PSA-nity Check:

Rethinking Fixed Cutoffs in Prostate Cancer Screening

Sarah Curtis, Hannah Fearon, Liverpool Clinical Laboratories

Aims

Prostate is the most common cancer in men in the UK, with 51,575 new cases diagnosed in 2021[1]. There is no national screening programme; NICE NG12 recommends any male over 50 years to be able to access a PSA test, even if asymptomatic. Many laboratories do not differentiate requests for asymptomatic screening versus individuals with symptoms, applying non-specific reference intervals to both categories.

The European Association of Urology (2025) recommend primary care physicians refer asymptomatic males with PSA >3.0 µg/L for further investigation, while NICE CKS Diagnosis of Prostate Cancer (2025) classifies PSA >3.0 µg/L in asymptomatic males as 'raised'. There are different, age-related, PSA cut offs outlined in NICE NG12 for use in those symptomatic of prostate cancer.

We performed a retrospective study on 45,369 primary care PSA results produced by three different methods at four different laboratories within Cheshire and Merseyside to assess the impact on potential referral rates for suspected prostate cancer of (1) symptomatic versus asymptomatic clinical cut-offs, and (2) the impact of analytical method.

Methods

PSA requests from primary care over 12 months from Liverpool Clinical Laboratories (LCL, Roche), St Helens and Knowsley (STHK, Siemens), Warrington and Halton (WHTH, Siemens), and Countess of Chester (COCH, Beckman) were reviewed. Inclusion criteria were: male, primary care, quantitative result, age >20 years, no renal, liver or bone co-morbidities (normal ALT, ALP and creatinine). These 45,369 results comprised the total PSA set. A 'screening' subset of 10,970 results was produced by exclusion of requests that contained any of 71 clinical details potentially suggestive of prostate cancer or symptoms of such; e.g. 'LUTS', 'CaP', 'Ca', 'retention'.

Results

The median PSA result varied between the four sites and exhibited the same pattern as would be expected given the bias evident in external quality assurance (EQA) reports for each of the analytical platforms in use, with a range between medians of 0.14 µg/L at 40-49 years, 0.20 µg/L at 50-59 years, 0.40 µg/L at 60-69 years, 0.60 µg/L at 70-79 years, and 0.90 µg/L at 80+ years. LCL (Roche, positive bias on EQA) produced the highest median for all age categories >50 years, and COCH (Beckman, negative bias on EQA) the lowest median values of all laboratories.

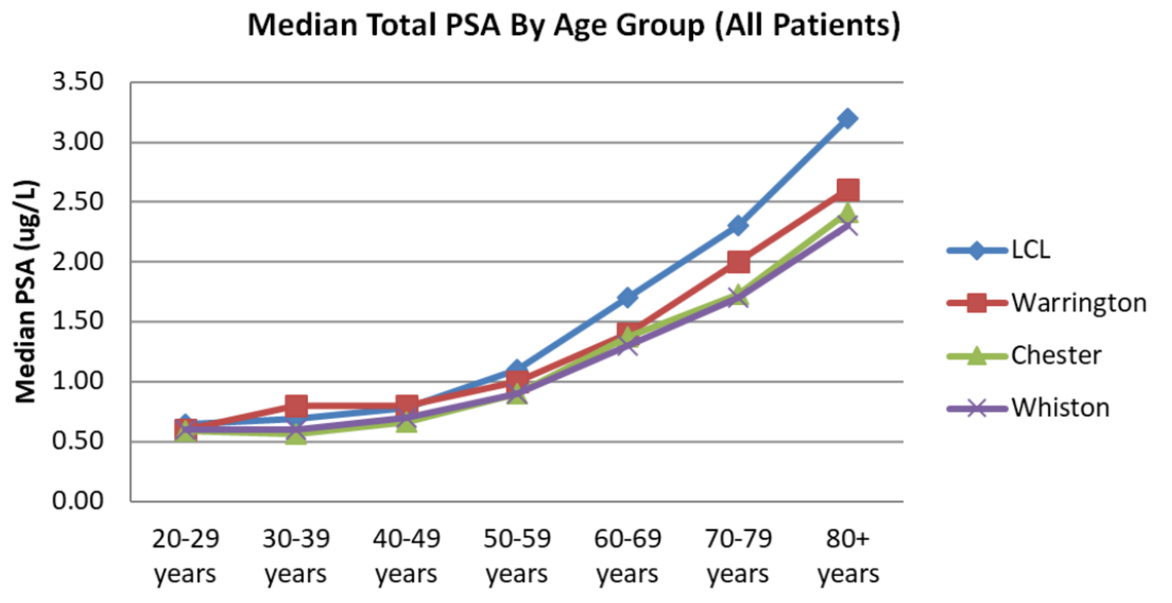

Figure 1: median PSA for all results across age categories according to method.

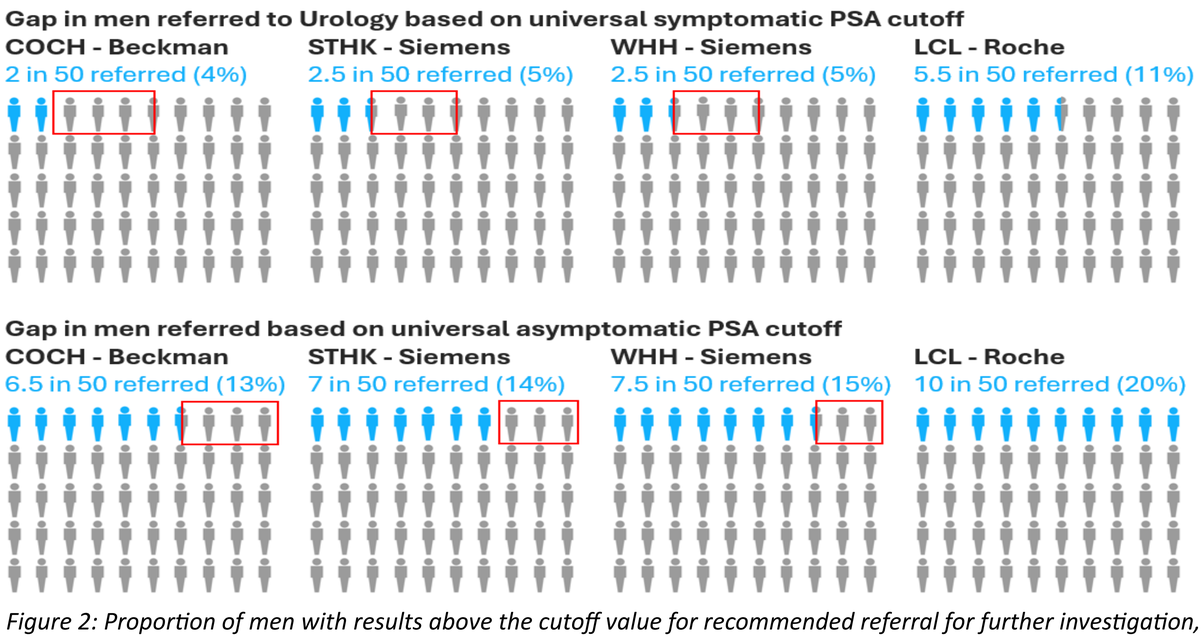

Figure 2: Proportion of men with results above the cutoff value for recommended referral for further investigation, according to site of analysis and analytical manufacturer.

The proportion of results that would be designated as 'raised' when the symptomatic age-related cut-offs from NG12 were applied to 50 to 69 year olds in the screening subset was 9.1% across all laboratories, increasing to 15.2% when the asymptomatic cut-off of >3.0 µg/L was used. The lowest proportion of results meeting the criteria for further investigation was at COCH (Beckman, negative bias on EQA) and the highest proportion at LCL (Roche, positive bias on EQA).

Conclusions

Our data suggests that using a universal PSA cut-off for referral for prostate cancer investigation may introduce **systemic bias and inequity** as patient populations that are tested via analytical methods with a relative positive bias to the mean (Roche) are more likely to have further investigations, and **those tested via assays with relative negative bias** (Siemens and Beckman) may miss follow up opportunities, leading to **delayed diagnosis, potential patient harm** and **poorer outcomes**.

Clinical outcome data is required to correlate these findings with the stage at which patients are being diagnosed with prostate cancer

Recommendations

1. Laboratories should introduce a question at the point of request to classify whether PSA requests are for symptomatic screening, monitoring, or asymptomatic screening, and should report reference intervals as appropriate to these categories to ensure correct flagging.

2. Laboratories should educate clinicians on the bias between different analytical platforms and the impact that this may have on the proportion of patients who exceed the clinical cut-offs for further investigation as published in the NICE and EAU guidelines.

References

1.UK cancer statistics | World Cancer Research Fund . https://www.wcrf.org/preventing-cancer/cancer-statistics/uk-cancer-statistics/. Accessed Sept 2025