Best current practice and research priorities in active surveillance for prostate cancer –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 varies significantly across different settings, as does the experience of surveillance – from which tests are offered, and when, to levels of psychological support.

Objective

To explore 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 healthcare 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 was 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 use of high quality MRI which allows DRE to be omitted, that repeat standard biopsy can be omitted when MRI and 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 active surveillance approach, reducing testing for those at 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

Current best practice in active surveillance includes 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 active surveillance for prostate cancer.

Patient summary

A diverse group of experts in active surveillance, including a broad range of healthcare professionals and researchers and those with lived experience of prostate cancer agreed that best practice includes use of high quality MRI, 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.

Introduction

Active surveillance (AS) for localised prostate cancer aims to defer or avoid treatment and its side effects, using repeat testing to detect disease which 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 which could be considered for AS. In the UK, where PSA testing can be requested by patients but is not routinely offered, MRI before biopsy is performed in 80% of men in 2016/2017[4], and biopsy is often omitted in men with a negative MRI and low PSA density. 2018-2019 National Prostate Cancer Audit (NPCA) data shows that low risk prostate cancer 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 the diagnoses of localised prostate cancer in a series assessing risk profile of prostate cancer at diagnosis over 10 years[6]. The United States Preventative Services Taskforce (USPSTF) recommendations in 2008[7] led to a reduction in the proportion of men seen with low risk disease, according to National Cancer Database (NCDB), 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 first year or two 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 which denote MR 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 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 framework.

Materials 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:

- Movember GAP3 [9-13]
- EAU DETECTIVE [14,15]
- Lancet commission[16]
- PIONEER data collaborative[17-20]
- University of Maryland initiative[21].

Some of these focus on the whole prostate cancer pathway (Lancet 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 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.

Study design (Figure 1)

The RAND-UCLA appropriateness method for assessing agreement in areas of uncertainty[22] was used. This includes:

- An evidence review comprising an overview of recent systematic reviews in active surveillance[23]
- Formation of an expert panel of healthcare and research professionals (HCP panel) and one of those with lived experience of prostate cancer (LE panel).
- Iterative development of discussion statements informed by the evidence review and modified by the panels
- Independent scoring of statements for strength of agreement from 1 (strongly disagree) to 9 (strongly agree)
- Analysis of group median scores (where 1-3 shows disagreement, 4-6 shows uncertainty and 7-9 shows agreement)
- Calculation of group consensus (yes, no, or uncertain) based on the inter-percentile range adjusted for symmetry[22]

After scoring, panellists received a summary of their own results, group median scores and consensus status, and the distribution of anonymised scores. Online discussions were held, where statements could be removed, added or modified, prior to re-scoring. 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 (figure 1).

An initial list of potential research priorities was identified from the literature. These were then discussed at each panel, following scoring of the statements across the 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.

Setting and participants (Figure 2, supplementary table 1)

The healthcare professional expert panel included expertise across urology, oncology, radiology, pathology, translational science, population health, psycho-oncology (including behavioural science), general practice, nursing, clinical trials, healthcare 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, 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.

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.

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 7 statements, added 74 statements, and rephrased 31 statements prior to final scoring. The additions were to address the panels' perceived gaps in the statements derived from the narrative review and the rephrasing was necessary to clarify meaning. A total of 307 statements underwent final scoring and analysis across both panels.

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.

Who should be offered active surveillance?

There was consensus and agreement across the two panels that a number of factors, including clinical factors, co-morbidities 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 the next most important (figure 3a). There was much discussion on the use of other

parameters, including cancer core length (in mm), 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.

Age and life expectancy

There was consensus in the LE panel that no upper age limit (e.g. 75 or 80 years old) should be applied, and 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 was also uncertainty and disagreement in the LE panel about whether life expectancy (e.g., 10 or 15 years) 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, that can lead to age discrimination. The HCP panel agreed that a life expectancy of $\geq$ 10 years should be considered within eligibility criteria for AS, with a shorter life expectancy requirement for intermediate risk prostate cancer.

Who is more likely to choose active surveillance?

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

Psychological impact of active surveillance

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.

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.

How should active surveillance be carried out?

a. 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, to learn about the disease, and to 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 to 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 healthcare team.

There was agreement in the LE panel that wellbeing, diet, exercise, and mindfulness are important during AS. There was also consensus among 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 (e.g., physical activity, vegan diet, 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 routinely offered 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 on the HCP panel that interventions designed to improve trust in AS should be utilised to improve adherence to AS.

b. Triggers for investigation and treatment

There was HCP agreement that PSA should be monitored every 3-6 months, 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 mpMRI or other routine imaging (e.g.TRUS) 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 a pre-biopsy MRI should be performed before any re-classification 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 (e.g. PIQUAL criteria[24]), and that repeat MRI on AS should be reported in a standardised manner (e.g. PRECISE[25]). 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 an MRI +/- biopsy, rather than a treatment discussion. There was also agreement that further research is warranted into the role of PSA velocity as a non-invasive predictor of histological progression.

There was overall agreement that a confirmatory biopsy should be done in AS, however that a negative MRI, in combination with other stable negative predictors (e.g., stable PSA, 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 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.

Switch to active treatment

Both the HCP and LE panels 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 treatment were similar to those for determining eligibility (figure 3b).

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 were in consensus disagreement that graduation to WW should occur at aged 75 or 80 or at a life expectancy of < 10 years, with uncertainty about whether this should occur at a life expectancy of less than 5 years.

Research priorities (figure 4)

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.

The most important priority for research, across both the LE and HCP panels, is the development of a personalised, dynamic, risk adapted approach according to an agreed framework, with less testing in men at 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 healthcare system, and across different healthcare systems, especially regarding access to MRI and newer biopsy approaches.

Discussion

Consensus agreement on best practice which differ 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:

- DRE can be omitted when MRI is used routinely in AS

- 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
- 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
- A change to active treatment should be based on a combination of clinical parameters, and discussion between clinician and patient rather than on any single parameter
- Men who are suitable for AS but experience, or are at 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 European Association of Urology (EAU) and the UK National Institute for Health & Care Excellence (NICE) 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 both those with clinical practice across a range of professions (urologists, oncologists, radiologists, pathologists & qualitative researchers, and including those with expertise by 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 which may not yet be reflected in published data, and hence in subsequent guidelines. In addition, for some areas eg omission of DRE when MRI is performed, there are data from area adjacent to AS which can be brought into the discussion eg diagnostic pathways that use MRI before biopsy may do 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, are ranked the most important in determining 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 detail of MRI data eg tumour volume, are not specificied in risk stratification systems yet. New risk stratification approaches are likely to incorporate MRI data to address this, but widespread data collection 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 to initiate a treatment choice, scored lowest of any 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 USA studies, it is clear to see the reduction in biopsy frequency as men progress through surveillance [26, 27], 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.

Recognition of wider social and psychological factors

Guidelines often concentrate on 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 tire of the process and uncertainty of surveillance, and choose active treatment despite the stability of objective disease parameters. It was acknowledged that including routine biopsies in surveillance increases surveillance fatigue, as does difficulty in accessing communication with the healthcare team[8]. Kinsella and colleagues showed that use of an educational intervention reduced drop out rates at 5 years, without evidence of progression from 41.5% at 5 years to 21.7%[28]. In contrast, an MRI-led active surveillance programme, with no routine biopsies, showed drop out rates at 5 years in the absence of progression at <1%[29],

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 were identified as key research priorities.

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, then later during surveillance.

Each of the identified research priorities will require specific development into a dedicated research project. The number one 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 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 such, this priority calls for a major programme of research, and Movember have set out a funding call to address this.

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 significant effort was made to accurately reflect diverse international thinking and practice across those countries where the conduct and practice of AS is widely reported. This included those with experience of different settings for managing patients with AS – in rural and urban settings, and with those offering a broad range of treatments. Similarly, efforts were made to include men with different lived experience of AS, including active treatment.

Conclusions

The current best practice of AS now includes 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, 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 additional support for those on active surveillance was recognised as an important alternative to immediate active treatment, especially for those with 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 of the other research priorities in the years ahead.

This report outlines future research priorities in AS agreed on by diverse healthcare 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 active surveillance in 2022.

Take home message

Current best practice in active surveillance involves the use of MRI before a biopsy decision, enabling digital rectal examination and some biopsies to be avoided. The highest research priority in active surveillance for prostate cancer has been identified as the development of a dynamic, risk adapted approach, according to an agreed framework, to reduce unnecessary testing, and to maximise detection of disease which would benefit from treatment.

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Figure 1 RAND UCLA consensus pathway

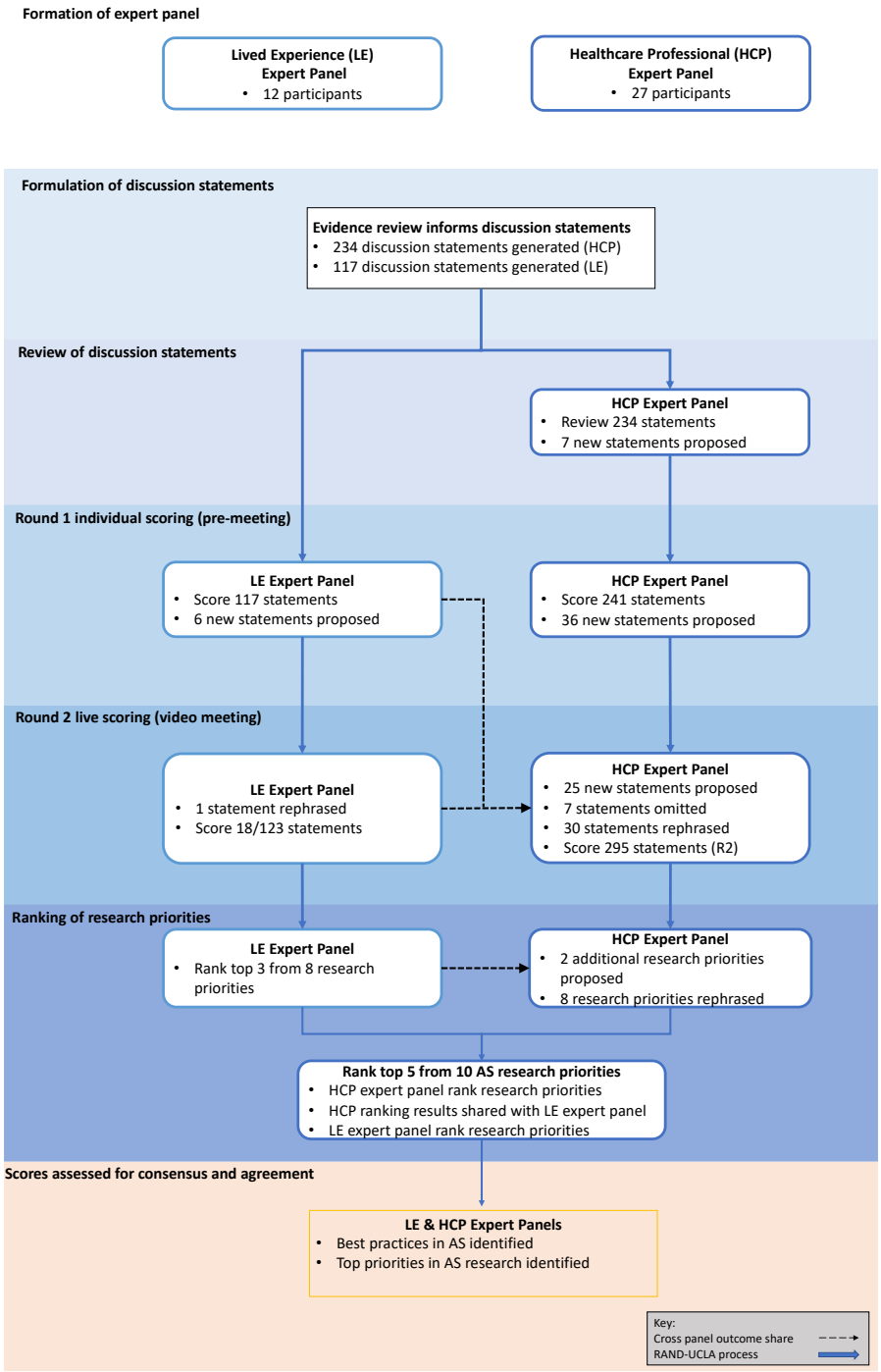


Figure 2 Expert panel participants

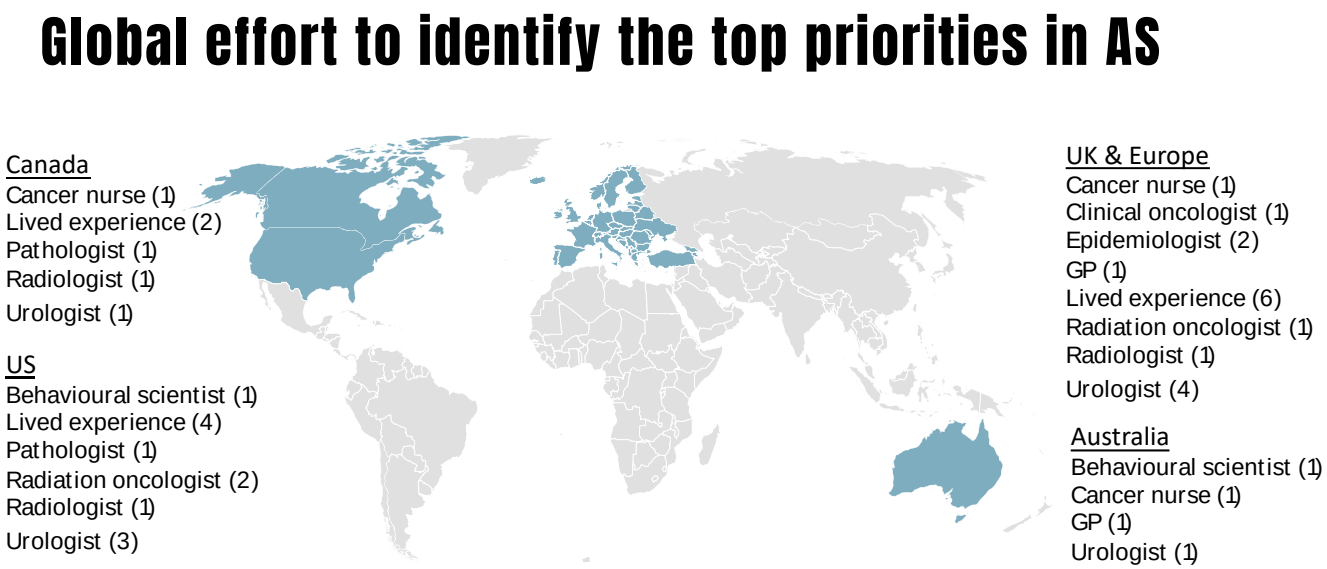
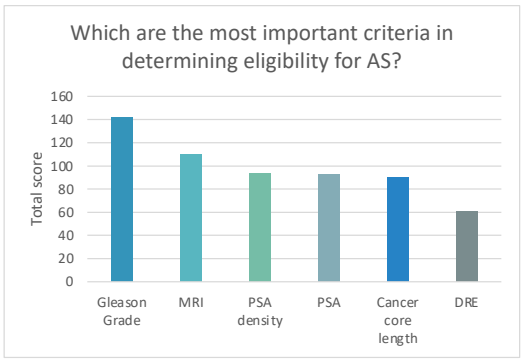
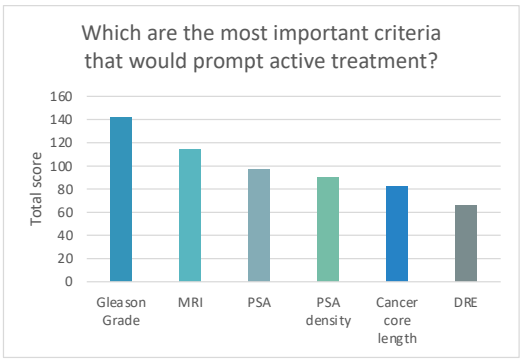


Figure 3 Ranking of factors for determining eligibility for surveillance and prompting active treatment

Fig 3 Ranking of factors for determining eligibility for surveillance and prompting active treatment

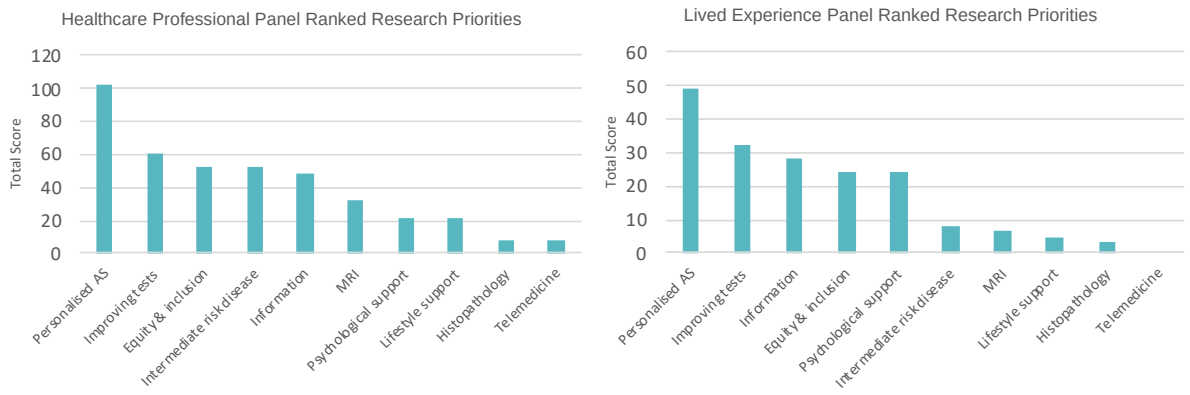


3a. Healthcare professionals



3b. Lived experience panel

Figure 4 Ranked research priorities (HCP and LE panel)



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

Table 1 Scored statements

Q-Num	HCP Statement	Q-Num	Lived Exp Statement	HCP Responses				Lived Exp Responses	
What factors influence the variation in approaches to active surveillance in different settings?				**R1 median**	**R1 Consensus**	**R2 median**	**R2 Consensus**	**Median score (after group discussion)**	**Consensus (after group discussion)**
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 (e.g. the USA) increases the likelihood of men being diagnosed with indolent disease	3	Checking 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 over-diagnosis (e.g. the US Preventive Services Task Force guidance) reduces the likelihood of men being diagnosed with indolent disease.**	**4**	**Checking PSA routinely risks over diagnosing prostate cancer that has a very low chance of causing harm**	**7**	**Yes**	**7**	**Yes**	6	**No**
5	Using multiparametric MRI (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 a 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 no prostate cancer is missed, but risks over diagnosing prostate cancer that has a very low chance of causing harm**	**7**	**Yes**	**7**	**Yes**	5.5	**No**
What factors which 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 active surveillance introduced*			N/A	N/A	8	Yes		
9	**NEW Men who have heard of active surveillance from a clinician before having a PSA test are more likely to choose surveillance for low risk disease than someone who has not*			N/A	N/A	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 (e.g. specialist nurse, surgeon, family doctor) will influence their decision between immediate treatment and AS	14	Who informs a patient about their prostate cancer diagnosis (e.g. 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 over-cautious about recommending AS because of fear of being sued if disease progresses during AS**	**15**	**Doctors might be over-cautious 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 health care system (such as in the USA) makes patients less likely to choose AS**			**6**	**Yes**	**6**	**Yes**	**7.5**	**Yes**
20	**A free at the point of use health care 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 do, 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 which 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 lowest risk needing less testing than those at higher risk	26	In an ideal system, testing *whilst on active surveillance* would be done according to risk, with patients at lowest risk needing less testing than those at higher risk	8	Yes	8	Yes	7.5	Yes
27	In an ideal system, most testing would be non-invasive, and biopsies would only be done 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, email 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 active surveillance 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 Active surveillance should be expanded to include men with a PSA or MRI suspicious of prostate cancer who have not had a biopsy*			N/A	N/A	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 over-monitoring			7	Yes	7	Yes	8	Yes
39	An ideal AS programme aims to reduce over-treatment			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 quality of life 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 active surveillance 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 (e.g. biopsy) during AS affects patients' quality of life**			**7**	**Yes**	**7**	**Yes**	**6.5**	**No**

51	*Side effects of testing (e.g. biopsy) during AS affects patients QoL in the short term*		N/A	N/A	7	Yes		
52	*Side effects of testing (e.g. biopsy) during AS affects patients QoL in the longer term*		N/A	N/A	6.5	Yes		
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 to in person visits*		N/A	N/A	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 active surveillance and should be used in counselling men considering AS*		N/A	N/A	7	Yes		

68	**White patients, *compared to 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 (i.e. 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 1st degree relative) can still be offered AS*			N/A	N/A	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*			N/A	N/A	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*			N/A	N/A	7	Yes		
73	Patients with PSA ≤20ng/mL should be offered AS			5	No	5	Yes		
74	Patients with PSA ≤15ng/mL should be offered AS			5.5	No	5	Yes		
75	Patients with PSA ≤10ng/mL should be offered AS			7	Yes	7	Yes		
76	Patients with PSA density ≤ 0.2 ng/mL/cc should be offered AS			5	Yes	5	Yes		
77	Patients with PSA density ≤ 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 ≤T2a should be offered AS			7	Yes	7	Yes		
80	Patients with clinical T-stage ≤T2b should be offered AS			7	Yes	7	Yes		
81	Patients with clinical T-stage ≤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 for AS		6	Yes	6	Yes
85	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 PIRADS 4 are not suitable for AS*		N/A	N/A	4	Yes
88	*Men with PIRADS 5 are not suitable for AS*		N/A	N/A	7	Yes
89	Patients who have not had multiparametric prostate MRI previously should be offered a 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*		N/A	N/A	6	Yes
94	*PSMA has a clear role in AS*		N/A	N/A	3	Yes
95	*PSMA may have a role in AS*		N/A	N/A	7	Yes
96	*Further studies are needed to determine the role of PSMA in AS*		N/A	N/A	9	Yes

97	Patients with Gleason grade 3+3 should be offered		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 ≤ 20% pattern 4 can be offered AS		7	Yes	7	Yes
100	Patients with Gleason grade 3+4 and ≤ 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 1mm 3 + 3 could be offered AS		7	Yes	7	Yes
103	Patients with ≤ 4 cancer containing cores of a 10-12 core standard biopsy can be offered AS		7	Yes	7	Yes
104	Patients with ≤ 3 cores positive can be offered AS		7	Yes	7.5	Yes
105	Patients with ≤ 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 multiparametric MRI should be used to determine eligibility for AS		5.5	Yes	5	Yes
108	Patients with ≤ 50% cancer in biopsy core can be offered AS		6	Yes	6	Yes
109	Patients with ≤ 33% cancer in biopsy core can be offered AS		7	Yes	7	Yes
110	Patients with ≤ 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 stronger than other methods, such as greatest linear percentage of cancer or greatest millimeter length in a single core, in predicting biochemical recurrence			5.5	No	5.5	Yes	
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 favorable intermediate-risk localized 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	Active surveillance may be offered to select patients with favorable intermediate-risk localized prostate cancer; however, patients should be informed that this comes with a higher risk of developing metastases compared to 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*		N/A	N/A	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	
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 non-carriers*				N/A	N/A	7	Yes		
137	**NEW ATM carriers can select AS but need closer surveillance than non-carriers*				N/A	N/A	7	Yes		
138	**NEW BRCA status should be determined for all men considering AS*				N/A	N/A	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*				N/A	N/A	7	Yes		
140	**NEW ATM status should be determined for all men considering AS*				N/A	N/A	4	Yes		
141	**NEW ATM status should be deternined for men diagnosed at a young age or with a positive family history of prostate cancer*				N/A	N/A	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*				N/A	N/A	7	Yes		
147	Only patients aged ≤ 80 years old should be offered AS				3	Yes	3	Yes	2 (2.5)	Yes (Yes)
148	Only patients aged ≤ 75 years old 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	**A life expectancy of ≥10 years is necessary to be considered for AS**			**7**	**Yes**	**7**	**Yes**	**4.5 (2)**	**No (Yes)**
152	**A life expectancy of ≥15 years is necessary to be considered for AS**			**4**	**Yes**	**4**	**Yes**	**4.5 (2)**	**No (Yes)**
153	A shorter life expectancy can be accepted in selecting men for AS if they have intermediate risk disease			7	Yes	7	Yes		
		154	Biopsy results (e.g. 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 ongoing risk assessment, with frequency and nature of testing based on this risk assessment*			N/A	N/A	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 first year to 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 two years 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*			N/A	N/A	3	Yes		
163	*Risk assessment tools should be informed by evidence gained from analysis of large datasets*			N/A	N/A	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 active surveillance are more likely to die from cardiovascular disease than prostate cancer and should be counseled on healthy lifestyle changes.*			N/A	N/A	8	Yes		
166	**NEW Men should be counseled that a randomized trial showed lifestyle modification including vegan diet, physical activity and relaxation are beneficial in active surveillance.*			N/A	N/A	8	Yes		
167	**NEW Men on active surveillance should be counseled that red/processed meat and whole dairy products are associated with a greater risk of prostate cancer progression.*			N/A	N/A	7	Yes		
168	**NEW Men on active surveillance should be counseled that physical activity (e.g., HIIT) may reduce the risk of progression.*			N/A	N/A	7.5	Yes		
169	Patients should have PSA checked *no more than* every 3 months while on AS			3.5	No	7	Yes		
170	Patients should have PSA checked *at least* every 6 months while on AS			7	Yes	8	Yes		

171	Patients should have PSA checked at intervals dependant on individual circumstance 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 multiparametric MRI 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*			N/A	N/A	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	Multi-parametric 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 10ng/mL during AS			6	Yes	6	Yes
188	Multiparametric MRI should be performed if PSADT is < 2 years during AS			6	Yes	6	Yes
189	Multiparametric MRI should be performed if PSADT is < 3 years during AS			6	Yes	6	Yes
190	**NEW Protocol-based biopsies can only be omitted 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	A pre-biopsy MRI should be performed before re-classification 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 done for men on AS, whatever the initial biopsy findings or MRI findings*			N/A	N/A	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 only be used in conjunction with systematic biopsies in AS			6	Yes	6	Yes
198	MRI and targeted biopsies is superior to systematic biopsies during AS			6	Yes	6	Yes

199	A 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*		N/A	N/A	7.5	Yes
201	**NEW Image quality for MRI should be recorded in a standardised manner eg PIQUAL criteria*		N/A	N/A	7	Yes
202	A 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 two years during AS		4	No	4	Yes
206	Repeat biopsy should be performed one year 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	Re-classification biopsy should be performed only if progression is seen on multiparametric MRI		3.5	Yes	3.5	Yes

211	Re-classification biopsy should be performed if PSA rises significantly during AS			7	Yes	7	Yes		
212	Re-classification biopsy should be performed if PSA rises above an absolute threshold of 10ng/mL during AS			5	Yes	5	Yes		
213	Re-classification biopsy should be performed if PSADT is < 2 years during AS			6	Yes	6	Yes		
214	Re-classification biopsy should be performed if PSADT is < 3 years during AS			5	Yes	5	Yes		
215	Re-classification 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 a 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 to stay on AS	8	Yes	8	Yes	9	Yes

221	**Patient anxiety should be considered a valid trigger for re-classification investigations during AS**	**221-223**	**If a patient experiences anxiety during AS, that 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 clinician***			N/A	N/A	**8**	**Yes**		
223	**Patient anxiety should be considered a trigger for treatment, even in the absence of re-classification during AS**			**4.5**	**Yes**	**4**	**Yes**		
224	**Patient depression should be considered a trigger for re-classification investigations during AS**	**224-225**	**If a patient experiences depression during AS, that should be used as a sign that tests are needed, and possibly active treatment**	**5.5**	**No**	**5**	**Yes**	**4.5**	**No**
225	**Patient depression should be considered a trigger for treatment, even in the absence of re-classification 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*			N/A	N/A	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 active surveillance when they meet the criteria*					7.5	Yes

		231	**NEW Nationally agreed guidelines would help support patients from a range of backgrounds and in a range of settings to consider active surveillance when they meet the criteria*					9	Yes
		232	**NEW Nationally available patient information would help support patients from a range of backgrounds and in a range of settings to consider active surveillance 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*			N/A	N/A	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	Wellbeing programs have an important role in supporting men during AS	243	Wellbeing programs have an important role in supporting patients during AS	7	Yes	7	Yes	7.5	Yes
244	Wellbeing programs have an important role in improving adherence during AS			7	Yes	7	Yes		
245	Further research is needed to determine the role of wellbeing programs in AS			8	Yes	8	Yes		
246	Dietary modification has an important role *for improving the overall health of men on active surveillance*	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			5	No	5	Yes		
When and how should AS end? Triggers for testing and treatment during AS									
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*			N/A	N/A	4	Yes		
253	A change in PSA or DRE should lead to an MRI with 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*			N/A	N/A	8	Yes		

255	**NEW MRI showing multifocal lesions should lead to additional biopsy*		N/A	N/A	7	Yes		
256	**NEW MRI showing multifocal lesions should lead to a discussion of active treatment*		N/A	N/A	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 re-classification biopsy should act as a trigger for *recommending treatment*		6	No	6	Yes		
267	An increase in the % positive cores at re-classification 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 e.g. MRI or biopsy		6	Yes	6	Yes		
269	A change in PSA density should act as trigger *for further investigation*		3	Yes	3.5	Yes		
270	A PSA doubling time < 3 years should act as a trigger *for further investigation*		4	Yes	4	Yes		
271	A PSA doubling time < 2 years should act as a trigger *for further investigation*		4.5	Yes	4	Yes		
272	A PSA doubling time < 1 year should act as a trigger *for further investigation*		5	Yes	5	Yes		
273	A PSA velocity > 1 ng/ml/year 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*		N/A	N/A	7	Yes		
276	Further research is warranted into the role of PSA velocity as a noninvasive predictor of underlying histologic 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 years old			3	Yes	3	Yes	3	Yes
279	**Patients should be 'graduated' to watchful waiting if they are on AS when they turn 80 years old**			**4**	**Yes**	**4**	**Yes**	**3**	**Yes**
280	**Patients should be 'graduated' to watchful waiting if they are on AS and it is determined their life expectancy is ≤ 10 years**			**7**	**Yes**	**7**	**Yes**	**2.5**	**Yes**
281	*A change in intent from active surveillance to watchful waiting, agreed between patient and clinician, should be recorded in the patient record and communicated to the GP*			N/A	N/A	9	Yes		
282	**Patients should be 'graduated' to watchful waiting if they are on AS and it is determined their life expectancy is ≤ 5 years**			**8**	**Yes**	**8**	**Yes**	**4**	**Yes**
		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 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*		N/A	N/A	7	Yes		
288	**NEW Future research should include the development of decision making aids for patients and health care professionals*		N/A	N/A	7	Yes		
289	**NEW Research should include ways to support men and their loved ones*		N/A	N/A	7	Yes		
290	**NEW Life expectancy tools for use in decision making in AS should be assessed*		N/A	N/A	6	Yes		
291	**NEW Exploring reasons why men did not choose AS would be a valuable research area*		N/A	N/A	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 over diagnosis 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 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		N/A	N/A	7	Yes		
297	The role of AI in AS should be explored		N/A	N/A	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*		N/A	N/A	7	Yes		
300	**NEW The role and sequence of MRI and biopsy in men on AS should be evaluated*		N/A	N/A	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*		N/A	N/A	7	Yes		
303	AS uptake and adherence is 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*		N/A	N/A	7	Yes		

305	**NEW The risks of adverse events (pelvic or extra pelvic mets, recurrence after radical treatment) need to be clarified in men on AS, including whether these are due to patient non-compliance or accuracy of tests on surveillance*		N/A	N/A	7	Yes	
306	**NEW Research should focus on how to improve communication and support offered by health care providers*		N/A	N/A	7	Yes	
307	**NEW Communication and support for preference sensitive decision making should be improved and available to all at diagnosis*		N/A	N/A	7	Yes	

Supplementary Table 1: Qualifying Criteria of Expert Panels

1. **Healthcare Professional Expert Panel**

	Panellist	Clinical and Academic Roles	Location	Discipline/ Expertise	Evidence Review	Relevant Collaborative Research
	Steven MacLennan **(chair)**	University of Aberdeen	UK	Health Services Research	DETECTIVE; (Willemse et al, 2022)	PIONEER
1	Caroline M. Moore	University College London; University College London Hospitals Trust	UK	Urology	PRECISE; PRECISION; (Bruinsma et al, 2017); (Merriel et al, 2019); (Schoots et al, 2018); (Schoots et al, 2014); (Stabile et al, 2018);	GAP3; Lancet Global Commission; START; TrueNTH Global Registry; PI-RADS; MAPPED; Movember Global Cancer Advisory Committee
`2	Thomas B. L. Lam	Aberdeen Royal Infirmary; University of Aberdeen	UK	Urology	DETECTIVE; EAU Guidelines 2021; (Willemse et al, 2022)	
3	Arnauld Villers	University Hospital Centre, Lille University	France	Urology	(Bruinsma et al, 2017); (Schoots et al, 2014); (van den Bergh et al, 2014); PRECISION	GAP3; ERSPC; START; ERSPC-study
4	Antonio Finelli	Princess Margaret Hospital; University Health Network and University of Toronto	Canada	Urology		(Timilshina et al, 2021); (Richard et al, 2020); (Wong et al, 2014); (Komisarenko et al, 2016); (Finelli et al, 2011)
5	M. Minhaj Siddiqui	University of Maryland School of Medicine	USA	Urology		Developing Provocative Questions – the Prostate Cancer Active Surveillance Research Initiative (DPQ-PCASRI)

6	Mark Frydenberg	Cabrini Health; Monash University	Australia	Urology	(Bruinsma et al, 2017)	GAP3
7	Ronald C. Chen	University of Kansas Cancer Centre	USA	Radiation Oncology	AUA Guidelines 2018	
8	Brandon A. Mahal	University of Miami	USA	Radiation Oncology	(Butler et al, 2019)	Lancet Global Commission; Movember Global Cancer Advisory Committee
9	Masoom A. Haider	University Health Network, Sinai Health System and University of Toronto	Canada	Radiology	PRECISE	PI-RADS
10	Clare M. C. Tempany	Brigham and Women's Hospital; Harvard Medical School	USA	Radiology		PI-RADS
11	Nicholas James	The Institute of Cancer Research London	UK	Clinical Oncology		Lancet Global Commission
12	Francesco Giganti	University College London; University College London Hospital NHS Foundation Trust	UK	Radiology	PRECISE; (Schoots et al, 2018); (Schoots et al, 2014); (Stabile et al, 2018); PRECISION	MAPPED
13	Theodorus H. van der Kwast	University Health Network, Princess Margaret Cancer Centre, University of Toronto	Canada	Pathology	DETECTIVE; EAU Guidelines 2021; (Willemse et al, 2022)	ERSPC; GAP3; ERSPC-study
14	Mahul B. Amin	University of Southern California, University of Tennessee	USA	Pathology	(Amin et al, 2014)	
15	Nynikka R. Palmer	University of California San Francisco	USA	Behavioural Science, Population Health, Public Health	(Kith et al, 2021)	(Osterberg et al, 2017)
16	Camille E. Short	University of Melbourne	Australia	Behavioural Science, Health Psychology, Public Health	(McIntosh et al, 2019)	
17	Netty Kinsella	The Royal Marsden Hospital; King's College London	UK	Cancer Nursing	(Kinsella et al, 2018); (Kinsella et al, 2018)	

18	Margaret I. Fitch	University of Toronto	Canada	Cancer Nursing		Movember Global Cancer Advisory Committee; (Fitch et al, 2017); (Fitch et al, 2020); (Pang et al, 2018)
19	Jane Crowe	Australian Prostate Centre	Australia	General Practice	(Murphy et al, 2014)	
20	Samuel W. D. Merriel	University of Exeter	UK	General Practice	(Merriel et al, 2019)	
21	Mieke Van Hemelrijck	King's College London	UK	Epidemiology	GAP3; (Kinsella et al, 2018); (Kinsella et al, 2018)	PIONEER
22	Monique J. Roobol	Erasmus University Medical Centre	The Netherlands	Epidemiology	DETECTIVE, GAP3, PRIAS, (Murphy et al, 2014); (Shill et al, 2021); (Bruinsma et al, 2017); (Merriel et al, 2019); (Schoots et al, 2018); (Loeb et al, 2015); PRECISION;	ERSPC; PIONEER; ERSPC-study
23	Stacy Loeb	New York University; Manhattan Veterans Affairs Medical Centre	USA	Urology	(Murphy et al, 2014); (Loeb et al, 2015)	
24	Francis I. Chinegwundoh	Barts Health NHS Trust; City University of London	UK	Urology		PROCESS
25	Matthew R. Cooperberg	University of California San Francisco	USA	Urology	(Murphy et al, 2014); (Dall'Era et al, 2012); (van den Bergh et al, 2014); (Leapman et al; 2022); (Washington et al, 2020)	(Osterberg et al, 2017)
26	Anita V. Mitra	University College London Hospitals	UK	Radiation Oncology		IMPACT; MAPPED
27	Catherine C. Paterson	University of Canberra, Canberra Health	Australia	Cancer Nursing	DETECTIVE; (Willemse et al, 2022)	

2. Lived Experience Expert Panel

	Panellist	Patient Advocacy Organisation	Location	Evidence Review	Relevant research/advocacy roles
	Steven MacLennan **(chair)**		as above	as above	as above
1	Ken Mastris	European Prostate Cancer Coalition/EUROPA UOMO (treasurer and acting secretary); Association of Prostate Cancer Patients in London and Essex (chair)	UK		PIONEER; European Cancer Patient Coalition (former president); Tackle Prostate Cancer UK (former chair);
2	Erik Briers	European Prostate Cancer Coalition/EUROPA UOMO (vice chair); Anticancer Fund (advisory board member)	Belgium	DETECTIVE; EAU Guidelines 2021; (Willemse et al, 2022)	PIONEER; European Society of Radiology (patient advisory group member); European Association of Urology (prostate cancer guidelines committee member)
3	Philip Segal	Prostate Cancer Support Canada- Active Surveillance Nationwide Support Group; Prostate Cancer Support Toronto (board member)	Canada		Movember True North - Peer Navigation Program (peer support); Active Surveillance Patients International (former board)
4	Howard Wolinksy	Answer Cancer (AnCan) Foundation (advisory board member)	USA		Active Surveillance Patients International (co-founder); AnCan Virtual Support Group (co-founder); TheActiveSurveillor.com (editor)
5	Mark Andrews		UK		
6	Anthony Henry	The Walnut Foundation (vice president)	Canada		Movember True North - Peer Navigation Program (peer support)
7	Mark Lichty	Active Surveillance Patients International (president)	USA		Developing Provocative Questions – the Prostate Cancer Active Surveillance Research Initiative (DPQ-PCASRI)
8	John Freeman		UK		

9	Stephen Gibbs		UK		
10	Joseph Gallo	Active Surveillance Patients International (board)	USA		AnCan (support group moderator)
11	James Schraidt	ZERO The End of Prostate Cancer (board)	USA		AnCan (support group moderator); Active Surveillance Patients International (former board)
12	Patient Advocate		Europe		