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Prostate-specific Antigen (PSA) Testing Is Prevalent and Increasing in Stockholm County, Sweden, Despite No Recommendations for PSA Screening: Results from a Population-based Study, 2003–2011

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Abstract

Background: Prostate-specific antigen (PSA) testing has increased in several countries. There is incomplete knowledge of PSA testing patterns.
Objective: Determine the prevalence of PSA testing and explore patterns of PSA retesting in Stockholm County, Sweden.
Design, setting, and participants: A population-based study was performed. Through registry linkages, we collected population information, data on PSA tests, pathology reports, and clinical information. The study population comprised males living in Stockholm County in 2011 (n = 1 034 129), of which 229 872 had a PSA test during the period 2003–2011.
Outcome measurements and statistical analysis: We determined limited-duration-point prevalence of PSA testing and performed survival analysis on PSA retesting for men aged 40–89 yr.
Results and limitations: The number of PSA tests increased from 54 239 in 2003 to 124 613 in 2011. During the 9-yr study period, 46%, 68%, and 77% of men without a prior prostate cancer (PCa) diagnosis and aged 50–59 yr, 60–69 yr, and 70–79 yr, respectively, had a PSA test. During 2010 and 2011, 25%, 40%, and 46% of men aged 50–59 yr, 60–69 yr, and 70–79 yr, respectively, had a PSA test. The prevalence of PSA testing increased from 2003 to 2011. The probability of retesting was PSA and age dependent, with a 26-mo cumulative incidence of 0.337 (95% confidence interval, 0.333–0.341) if the first PSA value was <1 ng/ml. The main limitations were (1) that PSA data prior to 2003 were not available and (2) that the study cohort was restricted to men who were alive in 2011.
Conclusions: Although screening for PCa is not recommended in Sweden, PSA testing in Stockholm County was high across ages ranging from 40 to 89 yr and increased during the period 2003–2011. The probability of PSA retesting was high, regardless of the original PSA level. These results contrast with current clinical recommendations and raise calls for a change, either through structured PCa testing or more detailed guidelines on PSA testing.

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1. Introduction

Prostate-specific antigen (PSA) is a cornerstone in prostate cancer (PCa) diagnostics [1]. Numerous studies have addressed the limited diagnostic accuracy of PSA, yet it remains the only widely adopted biomarker for PCa [2–6]. Data from the European Randomised Study of Screening for Prostate Cancer (ERSPC) showed a 21% reduction in PCa mortality in the PSA screening arm at 11 yr of follow-up [7]. These results were not confirmed in the Prostate, Lung, Colorectal, and Ovary (PLCO) screening trial, showing no mortality benefit for organised annual screening after 13 yr of follow-up [8]. Based on evidence review, the US Preventive Services Task Force recently recommended against PSA screening [9]. This recommendation has been opposed by the American Urological Association through a formal letter [10]. Thus PSA screening remains controversial. Neither European nor Swedish recommendations advocate population-based PSA screening. Rather, they recommend that PSA testing be considered for well-informed men [11,12].

Although no country has introduced organised population-level PSA screening, the incidence of PSA testing has increased in several countries [13–16], consistent with high levels of opportunistic screening. From recent survey data on changes in PSA uptake, 33%, 51%, and 44% of American males aged 50–59 yr, 60–74 yr, and ≥75 yr, respectively, were PSA tested the year preceding 2010 [17]. However, there is substantial variability in PSA uptake, as illustrated in the United Kingdom, where only 6% of men aged 45–89 yr underwent a PSA test in 2007 [18]. The intensity of PSA testing in Sweden has been studied using PCa incidence as a proxy variable. It was estimated that 6% of the total male population had an annual PSA test and that 56–59% of men aged 55–69 yr ever had a PSA test through 2007 [13]. To our knowledge, there is no population-based study with broad coverage of PSA levels.

The aim of this study was to describe the patterns of PSA testing in Stockholm County, Sweden, using population-based data. We utilized the STHLM0 cohort, which includes virtually all individual PSA tests in Stockholm for the period 2003–2011.

2. Methods

2.1. Data sources

Using the unique Swedish personal identification number, the study population was defined as males living in Stockholm County on 28 May 2012, as verified using the Swedish population register. Data on PSA testing, prostate biopsies, and PCa were collected through registry linkages after approval by the regional ethics committee in Stockholm.

Aggregated information on the study population was retrieved from Statistics Sweden. Population estimates were available by single year of age for men living in Stockholm County on 1 November. The study population estimates at 1 November 2011 were assumed to be represented by the population estimates at that date. Estimates of the study population at 1 November for 2003–2010 were estimated for each 1-yr birth cohort using the 2011 population times the probability of not immigrating to Stockholm in the intervening years, given residency in 2011.

Analyses of PSA tests in Stockholm County are performed at three official laboratories (Karolinska University Laboratory [KUL], Aleris, and Unilabs). Individual data, including date of PSA testing and PSA level, were reported by the laboratories for the period from 1 January 2003 to 31 December 2011.

Reports from prostate biopsies were retrieved from the three pathologic units in Stockholm (KUL, Unilabs, and Aleris), analysing all prostate biopsies in the county. Data included personal identification number and date and diagnoses of biopsies, following the Systematized Nomenclature of Coding (SNOMED), including coded reevaluation of the specimen. SNOMED M814** defined PCa in biopsy specimen.

Clinical data regarding PCa cases were collected from the National Cancer Register. The National Cancer Register was introduced in 1958 and is regulated by law. It is held by the National Board of Health and Welfare and covers 94.8% of diagnosed urologic cancers in Sweden [19]. It is mandatory for the responsible clinician to report newly found cancers to the register. International Classification of Diseases, 7th revision, code 177 defined PCa cases.

2.2. Statistical methods

Duration-specific test prevalence was calculated as the number of men with a PSA test in Stockholm in the period preceding a point in time divided by the population at that point in time. This estimate does not include those migrants who moved into Stockholm with a PSA history outside of Stockholm and who had no PSA test in Stockholm. As a sensitivity analysis, we investigated the effect of this assumption by assuming that immigrants had a similar PSA history to men already living in Stockholm; we found that the relative underestimation for the 9-yr prevalence estimates was at most 1.5%, whereas the bias was negligible for 1- and 2-yr prevalence. Due to the large number of PSA tests, we have only described the patterns using point estimates, without presenting confidence intervals based on the binomial distribution.

The pattern of PSA retesting was investigated using life-table analysis. Kaplan-Meier product limit estimators of survival and cumulative incidence (ie, 1 minus survival) were calculated using Stata v.11 (StataCorp LP, College Station, TX, USA). Time since the first recorded PSA test was used as the underlying time scale. The event of interest was the second PSA test. The end of follow-up was date of retesting, date of PCa diagnosis, date of biopsy, or 31 December 2011, whichever came first. Age was determined at the beginning of follow-up. Twenty-six months was chosen as time to event in the life-table analysis to include biennial screening.

SAS software (SAS Institute, Cary, NC, USA) was used for data management.

3. Results

The male population in the Stockholm region on 1 November 2011 totalled 1 034 129. For that cohort, we identified 875 265 PSA tests in 229 872 men for the period 2003–2011. To describe the prevalence of PSA testing, we restricted the analysis to men aged 40–89 yr, excluding 22 242 tests (2.5%) for those aged <40 yr and 3357 tests (0.4%) for those aged ≥90 yr. Another 137 951 (16%) tests were excluded due to PSA tests being undertaken after a PCa diagnosis.

The Stockholm population grew from 2003 to 2011. Table 1A shows the population growth together with the estimated population residing in Stockholm in a given year. Table 1B shows the number of men without and with prior diagnosis of PCa who had a PSA test and the proportion of men with no prior PCa diagnosis, by age and calendar

Table 1A – Men in Stockholm County, Sweden, in 2003–2011, counted as of 1 November and reported by Statistics Sweden

Year	No. of men in Stockholm County	Estimated population residing in Stockholm County	Estimated no. of men residing in Stockholm County with no prostate cancer
2003	912 382	712 581	708 667
2004	918 759	742 051	736 857
2005	927 274	772 398	765 753
2006	942 163	806 422	798 424
2007	959 155	847 658	838 367
2008	975 936	892 603	881 921
2009	995 292	937 960	925 490
2010	1 013 937	985 847	971 626
2011	1 034 129	1 034 129	1 018 063

Estimated populations describe number of men residing in Stockholm County a given year and 2011.

Table 1B – Prostate-specific antigen (PSA)–tested men in Stockholm County, Sweden, by year and age group and proportion of PSA-tested men not having a prior prostate cancer diagnosis

Year	Age group, yr									
	40–49		50–59		60–69		70–79		80–89	
	n	%	*n*	%	*n*	%	*n*	%	*n*	%
2003	4936	99.9	15 065	98.3	13 669	94.5	7029	87.9	1570	85.2
2004	5664	99.8	16 236	97.8	16 089	92.9	8206	86.5	2089	84.5
2005	5901	99.7	16 228	97.3	18 170	91.8	9035	84.6	2541	82.1
2006	7074	99.6	18 569	96.9	22 930	90.3	11 599	82.7	3632	79.5
2007	8467	99.6	20 649	96.5	27 706	88.9	14 592	81.1	4886	76.7
2008	8260	99.6	20 501	96.5	29 491	88.1	16 224	80.4	5558	74.8
2009	9164	99.4	22 375	96.6	33 222	88.5	18 689	79.8	6607	74.7
2010	9169	98.7	20 371	96.0	31 573	86.9	18 876	77.4	7138	72.4
2011	8734	99.4	20 830	95.8	32 094	86.0	20 054	75.9	7497	69.9

period. The age-specific number of men with a PSA test peaked in 2009 for men aged 50–69 yr, whereas the peak in number was in 2011 for those aged ≥70 yr. The proportion of PSA-tested men without prior PCa declined over time in all age groups.

Median age at PSA testing was 64.4 yr. In 2011, 46% of PSA tests for men aged 50–59 yr had PSA of <1 ng/ml, whereas 28% of men aged 60–69 yr and 19% of men aged 70–79 yr had a PSA test <1 ng/ml.

3.1. *Prevalence of prostate-specific antigen testing, 2003–2011*

The proportion of the 2011 male population that was PSA tested during the preceding 9 yr varied by age, at 46%, 68%, and 77% of men aged 50–59 yr, 60–69 yr, and 70–79 yr, respectively (Table 2); the similar proportions at 1 yr in those tested in 2011 were 17%, 27%, and 31%, respectively. The proportion rose slowly in all age groups from 2003 through 2009 and showed a small decline in 2010 and 2011 (Fig. 1). This trend was also seen for the 2- and 5-yr prevalence proportions of PSA testing (Fig. 2), consistent with increasing uptake of PSA testing through 2009.

3.2. *Prostate-specific antigen retesting*

Of the 229 872 men who had at least one PSA test between 2003 and 2011, we excluded men aged <40 yr at first PSA test (*n* = 17 208), aged ≥90 yr (*n* = 353), and men with PCa or a prostate biopsy prior to first PSA date (*n* = 2446). We also excluded men with first PSA before 2006, giving at least 3 yr of PSA test history. Among the remaining men, the cumulative incidence of having a second PSA test within 26 mo of the first test was 40%, 51%, and 58% in age groups 50–59 yr, 60–69 yr, and 70–79 yr, respectively (Table 3).

Table 2 – Population in Stockholm County, Sweden, by age group and 12-mo, 2-yr, 5-yr, and 9-yr prevalence of prostate-specific antigen testing in Stockholm County in 2011 by age group

Age group	Population	Prevalence of prostate-specific antigen testing in 2011							
		Last 12 mo		Last 2 yr		Last 5 yr		Last 9 yr	
yr	*n*	*n*	%	*n*	%	*n*	%	*n*	%
40–49	155 890	8670	5.6	13 572	8.7	23 780	15.3	27 743	17.8
50–59	121 260	20 036	16.5	30 618	25.2	48 675	40.1	55 207	45.5
60–69	103 344	27 821	26.9	41 236	39.9	62 063	60.1	69 942	67.7
70–79	50 266	15 348	30.5	22 953	45.7	34 138	67.9	38 736	77.1
80–89	22 546	5273	23.4	8698	38.6	14 021	62.2	16 339	72.5

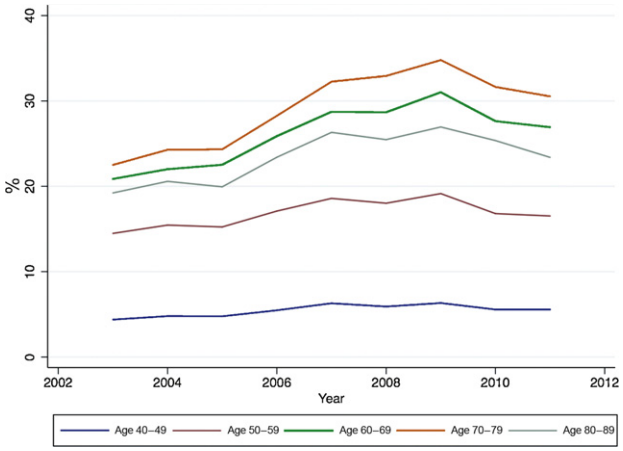

Fig. 1 – One-year prevalence proportion of prostate-specific antigen testing for men living in Stockholm County, Sweden, in 2011, presented by year and age group.

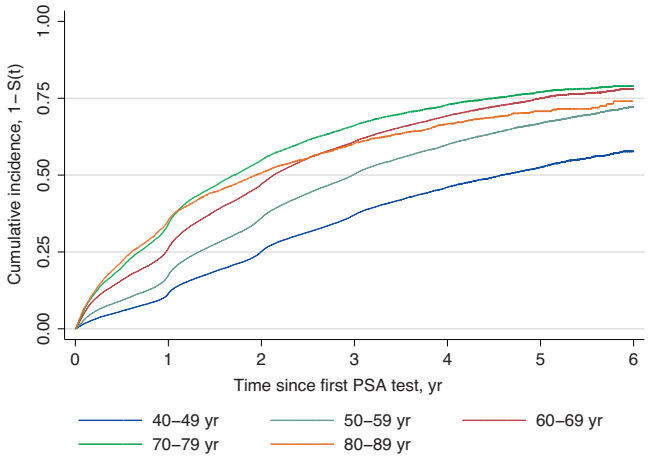

Fig. 3 – Cumulative incidence (1 minus survival [1 − S(t)]) for time between first and second prostate-specific antigen (PSA), tests stratified by age. Men with prostate cancer or a biopsy prior to the first test were excluded. All PSA tests were performed after 1 January 2006.

The cumulative incidence of having a second PSA test within 5 yr was 67%, 75%, and 77% of those aged 50–59 yr, 60–69 yr, and 70–79 yr, respectively. There was some evidence for annual and biannual testing, as illustrated by stepwise shifts in the Kaplan-Meier curve (Fig. 3).

For those aged 40–89 yr, the cumulative incidence of having a second PSA test within 26 mo of the first was 34%, 40%, 56%, 80%, and 88% for those with PSA <1 ng/ml, 1–2.9 ng/ml, 3–3.9 ng/ml, 4–9.9 ng/ml, and >10 ng/ml, respectively. The age-specific patterns of retesting by PSA test values are shown in Table 3 and Figures 4 and 5. PSA retesting within 2 yr was common, even when the previous PSA test level was <1 ng/ml, reaching 47% for men aged 70–79 yr (Table 3).

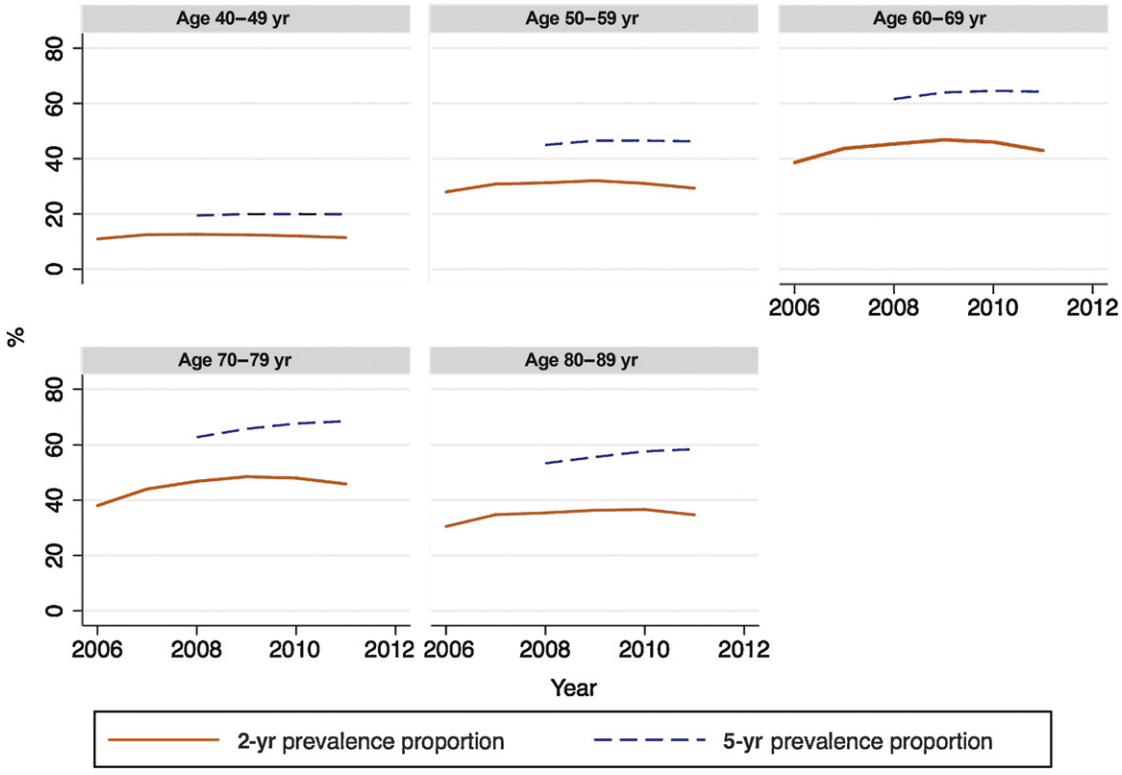

Fig. 2 – Two-year and 5-yr prevalence proportions of prostate-specific antigen testing for men living in Stockholm County, Sweden, in 2011, presented by year and age group.

Table 3 – Cumulative incidence with 95% confidence intervals of having a second prostate-specific antigen (PSA) test within 26 mo of the first, by PSA score and age at first test

	Age at first PSA test, yr					
	40–49	50–59	60–69	70–79	80–89	Total
PSA, ng/ml						
<1	0.264 (0.257–0.271)	0.348 (0.341–0.355)	0.414 (0.404–0.425)	0.466 (0.446–0.487)	0.367 (0.329–0.409)	0.337 (0.333–0.341)
1–2.9	0.284 (0.274–0.295)	0.379 (0.371–0.388)	0.451 (0.442–0.461)	0.482 (0.467–0.497)	0.414 (0.386–0.442)	0.396 (0.391–0.401)
3–3.9	0.578 (0.526–0.632)	0.566 (0.539–0.593)	0.582 (0.562–0.603)	0.537 (0.508–0.566)	0.480 (0.431–0.531)	0.561 (0.548–0.575)
4–9.9	0.750 (0.698–0.799)	0.837 (0.817–0.857)	0.822 (0.808–0.836)	0.796 (0.779–0.813)	0.639 (0.607–0.671)	0.795 (0.786–0.804)
>10	0.848 (0.760–0.917)	0.906 (0.860–0.942)	0.918 (0.892–0.939)	0.887 (0.861–0.910)	0.814 (0.778–0.847)	0.880 (0.866–0.894)
Total	0.281 (0.276–0.287)	0.395 (0.390–0.400)	0.507 (0.501–0.513)	0.575 (0.566–0.584)	0.528 (0.512–0.545)	–

PSA = prostate-specific antigen.
Men are included who had their first PSA test in 2006 or later, were biopsy- and prostate cancer–free, were between the ages of 40 and 89 at first test, and who were alive in 2011. Men with a diagnosis of prostate cancer or a biopsy after their first test were censored at date of diagnosis or biopsy.

4. Discussion

PSA testing in Stockholm County, where screening for PCa is not recommended, was common in all age groups at risk for PCa. PSA testing became more prevalent across the study period, possibly peaking in 2009. Of men aged 50–69 yr, 40–60% had a PSA test in the 5-yr period 2007–2011. The prevalence of PSA testing was highest among men aged 70–79 yr. PSA retesting was common, and we estimated that a third of men with a baseline PSA <1 ng/ml were retested within 2 yr.

This study has several strengths. We utilized individual data for all PSA tests collected in the region, and the coverage of the national PCa register is known to be high [19]. We are not aware of another population-level data set that includes PSA test levels.

There are some potential limitations to these data. First, PSA test data were not available prior to 2003. This introduces a potential misclassification into the analysis such that some men with a PSA test prior to 2003 were analysed as having a first PSA test between 2003 and 2011. We sought to address this issue by restricting the survival analysis to tests performed during 2006–2011, giving at least 3 yr of PSA test history. Second, the residential status of the study cohort was known only for May 2012, so our analysis was restricted to those men who were alive throughout the study period 2003–2011. We suggest a more cautious interpretation of trends for those men aged 80–89 yr, as the survivors may be less representative across the period 2003–2011. Third, it cannot be excluded that a very small number of men may have a PSA or pathology test outside of Stockholm. Any underreporting of pathology would affect only the censoring pattern and would have little effect on the final analysis. The population estimates assumed that migration was independent of PSA test status, and we did not adjust for migrants with a PSA test history outside of Stockholm County and with no PSA history in Stockholm. For this latter assumption, we calculated that the relative error due to underestimation of prevalence would be <1.5%.

PSA testing rates have increased over the last two decades in North America, Europe, and Australia [14,15,20,21]. Our results indicate higher 1-yr prevalence estimates than shown by Jonsson and co-workers, who estimated that 56%

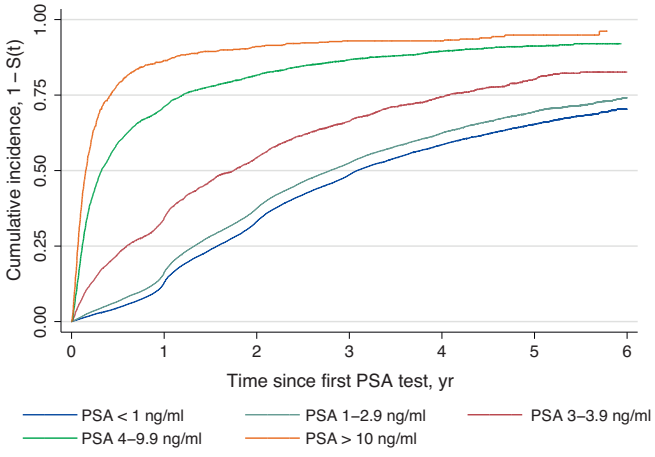

Fig. 4 – Cumulative incidence (1 minus survival [1 − S(t)]) for time between first and second prostate-specific antigen (PSA) test, stratified by PSA level at first test for men aged 50–69 yr. Men with prostate cancer or a biopsy prior to the first test were excluded. All PSA tests were performed after 1 January 2006.

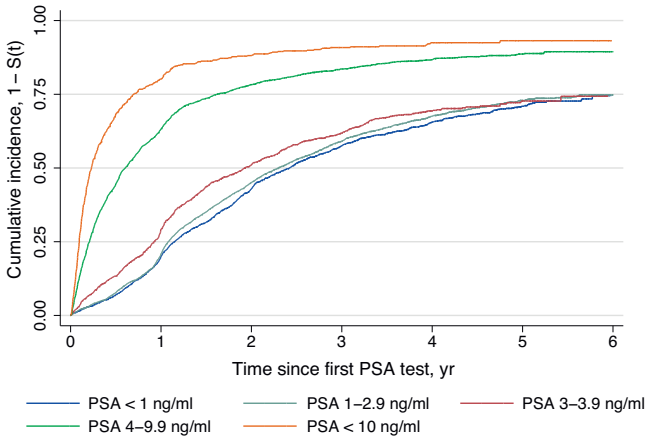

Fig. 5 – Cumulative incidence (1 minus survival [1 − S(t)]) for time between first and second prostate-specific antigen (PSA), test stratified by PSA level at first test for men aged 70–79 yr. Men with prostate cancer or a biopsy prior to the first test were excluded. All PSA tests were performed after 1 January 2006.

of Swedish men aged 50–69 yr in 2007 had ever a PSA test [13]. That study utilized PCa incidence as a proxy for PSA testing and reported on geographic variation in PSA uptake among Swedish counties, showing higher prevalence in urban regions such as Stockholm. Their findings of increasing PSA uptake are consistent with our findings. The prevalence estimates we present are lower than those estimated in the United States by Prasad and colleagues, where 51% of men aged 60–74 yr had a PSA test in the last year and PSA testing during the last year was more common in men >75 yr (44%) than in men aged 40–49 yr (13%) and 50–59 yr (33%) [17]. Results from the United Kingdom [18,22] suggest that levels of PSA testing in general practice remain low, with annual test rates of 6%. In line with our findings, Williams and colleagues [18] report more frequent PSA testing in older men. Mariotto and colleagues used US Medicare data to model PSA retesting for men aged ≥65 yr. They found that approximately 80% of men were retested every 5 yr [23]. In contrast to Mariotto and colleagues, we found strong evidence for nonproportionality across age groups.

The PSA-testing intensity in Stockholm County is comparable to participation rates in the screening arm of the ERSPC screening trial [7] but without the positive attributes of an organized screening program. With up to 77% of the male population having their PSA taken, together with a pattern of frequent PSA retesting, it is reasonable to say that unorganized, very frequent PSA testing exists in Stockholm today.

The high prevalence and increasing trend of PSA testing in men aged ≥70 yr conflict with evidence from the Scandinavian Prostate Cancer Group Study 4, in which the mortality benefit after radical prostatectomy was shown only for men aged <65 yr [24]. PSA testing in older men may lead to overdiagnosis and overtreatment of PCa, and this is why our findings are highly relevant. This trend is not easily explained and may be due to more frequent use of PSA in older men seeking medical care for reasons not related to urinary tract symptoms. Older men are also more likely to have elevated PSA test levels and PCa detected at biopsy, possibly leading physicians to recommend PSA testing to their patients, although it might not benefit a particular patient. In men aged 50–59 yr, PSA testing has been stable, and this is surprising because they possibly have more to gain from early detection of PCa. These findings indicate that risk evaluations preceding PSA testing are insufficiently performed.

Review of Figures 4 and 5 shows a high incidence of repeat PSA values during the first 6 mo after the initial PSA test. Early retesting was likely done to confirm a previously elevated test. This does not reflect rescreening. However, in the present study, retesting of men with PSA values <1 ng/ml was also frequent. Baseline PSA measurements for men aged <60 yr have been proposed as significant predictors of later PCa diagnosis and disease-specific outcomes [25], and a PSA value <1 ng/ml seems to be associated with a low risk of developing life-threatening PCa, even at long-term follow-up [26,27]. Thus frequent retesting of these men is probably not needed and may cause unnecessary anxiety and cost.

5. Conclusions

PSA testing in Stockholm County was common among all age groups at risk of PCa. PSA testing increased from 2003 to 2011. Retesting was common, regardless of the original PSA level. These results are in sharp contrast with current clinical recommendations and raise calls for a change, either through structured PCa testing or more detailed guidelines on PSA testing in the population.

Author contributions: Tobias Nordström had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Study concept and design: Nordström, Aly, Clements, Adolfsson, Grönberg.
Acquisition of data: Nordström, Aly.
Analysis and interpretation of data: Nordström, Aly, Clements, Weibull, Grönberg.
Drafting of the manuscript: Nordström, Aly, Clements, Adolfsson, Grönberg.
Critical revision of the manuscript for important intellectual content: Nordström, Aly, Clements, Weibull, Adolfsson, Grönberg.
Statistical analysis: Nordström, Clements, Weibull.
Obtaining funding: Nordström, Grönberg.
Administrative, technical, or material support: Clements.
Supervision: Grönberg.
Other (specify): None.

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