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Declining use of radical prostatectomy and pelvic lymphadenectomy despite more robotics: National population data over 15 years

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Running title: National radical prostatectomy trends

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ABSTRACT

Aim: To describe national surgical patterns of prostate cancer care considering radical prostatectomy with or without pelvic lymphadenectomy and consideration of robotic-assisted techniques.

Methods: Retrospective analysis of publicly accessible Medicare claims data was performed for the period 2001-2016 and included patients undergoing radical prostatectomy with or without pelvic lymphadenectomy relative to total and prostate cancer-specific populations among men aged 45-84 years. Proportion of cases performed robotically was considered.

Results: Total procedures performed increased from 2001, peaked in 2009 and subsequently decreased until 2016. Since 2009, the age-specific rate of surgery in men aged 75-84 increased by 2.3-fold, while the rates for men aged 55-64 and 45-54 reduced by 44% and 55%, respectively. Rates of concurrent pelvic lymphadenectomy fell until 2009 with subsequent stabilisation (ratio 1.05 – 1.14) through to 2016. Significant regional practice patterns were observed, as was an increasing trend toward a robotic assisted laparoscopic approach, comprising more than 80% of radical prostatectomies in 2016.

Conclusion: Since the peak in 2009, radical prostatectomy is performed less in men <65 years and more in men ≥65 years. An increasing proportion of cases omit concurrent pelvic lymphadenectomy and are performed robotically.

Keywords : Prostate cancer, radical prostatectomy, pelvic lymphadenectomy, treatments, trends

Introduction

Prostate cancer (PCa) remains the most commonly diagnosed and second most common cause of cancer deaths in Australian men [1,2], with similar trends observed internationally [3]. Curative treatment considerations are influenced by disease risk, as determined by serum prostate specific antigen (PSA), biopsy Gleason score, clinical stage, as well as patient factors (age, comorbidities, patient preferences, quality-of-life priorities). Men's acceptance of different risks and complications of treatment also influences choice of management [4]. Radical prostatectomy (RP) with or without pelvic lymph node dissection (PLND) or radiotherapy (including neoadjuvant androgen deprivation therapy(ADT)) are most commonly used for intermediate and high risk localized PCa[4,5].

Active surveillance (AS) of low risk PCa has been widely adopted to reduce over treatment of indolent PCa and is selectively used for those subsequently diagnosed with clinically significant PCa, including low volume intermediate risk disease[4,6,7]. Watchful waiting, as a similar approach has reduced active treatment in older men [5,8], where competing medical co-morbidities will influence PCa specific mortality. In contrast, higher risk patients who previously may have been more likely to adopt an expectant / palliative management approach, may be referred for local treatment such as radiotherapy or RP [6] to reduce localized disease progression and associated complications.

PLND is recommended within consensus guidelines for patients with high risk disease or in those of intermediate risk if the estimated risk of node positive disease is >5% [4] for accurate pathological staging to guide adjuvant therapy recommendations and prognosis estimates[9], given well described limitations in traditional imaging-based techniques [9,10]. A recent systematic review did not show any oncological benefit of performing any PLND during RP at the expense of longer operating times, more blood loss, increased length of stay, and postoperative complications [9].

Limited descriptions of patterns of prostate cancer care in Australia have been described to date[5-8,11]. Detailed considerations of surgical patterns of care, specifically relating to age groups treated, geographical locations of treatment and use of PLND, as well as the uptake of robotic-assisted laparoscopic prostatectomy (RALP), are yet to be described. The aim of this study was to describe the Australian national surgical patterns of PCa care considering utilisation of RP with or without PLND and uptake of RALP and consideration of robotic-assisted techniques.

Methods

Data sources

The Australian Government Department of Health Medicare Benefits Schedule (MBS) provides rebates to patients (Australian residents and certain visitors) as financial assistance for medical and allied health care. While public hospitals are funded by the federal and state governments independent of Medicare, patients treated in the private health care sector can have up to 75% of the schedule fees paid by Medicare, with private health reimbursement and out of pocket payments covering remaining expenses. Approximately 30% of hospital beds are located privately, where over 50% of elective surgical procedures in Australia are performed in private hospitals [12]. Thus, this proportion of elective surgical procedures would be expected to be reflected by MBS claims. Treatment patterns were also matched to PCa incidence according to Australian Institute for Health and Welfare (AIHW) Australian Cancer Incidence and Mortality books, which included incidence data for the time period 2001 - 2013. Incidence data after 2013 was not available for inclusion.

Data collection

MBS Item Statistics Reports (available from http://medicarestatistics.humanservices.gov.au/statistics/mbs_item.jsp) were queried in March 2017 per calendar year from 2001 to 2016 for MBS item numbers 37210

(Prostatectomy, radical, involving total excision of the prostate, sparing of nerves around the bladder and bladder neck reconstruction) and 37211 (Prostatectomy, radical, involving total excision of the prostate, sparing of nerves around the bladder and bladder neck reconstruction, with pelvic lymphadenectomy). Data were stratified as raw totals for each year per age group (45-54, 55-64, 65-74, 75-84) and Australian state or territory (New South Wales, NSW; Victoria, VIC; Queensland, QLD; Western Australia, WA; South Australia, SA; Tasmania, TAS; Australian Capital Territory, ACT; Northern Territory, NT), collated in Excel and described per 100,000 (10^5) men aged 45 – 84 years for each state or territory. The total procedures performed as RALPs were provided by Device Technologies Pty Ltd as part of routine data collection.

Institutional ethical board approval or informed consent were not required as the collected data released by the Australian Government is publicly available and research did not directly involve human participants.

Data analysis

Per capita estimates of RP performed with and without PLND were compared overall, for each age group and for Australian state or territory where the service was provided. The proportion of RP with or without PLND for PCa incidence (per AIHW) was calculated. A ratio of RP with PLND to RP without PLND was calculated as a reflection of the relative use of these two procedures. Figures were created using Stata version12.0 SE (StataCorp. College Station, Texas USA).

Results

Radical prostatectomy relative to total population

Total RPs performed increased from 2001 (1670 or 51.7/10^5 men) until peaking in 2009 (6407 or 164.6/10^5 men) with a subsequent decrease through to 2016 (5537 or 124/10^5 men), driven by reduced RPs in men <65 years (Figure 1a, Supplementary Table 1). Since

2009, the age-specific rate of RPs in men aged 75-84 increased by 2.3-fold, while the rates for men aged 55-64 and 45-54 reduced by 44% and 55%, respectively (Figure 1b). Rates in men aged 65-74 years were similar between 2009 and 2016 (<10% change).

When states and territories were considered, NSW consistently performed most RPs per 100,000 men across the study period. Trends observed for total RPs were maintained similar across all states (Figure 1c), including when rebased to 2009 levels (Figure 1d). Trends for ACT and NT were omitted due to small sample size.

Radical prostatectomy relative to prostate cancer incidence

The yearly fraction of RPs in the private health sector divided by PCa incidence increased from 2001 to 2009 in all age groups; men aged 45-54 years (45 to 51%), 55-64 years (35 to 45%), 65-74 years (13 to 30%) and 75-84 years (0.2 to 3.4%); Figure 2a). This increase continued for men aged ≥ 65 years to 2013, especially for men 75-84 years (3.4% to 6.5%) while slightly reduced proportions were observed for men aged < 65 years (Figure 2b).

Pelvic lymphadenectomy trends

When stratified according to RP with or without PLND (noPLND), overall use of PLND declined across the study period, with an observed reduction in the PLND:noPLND ratio from 3.61 to 1.06 (Figure 3a). The ratio remained stable between 2009 and 2016 (1.05 – 1.14; Supplementary Table 2).

The relative proportion of RP with PLND, compared to no PLND, declined over the study period for all age subgroups, shown by a reduction in PLND:noPLND ratios (Figure 3b). The point at which RP without PLND was performed more than RP with PLND (PLND:noPLND < 1) was first observed in 2008 for men 45-54 and in 2012 for men 55-64. RP with PLND was more commonly performed than noPLND for men aged between 65 and 84 years in 2016, indicated by a PLND:noPLND ratio greater than one.

When analysed according to treatment location, overall PLND:noPLND reductions were observed between 2001 and 2016 in all states (Figure 3c). The highest proportion of RPs with PLND were performed in NSW, with a reduction from 5.1 in 2001 to fluctuations between 2.0 and 2.8 since 2009. Ratios less than one in the past decade were consistently observed for RPs performed in Victoria, Queensland and Western Australia while a slightly higher ratio around one was observed in South Australia.

Association with robotic assisted laparoscopic prostatectomy (RALP)

When analysed considering RALPs performed in the private sector (data provided by Device Technologies), an increasing trend towards RALP was observed with more than 80% of RPs performed as RALPs in 2016 (Figure 4).

Discussion

This retrospective analysis of national health systems data between 2001 to 2016 reflects treatment patterns in the private health sector, where health insurance coverage has been relatively stable (51 to 57.1% between 2001 and 2012 %), and comprises more than 50% of nationally treated cases in some age groups [13]. RPs are now performed less than in 2009, driven by trends in younger patients. In contrast, RPs among men aged 75-84 years have continued to increase over time and were performed at a higher rate (per 10^5) than for men aged 45-54 years since 2013. Less concurrent PLND has been observed over time with an increased uptake of robotics.

These trends may be explained by an increased utilization of AS (15% of all men diagnosed with PCa in Victoria, 36% of low risk and 9% of intermediate risk cases) to reduce over treatment of PCa, particularly for men aged less than 65 years relative to the general (Figure 1) and PCa (Figure 2) populations [7]. Increasing use of 3 Tesla multiparametric magnetic resonance imaging (mpMRI) in Australia to triage men prior to biopsy may have also decreased low risk PCa diagnosis, as mpMRI omits a significant proportion of low volume,

low risk PCa [15,16]. Reduced serum PSA testing [11], potentially due to the "category D" recommendations of the USPSTF in 2012 [14], may further account for reduced overall PCa diagnoses since 2012 [2]. Reduced diagnosis of low risk PCa in young men, as demonstrated by Ruseckaite and colleagues[5], is presumed to be related to reduced PSA testing and may explain less treatment for men aged less than 65 years (Figure 1), as well as contributions from increased uptake of AS suggested by reduced active treatment in the younger PCa population (Figure 2).

Along with a trend towards older age at diagnosis[5], many factors may have contributed to an upward grade and stage "migration" described internationally and in Australia [5,17,18] and shift toward RP in the elderly (Figure 2). Furthermore, the introduction of the minimally invasive RALP technique was shown to decrease peri-operative complications compared to open surgery in a randomised controlled trial [19,20]. Minimally invasive laparoscopic surgery, such as RALP, has also allowed surgeons to be more confident performing surgery and achieving acceptable functional (e.g. continence) outcomes in older or overweight men, in preference to referral for radiation treatments. Life expectancy has continued to increase in Australia with a greater benefit observed in higher socioeconomic groups [21], such as privately insured patients. Thus, higher grade disease in older men expected to gain a mortality benefit from radical treatment may explain the observed increase in RP in this population.

The proportion of men with PCa not treated by RP in this dataset, representing private non-surgical management plans and public hospital patients, was observed to decline with time and may reflect reduced incidence as well as greater use of active, or expectant, monitoring approaches [5]. Furthermore, reduced utilization of radiotherapy techniques may be a contributing factor, with reductions from 25.6% to 15.6% observed between 2009 – 2013 in Australian registry data [5].

PLND was used less often in comparison to RP alone, with an overall PLND:noPLND ratio observed to be stable during 2008 – 2016 (Figure 3). A shift away from concurrent PLND

was observed across Australia, especially in Queensland, Victoria and Western Australia, with ratios less than 1 observed since before 2009. The greatest rates of decline appeared to occur with introduction of laparoscopic RP and RALP in each state (Figure 3). Indeed, PLND was performed on protocol during a Queensland-based randomised trial of open RP versus RALP in 36% (PLND:noPLND ratio 0.57) of cases (positive in 3% overall) among a contemporary cohort (61% organ confined disease) with a higher lymph node yield observed in favour of RALP [20]. Thus, we conclude that significant factors contributing to the reduced use PLND may include surgeon preference, the introduction of laparoscopic RP and RALP to Australian urological practice in the early 2000's, the absence of consensus on which patients should undergo PLND at time of RP [22] and the uncertainty regarding the long term oncological benefit of a PLND in the majority of men [9].

Experience with newer imaging, such as ^{68}Ga-labelled prostate-specific membrane antigen (PSMA) positron emission tomography (PET)[23,24], may influence whether PLND is performed, as some practitioners only perform PLND in the presence of PSMA-avid lymph node, thought to occur in approximately 25% of scans[25]. Other contributors to trends of practice may include limited sensitivity of preoperative nomograms (reported locally to be 38.2% in the primary setting[26]), availability and engagement of primary or post-operative radiotherapy considering geographic limitations in Australia and limited access to minimally invasive surgery (e.g. RALP platforms). The therapeutic value of PLND is supported by retrospective reports suggest that PLND may be curative in select cases of low volume nodal disease or with higher lymph node yield at RP [27]. Thus, the prognostic and potential survival benefit of PLND means that it is likely to continue to be performed in select cases based on surgeon and patient preference.

This study has several limitations. Most notably, the estimates are based on Medicare claims data that only reliably reflects treatment in the private health sector, thus omitting public treatment data. Furthermore, individual patient data regarding disease and patient factors

are unavailable when considering individual patient patterns of care. These limitations have been adjusted for using overall population and PCa incidence estimates wherever possible.

Conclusion

In this retrospective analysis of national health systems data representative of a significant proportion of PCa cases, RP is performed less men <65 years and more in men ≥65 years. PLND at the time of RP has mostly become performed less commonly, while RALP as a proportion of RP has increased since introduction in the early 21st century. In the absence of mature national PCa registry data, Medicare claims registry data describes change in surgical patterns of PCa care in Australia for consideration by clinicians and patients. These data suggest less overtreatment of PCa despite increased use of robotics, potentially both of which likely reflect reduced harm of PSA testing. Thus, these real world trends suggest that urological practice in our region uphold the NHMRC-endorsed PCFA PSA testing guidelines for evidence-based patient care

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Conflicts of Interest: none

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References

1. ABO. Underlying causes of death (Australia). 2016; http://www.aihw.gov.au/deaths/leading-causes-of-death/#leading-sex. Accessed 1/3/2016, 2016.
2. AIHW. *Australian Cancer Incidence and Mortality (ACIM) books: prostate cancer.* Canberra: Australian Institute of Health and Welfare.

3. Lozano R, Naghavi M, Foreman K, et al. Global and regional mortality from 235 causes of death for 20 age groups in 1990 and 2010: a systematic analysis for the Global Burden of Disease Study 2010. *Lancet.* 380(9859):2095-2128.

4. Mottet N, Bellmunt J, Bolla M, et al. EAU-ESTRO-SIOG Guidelines on Prostate Cancer. Part 1: Screening, Diagnosis, and Local Treatment with Curative Intent. *Eur Urol.* 2017;71(4):618-629.

5. Ruseckaite R, Beckmann K, O'Callaghan M, et al. A retrospective analysis of Victorian and South Australian clinical registries for prostate cancer: trends in clinical presentation and management of the disease. *BMC Cancer.* 2016;16:607.

6. Sampurno F, Earnest A, Kumari PB, et al. Quality of care achievements of the Prostate Cancer Outcomes Registry-Victoria. *Med J Aust.* 2016;204(8):319.

7. Weerakoon M, Papa N, Lawrentschuk N, et al. The current use of active surveillance in an Australian cohort of men: a pattern of care analysis from the Victorian Prostate Cancer Registry. *BJU Int.* 2015;115 Suppl 5:50-56.

8. Evans SM, Millar JL, Davis ID, et al. Patterns of care for men diagnosed with prostate cancer in Victoria from 2008 to 2011. *Med J Aust.* 2013;198(10):540-545.

9. Fossati N, Willemse PM, Van den Broeck T, et al. The Benefits and Harms of Different Extents of Lymph Node Dissection During Radical Prostatectomy for Prostate Cancer: A Systematic Review. *Eur Urol.* 2017; 72(1): 84-109.

10. Briganti A, Abdollah F, Nini A, et al. Performance characteristics of computed tomography in detecting lymph node metastases in contemporary patients with prostate cancer treated with extended pelvic lymph node dissection. *Eur Urol.* 2012;61(6):1132-1138.

11. 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 Int.* 2017;119(1):110-115.

12. Surgery in Australia's hospitals. 2017; http://www.aihw.gov.au/Haag13-14/surgery/. Accessed 22 April, 2017.

13. Private Health Insurance. *Australian Health Survey: Health Service Usage and Health Related Actions, 2011-12* 2013; http://www.abs.gov.au/ausstats/abs@.nsf/lookup/E334D0A98272E4DCCA257B39000F2DCF?opendocument. Accessed April, 2017.

14. McGinley KF, McMahon GC, Brown GA. Impact of the US Preventive Services Task Force Grade D Recommendation: Assessment of Evaluations for Elevated Prostate-specific Antigen and Prostate Biopsies in a Large Urology Group Practice Following Statement Revision. *Rev Urol.* 2015;17(3):171-177.

15. Pokorny MR, de Rooij M, Duncan E, et al. Prospective study of diagnostic accuracy comparing prostate cancer detection by transrectal ultrasound-guided biopsy versus magnetic resonance (MR) imaging with subsequent MR-guided biopsy in men without previous prostate biopsies. *Eur Urol.* 2014;66(1):22-29.

16. Ahmed HU, El-Shater Bosaily A, Brown LC, et al. Diagnostic accuracy of multi-parametric MRI and TRUS biopsy in prostate cancer (PROMIS): a paired validating confirmatory study. *Lancet.* 2017;389(10071):815-822.

17. Bhindi B, Mamdani M, Kulkarni GS, et al. Impact of the U.S. Preventive Services Task Force recommendations against prostate specific antigen screening on prostate biopsy and cancer detection rates. *J Urol.* 2015;193(5):1519-1524.

18. Fleshner K, Carlsson SV, Roobol MJ. The effect of the USPSTF PSA screening recommendation on prostate cancer incidence patterns in the USA. *Nat Rev Urol.* 2017;14(1):26-37.

19. Basto M, Sathianathen N, Te Marvelde L, et al. Patterns-of-care and health economic analysis of robot-assisted radical prostatectomy in the Australian public health system. *BJU Int.* 2016;117(6):930-939.

20. Yaxley JW, Coughlin GD, Chambers SK, et al. Robot-assisted laparoscopic prostatectomy versus open radical retropubic prostatectomy: early outcomes from a randomised controlled phase 3 study. *Lancet.* 2016;388(10049):1057-1066.

21. Korda RJ, Butler JRG, Clements MS, Kunitz SJ. Differential impacts of health care in Australia: trend analysis of socioeconomic inequalities in avoidable mortality. *Int J Epidemiol.* 2007;36(1):157-165.

22. Mohler J, Bahnson RR, Boston B, et al. NCCN clinical practice guidelines in oncology: prostate cancer. *J Natl Compr Canc Netw.* 2010;8(2):162-200.

23. Perera M, Papa N, Christidis D, et al. Sensitivity, Specificity, and Predictors of Positive (68)Ga-Prostate-specific Membrane Antigen Positron Emission Tomography in Advanced Prostate Cancer: A Systematic Review and Meta-analysis. *Eur Urol.* 2016;70(6):926-937.

24. Meredith G, Wong D, Yaxley J, et al. The use of 68 Ga-PSMA PET CT in men with biochemical recurrence after definitive treatment of acinar prostate cancer. *BJU Int.* 2016;118 Suppl 3:49-55.

25. Perera M, Papa N, Roberts MJ, et al. Gallium-68 Prostate-specific Membrane Antigen Positron Emission Tomography in Advanced Prostate Cancer—Updated Diagnostic Utility, Sensitivity, Specificity, and Distribution of Prostate-specific

Membrane Antigen-avid Lesions: A Systematic Review and Meta-analysis *Eur Urol.* (in press).

26. Yaxley JW, Raveenthiran S, Nouhaud FX, et al. Outcomes of Primary Lymph Node Staging of Intermediate and High Risk Prostate Cancer with 68Ga-PSMA Positron Emission Tomography/Computerized Tomography Compared to Histological Correlation of Pelvic Lymph Node Pathology: Can Preoperative 68Ga-PSMA Positron Emission Tomography/Computerized Tomography Replace Pelvic Lymph Node Dissection for Prostate Cancer Staging? *J Urol.* (in press).

27. Abdollah F, Gandaglia G, Suardi N, et al. More extensive pelvic lymph node dissection improves survival in patients with node-positive prostate cancer. *Eur Urol.* 2015;67(2):212-219.

Figure legends

Figure 1: Age specific total radical prostatectomy (RP) claims, including RP with and without pelvic lymphadenectomy, described per 100,000 men. A, B – age groups; C, D – states and territories; A, C – overall trends; B, D – rebased to 100 in 2009 (peak claims year).

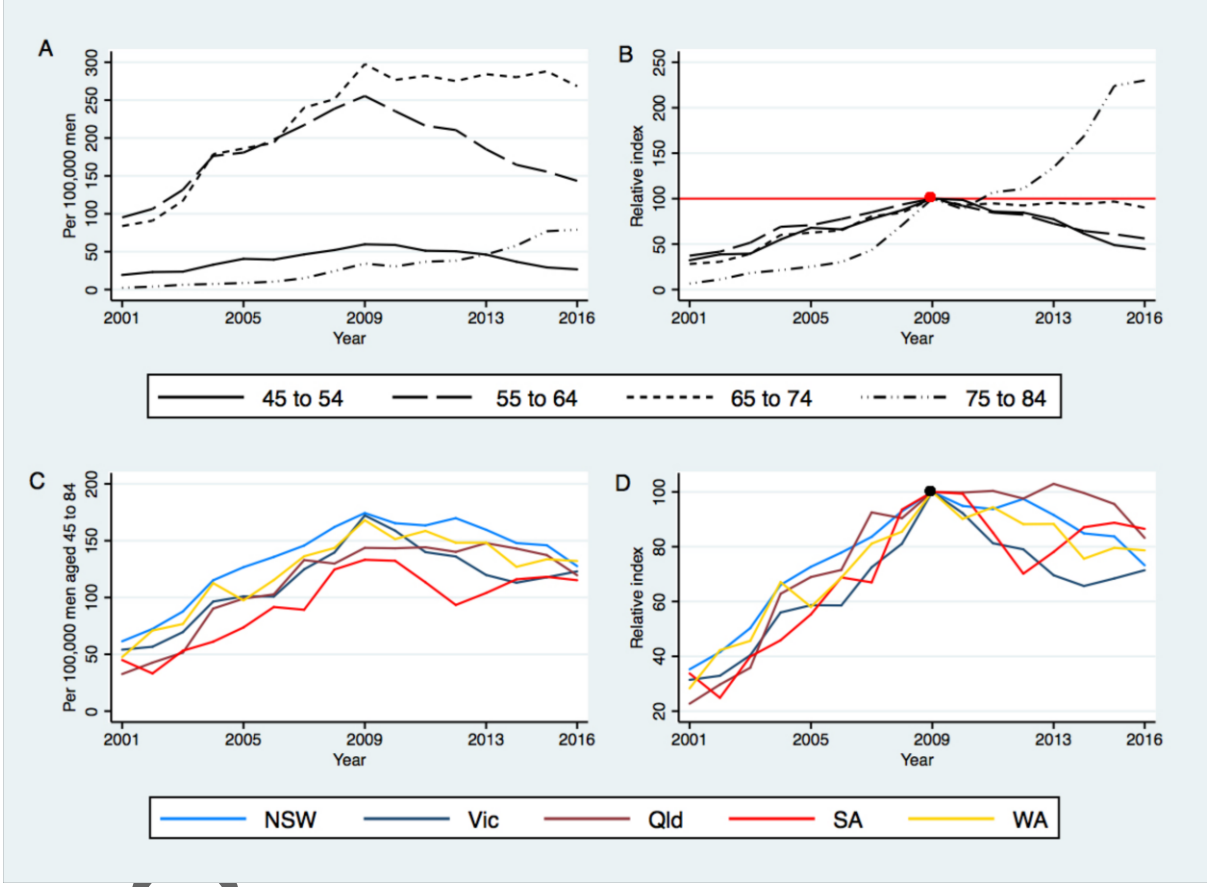


Figure 2: Prostate cancer (PCa) treatment by radical prostatectomy (RP) proportional to PCa incidence based on AIHW estimates [(RP/PCa incidence)*100). A – overall proportions; B – proportions relative to 2009.

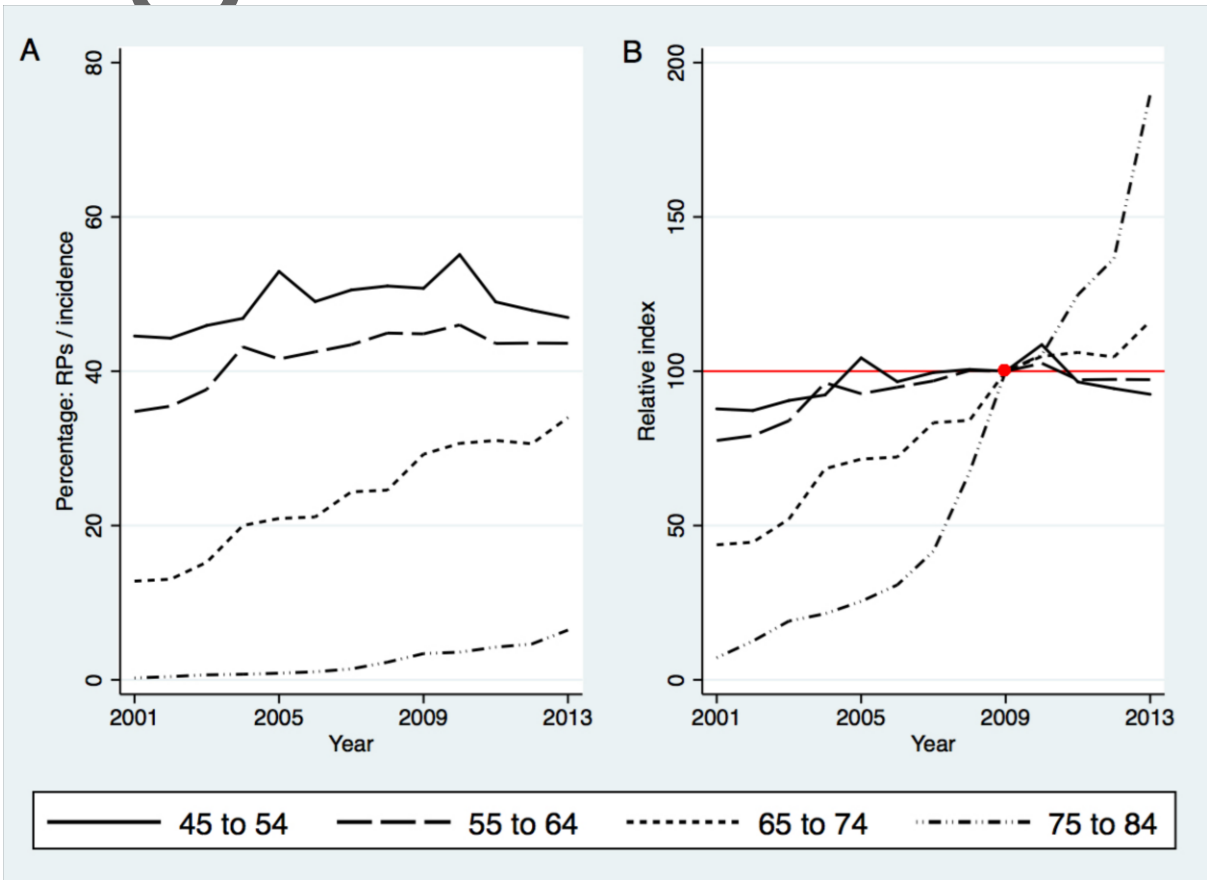
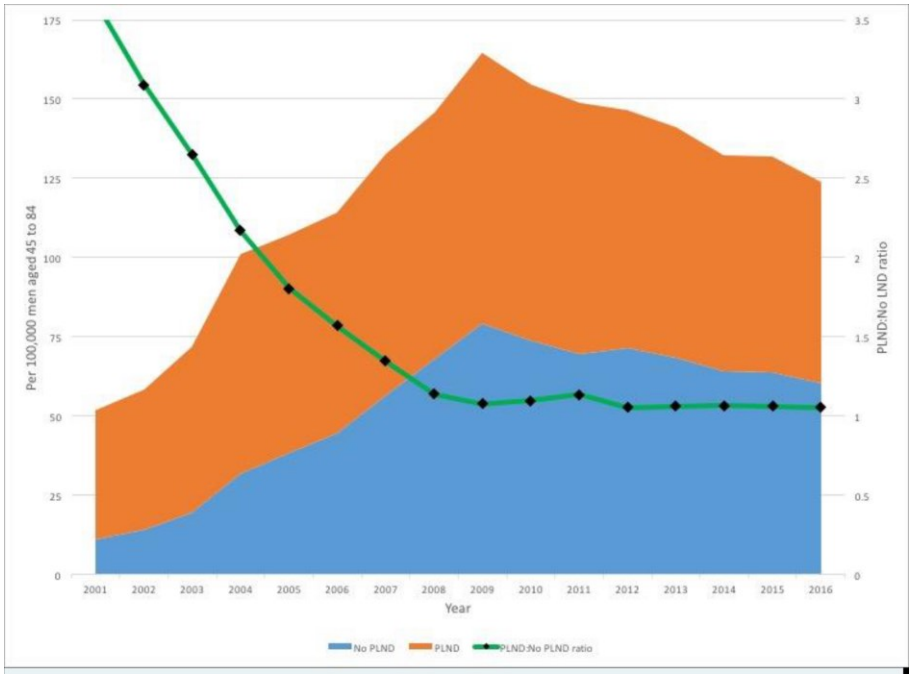


Figure 3: Relative index (/100,000 men) of radical prostatectomy (RP) with (orange) or without (blue; noPLND) pelvic lymphadenectomy (PLND). A – Overall PLND:noPLND ratio (green line) to reflect change in proportion over the study period. B - PLND:noPLND ratio for age groups; C – PLND:noPLND ratio for states and territories


Per 100,000 men aged 45 to 84
PLND:No LND ratio
Year
No PLND
PLND
PLND:No PLND ratio

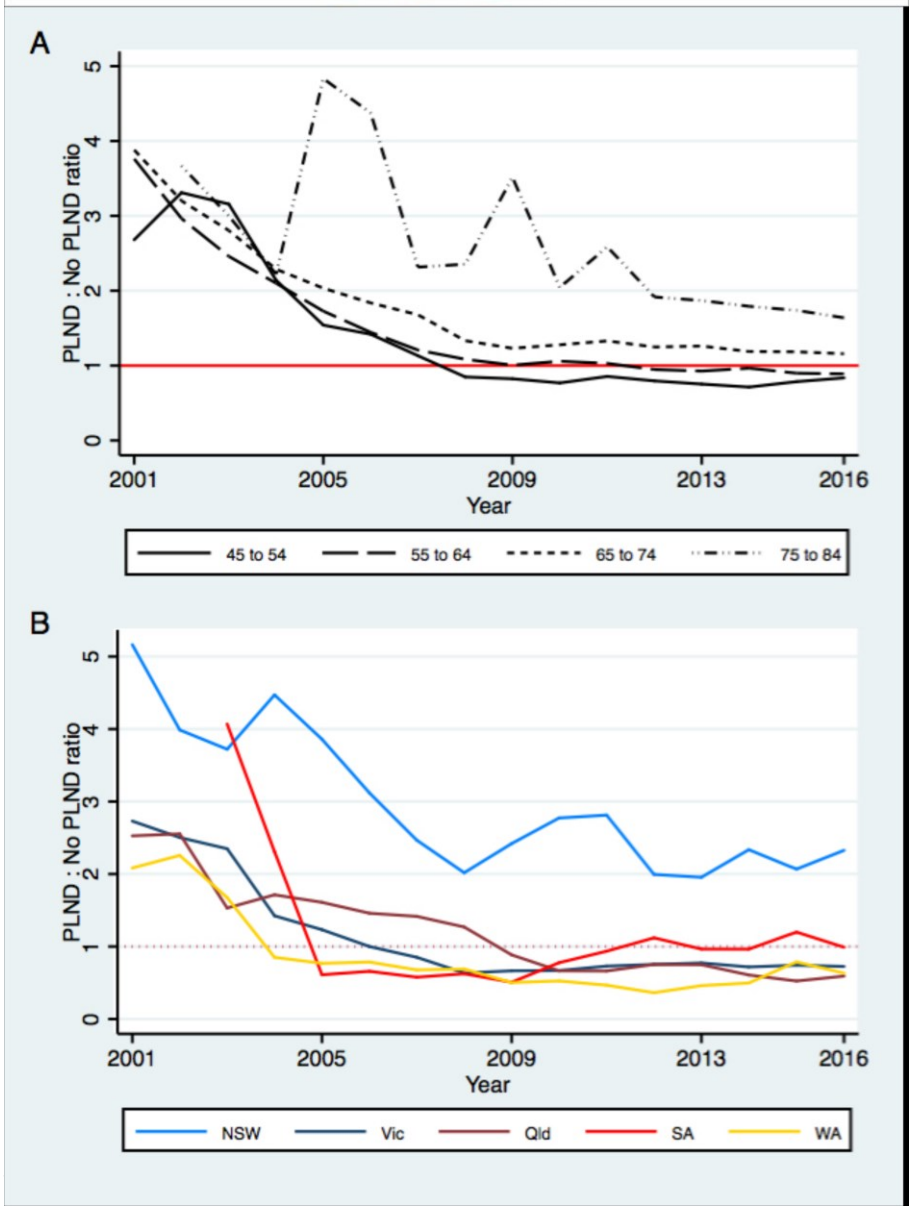

A
PLND : No PLND ratio
Year
45 to 54
55 to 64
65 to 74
75 to 84
B
PLND : No PLND ratio
Year
NSW
Vic
Qld
SA
WA

Figure 4: Proportion of radical prostatectomy (RP) performed using the robotic assisted laparoscopic (RALP) approach (calculated according to MBS data and RALP data from Device Technologies).