

Prostate-specific antigen levels in men aged 70 years and over: findings from the CHAMP study

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The benefits and risks of prostate-specific antigen (PSA) testing to screen unselected populations for prostate cancer remains controversial despite the recent publication of two large randomised controlled trials of PSA screening.^{1,2} These trials focused on men aged less than 75 years, as there is broad agreement that older men should not be screened for prostate cancer.³ However, Australian data indicate that as many as 76% of men aged over 70 years have been tested for prostate cancer.⁴ Knowing normal ranges of PSA values in older men may help doctors and patients make decisions about management in this increasingly complex area. However, there have been few population-based studies of PSA levels in men aged 70 years and over.

The level of PSA in the blood increases with age by about 3.2% per year.⁵ It has therefore been suggested that age-specific reference ranges for the PSA test should be available to increase the specificity and decrease the impetus for further, possibly unnecessary, investigations for the disease.⁵ While the age-independent cut-off point for investigating undiagnosed prostate cancer has traditionally been a serum PSA level of 4.0 ng/mL, the suggested PSA cut-off for a 50-year-old man is 3.5 ng/mL, and for a man aged 70 years or over is 6.5 ng/mL.⁵ These cut-off points are based on a study by Oesterling and colleagues that involved just 68 men aged 70–79 years, and none older than that.⁵

Age-specific serum PSA levels of men from different ethnic backgrounds vary.^{6–10} Research in this area is limited, but in the few published studies that compare PSA levels across countries in asymptomatic men, African-American men had the highest PSA levels¹⁰ and Chinese men the lowest.⁸

The Concord Health and Ageing in Men Project (CHAMP) is a population-based cohort study of a broad range of health issues in a representative

Abstract

Objective: To describe values of serum prostate-specific antigen (PSA) in older men without diagnosed prostate cancer, categorised by age and country of birth, and to describe self-reported prostate cancer screening.

Design, participants and setting: A cohort study (the Concord Health and Ageing in Men Project) involving a representative sample of 1434 eligible community-dwelling men with no diagnosis of prostate cancer who were aged 70 years and over and living in a defined geographic area in Sydney, with baseline data collected between 28 January 2005 and 4 June 2007.

Main outcome measures: Serum PSA levels and self-reported prostate cancer screening.

Results: 11% of men (155) had a PSA level of ≥ 6.5 ng/mL, increasing from 7.5% of men aged 70–74 years to 31.4% of men aged ≥ 90 years. PSA levels varied with ethnicity, with Australian-born men (695) having the highest levels (median, 2.3 ng/mL; 5th–95th percentile, 0.4–10.1 ng/mL), followed by men born in China ($n = 42$; 2.1 ng/mL; 0.4–12.4 ng/mL), United Kingdom and Ireland ($n = 70$; 1.9 ng/mL; 0.3–8.9 ng/mL), Greece ($n = 59$; 1.5 ng/mL; 0.2–6.1 ng/mL), and Italy ($n = 293$; 1.4 ng/mL; 0.3–7.2 ng/mL). A PSA test in the previous 2 years was reported by 48% of participants, and a digital rectal examination (DRE) in the previous 2 years by 37%.

Conclusions: A significant number of men aged over 70 years reported recent prostate cancer tests. The PSA level ranges reported in this cohort will help with interpreting serum PSA level findings in men aged over 70 years.

sample of men aged 70 years and over who live in the community in an ethnically diverse area of Sydney.¹¹ Our aim in this article is to describe serum PSA levels in men aged 70 years and over, without diagnosed prostate cancer, by age and by ethnic group. We also report the prevalence of self-reported PSA testing and digital rectal examinations (DREs) in this cohort of older men.

Methods

Details of the CHAMP methods have been reported elsewhere.¹¹ In this article, we focus on the results of the PSA test completed at the baseline examination.

CHAMP participants were men living in the community in three local government areas (Burwood, Canada Bay and Strathfield) surrounding Concord Hospital in Sydney. The New South Wales Electoral Roll was used as the sampling frame. Baseline data were collected between 28 January 2005 and 4 June 2007. Letters of invitation were sent to 3627 men, and contact was made with 3005. Some of

these (190) were not eligible for the study because they had moved out of the area, moved into a nursing home, or had died. This left 2815 men eligible for the study.

Data collection

Participants were asked to fill out a self-completed questionnaire before attending a 3-hour visit to the study clinic at Concord Repatriation General Hospital. Informed consent was obtained before blood collection and clinic examinations.

The questionnaire included demographic questions about age, country of birth and education level. It contained questions specific to prostate health, including history of previous PSA tests and DREs, the International Prostate Symptom Score (IPSS),¹² benign prostatic hyperplasia, prostatitis and prostate cancer.

A fasting blood sample was collected from participants on the morning of their clinic visit. The PSA assay was completed the same day in the Sydney South West Area Health Service laboratory. Total PSA levels were measured by electrochemiluminescence

1 Distribution of serum prostate-specific antigen (PSA) levels according to age group

Age (years)	Total men	Serum PSA levels (ng/mL)		
		0–6.4	6.5–9.9	≥10
70–74	586	542 (92.5%)	28 (4.8%)	16 (2.7%)
75–79	458	413 (90.2%)	26 (5.7%)	19 (4.1%)
80–84	251	213 (84.9%)	26 (10.4%)	12 (4.8%)
85–89	104	87 (83.7%)	11 (10.6%)	6 (5.8%)
90–99	35	24 (68.6%)	5 (14.3%)	6 (17.1%)

2 Medians and percentile ranges for serum prostate-specific antigen (PSA) levels according to age group

Age (years)	No. of men	Serum PSA level (ng/mL)		
		Median	25th to 75th percentile range	5th to 95th percentile range
70–74	586	1.6	0.8–3.3	0.4–7.5
75–79	458	1.8	0.9–3.6	0.4–9.1
80–84	251	2.2	1.0–4.7	0.3–9.8
85–89	104	2.5	1.4–4.8	0.2–10.2
90–99	35	2.8	0.9–7.2	0.1–18.0
All	1434	1.9	0.9–3.8	0.3–8.9

immunoassay on the Modular Analytics E170 (Elecsys module; Roche Diagnostics GmbH, Mannheim, Germany).

Statistical analysis

Descriptive statistics for PSA levels, including medians and percentiles, were calculated for each 5-year age group. PSA levels below the lower limits of quantification (12 in this study) were assigned values of 0.05 ng/mL. The IPSS was divided into two categories of lower urinary tract symptoms (LUTS): minor (IPSS 0–7) and moderate/severe (IPSS 8–35).¹² Logistic regression was used to determine the associations between self-reported screening and age, LUTS, level of education and country of birth. Multivariable adjusted odds

ratios and 95% CIs were calculated. The statistical package SAS, version 9.1 (SAS Institute, Cary, NC, USA) was used for analyses; *P* < 0.05 was considered statistically significant.

Ethics approval

Sydney South West Area Health Service Human Research Ethics Committee (Concord Repatriation General Hospital Zone) approved the study.

Results

Of the 2815 eligible men with whom contact was made, 1511 (54%) participated in the study. An additional 194 men aged 70 years or more living in the study area volunteered to be in the study before receiving an invitation

letter. Of the 1705 men who completed the baseline examination, 1675 provided a blood sample. Men with self-reported prostate cancer (178) were excluded from our analyses. In addition, 31 men did not answer the prostate cancer question and 32 men declined a PSA test, leaving 1434 men for this analysis.

Participants were aged between 70 and 97 years (mean, 77 years; SD, 5.4 years). Most participants were born in Australia (695/1434; 48%), followed by Italy (293/1434; 20%), the United Kingdom and Ireland (70/1434; 5%), Greece (59/1434; 4%) and China (42/1434; 3%). The remaining 275 men came from 52 other countries with numbers too small for meaningful analysis.

Serum PSA levels by age group

Overall, 155 men (11%) had a serum PSA level greater than or equal to the 6.5 ng/mL recommended reference cut-off point for men aged 70 years and over.⁵ The percentage of men with an elevated PSA level is shown in Box 1.

The median serum PSA level (5th to 95th percentile) for the entire cohort was 1.9 ng/mL (0.3–8.9 ng/mL). The median PSA levels (5th to 95th percentile) rose from 1.6 ng/mL (0.4–7.5 ng/mL) in men aged 70–74 years up to 2.8 ng/mL (0.1–18.0 ng/mL) in men aged 90 years and over (Box 2).

Australian-born men had the highest median serum PSA level of the five most common countries of birth (Box 3).

Self-reported history of prostate cancer screening

Of the 1398 men who answered the questions related to prostate cancer screening, 62% (867) reported they had ever had a PSA test, and 48% (670) reported they had had a PSA test in the previous 2 years. Men aged 70–74 years reported the highest rates of testing, with 64% (370/576) reporting they have ever had a PSA test and 54% (310/571) reporting a PSA test in the previous 2 years (Box 4). Of men aged 90 years and over, 39% (13/33) reported a PSA test in the previous 2 years. The median PSA levels (5th to 95th percentile) for men who reported they had ever had a PSA test was 2.1 ng/mL (0.4–9.5 ng/mL) compared

3 Median serum prostate-specific antigen (PSA) levels by age and country of birth

	Country of birth				
	Australia	Italy	United Kingdom and Ireland	Greece	China
No. of men*	695	293	70	59	42
Median serum PSA level in ng/mL (5th to 95th percentile range)					
Age (years)					
70–74	2.1 (0.4–8.9)	1.2 (0.3–6.0)	2.3 (0.5–6.8)	1.7 (0.2–6.2)	1.7 (0.3–7.5)
75–79	2.2 (0.5–10.5)	1.4 (0.3–8.0)	2.6 (0.4–8.6)	1.3 (0.3–5.4)	1.4 (0.6–12.4)
80–84	2.8 (0.5–9.8)	2.0 (0.2–7.2)	1.2 (0.1–15.1)	1.7 (0.2–6.1)	3.4 (0.8–44.4)
85–89	2.5 (0.3–11.0)	0.4 (0.1–3.4)	—	—	—
90–99	5.4 (0.1–18.0)	2.7 (0.2–6.1)	—	—	—
All	2.3 (0.4–10.1)	1.4 (0.3–7.2)	1.9 (0.3–8.9)	1.5 (0.2–6.1)	2.1 (0.4–12.4)

* 275 men from another 52 countries are not included in this table.

with 1.7 ng/mL (0.3–7.9 ng/mL) for men who reported they had never been tested.

Men with moderate or severe LUTS were significantly more likely to have had a PSA test in the previous 2 years (odds ratio [OR], 1.50; 95% CI, 1.14–1.96). Level of education was also significantly associated with reporting having had a PSA test (Box 4). Men with little or no formal education were about half as likely to report having had a PSA test in the previous 2 years (OR, 0.44; 95% CI, 0.24–0.79) than men with a university degree. Box 4 also shows that men born in China were significantly less likely to report having been tested for prostate cancer in the previous 2 years than Australian-born men (OR, 0.41; 95% CI, 0.20–0.84).

DREs were also common (Box 4); 70% (990/1417) of men who answered the screening questions reported they had ever had this examination and 37% (524/1400) reported having had this examination in the previous 2 years. Just over half of the men, 52% (722/1398), reported having ever had both a PSA test and a DRE, with 28% (388/1386) reporting having had both of these tests in the

previous 2 years. Self-reported moderate or severe LUTS was the strongest predictor of having a DRE in the previous 2 years (OR, 1.96; 95% CI, 1.50–2.55). Australian-born men were significantly more likely to report having had a DRE in the previous 2 years than men born in China (OR, 0.32; 95% CI, 0.14–0.71), the UK and Ireland (OR, 0.57; 95% CI, 0.33–0.99), and Italy (OR, 0.65; 95% CI, 0.45–0.93).

Discussion

PSA levels in men increase with age, and we have shown that this continues into very old age. PSA levels also vary with ethnicity. Given the high proportion of older men who report having had a recent PSA test, a greater understanding of the relationship between age and PSA levels is needed.

CHAMP is the largest population-based study to date to have measured PSA levels in a representative group of men aged 70 years and over and, to our knowledge, is the only study to include men aged 85 years and over (139). Most studies of normal PSA values involve clinic patients, partici-

pants enrolled in clinical trials, or volunteers attending screening programs. Among the true population-based studies are the Olmsted County study, which included 68 men aged 70–79 years,⁵ the Massachusetts Male Ageing Study (MMAS), which included 212 men aged 70–79 years,¹³ and the 2001–2002 National Health and Nutrition Examination Survey (NHANES 2001–2002), which included 343 men aged 70–79 years.¹⁴

The median PSA level in the 1044 men aged 70–79 years in our study (1.69 ng/mL) is similar to median value found in the MMAS study (1.75 ng/mL) and a little lower than those in the Olmsted County study (2.0 ng/mL) and the NHANES 2001–2002 study (70–74-year-old median, 1.5 ng/mL; 75–79-year-old median, 2.8 ng/mL).^{5,13,14} In our study, the 95th percentile PSA level in men aged 70–79 years was 9.0 ng/mL; again, similar to MMAS (8.84 ng/mL).¹³ This is much higher than the 6.5 ng/mL found in the Olmsted County study, on which current recommendations for men aged in their 70s are based.⁵

The only previous study to report PSA levels in men aged 80–84 years is NHANES 2001–2002.¹⁴ The median

4 Associations between prostate-specific antigen (PSA) screening and digital rectal examination in the previous 2 years and age, lower urinary tract symptoms, country of birth and education

Characteristic	PSA screening			Digital rectal examination		
	No. of men	No. screened	Adjusted odds ratio* (95% CI)	No. of men	No. screened	Adjusted odds ratio* (95% CI)
No. of men	1386			1400		
Age in years at baseline						
70–74	571	310 (54%)	1.00	571	214 (37%)	1.00
75–79	441	219 (50%)	0.78 (0.58–1.04)	450	172 (38%)	1.01 (0.75–1.36)
80–84	239	99 (41%)	0.45 (0.31–0.64)	244	85 (35%)	0.74 (0.52–1.06)
85–89	102	29 (28%)	0.23 (0.13–0.39)	101	40 (40%)	0.78 (0.47–1.30)
90–99	33	13 (39%)	0.32 (0.13–0.79)	34	13 (38%)	0.84 (0.36–2.00)
Lower urinary tract symptoms [†]						
Mild (IPSS 0–7)	928	425 (46%)	1.00	940	306 (33%)	1.00
Moderate/severe (IPSS 8–35)	442	240 (54%)	1.50 (1.14–1.96)	445	213 (48%)	1.96 (1.50–2.55)
Country of birth [‡]						
Australia	674	358 (53%)	1.00	682	303 (44%)	1.00
Italy	279	124 (44%)	0.80 (0.56–1.14)	283	89 (31%)	0.65 (0.45–0.93)
United Kingdom and Ireland	67	29 (43%)	0.61 (0.36–1.03)	68	21 (31%)	0.57 (0.33–0.99)
Greece	56	26 (46%)	0.74 (0.40–1.35)	57	19 (33%)	0.64 (0.34–1.20)
China	41	14 (34%)	0.41 (0.20–0.84)	42	9 (21%)	0.32 (0.14–0.71)
Education [‡]						
No schooling or primary only	163	57 (35%)	0.44 (0.24–0.79)	170	45 (26%)	0.61 (0.34–1.11)
Up to secondary school	444	205 (46%)	0.63 (0.41–0.97)	449	171 (38%)	0.79 (0.52–1.20)
Post-school — trade or certificate	569	294 (52%)	0.82 (0.54–1.25)	569	220 (39%)	0.81 (0.54–1.23)
University degree or higher	174	106 (61%)	1.00	175	81 (46%)	1.00

IPSS = International Prostate Symptom Score.

*Adjusted for all factors in the left-hand column of the table. † Total is less than 1386 (PSA screening) or 1400 (digital rectal examination) because of missing data. ‡ 269 men (PSA screening) or 268 men (digital rectal examination) were born in countries other than the five listed.

PSA was 2.4 ng/mL and the 75th percentile PSA level was 5.4 ng/mL (the 95th percentile was not reported). In CHAMP, the median PSA level in the 251 men aged 80–84 years was 2.2 ng/mL and the 75th percentile PSA level was 4.7 ng/mL. The 95th percentile PSA level was 10.2 ng/mL in men aged 85–89 years and 18.0 ng/mL in men aged 90 years and over.

Race-specific reference ranges for PSA have been suggested previously.^{5,7–10,15} We found that Australian-born men had higher serum PSA levels than men born in other countries. The median serum PSA levels for Australian men aged 70–74 years (2.1 ng/mL) and 75–79 years (2.2 ng/mL) were similar to values previously reported; 2.2 ng/mL¹⁶ and 2.0 ng/mL⁵ in American populations aged 70–79 years. In comparison, the median serum PSA levels for Italian-born men aged 70–74 years (1.2 ng/mL) and 75–79 years (1.4 ng/mL) in our study were low, and similar to levels reported elsewhere for Chinese (1.2 ng/mL)⁸ and Korean (1.3 ng/mL)¹⁵ populations aged 70–79 years. The low PSA levels in Italian-born men in this study is consistent with Australian data showing relatively low prostate cancer incidence among men born in Italy,¹⁷ and the low incidence of prostate cancer in Italy.¹⁸ The relatively high PSA levels for Chinese men (median, 2.1 ng/mL) in our cohort is consistent with a report of much higher incidence of prostate cancer in Chinese men living in Australia compared with their place of birth.¹⁷

We found a high rate of self-reported PSA testing, even among the very oldest men. The US Preventive Services Task Force recommends against prostate cancer screening for men over the age of 75 years, with moderate to high certainty that future research will not alter this position.³ Based on the results of our study, further research is needed to describe the management of older men with an elevated PSA level, and care of those diagnosed with prostate cancer to quantify whether overdiagnosis or overtreatment is occurring in this age group.

While we did not ask men why they had had a PSA test or DRE, data from the IPSS suggest that some of the testing is the result of lower urinary tract symptoms. We also found self-reported PSA testing rates in our study varied by

education and country of birth, with more educated men being more likely to report having had a PSA test, and men born in China being much less likely to report having had a PSA test or DRE than men born in Australia. This latter finding is consistent with a recent Australian study of screening behaviour in 15 275 men, that found that men born in East Asia had much lower prostate and bowel cancer screening rates than men born in Australia.¹⁹

The major strength of our study is its large representative sample of older men recruited from the community. The age distribution of the men in the CHAMP study is similar to that of men in the target population,¹¹ and the prevalence of self-reported disease in men in CHAMP is very similar to that found in a recent Australian national telephone survey of men's health, the Men in Australia Telephone Survey (MATEs) study.⁴ These data suggest that our PSA data are likely to reflect the range of values in older Australian men.

The major weakness of our observational study was our inability to exclude undiagnosed prostate cancer among the participants. The inclusion of some undiagnosed prostate cancers would be expected to result in higher PSA levels in CHAMP than in studies that have used prostate biopsy findings to exclude men with undiagnosed prostate cancer, such as the Olmsted County study.⁵ However, this may not be the case; in our study, median PSA levels in men in their 70s were lower than those reported in the Olmsted County study.

CHAMP is the largest study to date of PSA levels in a representative group of older men, and we found higher than expected serum PSA levels in the older age groups. Nearly half of the participants reported having a PSA test performed in the previous 2 years. Given that, despite recommendations, the PSA test is frequently used as a screening test for prostate cancer, doctors and patients should be aware of the effects of age and ethnicity on PSA levels when considering further investigations of elevated PSA levels, particularly in very elderly men.

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