NICE National Institute for Health and Care Excellence

March 2021 exceptional surveillance of suspected cancer: recognition and referral (NICE guideline NG12)

Surveillance report
Published: 25 March 2021

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Surveillance decision

We are reconsidering the evidence that is relevant to the recommendations on prostate-specific antigen (PSA) testing to guide referral for suspected prostate cancer. The recommendations could potentially be updated.

Exceptional surveillance review summary

Reasons for considering this area

The NICE guideline on suspected cancer covers identification of possible prostate cancer and recommends use of age-specific reference range for PSA. Clinicians have queried whether use of this age-specific reference range misses high grade cancers in older men and have advised that the recommendation is out of step with 2 studies which use a PSA level of 3 ng/mL to refer.

Methods

To review the impact on NICE guidance we took the following approach:

- We assessed the query against recommendations on PSA testing to guide referral for suspected prostate cancer and considered the evidence used to originally develop the recommendations.
- We examined the NICE event tracker for relevant ongoing and published events.

Full updated literature searches were not needed because the information we had obtained was enough to establish whether an update to the guideline was needed.

For further information see ensuring that published guidelines are current and accurate in developing NICE guidelines: the manual.

Surveillance proposal

How the guideline was developed

The relevant review questions in the NICE guideline are:

- What is the risk of prostate cancer in patients presenting in primary care with symptom(s)?
- Which investigations of symptoms of suspected prostate cancer should be done with clinical responsibility retained by primary care?

The recommendations currently state:

Recommendation 1.6.2: Consider a prostate-specific antigen (PSA) test and digital rectal examination to assess for prostate cancer in men with:

- any lower urinary tract symptoms, such as nocturia, urinary frequency, hesitancy, urgency or retention or
- erectile dysfunction or
- visible haematuria. **[2015]**

Recommendation 1.6.3: Refer men using a suspected cancer pathway referral (for an appointment within 2 weeks) for prostate cancer if their PSA levels are above the age-specific reference range. **[2015]**

During the development of the NICE guideline, the committee noted that there was no strong primary care evidence available on which to base a recommendation for what level of PSA should prompt a suspected cancer pathway referral. They therefore agreed to accept the age-specific reference range, which had previously been recommended by the UK Prostate Cancer Risk Management Programme (PCRMP) in 2008 (NHS Cancer Screening Programmes evidence document 2010).

As prostate cancer is less common in younger men, the committee considered whether or not to specify an age range in the recommendations for which symptoms should prompt PSA testing and digital rectal examination. They agreed not to do this as some risk factors, such as ethnicity, might warrant testing at a lower age.

A subsequent surveillance review in 2020 concluded that the NICE guideline did not need updating as the review did not find any new evidence specific for prostate cancer.

New intelligence

Clinicians have queried the age-specific PSA range used within NICE guidance. A clinical urologist suggested that use of an age-specific reference range for PSA levels risks missing high grade cancers in older men and is out of step with the following 2 studies which use a PSA level of 3 ng/mL to refer:

- The ProtecT trial (2020) is a prospective, multicentre PSA testing programme followed by a randomised trial of active monitoring, radical prostatectomy and radical radiotherapy in men aged 50 to 69 years with localised prostate cancer (n=82,429 men). In the ProtecT trial men with a PSA level of greater than or equal to 3 ng/mL were referred to secondary care as part of the enrolment criteria. The study found that there was no difference in disease-specific mortality between active monitoring, radical radiotherapy treatments, and radical prostatectomy at 10-year median follow up.
- The European Randomised study of Screening for Prostate Cancer (ERSPC) (2021) is a randomised study in 8 European countries on the benefits of screening for prostate cancer (n=184,000 men). The ERSPC study protocol shows that since 1997 a cut off value of greater than or equal to 3 ng/mL PSA was used for enrolment. A 13-year follow up of the ERSPC (2014) showed 1.28 fewer prostate cancer deaths per 1,000 men randomised to PSA screening, which was not felt to be sufficient to justify population-based screening.

Both of these studies were considered by the PCRMP and PSA referral values were realigned to the evidence from these 2 trials. Subsequently, Public Health England (PHE) issued guidance in 2020 on advising well men about the PSA test for prostate cancer: information for GPs. This guidance states: if the PSA is over 3 ng/mL, the GP is advised to refer.

Conclusions

Clinicians have queried the use of an age-specific PSA range, which relates to the prostate cancer section of the NICE guideline on suspected cancer. A clinical urologist suggested that use of an age-specific reference range for PSA levels risks missing high grade cancers in older men and is out of step with 2 studies that use a PSA level of 3 ng/mL to

refer, which informed the PCRMP reconsideration of PSA thresholds and subsequently PHE guidance.

As the PSA level for referral in the NICE guideline differs from recent studies and PHE guidance, further examination of the evidence is warranted to see if any update to the NICE guideline recommendations are needed.

Equalities

One enquirer considered that using age-specific PSA values may represent an inequality in care for older men. This issue does not appear to have been raised at the time of guideline development when age-specific PSA thresholds seem to have been clinical practice in the UK.

ISBN: 978-1-4731-4109-4