

Age specific trends in prostate cancer tests, incidence and mortality in Australia since the introduction of the Prostate Specific Antigen (PSA) test

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Research article

Keywords: Prostate cancer, incidence, PSA, biopsy, mortality, screening

Posted Date: March 2nd, 2020

DOI: <https://doi.org/10.21203/rs.3.rs-15620/v1>

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Abstract

Background

Population trends in PSA screening and prostate cancer incidence do not perfectly correspond. We aimed to better understand relationships between trends in PSA screening, prostate cancer incidence and mortality in Australia.

Methods

Description of age standardised time trends in PSA tests, prostate biopsies, cancer incidence and mortality within Australia for the age groups: 45-74, 75-84, and 85+ years.

Results

PSA testing increased from its introduction in 1989 to a peak in 2008. It then declined in men aged 45-84 years. Prostate biopsies and cancer incidence declined from 1995 to 2000, in parallel with decrease in trans-urethral resections of prostate (TURP). After 2000, changes in biopsies and cancer incidence paralleled PSA screening in men 45-84 years, while in men ≥ 85 years, biopsies stabilised and incidence declined. More recently a reduction in TURP correlated with increased Dutasteride and Tamsulosin usage. Prostate cancer mortality in men aged 45-74 years remained low throughout. Mortality in men 75-84 years gradually increased until the mid 1990s, then gradually decreased. Mortality in men ≥ 85 years increased until the mid 1990s, then stabilised.

Conclusions

Age specific prostate cancer incidence largely mirrors PSA screening rates. Most deviation may be explained by changes in management of benign prostatic disease and incidental cancer detection. The timing of the small mortality reduction in men 75-84 years is more consistent with benefits from advances in treatment than with early detection through PSA. The large increases in prostate cancer incidence with minimal changes in mortality suggest overdiagnosis.

Introduction

In Australia, after the introduction of PSA testing in 1989, age-standardised prostate cancer incidence more than doubled, from 80 per 100,000 in 1982 to 195 per 100,000 in 2009.¹ This rise in incidence is likely to reflect increased testing of asymptomatic men with PSA (PSA screening), which is a more sensitive test than digital rectal examination (the main screening test prior to 1989)^{2,3}, and which may lead to prostate cancer overdiagnosis.⁴

However, a comparison of the temporal trends in PSA screening and prostate cancer incidence does not reflect a perfect correspondence between the two parameters. Prostate cancer incidence rose before the introduction of PSA testing, and later declined even while PSA testing was increasing.

To better explain this incomplete association, we need to take a broader view, and explore other changes in urological practice during this time. The number of core biopsies taken to investigate elevated PSAs increased from 6 cores in the 1990s to 24 in contemporary practice, thus increasing the chance of a biopsy finding cancer.⁵ Prostate cancer may also be diagnosed through incidental detection in tissue from transurethral resection of prostate (TURP), which is offered to men with symptoms of benign prostatic hyperplasia (BPH).⁶ In the mid 1990s, medical treatment such as alpha-blockers such as prazosin, tamsulosin, and 5-alpha reductase inhibitors such as dutasteride were adopted as an alternative to TURP surgery as the initial treatment for BPH symptoms.⁷⁻⁹ Cancers discovered as a consequence of the PSA testing that is recommended for men taking these drugs, may have offset any reduction in cancers incidentally discovered through TURP.¹⁰ Furthermore, it's important to note that both surgical and medical treatments for BPH target hyperplasia of prostatic tissue in the transitional zone of prostate while the large majority of prostate cancers arise in the peripheral zone.¹¹

We aimed to describe the changes in PSA testing, prostate biopsy, TURP, alpha blocker and 5 alpha-reductase inhibitor prescribing, in order to better understand how each of these may have contributed to observed changes in prostate cancer incidence and mortality in Australia.

Methods

Annual data on PSA, TURP and prostate biopsy were obtained up to 2015 from the *Medicare Benefits Schedule* (MBS), which lists *Medicare* services subsidised by the Australian Government.^{9,12} The number of PSA tests performed from 1994 onwards were obtained from MBS items 66656 ('PSA used for either surveillance or screening purposes', data available from 1994) and 66655 ('PSA used only for screening purposes', data available only from 2001). For PSA test use prior to 1994, we used published data from New South Wales.³ The number of prostate biopsies performed from 1994 onwards were obtained from MBS data items 37218 and 37219; and the number of TURPs from MBS data item 37203.⁹ Annual data on Dutasteride, Prazosin, Dutasteride and Tamsulosin (combination) prescriptions as well as data on other treatment options for BPH were obtained from the *Pharmaceutical Benefits Schedule* (*PBS schedule*), which lists all Australian Government-subsidised medicines and therapeutic procedures.^{9,13} The item numbers and the years the data were available for these procedures are given in supplementary table 1. Prostate cancer incidence and mortality data from 1982 to 2015 were obtained from Australian Institute of Health and Welfare (AIHW), which compiles data provided by the individual state and territory cancer registries.¹

We used the direct standardization method based on the 30 June 2001 Australian standard male population^{1,14} to calculate annual age standardized rates for the following age groups: 45 – 74 years, 75 – 84 years, and ≥ 85 years. For each age group we described age standardised rates over time for the following parameters: PSA testing (PSA test for screening and surveillance, and for screening only), prostate biopsy, prostate cancer incidence, and prostate cancer mortality. In addition, we calculated total number of TURP procedures, number of men on drugs commonly used for BPH (Dutasteride, Prazosin,

Dutasteride and Tamsulosin), and number of men on endoscopic laser ablation. We compared our calculated rates of PSA testing in Australia to published survey estimates of PSA testing by searching PubMed using the terms: “prostate-specific antigen”, “prostate specific antigen”, “PSA”, “Australia” (from inception to September 2017, limited to English language). Ethics approval was not required as this was a secondary analysis of routinely collected deidentified, administrative data.

Results

Age-standardized rates of PSA testing (for screening or post cancer diagnosis surveillance) in all three age groups of men increased steeply after the test was first introduced in 1989 (Figure 1). From 2008 they gradually declined until 2015 (the most recent data available), except for men aged ≥ 85 years where testing continued to increase. Restricting the analysis only to PSA tests specifically ordered for screening (data available from 2001), shows similar trends, except in men aged ≥ 85 years where screening did not increase, suggesting the observed increase in overall tests for that age group was due to surveillance subsequent to increased rates of diagnosis (and treatment). The highest rates of PSA screening test use were in men aged 45-74 years, where a peak of 22% of men were screened in 2008.

Age standardized biopsy rates in all three age groups declined from 1995 to 2000, and then changed in correlation with PSA screening test use (Figure 2). In men aged 45-74 years and 75-84 years, biopsy rates increased to a peak rate in 2009, corresponding to a peak PSA screening test use in 2008. Both PSA screening tests and biopsy rates declined after this in these two age groups. In men aged ≥ 85 years biopsy rates were steady after 2000, corresponding with steady PSA screening test use during this time.

TURP numbers declined in the late 1990s, and from about 2000 onwards it appeared to increase to a peak in 2009, and then decreased (Supplementary figure 1). Prazosin usage closely followed this trend though it started to rise from 2013. Conversely, the number of men of combination Dutasteride and Tamsulosin showed a steep rise from 2011 when it was included in MBS while Dutasteride usage also increased since then. Number of men who underwent Endoscopic laser ablation as an alternative to TURP (included in MBS from 1995) increased, more markedly since around 2009.

Men aged 45-74 years had the lowest prostate cancer incidence rates (Figure 3). In this age group, incidence increased in the mid-1980s – before the introduction of the PSA test in 1989 – to a peak in 1994, declined up until 1999, and then increased again to greater peak in 2009. In men aged 75-84 and ≥ 85 years, the incidence rates were much higher, but showed similar temporal trends until 1996, after which they stayed steady until 2008 and then decreased. Prostate cancer specific mortality rates in men aged 45-74 years remained low throughout the study period. Mortality in the older two age groups increased until the mid-1990s, more so in men ≥ 85 years. The more gradual increase in men aged 75-84 years until the mid 1990s was followed by a gradual decrease, while mortality rates stabilised in men ≥ 85 years (around ~800 per 100,000).

Discussion

The results of our analysis suggest that PSA screening increased from its introduction in 1989 to a peak in 2008 in men aged ≥ 45 years of 22% in men 45-74 years, 20% in men 74-84 years, and 9% in men ≥ 85 years. After which it declined (in men 45-84 years) or remained steady (in men ≥ 85 years). While apparent incidence of prostate cancer was rising previously, it is clear the introduction of PSA test in 1989, and its use as a screening test, was associated with a dramatic increase in the incidence of prostate cancer, peaking in 1994.

These trends in use of screening PSA were comparable to previous estimates from surveys reporting ranges from 20 - 67% (Supplementary Table 2) as well as estimates based on Medicare data.¹⁵ Recent findings from the New South Wales 45 and Up Study reported PSA screening rates ranging from 41% in males aged 45–49 years through to 60% in those aged 60–69 years.¹⁶

The close association in rise and fall of prostate cancer incidence and PSA testing suggests much of the changes in incidence relate to PSA screening rates. However, some clear deviations from this association between PSA testing and prostate cancer incidence beg explanation. The rise before 1989 may have been caused by increased digital rectal screening and incidental detection of cancer as a consequence of management of BPH, (which prior to the 1990s was largely surgical – initially open prostatectomy, but increasingly replaced by TURP).¹⁷ In the setting of BPH, cancer may be diagnosed preoperatively (in biopsies performed to decide on management) or postoperatively from the resected tissue¹⁸

The rise of PSA testing in the early 1990s was likely the cause of the high biopsy rates and dramatic increases in prostate cancer incidence in this time. However despite further increases in PSA testing in the late 1990s, biopsy rates dropped, as did the apparent incidence of cancer. One potential explanation of this may be the coincident fall in the rates of TURP at this time which may have reduced both biopsies and cancer diagnoses. Additionally, many patients referred to urologists for biopsies following a raised PSA may have not proceeded to have the procedure or further investigations as a result of their comorbidities or general frailty which need to be considered in the context of the long natural history of prostate cancer. A further number of men also may not have proceeded due to concerns when the possible adverse effects of biopsies were explained.

We are unable to explain why the rates of TURP fell. We had hypothesised that increased use of drugs to manage BPH symptoms, may have been responsible. By reducing bladder outflow obstructive symptoms by either targeting prostatic epithelial cells (in the case of Dutasteride) or smooth muscle in the urethra and prostate (in the case of alpha blocker Tamsulosin), fewer patients would have been referred to urologists with lower urinary tract symptoms. However, we found no evidence of this from the pharmaceutical claims (PBS) data, as the main drug used for BPH symptoms at this time, Prazosin, also appears to have decreased in frequency in throughout the 1990s (Supplementary figure 1) .

From 2000-2010, for men aged 45-84 years, changes in biopsy and incidence followed changes in PSA screening. The decrease in PSA testing after 2008, was probably a response to the publication of a U.S. Preventive Services Task Force (USPSTF) statement in 2008, recommending against PSA screening for

men aged >75 years, and declaring that there was insufficient evidence for younger men to recommend screening.¹⁹ Two major screening trials were published in March 2009 describing unexpectedly small mortality benefit.^{20,21} In 2012, a USPSTF guideline update recommended against PSA based screening for prostate cancer in all age groups. Australia observed reductions in PSA testing in men aged 45-74 years after this^{22,23}, and there was increasing recognition of harms from overdiagnosis.^{24,25} For men aged ≥ 85 years, biopsy rates remained steady in line with PSA screening rates after 2000, but prostate cancer incidence decreased, especially after 2008. This may reflect earlier prostate cancer diagnosis in these men through PSA screening at a younger age.²⁶ Such earlier detection may have resulted in a longer time living with a prostate cancer diagnosis, but given the apparent lack of mortality reduction in this age group, may have not extended lives.

From 2010 to most recent data, for men aged 45-84 years biopsy and incidence trends followed decreases in PSA screening except in men aged over 85 years whose overall PSA testing rates increased. TURP has been replaced by medical treatment to relieve mild symptoms of BPH including Dutasteride and Tamsulosin Dutasteride combination (which was listed in PBS since 2011 and was to be prescribed under streamlined authority with treatment to be initiated by a urologist but can be continued by a general practitioner) and various operative procedures which utilize laser to treat more severe BPH²⁷ and as outlined in Supplementary table 1.

We observed small decreases in prostate cancer mortality rates after about 1996 in age groups other than those ≥ 85 years. Advocates assert that they may represent the mortality benefits from screening, especially in younger in men²⁰. However, the reductions began at the peak in incidence, though any beneficial effect from screening and subsequent treatment would have been delayed, by ten or more years. Thus it seems more likely that the mortality reductions are attributable to advances in the treatment of prostate cancer. Some developed countries (including the United States, Canada, and New Zealand) have reported similar changes in incidence. Others, including Switzerland and United Kingdom show slower rises in prostate cancer incidence over this time²⁸⁻³¹ which may be attributable to national differences in urological practice, and health care systems. Both groups of developed countries show similar reductions in mortality, even those that did little screening. This again suggests that mortality changes are due to improved treatment rather than the effects of early detection and screening.

The Australian National Health and Medical Research Council (NHMRC) endorsed Prostate Cancer Foundation of Australia Clinical Practice Guidelines for PSA testing published in late 2015 recommend that men who are considering having a PSA test should be offered evidence-based decision support, including the opportunity to discuss the benefits and harms of PSA testing, before making the decision to be tested. The guidelines recommend that men who are at average risk of prostate cancer who have been informed of the benefits and harms of testing, and who decide to undergo regular testing for prostate cancer, should be offered PSA testing every 2 years from age 50 to 69. Men aged 70 years or older who have been informed of the benefits and harms of testing, and who wish to start or continue regular testing, should be advised that the harms of testing may be greater than the benefits.³² The listing of

multiparametric magnetic resonance imaging (mpMRI) on the Medical Benefits Schedule in 2018, means that MRI may now be widely used to triage which men with an elevated PSA undergo prostate biopsy.³³ If this results in fewer biopsies in low risk men, then this may lead to fewer overdiagnosed cancers. The mpMRI will also be useful in active surveillance once a diagnosis is made through histopathology. Although mpMRI was included in the Medicare only last year, it was used considerably in private practice to bypass the need of a biopsy and therefore may have contributed to the drop in biopsy rates in the recent years. Analysis of trends in PSA tests, biopsies, incidence and mortality from 2016 onwards will enable assessment of the impact of both the Australian guideline and the MBS listing of MRI.

Our approach has some limitations. Although cancer registries gather high quality data, the reporting processes, (with varying diagnostic criteria used in different laboratories) are always a concern. Even using specific MBS item numbers, Medicare data cannot reliably differentiate between screening and surveillance (both before and after treatment) uses of PSA testing. Screening reasons probably dominate the data in young men, surveillance in the old. The problem of potential multiple observations from the same man do not arise for PSA item 66655 as they can only claim this once a year. However, this is an issue with PSA item 66656 and prostate biopsy items. We were able to obtain data on PSA testing only from 1994 onwards, as this test was not billed as a separate item in Medicare until then, and we could only differentiate screening claims from 2002. However, the PSA test rates were still low at this early stage, and the major increase in rates occurred only subsequently.

Conclusion

The incidence of prostate cancer appears to largely follow rates of PSA screening test use by age group. Deviations from this relationship may be explained by changes in management of BPH, and changes to screening practices following new guidelines based on new trials that showed limited benefit from PSA screening. That the low mortality rates were largely unaffected by fluctuations in incidence, suggests substantial overdiagnosis of prostate cancer. Future studies are needed to better measure the role of changing treatment in reducing death from prostate cancer, differentiate this from any benefit from screening, and to quantify the extent of overdiagnosis and other harms associated with PSA screening.

List Of Abbreviations

PSA - Prostate Specific Antigen

TURP – Trans urethral resection of prostate

BPH – Benign Prostatic Hyperplasia

MBS - Medicare Benefits Schedule

PBS – Pharmaceutical Benefits Schedule

AIHW – Australian Institute of Health and Welfare

USPSTF - U.S. Preventive Services Task Force

NHMRC - National Health and Medical Research Council

mpMRI - Multiparametric magnetic resonance imaging

Declarations

Ethics approval and consent to participate: Not applicable (Ethics approval was not required as this was a secondary analysis of routinely collected deidentified, administrative data.)

Consent for publication: Not applicable

Availability of data and materials: The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Competing interests: The authors declare that they have no competing interests

Funding:

The authors have received funding from the Australian National Health and Medical Research Council (NHMRC Fellowship No. 1080042, Centres of Research Excellence grant

No.1104136: Creating sustainable health care: ensuring new diagnostics avoid harms, improve outcomes and direct resources wisely, and Program grant No. 1113532: Using healthcare wisely: reducing inappropriate use of tests and treatments). The funders had no role in design and conduct of the study; collection, management, analysis, and interpretation of the data; and preparation, review, or approval of the manuscript.

Authors' contributions: PG conceived the ideas, developed them with all co-authors, and edited the paper. TP and RFS retrieved data from Australian Institute of Health and Welfare, did the analyses. TP wrote the first draft and edited the paper. CDM, JAD and KJLB developed the ideas and edited the paper.

Acknowledgements: Prof RA ('Frank') Gardiner AM, Emeritus Professor, UQ Centre for Clinical Research, University of Queensland for his valuable input.

Ms Melanie Vermeulen and Dr Mina Bakhit for their assistance in editing the graphs

Authors' information (optional) – Not applicable

References

1. Australian Institute of Health and Welfare. Australian Cancer Incidence and Mortality (ACIM) books: Prostate cancer. In: Welfare AloHa, editor. Canberra 2015.
2. Catalona WJ, Richie JP, Ahmann FR, Hudson MA, Scardino PT, Flanigan RC, et al. Comparison of digital rectal examination and serum prostate specific antigen in the early detection of prostate cancer: results of a multicenter clinical trial of 6,630 men. *The Journal of urology*. 1994;151(5):1283-90.
3. Smith DP, Armstrong BK. Prostate-specific antigen testing in Australia and association with prostate cancer incidence in New South Wales. *Medical Journal of Australia*. 1998;169(1):17-20.
4. Welch HG, Black WC. Overdiagnosis in Cancer. *JNCI: Journal of the National Cancer Institute*. 2010;102(9):605-13.
5. Prostate Cancer Foundation of Australia and Cancer Council Australia. Clinical practice guidelines PSA Testing and Early Management of Test-Detected Prostate Cancer. Sydney: Cancer Council Australia.
6. Potosky AL, Kessler L, Gridley G, Brown CC, Horm JW. Rise in prostatic cancer incidence associated with increased use of transurethral resection. *J Natl Cancer Inst*. 1990;82(20):1624-8.
7. Department of Health: Therapeutic Goods Administration. Australian Register of Therapeutic Goods (ARTG) 2015. Available from: <https://www.ebs.tga.gov.au/>.
8. Jiwrajka M, Yaxley W, Ranasinghe S, Perera M, Roberts MJ, Yaxley J. Drugs for benign prostatic hypertrophy. *Australian Prescriber*. 2018;41(5):150–153. doi:10.18773/austprescr.2018.
9. Department of Human Services. Medicare Item Reports Australia: Australian Government; 2015 [11 March 2015]. Available from: http://medicarestatistics.humanservices.gov.au/statistics/mbs_item.jsp.
10. NPS MedicineWise. Dutasteride (Avodart) and dutasteride with tamsulosin (Duodart) for lower urinary tract symptoms due to benign prostatic hyperplasia 2011. Available from: <https://www.nps.org.au/radar/articles/dutasteride-avodart-and-dutasteride-with-tamsulosin-duodart-for-lower-urinary-tract-symptoms-due-to-benign-prostatic-hyperplasia>
11. Roberts MJ, Teloken P, Chambers SK, Williams SG, Yaxley J, Samaratunga H, Frydenberg M, Gardiner RA. Prostate Cancer Detection. In: Endotext [Internet]. South Dartmouth (MA): MDText.com, Inc.; 2000-.2018 Jun 11. De Groot LJ, Chrousos G, Dungan K, Feingold KR, Grossman A, Hershman JM, Koch C, Korbonits M, McLachlan R, New M, Purnell J, Rebar R, Singer F, Vinik A, editors.
12. Australian Government Department of Health. Medicare Benefits Schedule 2011 [Available from: <http://www.health.gov.au/internet/hta/publishing.nsf/Content/mbs-1>].
13. Australian Government Department of Health. The Pharmaceutical Benefits Scheme (PBS) 2017 [Available from: <http://www.pbs.gov.au/info/about-the-pbs>].

14. Australian Bureau of Statistics. Australian Demographic Statistics, Sep 2014 Canberra 2015. Available from: <http://www.abs.gov.au/AUSSTATS/abs@.nsf/DetailsPage/3101.0Sep%202014?OpenDocument>.
15. Lo J, Papa N, Bolton DM, Murphy D, Lawrentschuk N. Australian patterns of prostate cancer care: Are they evolving?. *Prostate Int*. 2016;4(1):20–24. doi:10.1016/j.pnil.2015.11.001
16. Nair-Shalliker V, Bang A, Weber M, Goldsbury DE, Caruana M, Emery J, et al. Factors associated with prostate specific antigen testing in Australians: Analysis of the New South Wales 45 and Up Study. *Scientific Reports*. 2018;8(1):4261.
17. Merrill RM, Feuer EJ, Warren JL, Schussler N, Stephenson RA. Role of transurethral resection of the prostate in population-based prostate cancer incidence rates. *American Journal of Epidemiology*. 1999;150(8):848-60.
18. Perera M, Lawrentschuk N, Perera N, Bolton D, Clouston D. Incidental prostate cancer in transurethral resection of prostate specimens in men aged up to 65 years. *Prostate Int*. 2016;4(1):11–14. doi:10.1016/j.pnil.2015.10.016
19. Herget KA, Patel DP, Hanson HA, Sweeney C, Lowrance William T. Recent decline in prostate cancer incidence in the United States, by age, stage, and Gleason score. *Cancer Medicine*. 2016;5(1):136-41.
20. Schröder FH, Hugosson J, Roobol MJ, Tammela TLJ, Ciatto S, Nelen V, et al. Screening and Prostate-Cancer Mortality in a Randomized European Study. *New England Journal of Medicine*. 2009;360(13):1320-8.
21. Andriole GL, Crawford ED, Grubb RLI, Buys SS, Chia D, Church TR, et al. Mortality Results from a Randomized Prostate-Cancer Screening Trial. *New England Journal of Medicine*. 2009;360(13):1310-9.
22. Zargar H, van den Bergh R, Moon D, Lawrentschuk N, Costello A, Murphy D. The impact of the United States Preventive Services Task Force (USPTSTF) recommendations against prostate-specific antigen (PSA) testing on PSA testing in Australia. *BJU international*. 2016.
23. Moyer VA. Screening for prostate cancer: U.S. Preventive Services Task Force recommendation statement. *Annals of internal medicine*. 2012;157(2):120-34.
24. Postma R, Schröder FH, van Leenders GJLH, Hoedemaeker RF, Vis AN, Roobol MJ, et al. Cancer Detection and Cancer Characteristics in the European Randomized Study of Screening for Prostate Cancer (ERSPC) – Section Rotterdam: A Comparison of Two Rounds of Screening. *European urology*. 2007;52(1):89-97.
25. Draisma G, Boer R, Otto SJ, van der Cruijsen IW, Damhuis RA, Schroder FH, et al. Lead times and overdetection due to prostate-specific antigen screening: estimates from the European Randomized Study of Screening for Prostate Cancer. *Journal of the National Cancer Institute*. 2003;95(12):868-78.
26. Vis AN, Roemeling S, Reedijk AM, Otto SJ, Schroder FH. Overall survival in the intervention arm of a randomized controlled screening trial for prostate cancer compared with a clinically diagnosed cohort. *European urology*. 2008;53(1):91-8.

27. Ow D, Papa N, Perera M, Liodakis P, Sengupta S, Clarke S, Bolton DM, Lawrentschuk N. Trends in the surgical treatment of benign prostatic hyperplasia in a tertiary hospital. *ANZ J Surg*. 2018 Jan;88(1-2):95-99. doi: 10.1111/ans.13904.
28. Center MM, Jemal A, Lortet-Tieulent J, Ward E, Ferlay J, Brawley O, et al. International variation in prostate cancer incidence and mortality rates. *European urology*. 2012;61(6):1079-92.
29. Kachuri L, De P, Ellison LF, Semenciw R. Cancer incidence, mortality and survival trends in Canada, 1970-2007. *Chronic Dis Inj Can*. 2013;33(2):69-80.
30. Dickinson J, Shane A, Tonelli M, Gorber SC, Joffres M, Singh H, et al. Trends in prostate cancer incidence and mortality in Canada during the era of prostate-specific antigen screening. *CMAJ Open*. 2016;4(1):E73-E9.
31. Zhou CK, Check DP, Lortet-Tieulent J, Laversanne M, Jemal A, Ferlay J, et al. Prostate cancer incidence in 43 populations worldwide: An analysis of time trends overall and by age group. *International journal of cancer*. 2016;138(6):1388-400.
32. Prostate Cancer Foundation of Australia and Cancer Council Australia PSA Testing Guidelines Expert Advisory Panel. Clinical practice guidelines PSA Testing and Early Management of Test-Detected Prostate Cancer. Sydney: Cancer Council Australia. [Version URL:<http://wiki.cancer.org.au/australiawiki/index.php?oldid=134877>, cited 2019 May 24]. Available from:https://wiki.cancer.org.au/australia/Guidelines:PSA_Testing.
33. Goldman H, Singh N, Harding C, McGirr J, Seal A, Duncan I, Sowter S. Accuracy of multiparametric magnetic resonance imaging to detect significant prostate cancer and index lesion location. *ANZ J Surg*. 2019 Jan;89(1-2):106-110. doi: 10.1111/ans.14754.
34. Weller D, Pinnock C, Silagy C, Hiller JE, Marshall VR. Prostate cancer testing in SA men: influence of sociodemographic factors, health beliefs and LUTS. *Australian and New Zealand journal of public health*. 1998;22(3 Suppl):400-2.
35. Pinnock CB, Weller DP, Marshall VR. Self-reported prevalence of prostate-specific antigen testing in South Australia: a community study. *Med J Aust*. 1998;169(1):25-8.
36. Perkins JJ, Sanson-Fisher RW, Clarke SJ, Youman P. An exploration of screening practices for prostate cancer and the associated community expenditure. *Br J Urol*. 1998;82(4):524-9.
37. Ward JE, Gupta L, Taylor NJ. Do general practitioners use prostate-specific antigen as a screening test for early prostate cancer? *Med J Aust*. 1998;169(1):29-31.
38. Slevin TJ, Donnelly N, Clarkson JP, English DR, Ward JE. Prostate cancer testing: behaviour, motivation and attitudes among Western Australian men. *Med J Aust*. 1999;171(4):185-8.
39. Gattellari M, Young JM, Ward JE. GP and patient predictors of PSA screening in Australian general practice. *Family practice*. 2003;20(3):294-303.
40. Carrière P, Baade P, Newman B, Aitken J, Janda M. Cancer screening in Queensland men. *Med J Aust*. 2007;186(8):404-7.
41. Smith DP, Supramaniam R, Marshall VR, Armstrong BK. Prostate cancer and prostate-specific antigen testing in New South Wales. *Med J Aust*. 2008;189(6):315-8.

42. Weber MF, Banks E, Smith DP, O'Connell D, Sitas F. Cancer screening among migrants in an Australian cohort; cross-sectional analyses from the 45 and Up Study. BMC Public Health. 2009;9:144.
43. McDowell ME, Occhipinti S, Gardiner RA, Chambers SK. Patterns of prostate-specific antigen (PSA) testing in Australian men: the influence of family history. BJU international. 2012;109:64-70.
44. Carey M, Bryant J, Yoong SL, Russell G, Barker D, Sanson-Fisher R. Prostate specific antigen testing in family practice: a cross sectional survey of self-reported rates of and reasons for testing participation and risk disclosure. BMC Fam Pract. 2013;14:186.

Figures

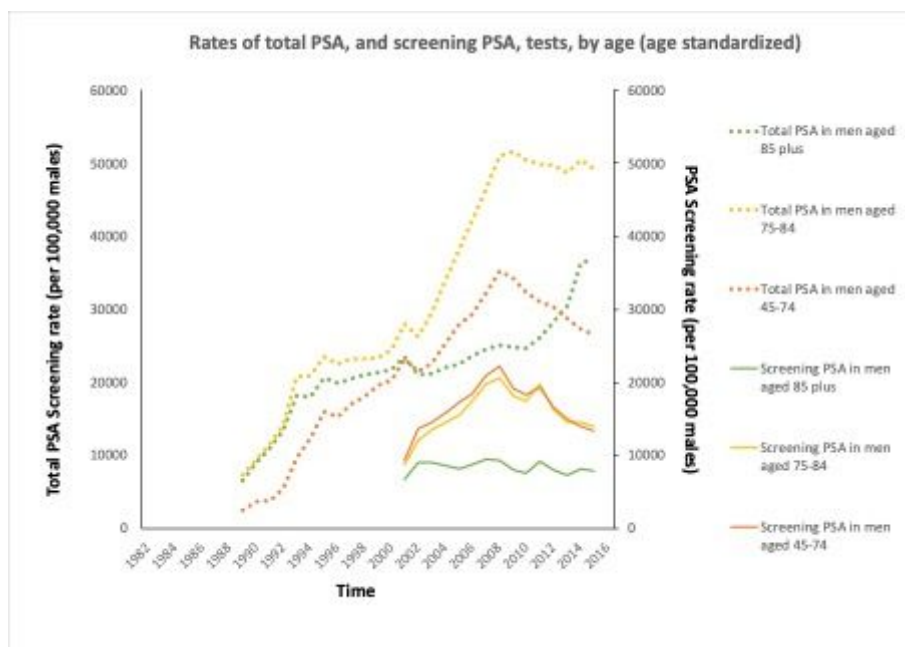


Figure 1

Rates of total PSA, and screening PSA, tests, by age (age standardized)

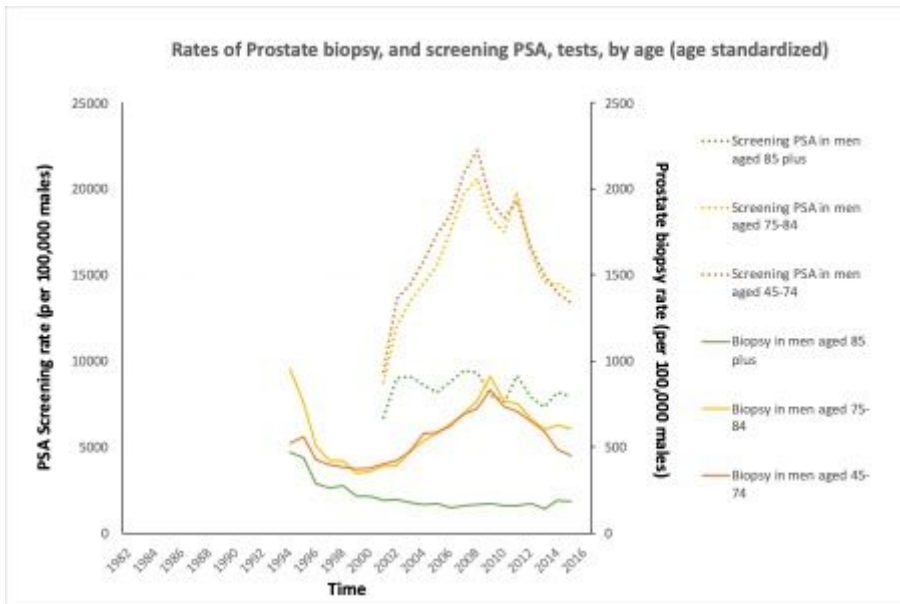


Figure 2

Rates of Prostate biopsy, and screening PSA, tests, by age (age standardized)

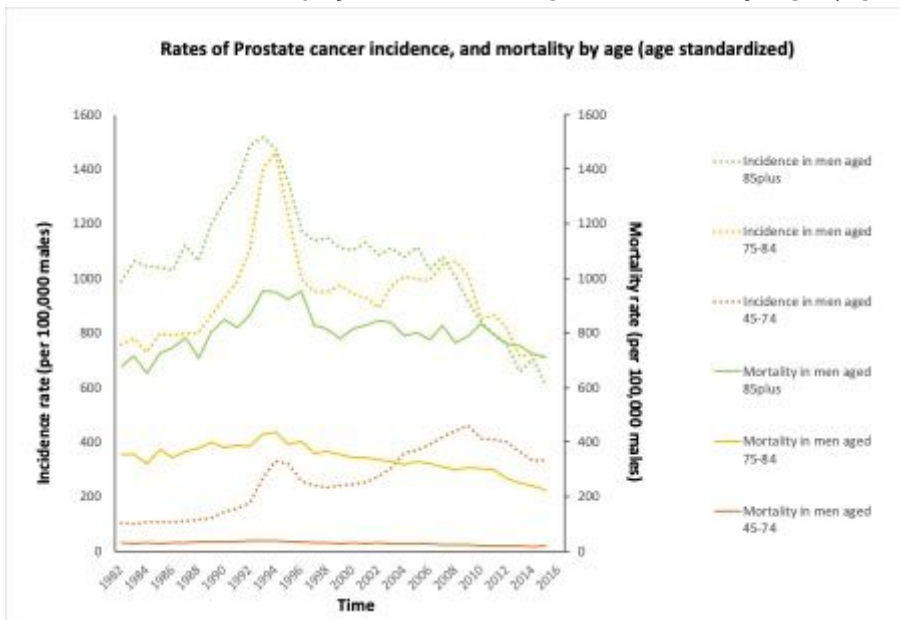


Figure 3

Rates of Prostate cancer incidence, and mortality by age (age standardized)