established guidelines. There was agreement that percentage cancer in a biopsy core is a flawed concept as it does not consistently reflect absolute tumour volume and that numbers of positive cores should not be considered indicative of tumour burden in the context of MRI-targeted biopsies.

#### 3.1.1. Age and life expectancy

There was consensus in the LE panel that no upper age limit (eg, 75 or 80 yrs old) should be applied, and there was uncertainty regarding a lower age limit. The HCP panel was uncertain about an upper age limit but agreed that there should be no lower age limit.

There were also uncertainty and disagreement in the LE panel about whether life expectancy (eg, 10 or 15 yr) should be used as an eligibility criterion. Discussion centred on the need to offer a full set of choices to men depending on their likelihood of benefitting from treatment, avoiding artificial barriers based on biological age or estimated life expectancy, which can lead to age discrimination. The HCP panel agreed that life expectancy of  $\geq 10$  yr should be considered within the eligibility criteria for AS, with a shorter life expectancy requirement for intermediate-risk prostate cancer.

### 3.2. Who is more likely to choose AS?

It was agreed that clinician confidence in AS, time to explain all the options, and the person or team informing patients of their diagnosis increase the likelihood of a choice of AS.

### 3.3. Psychological impact of AS

The HCP panel agreed that AS can lead to anxiety in some men, especially when awaiting test results, although the LE panel members were uncertain about this, suggesting that some men experience relief and positive psychological effects when able to have surveillance versus active treatment.

It was agreed that clinicians should aim to identify those with low-risk disease who might have, or be at risk of, negative psychological consequences of AS and offer psychological support, rather than immediate active treatment for the disease.

### 3.4. How should AS be carried out?

#### 3.4.1. Communication, education, and support

There was strong agreement that newly diagnosed patients should be offered separate appointments for diagnosis and decision-making, allowing time to process feelings, learn about the disease, and think of relevant questions. There was also strong agreement that better, clearer, and more consistent information is an unmet need for patients and their partners and families, that support groups can be an important support for men on AS, and that there is a need for clinician education to help men stay on AS when it is warranted.

There was strong agreement across both panels that patients should have an open line of communication with the health care team.

There was agreement in the LE panel that well-being, diet, exercise, and mindfulness are important during AS. There was also consensus in the HCP panel that men on AS are more likely to die from cardiovascular disease than prostate cancer and should be counselled about lifestyle modifications, with favourable results in AS populations (eg,



Table 1 – Scored statements

| Q-Num   | HCP statement  | Q-Num | Lived Exp statement   | HCP responses |              |           |              | Lived Exp responses                   |                                    |
|---|--|-------|---|---------------|--------------|-----------|--------------|---------------------------------------|------------------------------------|
|   |  |       |   | R1 median     | R1 consensus | R2 median | R2 consensus | Median score (after group discussion) | Consensus (after group discussion) |
| What factors influence the variation in approaches to AS in different settings?                                 |  |       |   |               |              |           |              |                                       |                                    |
| 1   | National and local policy on PSA testing affects the likelihood of men being diagnosed with indolent disease   | 1     | Checking PSA routinely will pick up more prostate cancers at early stage  | 8             | Yes          | 8         | Yes          | 8                                     | Yes                                |
| 2   | Reduced availability of PSA testing leads to lower absolute diagnosis of indolent disease  |       |   | 3             | Yes          | 5         | No           |                                       |                                    |
| 3   | Regular PSA testing in men with health insurance (eg, the USA) increases the likelihood of men being diagnosed with indolent disease   | 3     | Checking of PSA routinely will pick up more prostate cancers that do not need immediate treatment and could be managed with AS  | 8             | Yes          | 8         | Yes          | 9                                     | Yes                                |
| 4   | National guidance to reduce overdiagnosis (eg, the US Preventive Services Task Force guidance) reduces the likelihood of men being diagnosed with indolent disease                     | 4     | Checking PSA routinely risks overdiagnosing prostate cancer that has a very low chance of causing harm  | 7             | Yes          | 7         | Yes          | 6                                     | No                                 |
| 5   | Using mpMRI to assess men before biopsy reduces the likelihood of them being diagnosed with indolent disease   | 5     | Using MRI before biopsy to work out who needs a biopsy and in whom it can be avoided will reduce the risk of overdiagnosis  | 8             | Yes          | 8         | Yes          | 8.5                                   | Yes                                |
| 6   | Using standard biopsy for men with negative mpMRI increases the likelihood of being diagnosed with indolent disease  | 6     | Having a biopsy even if the MRI is negative would help make sure that no prostate cancer is missed, but risks overdiagnosing prostate cancer that has a very low chance of causing harm | 7             | Yes          | 7         | Yes          | 5.5                                   | No                                 |
| What factors influence the likelihood of patients with lower-risk disease choosing surveillance over treatment? |  |       |   |               |              |           |              |                                       |                                    |
| 7   | Cultural expectations that cancer diagnosis should lead to immediate active intervention are difficult to overcome when counselling men and their families about AS                    | 7     | Being diagnosed with cancer makes you feel that active treatment, rather than surveillance, should be undertaken  | 6             | Yes          | 7         | Yes          | 6                                     | No                                 |
| 8   | *NEW Men who discuss PSA testing with their urologist or primary care provider should have the concept of AS introduced  |       |   | NA            | NA           | 8         | Yes          |                                       |                                    |
| 9   | *NEW Men who have heard of AS from a clinician before having a PSA test are more likely to choose surveillance for low-risk disease than someone who has not                           |       |   | NA            | NA           | 7         | Yes          |                                       |                                    |
| 10  | *NEW Patients whose clinicians take the time to explain different options carefully are more likely to choose AS   |       |   | 8             | Yes          | 8         | Yes          |                                       |                                    |
| 11  | *NEW Patients whose doctors appear confident in their recommendation for AS will be more likely to choose AS   |       |   | 8             | Yes          | 8         | Yes          |                                       |                                    |
| 12  | Patients' families and loved ones are the main influence on their decision between immediate treatment and AS  |       |   | 6             | Yes          | 6         | Yes          | 4.5                                   | Yes                                |
| 13  | What patients hear about in the media is the main influence on their decision between immediate treatment and AS   |       |   | 4.5           | Yes          | 5         | Yes          | 4.5                                   | No                                 |
| 14  | The person who informs a patient about their prostate cancer diagnosis (eg, specialist nurse, surgeon, family doctor) will influence their decision between immediate treatment and AS | 14    | Who informs a patient about their prostate cancer diagnosis (eg, specialist nurse, surgeon, family doctor) might later influence their decision between active treatment and AS         | 8             | Yes          | 8         | Yes          | 8                                     | Yes                                |
| 15  | Clinicians are sometimes overcautious about recommending AS because of fear of being sued if disease progresses during AS  | 15    | Doctors might be overcautious about recommending AS because of fear of being sued if disease progresses during AS   | 6             | Yes          | 6         | Yes          | 7.5                                   | Yes                                |
| 16  | Clinicians working in countries that have national guidance recommending AS are more likely to recommend it for the management of low-risk prostate cancer                             | 16    | Doctors working in countries that have national guidance recommending AS are more likely to recommend it for the management of low-risk prostate cancer                                 | 8             | Yes          | 8         | Yes          | 8                                     | Yes                                |
| 17  | Patients with nationally available patient information recommending AS are more likely to choose it for the management of their low-risk prostate cancer                               |       |   | 8             | Yes          | 8         | Yes          | 7.5                                   | Yes                                |
| 18  | Advertisements for treatments (eg, surgery, radiotherapy) make patients less likely to choose AS   |       |   | 6             | Yes          | 6         | Yes          | 6                                     | Yes                                |
| 19  | An insurance-based healthcare system (such as in the USA) makes patients less likely to choose AS  |       |   | 6             | Yes          | 6         | Yes          | 7.5                                   | Yes                                |

(continued on next page)

Table 1 (continued)

| Q-Num  | HCP statement  | Q-Num | Lived Exp statement   | HCP responses |              |           |              | Lived Exp responses                   |                                    |
|--|--|-------|---|---------------|--------------|-----------|--------------|---------------------------------------|------------------------------------|
|  |  |       |   | R1 median     | R1 consensus | R2 median | R2 consensus | Median score (after group discussion) | Consensus (after group discussion) |
| 20   | A free at the point of use healthcare system (such as in the UK) makes patients more likely to choose AS   |       |   | 6             | Yes          | 6         | Yes          | 7                                     | Yes                                |
| 21   | A combination of approaches for funding healthcare (such as in Australia) makes patients more likely to choose AS  |       |   | 5             | Yes          | 6         | Yes          | 5                                     | Yes                                |
| 22   | A combination of approaches for funding healthcare (such as in Australia) makes patients less likely to choose AS  |       |   | 4             | Yes          | 4         | Yes          | 5                                     | Yes                                |
| 23   | Where doctors and hospitals get paid for the operations and interventions they perform, they are less likely to recommend AS                             |       |   | 7             | Yes          | 7         | Yes          | 7                                     | Yes                                |
| 24   | Where doctors and hospitals get paid simply for caring for patients, no matter whether they have operations or not, they are more likely to recommend AS |       |   | 7             | Yes          | 7         | Yes          | 8                                     | Yes                                |
| What would be the attributes of the ideal surveillance programme?        |  |       |   |               |              |           |              |                                       |                                    |
| 25   | In an ideal system, there would be no surveillance as patients would be diagnosed only if they had disease that needed treating                          | 25    | In an ideal system, there would be no surveillance as patients would be diagnosed only if they had disease that needed treating                             | 6.5           | No           | 7         | Yes          | 3.5                                   | No                                 |
| 26   | In an ideal system, testing would be done according to risk, with patients at the lowest risk needing less testing than those at a higher risk           | 26    | In an ideal system, testing whilst on AS would be done according to risk, with patients at the lowest risk needing less testing than those at a higher risk | 8             | Yes          | 8         | Yes          | 7.5                                   | Yes                                |
| 27   | In an ideal system, most testing would be noninvasive and biopsies would be performed only as needed   |       |   | 9             | Yes          | 9         | Yes          | 8.5                                   | Yes                                |
| 28   | Ideally, patients should be told about the risks of progression of cancer and the risks of harm from testing and treatment                               |       |   | 9             | Yes          | 9         | Yes          | 9                                     | Yes                                |
| 29   | Ideally, patients should be able to get additional testing on demand, more frequently than their clinicians feel necessary.                              |       |   | 4             | Yes          | 4         | Yes          | 8 (6)                                 | Yes (yes)                          |
| 30   | Ideally, patients should be able to have all testing closer to home or at home   |       |   | 8             | Yes          | 8         | Yes          | 8                                     | Yes                                |
| 31   | Ideally, patients should have an open line of communication with their healthcare team via telephone, e-mail, or app                                     |       |   | 8             | Yes          | 8         | Yes          | 9                                     | Yes                                |
| 32   | Ideally, patients should have access to peer support from others in a similar situation  |       |   | 8             | Yes          | 8         | Yes          | 9                                     | Yes                                |
| 33   | Ideally, patients should experience no more anxiety associated with having low-risk prostate cancer than a high blood pressure that is under treatment   |       |   | 8             | Yes          | 8         | Yes          | 8.5                                   | Yes                                |
| What are the goals of an ideal AS programme?                             |  |       |   |               |              |           |              |                                       |                                    |
| 34   | An ideal AS programme aims to avoid or defer the side effects of active treatment  |       |   | 9             | Yes          | 9         | Yes          | 9                                     | Yes                                |
| 35   | *NEW AS should be expanded to include men with PSA or MRI suspicious of prostate cancer who have not had a biopsy  |       |   | NA            | NA           | 3.5       | Yes          |                                       |                                    |
| 36   | An ideal AS programme aims to assess, using time, whether this is a cancer with the potential to become aggressive                                       |       |   | 9             | Yes          | 9         | Yes          | 8                                     | Yes                                |
| 37   | An ideal AS programme aims to improve general health and fitness   |       |   | 6             | Yes          | 8         | Yes          | 7 (8.5)                               | Yes (yes)                          |
| 38   | An ideal AS programme aims to reduce overmonitoring  |       |   | 7             | Yes          | 7         | Yes          | 8                                     | Yes                                |
| 39   | An ideal AS programme aims to reduce overtreatment   |       |   | 9             | Yes          | 9         | Yes          | 9                                     | Yes                                |
| 40   | An ideal AS programme aims to offer curative treatment with no negative consequences from having delayed that treatment                                  |       |   | 9             | Yes          | 9         | Yes          | 8.5                                   | Yes                                |
| 41   | An ideal AS programme aims to maximise QoL including urinary and sexual function, including fertility for those patients for whom that is important      |       |   | 9             | Yes          | 9         | Yes          | 9                                     | Yes                                |
| What are the burdens for patients and their families of an AS programme? |  |       |   |               |              |           |              |                                       |                                    |
| 42   | AS causes some patients to experience anxiety about cancer progression   | 42    | AS causes patients to experience anxiety about cancer progression   | 7             | Yes          | 7         | Yes          | 6.5                                   | Yes                                |
| 43   | AS causes some patients to experience anxiety about treatment  | 43    | AS causes patients to experience anxiety about treatment  | 5.5           | Yes          | 7         | Yes          | 5                                     | Yes                                |
| 44   | AS causes some patients to experience depression   | 44    | AS causes patients to experience depression   | 4             | Yes          | 6         | Yes          | 4.5                                   | Yes                                |
| 45   | AS costs patients money from hospital visits   |       |   | 6             | Yes          | 6         | Yes          | 6                                     | Yes                                |
| 46   | AS costs patients money from transport to attend hospital visits   |       |   | 6             | Yes          | 6         | Yes          | 5.5                                   | Yes                                |
| 47   | AS costs patients money from parking during hospital visits  |       |   | 6             | Yes          | 6         | Yes          | 5.5                                   | Yes                                |
| 48   | AS costs patients in terms of time off work  |       |   | 6             | Yes          | 6         | Yes          | 5.5                                   | Yes                                |
| 49   | AS causes patients to experience anxiety while waiting for test results  |       |   | 7             | Yes          | 7         | Yes          | 6.5                                   | No                                 |
| 50   | Side effects of testing (eg, biopsy) during AS affects patients' QoL   |       |   | 7             | Yes          | 7         | Yes          | 6.5                                   | No                                 |
| 51   | Side effects of testing (eg, biopsy) during AS affects patients' QoL in the short term   |       |   | NA            | NA           | 7         | Yes          |                                       |                                    |
| 52   | Side effects of testing (eg, biopsy) during AS affects patients' QoL in the longer term  |       |   | NA            | NA           | 6.5       | Yes          |                                       |                                    |

Table 1 (continued)

| Q-Num | HCP statement  | Q-Num | Lived Exp statement  | HCP responses |              |           |              | Lived Exp responses                   |                                    |
|-------|--|-------|--|---------------|--------------|-----------|--------------|---------------------------------------|------------------------------------|
|       |  |       |  | R1 median     | R1 consensus | R2 median | R2 consensus | Median score (after group discussion) | Consensus (after group discussion) |
| 53    | AS can distract patients from addressing other important health risks, such as obesity and high blood pressure   |       |  | 3             | Yes          | 3         | Yes          | 4                                     | Yes                                |
| 54    | AS can help patients to focus and reflect on their health-related behaviour, including diet and exercise   |       |  | 7             | Yes          | 7         | Yes          | 8                                     | Yes                                |
| 55    | The move to telehealth (phone or video) has reduced the burden of clinical appointments compared with in-person visits   |       |  | NA            | NA           | 8         | Yes          |                                       |                                    |
| 56    | Clinicians should offer active treatment instead of AS if they believe that a patient with low-risk disease might experience significant negative psychological effects from being on AS |       |  | 4             | Yes          | 4         | Yes          | 5.5 (5)                               | Yes (yes)                          |
| 57    | Clinicians should offer extra psychological support if they believe that a patient with low-risk disease might experience significant negative psychological effects from being on AS    |       |  | 8             | Yes          | 8         | Yes          | 8 (8.5)                               | Yes (yes)                          |
| 58    | Access to AS should not be denied to patients with the potential to experience negative psychological effects whilst on AS   |       |  | 8             | Yes          | 8         | Yes          | 7.5 (8.5)                             | Yes (yes)                          |
|       | Which patients are most likely to choose AS for low risk prostate cancer?  |       |  |               |              |           |              |                                       |                                    |
| 59    | Wealthy patients are more likely to choose AS for low-risk prostate cancer   |       |  | 5.5           | Yes          | 6         | Yes          | 5.5                                   | Yes                                |
| 60    | Married patients are more likely to choose AS for low-risk prostate cancer   |       |  | 5             | Yes          | 5         | Yes          | 5                                     | Yes                                |
| 61    | Patients with unrestricted access to healthcare are more likely to choose AS for low-risk prostate cancer  |       |  | 6             | Yes          | 6         | Yes          | 5                                     | Yes                                |
| 62    | Patients with high levels of anxiety are more likely to choose AS for low-risk prostate cancer   |       |  | 3             | Yes          | 3         | Yes          | 5                                     | Yes                                |
| 63    | Patients who are undergoing medical care for other conditions are more likely to choose AS for low-risk prostate cancer  |       |  | 7             | Yes          | 7         | Yes          | 7                                     | Yes                                |
| 64    | Younger patients are more likely to choose AS for low-risk prostate cancer   |       |  | 4             | Yes          | 4         | Yes          | 6                                     | Yes                                |
| 65    | Older patients are more likely to choose AS for low-risk prostate cancer   |       |  | 7             | Yes          | 7         | Yes          | 7                                     | Yes                                |
| 66    | Patients who are of the global majority are more likely to choose AS for low-risk prostate cancer  |       |  | 5             | Yes          | 5         | Yes          | 6.5                                   | Yes                                |
| 67    | *NEW Race should be seen as a risk factor for progression on AS and should be used in counselling men considering AS   |       |  | NA            | NA           | 7         | Yes          |                                       |                                    |
| 68    | White patients, compared with other ethnicities, are more likely to choose AS for low-risk prostate cancer   |       |  | 6.5           | Yes          | 6         | Yes          | 7                                     | Yes                                |
|       | How should we determine which patients should be offered AS?   |       |  |               |              |           |              |                                       |                                    |
|       |  | 69    | Stage of cancer (ie, how far it has grown inside the prostate) should be used to determine whether patients should have AS |               |              |           |              | 7.5                                   | Yes                                |
| 70    | *NEW Men with a family history of early diagnosis of prostate cancer (aged under 60 in a first-degree relative) can still be offered AS  |       |  | NA            | NA           | 7         | Yes          |                                       |                                    |
| 71    | *NEW Men with a family history of early death from prostate cancer (first-degree relative, aged under 65) can still be offered AS  |       |  | NA            | NA           | 7         | Yes          |                                       |                                    |
| 72    | *NEW Men with a family history of early death from prostate cancer (first-degree relative under 65) should be counselled about AS with increased monitoring                              |       |  | NA            | NA           | 7         | Yes          |                                       |                                    |
| 73    | Patients with PSA $\leq 20$ ng/ml should be offered AS   |       |  | 5             | No           | 5         | Yes          |                                       |                                    |
| 74    | Patients with PSA $\leq 15$ ng/ml should be offered AS   |       |  | 5.5           | No           | 5         | Yes          |                                       |                                    |
| 75    | Patients with PSA $\leq 10$ ng/ml should be offered AS   |       |  | 7             | Yes          | 7         | Yes          |                                       |                                    |
| 76    | Patients with PSA density $\leq 0.2$ ng/ml/cc should be offered AS   |       |  | 5             | Yes          | 5         | Yes          |                                       |                                    |
| 77    | Patients with PSA density $\leq 0.15$ ng/ml/cc should be offered AS  |       |  | 7             | Yes          | 7         | Yes          |                                       |                                    |
| 78    | Patients with clinically localised disease should be offered AS  |       |  | 7             | Yes          | 7         | Yes          |                                       |                                    |
| 79    | Patients with clinical T stage $\leq T2a$ should be offered AS   |       |  | 7             | Yes          | 7         | Yes          |                                       |                                    |
| 80    | Patients with clinical T stage $\leq T2b$ should be offered AS   |       |  | 7             | Yes          | 7         | Yes          |                                       |                                    |
| 81    | Patients with clinical T stage $\leq T2c$ should be offered AS   |       |  | 5             | Yes          | 5         | Yes          |                                       |                                    |
| 82    | Patients with clinical T stage T3a can be offered AS   |       |  | 2             | Yes          | 2         | Yes          |                                       |                                    |
| 83    | Stage, as determined on mpMRI, should be used to determine eligibility for AS  |       |  | 6.5           | Yes          | 6         | Yes          |                                       |                                    |
| 84    | Tumour volume on mpMRI should be used to determine eligibility   |       |  | 6             | Yes          | 6         | Yes          |                                       |                                    |

(continued on next page)



Table 1 (continued)

| Q-Num | HCP statement   | Q-Num | Lived Exp statement | HCP responses |              |           |              | Lived Exp responses                   |                                    |
|-------|---|-------|---------------------|---------------|--------------|-----------|--------------|---------------------------------------|------------------------------------|
|       |   |       |                     | R1 median     | R1 consensus | R2 median | R2 consensus | Median score (after group discussion) | Consensus (after group discussion) |
| 85    | for AS<br>Lesion visibility on mpMRI should be used to determine eligibility for AS   |       |                     | 6             | Yes          | 6         | Yes          |                                       |                                    |
| 86    | Men with mpMRI-invisible disease are not suitable for AS  |       |                     | 2             | Yes          | 2         | Yes          |                                       |                                    |
| 87    | Men with PI-RADS 4 are not suitable for AS  |       |                     | NA            | NA           | 4         | Yes          |                                       |                                    |
| 88    | Men with PI-RADS 5 are not suitable for AS  |       |                     | NA            | NA           | 7         | Yes          |                                       |                                    |
| 89    | Patients who have not had multiparametric prostate MRI previously should be offered multiparametric prostate MRI before commencing AS |       |                     | 8             | Yes          | 8         | Yes          |                                       |                                    |
| 90    | Patients with no aggressive features on MRI can be considered for AS  |       |                     | 7             | Yes          | 7         | Yes          |                                       |                                    |
| 91    | Patients in whom biopsy findings and MRI results do not agree should be offered a new MRI targeted biopsy before commencing AS        |       |                     | 8             | Yes          | 8         | Yes          |                                       |                                    |
| 92    | Patients with PI-RADS 4 or 5 lesions on MRI are unsuitable for AS even if they fulfil other AS eligibility criteria                   |       |                     | 4             | Yes          | 4         | Yes          |                                       |                                    |
| 93    | *NEW Where there is a mismatch between biopsy and MRI findings, PSMA can be considered  |       |                     | NA            | NA           | 6         | Yes          |                                       |                                    |
| 94    | PSMA has a clear role in AS   |       |                     | NA            | NA           | 3         | Yes          |                                       |                                    |
| 95    | PSMA may have a role in AS  |       |                     | NA            | NA           | 7         | Yes          |                                       |                                    |
| 96    | Further studies are needed to determine the role of PSMA in AS  |       |                     | NA            | NA           | 9         | Yes          |                                       |                                    |
| 97    | Patients with Gleason grade 3 + 3 should be offered AS  |       |                     | 9             | Yes          | 9         | Yes          |                                       |                                    |
| 98    | Patients with Gleason grade 3 + 4 can be offered AS   |       |                     | 7             | Yes          | 7.5       | Yes          |                                       |                                    |
| 99    | Patients with Gleason grade 3 + 4 and $\leq$ 20% pattern 4 can be offered AS  |       |                     | 7             | Yes          | 7         | Yes          |                                       |                                    |
| 100   | Patients with Gleason grade 3 + 4 and $\leq$ 10% pattern 4 can be offered AS  |       |                     | 8             | Yes          | 8         | Yes          |                                       |                                    |
| 101   | Number of cores containing cancer in a systematic biopsy should not be used to determine eligibility for AS                           |       |                     | 4             | No           | 4         | Yes          |                                       |                                    |
| 102   | Men with 12 cores of 1 mm 3 + 3 could be offered AS   |       |                     | 7             | Yes          | 7         | Yes          |                                       |                                    |
| 103   | Patients with $\leq$ 4 cancer-containing cores of a 10–12-core standard biopsy can be offered AS                                      |       |                     | 7             | Yes          | 7         | Yes          |                                       |                                    |
| 104   | Patients with $\leq$ 3 cores positive can be offered AS   |       |                     | 7             | Yes          | 7.5       | Yes          |                                       |                                    |
| 105   | Patients with $\leq$ 2 cores positive can be offered AS   |       |                     | 8             | Yes          | 8         | Yes          |                                       |                                    |
| 106   | Number of cores positive should not be considered indicative of tumour volume or extent if targeted biopsies have been performed      |       |                     | 7             | No           | 7         | Yes          |                                       |                                    |
| 107   | Tumour volume on mpMRI should be used to determine eligibility for AS   |       |                     | 5.5           | Yes          | 5         | Yes          |                                       |                                    |
| 108   | Patients with $\leq$ 50% cancer in biopsy core can be offered AS  |       |                     | 6             | Yes          | 6         | Yes          |                                       |                                    |
| 109   | Patients with $\leq$ 33% cancer in biopsy core can be offered AS  |       |                     | 7             | Yes          | 7         | Yes          |                                       |                                    |
| 110   | Patients with $\leq$ 20% cancer in biopsy core can be offered AS  |       |                     | 8             | Yes          | 8         | Yes          |                                       |                                    |
| 111   | Percentage cancer in biopsy core is a flawed concept, as it does not reflect absolute tumour volume                                   |       |                     | 7             | Yes          | 7         | Yes          |                                       |                                    |
| 112   | The total percentage of carcinoma in all cores and the number and percentage (fraction) of cores with cancer are significantly        |       |                     | 5.5           | No           | 5.5       | Yes          |                                       |                                    |

Table 1 (continued)

| Q-Num | HCP statement  | Q-Num | Lived Exp statement | HCP responses |              |           |              | Lived Exp responses                   |                                    |
|-------|--|-------|---------------------|---------------|--------------|-----------|--------------|---------------------------------------|------------------------------------|
|       |  |       |                     | R1 median     | R1 consensus | R2 median | R2 consensus | Median score (after group discussion) | Consensus (after group discussion) |
|       | stronger than other methods, such as greatest linear percentage of cancer or greatest millimetre length in a single core, in predicting biochemical recurrence   |       |                     |               |              |           |              |                                       |                                    |
| 113   | Patients with cribriform histology can never be offered AS   |       |                     | 6             | Yes          | 6         | Yes          |                                       |                                    |
| 114   | Patients with intraductal histology can never be offered AS  |       |                     | 6             | Yes          | 6         | Yes          |                                       |                                    |
| 115   | Patients with very-low-risk prostate cancer should be recommended to commence AS as best care  |       |                     | 9             | Yes          | 9         | Yes          |                                       |                                    |
| 116   | Patients with low-risk prostate cancer should be recommended to commence AS as best care   |       |                     | 9             | Yes          | 9         | Yes          |                                       |                                    |
| 117   | Patients with intermediate-risk prostate cancer can be offered AS  |       |                     | 7             | Yes          | 7         | Yes          |                                       |                                    |
| 118   | Selected patients with favourable intermediate-risk localised prostate cancer can be offered AS  |       |                     | 7.5           | Yes          | 7         | Yes          |                                       |                                    |
| 119   | Patients with intermediate-risk prostate cancer can be offered AS if they do not wish to undergo immediate treatment   |       |                     | 7             | Yes          | 7         | Yes          |                                       |                                    |
| 120   | AS may be offered to select patients with favourable intermediate-risk localised prostate cancer; however, patients should be informed that this comes with a higher risk of developing metastases than definitive treatment |       |                     | 8             | Yes          | 8         | Yes          |                                       |                                    |
| 121   | Developing multiple variable risk calculators would enable clinicians to provide objective, individualised advice to patients when discussing AS and other management options  |       |                     | 8             | Yes          | 8         | Yes          |                                       |                                    |
| 122   | Urine, tissue, or blood biomarkers should be used to determine whether patients should have AS   |       |                     | 7             | Yes          | 5         | Yes          | 7                                     | Yes                                |
| 123   | Urine, tissue, or blood biomarkers can be used to determine whether patients should have AS  |       |                     | NA            | NA           | 7         | Yes          |                                       |                                    |
| 124   | Genomic biomarkers now have a clear role in determining eligibility for AS   |       |                     | 3.5           | No           | 3         | Yes          |                                       |                                    |
| 125   | Genomic biomarkers may have a role in determining eligibility for AS in future   |       |                     | 7             | Yes          | 7         | Yes          |                                       |                                    |
| 126   | Further prospective studies are needed in order to define the role of genomic biomarkers in determining AS eligibility   |       |                     | 9             | Yes          | 8         | Yes          |                                       |                                    |
| 127   | Tissue-based molecular biomarkers now have a clear role in determining eligibility for AS  |       |                     | 4             | Yes          | 4         | Yes          |                                       |                                    |
| 128   | Tissue-based molecular biomarkers may have a role in determining eligibility for AS in future  |       |                     | 7             | Yes          | 7         | Yes          |                                       |                                    |
| 129   | Further prospective studies are needed in order to define the role of tissue-based molecular biomarkers in determining AS eligibility  |       |                     | 9             | Yes          | 9         | Yes          |                                       |                                    |
| 130   | Serum molecular biomarkers now have a clear role in determining eligibility for AS   |       |                     | 3             | Yes          | 3         | Yes          |                                       |                                    |
| 131   | Serum molecular biomarkers may have a role in determining eligibility for AS in future   |       |                     | 7             | Yes          | 7         | Yes          |                                       |                                    |
| 132   | Further prospective studies are needed in order to define the role of serum molecular biomarkers in determining AS eligibility   |       |                     | 8             | Yes          | 8         | Yes          |                                       |                                    |
| 133   | Urine molecular biomarkers now have a clear role in determining eligibility for AS   |       |                     | 3             | Yes          | 3         | Yes          |                                       |                                    |
| 134   | Urine molecular biomarkers may have a role in determining eligibility for AS in future   |       |                     | 7             | Yes          | 7         | Yes          |                                       |                                    |

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Table 1 (continued)

| Q-Num   | HCP statement   | Q-Num | Lived Exp statement   | HCP responses |              |           |              | Lived Exp responses                   |                                    |
|---|---|-------|---|---------------|--------------|-----------|--------------|---------------------------------------|------------------------------------|
|   |   |       |   | R1 median     | R1 consensus | R2 median | R2 consensus | Median score (after group discussion) | Consensus (after group discussion) |
| 135   | Further prospective studies are needed in order to define the role of urine molecular biomarkers in determining AS eligibility  |       |   | 8             | Yes          | 8         | Yes          |                                       |                                    |
| 136   | *NEW BRCA carriers can select AS but need closer surveillance than noncarriers  |       |   | NA            | NA           | 7         | Yes          |                                       |                                    |
| 137   | *NEW ATM carriers can select AS but need closer surveillance than noncarriers   |       |   | NA            | NA           | 7         | Yes          |                                       |                                    |
| 138   | *NEW BRCA status should be determined for all men considering AS  |       |   | NA            | NA           | 4         | Yes          |                                       |                                    |
| 139   | *NEW BRCA status should be determined for men diagnosed at a young age or with a positive family history of prostate cancer   |       |   | NA            | NA           | 7         | Yes          |                                       |                                    |
| 140   | *NEW ATM status should be determined for all men considering AS   |       |   | NA            | NA           | 4         | Yes          |                                       |                                    |
| 141   | *NEW ATM status should be determined for men diagnosed at a young age or with a positive family history of prostate cancer  |       |   | NA            | NA           | 7         | Yes          |                                       |                                    |
| 142   | Other medical conditions and predicted life expectancy should be used to determine whether patients should have AS  |       |   | 8             | Yes          | 8         | Yes          | 7                                     | Yes                                |
| 143   | Patients' preferences should be used to determine whether they should have AS   |       |   | 9             | Yes          | 9         | Yes          | 7.5                                   | Yes                                |
| 144   | Risk calculator tools, taking into account 62–65, should be used to determine whether patients should have AS   | 144   | Risk calculator tools should be used to determine whether patients should have AS                                 | 8             | Yes          | 8         | Yes          | 8                                     | Yes                                |
| 145   | Only patients fit for radical treatment should be offered AS  | 145   | Only patients fit for active treatment should be offered AS   | 6             | No           | 6         | Yes          | 5 (5)                                 | No (no)                            |
| 146   | Only patients fit for definitive local treatment should be offered AS   |       |   | NA            | NA           | 7         | Yes          |                                       |                                    |
| 147   | Only patients aged ≤80 yr should be offered AS  |       |   | 3             | Yes          | 3         | Yes          | 2 (2.5)                               | Yes (yes)                          |
| 148   | Only patients aged ≤75 yr should be offered AS  |       |   | 3             | Yes          | 3         | Yes          | 2 (2.5)                               | Yes (yes)                          |
| 149   | There is no upper age limit below which AS can be offered   |       |   | 5             | No           | 5         | Yes          | 7.5 (9)                               | No (yes)                           |
| 150   | There is no lower age limit below which AS can be offered   |       |   | 8             | Yes          | 8         | Yes          | 6.5 (9)                               | No (yes)                           |
| 151   | Life expectancy of ≥10 yr is necessary to be considered for AS  |       |   | 7             | Yes          | 7         | Yes          | 4.5 (2)                               | No (yes)                           |
| 152   | Life expectancy of ≥15 yr is necessary to be considered for AS  |       |   | 4             | Yes          | 4         | Yes          | 4.5 (2)                               | No (yes)                           |
| 153   | Shorter life expectancy can be accepted in selecting men for AS if they have intermediate-risk disease  |       |   | 7             | Yes          | 7         | Yes          |                                       |                                    |
|   |   | 154   | Biopsy results (eg, cancer grade or “aggressiveness”) should be used to determine whether patients should have AS |               |              |           |              | 8                                     | Yes                                |
| What should happen during AS? Surveillance approaches |   |       |   |               |              |           |              |                                       |                                    |
| 155   | AS should be carried out according to a standardised protocol   | 155   | AS should be carried out according to a management plan   | 7             | Yes          | 7         | Yes          | 8                                     | Yes                                |
| 156   | *NEW AS should be carried out according to a personalised risk-adjusted protocol based on baseline and on-going risk assessment, with frequency and nature of testing based on this risk assessment |       |   | NA            | NA           | 8         | Yes          |                                       |                                    |
| 157   | AS should be carried out according to a protocol that is personally risk adjusted for each individual patient   |       |   | 8             | Yes          | 8         | Yes          | 9                                     | Yes                                |
| 158   | AS should be carried out according to a protocol that is different in the 1st year from that in later years   |       |   | 6.5           | Yes          | 7         | Yes          | 8                                     | Yes                                |
| 159   | AS should be carried out according to a protocol that is different in the first 2 yr to later years   |       |   | 6             | Yes          | 6         | Yes          | 7                                     | Yes                                |
| 160   | When deciding on a risk-adjusted approach to testing during surveillance, test results (biopsy, MRI, rectal examination, and PSA) should be used  |       |   | 9             | Yes          | 9         | Yes          | 8                                     | Yes                                |
|   |   | 161   | When deciding on a risk-adjusted approach to testing during surveillance, personal experience should be used      |               |              |           |              | 8                                     | Yes                                |
| 162   | We are ready to apply a universal risk calculator in AS   |       |   | NA            | NA           | 3         | Yes          |                                       |                                    |

Table 1 (continued)

| Q-Num | HCP statement   | Q-Num | Lived Exp statement | HCP responses |              |           |              | Lived Exp responses                   |                                    |
|-------|---|-------|---------------------|---------------|--------------|-----------|--------------|---------------------------------------|------------------------------------|
|       |   |       |                     | R1 median     | R1 consensus | R2 median | R2 consensus | Median score (after group discussion) | Consensus (after group discussion) |
| 163   | Risk assessment tools should be informed by evidence gained from analysis of large datasets   |       |                     | NA            | NA           | 8         | Yes          |                                       |                                    |
| 164   | When deciding on a risk-adjusted approach to testing during surveillance, family history should be used   |       |                     | 8             | Yes          | 8         | Yes          | 8                                     | Yes                                |
| 165   | *NEW Men on AS are more likely to die from cardiovascular disease than prostate cancer and should be counselled on healthy lifestyle changes                      |       |                     | NA            | NA           | 8         | Yes          |                                       |                                    |
| 166   | *NEW Men should be counselled that a randomised trial showed lifestyle modifications including vegan diet, physical activity, and relaxation are beneficial in AS |       |                     | NA            | NA           | 8         | Yes          |                                       |                                    |
| 167   | *NEW Men on AS should be counselled that red/processed meat and whole dairy products are associated with a greater risk of prostate cancer progression            |       |                     | NA            | NA           | 7         | Yes          |                                       |                                    |
| 168   | *NEW Men on AS should be counselled that physical activity (eg, HIIT) may reduce the risk of progression  |       |                     | NA            | NA           | 7.5       | Yes          |                                       |                                    |
| 169   | Patients should have PSA checked no more than every 3 mo while on AS  |       |                     | 3.5           | No           | 7         | Yes          |                                       |                                    |
| 170   | Patients should have PSA checked at least every 6 mo while on AS  |       |                     | 7             | Yes          | 8         | Yes          |                                       |                                    |
| 171   | Patients should have PSA checked at intervals depending on individual circumstances during AS   |       |                     | 7             | Yes          | 7         | Yes          |                                       |                                    |
| 172   | PSA kinetics should be monitored during AS  |       |                     | 8             | Yes          | 8         | Yes          |                                       |                                    |
| 173   | PSA density should be monitored during AS   |       |                     | 7.5           | Yes          | 8         | Yes          |                                       |                                    |
| 174   | PSA can be monitored in primary care, if there are mechanisms and protocols in place to facilitate shared care  |       |                     | 7             | Yes          | 7         | Yes          |                                       |                                    |
| 175   | PSA should be monitored in secondary/tertiary care only   |       |                     | 3             | Yes          | 3         | Yes          |                                       |                                    |
| 176   | DRE should be performed routinely during AS   |       |                     | 3             | No           | 3         | Yes          |                                       |                                    |
| 177   | DRE should be performed annually during AS  |       |                     | 4             | Yes          | 3         | Yes          |                                       |                                    |
| 178   | DRE should be performed more frequently than annually during AS   |       |                     | 2             | Yes          | 2         | Yes          |                                       |                                    |
| 179   | DRE needs to be done as frequently as PSA during AS   |       |                     | 2             | Yes          | 2         | Yes          |                                       |                                    |
| 180   | DRE is unnecessary if routine mpMRI is being performed during AS  |       |                     | 8             | Yes          | 8         | Yes          |                                       |                                    |
| 181   | DRE does not need to be used routinely to identify progression in AS if routine imaging is available  |       |                     | NA            | NA           | 8         | Yes          |                                       |                                    |
| 182   | Multiparametric MRI should be performed routinely during AS   |       |                     | 7.5           | Yes          | 7         | Yes          |                                       |                                    |
| 183   | Multiparametric MRI should be performed annually during AS  |       |                     | 4             | Yes          | 4         | Yes          |                                       |                                    |
| 184   | Multiparametric MRI should be performed more frequently than annually during AS   |       |                     | 2             | Yes          | 2         | Yes          |                                       |                                    |
| 185   | Multiparametric MRI should be performed if PSA rises significantly during AS  |       |                     | 8             | Yes          | 8         | Yes          |                                       |                                    |
| 186   | Multiparametric MRI should be done based on a change in PSA density during AS   |       |                     | 6             | Yes          | 6         | Yes          |                                       |                                    |
| 187   | Multiparametric MRI should be performed if PSA rises above an absolute threshold of 10 ng/ml during AS  |       |                     | 6             | Yes          | 6         | Yes          |                                       |                                    |
| 188   | Multiparametric MRI should be performed if PSADT is <2 yr during AS   |       |                     | 6             | Yes          | 6         | Yes          |                                       |                                    |
| 189   | Multiparametric MRI should be performed if PSADT is <3 yr   |       |                     | 6             | Yes          | 6         | Yes          |                                       |                                    |

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Table 1 (continued)

| Q-Num | HCP statement   | Q-Num | Lived Exp statement | HCP responses |              |           |              | Lived Exp responses                   |                                    |
|-------|---|-------|---------------------|---------------|--------------|-----------|--------------|---------------------------------------|------------------------------------|
|       |   |       |                     | R1 median     | R1 consensus | R2 median | R2 consensus | Median score (after group discussion) | Consensus (after group discussion) |
| 190   | during AS<br>*NEW Protocol-based biopsies can be omitted only if a centre is confident that their MRI has a sufficiently high negative predictive value   |       |                     | 7             | Yes          | 7         | Yes          |                                       |                                    |
| 191   | *NEW MRI during surveillance should be reported according to the PRECISE criteria   |       |                     | 7             | Yes          | 7         | Yes          |                                       |                                    |
| 192   | *NEW MRI targeted biopsies during AS can cause "grade inflation"  |       |                     | 7             | Yes          | 7         | Yes          |                                       |                                    |
| 193   | *NEW Grade inflation from MRI targeted biopsies can lead to overtreatment   |       |                     | 6             | No           | 6         | Yes          |                                       |                                    |
| 194   | Prebiopsy MRI should be performed before reclassification systematic TRUS-guided biopsies in men on AS, together with MRI targeted biopsies when indicated  |       |                     | 8             | Yes          | 8         | Yes          |                                       |                                    |
| 195   | *NEW A confirmatory biopsy should always be performed for men on AS, whatever be the initial biopsy findings or MRI findings  |       |                     | NA            | NA           | 6.5       | Yes          |                                       |                                    |
| 196   | MRI and targeted biopsies should replace systematic biopsies in AS  |       |                     | 6             | No           | 5.5       | Yes          |                                       |                                    |
| 197   | MRI and targeted biopsies should be used only in conjunction with systematic biopsies in AS   |       |                     | 6             | Yes          | 6         | Yes          |                                       |                                    |
| 198   | MRI and targeted biopsies are superior to systematic biopsies during AS   |       |                     | 6             | Yes          | 6         | Yes          |                                       |                                    |
| 199   | Negative MRI indicates that a scheduled surveillance biopsy is no longer necessary  |       |                     | 4             | Yes          | 4         | Yes          |                                       |                                    |
| 200   | *NEW MRI in AS should be reported in a standardised manner (eg, PRECISE criteria)   |       |                     | NA            | NA           | 7.5       | Yes          |                                       |                                    |
| 201   | *NEW Image quality for MRI should be recorded in a standardised manner (eg, PIQUAL criteria)  |       |                     | NA            | NA           | 7         | Yes          |                                       |                                    |
| 202   | Negative MRI, in combination with other stable negative predictors (low PSA kinetics, low PSA density), may support the decision to omit additional TRUS-guided biopsies at routine repeat biopsies, at least on an individual basis, with adequate counselling |       |                     | 8             | Yes          | 8         | Yes          |                                       |                                    |
| 203   | Repeat biopsy should be performed based on a time-based protocol without specific triggers to prompt a biopsy during AS   |       |                     | 5.5           | No           | 6         | Yes          |                                       |                                    |
| 204   | Repeat biopsy should be performed annually during AS  |       |                     | 3             | Yes          | 3         | Yes          |                                       |                                    |
| 205   | Repeat biopsy should be performed every 2 yr during AS  |       |                     | 4             | No           | 4         | Yes          |                                       |                                    |
| 206   | Repeat biopsy should be performed 1 yr after commencing AS, then only if indicated based on other criteria  |       |                     | 4             | No           | 4         | Yes          |                                       |                                    |
| 207   | Repeat biopsies should be performed at routinely scheduled intervals throughout AS  |       |                     | 4             | Yes          | 4         | Yes          |                                       |                                    |
| 208   | Protocols that include scheduled biopsies are more likely to have higher rates of conversion to active intervention   |       |                     | 7             | Yes          | 7         | Yes          |                                       |                                    |
| 209   | Downgrading on repeat biopsy should influence the subsequent intervals and nature of repeat diagnostic testing in AS  |       |                     | 6             | Yes          | 6         | Yes          |                                       |                                    |
| 210   | Reclassification biopsy should be performed only if progression is seen on mpMRI  |       |                     | 3.5           | Yes          | 3.5       | Yes          |                                       |                                    |
| 211   | Reclassification biopsy should be performed if PSA rises significantly during AS  |       |                     | 7             | Yes          | 7         | Yes          |                                       |                                    |

Table 1 (continued)

| Q-Num | HCP statement   | Q-Num   | Lived Exp statement   | HCP responses |              |           |              | Lived Exp responses                   |                                    |
|-------|---|---------|---|---------------|--------------|-----------|--------------|---------------------------------------|------------------------------------|
|       |   |         |   | R1 median     | R1 consensus | R2 median | R2 consensus | Median score (after group discussion) | Consensus (after group discussion) |
| 212   | Reclassification biopsy should be performed if PSA rises above an absolute threshold of 10 ng/ml during AS  |         |   | 5             | Yes          | 5         | Yes          |                                       |                                    |
| 213   | Reclassification biopsy should be performed if PSADT is <2 yr during AS   |         |   | 6             | Yes          | 6         | Yes          |                                       |                                    |
| 214   | Reclassification biopsy should be performed if PSADT is <3 yr during AS   |         |   | 5             | Yes          | 5         | Yes          |                                       |                                    |
| 215   | Reclassification biopsy should be performed if progression is suspected based on DRE  |         |   | 7             | Yes          | 7         | Yes          |                                       |                                    |
| 216   | A scheduled surveillance biopsy should be done regardless of negative MRI   |         |   | 4             | Yes          | 4         | Yes          |                                       |                                    |
| 217   | When first diagnosed, patients may benefit from separate appointments for discussing diagnosis and decision-making, to allow them time to process emotions, gather information, and formulate questions   | 217     | When first diagnosed, patients may benefit from separate appointments for discussing diagnosis and decision-making, to allow them time to process their feelings, read-up, and think of questions | 8             | Yes          | 8         | Yes          | 8                                     | Yes                                |
| 218   | Patients should be offered intervention at every AS consultation, irrespective of surveillance parameters   | 218     | Patients should be offered active treatment at every AS consultation, no matter what their test results show  | 3             | Yes          | 3         | Yes          | 3                                     | Yes                                |
|       |   | 219     | Being repeatedly offered active treatment when test results are stable causes anxiety and unnecessary acceptance of active treatment  |               |              |           |              | 8                                     | Yes                                |
| 220   | Patients for whom AS remains a safe management plan should be reassured and their decision to remain on AS actively encouraged to improve adherence   | 220     | Patients for whom AS remains a safe management plan should be reassured and their decision to remain on AS actively encouraged to help them stay on AS  | 8             | Yes          | 8         | Yes          | 9                                     | Yes                                |
| 221   | Patient anxiety should be considered a valid trigger for reclassification investigations during AS  | 221-223 | If a patient experiences anxiety during AS, it should be used as a sign that tests are needed, and possibly active treatment  | 6             | Yes          | 6         | Yes          | 5                                     | No                                 |
| 222   | Patient anxiety or depression should trigger a detailed conversation between the patient and the clinician  |         |   | NA            | NA           | 8         | Yes          |                                       |                                    |
| 223   | Patient anxiety should be considered a trigger for treatment, even in the absence of reclassification during AS   |         |   | 4.5           | Yes          | 4         | Yes          |                                       |                                    |
| 225   | Patient depression should be considered a trigger for treatment, even in the absence of reclassification during AS  |         |   | 5             | Yes          | 4         | Yes          |                                       |                                    |
| 226   | Holistic needs assessment should be considered at the outset of surveillance and during surveillance, with further assessment and support available to them   |         |   | NA            | NA           | 8         | Yes          |                                       |                                    |
| 227   | Interventions designed to improve trust in AS should be utilised during AS to improve adherence   |         |   | 8             | Yes          | 8         | Yes          |                                       |                                    |
| 228   | Identifying when men are making assessments of risk based mainly on their emotions (and not the synthesis of information provided by their clinician) is important when making shared decisions during AS | 228     | If patients seem to be making decisions based mainly on how they feel, they would benefit from more information and support   | 7             | Yes          | 7         | Yes          | 8                                     | Yes                                |
| 229   | Partner and family attitudes are strongly associated with men's decision-making before and during AS  |         |   | 7             | Yes          | 7         | Yes          |                                       |                                    |
|       |   | 230     | *NEW More research is needed on supporting patients from a range of backgrounds and in a range of settings to consider AS when they meet the criteria   |               |              |           |              | 7.5                                   | Yes                                |
|       |   | 231     | *NEW Nationally agreed guidelines would help support  |               |              |           |              | 9                                     | Yes                                |

(continued on next page)



Table 1 (continued)

| Q-Num | HCP statement  | Q-Num   | Lived Exp statement   | HCP responses |              |           |              | Lived Exp responses                   |                                    |
|-------|--|---------|---|---------------|--------------|-----------|--------------|---------------------------------------|------------------------------------|
|       |  |         |   | R1 median     | R1 consensus | R2 median | R2 consensus | Median score (after group discussion) | Consensus (after group discussion) |
|       |  | 232     | patients from a range of backgrounds and in a range of settings to consider AS when they meet the criteria<br>*NEW Nationally available patient information would help support patients from a range of backgrounds and in a range of settings to consider AS when they meet the criteria |               |              |           |              | 9                                     | Yes                                |
| 233   | Adequate, clear, and consistent information is a major unmet support need for men undergoing AS  | 233     | Better, clearer, and more consistent information is a major unmet support need for patients undergoing AS   | 8             | Yes          | 8         | Yes          | 8.5                                   | Yes                                |
| 234   | Educating partners is important during AS, as a means of improving adherence   | 234     | Educating partners is important during AS, as a means of helping patients to stay on surveillance   | 8             | Yes          | 8         | Yes          | 9                                     | Yes                                |
| 235   | Support groups are an important support for men during AS  | 235     | Support groups are an important support for patients during AS  | 8             | Yes          | 8         | Yes          | 9                                     | Yes                                |
| 236   | Support groups may be actively unhelpful for men during AS   | 236     | Support groups may be actively unhelpful for patients during AS   | 5             | Yes          | 5         | Yes          | 2                                     | Yes                                |
| 237   | Clinician attitudes are strongly associated with men's decision-making before and during AS  | 237     | The attitudes of doctors and nurses have a strong influence on patients' decisions around AS  | 9             | Yes          | 8         | Yes          | 7.5                                   | Yes                                |
| 238   | Educating clinicians on AS is important as a means of improving patients' adherence  | 238     | Educating clinicians on AS is important to help keep patients on surveillance   | 8             | Yes          | 8         | Yes          | 9                                     | Yes                                |
| 239   | AS should be considered a subspecialty area of practice  |         |   | 5             | Yes          | 5         | Yes          |                                       |                                    |
| 240   | The AS protocol for an individual patient should be communicated to their GP/primary care physician, including frequency of monitoring testing and triggers suggesting possible progression for urgent re-referral |         |   | NA            | NA           | 9         | Yes          |                                       |                                    |
| 241   | AS uptake and adherence could be improved by the introduction of clearer national guidelines   | 241–242 | More patients would take up and stick with AS if there were clearer national and international guidelines   | 8             | Yes          | 8         | Yes          | 9                                     | Yes                                |
| 242   | AS uptake and adherence could be improved by the introduction of clearer international guidelines  |         |   | 8             | Yes          | 8         | Yes          |                                       |                                    |
| 243   | Well-being programmes have an important role in supporting men during AS   | 243     | Well-being programmes have an important role in supporting patients during AS   | 7             | Yes          | 7         | Yes          | 7.5                                   | Yes                                |
| 244   | Well-being programmes have an important role in improving adherence during AS  |         |   | 7             | Yes          | 7         | Yes          |                                       |                                    |
| 245   | Further research is needed to determine the role of well-being programmes in AS  |         |   | 8             | Yes          | 8         | Yes          |                                       |                                    |
| 246   | Dietary modification has an important role for improving the overall health of men on AS   | 246     | Adjusting diet is important during AS   | 6             | Yes          | 7         | Yes          | 8.5                                   | Yes                                |
| 247   | Further research is needed to inform recommendations on the importance of dietary modification during AS   |         |   | 8             | Yes          | 8         | Yes          |                                       |                                    |
|       |  | 248     | Exercise is important during AS   |               |              |           |              | 8.5                                   | Yes                                |
|       |  | 249     | Mindfulness is helpful during AS  |               |              |           |              | 7                                     | Yes                                |
| 250   | Daily 5-alpha reductase inhibitors may have a role in men on AS<br>When and how should AS end? Triggers for testing and treatment during AS  |         |   | 5             | No           | 5         | Yes          |                                       |                                    |
| 251   | A change in PSA or DRE should lead to a biopsy being done  |         |   | 4             | Yes          | 4         | Yes          | 2.5                                   | No                                 |
| 252   | A change in DRE should lead to a biopsy being done   |         |   | NA            | NA           | 4         | Yes          |                                       |                                    |
| 253   | A change in PSA or DRE should lead to MRI with a biopsy if the MRI shows a change  |         |   | 8             | Yes          | 8         | Yes          | 7                                     | Yes                                |
| 254   | A change in DRE does not need a biopsy if the MRI is reassuring  |         |   | NA            | NA           | 8         | Yes          |                                       |                                    |
| 255   | *NEW MRI showing multifocal lesions should lead to additional  |         |   | NA            | NA           | 7         | Yes          |                                       |                                    |

Table 1 (continued)

| Q-Num                            | HCP statement  | Q-Num | Lived Exp statement | HCP responses |              |           |              | Lived Exp responses                   |                                    |
|----------------------------------|--|-------|---------------------|---------------|--------------|-----------|--------------|---------------------------------------|------------------------------------|
|                                  |  |       |                     | R1 median     | R1 consensus | R2 median | R2 consensus | Median score (after group discussion) | Consensus (after group discussion) |
| 256                              | biopsy<br>*NEW MRI showing multifocal lesions should lead to a discussion of active treatment  |       |                     | NA            | NA           | 5.5       | Yes          |                                       |                                    |
| 257                              | A change in PSA or DRE should lead to discussion of active treatment   |       |                     | 3.5           | Yes          | 4         | Yes          | 5                                     | No                                 |
| 258                              | Switching from AS to active treatment should be decided based on PSA alone   |       |                     | 1             | Yes          | 1         | Yes          | 1                                     | Yes                                |
| 259                              | Switching from AS to active treatment should be decided based on biopsy results alone  |       |                     | 4             | No           | 4         | Yes          | 3                                     | Yes                                |
| 260                              | Switching from AS to active treatment should be decided based on MRI changes alone   |       |                     | 2             | Yes          | 2         | Yes          | 3                                     | Yes                                |
| 261                              | MRI targeted biopsy should be used to determine the need for intervention  |       |                     | 6.5           | Yes          | 6.5       | Yes          |                                       |                                    |
| 262                              | Switching from AS to active treatment should be decided based on patient preference alone  |       |                     | 4             | Yes          | 4         | Yes          | 2.5                                   | Yes                                |
| 263                              | Switching from AS to active treatment should be decided based on a combination of changes in test results and patient discussion   |       |                     | 9             | Yes          | 9         | Yes          | 8                                     | Yes                                |
| 264                              | Upgrading to Gleason grade 3 + 4 should act as a trigger for discussion of intervention  |       |                     | 6             | Yes          | 6         | Yes          |                                       |                                    |
| 265                              | Upgrading to Gleason grade 4 + 3 should act as a trigger for recommending treatment  |       |                     | 8             | Yes          | 8         | Yes          |                                       |                                    |
| 266                              | An increase in the number of positive cores at reclassification biopsy should act as a trigger for recommending treatment  |       |                     | 6             | No           | 6         | Yes          |                                       |                                    |
| 267                              | An increase in the % positive cores at reclassification biopsy should act as a trigger for discussing treatment in AS  |       |                     | 6             | Yes          | 6         | Yes          |                                       |                                    |
| 268                              | A change in PSA density should act as a trigger for further investigation (eg, MRI or biopsy)  |       |                     | 6             | Yes          | 6         | Yes          |                                       |                                    |
| 269                              | A change in PSA density should act as a trigger for further investigation  |       |                     | 3             | Yes          | 3.5       | Yes          |                                       |                                    |
| 270                              | PSA doubling time of < 3 yr should act as a trigger for further investigation  |       |                     | 4             | Yes          | 4         | Yes          |                                       |                                    |
| 271                              | PSA doubling time of <2 yr should act as a trigger for further investigation   |       |                     | 4.5           | Yes          | 4         | Yes          |                                       |                                    |
| 272                              | PSA doubling time of <1 yr should act as a trigger for further investigation   |       |                     | 5             | Yes          | 5         | Yes          |                                       |                                    |
| 273                              | A PSA velocity of >1 ng/ml/yr should act as a trigger for further investigation  |       |                     | 4.5           | Yes          | 4         | Yes          |                                       |                                    |
| 274                              | PSA kinetics should not be used as stand-alone triggers for discussing treatment   |       |                     | 7             | Yes          | 7.5       | Yes          |                                       |                                    |
| 275                              | PSA kinetics should be used to determine further investigation   |       |                     | NA            | NA           | 7         | Yes          |                                       |                                    |
| 276                              | Further research is warranted into the role of PSA velocity as a noninvasive predictor of underlying histological progression in men who have been stable on AS for a significant period of time |       |                     | 8             | Yes          | 8         | Yes          |                                       |                                    |
| “Graduating to watchful waiting” |  |       |                     |               |              |           |              |                                       |                                    |
| 277                              | Patients who are on AS and reach a point at which they would no longer be recommended AS due to age or life expectancy should be “graduated” to watchful waiting                                 |       |                     | 8             | Yes          | 8         | Yes          | 6                                     | No                                 |
| 278                              | Patients should be “graduated” to watchful waiting if they are on AS when they turn 75 yr old  |       |                     | 3             | Yes          | 3         | Yes          | 3                                     | Yes                                |
| 279                              | Patients should be “graduated” to watchful waiting if they are on AS when they turn 80 yr old  |       |                     | 4             | Yes          | 4         | Yes          | 3                                     | Yes                                |
| 280                              | Patients should be “graduated” to watchful waiting if they are on AS, and it is determined that their life expectancy is $\leq 10$ yr  |       |                     | 7             | Yes          | 7         | Yes          | 2.5                                   | Yes                                |
| 281                              | A change in intent from AS to watchful waiting, agreed between the patient and the clinician, should be recorded in the patient record and communicated to the GP                                |       |                     | NA            | NA           | 9         | Yes          |                                       |                                    |
| 282                              | Patients should be ‘graduated’ to watchful waiting if they are on AS and it is determined their life expectancy is $\leq 5$ years  |       |                     | 8             | Yes          | 8         | Yes          | 4                                     | Yes                                |

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Table 1 (continued)

| Q-Num | HCP statement  | Q-Num | Lived Exp statement  | HCP responses |              |           |              | Lived Exp responses                   |                                    |
|-------|--|-------|--|---------------|--------------|-----------|--------------|---------------------------------------|------------------------------------|
|       |  |       |  | R1 median     | R1 consensus | R2 median | R2 consensus | Median score (after group discussion) | Consensus (after group discussion) |
|       |  | 283   | *NEW Transition to less intensive monitoring, or watchful waiting, should be based on a combination of age/life expectancy                         |               |              |           |              | 5                                     | Yes                                |
|       |  | 284   | *NEW Transition to less intensive monitoring, or watchful waiting, should be based on a combination of test results (eg, stability of PSA/DRE/MRI) |               |              |           |              | 7                                     | Yes                                |
|       |  | 285   | *NEW Transition to less intensive monitoring, or watchful waiting, should be based on a combination of joint discussion with the patient           |               |              |           |              | 8                                     | Yes                                |
|       | What are the priorities for future research?   |       |  |               |              |           |              |                                       |                                    |
| 286   | Further research should focus on ensuring that all patients have access to best practice care wherever and whoever they are  |       |  | 8             | Yes          | 8         | Yes          | 9                                     | Yes                                |
| 287   | *NEW Future research should assess the role of germline determinants of aggressive prostate cancer   |       |  | NA            | NA           | 7         | Yes          |                                       |                                    |
| 288   | *NEW Future research should include the development of decision-making aids for patients and healthcare professionals  |       |  | NA            | NA           | 7         | Yes          |                                       |                                    |
| 289   | *NEW Research should include ways to support men and their loved ones  |       |  | NA            | NA           | 7         | Yes          |                                       |                                    |
| 290   | *NEW Life expectancy tools for use in decision-making in AS should be assessed   |       |  | NA            | NA           | 6         | Yes          |                                       |                                    |
| 291   | *NEW Exploring reasons why men did not choose AS would be a valuable research area   |       |  | NA            | NA           | 7         | Yes          |                                       |                                    |
| 292   | Future studies should focus on determining the best standardised protocol for AS in all patients   |       |  | 8             | Yes          | 8         | Yes          | 8.5                                   | Yes                                |
| 293   | Future studies should focus on determining how to adjust the timing and nature of assessments for individual patients, according to their risk assessment  |       |  | 9             | Yes          | 8         | Yes          | 8                                     | Yes                                |
| 294   | Improving diagnostic pathways to address overdiagnosis is essential in reducing the number of patients who will never progress on surveillance and would benefit from not knowing about a very-low-risk cancer |       |  | 7             | Yes          | 7         | Yes          | 7                                     | Yes                                |
| 295   | Improving tests such as MRI and biopsy promises to improve adherence to AS and reduce the rates of unnecessary active treatment, based on anxiety alone  |       |  | 7             | Yes          | 7         | Yes          | 8                                     | Yes                                |
| 296   | Novel pathological and molecular diagnostic techniques should be assessed for their role in AS   |       |  | NA            | NA           | 7         | Yes          |                                       |                                    |
| 297   | The role of AI in AS should be explored  |       |  | NA            | NA           | 8         | Yes          |                                       |                                    |
| 298   | The role of MRI during AS needs to be clarified  |       |  | 8             | Yes          | 8         | Yes          | 7                                     | Yes                                |
| 299   | *NEW The role of advanced ultrasound technologies in AS needs to be clarified  |       |  | NA            | NA           | 7         | Yes          |                                       |                                    |
| 300   | *NEW The role and sequence of MRI and biopsy in men on AS should be evaluated  |       |  | NA            | NA           | 8         | Yes          |                                       |                                    |
| 301   | Understanding how to safely reduce the burden on AS for individual patients, healthcare providers, and healthcare systems should be considered a research priority   |       |  | 7             | Yes          | 7         | Yes          | 9                                     | Yes                                |
| 302   | *NEW The role of ancillary practice providers in efficient AS programmes should be explored  |       |  | NA            | NA           | 7         | Yes          |                                       |                                    |
| 303   | AS uptake and adherence are known to vary between self-identifying racial groups and between socioeconomic classes. Research is now needed to ensure that AS is inclusive of all                               |       |  | 8             | Yes          | 7         | Yes          | 9                                     | Yes                                |
| 304   | *NEW The role of telemedicine in improving access and lessening disparities in adoption and continuance of AS needs to be explored   |       |  | NA            | NA           | 7         | Yes          |                                       |                                    |
| 305   | *NEW The risks of adverse events (pelvic or extrapelvic mets, recurrence after radical treatment) need to be clarified in men on   |       |  | NA            | NA           | 7         | Yes          |                                       |                                    |

Table 1 (continued)

| Q-Num | HCP statement  | Q-Num | Lived Exp statement | HCP responses       |              |                     | Lived Exp responses |                                       |                                    |
|-------|--|-------|---------------------|---------------------|--------------|---------------------|---------------------|---------------------------------------|------------------------------------|
|       |  |       |                     | R1 median consensus | R1 consensus | R2 median consensus | R2 consensus        | Median score (after group discussion) | Consensus (after group discussion) |
| 306   | *NEW Research should focus on how to improve communication and support offered by healthcare providers                       | NA    | NA                  | NA                  | 7            | Yes                 |                     |                                       |                                    |
| 307   | *NEW Communication and support for preference sensitive decision-making should be improved and available to all at diagnosis | NA    | NA                  | NA                  | 7            | Yes                 |                     |                                       |                                    |

AS, including whether these are due to patient noncompliance or accuracy of tests on surveillance

AI = artificial intelligence; AS = active surveillance; DRE = digital rectal examination; GP = general practitioner; Exp = experience; HCP = healthcare and research professionals; HIIT = high-intensity interval training; mets = metastases; LE = lived experience of prostate cancer; mpMRI = multiparametric magnetic resonance imaging; MRI = magnetic resonance imaging; NA = not available; PI-RADS = Prostate Imaging Reporting and Data System; PSA = prostate-specific antigen; PSADT = PSA doubling time; PSMA = prostate-specific membrane antigen; QoL = quality of life; TRUS = transrectal ultrasonography. The bold text indicates discordance between HCP and LE (group medium category/group consensus); italics indicate additional statements or modifications proposed live during consensus meetings; and italics \*NEW indicates additional statements proposed during review period and R1.

physical activity, vegan diet, and relaxation).The HCP panel agreed that further research is needed to inform their role in improving the experience of AS and adherence to AS when the disease is stable.

There was strong agreement that, once the AS decision has been made, active treatment should not be offered routinely at each subsequent visit, as this causes unnecessary anxiety and increased rates of acceptance of active treatment when tests results are stable. There was agreement in the HCP panel that interventions designed to improve trust in AS should be utilised to improve adherence to AS.

3.4.2. Triggers for investigation and treatment

There was HCP agreement that PSA should be monitored every 3–6 mo, and that this could be done in primary care if there are mechanisms and protocols in place to facilitate shared care. There was consensus disagreement with the use of routine DRE but a recognition that DRE may be done for reasons other than assessment of disease progression. There was strong agreement that DRE is unnecessary if multiparametric MRI or other routine imaging (eg, transrectal ultrasonography) is being carried out during AS.

There was agreement that MRI should be done routinely during surveillance, but less frequently than annually. Triggers for requesting MRI include a significant PSA rise, although no agreement about a numerical threshold for this was reached. There was consensus agreement that prebiopsy MRI should be performed before any reclassification biopsies and that MRI-targeted biopsy should be added to standard cores when there is an MRI target. There was agreement that MRI quality should be reported (eg, PIQUAL criteria [23]) and that repeat MRI on AS should be reported in a standardised manner (eg, PRECISE [24]). There was agreement that MRI targeting can cause “grade inflation”, although there was HCP uncertainty that this would lead to overtreatment.

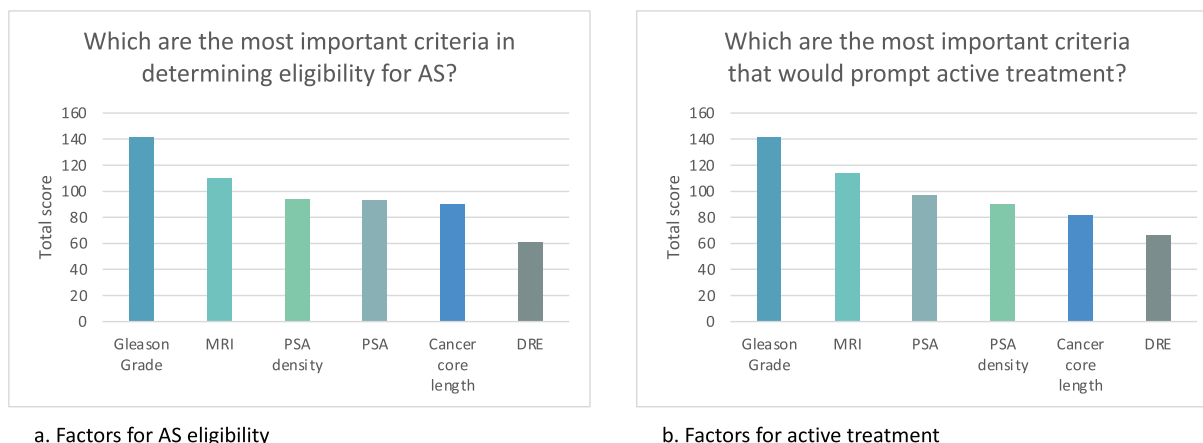
There was agreement that a change in PSA kinetics, PSA density, or DRE should lead to MRI ± biopsy, rather than a treatment discussion. There was also agreement that further research is warranted into the role of PSA velocity as a noninvasive predictor of histological progression.

There was overall agreement that a confirmatory biopsy should be done in AS, but that negative MRI, in combination with other stable negative predictors (eg, stable PSA and low PSA density), can support the decision to omit additional prostate biopsies, at least on an individual basis with adequate counselling.

It was agreed that repeat biopsy should not be performed annually, and there was uncertainty that it should be done routinely, with recognition that protocols that include scheduled biopsies are more likely to have higher rates of conversion to active treatment.

3.5. Switch to active treatment

Both the HCP and the LE panel agreed that switching to active treatment should be done on the basis of a combination of changes in test results and patient discussion, although there was agreement that upgrading to Gleason 4 + 3 should act as a trigger for recommending active treatment. The ranking of factors determining the need for active



**Fig. 3 – Ranking of factors for (A) determining eligibility for surveillance and (B) prompting active treatment. AS = active surveillance; DRE = digital rectal examination; MRI = magnetic resonance imaging; PSA = prostate-specific antigen.**

treatment was similar to that for determining eligibility (Fig. 3B).

### 3.6. Graduation to watchful waiting

There was HCP agreement that those who reach a point where they would no longer be recommended treatment for localised disease should be graduated to less intensive monitoring or watchful waiting (WW), although not based on age or life expectancy alone. The LE panel was in consensus disagreement that graduation to WW should occur at age 75 or 80 yr or for life expectancy of <10 yr, with uncertainty about whether this should occur for life expectancy of <5 yr.

### 3.7. Research priorities

The panel discussions on the AS pathway helped identify, shape, and reach agreement on the final list of ten AS research priorities, across the patient journey (Fig. 4).

The most important priority for research, across both the LE and the HCP panel, is the development of a personalised, dynamic, risk-adapted approach according to an agreed framework, with less testing in men at the lowest risk of progression. This risk-adapted approach contrasts with the current guideline-approved standardised approach.

There was a significant concern raised by the LE panel that a personalised approach might lead to patients being at the discretion of an individual clinician, leading to variable standards of care.

There were also concerns raised about the variation in offering AS across patients in the same health care system and across different health care systems, especially regarding access to MRI and newer biopsy approaches.

## 4. Discussion

### 4.1. Consensus agreement on best practice that differs from current international guidelines

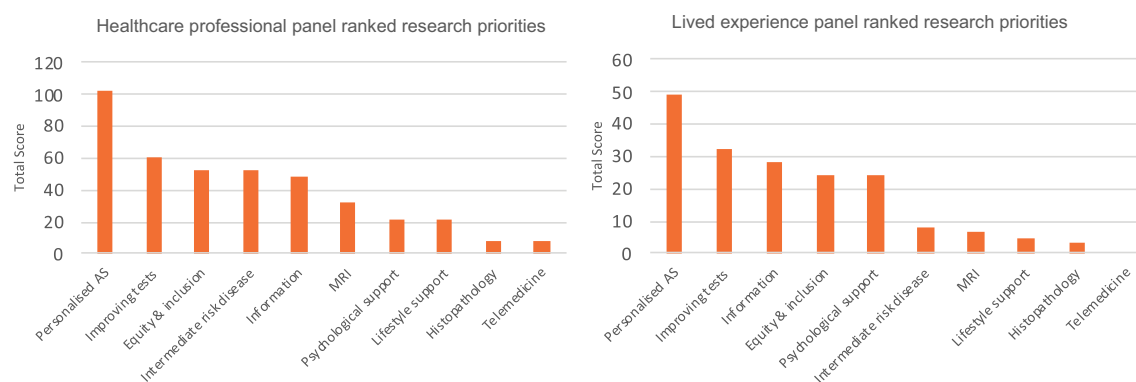
A number of differences between the current consensus opinion (often based on clinical practice) and current guideline recommendations were evident in this work:

1. DRE can be omitted when MRI is used routinely in AS.
2. In men with stable MRI and other stable parameters (PSA kinetics and density), consideration can be given to omitting routine biopsy, with discussion between the clinician and the patient.
3. A change in PSA or DRE (if done) should lead to MRI with the option of a biopsy after this, rather than immediate biopsy or discussion of active treatment.
4. A change to active treatment should be based on a combination of clinical parameters, and the discussion between the clinician and the patient rather than on any single parameter.
5. Men who are suitable for AS but experience, or are at a risk of, significant psychological consequences of AS should be offered additional support rather than immediate active treatment.

It may seem surprising that these findings differ from current guidelines. Part of the reason for this is that guidelines, particularly the more robust ones such as those from the EAU and the UK National Institute for Health & Care Excellence are, quite understandably, based on published data. They also often recommend what is most feasible across a wide range of settings, rather than the latest advances. This can mean that the guidelines take some time to catch up with the most modern practice, started at a small number of pioneering centres, which were well represented in this consensus panel.

The explicit point of expert consensus is to give opinion in areas where data may be less robust and in the process of changing, based on expertise of the consensus panel. The expertise aggregated here is broad, across those with clinical practice across a range of professions (urologists, oncologists, radiologists, pathologists and qualitative researchers) and including those with lived experience of localised prostate cancer, from those on AS, those who have had active treatment, and family members of those with localised prostate cancer.

Expert opinion is also able to draw on common practice that may not yet be reflected in published data and hence in subsequent guidelines. In addition, for some areas, for example, omission of DRE when MRI is performed, there



**Personalised AS:** Understanding how to personalise AS, within an agreed framework, using a dynamic, risk-adapted approach to reduce unnecessary tests and treatment

**Improving tests:** Improving current and emerging tests (including imaging and biomarkers) at diagnosis and during AS to reduce overtreatment

**Equity & inclusion:** Acknowledging and addressing inequities in access to best care in AS. Working to address inequities, including self-identified race, age and socioeconomic factors, to ensure inclusion and retention of all who are eligible to be offered AS

**Intermediate-risk disease:** Exploring the inclusion of men with intermediate risk disease in AS, and adapting monitoring programmes for men with intermediate risk disease

**Information:** Exploring where people go for information about AS. Understanding how information and misinformation are spread. Addressing communication and information gaps with clinicians, patients, families and communities

**MRI:** Defining the role of MRI in AS, including best sequences, targeted and systematic biopsies, and access to high-quality scanning

**Psychological support:** Addressing the need for high-quality, personalised psychological support at diagnosis and during AS, to reduce negative psychological impacts of a new cancer diagnosis and AS

**Lifestyle support:** Understanding the role of support for positive changes in lifestyle and behaviour, in terms of their potential benefits to both prostate and general health, including diet, exercise and other factors

**Histopathology:** Defining the role of histopathology in AS, including the incorporation of new modifications to grading systems and new approaches to biopsies

**Telemedicine:** Understanding the current and future role of telemedicine in delivering best care in AS, including its potential impact on access to care

Fig. 4 – Ranked research priorities (HCP and LE panels). AS = active surveillance; HCP = health care and research professionals; LE = lived experience of prostate cancer; MRI = magnetic resonance imaging.



are data from the area adjacent to AS that can be brought into the discussion; for example, diagnostic pathways that use MRI before biopsy may perform the MRI first and omit DRE, whilst still accepting an abnormal DRE in primary care as an entry route to the pathway. The clinical relevance of this expert consensus process is that the wider community can be reassured that common practice (eg omission of DRE when MRI is done) is supported by expert agreement.

In terms of modern risk stratification, this consensus process acknowledged that the use of Gleason grade and MRI findings, which give an indication of the volume and aggressivity of the tumour, is ranked as the most important criterion in determining the eligibility for and continuation on AS. This reflects a current gap in the guidelines where, whilst MRI is recommended before biopsy and therefore MRI data are widely available in clinical practice, the granular details of MRI data (eg tumour volume) are not specified in risk stratification systems yet. New risk stratification approaches are likely to incorporate MRI data to address this, but widespread data on MRI parameters including tumour volume need to be collected and published.

The use of DRE ranked lowest for both determining eligibility for and continuation on AS, due to its poor positive predictive value and impact on the patient.

In fact, the use of DRE to initiate either additional tests (such as biopsy or MRI) or a treatment choice scored lowest among all tests, including PSA density, which is not commonly included in any of the guidelines. When community practice of AS is considered, according to both European and US studies, the reduction in biopsy frequency as men progress through surveillance can clearly be seen [1,25], as both patients and clinicians see less value in biopsies where PSA, DRE, or MRI findings are stable. This expert consensus is able to recognise this.

#### 4.2. Recognition of wider social and psychological factors

Guidelines often concentrate on the clinical aspects of disease management, whilst this consensus process explicitly sought to acknowledge important social and psychological determinants of entry into and maintaining participation in AS. Having a dedicated lived experience panel was particularly helpful in this regard.

The concept of “surveillance fatigue” was discussed where men and their families become tired of the process and uncertainty of surveillance, and choose active treatment despite the stability of objective disease parameters. It was acknowledged that the inclusion of routine biopsies in surveillance increases surveillance fatigue, as does difficulty in accessing communication with the health care team [8]. Kinsella and colleagues [26] showed that the use of an educational intervention reduced dropout rates at 5 yr, without evidence of progression from 41.5% at 5 yr to 21.7%. By contrast, an MRI-led AS programme, with no routine biopsies, showed dropout rates at 5 yr in the absence of progression at <1% [27], highlighting that education, support, and a more acceptable surveillance schedule all have an impact.

Similarly, this consensus process identified agreement that men experiencing adverse psychological consequences

from surveillance should be offered additional support, rather than immediate active treatment.

The theme that communication and support are of paramount importance throughout surveillance emerged clearly. Furthermore, addressing both the need for high-quality, personalised psychological support, and communication and information gaps with clinicians, patients, families, and communities was identified as a key research priority.

One priority, that of working to address inequities, including self-identified race, age, and socioeconomic factors, to ensure inclusion and retention of all who are eligible to be offered AS, was felt by many expert panel members to be a priority that ought to be seen as “cutting across” or “threading through” all the others. For instance, improving our understanding of MRI must be approached in a way that takes into account potential disparities in access to the most high-quality imaging, both at diagnosis and later during surveillance.

Each of the identified research priorities will require specific development into a dedicated research project. The topmost priority, across both expert panels, is the development of a personalised, dynamic, risk-adapted approach according to an agreed framework, with less testing in men at the lowest risk of progression. This represents a fundamental break with guideline-based practice in AS, not just in terms of practice, but in terms of the philosophy of care as well. As such, this priority calls for a major programme of research, and Movember has set out a funding call to address this.

#### 4.3. Limitations

There are many more experts in AS for prostate cancer than could be included, and a different panel may have had different outcomes. However a significant effort was made to accurately reflect diverse international thinking and practice across those countries where the conduct and practice of AS are reported widely. This included those with experience of different settings for managing patients with AS—in rural and urban settings, and those offering a broad range of treatments. Similarly, efforts were made to include men with different lived experience of AS, including active treatment.

#### 5. Conclusions

The current best practice of AS includes the use of high-quality MRI to be able to omit routine DRE, and to avoid routine repeat biopsy in those with stable MRI findings and PSA kinetics. In addition, for those settings where MRI access is limited, the use of MRI to determine the need for biopsy is favoured over standard transrectal biopsy promoted by a rise in PSA or a change in DRE.

The importance of an additional support for those on AS was recognised as an important alternative to immediate active treatment, especially for those with a significant risk of greater psychological impact of surveillance.

Working to address inequities, including self-identified race, age, and socioeconomic factors, to ensure inclusion and retention of all who are eligible to be offered AS was

viewed as a research priority and as a potential theme that could inform work on all the other research priorities in the years ahead.

This report outlines future research priorities in AS agreed on by diverse health care professional and lived experience experts. Movember has published an expression of interest for participants in a collaborative research programme on the highest ranked priority of personalised, dynamically adapted AS in 2022.

**Author contributions:** Caroline M. Moore had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

**Study concept and design:** Moore, MacLennan, King, Withington.

**Acquisition of data:** All authors.

**Analysis and interpretation of data:** Moore, MacLennan, King, Withington.

**Drafting of the manuscript:** Moore, MacLennan, King, Withington.

**Critical revision of the manuscript for important intellectual content:** All authors.

**Statistical analysis:** MacLennan.

**Obtaining funding:** Moore.

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**Supervision:** Moore, MacLennan.

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## Appendix A. Supplementary data

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