

# **Urological referral in men with raised Prostate Specific Antigen levels and patterns of testing in General Practice 2002-2004**

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## EXECUTIVE SUMMARY

**Background:** The NHS Prostate Cancer Risk Management Programme (PCRMP) was set up to provide materials to help men requesting a PSA test make an informed choice about the potential benefits and harms of screening. In September 2002, the PCRMP information packs were sent to all general practitioners (GPs) and urologists in England. The packs included guidelines to GPs about the age related cut-off levels of prostate specific antigen (PSA) for urological referral when screening for prostate cancer. The impact of the PCRMP on rates of referral to urology in general practice or on rates of PSA testing is not known. The present study was set up to investigate urological referrals, and changes in rates of testing, using baseline data on rates of testing collected in a previous study.

**Aims:** The main aim was to compare the proportion of asymptomatic men with raised PSA levels who were subsequently referred to urology, before and after the launch of the guidelines. Subsidiary aims were to report trends in the rate of PSA testing over a 2½ year period, and patterns of PSA testing in general practice by reason for test over a two period, and to pilot extraction of data on referrals from hospital sources.

**Study areas:** In the previous study four pathology laboratories which provided timely, reliable data were identified in Chichester, Sutton & Merton, Truro, and York, and all general practices which participated in these areas were invited to take part in the present study. No local initiatives for PSA testing or referral were reported by the urologists or chairs of the Primary Care Trusts (PCTs) in these areas.

**Study population:** Men who, at the time of their first recorded test in the study period, were

aged 45 to 84 years and were registered at the consenting practices formed the study population.

**Time periods:** Data on PSA requests were collected for the period 1<sup>st</sup> December 2001 to 31<sup>st</sup> May 2004. Data on urological referrals were collected for the period 1<sup>st</sup> December 2001 to 31<sup>st</sup> May 2002 (pre-launch period) and 1<sup>st</sup> December 2003 to 31<sup>st</sup> May 2004 (post-launch period).

**Data collection:** Pathology laboratories provided data on PSA requests submitted by the GP practices during the study period. Data were collected from the general practices on reason for test, date of subsequent urological referrals and reasons for non-referral. The four categories of reason for test were the same as those used in previous research: men with no prior diagnosis of prostate cancer who were either asymptomatic, symptomatic or being re-tested, and men who were already diagnosed with prostate cancer at the time of the test. To limit the workload of the practices, these data were requested on a stratified sample of PSA requests: records for all men with a test value of 3 ng/mL or more (raised PSA levels), all men with more than one test during the two time periods, and a random 25% sample of men with a single test value below 3 ng/mL (low PSA levels) were selected.

**Outcome measures:** Rates of PSA testing were studied in six month periods by counting the number of men aged 45 to 84 years with at least one PSA test in each period divided by the total number of men registered at the study practices. Reason for test and urological referral were studied using data associated with the first test reported for an individual either during the pre-launch or post-launch period. The definition of 'first test' did not take into account PSA testing outside the study periods. Patterns of testing are reported for men with at least one PSA test in the pre-launch period for whom data on further tests were studied for a two

year period after their first recorded test.

**Uptake rate of practices:** In the previous study, 71 practices in the four areas had taken part. Two of these practices no longer existed at the time of the present study, and, out of 69 practices, 48 (70%) took part. A total of 67162 and 70658 men aged 45 to 84 years were registered at the consenting practices in the pre- and post-launch periods respectively, based on numbers provided by the national PCT database.

**Data completeness:** During the pre- and post- launch periods, 2318 and 3030 men respectively had at least one PSA request. Data were collected on stratified samples of 1418 and 1788 men pre- and post-launch respectively. Exclusion of men who had died or left the practices resulted in 1224 and 1647 men aged 45 to 84 available for analysis pre- and post-launch respectively. In the pre-launch period, PSA levels were low in 515/1224 and raised in 709/1224 men, including men with multiple tests. In the post-launch period, PSA levels were low in 607/1647 and raised in 1040/1647 men. Patterns of PSA testing were studied in 2318 men who had at least one PSA test pre-launch.

**Rates of testing:** The six monthly rate of men having at least one PSA test, age standardized to the male population in England in 2004, increased from 3.4 to 4.3 per 100 men in the pre- and post-launch periods respectively. The rate increased significantly with time and age, and differed significantly between areas ( $p<0.001$ ). Thus the annual rate of testing is estimated to have increased from 6.8 to 8.6 per 100 men.

**Reason for test:** The proportion of men tested who were asymptomatic was similar in the two time periods. A higher proportion of men with low PSA levels than men with raised levels were asymptomatic (39% and 20% respectively post-launch,  $p<0.001$ ).

**Urological referrals according to PCRMP age specific cut-off levels:** There was a small non-significant increase in the proportion of asymptomatic men with low PSA levels referred, from no men pre-launch to 1.6% post-launch (Fisher's exact test  $p=0.07$ ). The proportion of asymptomatic men with raised PSA levels referred increased from 24% pre-launch to 29% post-launch, but this increase was also not significant ( $p=0.42$ ). The PCRMP cut-off levels did not apply to symptomatic men. Overall the proportion of these men referred was higher than that in asymptomatic men, but there was also no significant increase in the referral rate over time. In symptomatic men with raised PSA levels, the proportion referred increased from 38% pre-launch to 45% post launch ( $p=0.067$ ).

**Awareness of receiving the PCRMP information packs :** 56% of GPs acknowledged awareness of receiving the PCRMP packs at the time of data collection.

**Patterns of PSA testing over time:** The distributions of men by number of tests in the two year period following their first test recorded during the pre-launch period were very similar for asymptomatic and symptomatic men, with 67% having one test only, and 22% two tests. In men already diagnosed with prostate cancer, 56% had three or more tests taken. The time interval between the first and second tests decreased significantly with increasing level of PSA at first recorded test ( $p<0.001$ ), but this effect was less evident in men with prostate cancer. Asymptomatic men with low PSA levels were most frequently re-tested at about 12 months after the first recorded test, and, if the first recorded test was raised, most frequently within 6 months of the first recorded test.

**Hospital data on referrals:** Electronic linkage between hospital and laboratory data was only possible at two of the four hospitals. Linkage was very limited because NHS and hospital

numbers were frequently not recorded on the pathology data, partly because many men receiving PSA tests had not previously attended the hospital.

**Limitations:** A randomized controlled trial could not be conducted because the PCRMP packs were distributed nationwide, so an observational approach was adopted. Two distinct six month periods were studied as it was impractical to collect data for longer. It is possible that use of the guidelines could have varied over time. The general practices were a sub-sample of those which had taken part in previous research so that the workload extracting data from patient notes could be reduced. The previous practices were not a random sample and represented just over 30% of those recorded as using the pathology laboratories. The sample under-represented single handed practices and those in deprived areas. The relation of the PCRMP guidelines to decisions about referral could not be studied retrospectively because there were no routinely recorded data on use of the PCRMP packs at the time of each consultation. There was a higher proportion of data on referrals missing on patients who had died or were no longer registered at the practices for the pre- than the post-launch period. As different assays were used to measure PSA at the laboratories, there will have been some variation in the accuracy of measurement which could affect referral rates along with local factors. Finally, the distribution of men by number of tests in the longitudinal period will slightly under-estimate the proportions with multiple tests because the data on those who had left the cohort through death or moving were incomplete.

**Conclusions:** There was no significant change in the proportion of urological referrals in asymptomatic or symptomatic men, over the period before and after the introduction of the PCRMP information packs. Overall the referral rate in asymptomatic men was much lower than expected if the guidelines had been followed, and the proportion of GPs reporting that they were aware of the PCRMP packs was low. The factors affecting urological referrals and

their implications for patient management and diagnosis of prostate cancer need further investigation. The overall rates of testing continue to increase over time, and show significant variation between areas. Without the availability of standardized, routinely available data it will not be possible to study the impact of future trends in PSA testing on general practice workload, the incidence or detection of prostate cancer, or the impact of new initiatives. The impact of the PCRMP guidelines PSA cut off levels appears to be low in this select group of general practices. New approaches to provide effective guidelines need to be developed and piloted but there remains further potential to increase use of the guidelines. The linkage of data on PSA tests and urological appointments was not feasible but recent developments in hospital data systems should improve linkage.

## INTRODUCTION

The rate of Prostate Specific Antigen (PSA) testing for prostate cancer has been increasing in the UK since the early 1990's<sup>1,2</sup>. In 1994 the annual rate in general practices in England and Wales was estimated to be 1.4%<sup>3</sup>. By 2002 the annual rate of testing by GPs in men aged 45-84 years was estimated to be 7% and the rate of asymptomatic testing 1.6%<sup>2</sup>. In September 2002 the NHS Prostate Cancer Risk Management Programme (PCRMP) (<http://www.cancerscreening.nhs.uk/prostate/informationpack.html>) was launched and PCRMP information packs were distributed to all GPs and urologists in England. The programme provided materials to help men requesting a PSA test make an informed choice about the potential benefits and harms of screening. An evaluation study took place in 11 GP practices<sup>4</sup> to study the impact of the provision of a brief decision aid developed for the PCRMP. Men who received the aid and questionnaire, compared with men who only received the questionnaire, had a significantly greater knowledge of PSA testing and prostate cancer and understanding of the risk of the PSA tests, but the proportion of men intending to be tested in the next 12 months was similar in each group.

The information pack also included guidelines to GPs on the age specific PSA cut-off levels for urological referral in asymptomatic men: aged 50-59 years  $\geq 3\text{ng/mL}$ , aged 60-69 years  $\geq 4\text{ng/mL}$  and aged 70 years or more  $> 5\text{ng/mL}$ . The impact of the initiative on referral rates for men with a raised PSA is unknown.

This study was set up to compare the rates of urological referral between two six month periods before and after the introduction of the PCRMP information packs, and to study trends in population-based rates of PSA testing. A randomized controlled trial could not be conducted because of the nationwide distribution of packs. Data from the previous study<sup>2</sup> in England provided a baseline, and the present study was conducted in a subset of the

pathology laboratories and general practices from the first study. In addition, the laboratory data, which were collected over a 2½ year period from 1<sup>st</sup> December 2001, were used to study patterns and frequency of repeat testing in general practice by reason for test. The laboratory data were also used to test the feasibility of linking to hospital appointments to collect data on referrals, compared with collecting data from GPs.

## **AIMS**

The main aims were to study

1. the referral rate, defined as the proportion of asymptomatic men with no prior diagnosis of prostate cancer who were referred to urology by their GPs following a PSA test, according to the level of PSA
2. changes in the referral rate between two six month periods before and after the distribution of PCRMP information packs

Over a 2 ½ year period the rates of PSA testing were studied, and changes in the patterns and frequency of PSA testing in general practice by reason for test were studied. An investigation into the feasibility of linking data on PSA requests electronically to information on subsequent urological referral within each study hospital was conducted. These data were used to check the completeness of data on referrals to those hospitals provided by GPs. The data were not expected to provide an overall measure of referral rates as men will sometimes be referred to other hospitals.

## **MATERIALS AND METHODS**

### ***Approval***

The study had approval from COREC (04/MRE01/39) and the Patient Information Advisory Group (PIAG 2-06(f)/2004).

### ***Study areas and population***

Four laboratories, which took part in the previous study<sup>2</sup> and had provided timely data, all agreed to take part in the study: these were in Chichester, Sutton & Merton, Truro and York. A fifth laboratory, Kidderminster, was considered but the number of practices (2 out of 4 consenting) was too small to provide meaningful results. Practices which had participated in the previous study within each area were invited to take part. The practice addresses and details of GP partners were updated. Each partner provided signed informed consent and completed a one page questionnaire on demographic data, membership of the Royal College of General Practitioners (MRCGP) and awareness of receiving the PCRMP pack. The criteria for study participation were that within each practice all NHS PSA requests were routinely sent to the same laboratory, and all GP partners should give signed consent. This enabled population based rates of testing to be calculated using counts of the male population registered at the practice.

### ***Data collection***

Data on PSA requests were provided by the pathology laboratories for a 2½ year period from 1st December 2001 to 31st May 2004. The variables were specimen number, date of test, name and date of birth of man receiving test, name of GP and practice, total PSA level (ng/mL), NHS number and hospital number. These variables were used by our Unit (the Cancer Screening Evaluation Unit, CSEU) to link records and form a patient-based set of records to investigate the urological referral rates.

Data on referrals were collected from the general practices for two time periods: pre-launch 1<sup>st</sup> December 2001 to 31<sup>st</sup> May 2002 and post-launch 1<sup>st</sup> December 2003 to 31<sup>st</sup> May 2004. The first time period was chosen because data had already been collected on reason for test<sup>2</sup>.

The second time period was chosen at the same time of year to avoid confounding from seasonal variation in the rate of testing PSA and PSA levels<sup>5</sup> and to ensure that GPs would have had time to assess and actively use the packs distributed in September 2002.

To reduce the workload incurred by the practice staff searching patient notes, referral data were collected on a stratified sample of men in each time period. Records for all men with a test value of 3 ng/mL or more, all men with more than one test over the two time periods, and a random 25% sample of men with a single test value below 3 ng/mL were selected. A standardised proforma was prepared for each man, listing all his PSA tests recorded by the laboratory during the study periods (Appendix 1). The coding of reason for testing, which only needed to be collected for the second time period, was the same as that in our previous study. There were four categories: men with no prior diagnosis of prostate cancer who were asymptomatic or symptomatic or being re-tested, and men already diagnosed with prostate cancer (Appendix 1). The focus of the study was on men who were asymptomatic at the time they had their PSA test taken, although data on men tested for other reasons have also been analyzed. Asymptomatic men were defined as those with no prior diagnosis of prostate cancer who:

- requested screening, but did not attend because of prostate symptoms
- were offered PSA screening or re-screening as part of a general health check eg. Well Man Clinic
- were given an opportunistic test by their GP while attending for health reasons unrelated to prostate cancer

(use of these categories was independent of any findings from rectal examination)

If there was any urological referral following a PSA test, the date of referral and hospital name were requested. Reasons for non-referral or for not being able to complete a proforma

were reported eg patient had moved or died. Each general practice was paid a flat rate per patient record checked.

To assess whether any local initiatives might have affected referrals during the study period, questionnaires were sent to the consultant urologists, chairs of the Primary Care Trusts (PCTs) and Directors of Public Health. However, no initiatives were identified up to the end of the post-launch study period.

The numbers of men registered at each practice, used to calculate population based rates of testing, were provided by General Medical Services Statistics, National Primary Care Trust (PCT) Database, National Primary Care Research and Development Centre, University of Manchester. Data were provided by age group and practice for the years 2001, 2002, 2003 and 2004.

### ***Hospital linkage***

To investigate urological referrals using hospital data sources, we first discussed feasibility of linkage with hospital staff responsible for the Patient Appointments System. We then prepared an electronic data file of PSA requests based on the laboratory data using an agreed format. The staff were asked to provide dates of any urological appointments at the hospital which occurred within six months of the date of the PSA request.

There were two steps to linkage:

Step 1: The identifiers of men with PSA records provided by the pathology laboratories were linked to the hospital appointment systems. Limitations with linkage included the absence of NHS numbers from pathology records, and hospital numbers also not always being recorded on the pathology system of one laboratory (in three out of four hospitals studied patients were only given a hospital number if they became an outpatient or in-patient).

Step 2: The hospital system was searched for urological appointments. The main limitation was that the search for urological appointments was restricted to six month time periods and was carried out using consultant urologists' names to identify urological appointments. It is possible that this will have led to some matching being missed.

### ***Sample size***

In the original protocol, it was estimated that, in a sample of 900 PSA requests, 180 might have levels above the recommended age related cut-offs defined by the PCRMP and 720 levels below the cut-offs. The sample size gave 80% power to detect, at the 5% level of significance, a difference for example of 70% vs 83% in the proportions of tests above the age related cut-offs which resulted in referrals before and after the distribution of leaflets. In practice there were more men tested for PSA in the study, and lower rates of urological referral. In the pre-launch period, 131 men were asymptomatic among 709 with raised levels, and 203 among 1040 in the post-launch period. However the proportions referred were considerably lower than we had estimated (< 20%), and the size of increase the study was powered to detect would be equivalent to almost a doubling of the referral rate.

### ***Inclusion criteria and outcome measures***

Rates of PSA testing over time: Men aged 45 to 84 years at the time of their first recorded test in each six month period were included in these analyses. The main outcome measure was the number of men with at least one PSA test within each six month period.

PSA tests by reason for test and urological referral: Analyses were conducted on the first PSA test recorded for each man within the pre- and post-launch periods. Thus the definition

of 'first recorded test' is restricted to PSA tests reported within a strict time period and does not refer to the first PSA test ever taken for an individual. The inclusion criteria were that the men were aged 45 to 84 years at the time of their first recorded test, had a PSA test within either of the two time periods pre- and post-launch, and were not reported dead or no longer registered at their study practice. Outcome measures included the reason for test, and urological referral among men grouped by their PSA levels within each study period. Reason for test identified tests which were associated with screening but this did not necessarily exclude the possibility that some men may well have been screened before or after the study periods.

Patterns of PSA testing over time: All PSA tests recorded for an individual occurring in a two year period following the date of their first PSA test recorded during the pre-launch period were included in the analyses. The men were aged 45 to 84 years at the time of their first recorded test in the pre-launch period. The 'first test' again strictly refers to testing within the study period and did not include reference to any testing prior to study period. The main outcome measures were the number of tests occurring during the time period, and the time interval between first and second tests.

### ***Analysis***

Rates of PSA testing over time: Population-based rates of testing were calculated using the number of men with at least one PSA test within a defined time period as the numerator, and the total number of men registered at the participating practices as the denominator. The annual populations in the participating centres, which were provided by the National PCT database, rose sharply during the study period. For this reason, we wished to estimate the population for each six monthly interval. Using a code for each six month period ( $x=1$  to 5), the equation (population =  $a * x^3 + b$ ) provided a reasonable fit and was used to predict the

population at six monthly intervals. Using the predicted population, the six monthly rate of men test was calculated from 1<sup>st</sup> December 2001 to 31<sup>st</sup> May 2004 and was further age adjusted to the male population of England in 2004 (Appendix 2). The rates were analysed in simple tabulations and Poisson regression.

PSA tests by reason for test and urological referral: The PSA records were grouped according to the stratified sampling: records <3 ng/mL (low PSA levels), and records  $\geq 3$  ng/mL (raised PSA levels), and by time period pre- and post-launch. Men with multiple tests were included. The distribution of reason for test, and proportion of men referred (referral rate) were studied in simple tabulations within these groups of men and also within groups of men categorised by the age specific PSA cut-off levels defined by the PCRMP. Chi-square tests were conducted to test for differences between certain subgroups, and Fisher's Exact test was used when predicted numbers in the cells were below 5. Social deprivation was not included in the analyses as postcodes of individuals were not known. Social deprivation scores were linked to the postcode of the practices, but the range of values was fairly narrow and several practices within each area shared the same score so the interpretation of these data would have been very limited (the mean Townsend score for the participating practices were -2.62 S.D.  $\pm$  0.08, -1.46 S.D.  $\pm$  0.99, -1.32 S.D.  $\pm$  0.50 and -2.16 S.D.  $\pm$  0.83 in Chichester, Sutton & Merton, Truro and York respectively). Given the lack of individual data and small number of referrals it was not feasible to conduct regression analyses of the relation between referral rates and deprivation. It was also not feasible to study variation in referral rates by practice, or between GPs within practices, because of the small number of men being referred.

Patterns of PSA testing over time: All men in the analyses had at least one test in the six month pre-launch period, and their follow-up was truncated to 24 months following their first recorded test. The distributions of men by number of tests in the two year period following their first recorded test in the pre-launch period were studied in simple tabulations. Survival analyses were used to calculate the probability of having a second PSA test over time. Cox proportional hazards model was used to study the effect of age at and PSA level of first test on the probability of having a second test by time interval following the first test. Analyses were conducted separately for each reason for first test. A limitation of the use of survival analyses is that data on date of death or date a man left a GP practice were incomplete, and the assumption had to be made that all men in the analyses stayed in the cohort for the whole two year period.

## RESULTS

### *Uptake of practices*

In the previous study 71 practices participated in the four study areas. Of these, two no longer existed in the post-launch stage, so 69 were invited of which 48 (70%) took part in the present study. The uptake rate was 75% or more in all areas except Truro which had an uptake rate of 57% (Fisher's exact test  $p=0.47$  comparing the response rate in Truro with the other areas). The total male populations aged 45 to 84 years registered at the participating practices were 67162 and 70658 in the pre- and post-launch periods respectively. The uptake rate of practices in the previous study was estimated to be 32%. However, it was considered to be low because many non-responding practices were in fact ineligible i.e. did not use the study laboratory for all their PSA requests. In this study, there were a total of 200 GPs partners at these practices at the time of data collection. The proportions of practices with one, 2-4, 5-6, and 7 or more GP partners were 10% (5), 42% (20), 40% (19) and 8% (4) respectively.

### ***GP characteristics and awareness of PCRMP information pack***

Out of a total of 200 GPs, there were 133 male and 67 female GP partners in the study practices (Table 1). A total of 79% were aged 40 or more years, 60% had membership of the MRCGP, and 76% did seven or more sessions per week. Awareness of receiving the PCRMP pack was acknowledged by 56% of GPs (112/200) with 24 reporting that they were unaware of the pack and 64 reporting that they did not know if they had received it. Awareness did not differ significantly between areas ( $\chi^2_3=6.4$ ,  $p=0.10$ ) but the proportion of GPs aware of the information pack was highest in Truro (69%, 40/58), followed by Chichester with 57% (20/35), Sutton & Merton with 49% (29/59) and York with 48% (23/48). There was some variation in the proportion of GPs aware by age group but the differences were not significant ( $\chi^2_2=2.1$ ,  $p=0.35$ ): 54% in those aged under 40 years, 63% in 40-49 year olds, and 52% in those aged 50 or more years. In Poisson regression analyses, awareness was not significantly related to the factors age, gender, MRCGP, number of years working as a GP, and number of sessions per week. The proportion of GP partners per practice who were aware of the PCRMP pack varied independently of size of practice. In one of the five single partner practices, the GP partner was aware of the pack. In practices with two or more GP partners, all GP partners were aware of the PCRMP pack in 12 of the 43 practices.

### ***Data completeness***

Rates of PSA testing over time: The pathology laboratories provided data on over 2500 GP PSA requests in men aged 45 to 84 years in each of the six month periods from 1<sup>st</sup> December 2001 to 31<sup>st</sup> May 2004. There were fewer than 15 records per period with missing data on PSA value or patient name, or with gender recorded as

female. Following record linkage within each six month period, the total numbers of men with at least one PSA test were over 2300 in each period.

PSA tests by reason for test and urological referral: The pathology laboratories provided data on GP PSA requests in men aged 45 to 84 years for totals of 2494 and 3209 records in the pre- and post-launch periods respectively. Records with missing data on PSA value or patient name, and recording gender as female (12 and 1 records respectively) were excluded. Following record linkage, there were a total of 2318 and 3030 men with at least one PSA test in the pre- and post-launch periods respectively (Table 2). After selecting all men in each period whose first recorded test was raised, all those with more than one test and a 25% random sample of men with single low PSA levels, there were 1418 and 1788 men included in data collection (Table 2). Following further exclusions including men reported by their GP to be deceased or no longer registered at the study practices there were 1224 and 1647 available for analysis pre- and post-launch respectively. Thus in the pre-launch period, 515/1420 men with low records and 709/898 men with raised PSA levels were available for analysis including those with multiple tests (Table 2). The corresponding figures for the post-launch period were 607/1873 and 1040/1157 respectively (Table 2). There were 1111 men with a single test and 113 with multiple tests pre-launch, and correspondingly 1520 and 127 post-launch.

Completeness of data on reason for test was high and similar in both time periods (99% and 98% respectively). The data for this variable were collected close to each time period (pre-launch data collected in the previous study in 2001/2 and post-launch in the present study in 2004/5). A higher proportion of records had data on referral missing as these were all collected in 2004/5 and information was not available for some patients who had died or were no longer registered at the study practices (numbers given in Table 2). The characteristics of

these men were compared with those remaining in the main analyses (Appendix 3). Men who were deceased or no longer registered were significantly older both pre- ( $p<0.001$ ) and post-launch ( $p<0.05$ ), and had a higher proportion of PSA levels above 10ng/mL within each age group (significant for 60-69 year olds and  $\geq 70$  year olds,  $p<0.01$ , pre-and post-launch Appendix 3). Only in the pre-launch period did there appear to be more men already diagnosed with prostate cancer in the deceased or no longer registered group compared with those remaining in the analyses.

Data from the proformas on ethnic group and family history of prostate cancer could not be included in the analyses as high proportions of records had missing data. Ethnicity was missing for 35% (424/1224) and 31% (516/1647) pre-and post-launch respectively. Family history was missing for 86% in both time periods (1058/1224 and 1412/1647 pre-and post-launch respectively). In total over the two periods, only 25 and 44 men were reported to be Afro-Caribbean or have a family history of prostate cancer respectively.

Patterns of PSA testing over time: There were 2318 men aged 45 to 84 years who had had at least one PSA test pre-launch (Table 2) and whose subsequent tests were studied in a two year period following their first recorded test pre-launch. Data on reason for test in the pre-launch period had been collected in the previous study for all tests recorded by the pathology laboratories. Reason for the first recorded test was not known for 243 men (10%) but they were included in the analyses as a not known category.

### ***Rates of testing***

The crude six monthly rate of PSA testing increased from 3.7 (2494/67162) pre-launch to 4.5 (3209/70658) post-launch per 100 men (Table 3). The overall crude six monthly rates of men tested increased from 3.5 (2318/67162) pre-launch to 4.2 (3030/70658) post-launch per 100

men (Table 3). The rates of men tested varied significantly by area ( $p < 0.001$ ) and increased significantly with time ( $p < 0.001$ ) and across the age groups 45-64, 65-74 and 75-84 years ( $p < 0.001$ ).

### **Reason for test**

The percentage distributions of reason for test in men with low and men with raised PSA levels were similar in both time periods (Table 4). Within each time period a higher proportion of men with low PSA levels were asymptomatic compared with men with raised PSA levels (pre-launch 38% and 19% respectively,  $\chi^2_1 = 56.3$   $p < 0.001$ , and post-launch 39% and 20% respectively  $\chi^2_1 = 71.2$   $p < 0.001$ ).

The population based rates of testing per 100 men were calculated by reason, adjusting for the proportion of records without data on reason for test, based on the numbers in Tables 2 and 4, although the calculations should be treated with caution given the high number of low records excluded from data collection, and potential bias arising from missing data in men who were deceased or had moved. Pre-launch it was estimated that there might have been a total of 704 asymptomatic men giving a population based six monthly rate of 1.1%, and post-launch 948 asymptomatic men giving a six monthly rate of 1.3%. There also appeared to be a slight increase in the estimated rates for symptomatic men and for men already diagnosed with prostate cancer.

The distribution of men by reason for test varied by area. Results were similar in each time period. Post-launch in men with low PSA levels, the proportions of tests which were in asymptomatic men were 41% (67/162), 53% (82/155), 26% (51/197) and 37% (34/93) in

Chichester, Sutton & Merton, Truro and York respectively ( $\chi^2_3 = 27.5$   $p < 0.001$ ). Post-launch in men with raised PSA levels, the proportions of tests which were in asymptomatic men were 26% (68/264), 25% (54/219), 14% (53/386) and 16% (28/171) in Chichester, Sutton & Merton, Truro and York respectively ( $\chi^2_3 = 19.5$   $p < 0.001$ ).

### ***Urological referrals in asymptomatic men***

There were no referrals in asymptomatic men with low PSA levels (PSA level  $< 3$ ng/mL) pre- or post-launch (Table 5). The proportion of asymptomatic men referred in those with raised PSA levels increased from the pre- to post-launch period (13.7% and 18.2% respectively) but the difference was not statistically significant. There was also no significant difference in the referral rates by area in either time period. Among those not referred, the most frequent reason was PSA too low (87%, 347/400 post-launch), and re-testing scheduled by GP in general practice (7%, 29/400 post-launch). In the raised PSA group, additional reasons for non-referral included serious co-morbidity.

Analysis of referral according to the PCRMP age specific cut-off levels, restricted to men aged 50 to 84 years, showed that there were non-significant increases in the proportion of men referred over time for men with PSA levels below (0.0 to 1.6%, Fisher's exact test  $p = 0.07$ ) and above the age specific cut-off levels (24.0 to 29.4%  $p = 0.42$ , Table 6). The proportion of men referred appeared to increase across the age groups in the post-launch period but there was no statistically significant trend (Table 6: in men with PSA levels below the cut offs  $p = 0.15$ ; in men with PSA levels above the cut offs  $p = 0.32$ ). Similarly there was no significant trend with age pre-launch (in men with PSA levels below the cut offs  $p = 0.15$ ; in men with PSA levels above the cut offs  $p = 0.21$ ). A more detailed breakdown for all age

groups and using 3ng/mL as well as the PCRMP cut off levels is shown in Table 7.

Of all 55 men referred, 45 (82%) were referred within two months of their test. The levels of PSA actually associated with referral in men with raised PSA levels are shown in Table 8. Post-launch the median PSA value associated with referral increased with age from 6.2 ng/mL in 50-59 year olds to 13.0 ng/mL in 70-84 year olds. (Only five men with PSA levels below the PCRMP age specific cut-offs were referred: PSA levels ranged from 3 to 4.9 ng/mL in men aged 60-84 years). The number of men is small so the results should be interpreted with caution. The median values for the distributions of PSA levels associated with referral showed little difference pre- and post-launch.

The PSA levels in asymptomatic men who were not referred with reason given as PSA level too low were also studied (Table 9). Of particular interest are those for whom the PSA level was above the PCRMP age specific cut-offs. Post-launch, in men aged 50-59, 13 out of 72 had levels above the guidelines with range 3 to 5.2 ng/mL; in men aged 60-69, 13 out of 125 had levels above the guidelines with range 4 to 8.9 ng/mL; and in men aged 70-84, 9 out of 138 had levels above the guidelines with range 5.3 to 7.5 ng/mL. The levels were similar pre-launch. All levels associated with non-referral in this group of men were below 10 ng/mL.

### ***Urological referrals in symptomatic men***

Urological referral of symptomatic men will be determined by several factors besides the level of PSA. It was not practical to collect these data retrospectively. Nevertheless the opportunity is taken to report referral rates in symptomatic men so that some comparison may be made with referrals in asymptomatic men.

Among symptomatic men with low PSA levels, 11% (21/188) and 9% (18/201) of men were

referred following their first recorded test pre- and post-launch respectively (no significant difference, Table 10). About 90% of non-referrals with low records in both periods were because the GP considered the PSA level to be low.

Among symptomatic men with raised PSA records, 38% (110/284) and 45% (203/445) were referred following their first recorded test in the pre- and post- time periods respectively (difference not significant,  $p=0.067$ , Table 10). Among non-referrals with raised PSA levels, just over 48% in both time periods were reported by their GPs as having PSA levels too low for referral. In symptomatic men who were non-referrals there was a significant increase in the proportion of men scheduled for a re-test initiated by the urologist (6.2%, 21/341, and 11.5%, 44/381, pre- and post-launch respectively,  $\chi^2_1 = 4.29$ ,  $p=0.04$ ). These men had presumably had a urological referral prior to the date of the PSA test being studied. There was no significant increase in the proportion of non-referrals scheduled for a re-test at the initiative of their GP.

Of 352 men referred, 321 (91%) were referred within two months of their test. There was little difference in the distribution of the PSA levels actually associated with referral between the pre- and post-launch periods. For men with low PSA levels, there was little difference in the PSA levels associated with referral by age. Overall the levels ranged from 0.3 to 2.7 ng/mL. For men with raised PSA levels pre-launch, in 45-49 year olds two men were referred with PSA levels of 8.0 and 11.1 ng/mL, in 50-59 years 13 referred with levels ranging from 3.4 to 29.5 ng/mL (median 6), in 60-69 year olds 31 referred with levels ranging from 4.0 to 62.8 ng/mL (median 7) and in 70-84 year olds 64 referred with levels ranging from 3.0 to 1364.0 ng/mL (median 9.5).

### ***Patterns of PSA testing***

The distribution of men according to the total number of GP PSA requests recorded during a two year period from the date of their first test recorded from 1st December 2001 to 31<sup>st</sup> May 2002 is presented by reason for first recorded test (Table 11). In 614 men reported to be asymptomatic and 862 symptomatic, the distributions of number of tests were very similar with about 67% having one test only, and 22% two tests. Among 369 men whose first recorded test in the study period was a retest, there were higher proportions with 3-5 tests (39%), and 6-10 tests (1.4%). The number of tests was highest for the 230 men already diagnosed with prostate cancer: 42% having 3-5 tests, 12% 6-10 tests and 2% more than 10 tests. Those with reason for test not known (243) had a distribution of number of tests similar to asymptomatic and symptomatic men.

The relationship between PSA level of first recorded test and time interval to second test is illustrated for asymptomatic men grouped by whether their first recorded test was <4ng/mL or  $\geq$ 4ng/mL (Figure 1). The value of 4ng/mL was chosen because this has often been studied in the literature as a cut-off level for PSA. In men whose first recorded test was <4 ng/mL, the most frequent time interval to the second test was 11 to 13 months (40/147, 27%), but in men whose first recorded test was  $\geq$ 4 ng/mL, the men were most frequently re-tested 1 to 7 months after the first recorded test ( 30/56, 54%).

The interpretation of patterns of testing in symptomatic men and those with prostate cancer is limited without other information such as presence of symptoms, and choice of management and treatment. However, the relationship between PSA level of first recorded test and time interval to second test in symptomatic men and those being re-tested at their first recorded test (Figures 2 and 3) was similar to that in asymptomatic men. Men already diagnosed with prostate cancer were most frequently re-tested within 7 months of the first recorded test

whether they had a low PSA level (52%, 62/120) or a raised PSA level (79%, 72/91) (Figure 4). Results for men with reason for test not known were similar to those for asymptomatic men (Figure 5).

The results of the survival analyses to study the probability of having a second test over time by PSA level (<4 ng/mL and  $\geq$ 4 ng/mL) and age ( $\leq$ 69 years and >69 years) at first test are presented by reason for test (Figures 6 to 10). In asymptomatic men (Figure 6) and those with reason for test not known (Figure 10), the cumulative probability of a second test was significantly greater in men with higher PSA levels and in men in older age groups. In symptomatic men there was a significant interaction between level of first PSA test and age; the probability of a second test increasing more with older age when the PSA test was <4 ng/mL than when the PSA test was higher, but the probability of a second test being highest in men a raised PSA level (Figure 7). In men being re-tested at their first test recorded in the pre-launch period the probability of a second test only increased significantly with increasing level of first PSA test (Figure 8), and in men already diagnosed with prostate cancer the probability of a second test was independent of age or level of first PSA test (Figure 9).

### ***Hospital linkage***

It was only possible to submit all records from the pathology laboratory for linkage to the hospital appointment system in two out of the four hospitals (Table 12). At the two other hospitals manual linkage would have been required. Therefore results are only quantified for two hospitals (Table 13). A total of 47% of pathology records were linked to the hospital system in both hospitals. Of the PSA records reported by the GPs to be followed by a urological referral, 43% were identified in Sutton & Merton and 55% by the hospital in Chichester. It was expected that some appointments would be recorded by the GPs but not found by the hospital studied as some men may have chosen to go privately. Appointments

recorded by the hospital, and not the GP (8% for Sutton & Merton and 7% for Chichester), may be follow-up appointments organised within the hospital as the time period covered by the hospital linkage was six months following the date of each PSA test.

## **DISCUSSION**

The main aim of this study was to investigate whether the PCRMP guidelines for age specific cut-off levels for PSA had influenced GP referrals to urology in asymptomatic men by comparing urological referrals in two time periods pre- and post-launch of the PCRMP information packs. There was no significant increase in the proportion of asymptomatic men being referred following a PSA test between the pre-launch and post-launch periods. Using the PCRMP age specific cut-off levels, the proportions referred when their PSA level was above the cut-offs were 24% and 29% pre- and post-launch respectively ( $p=0.42$ , Table 6). Moreover, the proportions referred were lower than anticipated when planning the study. Thus the influence of the PCRMP PSA cut off levels seems to have been low: 56% of GPs in the study reported being aware that they had received the information packs. There was also no significant increase in the proportion of referrals in symptomatic men: in those with raised PSA levels the proportions of urological referrals were 39% and 46% pre- and post-launch respectively ( $p=0.067$ ). The relation of the PCRMP PSA cut off levels to decisions about referral could not be studied retrospectively because there were no routinely recorded data on use of the PCRMP packs at the time of each consultation.

There was no consistent cut-off level for PSA associated with referral following testing in asymptomatic men. No local guidelines for asymptomatic men were reported. Review of the guidance provided in the study laboratories' pathology reports were primarily concerned with symptomatic patients and those already diagnosed with prostate cancer. At one laboratory,

for symptomatic men, values  $>10$  ng/mL were advised to be significant. In prostate cancer patients PSA levels  $<10$  ng/mL was reported associated with prolonged remission, and those with a PSA level of  $>10$  ng/mL associated with progression of the disease. The laboratory advised that “measuring PSA in men under 50 years is not indicated unless on the advice of a urologist”. At a second laboratory prostate cancer was reported on the pathology report to be found in 15% of men with PSA  $<4$  ng/mL, 20% with PSA 4-10 ng/mL and 65% of men with PSA  $>10$  ng/mL. A third laboratory provided no guidelines on the report. The fourth laboratory used  $\geq 4$  ng/mL as the cut off level during the pre-launch period but in the post-launch period they used age specific levels: at age 50-59  $\geq 3$  ng/ml, at 60-69 years  $\geq 4$  ng/ml, at 70 or more years  $\geq 5$  ng/ml.

Additional analyses were conducted on the pattern and frequency of GP PSA requests longitudinally over a two year period, the overall rate of PSA testing, and the feasibility of using hospital data to study referral rates.

The frequency and time intervals between PSA tests showed great variation and were partly determined by the reason for test and the PSA level recorded. During the 2 year follow-up period, the majority of men who were asymptomatic or symptomatic at their first recorded test were tested just once (67%, Table 4). Multiple testing was far more frequent in men tested for other reasons at their first recorded test (those not diagnosed with prostate cancer being re-tested or those already diagnosed with prostate cancer). The time interval between the first and second test was significantly lower in those men whose first test was  $\geq 4$  ng/mL than in those whose first test was  $<4$  ng/mL ( $p<0.01$ ) for all groups except men already diagnosed with prostate cancer. In asymptomatic men the probability of a second test was higher in older age groups than those aged  $\leq 69$  years ( $p=0.003$ ) (Figures 6 – 10) . It was not feasible in this study to collect detailed data on all factors which might have influenced the pattern of

testing such as the presence or absence of infections or benign prostatic hyperplasia in symptomatic patients, and progression and management of prostate cancer patients. Therefore the results should be interpreted with caution.

Overall the six monthly rate of men tested increased over time from 3.4 to 4.3 per 100 men aged 45 to 84 years, age adjusted to the male population in England in 2004 (Table 3). There was evidence that the GPs were testing more asymptomatic and symptomatic men, as well as men already diagnosed with prostate cancer.

The study helps to illustrate the amount of re-testing of PSA which GPs carry out. Post-launch, a total of 20% of men with low and raised PSA levels were being re-tested at their first recorded test, and a further 12.3% of men tested were already diagnosed with prostate cancer (Table 4). In symptomatic men who were non-referrals there was a significant increase in the proportion of men scheduled for a re-test initiated by the urologist (6%, 21/341 and 11.5%, 44/381 pre- and post-launch respectively,  $p=0.04$ , Table 10). These men had presumably been seen by a urologist before the date of the PSA test being studied.

Electronic linkage of pathology PSA records to hospital appointments was only possible in two out of four hospitals and required some manual checking and identification of patients. Fifty percent of urological referrals to the study hospitals reported by GPs were identified in the linkage exercise. There are a number of reasons why details of a referral may not have been identified including patients deciding not to be referred or opting for a private referral.

### ***Study limitations***

The study limitations include the design of evaluation, and timing of data collection, selection of practices, incomplete data, and accuracy of PSA measurements.

Ideally interventions should be evaluated in a randomized controlled trial but this was not possible because the PCRMP information packs were distributed nationwide. The results of observational data cannot provide conclusive evidence of the effect of the programme. Although no local initiatives were reported by the urologists and PCTs in the study areas during the study periods, other factors including events reported in the national or local media could have influenced men's awareness of prostate cancer and their demands on GP services. However, if the PCRMP PSA cut off levels had had a strong impact on PSA testing and referrals, this should have been reflected in changes in the referral rates in asymptomatic men. It was not feasible in this evaluation to ask GPs retrospectively if they had used the PCRMP information packs for each referral decision or to study men's experiences of PSA testing but these merit specific research studies<sup>6</sup>.

There is also the fact that the observational periods were restricted to two six month periods, December to May, 18 months apart. Controlling for time of year removes potential bias from seasonal variation in rates of testing and levels of PSA<sup>5</sup>. The second period was a year after the launch of the PCRMP information packs which might have allowed GPs and urologists to take on board any recommendations and alter local guidelines for referral. Alternatively, the impact of the PCRMP may not have been sustained. Although it would have been informative to study referral rates over a continuous period this was not practical because of the lack of routine data on reason for test or on referral. The overall rate of testing increased significantly over time (Table 3)

The practices were highly selected as only those practices which had taken part in the earlier study were invited to join this study, so that previous data could be used, thus reducing the workload associated with searching patient notes. The earlier study had a low uptake rate by

GPs (32%), although this is likely to be an under-estimate because ineligible practices were among the non-responders. In both studies the participating practices represent a smaller proportion of single-handed practices (10% in the present study) than nationally (27% in 2004<sup>7</sup>) and represented a fairly narrow range of Townsend scores. As the rate of testing increases with affluence, it is likely that, on the one hand, the rate in this study is an over-estimate of the national rate, but on the other hand it is also an under-estimate as data on private testing were not available. It is possible that the participating GPs may have been more likely than other GPs to have used the PCRMP packs and more likely to make urological referrals than other GPs if a special interest in prostate cancer was associated with their willingness to participate in both of our studies,.

Data on referral were incomplete for men who had died or who were no longer registered at the practices as their notes were not available. Out of all men for whom data on referral were requested, the proportion of men deceased or no longer registered was greater pre-launch than post-launch (13.7%, 194/1418, and 7.9%, 141/1788, respectively:  $\chi^2_1 = 28.4$   $p < 0.001$ ), was greater in older age groups and within these older groups, they had a higher proportion with PSA level  $\geq 10$ ng/mL compared with men for whom data on referral were complete ( $p < 0.01$ ). This suggests that those excluded from the analyses were more likely to have been symptomatic or diagnosed with prostate cancer than men for whom data were complete. Thus, referral rates in asymptomatic men, the main outcome measure of the study, are less likely to have been affected by the loss of men who had died or were no longer registered at the study practices than referral rates in men tested for other reasons. Missing data on deaths and on men leaving the practices will also have affected the analyses of patterns of PSA testing, but this is less likely for the analyses of testing in asymptomatic men.

Data on reason for test was not known for 10% of men in the analyses of patterns of testing.

However their results were very similar to men recorded as asymptomatic. It is conceivable that nearly all men with a history of symptoms or prostate cancer will have this recorded in their notes, but those tested without symptoms will have less information in the notes and so were more likely to be recorded as not known. In addition in the longitudinal analyses, the distribution of men by number of tests will slightly under-estimate the proportions with multiple tests because the data on those who had left the cohort through death or moving were incomplete.

The proportion of asymptomatic men being tested may be over-estimated, because of the loss of men who were deceased or who had moved, the former being old and more likely to be symptomatic or diagnosed with prostate cancer. On the other hand, the overall proportion of asymptomatic men being tested within defined populations will have been under-estimated because a proportion will have been tested privately.

All of the laboratories participated in the Quality Assurance scheme for PSA measurement<sup>8</sup>. Their methods of measurement were Bayer Immunol, Bayer Centaur and DPC Immulite used by two. There may have been variation in the accuracy of the PSA measurements which could contribute towards variation in referral rates. In addition, one laboratory rounded all PSA values to whole numbers so the distribution of PSA values in this area will represent slightly higher values than the other areas. In turn this may have raised the age related referral rates. Using data from the previous study, we are able to compare the distribution of the laboratory's data on the original values to one decimal place with the distribution of the rounded values. Of 320 men with at least one PSA test pre-launch, 99 were asymptomatic. When these men were grouped by the PCRMP age specific cut-off levels, a total of seven were classified as above the cut-offs for 50-59, and 60-69 year olds when their true value was below the cut-offs, and five men over 70 years were classified as below the cut-off for that

age group (>5ng/mL) when their true value was 5.0/mL. It is unlikely that these small numbers would have had a significant effect on the analyses of referral rates. The cut-off levels associated with referral in asymptomatic men varied greatly, so it is unclear what effect the rounded values would have had overall on referral rates. The study areas were selected because their pathology laboratories were known to provide reliable and timely results but this is unlikely to have directly affected use of the PSA test by GPs.

The practices were asked about reasons for non-referral, but they were not asked if the PCRMP packs influenced their decision to refer. This can only be assessed indirectly by the fact that there was variation in referral rates by age and PSA level which did not conform with the PCRMP age specific cut-off levels.

Finally, assessments were made of the quality of the data collected in the proformas. At some practices the proformas were completed partly by a practice nurse or manager and not by the patient's GP. Any concerns about quality of the data could have affected reason for test but not the referral data, as the latter required a date of referral and consultant name. A series of internal checks provide reassurance about the reliability of reason for test. Analysis of reason for test by PSA level showed that low levels were associated with asymptomatic testing, as has been found in screening trials<sup>9</sup>. Tests recorded as a re-test were checked, where possible, against the full record of PSA tests for each patient and re-testing was confirmed. Reason given as patient already diagnosed with prostate cancer correlated with other data on the proforma including the date of prostate cancer diagnosis. It was not feasible to collect data on the full history of testing in an individual: without these data, reason for test has to depend on reporting by the general practices.

### ***Comparisons of results with other studies***

**Referral studies:** There are very few studies reporting on urological referral rates in general

practice, partly because there is considerable workload involved in retrospectively searching patient notes. Some studies have investigated PSA tests prior to a diagnosis of prostate cancer. One study in Liverpool showed that among 219 men referred to urology via the fast track service (191 from primary care and 28 from secondary care, 100% response rate) 41.5% were aware of having a PSA test prior to referral. An NHS survey of 10719 prostate cancer patients<sup>10</sup> showed that 85% had seen their GP prior to diagnosis, mean age being 73 years, and 55% received care by GP post-discharge.

In the USA<sup>11</sup>, referral rates were studied in men aged  $\geq 75$  years with no prior prostate cancer diagnosis attending one centre in Iowa: in those with PSA levels between 0.1 and 4.0 ng/mL 28.6% were referred, and in those with PSA levels  $>4.0$  ng/mL 52% were referred. For the comparable populations defined by age and PSA level in our study, 7% (8/120) and 30% (56/186) were referred respectively pre-launch with similar proportions post-launch.

**Patterns of PSA testing:** There are few reports of patterns of testing in general practice, with most studies simply reporting the proportions of men having their first recorded test or repeat test in defined periods. In Northern Ireland<sup>1</sup> overall 38% of men had more than one test either requested by their GP or by a urologist, and this was more likely in older men and those whose previous PSA tests was  $>4$  ng/mL. Repeat testing was more frequent in secondary care (42%) than in primary care (36%). In Tayside<sup>12</sup> the number of PSA tests per patient increased from 1.1 in 1992 to 2.6 in 2001.

In the USA one study linked data from the SEER dataset to Medicare physician claims of PSA testing<sup>13</sup>. The cohort of 20894 men was free of cancer prior to 1st January 1988 and aged 65 years or more by that date. By 1994 53% of white men and 45% of black men had had a test. After the 1st test 35% of white men were tested within a year, 68% within two years and

by four years 87%. The time interval between tests shortened as men had more tests. However there was variation in this practice given the distribution of time intervals from less than one year to four years between tests.

**Rates of testing:** The age adjusted six monthly rates of men tested were doubled to provide estimates of the annual rates of men tested: 6.8 per 100 men and 8.5 per 100 men pre-launch and post-launch respectively age adjusted to men in England in 2004. In the UK there are no standardized, longitudinal data to study time trends in rates of testing, but the results of several studies strongly indicate that PSA testing has been increasing in England and Wales<sup>14</sup>, and in Northern Ireland<sup>1</sup>. The rate of testing varies between areas, although comparison between studies should be made with caution because of differences in methodology and time periods<sup>1,2,12</sup>. For example, in Northern Ireland, in primary care the annual rate of first PSA testing was 9.2 per 1000 men for 1994-96 rising to 11.8 per 1000 men in 1997-99. Although reason for test was not known, the proportion of tests with level of PSA  $\leq 4$  ng/mL increased over time indicating more testing of asymptomatic men in general practice. This study and our previous study in England and Wales confirm a wide variation in the rate of testing between general practices. Other research in the UK has asked GPs about their use of the PSA test and attitudes towards screening<sup>15</sup>. This confirmed that testing of asymptomatic men is a regular occurrence in the UK, and that there was general support from the GPs for the use of guidelines on informed consent.

In the USA rates of testing have been increasing since the early 1990s and the rates are high compared with most other countries<sup>16</sup> (Table 14). Population based rates of testing in men attending outpatient visits to office based physicians from 1999 to 2002<sup>17</sup> were found to be 6.1% in 40-49 year olds, 26.0% in 50-75 year olds, and 27.8% in those aged 75 or more. In a study of asymptomatic testing in primary care<sup>18</sup>, screening increased from 19% before to 26%

after the publication of the American Cancer Society guidelines. Testing is far more frequent in older men in the USA compared with the UK. In 2003, 56% of men aged 70 or more years with no history of prostate cancer received a PSA test, and over 30% of men aged 85 or older were tested.<sup>19</sup> Whereas, in the present study pre-launch 6.3% (603/9600) men aged 75 to 84 years were tested. There is wide variation in the rates in other countries but the methods of data collection and outcome measure contribute to this variation (Table 14).

## CONCLUSIONS

With the observational approach used and the highly selected samples of practices, there appeared to be no marked effect of the guidelines on the proportion in asymptomatic men being referred by GPs. GPs appear to have adopted a varied, but cautious approach to referral, with all non-referrals having PSA levels below 10 ng/mL and the proportions referred being lower than expected. The proportion of referrals was higher in symptomatic men. Re-testing was the most frequent management in non-referrals.

The effect of the PCRMP PSA cut off levels on asymptomatic testing is uncertain but the rate of testing increased over time. With 56% of GPs acknowledging awareness of receiving the packs, this suggested that use of the materials to provide men with informed consent on PSA testing is limited but there remains further potential to increase use of the guidelines. The proportion could be lower in non-participating study practices. The fact that there is considerable variation in the frequency of testing and time intervals between PSA tests indicates that the present work to revise, pilot and evaluate<sup>4</sup> the PCRMP information packs is timely and urgently needed. Without routine, standardized data collection on reasons for PSA tests and urological referral in general practice, it will be impractical to monitor future trends in use of the PSA test, its impact on GP workload and its long-term effects of the detection rates of prostate cancer nationwide.

The results of linkage of PSA data to urological referrals within hospitals cannot be reliably reported. However, as new hospital systems are currently being introduced, it is expected that linkage within the hospital system will improve, and provide useful data for monitoring, and for research and development.

**Recommendations for future research:**

Further investigation is required into:

- the factors which influence or motivate men to request a PSA test
- whether GPs discuss the PSA result with their patient and options for management including referral or retesting
- variation in referral rates among a wider group of general practices and the implications of this variation for patient management and diagnosis of prostate cancer
- the factors which influence a GP's decision to refer or not to refer including use of any specific guidelines
- the reasons for the apparent increase in re-testing of PSA by GPs both initiated by the GPs themselves and by urologists
- the workload and economic costs associated with different referral strategies which would help to inform future recommendations for patient management
- methods to improve the availability of routine data to aid future research into screening and its impact on detection rates of prostate cancer.

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**TABLES****TABLE 1** Distribution (%) of GPs by characteristics and awareness of receiving the PCRMP information pack

<b>Variable</b>	<b>Categories</b>	<b>Percentage distribution</b>	<b>Number</b>
<b>Sex</b>	Male	66.5	133
	Female	33.5	67
	Total	100.0	200
<b>Age (years)</b>	% <40 years	21.0	37
	% ≥40 years	79.0	139
	Total	100.0	176
	Not known		24
<b>Membership of RCGP</b>	Yes	59.8	113
	No	40.2	76
	Total	100.0	189
	Not known		11
<b>No. sessions per week pre-launch</b>	% <7	23.6	41
	% ≥7	76.4	133
	Total	100.0	174
	DNA*		8
	Not known		18
<b>Awareness of receiving the PCRMP pack</b>	Yes aware	56.0	112
	Not aware	12.0	24
	Did not know	32.0	64
	Total	100.0	200

\*DNA Does not apply as GP did not work at practice in pre-launch period

**TABLE 2** Number of men for whom data were collected and counts of exclusions by time period and PSA level (low <3ng/mL, raised ≥3ng/mL)

	<b>Pre Launch 1<sup>st</sup> Dec 2001 to 31<sup>st</sup> May 2002</b>			<b>Post Launch 1<sup>st</sup> Dec 2003 to 31<sup>st</sup> May 2004</b>		
	<b>Total</b>	<b>No. with 1<sup>st</sup> test low record</b>	<b>No. with 1<sup>st</sup> test raised record</b>	<b>Total</b>	<b>No. with 1<sup>st</sup> test low record</b>	<b>No. with 1<sup>st</sup> test raised record</b>
<b>No. men aged 45-84 before stratified sampling</b>	2318	1420	898	3030	1873	1157
<b>Reasons for exclusions from laboratory data files:</b>						
<b>Removed by sampling procedure</b>		848	0		1199	0
<b>One practice reduced workload</b>		9	23		11	32
<b>At one lab , GPs only notified of rounded values so some PSA levels were classified as low</b>		NA	20		NA	0
<b>No. men aged 45-84 after stratified sampling</b>	1418	563	855	1788	663	1125
<b>Reasons for exclusion from data analysis after data collection from general practices:</b>						
<b>Men's records not available through death or no longer registered at practice</b>	194	48	146	141	56	85
<b>No. men aged 45-84 alive and still registered at practice</b>	1224	515	709	1647	607	1040

NA: not applicable

**TABLE 3** Number of GP PSA requests and number of men tested aged 45 to 84 years within each six month period from 1<sup>st</sup> December 2001 to 31<sup>st</sup> May 2004

Time period	01/12/2001- 31/05/2002	01/06/2002- 30/11/2002	01/12/2002- 31/05/2003	01/06/2003- 30/11/2003	01/12/2003- 31/05/2004
<b>No. PSA requests</b>	2494	2692	2657	2784	3209
<b>No. of Men</b>	2318	2552	2496	2620	3030
<b>Total Population no.<sup>+</sup></b>	67162	67491	68131	69187	70658
<b>Rates</b>					
<b>requests/100 men</b>	3.71	3.99	3.90	4.02	4.54
<b>men tested/100 men</b>	3.45	3.78	3.66	3.79	4.24
<b>Age adjusted<sup>†</sup></b>					
<b>men tested/100 men</b>	3.43	3.79	3.67	3.81	4.25
<b>Age*</b>					
<b>Mean</b>	67.4	67.2	67.7	67.7	70.8
<b>St. Dev</b>	9.62	9.50	9.29	9.27	8.16
<b>PSA levels ng/mL</b>					
<b>* 25%</b>	0.8	1.0	1.0	1.0	1.0
<b>at points in</b>					
<b>50%</b>	2.0	1.9	2.0	2.0	2.0
<b>% distribution</b>					
<b>75%</b>	4.9	4.5	4.9	5.0	4.7
<b>Maximum</b>	1694	2295	2338	2590.7	3894

<sup>+</sup> Based on data provided from the National PCT database

<sup>†</sup> Adjusted to the male population of England aged 45 to 84 years in 2004

\* Men at 1<sup>st</sup> test

**TABLE 4** Distribution of men by reason for test for two time periods and PSA level low (<3 ng/mL) or raised (≥ 3 ng/mL)

Reason for test	Pre-launch 1 <sup>st</sup> Dec 2001 to 31 <sup>st</sup> May 2002				Post-launch 1 <sup>st</sup> Dec 2003 to 31 <sup>st</sup> May 2004			
	Low records*		Raised records		Low records*		Raised records	
	no.	%	no.	%	no.	%	no.	%
Asymptomatic	194	37.7	131	18.5	234	38.6	203	19.5
Symptomatic	188	36.4	284	40.1	201	33.1	445	42.8
Re-test	56	10.9	220	31.0	56	9.2	273	26.3
Prostate cancer already diagnosed	72	14.0	68	9.6	100	16.5	103	9.9
Not known	5	1.0	6	0.8	16	26.4	16	1.5
<b>Total included in data collection</b>	<b>515</b>	<b>100</b>	<b>709</b>	<b>100</b>	<b>607</b>	<b>100</b>	<b>1040</b>	<b>100</b>
<b>Significance of difference in distribution of reason for test between low and raised records</b>	$\chi^2 = 100.3, p < 0.001$				$\chi^2 = 132.9, p < 0.001$			

No significant differences between the two time periods were found in the distribution of reason for test among men with low or men with raised PSA levels

\* based on sub-sample, see Table 2

**TABLE 5** Number of urological referrals and reasons for non-referral in asymptomatic men aged 45-84 years by time period and PSA level low (<3 ng/mL) or raised ( $\geq 3$  ng/mL)

	Total number of men	Referrals		Non-referrals		Significance of difference in proportion referred between low and raised records	Distribution of non-referrals by reason						
		no.	%	no.	%		PSA too low	Re-test scheduled and initiated by		Serious co-morbidity	Other	Lost to Follow up	Not known
								GP Practice	Urologist				
<b>Pre-launch</b>													
Low records*	194	0	(0.0)	194	(100)	Fisher's exact test  p<0.001	187	3	0	0	3	0	1
Raised PSA levels	131	18	(13.7)	113	(82.3)		71	21	2	6	3	3	7
<b>Total</b>	<b>325</b>	<b>18</b>	<b>(5.5)</b>	<b>307</b>	<b>(94.5)</b>		<b>258</b>	<b>24</b>	<b>2</b>	<b>6</b>	<b>6</b>	<b>3</b>	<b>8</b>
<b>Post-launch</b>													
Low records*	234	0	(0.0)	234	(100)	Fisher's exact test  p<0.001	230	3	0	1	0	0	0
Raised PSA levels	203	37	(18.2)	166	(81.8)		117	26	4	6	7	1	5
<b>Total</b>	<b>437</b>	<b>37</b>	<b>(8.5)</b>	<b>400</b>			<b>347</b>	<b>29</b>	<b>4</b>	<b>7</b>	<b>7</b>	<b>1</b>	<b>5</b>

No significant differences between the two time periods in distributions of proportion referred for either low or raised PSA levels

\* based on sub-sample, see Table 2

**TABLE 6** Proportion of asymptomatic men referred pre- and post-launch whose PSA levels were above or below the age specific PSA cut-off levels recommended by the PCRMP (restricted to men aged 50 to 84 years)

	Age (yrs)	50 - 59		60 - 69		70 - 84		Total percentage of men referred below and above the age specific cut-off levels	
		PSA level (ng/mL)	<3	≥3	<4	≥4	≤5	>5	Below
<b>Pre-launch</b>	%	0.0	37.5	0.0	22.9	0.0	16.7	0.0	24.0
	No. referred	0	6	80	8	0	4	0	18
	Total no. men	65	16		35	95	24	240	75
<b>Post-launch</b>	%	0.0	18.2	0.9	31.0	2.9	33.3	1.6	29.4
	No. referred	0	4	1	13	4	15	5	32
	Total no. men	60	22	115	42	140	45	315	109

No significant difference in the overall proportion of referrals between pre and post-launch periods.

**TABLE 7** Proportion of asymptomatic men referred pre- and post-launch aged 45-84 years grouped by PSA level and age

	Age (yrs)	45 - 49		50 - 59		60 - 69				70 - 84				Total % men referred below & above age specific cut-off	
		PSA level (ng/ml)	<3	≥3	<3	≥3	<3	≥3 - <4	Total <4	Total ≥4	<3	≥3 - ≤5	Total ≤5	Total >5	Below
<b>Pre - launch</b>	%	0.0	0.0	0.0	37.5	0.0	0.0	0.0	22.9	0.0	0.0	0.0	16.7	0.0	24.0
	No. Referred	0	0	0	6	0	0	0	8	0	0	0	4	0	18
	Total no. men	10	0	65	16	61	19	80	35	58	37	95	24	250	75
<b>Post - launch</b>	%	0.0	0.0	0.0	18.2	0.0	3.4	0.9	31.0	0.0	6.5	2.9	33.3	1.5	28.6
	No. Referred	0	0	0	4	0	1	1	13	0	4	4	15	5	32
	Total no. men	10	3	60	22	86	29	115	42	78	62	140	45	325	112

No significant difference in the proportion of referrals between pre and post-launch periods.

**TABLE 8** The levels of PSA associated with referral in asymptomatic men with no prostate cancer diagnosis and PSA levels above the PCRMP age specific cut-offs by time period and age

Time period and age (years)	No. men	Range and median values of PSA levels		
		Lowest value	Median value	Highest value
Pre-launch				
45-49	0	-	-	-
50-59	6	4.5	5.2	7.4
60-69	8	5.1	6.4	16.1
70-84	4	6.4	6.8	15.8
Post-launch				
45-49	0	-	-	-
50-59	4	5.0	6.2	21
60-69	13	5.0	8.0	188.9
70-84	15	5.3	13.0	101

**TABLE 9** Number of asymptomatic men not referred for whom the GP specifically reported the reason for non-referral as level too low. Number of men grouped by their PSA levels presented below and above the PCRMP age specific guidelines and the cut-off at 3 ng/mL used in data collection to define low and raised PSA levels

Age specific cut-off levels	Age (yrs)	45 - 49		50 - 59		60 - 69				70 - 84				Total	
		PSA level (ng/ml)	<3	≥3	<3	≥3	<3	≥3 - <4	Total <4	Total ≥4	<3	≥3 - ≤5	Total ≤5	Total >5	Below <3
<b>Pre - launch</b>	% within age group	100	0	89	11	63	20	83	17	66	28	4	6	72	28
	No. of men	9	0	63	8	57	18	75	15	58	25	83	5	187	71
<b>Post - launch</b>	% within age group	83	17	82	18	68	22	90	10	54	39	93	7	66	34
	No. of men	10	2	59	13	85	27	112	13	76	53	129	9	230	117

**TABLE 10** Number (%) of urological referral and non-referral, and reasons for non-referral in symptomatic men by time period and PSA level (low <3 ng/mL or raised  $\geq$  3 ng/mL))

	Total number of men	Referrals		Non-referrals		Significance of difference in proportion referred between low and raised records	Distribution of non-referrals by reason							
		no.	%	no.	%		PSA too low	Re-test scheduled and initiated by		Serious co-morbidity	Other	Lost to Follow up	Not known	
								GP Practice	Urologist					
<b>Pre-launch</b>														
Low records*	188	21	11.2	167	88.8	$\chi^2=42.9$ p<0.001	149	6	4	1	3	0	4	
Raised PSA levels	284	110	38.7	174	61.3		88	35	17	7	13	0	14	
<b>Total</b>	<b>472</b>	<b>131</b>	<b>27.8</b>	<b>341</b>	<b>72.2</b>		<b>237</b>	<b>41</b>	<b>21</b>	<b>8</b>	<b>16</b>	<b>0</b>	<b>18</b>	
<b>Post-launch</b>														
Low records*	201	18	9.0	183	91.0	$\chi^2=82.7$ p<0.001	163	7	6	0	7	0	0	
Raised PSA levels	445	203	45.6	242	54.4		121	52	38	10	16	0	5	
<b>Total</b>	<b>646</b>	<b>221</b>	<b>34.2</b>	<b>425</b>	<b>65.8</b>		<b>284</b>	<b>59</b>	<b>44</b>	<b>10</b>	<b>23</b>	<b>0</b>	<b>5</b>	

\* based on sub-sample, see Table 2

No significant difference between the two time periods in proportions referred in low PSA records

No significant difference between the two time periods in proportions referred in raised PSA records

**TABLE 11** The distribution of men who had their first test between 1<sup>st</sup> Dec. 2001 and 31<sup>st</sup> May 2002 with one or more tests in the period 1<sup>st</sup> December 2001 to 31<sup>st</sup> May 2004 according to reason for first PSA test within time period and number of tests

Reason for test	Number of tests										Total	
	1		2		3 – 5		6 - 10		> 10		no.	%
	no.	%	no.	%	no.	%	no.	%	no.	%	no.	%
Asymptomatic	411	66.9	136	22.1	66	10.7	1	0.2	0	0.0	614	100
Symptomatic	574	66.6	192	22.3	92	10.7	4	0.5	0	0.0	862	100
Re-test	124	33.6	94	25.5	145	39.3	5	1.4	1	0.3	369	100
Prostate cancer already diagnosed	53	23.0	49	21.3	96	41.7	28	12.2	4	1.7	230	100
Not Known	170	70.0	47	19.3	21	8.6	5	2.1	0	0.0	243	100
<b>Total</b>	1332	57.5	518	22.3	420	18.1	43	1.9	5	0.02	2318	100

Significance of overall difference in distribution of men by number of PSA tests by reason for test:  $\chi^2_{16} = 513.9, p < 0.001$

**TABLE 12** Pilot results for linking PSA records from pathology laboratories for men aged 45 to 84 years to urological appointments within the same hospital

<b>Area covered by hospital</b>	<b>Total records to be linked</b>	<b>Number of records linked</b>	<b>Comments</b>
Sutton & Merton	1269	593 (47%)	Linked only on records with NHS number.
Chichester	1478	695 (47%)	Linked on NHS number and 6 digit hospital number.
Truro	2270	Not applicable	Unable to set up automatic link.
York	1081	Not applicable	Unable to set up automatic link.

**TABLE 13** Comparison of GP reports of referral with hospital linkage results for men aged 45 to 84 years

Report from hospital database	Report from General Practice					
	Yes referred		No record of referral		Total	
Sutton & Merton Excludes 53 records GPs reported having urological referral prior to PSA test						
	no.	%	no.	%	no.	%
Yes referred	51	43	34	8	85	16
No record of urology appointment within 6 months of test	14	12	179	42	193	36
No link	53	45	209	50	262	48
Total	118	100	422	100	540	100
Chichester Excludes 82 records GPs reported having urological referral prior to PSA test						
	no.	%	no.	%	no.	%
Yes referred	80	55	32	7	112	18
No record of urology appointment within 6 months of test	19	13	300	64	319	52
No link	47	22	135	29	182	30
Total	146	100	467	100	613	100

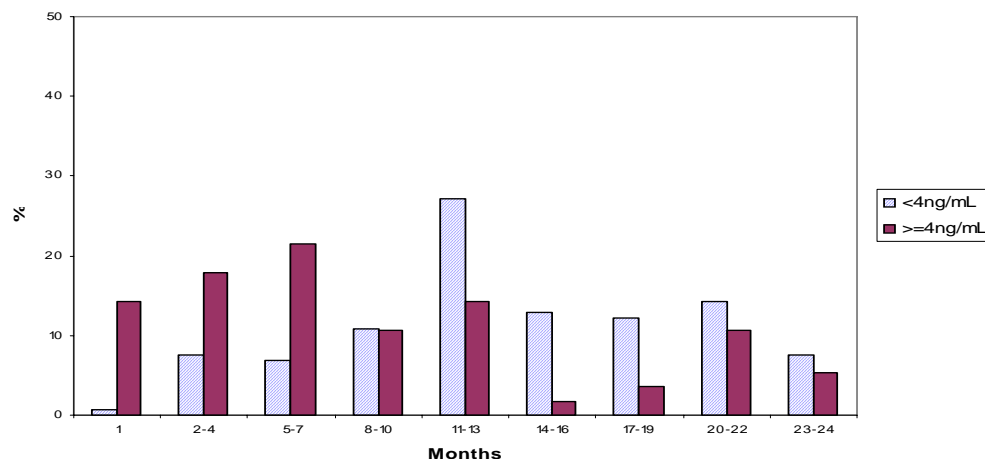
**TABLE 14** Summary of reports on rates of PSA testing

Place	Year	Rate of testing
UK <sup>3 14</sup>	1994 1999	In men aged >45 years tested in general practice p.a. where no prior diagnosis of prostate cancer: 1.4% men tested pa 3.4% men tested pa
England and Wales <sup>2</sup>	2001-2002	In men aged 45-84 years tested in general practice p.a. where no prior diagnosis of prostate cancer: 5.4 tests per 100 men in one year
Northern Ireland <sup>1</sup>	1993-1999 After 1995	30% of men aged $\geq 50$ years had at least one PSA test either in general practice or at hospital. 6% men aged $\geq 50$ years estimated to have a PSA test pa.
Scotland <sup>12</sup>	1992-2001	In men aged $\geq 30$ years, annual rate of testing increased from 5.1 per 1000 man years in 1992 to 21.3 per 1000 men years in 2001.
USA	1992 1994-1997 1995-1996 1998 1999-2002	In Minnesota <sup>20</sup> Over 40% of men aged 60 or more had had at least one test in their lifetime. In a telephone survey <sup>21</sup> rate increased from 33% to 54% in men aged 50 years or more. In visits to US primary care physicians <sup>22</sup> 7% of men aged 60 to 79 years had test In Medicare records <sup>23</sup> 38% of black men and 31% of white men aged $\geq 65$ years had a test. Population based rates of attending outpatients of office based physicians <sup>17</sup> increased from 6% in 40 to 49 years old to 28% in $\geq 75$ years old.
Canada <sup>24</sup>	1984	In men aged 40-74 years, the percentage of men ever having had a test increased from 5% in 40-49 years old to 22% in 60-74 years old.
Australia South <sup>25</sup> South <sup>26</sup> New South Wales <sup>27</sup> Sydney <sup>28</sup>	1995 1996 1995-1996 1999	25% aged $\geq 40$ and no previous prostate cancer had had at least one test 20% aged $\geq 40$ had had a test in the previous year 27% aged > 50 years had had at least on test 23% aged 40-70 years consulting their GP for any condition reported having had a PSA test
Spain <sup>29</sup>	1997-1999	21.6 per 1000 person years
Milan, Italy <sup>30</sup> Florence, Italy <sup>31</sup>	1999-2000 2000 2000-2002	26.9% in men $\geq 40$ years Range of 12 to 16% in men $\geq 50$ years old tested at least once in one year. In men > 50 years <sup>32</sup> , 31% had had opportunistic screening. Annual rate of testing increased from 13% in 2000 to 16% in 2002.
Rotterdam <sup>33</sup>	1997-2000	Defined by PSA $\geq 3$ ng/mL followed by biopsy, in 2.9 years, general population had rate of 33 per 1000 person years, control arm of screening study had rate of 20,0% or 73 per 1000 person years.
Norway <sup>34</sup>	1999	7% in 50-65 year olds - not population based.

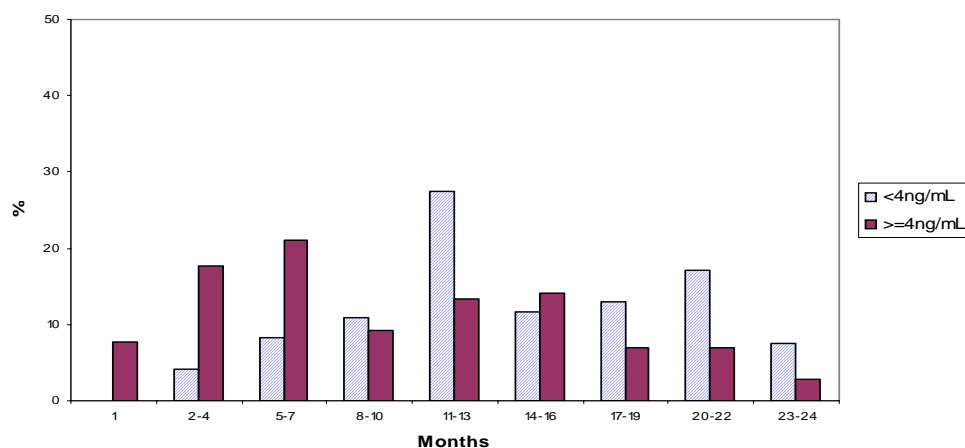
## FIGURES

**Figures 1 – 5:** Distribution (%) of number of men, aged 45 to 84 years, with a first test taken during 1st December 2001 to 31<sup>st</sup> May 2002 and at least one further test, according to the time interval between their first recorded test and second PSA test which occurred within 2 years of the first recorded test, presented by reason for first recorded test and value of test (<4 ng/mL or ≥4 ng/mL)

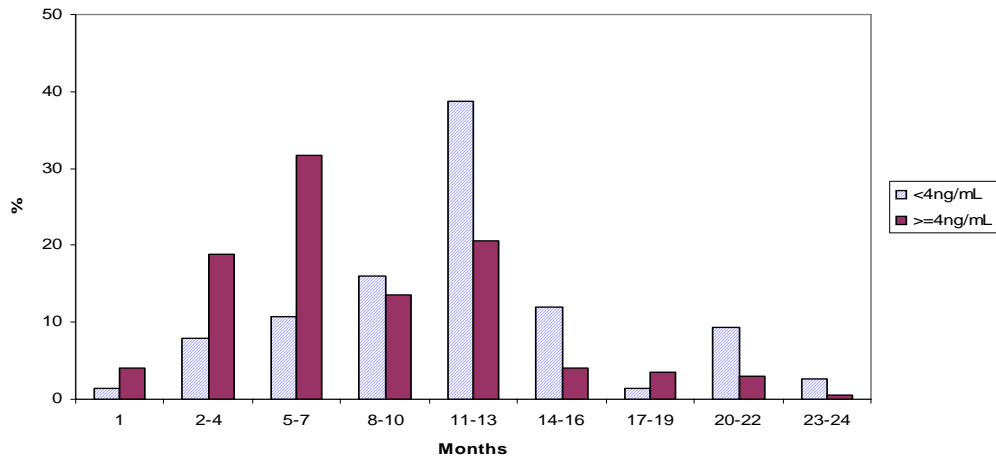
**Figure 1** Asymptomatic men only with no prior diagnosis of prostate cancer, (<4 ng/mL N=147, ≥4 ng/mL N=56)



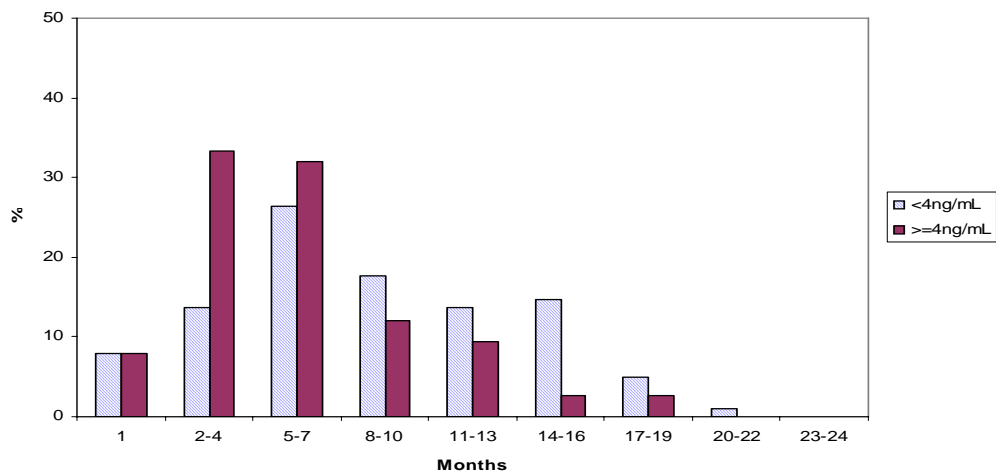
**Figure 2** Symptomatic men with no prior diagnosis of prostate cancer (<4 ng/mL N=146, ≥4 ng/mL N=142)



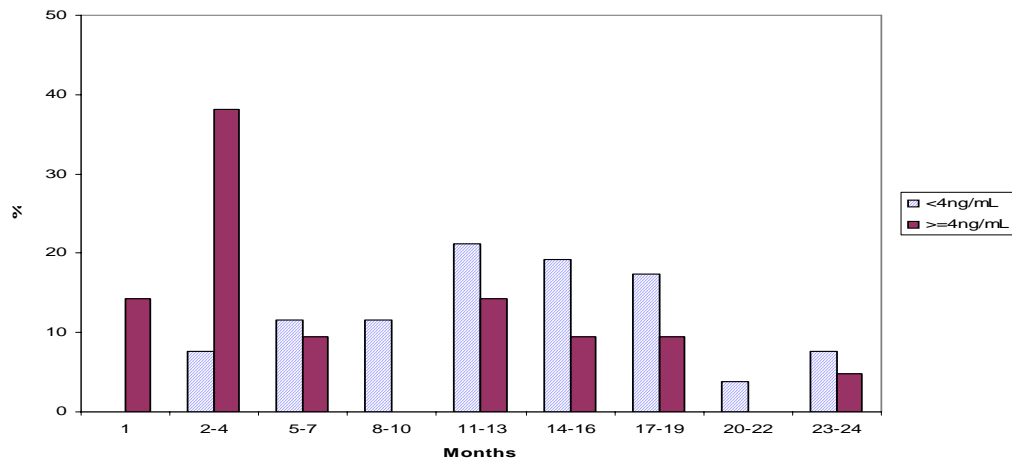
**Figure 3** Men with no prior diagnosis of prostate cancer having a repeat test (<4 ng/mL N=75, ≥4 ng/mL N=170)



**Figure 4** Men already diagnosed with prostate cancer (<4 ng/mL N=102, ≥4 ng/mL N=75)

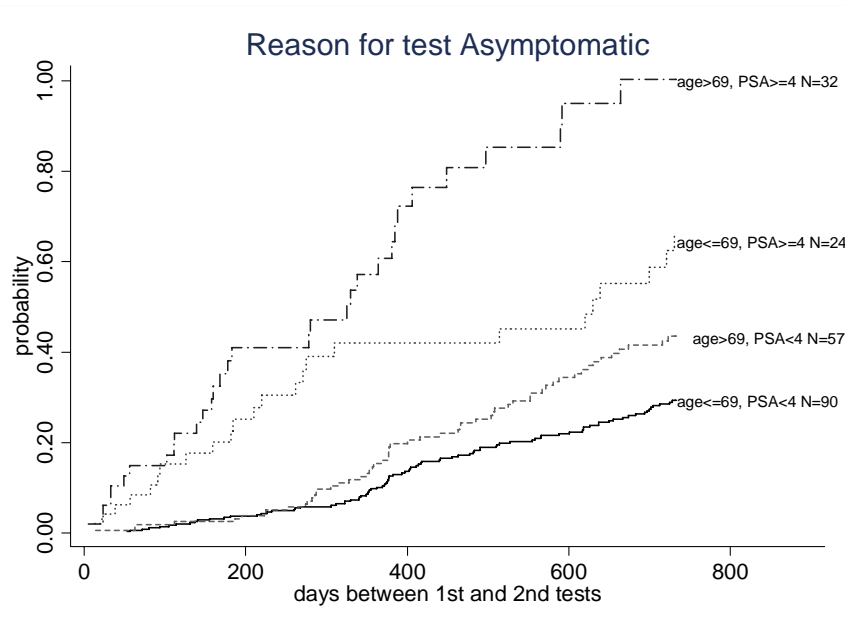


**Figure 5** Men with reason for test not known (<4 ng/mL N=52, ≥4 ng/mL N=21)



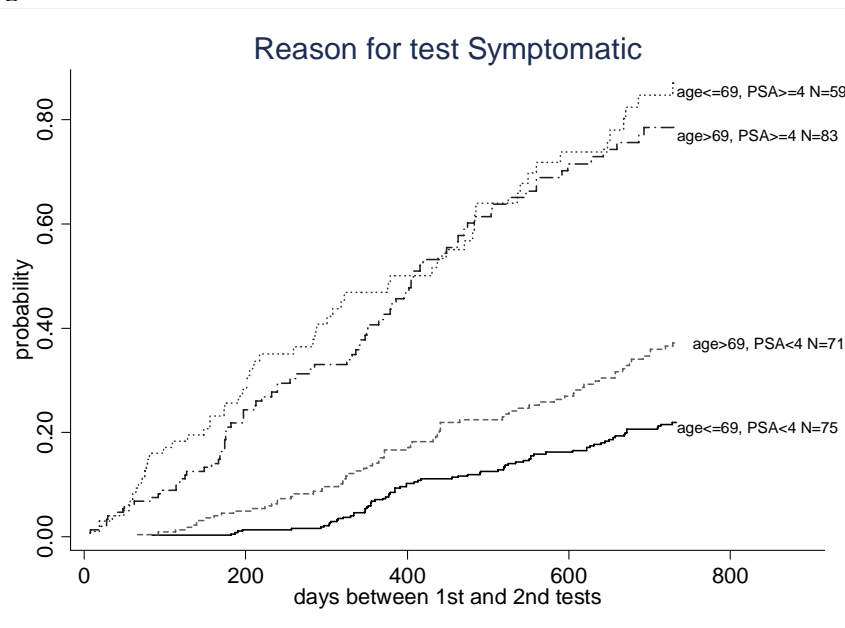
**Figures 6 to 10** Cumulative probability of having a second test up to two years following a first test in the period 1<sup>st</sup> December 2001 to 31st May 2002. Results presented by reason for test, and age at and level of the first test. Restricted to men aged 45 to 84 with one or more tests in the period followed up for a maximum of two years to the date of their second test in the study period

**Figure 6**



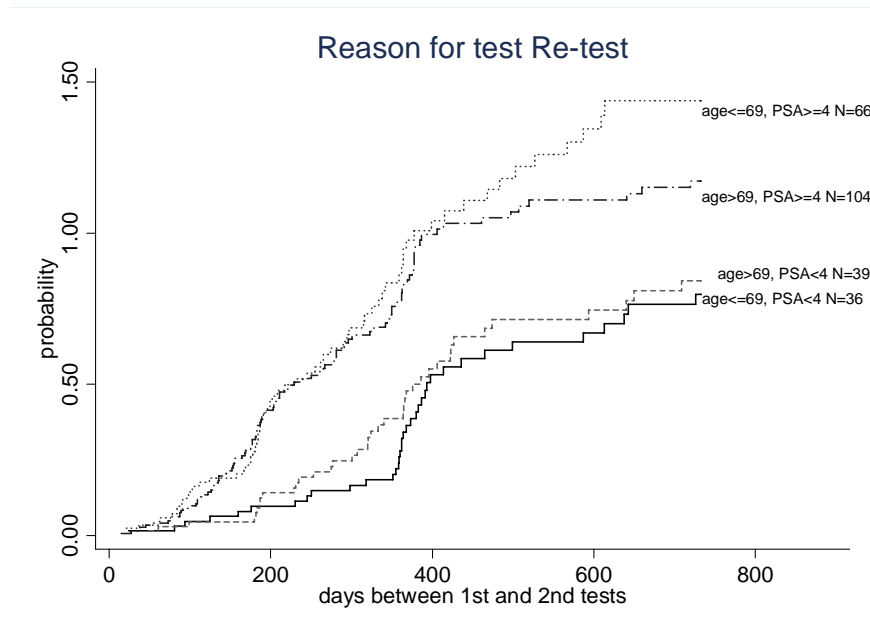
Difference in probability of second test over time in Cox proportional hazard model significant for age group ( $z=2.93$ ,  $p=0.003$ ), and PSA level ( $z=6.03$ ,  $p<0.001$ ). Interaction between PSA level and age not significant

**Figure 7**



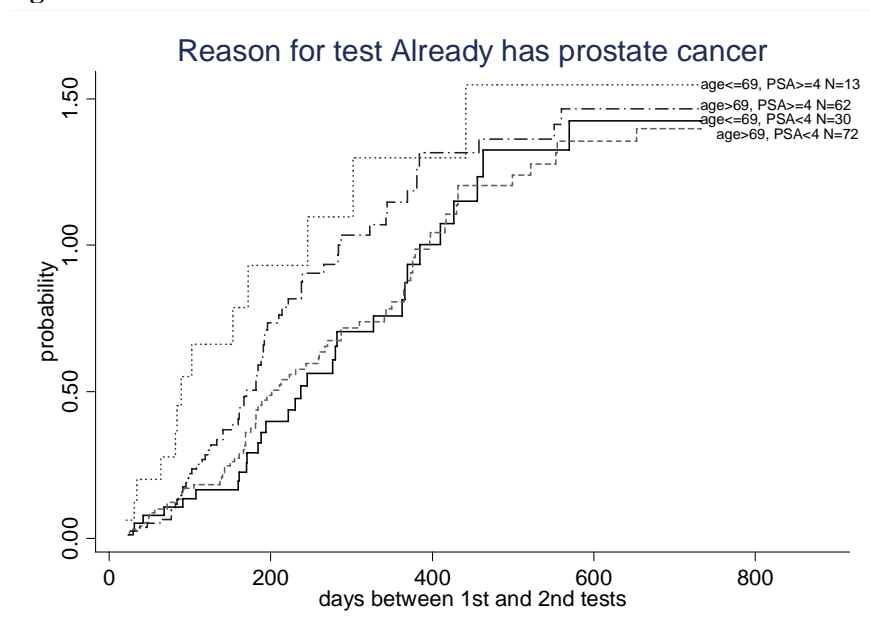
Difference in probability of second test over time in Cox proportional hazard model significant for age group ( $z=3.22$ ,  $p=0.001$ ), PSA level ( $z=8.47$ ,  $p<0.001$ ) and interaction between PSA level and age ( $z=-2.73$ ,  $p=0.006$ )

**Figure 8**

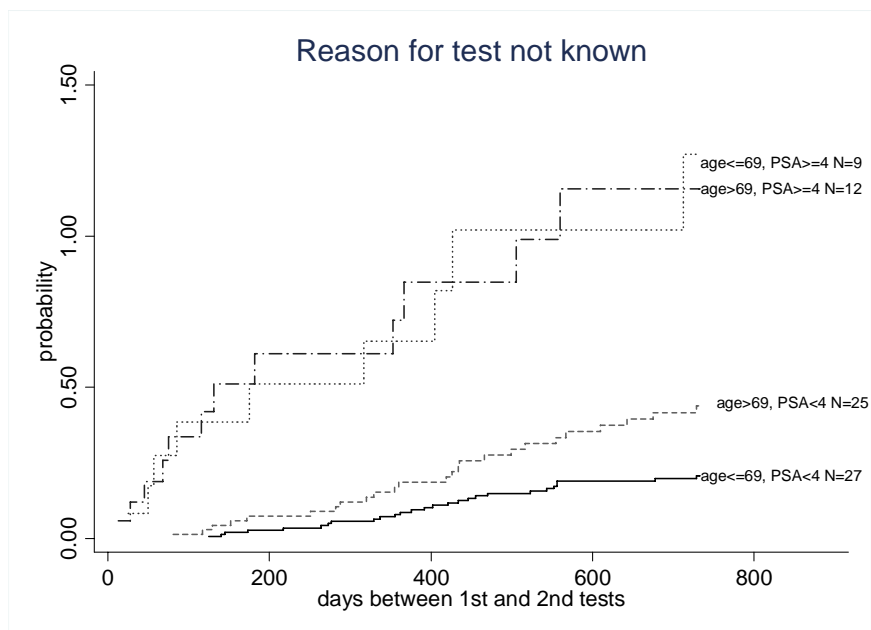


Difference in probability of second test over time in Cox proportional hazard model significant for PSA level ( $z=4.14, p<0.001$ ), and not for age group or interaction between PSA level and age

**Figure 9**



Difference in probability of second test over time in Cox proportional hazard model not significantly related to age group or PSA level

**Figure 10**

Difference in probability of second test over time in Cox proportional hazard model significant for age group ( $z=2.16$ ,  $p=0.03$ ), and PSA level ( $z=5.75$ ,  $p<0.001$ ). Interaction between PSA level and age not significant

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## APPENDICES

### PSA Referral Study: Code Sheet Instructions

### APPENDIX 1

#### Code for Reason for Test

<b>Asym</b>	<p><u>ASYMPTOMATIC</u> MEN WITH NO PRECEDING DIAGNOSIS OF PROSTATE CANCER</p> <ul style="list-style-type: none"> <li><input type="checkbox"/> Men who request screening, but not those who have attended because of prostate symptoms</li> <li><input type="checkbox"/> Men offered PSA screening or re-screening as part of general health check eg Well Man Clinic</li> <li><input type="checkbox"/> Opportunistic test by GP while patient attended for health reasons unrelated to prostate cancer</li> </ul> <p>(use of these categories should be independent of any findings from rectal examination)</p>
<b>Sym</b>	<p><u>SYMPTOMATIC</u> MEN WITH NO PRECEDING DIAGNOSIS OF PROSTATE CANCER</p> <p>Men attending because of concerns about prostate symptoms</p>
<b>Re-test</b>	<p><u>RETEST</u> OF MEN WITH NO PRECEDING DEFINITIVE DIAGNOSIS OF PROSTATE CANCER</p> <ul style="list-style-type: none"> <li><input type="checkbox"/> Men undergoing review who had a previous negative biopsy, but raised PSA</li> <li><input type="checkbox"/> Men undergoing review because previous PSA level within the normal range, but higher than average</li> </ul>
<b>PrCa</b>	<p>MEN WITH PRECEDING DEFINITIVE DIAGNOSIS OF PROSTATE CANCER</p> <p>Men undergoing regular PSA measurement as a marker of disease activity</p>
<b>NK</b>	Not known

#### Code for Reason for No Referral

- 1** - PSA too low (no known Prostate Cancer diagnosis)
- 2** - Patient diagnosed with prostate cancer prior to this test
- 3** - Patient has other serious co-morbidity including senility / old age
- 4a** - Re-test was scheduled, no previous referral (no known Prostate Cancer diagnosis)
- 4b** - Re-test was scheduled, previous referral (no known Prostate Cancer diagnosis)
- 5** - Other
- 6** - Lost to follow up
- NK** - Not known

**Example of how to complete a Patient Proforma is on the reverse of this sheet**

**Version 1 May 2005**

## EXAMPLE OF COMPLETED FORM (answers that would be completed in surgery shown in italics)

PSA Referral Study: GP Patient Proforma

GP Practice Name:

Practice ID:

Patient Name:

DOB

Sex:

Name of GP:

PLEASE COMPLETE by circling answers and completing the table. Please indicate if any corrections are needed to pre-coded data eg. Reason for Test

African or African -Caribbean origin: NO YES Not Known Family history of prostate cancer: NO YES NOT KNOWN

Date of PSA Test	Total PSA Result (ng/mL)	Reason for Test (see code sheet)	NO urological referral following test: Reason (see code sheet)	YES - urological referral following test			
				Date	Hospital	Consultant	NHS / Private
2/3/2001	2.9						
3/5/2004	5.1						

If reason for NO urological referral is 'Other' please describe .....

If patient has been diagnosed with prostate cancer please give date of diagnosis .... / ..... / .....

IF UNABLE TO COMPLETE FORM (please circle)

Patient has: Moved Died Other If 'Other' give reason .....

THANK YOU.

Please return to the Cancer Screening Evaluation Unit, Institute of Cancer Research, SM2 5NG.

Version 2 May 2005

## APPENDIX 2

**Calculation of six monthly rates of men having at least one PSA test adjusted to the male population of England, aged 45 to 84 years in 2004**

**Source of male population for standardization: Table 2, Estimated resident male population: sex and age as at 30 June 2004, Series MB1 no.35 Table 2, England, Government Office Regions**

Age (years)		45-64	65-74	75-84	Total	Adj rate/100 men
<b>Male population, England 2004</b>		5976900	1980900	1174700	9132500	
<b>Study areas</b>						
Dec01- May02	No. PSA	866	806	646	2318	3.43
	Population	43790	14507	8886	67162	
	Crude rate(R)	.0198	.0556	.0727	.0345	
	R x Eng pop	118200	110058	85399	313657	
Jun- Nov02	No. PSA	998	888	666	2552	3.79
	Population	44388	14294	8808	67491	
	Crude rate(R)	.225	.062	.0756	.0378	
	R x Eng pop	134382	123061	88823	346266	
Dec02- May03	No. PSA	904	909	683	2496	3.67
	Population	44830	14444	8925	68131	
	Crude rate(R)	.020	.063	.0765	.0366	
	R x Eng pop	120525	124663	89896	335084	
Jun- Nov03	No. PSA	964	930	726	2620	3.81
	Population	45633	14495	9058	69187	
	Crude rate(R)	.021	.064	.080	.0379	
	R x Eng pop	126262	127095	94152	347509	
Dec03- May04	No. PSA	1075	1084	835	2994	4.25
	Population	46634	14838	9256	70658	
	Crude rate(R)	.0231	.0731	.090	.0424	
	R x Eng pop	137779	144716	105972	388467	

## APPENDIX 3

**Table A3.1** Distribution of the deceased and men no longer registered at the study practices by age, time period and reason for test. The range, median and % of PSA levels  $\geq 10\text{ng/mL}$  are also given.

Reason for test	Pre-launch 1 <sup>st</sup> Dec 2001 to 31 <sup>st</sup> May 2002						Post-launch 1 <sup>st</sup> Dec 2003 to 31 <sup>st</sup> May 2004					
	Age(yrs)						Age(yrs)					
	<60		60 - 69		$\geq 70$		<60		60 - 69		$\geq 70$	
	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.
Asymptomatic	21.1	4	15.4	6	12.5	17	12.5	2	8.1	3	9.1	8
Symptomatic	31.6	6	51.3	20	25.0	34	12.5	2	8.1	3	9.1	8
Re-test	21.1	4	12.8	5	19.9	27	12.5	2	2.7	1	5.7	5
Prostate cancer already diagnosed	0.0	0	12.8	5	30.9	42	0.0	0	8.1	3	19.3	17
Not known	0.0	0	0.0	0	0.7	1	0.0	0	0.0	0	0.0	0
Record not found	26.3	5	7.7	3	11.0	15	62.5	10	73.0	27	56.8	50
<b>Total</b>	100	19	100	39	100	136	100	16	100	37	100	88
<b>PSA levels</b>												
Range	0.5 – 18.6		0.1 – 850.5		0.1 – 995		0.6 – 10.7		0.6 – 1001		0.1 – 3894	
Median	1		5		7.2		1		3		6.3	
% tests $\geq 10\text{ng/mL}$	11		26		40		6		24		35	
No.	2		10		54		1		9		31	

## APPENDIX 3 contd.

**Table A3.2** Distribution of men in the main analyses (which excludes the deceased and men no longer registered at the study practices) by age, time period and reason for test. The range, median and % of PSA levels  $\geq 10\text{ng/mL}$  are also given.

Reason for test	Pre-launch 1 <sup>st</sup> Dec 2001 to 31 <sup>st</sup> May 2002						Post-launch 1 <sup>st</sup> Dec 2003 to 31 <sup>st</sup> May 2004					
	<60		Age(yrs) 60 - 69		$\geq 70$		<60		Age(yrs) 60 - 69		$\geq 70$	
	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.
Asymptomatic	41.2	91	29.8	115	19.3	119	37.5	95	28.5	157	21.9	185
Symptomatic	43.4	96	37.6	145	37.4	231	44.3	112	37.0	204	39.1	330
Re-test	11.8	26	22.8	88	26.3	162	12.6	32	20.3	112	21.9	185
Prostate cancer already diagnosed	3.2	7	8.0	31	16.5	102	3.9	10	10.3	57	14.7	124
Not known	0.4	1	1.8	7	0.5	3	15.8	4	3.1	17	1.3	11
Record not found	0.0	0	0.0	0	0.0	0	0.0	0	0.7	4	0.9	8
<b>Total</b>	100	221	100	386	100	617	100	253	100	551	100	843
<b>PSA levels</b>												
Range	0.1 – 467		0.1 – 167		0.1 – 1694		0.05 – 23.2		0.05– 188.9		0.05-1287	
Median	1.3		3.5		4.3		1.9		3.4		4.7	
% tests $\geq 10\text{ng/mL}$	4		11		18		6		10		21	
no.	9		41		110		14		54		176	

**Results of significance tests: contd. next page**

**APPENDIX 3 contd.**

$\chi^2$  test on difference in age distribution

Pre-launch No.s 19 39 136\221 386 617 Pearson  $\chi^2_2 = 26.2879$  Pr = 0.000

Post-launch No.s 16 37 88\253 551 843 Pearson  $\chi^2_2 = 6.5902$  Pr = 0.037

	Pre-launch			Post-launch		
	<60	Age(yrs) 60 - 69	≥70	<60	Age(yrs) 60 - 69	≥70
$\chi^2_1$	1.66	7.57	31.3	0.01	7.65	9.49
P value	0.20	0.006	0.0001	0.90	0.006	0.002