

Research Communication

Large variation in conservative management of low-risk prostate cancer in Australia and New Zealand

Most men with low-risk prostate cancer (LRPC) do not require immediate local treatment, with conservative management, either active surveillance (AS) or watchful waiting (WW), being the preferred management option. Multiple population-based studies have reported increasing uptake of conservative management for LRPC, with wide variations in practice across different countries [1–4].

In Australia, only limited regional data exist [5], but the establishment of the bi-national Prostate Cancer Outcomes Registry Australia and New Zealand (PCOR-ANZ) [6] has allowed for expanded data. It is estimated that PCOR-ANZ captures approximately 72% of all new prostate cancer cases in these jurisdictions. In this population-based study, we aimed to report on the changing trends in conservative management for men with LRPC (i.e. Gleason Grade Group 1, PSA < 10 ng/mL, and cT1c–cT2a), which constitutes approximately 20% of all prostate cancer diagnoses, between 2015 and 2018, in three states in Australia (New South Wales, Victoria and Queensland) and New Zealand, as captured in PCOR-ANZ [6], and to identify institutional and jurisdiction variations in practice.

We defined men on ‘conservative management’ as those who did not receive active treatment in the first 12 months after LRPC diagnosis (confirmed through patient contact 12 months post-diagnosis and verified by cross-checking with medical records); these included men documented to be on either AS or WW by their clinicians in the medical records. The Cochran–Armitage test for trend was used to evaluate the temporal change in conservative management of LRPC. Multivariable logistic regression was used to evaluate the association of covariates with the likelihood of conservative management. A two-sided P value < 0.05 was considered statistically significant. All statistical analyses were performed using Stata/MP 16 (StataCorp, College Station, TX, USA). This study was approved by the Monash University Human Research Ethics Committee.

Of the 3799 men with LRPC in the study, 2816 (74%) had conservative management, of whom 2571 (68%) were documented to be on AS (Table 1). There were marked differences in conservative management use across jurisdictions: 80% in New South Wales, 77% in Victoria, 72% in Queensland and 67% in New Zealand ($P < 0.001$). A higher proportion of men diagnosed in public metropolitan (77%) and public regional centres (78%), compared to private regional centres (66%), received conservative management

($P < 0.001$). Institutional variation in practice was observed across all jurisdictions. In NSW, the proportion of those receiving conservative management was highest in men diagnosed in public metropolitan centres (84%) and lowest in men diagnosed in private regional centres (62%). Similarly, the proportion of patients receiving conservative management was lowest in men diagnosed in private regional centres in Victoria (65%) and Queensland (67%). However, in New Zealand, the proportion of those with conservative management was highest in public regional centres (76%) and lowest in private metropolitan centres (57%). There was a progressive increase in conservative management over time, from 70% in 2015 to 76% in 2018 (P -trend = 0.001).

In multivariate analyses, there was a progressive increase in conservative management over time after adjusting for other covariates. Men diagnosed in 2018 were more likely to be managed conservatively than men diagnosed in 2015 (odds ratio [OR] 1.6, 95% CI 1.2–2.0; $P < 0.001$). Compared to men diagnosed in NSW, men diagnosed in Queensland (OR 0.71, 95% CI 0.54–0.93; $P = 0.01$) and New Zealand (OR 0.42, 95% CI 0.32–0.56; $P < 0.001$) were less likely to be managed conservatively. Compared to men diagnosed in public metropolitan centres, those diagnosed in private metropolitan (OR 0.71, 95% CI 0.58–0.87; $P = 0.001$) and private regional centres (OR 0.44, 95% CI 0.34–0.57; $P < 0.001$) were less likely to be managed conservatively.

It is important to acknowledge that men who received conservative management within 12 months of LRPC represent a heterogeneous group, ranging from fit healthy men on AS (with intention of deferring, or avoiding curative treatment) to frail elderly men on WW. The rationale for the use of the term ‘conservative management’ is the inconsistency in clinicians’ reporting of AS and WW. This is evident in the large variation in the proportion of men undergoing WW observed among institutions, and in changing trends in WW, when no new evidence or guidelines have recommended a change in criteria for WW. Also, earlier Victorian studies showed that only one in four men documented by clinicians to be on AS adhered to guideline-recommended AS protocols [7]. The broader term ‘conservative management’ is therefore used for the purpose of this study, and is consistent with multiple earlier studies [1–4].

Overall, the proportion of those on conservative management for LRPC in our cohort was much higher than reported in

Table 1 Characteristics of men with low-risk prostate cancer who had conservative management (i.e. no active treatment within 12 months of diagnosis, including active surveillance and watchful waiting) and multivariate analyses of factors associated with conservative management.

	Conservative management 2816 (74%)	Active surveillance 2571 (68%)	Watchful waiting 245 (6%)	Active treatment 983 (26%)	Multivariate analyses OR (95% CI)	P value
Age at LRPC diagnosis , Mean (SD), years	64.0 (7.7)	63.6 (7.4)	68.2 (9.0)	62.0 (7.2)	1.05 (1.04–1.06)	<0.001
Age category, n (%)						
<55 years	333 (67)	314 (63)	19 (4)	165 (33)	–	–
55–59 years	510 (70)	483 (66)	27 (4)	219 (30)	–	–
60–64 years	653 (74)	611 (69)	42 (5)	235 (26)	–	–
65–69 years	764 (76)	713 (71)	51 (5)	243 (24)	–	–
70–74 years	350 (77)	309 (68)	41 (9)	102 (23)	–	–
≥75 years	206 (92)	141 (63)	65 (29)	19 (8)	–	–
PSA at LRPC diagnosis , Median (IQR), ng/mL	5.2 (3.9–6.7)	5.2 (3.9–6.7)	5.0 (2.9–7.0)	5.3 (4.2–6.7)	0.92 (0.88–0.95)	<0.001
Clinical category, n (%)						
cT1	2597 (76)	2369 (69)	228 (7)	814 (24)	Reference	
cT2a	219 (56)	202 (52)	17 (4)	169 (44)	0.39 (0.31–0.49)	<0.001
Jurisdiction/State, n (%)						
NSW	457 (80)	423 (74)	34 (6)	113 (20)	Reference	
VIC	1126 (77)	1018 (70)	108 (7)	337 (23)	0.94 (0.74–1.21)	0.6
QLD	714 (72)	636 (64)	78 (8)	275 (28)	0.71 (0.54–0.93)	0.01
NZ	519 (67)	494 (64)	25 (3)	258 (33)	0.42 (0.32–0.56)	<0.001
Institutions where LRPC diagnosed, n (%)						
Public metropolitan	694 (77)	629 (70)	65 (7)	209 (23)	Reference	
Private metropolitan	1377 (74)	1264 (68)	113 (6)	474 (26)	0.71 (0.58–0.87)	0.001
Public regional	357 (78)	319 (70)	38 (8)	100 (22)	1.03 (0.78–1.37)	0.8
Private regional	388 (66)	359 (61)	29 (5)	200 (34)	0.44 (0.34–0.57)	<0.001
Year of LRPC diagnosis, n (%)						
2015	490 (70)	429 (61)	61 (9)	213 (30)	Reference	
2016	602 (72)	543 (65)	59 (7)	238 (28)	1.09 (0.87–1.37)	0.5
2017	882 (77)	810 (71)	72 (6)	260 (23)	1.64 (1.31–2.05)	<0.001
2018	842 (76)	789 (71)	53 (5)	272 (24)	1.55 (1.23–1.96)	<0.001

LRPC, low-risk prostate cancer; NSW, New South Wales; NZ, New Zealand; QLD, Queensland; VIC, Victoria.

the US Surveillance Epidemiology and End Results (SEER) study, and even when patterns of practice in the same year were considered, those on conservative management for LRPC constituted only 42% of men in the US SEER 'Prostate with Watchful Waiting Database' in 2015 [3], compared to 70% in our cohort. The proportion of those receiving conservative management in a Swedish population-based study was more similar to that in our cohort [4], which is probably attributable to similarities between the Australian and New Zealand healthcare systems and Sweden, compared to the United States. Another consideration is that the SEER database was restricted to men aged >65 years and above, whereas PCOR-ANZ captured men of all age groups. In contrast, in the UK National Prostate Cancer Audit, the proportion of 5588 men with LRPC diagnosed during 2014–2017 who were managed conservatively was much higher, at 95%, and when classified using the Cambridge Prognostic Group (CPG) system, 89% of 10 963 men in CPG Group 1 were managed conservatively [8]; this represents the highest reported population-based use of conservative management for LRPC in the literature.

We observed marked variations in practice among the jurisdictions in our cohort, the reason for which is probably multifactorial and driven by a combination of patient and

clinician factors. Across the three Australian jurisdictions, conservative management was consistently the lowest in men diagnosed in private regional centres. However, it is reassuring to observe an increasing trend in uptake of conservative management in private regional centres over time. It is also important to acknowledge that 'public/private' and 'metropolitan/regional' is a broad classification for institutions in our study, and it has been shown in earlier studies in Victoria that there is significant heterogeneity and variations in practice between institutions that were classified as public/private and metropolitan/regional [5].

The lower proportion of patients on conservative management in private settings raises several hypotheses. A higher proportion of active treatment in private settings may reflect lower comorbidities in men diagnosed in private institutions; this is also reflected in the lower proportion of men diagnosed in private institutions being put on WW as compared to AS. It may also be a result of a financial incentive for clinicians to offer these men curative treatment (surgery or radiotherapy). This trend could also be driven by patient preference, whereby men who have private insurance may be more interested, or willing to pursue active treatment.

Findings from this study have highlighted opportunities for future efforts to identify factors driving practice variation.

Key themes influencing men's choice and adherence to AS may include: fear of progression; family and social support; healthcare providers' communication and attitudes; and the location and type of institutions, among others. Further qualitative research is currently underway within our group to better understand clinicians' barriers to increasing the adoption of conservative management for LRPC.






In summary, in this first ANZ population-based cohort of men with LRPC, we observed increasing conservative management for LRPC over time. However, large variations in practice exist across institutions and jurisdictions. This suggests opportunities for future quality improvement initiatives to further increase the adoption of conservative management for LRPC, and importantly to reduce variations in care for men with LRPC.

Acknowledgement

This work was funded by the Movember Foundation PCOR-ANZ Clinical Quality Improvement Research Fund. Open access publishing facilitated by Monash University, as part of the Wiley - Monash University agreement via the Council of Australian University Librarians.

Disclosure of Interests

Declan Muphy reports personal fees from Janssen, Astellas, Bayer, Ferring, Astra Zeneca, and Ipsen outside of the submitted work. David Pryor reports personal fees from Bayer, and Roche outside the submitted work. No other disclosures were reported.

Wee Loon Ong^{1,2,3,4,5} , Isaac Thangasamy⁶ , Declan Murphy⁶ , Elizabeth Pritchard⁴, Susan Evans⁴, Jeremy Millar^{1,7}, Venu Chalasani⁸, Prem Rashid⁹, Matthew Winter¹⁰, Ian Vela^{11,12}, David Pryor¹³ , Stephen Mark¹⁴ and Nathan Lawrentschuk^{6,15,16} 

¹Alfred Health Radiation Oncology, Melbourne, Victoria, Australia, ²Department of Radiation Oncology, Olivia Newton-John Cancer Wellness and Research Centre, Austin Health, Heidelberg, Victoria, Australia, ³Department of Radiation Oncology, Peter MacCallum Cancer Centre, Melbourne, Victoria, Australia, ⁴Department of Epidemiology and Preventive Medicine, Monash University, Melbourne, Victoria, Australia, ⁵School of Clinical Medicine, University of Cambridge, Cambridge, UK, ⁶Department of Cancer Surgery, Peter MacCallum Cancer Centre, Melbourne, Victoria, Australia, ⁷Central Clinical School, Monash University, Melbourne, Victoria, Australia, ⁸Horbsby Hospital, Hornsby, New South Wales, Australia, ⁹Port Macquarie Base Hospital,

Port Macquarie, New South Wales, Australia, ¹⁰Urology Research Group, Nepean Hospital, Kingswood, New South Wales, Australia, ¹¹Department of Urology, Princess Alexandra Hospital, Woolloongabba, Queensland, Australia, ¹²Australian Prostate Cancer Research Centre, Queensland University of Technology, Brisbane, Queensland, Australia, ¹³Department of Radiation Oncology, Princess Alexandra Hospital, Woolloongabba, Queensland, Australia, ¹⁴Department of Urology, Christchurch Hospital, Christchurch, New Zealand, ¹⁵EJ Whitten Prostate Cancer Research Centre, Epworth Hospital, Melbourne, Victoria, and ¹⁶Department of Surgery, University of Melbourne, Royal Melbourne Hospital, Melbourne, Victoria, Australia

WLO and IT contributed equally as co-first author.

References

- Gray PJ, Lin CC, Cooperberg MR, Jemal A, Efsthathiou JA. Temporal trends and the impact of race, insurance, and socioeconomic status in the Management of Localized Prostate Cancer. *Eur Urol* 2017; 71: 729–37
- Loeb S, Byrne N, Makarov DV, Lepor H, Walter D. Use of conservative Management for low-Risk Prostate Cancer in the veterans affairs integrated health care system from 2005-2015. *JAMA* 2018; 319: 2231–3
- Mahal BA, Butler S, Franco I et al. Use of active surveillance or watchful waiting for low-risk prostate cancer and management trends across risk groups in the United States, 2010-2015. *JAMA* 2019; 321: 704–6
- Loeb S, Folkvaljon Y, Curnyn C, Robinson D, Bratt O, Stattin P. Uptake of active surveillance for very-low-risk prostate cancer in Sweden. *JAMA Oncol* 2017; 3: 1393–8
- Ong WL, Evans SM, Evans M et al. Trends in conservative management for low-risk prostate cancer in a population-based cohort of Australian men diagnosed between 2009 and 2016. *Eur Urol Oncol* 2021; 4: 319–22
- Evans SM, Nag N, Roder D et al. Development of an international prostate cancer outcomes registry. *BJU Int* 2016; 117(Suppl 4): 60–7
- Evans MA, Millar JL, Earnest A et al. Active surveillance of men with low risk prostate cancer: evidence from the prostate cancer outcomes registry-Victoria. *Med J Aust* 2018; 208: 439–43
- Parry MG, Cowling TE, Sujenthiran A et al. Risk stratification for prostate cancer management: value of the Cambridge prognostic group classification for assessing treatment allocation. *BMC Med* 2020; 18: 114

Correspondence: Wee Loon Ong, Alfred Health Radiation Oncology, 55 Commercial Road, Melbourne 3000 VIC, Australia.

e-mail: weeloonong@cantab.net

Abbreviations: AS, active surveillance; CPG, Cambridge Prognostic Group; LRPC, low-risk prostate cancer; OR, odds ratio; PCOR-ANZ, Prostate Cancer Outcomes Registry Australia and New Zealand; SEER, Surveillance Epidemiology and End Results; WW, watchful waiting.