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Prostate-specific antigen testing prevalence and prostate cancer risk factors in general practice: a cross-sectional study in inner London

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Main title: Prostate-specific antigen testing prevalence and prostate cancer risk factors in general practice: a cross-sectional study in inner London

Running title: PSA testing prevalence and prostate cancer risk factors

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Abstract

Objectives: To investigate the association between PSA testing prevalence and prostate cancer risk factors (age and ethnicity), obesity, social deprivation and comorbidity.

Setting: A cross-sectional database of 136 inner London general practices from 1st August 2009 to 31st July 2014.

Participants: Men aged 40 years and over without prostate cancer were included (*n*=150,481).

Primary Outcome: Logistic regression analyses were used to estimate the association between PSA testing and age, ethnicity, social deprivation, body mass index (BMI) and comorbidity cluster while adjusting for age, benign prostatic hypertrophy, prostatitis and tamsulosin or finasteride use.

Results: PSA testing prevalence was 8.2% (2013-14), mean age of 54 years (SD: 11). PSA testing was positively associated with age (Odds Ratio (OR) 70-74y compared to 40-44y: 7.34 (95%CI: 6.82-7.90)), Black ethnicity (OR compared to White ethnicity: 1.78 (95%CI: 1.71-1.85)), increasing BMI and cardiovascular comorbidity. Testing was negatively associated with Chinese ethnicity and with increasing social deprivation.

Conclusions: In this study, PSA testing amongst black patients was higher compared to white patients which differs from the lower testing rates seen in previous studies. PSA testing in general practice appears to be positively associated with prostate cancer risk factors and cardiovascular comorbidities but is inversely associated with social deprivation.

Keywords: Prostate-specific antigen, testing prevalence, general practice, prostate cancer, ethnicity, comorbidity.

Strengths and limitations of this study

- This study features a large, inclusive GP registered population with representation from a wide range of ethnicity groups.
- Use of computerised general practice coded and PSA data minimised information entry errors.
- This study explores the important associations between PSA testing and important comorbidities which may influence the testing threshold.
- This study shows an increased testing rate amongst Black men which marks a positive change in testing behaviour compared to prior studies.
- Data on the reasoning for PSA testing were not available in this study.

Background

Prostate cancer is the commonest male cancer in the UK with 41,736 new cases in 2011 and the second commonest cause of cancer death in men in the UK with 10,837 deaths in 2012.[1,2] Known prostate cancer risk factors are increasing age, family history and black ethnicity.[2,3] Prostate cancer is rare in the under 50s but the incidence rises rapidly with those aged 75-79 years at five times higher risk compared to 55-59 year olds.[2] Black males are reported to have a three times greater risk of developing prostate cancer compared to white males.[4,5] A raised BMI has also been implicated as possible prostate cancer risk factor with some studies reporting a 2-fold increased risk in obese men.[3,6]

Currently, no prostate cancer screening programme exists in the UK and a policy for screening men aged 50-74 years every four years would cost an additional £800 million per

annum.[7] Current UK recommendations are that asymptomatic men aged over 50 who wish to have a Prostate-Specific Antigen (PSA) test may do so after careful consideration of the implications.[8] The prostate cancer risk management programme (PCRMP), introduced in 2002, provides patients and clinicians with balanced information on the advantages and disadvantages of PSA testing.[8] There still remains a high degree of variability in PSA testing, with a recent qualitative study showing that general practitioners (GPs) have varied beliefs about the risks of prostate cancer over or under diagnosis which influences the likelihood of testing.[9]

PSA screening remains controversial and conflicting evidence exists as to the benefits of screening on prostate cancer mortality. Whilst the European Randomised Study of Screening for Prostate Cancer (ERSPC) showed a reduced mortality rate in patients undergoing PSA screening[10], the US Prostate, Lung, Colorectal and Ovarian (PLCO) trial showed no statistically significant difference in mortality rates.[11] However, the PLCO study had a higher contamination rate in the control group with 45% of patients having had an opportunistic PSA test in the 3 years prior to study randomisation.[11] The PSA test has poor specificity in regards to prostate cancer diagnosis with up to 76% of men having a falsely raised PSA level.[7] Moreover, the large number of men screened for prostate cancer have local or indolent disease and up to 84% of men diagnosed with prostate cancer survive 10 years or more[2,10,12,13] hence the risk of unnecessary invasive diagnostic or treatment strategies with associated harmful side effects such as sexual dysfunction and incontinence is ever present.[10,12,13] Conversely, prostate cancer remains the second commonest cause of male cancer death in the UK and earlier diagnosis and treatment, especially in some patients with aggressive disease could reduce morbidity and mortality.[12] Moreover, active surveillance is used as an initial management option for some patients with low risk prostate cancer reducing the negative risks of invasive treatment.[12]

The PSA testing rate per year in the UK is estimated to be around 6% in men aged 45-89y and remained unchanged between 2004-11.[14,15] PSA testing has previously been reported to vary with increasing age, ethnicity (decreased in Black patients), geographical location, social deprivation, decision tool use and test indication.[14-16] However, previous studies have relied upon self-reported data[16] or have had a restrictive age inclusion criteria.[14,15] Moreover, previous studies have not fully explored the influence of ethnicity in detail[14] nor investigated the possible influence of comorbidity on PSA testing. The aim of this study is to investigate the association between PSA testing prevalence and the prostate cancer risk factors of age and ethnicity. Furthermore, we aim to quantify the influence of obesity, social deprivation and comorbidity on PSA testing.

Methods

Study data and setting

Data for the study was taken from the inner east London boroughs of Newham, City and Hackney and Tower Hamlets and covered more than 95% of the general practice-registered population. Routine clinical data were entered on practice computers using EMIS Web software. Anonymised Read coded clinical and prescription data recorded over a 5-year period were extracted from 136 participating practices in July 2014. Data were managed according to the UK NHS information governance requirements.

Participant selection

We included all male patients aged 40 years and over on the 31st of July 2014. Patients with a recorded history of prostate cancer during the 5-year study period and prior to the 1st Aug

2009 were excluded as PSA testing in this setting would be for monitoring purposes and not for the detection of incident cases. Data from 150,481 patients were included in the cross-sectional study as shown in **Figure 1**.

Figure 1. PSA testing study selection flow chart

PSA measurement

The latest PSA measurement per patient recorded during the 5-year study period was used to categorise patients into tested and untested PSA groups; free and total PSA measurements were included. Patients with a PSA measurement were categorised into 0 to 0.99ng/ml, 1 to 3.99ng/ml, 4 to 9.99ng/ml and ≥10ng/ml groups. The PSA testing prevalence was calculated as the percentage of tested study participants over the 5-year and one-year (Aug 2013-14) period. Data on the reasoning for PSA testing were not available in this study.

Study cofactors

Socio-demographics

Data on patient age, ethnicity and individual-level Townsend score as a measure of deprivation were extracted. The Townsend score is a census-based measure of deprivation and is widely used to assess deprivation in the UK.[17] Patients were categorised into 5-year age groups and were placed into approximate deprivation quintiles based on the relative Townsend scores; 272 (0.18%) patients did not have a Townsend score on record. Ethnicity was self-reported by patients during practice visits and recorded using 2001 UK census ethnicity codes. For the purposes of this study, ethnic groups where grouped into White (British, Irish, other White), Black (African, Caribbean, other Black), mixed Black, South

Asian (Indian, Pakistani, Bangladeshi, other Asian), Chinese, mixed Asian, other mixed and other ethnicity. Those without a recorded ethnicity were categorised as "not defined" and included in the analysis. There were 13,149 patients (8.7%) without a recorded ethnicity.

Body mass index

Data on the body mass index (BMI, kg/m2) were extracted for the study period with the latest BMI used to categorise patients. Patients were categorised into normal weight (18.5 to 24.9), underweight (<18.5), overweight (25 to 29.9), obese class I (30 to 34.9), class II (35 to 39.9) and class III (≥40) groups. There were 11,462 (7.6%) patients without a recorded BMI.

Comorbidity

Comorbidities included in this study were placed into four disease clusters.

(i) The cardiovascular cluster, which included ischaemic heart disease (IHD), peripheral vascular disease (PVD), heart failure (HF) and atrial fibrillation (AF) grouped together as cardiovascular disease (CVD). Hypertension (HTN), type I and II diabetes mellitus (DM), chronic kidney disease (CKD, stage 3-5) and stroke/transient ischaemic attack (TIA) were also individually included in the cardiovascular cluster.

(ii) The respiratory cluster, which included asthma and chronic obstructive pulmonary disease (COPD).

(iii) The mental health cluster, which included dementia and serious mental illness (SMI). SMI group included schizophrenia, bipolar disorder, mania and psychosis.

(iv) Other cancer (excluding prostate cancer).

The selected comorbidities were chosen as they were all Quality Outcome Framework (HSCIC, 2014)related domains hence were well recorded and represented prevalent, clinical conditions that GPs may take into consideration when deciding upon the appropriateness of PSA testing. Presence of the select comorbidities was identified from the data using unique clinical codes (Read codes) used in UK general practice data coding.

Adjusted covariates

Presence of benign prostatic hypertrophy (BPH) or prostatitis was defined as a diagnosis existing at any point throughout the patient records. Data on tamsulosin or finasteride use, used for the treatment of symptomatic BPH, were also extracted and were defined as the issue of a prescription of at any point during the 5-year study period.

Statistical methods

Normally distributed continuous variables were analysed as means and standard deviations (SD) and dichotomous variables were analysed as counts and percentages. Parametric tests for significant differences were determined using unpaired *t*-test or Chi-squared ($\chi 2$) test as appropriate.

Logistic regression analyses, with 95% confidence intervals (CI), were used to assess the association between the odds of PSA testing and age, ethnicity, deprivation quintile, BMI and comorbidity (both the comorbidity cluster and individual comorbidities were tested). The 40-44y, White, least deprived quintile, normal weight, absence of the comorbidity cluster or individual comorbidity acted as the reference for the aforementioned cofactors respectively. Two adjusted models were derived per cofactor analyses; (i) an age-adjusted model and (ii)

an age and covariate (BPH, prostatitis, tamsulosin or finasteride use) adjusted model. All statistical analyses were carried out on SPSS, version 20.0, IBM, USA.

Results

Characteristics of PSA tested and untested patients

The prevalence of PSA testing over the previous five years was 17.6% (*n*=26,427, practice inter-quartile range (IQR) 12.2%-20.3%) for male patients aged ≥40 years. The one year PSA testing prevalence (1st Aug 2013 - 31st Jul 2014) was 8.2% (*n*=11,065, practice IQR 4.8%-9.7%). The mean age of included patients was 53.6 years (SD: 11.4). Over 66% were classed as overweight or obese and a significant proportion had HTN (25.5%), DM (15.6%) or CVD (9.1%). There were significant differences in the age, ethnicity, social deprivation, BMI, comorbidity and covariate status between PSA tested and untested patients (p<0.001, **Table 1**).

Table 1. Baseline characteristics of PSA tested and untested patients

PSA testing prevalence, level and age

As shown in **Figure 2a**, the PSA testing prevalence increased significantly with age from 5.1% at age 40-44y to 39.7% at age 70-74y (p<0.001). However, the greatest proportion of PSA tests performed occurred in patients aged 55-59y (16.1%) with just 7% of all PSA tests performed in patients aged 70-74y.

The PSA level rose significantly with age, with 0.8% of patients aged 40-44y having a PSA level of 4ng/ml or greater, rising to 17.5% by age 70-74y and 36.9% by age 90-94y (**Figure 2b**). The median [IQR] PSA values were 0.68ng/ml [0.45-1.00] for 40-49y, 0.81ng/ml [0.50-1.40] for 50-59y, 1.20ng/ml [0.65-2.30] for 60-69y, 1.63ng/ml [0.80 -3.30] for 70-79y, 2.08ng/ml [0.93-4.28] for 80-89y and 2.90ng/ml [1.25-6.31] for 90y and over.

Figure 2a,b. PSA testing prevalence, level and age

Association between PSA testing and age, ethnicity, social deprivation, BMI and comorbidity

PSA testing was positively associated with age. The adjusted odds ratio (OR) of PSA testing in the 70-74y age group was 7.34 (95%CI: 6.82-7.90), compared to those baseline 40-44y group (**Table 2**). Moreover, the odds of PSA testing increased in each age cohort peaking at 70-74y and decreasing thereafter up to the ≥95y age group.

Compared to White patients, Black (adjusted OR: 1.78 (95%CI: 1.71-1.85), mixed Black and to lesser degree south Asian patients were significantly more likely to undergo PSA testing. This remained true for Black and mixed Black patients after further adjustment for included comorbidity clusters, Black (adjusted OR: 1.73 (95%CI: 1.66-1.80) but the OR for south Asians become non-significant. Conversely, Chinese patients were significantly less likely to undergo PSA testing than White patients (**Table 2**); there was minimal change in the OR after adjusting for included comorbidities.

Increasing social deprivation was inversely associated with the odds of PSA testing (**Table 2**).

Compared to patients of a normal BMI, obese patients were significantly more likely to undergo PSA testing (adjusted OR: 1.29 (95%CI: 1.24-1.35)). The likelihood of PSA testing increased with each BMI class above normal weight and decreased in underweight patients (**Table 2**).

PSA testing was significantly associated with cardiovascular comorbidity, especially with HTN. Dementia but not SMI showed an inverse association with PSA testing. There was a weak association between PSA testing and respiratory disease with no significant difference in testing in patients with a diagnosis of other cancer (**Table 2**).

Table 2. Association between PSA testing and age, ethnicity, social deprivation, BMI and comorbidity

Discussion

Summary

PSA testing prevalence was positively associated with increasing age, Black, mixed Black and South Asian ethnicity, increasing BMI and cardiovascular comorbidity. In contrast, PSA testing was inversely associated with Chinese ethnicity and greater social deprivation.

Prevalence of PSA testing

Based on our findings, the one year PSA testing prevalence in inner east London (8.2%) was higher than the 6.2% reported in previous studies by Melia et al., (2004)[14] and

Williams et al., (2011)[15]. However, both studies excluded older patients with an inclusion age criteria of 45-84 and 45-89 years respectively.[14,15] Additionally, Williams *et al*, (2011)[15] reported higher PSA testing rates (7.1%-8.9%) in the southern UK general practices. Differences are likely to be multifactorial including north and south social deprivation differences.[15] Based on reported one year PSA testing rates in the UK, there has been a modest 2% rise in testing rates from 6.2%[14,15] to the current rate of 8.2% in our study.

We observed a significant degree of variability in the PSA testing rate between practices, which is similar to previous findings, IQR 3.6%-8.4% (Williams *et al*, 2011)[15], and may be a reflection of differences in practice organisation, GP attitudes to testing or patient demographics. Yearly PSA testing rates also vary greatly between developed countries with greater testing in some EU countries (Germany 35%)[16], New Zealand (22%)[18] and a greater degree of testing in the USA (57%)[19]. Hjertholm *et al*, (2015) found no difference in prostate cancer specific mortality between Danish practices with the highest and lowest relative levels of PSA testing but there was a significant increase in prostate cancer diagnoses (mainly local disease), prostate biopsy and prostatectomy.[13]

PSA testing, level and age

Similar to the findings of others, PSA testing rates increase with age[14-16,18-20], and peak testing prevalence is amongst the patients aged 70-80 years old.[14,15,18-20]. A third of those aged 70 years or more have PSA levels ≥4ng/ml[14,15,21] which was consistent with our own findings.

PSA testing and ethnicity

In contrast to our study, Melia *et al*, (2004) reported a decrease in PSA testing with increasing proportions of Black and South Asian men.[14] This finding was echoed by Gorday *et al*, (2014) who found a decreased rate of PSA testing amongst Black Canadian men.[22] Further US studies have found little difference in PSA uptake between Black and White patients.[23-25] This is despite the increased incidence and mortality of prostate cancer amongst Black men.[4,5,26,27] To the best of our knowledge, our study results are first to show higher rates of PSA testing amongst Black men which marks a positive change in testing behaviour potentially reflecting the increased underlying risk of prostate cancer and possibly driven by increased awareness of risk both by patients and GPs. However, given that black men are at up to 3 times greater risk of developing prostate cancer, the raised odds ratios for testing found in our study do not sufficiently reflect the increased risk of prostate cancer in this group. The decreased PSA testing amongst Chinese men may reflect the reduced incidence and mortality risk of prostate cancer in the native Chinese population.[28]

PSA testing and social deprivation

The inverse relationship between socioeconomic status and PSA testing observed in this study has been reported both in the UK[14,15] and internationally.[16,25] Purported reasons for this relationship are, reduced access to health services in deprived areas and increased health awareness with greater patient driven testing among less deprived patients.[15,16] Prostate cancer mortality has also been found to be higher in more deprived populations.[27] Although we used internal quartiles of deprivation and the studied London boroughs had high levels of deprivation, PSA testing should still be a patient and clinician driven process and efforts should to be made to reduce any socioeconomic disparities in testing.

PSA testing and BMI

Similar to our study findings, US studies by Fontaine *et al*, (2005) and Fowke *et al*, (2006) found a trend of increasing PSA testing with increasing BMI.[29-30] A raised BMI is a proposed risk factor for prostate cancer, especially for advanced tumours.[6] In this study, the increased PSA testing in obese patients more likely represents opportunistic testing in such patients who are more likely to have CVD associated with increased healthcare access.[30]

PSA testing and comorbidity

Fowke *et al*, (2006) found an increased rate of PSA testing in patients with comorbidity, particularly CVD (HTN, DM and high cholesterol) but no association with coronary heart disease or respiratory disease.[30] Minor dissimilarities between the findings are likely to be the result of methodological differences such as their inclusion of a younger age range and adjustment for differing co-factors (Fowke *et al*, 2006).[30]

A possible mechanism for the observed relationship between some comorbidities and PSA testing is that increased consultation rates and routine blood test monitoring for comorbidity could increase the opportunity to add PSA testing to existing monitoring tests. This hypothesis was also suggested by Fowke *et al*, (2006) who first reported for the positive association between CVD and PSA testing amongst obese men.[30] Lack of association between PSA testing rates and other comorbidities may be related to lack of routine blood test monitoring in these comorbidities although this is unlikely to be the sole explanation since increased PSA screening rates were also seen in patients with asthma, a comorbidity not associated with blood test monitoring.

Strengths and limitations

The results of this study are reflective of current clinical practice as it features a large GP registered population with an inclusive criteria featuring a broad age range with representation from various ethnicity groups, conducted over a five year period. Our study utilised routinely collected PSA testing data directly linked to computerised general practice systems largely avoiding data entry errors and reporting bias that occur with self-reported data. The use of a retrospective study design meant that PSA testing behaviour at the general practice level was not altered by the knowledge of an ongoing study.

Study limitations were that data on the PSA testing intent and whether patients were symptomatic or asymptomatic were not available. Similarly, we did not have data on whether PSA testing was initiated by the patient or GP.

Conclusions

Based on our data from inner east London, one year PSA testing prevalence showed a modest increase from previous studies but was relatively low compared to other EU countries and the US. Those at higher risk (older patients, Black men and obese patients) had higher PSA testing rates; those at lower risk (patients of Chinese ethnicity) had lower testing rates. Independent of risk, patients living in more socially deprived areas had lower PSA testing rates; those with cardiovascular comorbidities had higher test rates which were likely to have been driven by opportunistic testing. Future studies should explore the intention for PSA testing in general practice, especially in relation to ethnicity, comorbidity and social deprivation.

Competing interest

The authors declare no competing interest.

Authors Declaration

PN, MVH, MA, AD and SC conceived and refined the initial study design. PN and AD performed the background review. PN, MVH, RM and SH collated the study data and PN carried out the primary data analysis. PN, MVH, MA, RM, SH, AD and SC were involved in the data interpretation and refined the primary study design and data analysis. PN drafted the initial manuscript. PN, MVH, MA, RM, SH, AD and SC refined the draft manuscript and approved the final submitted article.

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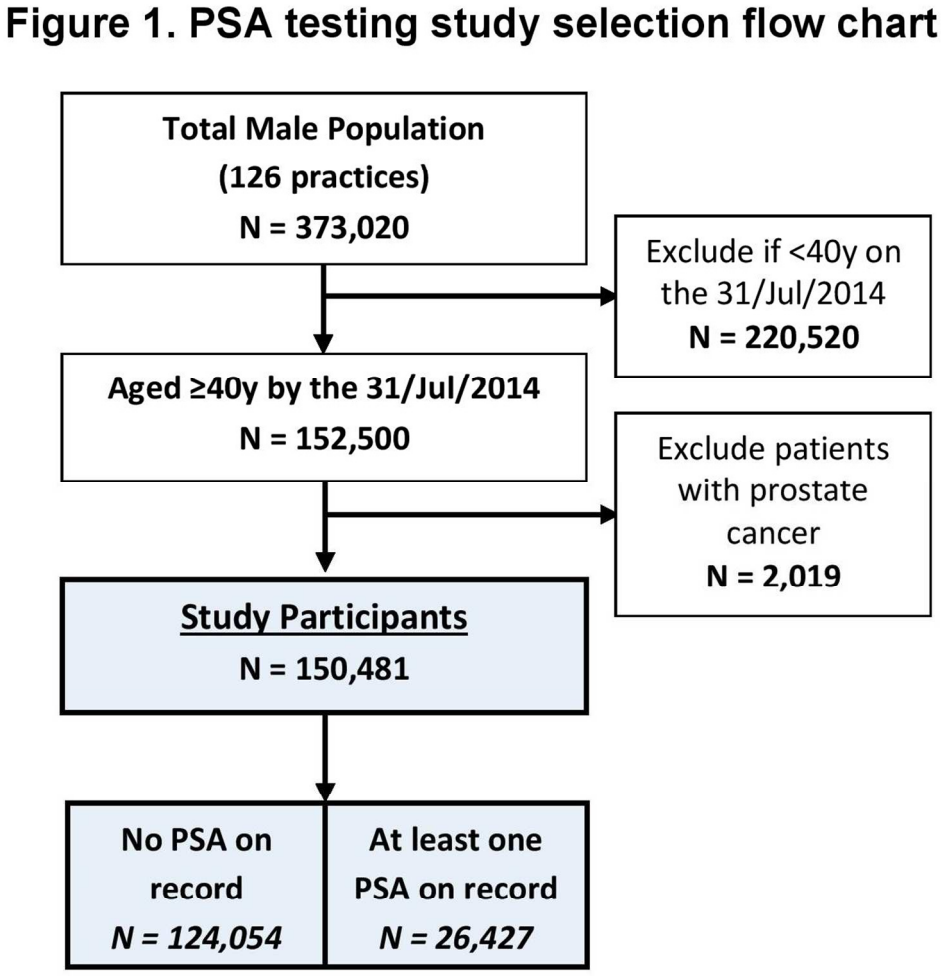

Figure 1. PSA testing study selection flow chart
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Figure 2a. PSA testing prevalence and age

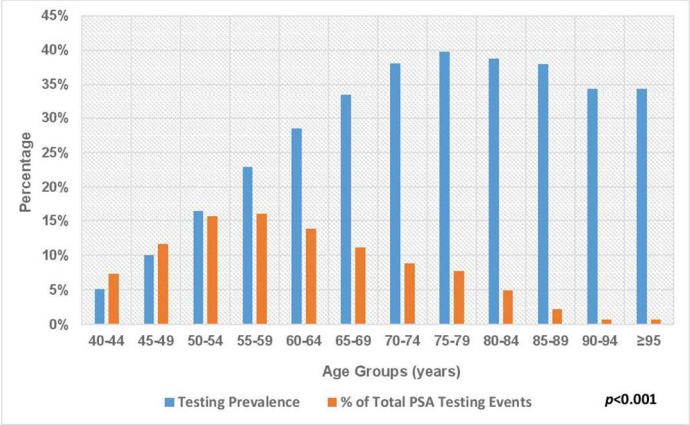

Figure 2b. PSA level and age

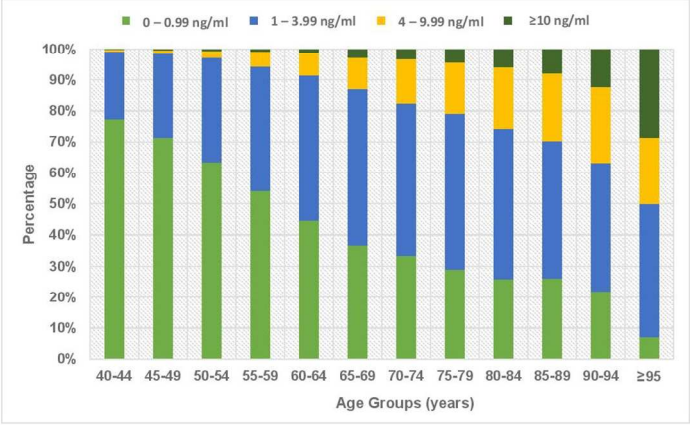

Figure 2a,b. PSA testing prevalence, level and age
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Table 1. Baseline characteristics of PSA tested and untested patients

Baseline characteristics	ALL (n=150,481)	PSA Untested (n=124,054)	PSA Tested (n=26,427)	*p*-value[a]
Age, mean (SD)	**53.6** (11.4)	**52.1** (10.7)	**60.8** (11.9)	**<0.001**
Ethnicity, % (N)				
White	**40.9** (61,621)	**41.0** (50,897)	**40.6** (10,724)	
Black	**17.2** (25,956)	**16.0** (19,835)	**23.2** (6,121)	
[1]South Asian	**26.1** (39,341)	**26.5** (32,858)	**24.5** (6,483)	
Chinese	**0.9** (1,363)	**1.0** (1,200)	**0.6** (163)	
Mixed Black	**1.5** (2,299)	**1.3** (1,647)	**2.5** (652)	**<0.001**
[1]Mixed Asian	**0.2** (235)	**0.2** (195)	**0.2** (40)	
Other Mixed	**0.4** (608)	**0.4** (535)	**0.3** (73)	
Other Ethnicity	**3.9** (5,909)	**3.9** (4,857)	**4.0** (1,052)	
Not Specified	**8.7** (13,149)	**9.7** (12,030)	**4.2** (1,119)	
[2]**Deprivation, %** (N)				
Least Deprived	**21.8** (32,780)	**21.5** (26,646)	**23.2** (6,134)	
Q2	**16.6** (25,022)	**16.6** (20,519)	**17.1** (4,503)	
Q3	**17.1** (25,802)	**17.2** (21,253)	**17.2** (4,549)	**<0.001**
Q4	**19.0** (28,637)	**19.1** (23,654)	**18.9** (4,983)	
Most Deprived	**25.2** (37,968)	**25.6** (31,748)	**23.6** (6,220)	
[3]**BMI Class, %** (N)				
Normal Weight	**31.6** (47,619)	**35.4** (40,140)	**29.1** (7,479)	
Underweight	**1.0** (1,558)	**1.2** (1,321)	**0.9** (237)	
Overweight	**39.1** (58,787)	**42.0** (47,614)	**43.5** (11,173)	**<0.001**
Obese Class I	**15.3** (22,985)	**15.9** (17,993)	**19.4** (4,992)	
Obese Class II	**4.0** (6,026)	**4.1** (4,653)	**5.3** (1,373)	
Obese Class III	**1.4** (2,044)	**1.4** (1,586)	**1.8** (458)	
Comorbidity, % (N)				
HTN	**25.5** (38,399)	**21.6** (26,814)	**43.8** (11,585)	**<0.001**
CVD	**9.1** (13,635)	**7.4** (9,220)	**16.7** (4,415)	**<0.001**
DM	**15.6** (23,421)	**13.8** (17,100)	**23.9** (6,321)	**<0.001**
CKD stage 3-5	**4.1** (6,098)	**3.2** (3,918)	**8.2** (2,180)	**<0.001**
Stroke	**2.4** (3,583)	**2.0** (2,458)	**4.3** (1,125)	**<0.001**
Asthma	**8.5** (12,792)	**8.1** (10,012)	**10.5** (2,780)	**<0.001**
COPD	**3.5** (5,206)	**2.9** (3,550)	**6.3** (1,656)	**<0.001**
Dementia	**0.6** (920)	**0.5** (600)	**1.2** (320)	**<0.001**
SMI	**2.5** (3,699)	**2.5** (3,094)	**2.3** (605)	0.510
[4]Cancer	**1.8** (2,719)	**1.5** (1,898)	**3.1** (821)	**<0.001**
BPH, % (N)	**3.5** (5,271)	**1.4** (1,787)	**13.2** (3,484)	**<0.001**
Prostatitis, % (N)	**1.6** (2,405)	**0.9** (1,113)	**4.9** (1,292)	**<0.001**
Tamsulosin use, % (N)	**7.2** (10,825)	**3.2** (4,021)	**25.7** (6,804)	**<0.001**
Finasteride use, % (N)	**2.4** (3,610)	**1.1** (1,419)	**8.3** (2,191)	**<0.001**

[a]Chi-squared between tested and untested groups.[1]Indian, Pakistani, Bangladeshi or other Asian, [2]Townsend score quintiles (272 scores missing), [3]11,462 BMI values missing, [4]Excludes benign or malignant prostate cancer.

Table 2. Association between PSA testing and age, ethnicity, social deprivation, BMI and comorbidity

Co-Factor	Description	PSA Study Group (N=150,481)		
		Unadjusted OR (95%CI)	*Age Adjusted OR (95%CI)*[1]	*Age and Covariate Adjusted OR (95%CI)*[2]
Age	***40-44y*** *(n=37,668)*	*1.00 (Ref)*	*N/A*	*1.00 (Ref)*
	45-49y *(n=30,792)*	2.04 (1.92 - 2.17)	*N/A*	**2.00 (1.88 - 2.12)**
	50-54y *(n=24,982)*	3.66 (3.45 - 3.87)	*N/A*	**3.44 (3.25 - 3.65)**
	55-59y *(n=18,658)*	5.47 (5.17 - 5.79)	*N/A*	**4.81 (4.54 - 5.10)**
	60-64y *(n=12,814)*	7.37 (6.94 - 7.82)	*N/A*	**5.91 (5.56 - 6.29)**
	65-69y *(n=8,839)*	9.21 (8.64 - 9.81)	*N/A*	**6.71 (6.28 - 7.17)**
	70-74y *(n=6,105)*	11.31 (10.55 - 12.11)	*N/A*	**7.34 (6.82 - 7.90)**
	75-79y *(n=5,152)*	12.14 (11.29 - 13.05)	*N/A*	**6.86 (6.35 - 7.42)**
	80-84y *(n=3,320)*	11.64 (10.71 - 12.65)	*N/A*	**6.02 (5.49 - 6.60)**
	85-89y *(n=1,527)*	11.24 (10.04 - 12.59)	*N/A*	**5.41 (4.77- 6.14)**
	90-94y *(n=522)*	9.63 (7.99 - 11.61)	*N/A*	**4.35 (3.54 - 5.35)**
	≥95y *(n=102)*	6.98 (4.51 - 10.81)	*N/A*	**3.25 (2.02 - 5.24)**
Ethnicity	**White** *(n=61,621)*	*1.00 (Ref)*	*1.00 (Ref)*	*1.00 (Ref)*
	Black *(n=25,956)*	1.47 (1.41 - 1.52)	**1.74 (1.68 - 1.81)**	**1.78 (1.71 - 1.85)**
	South Asian[a] *(n=39,341)*	0.94 (0.91 - 0.97)	**1.13 (1.09 - 1.17)**	**1.08 (1.04 - 1.12)**
	Chinese *(n=1,363)*	0.65 (0.55 - 0.76)	**0.66 (0.56 - 0.78)**	**0.67 (0.56 - 0.80)**
	Mixed Black *(n=2,299)*	1.88 (1.71 - 2.06)	**2.23 (2.02 - 2.46)**	**2.25 (2.03 - 2.50)**
	Mixed Asian[a] *(n=235)*	0.97 (0.69 - 1.37)	1.23 (0.86 - 1.76)	1.21 (0.83 - 1.76)
	Other Mixed *(n=608)*	0.65 (0.51 - 0.83)	1.03 (0.80 - 1.32)	1.00 (0.77 - 1.30)
	Other Ethnicity *(n=5,909)*	1.03 (0.96 - 1.10)	**1.19 (1.11 - 1.29)**	**1.10 (1.02 - 1.19)**
	Not Defined *(n=13,149)*	0.44 (0.41 - 0.48)	**0.57 (0.53 - 0.61)**	**0.60 (0.56 - 0.65)**
Deprivation Quintiles[4b]	**Least Deprived** *(n=32,780)*	*1.00 (Ref)*	*1.00 (Ref)*	*1.00 (Ref)*
	Q2 *(n=25,022)*	0.95 (0.91 - 1.00	0.97 (0.92 - 1.01)	0.96 (0.92 - 1.01)
	Q3 *(n=25,802)*	0.93 (0.89 - 0.97)	**0.95 (0.90 - 0.99)**	**0.94 (0.90 - 0.99)**
	Q4 *(n=28,637)*	0.92 (0.88 - 0.95)	**0.90 (0.86 - 0.94)**	**0.89 (0.85 - 0.93)**
	Most Deprived *(n=37,968)*	0.85 (0.82 - 0.89)	**0.85 (0.82 - 0.89)**	**0.83 (0.80 - 0.87)**

BMI[3]	**Normal weight** *(n=47,619)*	*1.00 (Ref)*	*1.00 (Ref)*	*1.00 (Ref)*
	Underweight *(n=1,558)*	0.96 (0.84 - 1.11)	**0.79 (0.68 - 0.92)**	**0.82 (0.70 - 0.95)**
	Overweight *(n=58,787)*	1.26 (1.22 - 1.30)	**1.19 (1.15 - 1.23)**	**1.18 (1.14 - 1.22)**
	Obese Class I *(n=22,985)*	1.49 (1.43 - 1.55)	**1.31 (1.26 - 1.37)**	**1.29 (1.24 - 1.35)**
	Obese Class II *(n=6,026)*	1.58 (1.48 - 1.69)	**1.34 (1.26 - 1.44)**	**1.31 (1.22 - 1.41)**
	Obese Class III *(n=2,044)*	1.55 (1.39 - 1.73)	**1.36 (1.22 - 1.52)**	**1.38 (1.23 - 1.55)**
Comorbidity[5]	**Cardiovascular Cluster** (*n*=53,120)	2.92 (2.87 - 3.03)	**1.60 (1.55 - 1.65)**	**1.51 (1.46 - 1.56)**
	HTN (*n*=38,,399)	2.83 (2.75 - 2.91)	**1.53 (1.50 - 1.60)**	**1.49 (1.44 - 1.54)**
	CVD[c] (*n*=13,635)	2.50 (2.40 - 2.60)	**1.19 (1.14 - 1.24)**	**1.07 (1.02 - 1.12)**
	DM (*n*=23,421)	1.97 (1.90 - 2.03)	**1.22 (1.18 - 1.27)**	**1.16 (1.12 - 1.21)**
	CKD Stage 3-5 (*n*=6,098)	2.76 (2.61 - 2.91)	1.23 (1.16 - 1.31)	**1.14 (1.06 - 1.21)**
	Stroke (*n*=3,583)	2.20 (2.05 - 2.36)	1.03 (0.96 - 1.11)	0.98 (0.90 - 1.06)
	Respiratory Cluster (*n*=16,616)	1.55 (1.28 - 1.40)	**1.18 (1.13 - 1.22)**	**1.08 (1.03 - 1.13)**
	Asthma (*n*=12,792)	1.34 (1.28 - 1.40)	**1.25 (1.19 - 1.31)**	**1.15 (1.10 - 1.21)**
	COPD (*n*=5,206)	2.27 (2.14 - 2.41)	**1.06 (1.00 - 1.13)**	0.95 (0.89 - 1.02)
	Mental Health Cluster (*n*=4,572)	1.18 (1.09 - 1.27)	0.94 (0.87 - 1.02)	**0.91 (0.84 - 0.99)**
	Dementia (*n*=920)	2.52 (2.20 - 2.89)	0.92 (0.80 - 1.05)	**0.82 (0.70 - 0.96)**
	SMI (*n*=3,699)	0.92 (0.84 - 1.00)	0.95 (0.86 - 1.04)	0.95 (0.86 - 1.04)
	Other Cancer[d] (*n*=2,719)	2.06 (1.90 - 2.24)	**1.13 (1.03 - 1.23)**	1.02 (0.93 - 1.12)

[1]Age-adjusted in age groups, 40-44, 45-49, 50-54, 55-59, 60-64, 65-69, 70-74, 75-79, 80-84, 85-89, 90-94, ≥95, [2]Adjusted for age, BPH, prostatitis, Tamsulosin or Finasteride use. [3]11,462 BMI values missing. [4]272 Townsend scores missing.[5]Absence of comorbidity (individual or cluster) acts as reference group. [a]Indian, Pakistani and Bangladeshi, other Asian. [b]Quintiles based on Townsend Scores -5 to +10. [c]Includes IHD, PAD, AF and HF. [d]Excludes benign or malignant prostate cancer.

STROBE Statement—checklist of items that should be included in reports of observational studies

	PAGE	Recommendation
Title and abstract	1-2	(*a*) Indicate the study's design with a commonly used term in the title or the abstract
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found
Introduction		
Background/rationale	3-5	Explain the scientific background and rationale for the investigation being reported
Objectives	5	State specific objectives, including any prespecified hypotheses
Methods		
Study design	5	Present key elements of study design early in the paper
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection
Participants	5-6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case
Variables	6-8	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable
Data sources/ measurement	5-8	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group
Bias	15	Describe any efforts to address potential sources of bias
Study size	6	Explain how the study size was arrived at
Quantitative variables	8	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why
Statistical methods	8	(*a*) Describe all statistical methods, including those used to control for confounding
		(*b*) Describe any methods used to examine subgroups and interactions
		(*c*) Explain how missing data were addressed
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy
		(*e*) Describe any sensitivity analyses

Continued on next page

Results		
Participants	9	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed
		(b) Give reasons for non-participation at each stage
		(c) Consider use of a flow diagram
Descriptive data	9-10	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders
		(b) Indicate number of participants with missing data for each variable of interest
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)
Outcome data	10-11	*Cohort study*—Report numbers of outcome events or summary measures over time
		Case-control study—Report numbers in each exposure category, or summary measures of exposure
		Cross-sectional study—Report numbers of outcome events or summary measures
Main results	10-11	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included
		(*b*) Report category boundaries when continuous variables were categorized
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period
Other analyses	N/A	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses
Discussion		
Key results	11	Summarise key results with reference to study objectives
Limitations	14-15	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias
Interpretation	11-14	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence
Generalisability	14-15	Discuss the generalisability (external validity) of the study results
Other information		
Funding	16	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based

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Prostate-specific antigen testing in inner London general practices: are those at higher risk most likely to get tested?

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Main title: Prostate-specific antigen testing in inner London general practices: are those at higher risk most likely to get tested?

Running title: PSA testing: are those at higher risk most likely to get tested?

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Abstract

Objectives: To investigate the association between factors influencing PSA testing prevalence including prostate cancer risk factors (age, ethnicity, obesity) and non-risk factors (social deprivation and comorbidity).

Setting: A cross-sectional database of 136 inner London general practices from 1st August 2009 to 31st July 2014.

Participants: Men aged 40 years and over without prostate cancer were included (*n*=150,481).

Primary Outcome: Logistic regression analyses were used to estimate the association between PSA testing and age, ethnicity, social deprivation, body mass index (BMI) and comorbidity while adjusting for age, benign prostatic hypertrophy, prostatitis and tamsulosin or finasteride use.

Results: PSA testing prevalence was 8.2% (2013-14), mean age of 54 years (SD:11). PSA testing was positively associated with age (Odds Ratio (OR) 70-74y compared to 40-44y: 7.34 (95%CI: 6.82-7.90)), ethnicity (Black) (OR compared to White: 1.78 (95%CI: 1.71-1.85)), increasing BMI and cardiovascular comorbidity. Testing was negatively associated with Chinese ethnicity and with increasing social deprivation.

Conclusions: PSA testing amongst black patients was higher compared to white patients which differs from lower testing rates seen in previous studies. PSA testing was positively associated with prostate cancer risk factors and non-risk factors. Association with non-risk factors may increase the risk of unnecessary invasive diagnostic procedures.

Keywords: Prostate-specific antigen, testing prevalence, general practice, prostate cancer, ethnicity, comorbidity.

Strengths and limitations of this study

- This study features a large, inclusive GP registered population with representation from a wide range of ethnicity groups.
- Use of computerised general practice coded and PSA data minimised information entry errors.
- This study explores the important associations between PSA testing and factors that may influence testing threshold including prostate cancer risk factors, social deprivation and comorbidity.
- This study shows an increased testing rate amongst Black men which marks a positive change in testing behaviour compared to prior studies.
- Data on the reasoning for PSA testing were not available in this study.

Background

Prostate cancer is the commonest male cancer in the UK with 41,736 new cases in 2011 and the second commonest cause of cancer death in men in the UK with 10,837 deaths in 2012.[1,2] Known prostate cancer risk factors are increasing age, family history, ethnicity (black men) and obesity.[2,3] Prostate cancer is rare in the under 50s but the incidence rises rapidly with those aged 75-79 years at five times higher risk compared to 55-59 year olds.[2] Black males are reported to have a three times greater risk of developing prostate cancer compared to white males.[4,5] In the UK, the reported age-adjusted incidence rates for African Caribbeans is 647 per 100 000 compared to 213 for Europeans and 199 for South Asians.[5] A raised BMI has also been implicated as possible prostate cancer risk factor with some studies reporting a 2-fold increased risk in obese men.[3,6]

Currently, no prostate cancer screening programme exists in the UK and a policy for screening men aged 50-74 years every four years would cost an additional £800 million per annum.[7] Current UK recommendations are that asymptomatic men aged over 50 who wish to have a Prostate-Specific Antigen (PSA) test may do so after careful consideration of the implications but GPs are not encouraged to proactively raise the issue of PSA testing.[8] The prostate cancer risk management programme (PCRMP), introduced in 2002, provides patients and clinicians with balanced information on the advantages and disadvantages of PSA testing and is used to help concerned men make informed decisions regarding PSA testing.[8] There still remains a high degree of variability in PSA testing, with a recent qualitative study showing that general practitioners (GPs) have varied beliefs about the risks of prostate cancer over or under diagnosis which influences the likelihood of testing.[9] Therefore, PSA testing may be influenced by other factors, such as comorbidity, that are not directly associated with prostate cancer but which may be associated with the GPs beliefs about the impact of invasive testing or diagnosis of prostate cancer.

PSA screening remains controversial and conflicting evidence exists as to the benefits of screening on prostate cancer mortality. Whilst the European Randomised Study of Screening for Prostate Cancer (ERSPC) showed a reduced mortality rate in patients undergoing PSA screening[10], the US Prostate, Lung, Colorectal and Ovarian (PLCO) trial showed no statistically significant difference in mortality rates.[11] However, the PLCO study had a higher contamination rate in the control group with 45% of patients having had an opportunistic PSA test in the 3 years prior to study randomisation.[11] The PSA test has poor specificity in regards to prostate cancer diagnosis with up to 76% of men having a falsely raised PSA level.[7] Moreover, the large number of men screened for prostate cancer have local or indolent disease and up to 84% of men diagnosed with prostate cancer survive 10

years or more[2,10,12,13] hence the risk of unnecessary invasive diagnostic or treatment strategies with associated harmful side effects such as sexual dysfunction and incontinence is ever present.[10,12,13] Conversely, prostate cancer remains the second commonest cause of male cancer death in the UK and earlier diagnosis and treatment, especially in some patients with aggressive disease could reduce morbidity and mortality.[12] Moreover, active surveillance is used as an initial management option for some patients with low risk prostate cancer reducing the negative risks of invasive treatment.[12]

The PSA testing rate per year in the UK is estimated to be around 6% in men aged 45-89y and remained unchanged between 2004-11.[14,15] PSA testing has previously been reported to vary with increasing age, ethnicity (decreased in Black patients), geographical location, social deprivation, decision tool use and test indication.[14-16] However, previous studies have relied upon self-reported data[16] or have had a restrictive age inclusion criteria.[14,15] Moreover, previous studies have not fully explored the influence of ethnicity in detail[14] nor investigated the possible influence of comorbidity on PSA testing. The aim of this study is to investigate the association between PSA testing prevalence and factors that may influence testing including prostate cancer risk factors (age, ethnicity and obesity) and non-risk factors of social deprivation and comorbidity.

Methods

Study data and setting

Data for the study was taken from the inner east London boroughs of Newham, City and Hackney and Tower Hamlets and covered more than 95% of the general practice-registered population. Routine clinical data were entered on practice computers using EMIS Web

software. Anonymised Read coded clinical and prescription data recorded over a 5-year period were extracted from 136 participating practices in July 2014. Data were managed according to the UK NHS information governance requirements and ethical approval was not required for this anonymised observational study.

Participant selection

We included all male patients aged 40 years and over on the 31st of July 2014. Patients with a recorded history of prostate cancer ever were excluded as PSA testing in this setting would be for monitoring purposes and not for the detection of incident cases. Data from 150,481 patients were included in the cross-sectional study as shown in **Figure 1**.

Figure 1. PSA testing study selection flow chart

PSA measurement

The latest PSA measurement per patient recorded during the 5-year study period was used to categorise patients into tested and untested PSA groups; free and total PSA measurements were included. Patients with a PSA measurement were categorised into 0 to 0.99ng/ml, 1 to 3.99ng/ml, 4 to 9.99ng/ml and ≥10ng/ml groups. The PSA testing prevalence was calculated as the percentage of tested study participants over the 5-year and one-year (Aug 2013-14) period. Data on the reasoning for PSA testing were not available in this study.

Study cofactors

Socio-demographics

Data on patient age, ethnicity and individual-level Townsend score (calculated using patient postcodes) as a measure of deprivation were extracted. The Townsend score is a census-based measure of deprivation and is widely used to assess deprivation in the UK.[17] Patients were categorised into 5-year age groups and were placed into approximate deprivation quintiles based on the relative Townsend scores; 272 (0.18%) patients did not have a Townsend score on record. Ethnicity was self-reported by patients during practice visits and recorded using 2001 UK census ethnicity codes. For the purposes of this study, ethnic groups where grouped into White (British, Irish, other White), Black (African, Caribbean, other Black), mixed Black, South Asian (Indian, Pakistani, Bangladeshi, other Asian), Chinese, mixed Asian, other mixed and other ethnicity. Those without a recorded ethnicity were categorised as "not defined" and included in the analysis. There were 13,149 patients (8.7%) without a recorded ethnicity.

Body mass index

Data on the body mass index (BMI, kg/m2) were extracted for the study period with the latest BMI used to categorise patients. Patients were categorised into normal weight (18.5 to 24.9), underweight (<18.5), overweight (25 to 29.9), obese class I (30 to 34.9), class II (35 to 39.9) and class III (≥40) groups. There were 11,462 (7.6%) patients without a recorded BMI.

Comorbidity

Comorbidities included in this study were placed into four disease clusters.

(i) The cardiovascular cluster, which included ischaemic heart disease (IHD), peripheral vascular disease (PVD), heart failure (HF) and atrial fibrillation (AF) grouped together as cardiovascular disease (CVD). Hypertension (HTN), type I and II diabetes mellitus (DM), chronic kidney disease (CKD, stage 3-5) and

stroke/transient ischaemic attack (TIA) were also individually included in the cardiovascular cluster.

(ii) The respiratory cluster, which included asthma and chronic obstructive pulmonary disease (COPD).

(iii) The mental health cluster, which included dementia and serious mental illness (SMI). SMI group included schizophrenia, bipolar disorder, mania and psychosis.

(iv) Other cancer (excluding prostate cancer).

The selected comorbidities were chosen as they were all Quality Outcome Framework (HSCIC, 2014) related domains hence were well recorded and represented prevalent, clinical conditions that GPs may take into consideration when deciding upon the appropriateness of PSA testing. Presence of the select comorbidities was identified from the data using unique clinical codes (Read codes) used in UK general practice data coding.

Adjusted covariates

Presence of benign prostatic hypertrophy (BPH) or prostatitis was defined as a diagnosis existing at any point throughout the patient records. Data on tamsulosin or finasteride use, used for the treatment of symptomatic BPH, were also extracted and were defined as the issue of a prescription of at any point during the 5-year study period. BPH and prostatitis symptoms and presentation overlap with those of prostate cancer which may prompt PSA testing, hence their inclusion. Similarly, finasteride and tamsulosin, used for the treatment of BPH influence PSA levels or disease symptomology hence may influence the decision to undertake PSA testing.

Statistical methods

Normally distributed continuous variables were analysed as means and standard deviations (SD) and dichotomous variables were analysed as counts and percentages. Parametric tests for significant differences were determined using unpaired *t*-test or Chi-squared ($\chi 2$) test as appropriate.

Logistic regression analyses, with 95% confidence intervals (CI), were used to assess the association between the odds of PSA testing and age, ethnicity, deprivation quintile, BMI and comorbidity (both the comorbidity cluster and individual comorbidities were tested). The 40-44y, White, least deprived quintile, normal weight, absence of the comorbidity cluster or individual comorbidity acted as the reference for the aforementioned cofactors respectively. Two adjusted models were derived per cofactor analyses; (i) an age-adjusted model and (ii) an age and covariate (BPH, prostatitis, tamsulosin or finasteride use) adjusted model. All statistical analyses were carried out on SPSS, version 20.0, IBM, USA.

Results

Characteristics of PSA tested and untested patients

The prevalence of PSA testing over the previous five years was 17.6% (*n*=26,427, practice inter-quartile range (IQR) 12.2%-20.3%) for male patients aged ≥40 years. The one year PSA testing prevalence (1st Aug 2013 - 31st Jul 2014) was 8.2% (*n*=11,065, practice IQR 4.8%-9.7%). The mean age of included patients was 53.6 years (SD: 11.4). Over 66% were classed as overweight or obese and a significant proportion had HTN (25.5%), DM (15.6%) or CVD (9.1%). There were significant differences in the age, ethnicity, social deprivation, BMI, comorbidity and covariate status between PSA tested and untested patients ($p<0.001$, **Table 1**).

Table 1. Baseline characteristics of PSA tested and untested patients

Baseline characteristics	ALL (n=150,481)	PSA Untested (n=124,054)	PSA Tested (n=26,427)	*p*-value[a]
Prostate Cancer Risk Factors				
Age, mean (SD)	**53.6** (11.4)	**52.1** (10.7)	**60.8** (11.9)	**<0.001**
Ethnicity, % (N)				
White	**40.9 (**61,621)	**41.0** (50,897)	**40.6** (10,724)	
Black	**17.2** (25,956)	**16.0** (19,835)	**23.2** (6,121)	
[1]South Asian	**26.1** (39,341)	**26.5** (32,858)	**24.5** (6,483)	
Chinese	**0.9** (1,363)	**1.0** (1,200)	**0.6** (163)	
Mixed Black	**1.5** (2,299)	**1.3** (1,647)	**2.5** (652)	**<0.001**
[1]Mixed Asian	**0.2** (235)	**0.2** (195)	**0.2** (40)	
Other Mixed	**0.4** (608)	**0.4** (535)	**0.3** (73)	
Other Ethnicity	**3.9** (5,909)	**3.9** (4,857)	**4.0** (1,052)	
Not Specified	**8.7** (13,149)	**9.7** (12,030)	**4.2 (**1,119)	
[2]**BMI Class, %** (N)				
Normal Weight	**31.6** (47,619)	**35.4** (40,140)	**29.1** (7,479)	
Underweight	**1.0** (1,558)	**1.2** (1,321)	**0.9** (237)	
Overweight	**39.1** (58,787)	**42.0** (47,614)	**43.5** (11,173)	**<0.001**
Obese Class I	**15.3** (22,985)	**15.9** (17,993)	**19.4** (4,992)	
Obese Class II	**4.0** (6,026)	**4.1** (4,653)	**5.3** (1,373)	
Obese Class III	**1.4** (2,044)	**1.4** (1,586)	**1.8** (458)	
Non-Risk Factors				
[3]**Deprivation, %** (N)				
Least Deprived	**21.8** (32,780)	**21.5** (26,646)	**23.2** (6,134)	
Q2	**16.6** (25,022)	**16.6** (20,519)	**17.1** (4,503)	
Q3	**17.1** (25,802)	**17.2** (21,253)	**17.2** (4,549)	**<0.001**
Q4	**19.0** (28,637)	**19.1** (23,654)	**18.9** (4,983)	
Most Deprived	**25.2** (37,968)	**25.6** (31,748)	**23.6** (6,220)	
Comorbidity, % (N)				
HTN	**25.5** (38,399)	**21.6** (26,814)	**43.8** (11,585)	**<0.001**
CVD	**9.1** (13,635)	**7.4** (9,220)	**16.7** (4,415)	**<0.001**
DM	**15.6** (23,421)	**13.8** (17,100)	**23.9** (6,321)	**<0.001**
CKD stage 3-5	**4.1** (6,098)	**3.2** (3,918)	**8.2** (2,180)	**<0.001**
Stroke	**2.4** (3,583)	**2.0** (2,458)	**4.3** (1,125)	**<0.001**
Asthma	**8.5** (12,792)	**8.1** (10,012)	**10.5** (2,780)	**<0.001**
COPD	**3.5** (5,206)	**2.9** (3,550)	**6.3** (1,656)	**<0.001**
Dementia	**0.6** (920)	**0.5** (600)	**1.2** (320)	**<0.001**
SMI	**2.5** (3,699)	**2.5** (3,094)	**2.3** (605)	0.510

[4]Cancer	**1.8** (2,719)	**1.5** (1,898)	**3.1** (821)	**<0.001**
Covariates				
BPH, % (N)	**3.5** (5,271)	**1.4** (1,787)	**13.2** (3,484)	**<0.001**
Prostatitis, % (N)	**1.6** (2,405)	**0.9** (1,113)	**4.9** (1,292)	**<0.001**
Tamsulosin use, % (N)	**7.2** (10,825)	**3.2** (4,021)	**25.7** (6,804)	**<0.001**
Finasteride use, % (N)	**2.4** (3,610)	**1.1** (1,419)	**8.3** (2,191)	**<0.001**

[a]Chi-squared between tested and untested groups.[1]Indian, Pakistani, Bangladeshi or other Asian, [2]11,462 BMI values missing, [3]Townsend score quintiles (272 scores missing), [4]Excludes benign or malignant prostate cancer. PSA – Prostate specific antigen, HTN – Hypertension, CVD – Cardiovascular disease, DM – Diabetes mellitus, CKD – Chronic kidney disease, COPD – Chronic obstructive pulmonary disease, SMI – Significant mental illness, BPH – Benign prostate hypertrophy.

PSA testing prevalence, level and age

As shown in **Figure 2a**, the PSA testing prevalence increased significantly with age from 5.1% at age 40-44y to 39.7% at age 70-74y (p<0.001). However, the greatest proportion of PSA tests performed occurred in patients aged 55-59y (16.1%) with just 7% of all PSA tests performed in patients aged 70-74y.

The PSA level rose significantly with age, with 0.8% of patients aged 40-44y having a PSA level of 4ng/ml or greater, rising to 17.5% by age 70-74y and 36.9% by age 90-94y (**Figure 2b**). The median [IQR] PSA values were 0.68ng/ml [0.45-1.00] for 40-49y, 0.81ng/ml [0.50-1.40] for 50-59y, 1.20ng/ml [0.65-2.30] for 60-69y, 1.63ng/ml [0.80 -3.30] for 70-79y, 2.08ng/ml [0.93-4.28] for 80-89y and 2.90ng/ml [1.25-6.31] for 90y and over.

Figure 2a,b. PSA testing prevalence, level and age

Association between PSA testing and age, ethnicity, social deprivation, BMI and comorbidity

PSA testing was positively associated with age. The adjusted odds ratio (OR) of PSA testing in the 70-74y age group was 7.34 (95%CI: 6.82-7.90), compared to those baseline 40-44y group (**Table 2**). Moreover, the odds of PSA testing increased in each age cohort peaking at 70-74y and decreasing thereafter up to the ≥95y age group.

Compared to White patients, Black (adjusted OR: 1.78 (95%CI: 1.71-1.85), mixed Black and to lesser degree south Asian patients were significantly more likely to undergo PSA testing. This remained true for Black and mixed Black patients after further adjustment for included comorbidity clusters, Black (adjusted OR: 1.73 (95%CI: 1.66-1.80) but the OR for south Asians become non-significant. Conversely, Chinese patients were significantly less likely to undergo PSA testing than White patients (**Table 2**); there was minimal change in the OR after adjusting for included comorbidities.

Increasing social deprivation was inversely associated with the odds of PSA testing (**Table 2**).

Compared to patients of a normal BMI, obese patients were significantly more likely to undergo PSA testing (adjusted OR: 1.29 (95%CI: 1.24-1.35)). The likelihood of PSA testing increased with each BMI class above normal weight and decreased in underweight patients (**Table 2**).

PSA testing was significantly associated with cardiovascular comorbidity, especially with HTN. Dementia but not SMI showed an inverse association with PSA testing. There was a weak association between PSA testing and respiratory disease with no significant difference in testing in patients with a diagnosis of other cancer (**Table 2**).

Table 2. Association between PSA testing and age, ethnicity, social deprivation, BMI and comorbidity

Co-Factor	Description	PSA Study Group (N=150,481)		
		Unadjusted OR (95%CI)	*Age Adjusted OR (95%CI)*[1]	*Age and Covariate Adjusted OR (95%CI)*[2]
Prostate Cancer Risk Factors				
Age	***40-44y*** *(n=37,668)*	*1.00 (Ref)*	*N/A*	*1.00 (Ref)*
	45-49y *(n=30,792)*	2.04 (1.92 - 2.17)	*N/A*	**2.00 (1.88 - 2.12)**
	50-54y *(n=24,982)*	3.66 (3.45 - 3.87)	*N/A*	**3.44 (3.25 - 3.65)**
	55-59y *(n=18,658)*	5.47 (5.17 - 5.79)	*N/A*	**4.81 (4.54 - 5.10)**
	60-64y *(n=12,814)*	7.37 (6.94 - 7.82)	*N/A*	**5.91 (5.56 - 6.29)**
	65-69y *(n=8,839)*	9.21 (8.64 - 9.81)	*N/A*	**6.71 (6.28 - 7.17)**
	70-74y *(n=6,105)*	11.31 (10.55 - 12.11)	*N/A*	**7.34 (6.82 - 7.90)**
	75-79y *(n=5,152)*	12.14 (11.29 - 13.05)	*N/A*	**6.86 (6.35 - 7.42)**
	80-84y *(n=3,320)*	11.64 (10.71 - 12.65)	*N/A*	**6.02 (5.49 - 6.60)**
	85-89y *(n=1,527)*	11.24 (10.04 - 12.59)	*N/A*	**5.41 (4.77- 6.14)**
	90-94y *(n=522)*	9.63 (7.99 - 11.61)	*N/A*	**4.35 (3.54 - 5.35)**
	≥95y *(n=102)*	6.98 (4.51 - 10.81)	*N/A*	**3.25 (2.02 - 5.24)**
Ethnicity	**White** *(n=61,621)*	*1.00 (Ref)*	*1.00 (Ref)*	*1.00 (Ref)*
	Black *(n=25,956)*	1.47 (1.41 - 1.52)	**1.74 (1.68 - 1.81)**	**1.78 (1.71 - 1.85)**
	South Asian[a] *(n=39,341)*	0.94 (0.91 - 0.97)	**1.13 (1.09 - 1.17)**	**1.08 (1.04 - 1.12)**
	Chinese *(n=1,363)*	0.65 (0.55 - 0.76)	**0.66 (0.56 - 0.78)**	**0.67 (0.56 - 0.80)**
	Mixed Black *(n=2,299)*	1.88 (1.71 - 2.06)	**2.23 (2.02 - 2.46)**	**2.25 (2.03 - 2.50)**
	Mixed Asian[a] *(n=235)*	0.97 (0.69 - 1.37)	1.23 (0.86 - 1.76)	1.21 (0.83 - 1.76)
	Other Mixed *(n=608)*	0.65 (0.51 - 0.83)	1.03 (0.80 - 1.32)	1.00 (0.77 - 1.30)
	Other Ethnicity *(n=5,909)*	1.03 (0.96 - 1.10)	**1.19 (1.11 - 1.29)**	**1.10 (1.02 - 1.19)**
	Not Defined *(n=13,149)*	0.44 (0.41 - 0.48)	**0.57 (0.53 - 0.61)**	**0.60 (0.56 - 0.65)**
BMI[3]	**Normal weight** *(n=47,619)*	*1.00 (Ref)*	*1.00 (Ref)*	*1.00 (Ref)*
	Underweight *(n=1,558)*	0.96 (0.84 - 1.11)	**0.79 (0.68 - 0.92)**	**0.82 (0.70 - 0.95)**

	Overweight *(n=58,787)*	1.26 (1.22 - 1.30)	**1.19 (1.15 - 1.23)**	**1.18 (1.14 - 1.22)**
	Obese Class I *(n=22,985)*	1.49 (1.43 - 1.55)	**1.31 (1.26 - 1.37)**	**1.29 (1.24 - 1.35)**
	Obese Class II *(n=6,026)*	1.58 (1.48 - 1.69)	**1.34 (1.26 - 1.44)**	**1.31 (1.22 - 1.41)**
	Obese Class III *(n=2,044)*	1.55 (1.39 - 1.73)	**1.36 (1.22 - 1.52)**	**1.38 (1.23 - 1.55)**
	Non-Risk Factors			
Deprivation Quintiles[4b]	**Least Deprived** *(n=32,780)*	*1.00 (Ref)*	*1.00 (Ref)*	*1.00 (Ref)*
	Q2 *(n=25,022)*	0.95 (0.91 - 1.00	0.97 (0.92 - 1.01)	0.96 (0.92 - 1.01)
	Q3 *(n=25,802)*	0.93 (0.89 - 0.97)	**0.95 (0.90 - 0.99)**	**0.94 (0.90 - 0.99)**
	Q4 *(n=28,637)*	0.92 (0.88 - 0.95)	**0.90 (0.86 - 0.94)**	**0.89 (0.85 - 0.93)**
	Most Deprived *(n=37,968)*	0.85 (0.82 - 0.89)	**0.85 (0.82 - 0.89)**	**0.83 (0.80 - 0.87)**
Comorbidity[5]	**Cardiovascular Cluster** (*n*=53,120)	2.92 (2.87 - 3.03)	**1.60 (1.55 - 1.65)**	**1.51 (1.46 - 1.56)**
	HTN (*n*=38,399)	2.83 (2.75 - 2.91)	**1.53 (1.50 - 1.60)**	**1.49 (1.44 - 1.54)**
	CVD[c] (*n*=13,635)	2.50 (2.40 - 2.60)	**1.19 (1.14 - 1.24)**	**1.07 (1.02 - 1.12)**
	DM (*n*=23,421)	1.97 (1.90 - 2.03)	**1.22 (1.18 - 1.27)**	**1.16 (1.12 - 1.21)**
	CKD Stage 3-5 (*n*=6,098)	2.76 (2.61 - 2.91)	1.23 (1.16 - 1.31)	**1.14 (1.06 - 1.21)**
	Stroke (*n*=3,583)	2.20 (2.05 - 2.36)	1.03 (0.96 - 1.11)	0.98 (0.90 - 1.06)
	Respiratory Cluster (*n*=16,616)	1.55 (1.28 - 1.40)	**1.18 (1.13 - 1.22)**	**1.08 (1.03 - 1.13)**
	Asthma (*n*=12,792)	1.34 (1.28 - 1.40)	**1.25 (1.19 - 1.31)**	**1.15 (1.10 - 1.21)**
	COPD (*n*=5,206)	2.27 (2.14 - 2.41)	**1.06 (1.00 - 1.13)**	0.95 (0.89 - 1.02)
	Mental Health Cluster (*n*=4,572)	1.18 (1.09 - 1.27)	0.94 (0.87 - 1.02)	**0.91 (0.84 - 0.99)**
	Dementia (*n*=920)	2.52 (2.20 - 2.89)	0.92 (0.80 - 1.05)	**0.82 (0.70 - 0.96)**
	SMI (*n*=3,699)	0.92 (0.84 - 1.00)	0.95 (0.86 - 1.04)	0.95 (0.86 - 1.04)
	Other Cancer[d] (*n*=2,719)	2.06 (1.90 - 2.24)	**1.13 (1.03 - 1.23)**	1.02 (0.93 - 1.12)

[1]Age-adjusted in age groups, 40-44, 45-49, 50-54, 55-59, 60-64, 65-69, 70-74, 75-79, 80-84, 85-89, 90-94, ≥95, [2]Adjusted for age, BPH, prostatitis, Tamsulosin or Finasteride use. [3]11,462 BMI values missing. [4]272 Townsend scores missing.[5]Absence of comorbidity (individual or cluster) acts as reference group. [a]Indian, Pakistani and Bangladeshi, other Asian. [b]Quintiles based on Townsend Scores -5 to +10. [c]Includes IHD, PAD, AF and HF. [d]Excludes benign or malignant prostate cancer. PSA – Prostate specific antigen, HTN – Hypertension, CVD – Cardiovascular disease, DM – Diabetes mellitus, CKD – Chronic kidney disease, COPD – Chronic obstructive pulmonary disease, SMI – Significant mental illness, BPH – Benign prostate hypertrophy.

Discussion

Summary

PSA testing prevalence was positively associated with increasing age, Black, mixed Black and South Asian ethnicity, increasing BMI and cardiovascular comorbidity. In contrast, PSA testing was inversely associated with Chinese ethnicity and greater social deprivation.

Prevalence of PSA testing

Based on our findings, the one year PSA testing prevalence in inner east London (8.2%) was higher than the 6.2% reported in previous studies by Melia *et al*., (2004)[14] and Williams *et al*., (2011)[15]. However, both studies excluded older patients with an inclusion age criteria of 45-84 and 45-89 years respectively.[14,15] Additionally, Williams *et al*, (2011)[15] reported higher PSA testing rates (7.1%-8.9%) in the southern UK general practices. Differences are likely to be multifactorial including north and south social deprivation differences.[15] Based on reported one year PSA testing rates in the UK, there has been a modest 2% rise in testing rates from 6.2%[14,15] to the current rate of 8.2% in our study.

We observed a significant degree of variability in the PSA testing rate between practices, which is similar to previous findings, IQR 3.6%-8.4% (Williams *et al*, 2011)[15], and may be a reflection of differences in practice organisation, GP attitudes to testing or patient demographics. Yearly PSA testing rates also vary greatly between developed countries with greater testing in some EU countries (Germany 35%)[16], New Zealand (22%)[18] and a greater degree of testing in the USA (57%)[19]. Hjertholm *et al*, (2015) found no difference in prostate cancer specific mortality between Danish practices with the highest and lowest

relative levels of PSA testing but there was a significant increase in prostate cancer diagnoses (mainly local disease), prostate biopsy and prostatectomy.[13]

PSA testing, level and age

Similar to the findings of others, PSA testing rates increase with age[14-16,18-20], and peak testing prevalence is amongst the patients aged 70-80 years old.[14,15,18-20]. A third of those aged 70 years or more have PSA levels ≥4ng/ml[14,15,21] which was consistent with our own findings.

PSA testing and ethnicity

In contrast to our study, Melia *et al*, (2004) reported a decrease in PSA testing with increasing proportions of Black and South Asian men.[14] This finding was echoed by Gorday *et al*, (2014) who found a decreased rate of PSA testing amongst Black Canadian men.[22] Further US studies have found little difference in PSA uptake between Black and White patients.[23-25] This is despite the increased incidence and mortality of prostate cancer amongst Black men.[4,5,26,27] To the best of our knowledge, our study results are first to show higher rates of PSA testing amongst Black men which marks a positive change in testing behaviour potentially reflecting the increased underlying risk of prostate cancer and possibly driven by increased awareness of risk both by patients and GPs. However, given that black men are at up to 3 times greater risk of developing prostate cancer, the raised odds ratios for testing found in our study do not sufficiently reflect the increased risk of prostate cancer in this group. The decreased PSA testing amongst Chinese men may reflect the reduced incidence and mortality risk of prostate cancer in the native Chinese population.[28]

PSA testing and social deprivation

The inverse relationship between socioeconomic status and PSA testing observed in this study has been reported both in the UK[14,15] and internationally.[16,25] Purported reasons for this relationship are, reduced access to health services in deprived areas and increased health awareness with greater patient driven testing among less deprived patients.[15,16] Prostate cancer mortality has also been found to be higher in more deprived populations.[27] Although we used internal quartiles of deprivation and the studied London boroughs had high levels of deprivation, PSA testing should still be a patient and clinician driven process and efforts should to be made to reduce any socioeconomic disparities in testing.

PSA testing and BMI

Similar to our study findings, US studies by Fontaine *et al*, (2005) and Fowke *et al*, (2006) found a trend of increasing PSA testing with increasing BMI.[29-30] A raised BMI is a proposed risk factor for prostate cancer, especially for advanced tumours.[6] In this study, the increased PSA testing in obese patients more likely represents opportunistic testing in such patients who are more likely to have CVD associated with increased healthcare access.[30]

PSA testing and comorbidity

Fowke *et al*, (2006) found an increased rate of PSA testing in patients with comorbidity, particularly CVD (HTN, DM and high cholesterol) but no association with coronary heart disease or respiratory disease.[30] Minor dissimilarities between the findings are likely to be the result of methodological differences such as their inclusion of a younger age range and adjustment for differing co-factors (Fowke *et al*, 2006).[30]

A possible mechanism for the observed relationship between some comorbidities and PSA testing is that increased consultation rates and routine blood test monitoring for comorbidity could increase the opportunity to add PSA testing to existing monitoring tests. This hypothesis was also suggested by Fowke *et al*, (2006) who first reported for the positive association between CVD and PSA testing amongst obese men.[30] Lack of association between PSA testing rates and other comorbidities may be related to lack of routine blood test monitoring in these comorbidities although this is unlikely to be the sole explanation since increased PSA screening rates were also seen in patients with asthma, a comorbidity not associated with blood test monitoring.

Strengths and limitations

The results of this study are reflective of current clinical practice as it features a large GP registered population with an inclusive criteria featuring a broad age range with representation from various ethnicity groups, conducted over a five year period. Our study utilised routinely collected PSA testing data directly linked to computerised general practice systems largely avoiding data entry errors and reporting bias that occur with self-reported data. The use of a retrospective study design meant that PSA testing behaviour at the general practice level was not altered by the knowledge of an ongoing study.

Study limitations were that data on the PSA testing intent and whether patients were symptomatic or asymptomatic were not available. Similarly, we did not have data on whether PSA testing was initiated by the patient or GP. There are other drugs used on occasion for patients with prostatic symptoms or that may influence PSA levels that were not adjusted for in this study.

Conclusions

Based on our data from inner east London, one year PSA testing prevalence showed a modest increase from previous studies but was relatively low compared to other EU countries and the US. Patients at higher risk of prostate cancer (older patients, Black men and obese patients) had higher PSA testing rates; those at lower risk (patients of Chinese ethnicity) had lower testing rates. Independent of prostate cancer risk factors, patients living in more socially deprived areas had lower PSA testing rates and those with cardiovascular comorbidities had higher test rates likely due to opportunistic testing. This study indicates that PSA testing may be influenced by both prostate cancer risk factors and non-risk factors. In light of the current lack of evidence demonstrating a benefit in outcomes in testing asymptomatic men, positive associations with non-prostate risk factors may potentially increase the risk of invasive diagnostic procedures. Future studies should explore the intention for PSA testing in general practice, especially in relation to ethnicity, comorbidity and social deprivation.

Competing interest

The authors declare no competing interest.

Authors Declaration

PN, MVH, MA, AD and SC conceived and refined the initial study design. PN and AD performed the background review. PN, MVH, RM and SH collated the study data and PN carried out the primary data analysis. PN, MVH, MA, RM, SH, AD and SC were involved in the data interpretation and refined the primary study design and data analysis. PN drafted the initial manuscript. PN, MVH, MA, RM, SH, AD and SC refined the draft manuscript and approved the final submitted article.

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Data Sharing

No additional data is available for this study.

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Figure 1. PSA testing study selection flow chart

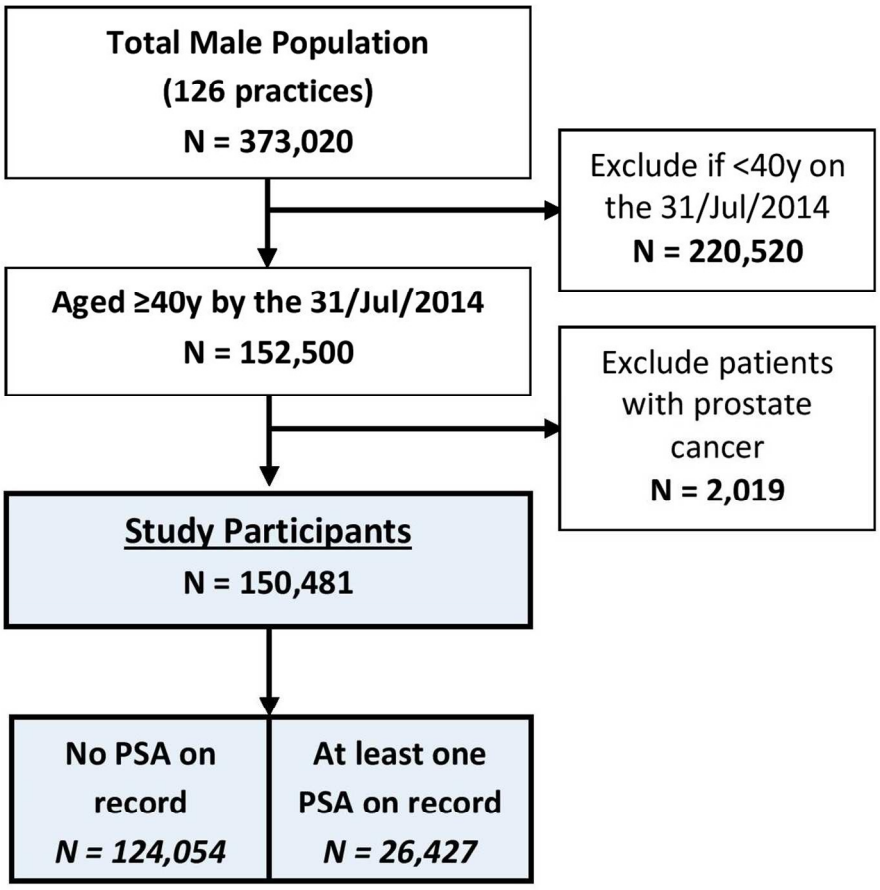

Figure 1. PSA testing study selection flow chart
111x115mm (300 x 300 DPI)

Figure 2a. PSA testing prevalence and age

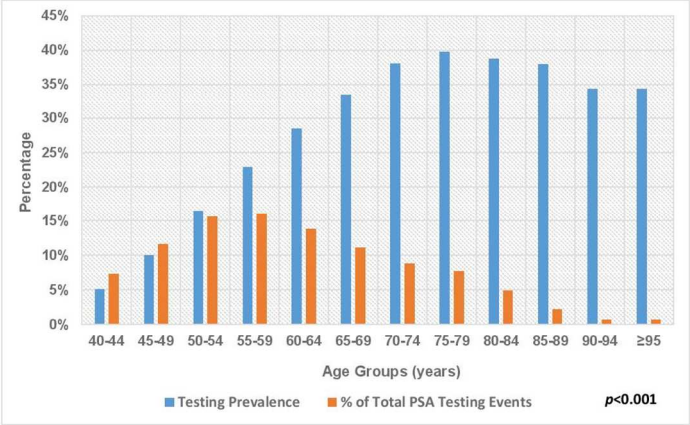

Figure 2b. PSA level and age

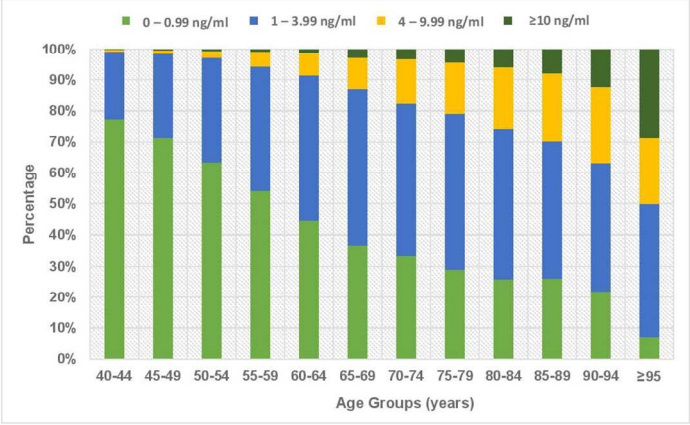

Figure 2a,b. PSA testing prevalence, level and age
209x297mm (150 x 150 DPI)

STROBE Statement—checklist of items that should be included in reports of observational studies

	PAGE	Recommendation
Title and abstract	1-2	(*a*) Indicate the study's design with a commonly used term in the title or the abstract
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found
Introduction		
Background/rationale	3-5	Explain the scientific background and rationale for the investigation being reported
Objectives	5	State specific objectives, including any prespecified hypotheses
Methods		
Study design	5	Present key elements of study design early in the paper
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection
Participants	5-6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case
Variables	6-8	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable
Data sources/ measurement	5-8	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group
Bias	15	Describe any efforts to address potential sources of bias
Study size	6	Explain how the study size was arrived at
Quantitative variables	8	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why
Statistical methods	8	(*a*) Describe all statistical methods, including those used to control for confounding
		(*b*) Describe any methods used to examine subgroups and interactions
		(*c*) Explain how missing data were addressed
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy
		(*e*) Describe any sensitivity analyses

Continued on next page

Results		
Participants	9	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed
		(b) Give reasons for non-participation at each stage
		(c) Consider use of a flow diagram
Descriptive data	9-10	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders
		(b) Indicate number of participants with missing data for each variable of interest
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)
Outcome data	10-11	*Cohort study*—Report numbers of outcome events or summary measures over time
		Case-control study—Report numbers in each exposure category, or summary measures of exposure
		Cross-sectional study—Report numbers of outcome events or summary measures
Main results	10-11	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included
		(*b*) Report category boundaries when continuous variables were categorized
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period
Other analyses	N/A	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses
Discussion		
Key results	11	Summarise key results with reference to study objectives
Limitations	14-15	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias
Interpretation	11-14	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence
Generalisability	14-15	Discuss the generalisability (external validity) of the study results
Other information		
Funding	16	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based