Active surveillance for prostate cancer: an update

Sam Merriel, GP and Clinical Senior Research Fellow, University of Exeter

An increasing number of men diagnosed with localised prostate cancer has been accompanied by more men being considered for active surveillance as a management option. Here the author provides an update on recent developments in active surveillance and changes to NICE guidance.

Active surveillance is a management strategy for men with prostate cancer that involves regular monitoring for signs of cancer progression in order to avoid, or delay, more radical treatments in patients whose prostate cancer does not progress rapidly.

Active surveillance is commonly offered as a treatment option to men with localised low-risk, and sometimes intermediate-risk, prostate cancer. Increasing numbers of men are being considered for active surveillance in the context of the rise in the number diagnosed with localised prostate cancer in recent years.

The issue of active surveillance was last addressed in *Trends in Urology and Men's Health* in 2014,[1] and this article seeks to update readers on developments in active surveillance in recent years and changes introduced by the latest NICE guidance for prostate cancer diagnosis and management.[2]

Long-term outcomes for active surveillance

Two major randomised controlled trials with long-term follow up data comparing outcomes for men on watchful waiting/active monitoring, versus surgery/radiotherapy have recently published their results. The Prostate Testing for Cancer and Treatment (ProtecT) trial recruited men from the positive screening arm of a UK-wide PSA screening study, and randomly assigned them to active monitoring, radical prostatectomy and radiotherapy from 1999 to 2009. These men were then followed up for a median of 10 years. The ProtectT trial found no difference in cancer-related or all-cause mortality between the three study arms, although the mortality rate across the entire study population was low.[3] Men randomised to active monitoring had a higher risk of cancer progression compared with those receiving surgery or radiotherapy, but a lower risk of urinary incontinence or erectile dysfunction.[4] These findings were consistent with the PIVOT study conducted in the USA.[5]

The Swedish Prostate Cancer Group-4 (SPCG-4) study randomly assigned men with localised prostate cancer to radical prostatectomy or watchful waiting, recruited over 10 years from 1989 to 1999, and followed them for 29 years through to 2017. Men on watchful waiting in this study received no immediate treatment or active monitoring, except a transurethral resection of the prostate (TURP) if indicated, which is different from modern active surveillance protocols. The SPCG-4 study found men with localised prostate cancer and a longer life expectancy gained a mean 2.9 years of life from surgery compared with watchful waiting.[6]

NICE, 2019[2]	British Association of Urological Surgeons, 2017[8]	European Association of Urology (EAU), 2018[9]
Prostate-specific antigen (PSA) <10ng/mL Gleason score ≤6 Clinical stage T1–T2a	PSA <10ng/mL Gleason score ≤6 Clinical stage T1–T2 <50% of biopsy cores positive	PSA <10ng/mL Gleason score ≤6 Clinical stage T1–T2a

Table 1. UK and European guidance for identifying low-risk prostate cancer patients

Assessing risk

Following a diagnosis of prostate cancer, risk stratification is performed to estimate whether a man is a low-, intermediate-, or high-risk of cancer progression and mortality. There are numerous factors that can be used to perform this risk stratification.[7] Most guideline recommendations include prostate specific antigen (PSA), clinical stage from a digital rectal examination (DRE) and Gleason score as important factors. Table 1 shows current guidance from the UK and Europe.

Treatment discussions

Men diagnosed with low-risk prostate cancer, who are suitable for radical

What effect does each treatment option have on survival?	The evidence does not show a difference in the number of deaths from prostate cancer among people offered active surveillance, prostatectomy or radical radiotherapy. People who had not died of prostate cancer were: • 98 out of 100 patients offered active surveillance • 99 out of 100 patients offered radical prostatectomy • 99 out of 100 patients offered radical radiotherapy
What effect does each treatment option have on disease progression?	There is good evidence that both prostatectomy and radiotherapy reduce disease progression compared with active surveillance. Signs of disease progression were reported in: • 21 out of 100 patients offered active surveillance • 8 out of 100 patients offered radical prostatectomy • 8 out of 100 patients offered radical radiotherapy
What effect does each treatment option have on urinary function?	There is some evidence that urinary function is better for people offered active surveillance or radiotherapy than those offered prostatectomy. At six months, problems were reported in: • 39 out of 100 patients offered active surveillance • 71 out of 100 patients offered radical prostatectomy • 38 out of 100 patients offered radical radiotherapy
What effect does each treatment option have on erectile dysfunction?	There is some limited evidence that sexual function is better for people offered active surveillance or radiotherapy than those offered prostatectomy. At six months, moderate/severe problems in erectile function were reported in: • 29 out of 100 patients offered active surveillance • 66 out of 100 patients offered radical prostatectomy • 48 out of 100 patients offered radical radiotherapy

Table 2. NICE guidance on discussing benefits and harms of treatment options for low-risk localised prostate cancer[2]

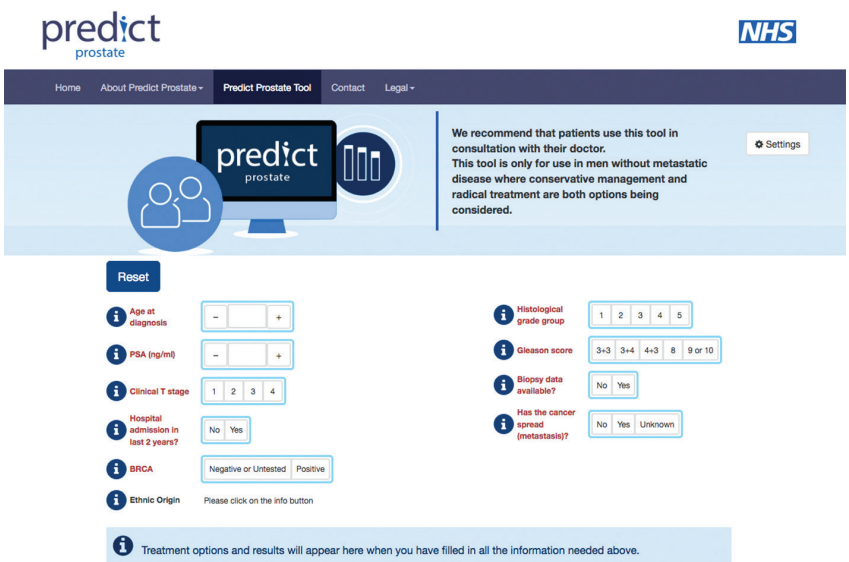

Figure 1. Predict Prostate, an online individualised prognostic tool for men with localised prostate cancer (https://prostate.predict.nhs.uk)

treatment, should be given the choice of active surveillance, radical prostatectomy or radical radiotherapy.[2] This choice is not a straightforward one for patients, as they have to weigh up the risk of cancer progression versus the potential side-effects of radical treatments. Table 2 shows the NICE recommendations for treatment discussions with men in this situation, informed by the findings from the ProtecT trial.

Communicating risk to patients is an important skill for any clinician, and men faced with the decision about whether to commence active surveillance value clear information about all of their options.[10] The updated NICE guidance employs numerical methods to try to translate population level risks to the individual patient. A new tool that produces personalised risk information for men with prostate cancer, called Predict Prostate, is freely available for patients and clinicians to use online (see Figure 1). Predict Prostate uses individual patient data to provide prognostic and treatment information, and presents it in six different modes to help tailor this information to meet a patient's communication preferences. It has been developed as a collaboration between clinicians, scientists and communications experts, and has been shown to reduce variation in clinicians' estimates of mortality risk.

Active surveillance protocols

Patients undergoing active surveillance for prostate cancer are regularly monitored by their treatment team for signs of cancer progression. Following an initial consultation, patients will have PSA testing, DRE, and imaging and/or biopsy at regular intervals. The timing and frequency of these monitoring tests, and which tests are done, varies significantly within the UK, and internationally.[10] The recommended protocol from the recently update NICE guidance can

Timing	Tests
Year 1 of active surveillance	Measure prostate- specific antigen (PSA) every three to four months Monitor PSA kinetics throughout active surveillance A digital rectal examination (DRE) at 12 months A multiparametric MRI at 12 to 18 months
Year 2 and every year thereafter until active surveillance ends	Measure PSA every six months Monitor PSA kinetics throughout active surveillance DRE every 12 months

Table 3. NICE NG131 protocol for active surveillance[2]

be found in Table 3.

Future of active surveillance

The use of active surveillance for prostate cancer remains an evolving area of clinical practice, but many questions are still unanswered by currently available evidence. For example, which patients should be offered active surveillance? How can progression for localised prostate cancer be accurately predicted? What is the best protocol to use for men undergoing active surveillance? And what is the role of multiparametric MRI in follow up for patients on active surveillance? Further large trials of men with prostate cancer on active surveillance with long-term follow up are ongoing[11,12] and will publish their results in the future that may continue the evolution of active surveillance as a treatment modality.

Declarations of interest: *none declared.*

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Key points

- Active surveillance is a treatment option for men with low-risk prostate cancer
- Risk of mortality for men with prostate cancer on active surveillance is almost the same as for men who receive surgery or radiotherapy. Their risk of cancer progression is higher, but the risk of urinary symptoms and erectile dysfunction is lower
- Active surveillance protocols vary significantly between and within countries