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Original Article

General practitioner perception of prostate-specific antigen testing has improved, but more awareness of prostate cancer risk in younger patients is still awaited

David R. Thurtle [a, *, †], Emma M. Gordon [b, *, †], Robert D. Brierly [c], Ciaran J. Conway [d], John McLoughlin [b]

[a] Academic Urology Group, Department of Surgery, University of Cambridge, UK and West Suffolk Hospital NHS Foundation Trust, Bury St Edmunds, UK
[b] Department of Urology, West Suffolk Hospital NHS Foundation Trust, Bury St Edmunds, UK
[c] Department of Urology, Ipswich Hospital NHS Trust, Ipswich, UK
[d] General Practice Registrar, Severn Deanery, University of Bristol, Bristol, UK

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ABSTRACT

Background: In 2006, a county-wide survey of general practitioners (GPs) in the United Kingdom (UK) identified a reluctance to refer younger men with abnormal prostate specific antigen (PSA) levels. Younger men have the most to gain from early-detection of prostate cancer (PCa), which remains a national government priority in the UK and around the world. We sought to assess changes in perception of abnormal PSA-values amongst UK GPs over the past 10 years.

Materials and methods: A total of 500 self-administered paper questionnaires were distributed to individually named GPs. One hundred and forty two responded (28.4%), representing a patient population of ~600,000. A series of visual analogue questions assessed referral thresholds and understanding of risk factors related to the development of PCa.

Results: GPs with a median of 23-years experience responded. Although mean PSA threshold for referral to urology did fall between 2006 and 2016 in both the 45-year (5.42 ng/mL vs. 4.61 ng/mL $P = 0.0003$) and 55-year (5.81 ng/mL vs. 5.30 ng/mL $P = 0.0164$) age groups, the median referral values were unchanged. Significantly, referral thresholds quoted for younger men (<65 years) were considerably higher than recommended UK maximum PSA-levels. Using case-based scenarios, practitioners appeared more likely to refer older men with abnormal PSA values, with GPs reporting an average 56.2% likelihood of referring an asymptomatic 55-year-old with elevated age-adjusted PSA of 4.6 ng/mL. A total of 95.1% recognised a family history of PCa to be a potential risk factor but other at-risk categories were not so clearly understood.

Conclusion: Awareness of abnormal PSA values in UK primary care is improving, but continues to lag behind the evidence. Strategies to disseminate knowledge of maximum PSA-values to GPs should focus especially on those for younger patients.

1. Introduction

Prostate cancer (PCa) is the commonest male cancer across Europe; one in eight United Kingdom (UK) men will be diagnosed with PCa in their lifetime.[1] Prostate specific antigen (PSA) testing was introduced in the 1990s. It has subsequently been used as an *ad hoc* diagnostic tool in the UK. The use of PSA and an increasing awareness of PCa has facilitated a migration towards increased detection and at an earlier stage,[2] but with it has brought concerns of overdiagnosis and overtreatment.[3] It was on this basis that age-adjusted PSA levels were introduced in 1993[4] in an attempt to both highlight younger men at risk of PCa and also to reduce the number of older men having unnecessary invasive investigations. These same PSA ranges have actually been revised downwards over the

* Corresponding author. Academic Urology Group, Department of Surgery, University of Cambridge, Addenbrooke's Hospital, Hills Road, Cambridge, CB2 0QQ, United Kingdom.
E-mail address: dt433@cam.ac.uk (DR Thurtle).
† Authors contributed equally to this work.

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past 10 years (Table 1) with the appreciation that a proportion of men with lower PSA can harbour significant PCa.[5,6] It is in younger men (aged < 60 years) with high-risk disease that the survival impact of surgical intervention may be most valuable.[7] Unlike some European countries, there is no formal PSA screening programme in the UK, but the National Institute of Health and Clinical Excellence (NICE) have clear recommendations that informed men over 50 years of age who ask for the test should be offered the test,[8] as well as those with lower urinary tract symptoms or abnormal digital rectal examination.[9] GPs are to refer to urology if the patient's PSA is above the age-adjusted reference range.[10]

In 2006 a survey of general practitioners (GPs) throughout Suffolk, in England, showed a particular reluctance to refer younger men with abnormal PSA levels.[11] It is logical, that younger men have the most to gain from early diagnosis and curative treatment. Indeed, the latest evidence suggests a particular advantage to curative surgical therapy in younger men and those with high-risk disease.[7,12]

Given that early diagnosis of malignancy has been a consistent UK government policy over the past decade,[13] and in the context of this updated evidence, it would be hoped there has been a shift in GP perception of abnormal PSAs particularly in younger men.

A repeated survey of GPs was performed in 2015/2016 to assess change in perception of abnormal PSA-values in primary care. We hypothesised that PSA values for referral would have fallen in line with the latest maximum age-adjusted PSA values.

2. Materials and methods

Following local study approval, a self-administered questionnaire was developed at the West Suffolk Hospital and Ipswich Hospital based upon the previously used questionnaire. A series of visual analogue questions assessed referral behaviour. Demographic information, years since qualification, and questions on exposure to PCa was also sought in addition to questions surrounding brief clinical vignettes. The full questionnaire is available in the appendices with additional questions added regarding risk factors for high-risk groups. A total of 500 paper questionnaires were distributed, by mail, to named GPs in the two hospitals' combined catchment area. All responses were anonymous to maintain confidentiality. Individuals inputting data were blinded to the providence of each response. Anonymized returns precluded the chasing of responses. Data was recorded and analysed in MS Excel 2010 (Microsoft, Washington, USA). Statistical analysis was performed using StatsDirect (StatsDirect Ltd, Cheshire, UK).

3. Results

The population of the surveyed area was ~600,000. A total of 142 GPs responded (28.4%) of which 125 (88.0%) contained complete data. Eighty one (57.0%) responders were male, 103 (72.5%) had been qualified longer than 15 years. The median estimated number of men investigated by PSA per GP each month was two (range 0–30), this was unchanged since the 2006 survey. Male GPs reported seeing, on average, an estimated 4.4 men per month for PSA tests, significantly more than female GPs who saw 2.0 ($P < 0.0001$). Median estimated number of new patients with PCa seen per year was six (range 0–36), much higher than the median estimate of two (range 0–12) in 2006.

Fig. 1 shows the proportion of GPs using each referral threshold in each of the 2006 and 2016 surveys. The median (range) PSA thresholds that GPs reported for referral at ages 45, 55, 65, 75, and

Table 1
Recommended maximum PSA values (British Association of Urological Surgeons).[6]

Patient age (y)	Maximum PSA level (ng/mL)
40–49	2.7
50–59	3.9
60–69	5.0
70–75	7.2

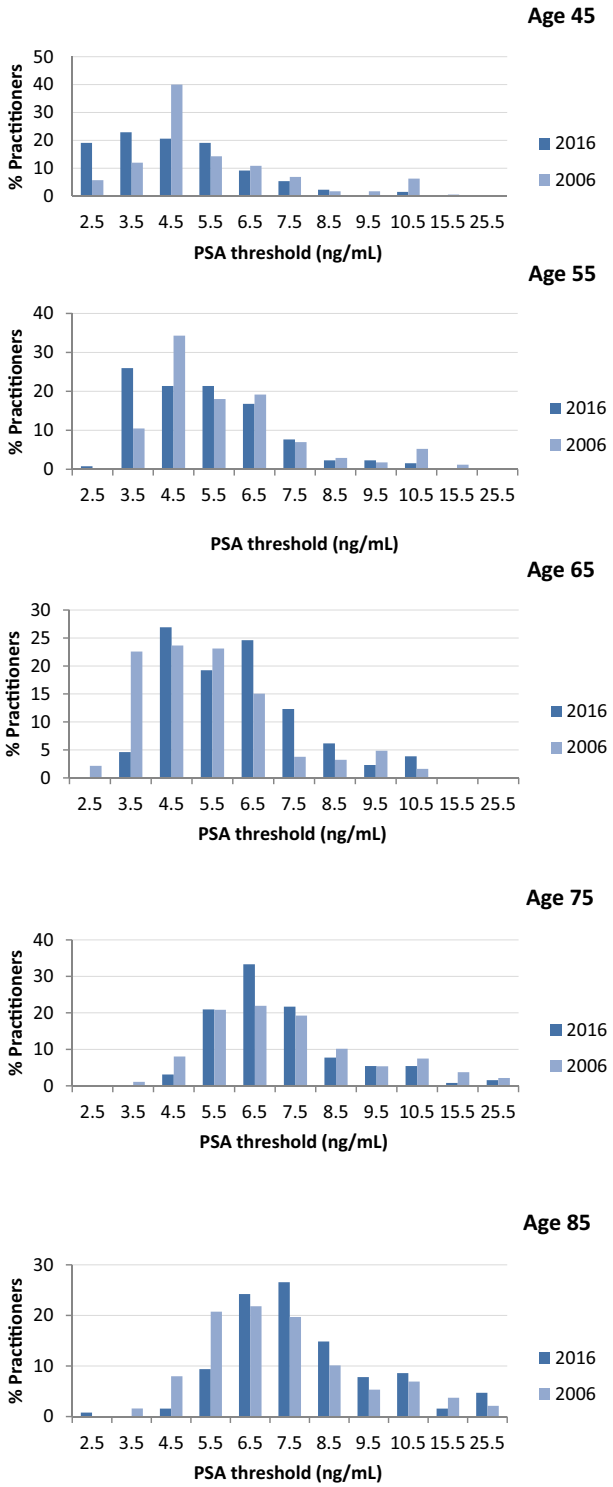

Fig 1. Graphs showing the proportion of GPs quoting each PSA value as a referral threshold, for each age category, in the 2016 and 2006 questionnaire. GP, general practitioners; PSA, prostate specific antigen.

85 were 4.5 ng/mL (2.5–10.5), 5.5 ng/mL (2.5–10.5), 5.5 ng/mL (3.5–10.5), 6.5 ng/mL (4.5–25.5), and 7.5 ng/mL (4.5–25.5) respectively. These were the same as their respective values in the 2006 survey, except for 65 year-olds, where median PSA fell from 6.5 ng/mL in 2006 to 5.5 ng/mL in 2016. Using mean PSA values, there were significant reductions in mean PSA values for 45- and 55-year-old men (Table 2). For 65-year-old men there was an increase in reported referral threshold between 2006 and 2016 from 5.34 (ng/mL) to 6.10 (ng/mL) ($P = 0.0001$). For 85-year-old men there was also a trend towards higher PSA referral values ($P = 0.058$) in the latest survey.

In younger men (aged 45, 55, and 65 years), both median and mean values are still considerably higher than the recommended age-adjusted maximum PSA-levels (Table 1).[6] However, for 75-year-olds, the median referral threshold (6.5 ng/mL) was actually lower than recommended maximum PSA values (7.2 ng/mL).

When GP responses were analysed by GP experience, GPs with <15 years since qualification referred at lower mean PSA values for each age category, although this did not reach significance (Table 3).

Table 2
Mean PSA referral thresholds reported by GPs in the 2006 and 2016 GP survey.

Patient age (y)	2006 Mean (±SD) PSA (ng/mL)	2016 Mean (±SD) PSA (ng/mL)	*P* (difference)
45	5.42 (±2.08)	4.61 (±1.72)	0.0003
55	5.81 (±2.04)	5.30 (±1.65)	0.0164
65	5.34 (±1.76)	6.10 (±1.65)	0.0001
75	7.70 (±3.70)	7.34 (±2.79)	0.3211
85	7.66 (±3.50)	8.51 (±4.18)	0.0579

GP, general practitioners; PSA, prostate specific antigen; SD, standard deviation.

Table 3
Mean PSA referral thresholds reported by GPs in 2016, analysed by GP experience.

Patient age (y)	GPs with <15 y since qualification. Mean (±SD) PSA (ng/mL)	GPs with >15 y since qualification. Mean (±SD) PSA (ng/mL)	*P* (difference)
45	4.55 (±1.52)	4.63 (±1.80)	0.8058
55	5.03 (±1.41)	5.41 (±1.74)	0.1862
65	5.87 (±1.50)	6.20 (±1.71)	0.2784

GP, general practitioners; PSA, prostate specific antigen; SD, standard deviation.

Even in this subgroup, reported PSA referral thresholds were still considerably higher than the recommended maximum PSA levels, particularly for 45 and 65-year-old men.

Five hypothetical brief clinical vignettes were described, as shown on page 4 of the questionnaire (online supplementary file). These demonstrated a median 80% likelihood of referring an 85-year-old with an incidental finding of PSA 18 ng/mL. This compared with 65% likelihood of referral for a 55-year-old man with PSA of 4.6 ng/mL, up from 3.6 ng/ml 12 months earlier (Fig. 2). The mean likelihood for referral of this 55-year-old case was only 56.2%.

A total of 95.1% of respondents recognised a family history of PCa to be a potential risk factor for PCa. It was found that 43.6% and 27.3% thought a family history of breast cancer, or ovarian cancer was a potential risk factor respectively and 67.9% and 10.9% of respondents respectively thought smoking and lead exposure were risk factors. These questions were not asked in 2006.

4. Discussion

4.1. Summary

This study demonstrates that GPs still individually see relatively few men per month for PSA testing. Despite this, the recognition of abnormal PSA values in younger men <55 years has improved over the past decade. However, this still lags behind accepted referral thresholds and actually worsened for 65-year-old men. There still appears to be a preponderance for better recognition and better referral trends for older men with abnormal PSA values in general practice, compared with younger men, both when assessed using the estimated referral thresholds and hypothetical clinical scenarios. This is paradoxical as the evidence for positive impact of earlier detection is stronger for younger men.

4.2. Strengths and limitations

This study surveyed GPs representing a large patient population, in a mixed urban and rural catchment which is likely to be typical of UK primary care. The reassessment, within the same geographical region allows for changes in perceptions to be assessed within a similar cohort. These data may be generalizable to other nonscreened populations, with similar healthcare systems to the

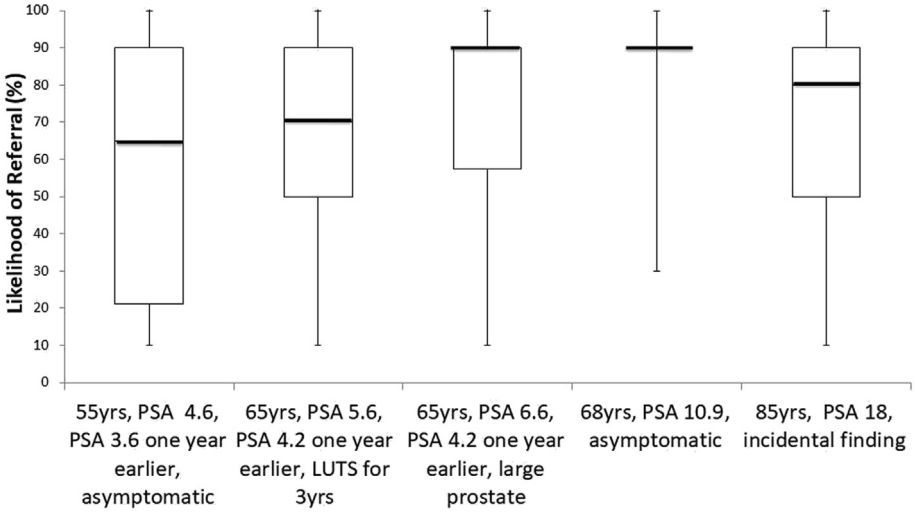

Fig 2. Box-plots demonstrating likelihood of referral for five hypothetical clinical vignettes, with age and PSA levels (ng/mL) indicated (median, interquartile range, maximum and minimum reported values shown). LUTS, lower urinary tract symptoms; PSA, prostate specific antigen.

UK, but will not be relevant to countries with formal screening programmes.

The overall response rate was relatively low, which may produce a selection bias. As responses were anonymized we did not attempt a second trawl of responses. As such it is possible we may have captured those GPs that are most engaged or interested in urology. The clinical vignettes used within the survey were deliberately brief and lacked background information that GPs would ordinarily take into account. Many GPs would not act upon a single PSA value but may appropriately repeat PSA tests or assess trends. As with any survey, there is the potential for difference between reported, and actual referral behaviour and our findings should be correlated with actual referral practice.

4.3. Comparison with existing literature

Our clinical vignettes suggest an ongoing preponderance to refer older men with abnormal PSAs, compared with younger men. This mirrors a finding of differences in PSA-testing from a 2011 study in six UK cities which found that only 1.4% of men aged 45–49 years were tested, compared with 11.3% in men aged 75–79 years.[14] There has been very little research into GP awareness of abnormal PSA values or referral patterns.

Other studies have focussed on PSA testing behaviours amongst GPs and demonstrated considerable variability in PSA testing, even prior to assessing PSA interpretation. A study in 2015 found that GPs with low tolerance levels for ambiguity, or high anxiety regarding adverse outcomes, were more likely to perform incidental PSA tests.[15] A separate study in 2015 amongst New Zealand GPs found PSA testing to be related to a GP's approach to over- and underdiagnosis of prostate cancer.[16] Elsewhere, geographical and socioeconomic differences in rates of PSA-testing have been reported.[14]

In 2006, a GP survey, performed in Northern Ireland, found that only 49% of responders were aware of national guidelines related to PSA. They also found that male GPs, who had attended postgraduate urology teaching were more likely to request PSA tests, and that GPs with >21 years of experience requested the most tests.[17]

Putting our results in the context of this literature, not only is there an ongoing reluctance to refer younger men, this may well be within a group that are already 'under-tested' by PSA initially. In our data, GPs with less experience, appear to have a better appreciation of PSA referral thresholds. Yet, it appears these GPs may not be the practitioners performing the majority of PSA tests.

The improvement and reduction of PSA referral thresholds in patients younger than 55 years should be applauded. The potential superiority of GPs with less experience, may also suggest an improving pattern over time. However, there remains some distance between reported GP behaviour and accepted guideline referral values.

In terms of potential risk factors, GPs were very good at recognising the importance of family history of PCa (95.1%). Indeed, between 5% and 10% of PCa has been shown to have an inherited component[18] with the relative-risk increasing with number of first degree relatives affected. Recognition of the importance of family history of breast or ovarian cancer was lower. The BRCA1 and BRCA2 genes have been implicated[19,20] in PCa such that family history of breast or ovarian cancer should be regarded as a potential risk. Very limited evidence of dietary risk factors exist; however, there may be a degree of protection offered by dietary intake of lycopenes, and an increased PCa risk associated with obesity.[21] There is no convincing evidence of association between lead exposure or smoking and PCa, which 10.6% and 66.9% of respondents respectively thought was the case.

5. Conclusion

Awareness of abnormal PSA values in primary care, particularly in younger patients, is still lagging behind the evidence and latest guidelines. Strategies to disseminate knowledge of maximum PSA-values to GPs should focus on those for younger patients. Postgraduate teaching on urology may be an effective mechanism of change. Educational campaigns could remind practitioners that current UK national guidelines require only a single PSA value above the 'age-specific reference range' to make a urology referral.[10]

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Conflicts of interest

The authors have no conflicts of interests to declare.

Appendix A. Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.prnil.2017.10.001.

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