ANDROLOGY AUSTRALIA
What every man needs to know

The early detection of prostate cancer

Review and summary of current professional guidelines & position statements

Many professional bodies in Australia and overseas have published position statements or professional guidelines/recommendations on the early detection of prostate cancer, with a focus on PSA testing. Despite the publication of findings from several large randomised trials in recent years there is still much discussion about the merits and harms of the PSA test with no consensus on the appropriate use of PSA testing in men with no history of prostate cancer. All position statements and guidelines are based on a similar body of evidence, although some are more inclusive than others, but interpretation of the evidence and implications for practice differ, causing some confusion for doctors, and for men.

This summary provides a review of current guidelines and position statements from the major cancer organisations, urological societies and public health agencies in Australia, USA, Europe and Canada, that are most likely to be used by Australian health practitioners. The points of agreement and points of contention have been highlighted to provide some assistance with making decisions about the use of the PSA test in the early detection of prostate cancer.

Points of general agreement

- Mass population screening is not warranted based on current evidence
- The early detection of prostate cancer is complex with many factors to consider
- Informed (or shared) decision making should be supported and testing should not take place in uninformed men, if at all
- Harms as well as benefits of testing should be considered by men and their doctors
- For patients diagnosed with prostate cancer who have a low-level risk of disease progression, active surveillance is a treatment option that can ameliorate harms of over-treatment and side-effects of treatment in some men
- An individual's life expectancy should be considered in offering PSA testing to older men or those with co-morbidities; there is general agreement that less than about 10-15 years life expectancy should preclude testing
- Higher risk men (mainly those with a family history) may benefit from testing at a younger age than men at general (population) risk
- There is a need for more research on: better screening tests or tests/risk factors that will discriminate cancers leading to metastases or death; benefits and harms of early detection; and the efficacy and side-effects of treatments, including active surveillance.

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Points of contention

- The USPSTF, CTFPHC and the RACGP recommend against offering testing to any men; however, each organisation acknowledges that men asking about screening need to be informed before making a decision. Other organisations suggest offering a PSA test to (or at least discussing PSA testing with) men of varying ages (see Appendix Table)
- Among those recommending routine screening, the proposed age at commencement varies (see Appendix Table). Risk-based screening is contentious, with USANZ and EAU recommending a single PSA test from age ~ 40 years whereas ACS or AUA do not recommend due to lack of robust evidence of effectiveness. CUA mentions this approach but does not strongly recommend it.
- The statements vary with regard to both the number of studies reviewed (including which RCTs), and the interpretation of the RCT findings
- Intervals for testing and PSA level for biopsy differ across statements although there is general agreement that initial PSA results should guide the interval for subsequent testing.
- Including DRE with PSA is recommended by USANZ, RACGP and CUA but not ACS or CTFPHC due to lack of convincing evidence. EAU and AUA do not discuss this issue.

Documents included in this summary:

Australia*

- CCA & the Screening Subcommittee of the Australian Population Health Development Principal Committee of AHMAC, Position Statement, 2010
- USANZ, Policy, 2009
- RACGP, Guidelines, 2012

* CCA and Prostate Cancer Foundation of Australia (PCFA) clinical guidelines currently in development (draft available)

USA

- ACS, Guidelines, 2010
- AUA, Guidelines, 2013
- USPSTF, Recommendation Statement, 2012

Europe

- EAU, Recommendation, 2013

Canada

- CUA, Guidelines, 2011
- CTFPHC, Recommendation Statement, 2014

See summary tables pp. 4–7.

Abbreviations

ACS	American Cancer Society
AS	Active Surveillance
AUA	American Urological Association
CCA	Cancer Council Australia
CTFPHC	Canadian Task Force on Preventive Health Care
CUA	Canadian Urological Association
DRE	Digital rectal examination
EAU	European Association of Urology
ERSPC	European Randomised Study of Screening for Prostate Cancer
PCFA	Prostate Cancer Foundation of Australia
PLCO	Prostate Lung Colorectal and Ovarian Cancer Screening Trial
RACGP	Royal Australian College of General Practitioners
RCT	Randomised controlled trial
USANZ	Urological Society of Australia and New Zealand
USPSTF	United States Preventive Services Taskforce
WW	Watchful waiting

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Resources

Chapman S, Barratt A, Stockler M. Let Sleeping Dogs Lie? What men should know before getting tested for prostate cancer (Sydney University Press, 2010). http://purl.library.usyd.edu.au/sup/9781920899684

Draft clinical practice guidelines: PSA testing and early management of test-detected prostate cancer (Cancer Australia and PCFA, 2014). http://wiki.cancer.org.au/australia/Guidelines:PSA_Testing

Gardiner RA, Chambers SK, Yaxley J, et al. Prostate cancer – Part one: Detection (2014 update). In: McLachlan R (Ed), Endotext: Endocrinology of Male Reproduction. http://www.endotext.org/section/male/

PSA Testing for Prostate Cancer in Asymptomatic Men: Information for Health Practitioners (NHMRC, 2014). https://www.nhmrc.gov.au/guidelines/publications/men4

The early detection of prostate cancer in the general practice setting: supporting patient choice (Cancer Council Queensland, 2009). https://www.andrologyaustralia.org/patient-assessment-tools/

Prostate Cancer—Harms and Benefits (Canadian Task Force on Preventive Health Care (2015) http://canadiantaskforce.ca/ctfphc-guidelines/2014-prostate-cancer/harms-and-benefits/

Appendix Table: Age ranges for offering PSA testing to men of average risk*

ORGANISATION	AGE (YEARS) TO START PSA TESTING	WHEN TO STOP OR NOT OFFER PSA TESTING, BASED ON AGE AND/OR LIFE EXPECTANCY	
		Age (years)	Life expectancy (years)
CCA	Not stated	Not stated	Not stated
CUA	50	75	< 10 years
ACS	50	–	< 10 years
AUA	55	> 69	< 10–15 years
EAU	40–45 (baseline test)	~70	< 10 years
USANZ	40 (single baseline test) 55 (more frequent)	55 (single test) > 69	Not stated
CTFPHC	Recommend against screening at any age		
RACGP	Recommend against screening at any age		
USPSTF	Recommend against screening at any age		

* Note: General agreement that men with a higher risk due to family history, race or other risk factors, are likely to gain greater benefit from testing and perhaps at younger ages than those at average risk.

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Summaries of position statements and guidelines

ORGANISATION (YEAR) TITLE (INTENDED AUDIENCE)	MAIN ADVICE	OTHER BACKGROUND/DISCUSSION INCLUDED IN THE DOCUMENT	EVIDENCE USED
AUSTRALIA			
Cancer Council Australia & Screening Subcommittee of the Australian Population Health Development Principal Committee of AHMAC (2010) Position Statement: Prostate cancer screening in Australia: Key joint messages (general audience)	PSA is not a suitable test for population screening as harms outweigh benefits The risk of prostate cancer is higher if first-degree relative has prostate cancer Men and doctors need to consider harms as well as benefits, and side-effects of treatments Active surveillance (AS) is an appropriate option for some men Speak to a doctor to make informed decision.	Prostate cancer is a major health concern in Australia Early detection of prostate cancer is a complex issue.	3 references ERSPC (2009), PLCO (2009), US Preventive Services Task Force (2002)
Urological Society of Australia and New Zealand (USANZ) (2009) PSA Testing Policy (for urologists and other health professionals)	Population screening not supported by evidence However, based on ERSPC study (2009), men aged 55-69 should be offered PSA and DRE after providing information on risks and benefits Men <55 years of age (and over 40) could have a single PSA/DRE to estimate 10-20 year risk and intensity of subsequent testing adjusted according to PSA level (a stronger recommendation to test men in their 40s in 2011 media release) After a single PSA test in the 40s, recommend that those with PSA above age-specific median are carefully monitored and considered for biopsy – include other factors family history, ethnicity, DRE, PSA velocity, PSA derivatives; PSA below the median indicates low risk and should be monitored less frequently AS should be discussed with selected patients to reduce over-treatment and side-effects.	Younger men are less likely to be diagnosed with prostate cancer but if diagnosed more likely to die USANZ supports research into novel diagnostic markers and AS protocols to enhance AS safety Men aged 70 and over not mentioned.	14 references Reviewed 2 RCTs – ERSPC, PLCO – and 1 non-randomised study (Tyrol, 2008) for mortality reduction Reviewed evidence to support doing DRE with PSA Observational studies cited to support testing men in 40s to indicate future risk of cancer and monitoring frequency (exact frequency not specified) Reviewed AS studies – most short follow-up but suggest careful selection of patients needed for AS

ORGANISATION (YEAR) TITLE (INTENDED AUDIENCE)	MAIN ADVICE	OTHER BACKGROUND/DISCUSSION INCLUDED IN THE DOCUMENT	EVIDENCE USED
Royal Australian College of GPs (RACGP) (2012) Guidelines for Preventive Activities in General Practice (Red Book) 8th Edition (for GPs)	Routine screening with DRE, PSA or trans-abdominal ultrasound not recommended GPs recommended to not raise the issue but if men ask they need to be fully informed of potential benefits, risks and uncertainties of testing If patient chooses screening, both PSA and DRE should be done Decision aids may be useful for discussions with patients who ask about testing.	Refers to "Let Sleeping Dogs Lie" as a source of balanced information for patients.	19 references Recommendation based on USPSTF statement, American College of Preventive Medicine and Cochrane review.
USA			
American Cancer Society (ACS) (2010) Guideline for the early detection of prostate cancer: update 2010 (primarily for healthcare providers but not specified)	Population screening not recommended If a man's life expectancy less than 10 years, do not offer testing If life expectancy 10 or more years, offer the opportunity for testing from age 50 years (average risk) but only if decision informed Encourage use of decision aids by health professional with men to ensure informed decision If man at higher risk (positive family history) offer opportunity for testing earlier (45+ years or 40 years if very high risk) Frequency of testing based on PSA level: 2.5ng/mL or higher – annually; less than 2.5 ng/mL – 2-yearly 4.0 ng/mL is the general cut-off for further evaluation but at 2.5 - 4.0 ng/mL it may also be indicated based on other risk factors (tools are provided for individualised risk assessment) DRE could be included with PSA but evidence for benefit not clear.	PSA testing may lead to a lower risk of dying from prostate cancer but evidence conflicting regarding the value of screening Currently unable to distinguish men who will benefit from treatment Biopsy and treatment side-effects can be serious and false positive tests can lead to anxiety Men not having immediate treatment still need biopsies with associated risks.	154 references Systematic reviews of evidence: Evidence for impact of screening – PLCO and ERSPC (2009); case-control studies; mortality and incidence trends. Evidence of harms including over-diagnosis and over-treatment, biopsy risks, risks of treatment; harms of AS/WW. Test performance at different PSA thresholds, PSA velocity, effect of adding DRE to PSA

ORGANISATION (YEAR) TITLE (INTENDED AUDIENCE)	MAIN ADVICE	OTHER BACKGROUND/DISCUSSION INCLUDED IN THE DOCUMENT	EVIDENCE USED
American Urological Association (AUA) (2013) AUA Guideline: Early detection of prostate cancer (for urologists and other health professionals)	Do not screen men under 40 years of age No routine screening in average risk men 40-54 years of age For men at higher risk – individualised decisions in men under 55 55-69 years: greatest benefit in this age band – recommend shared decision-making No routine screening in men over 70 years (except some in excellent health) or less than 10 to 15 years life expectancy Screening every two years rather than annually, or rescreening interval based on initial PSA, may maintain the benefit and reduce harms.	Noted that guidance does not include use of secondary tests such as PSA isoforms, PCA3, imaging Shared decision making emphasised throughout Recognise the limitations of current literature to inform men about the benefits/ harms for prostate cancer screening and the need for further research.	112 references Statements accompanied by strength of evidence grading Systematic review by multidisciplinary panel addressing similar questions to ACS (above) Age ranges based on RCT evidence for average risk men 6 RCTs (Stockholm, Norrkoping, Quebec, ERSPC, Goteborg, PLCO) and published meta-analyses reviewed.
United States Preventive Services Task Force (USPSTF) (2012) Recommendation Statement: Screening for prostate cancer (mainly for health care providers plus 1-page summary for men) Ann Intern Med 2012;157:120-134	Recommends against PSA-based screening for prostate cancer at any age as harms outweigh benefits in the screened population However, recognise that some men will request screening and some doctors will offer screening despite recommendation; this decision needs to be informed Physicians should not offer PSA unless willing to engage in shared decision-making; discuss with man benefits and harms Discontinue community and employer-based PSA screening Focusing screening on higher risk men may improve benefit/ harm ratio but existing studies can't answer this question Harms could be reduced by longer screening interval, increased PSA threshold for biopsy, increasing AS/WW, use of periodic DRE. but more research needed for optimal approach Recommendation not applicable to PSA tests after a cancer diagnosis; recommendation may change with new studies.	Studies show number of men benefiting from early detection and treatment is likely very small (small prostate cancer mortality and no all-cause mortality benefit shown) - only 0 to 1 prostate cancer death for every 1000 men screened Good evidence that PSA screening can cause harms including complications of biopsies and worry about test results; and side effects of treatments that may have been unnecessary Applies to men of ALL ages More research needed on: cause of death for validity of prostate cancer mortality outcome measure; use of 5 alpha reductase inhibitors for prevention – possible increase in high-grade cancer; patient/provider knowledge, values, informed decision tools.	63 references plus supporting documents containing evidence review Review of benefits of early detection and treatment used only mortality (PLCO and ERSPC trials ranked fair quality - others poor quality); insufficient evidence for other outcomes. Updated results from ERSPC and PLCO included even though they came after the systematic review (median 11-yr follow-up in ERSPC). Review of harms covered the following: harms from test itself (psychological), biopsies, over-diagnosis, treatment side-effects.

ORGANISATION (YEAR) TITLE (INTENDED AUDIENCE)	MAIN ADVICE	OTHER BACKGROUND/DISCUSSION INCLUDED IN THE DOCUMENT	EVIDENCE USED
EUROPE			
European Association of Urology (EAU) (2013) EAU Recommendation: Early detection of prostate cancer (for urologists and other health professionals) European Urology 2013;64:347-354	Do not recommend population screening but strong recommendation of testing in well-informed men Baseline PSA at 40-45 years of age and subsequent screening interval according to PSA level Screening of men with life expectancy of 10 years or more recommended independent of chronological age; screening in men older than 70 years may not be cost-effective; consider co-morbidities in assessing life expectancy Risks of over-diagnosis/over-treatment ameliorated by stratification of men by risk of future clinically apparent prostate cancer (need more data for this) and informing men about AS approaches to treatment Intervals for testing men aged 45-59 years: 2-4 yearly if PSA > 1.0 ng/mL up to 8-yearly for 1 ng/mL or lower.	Comparison with AUA guidelines noting that EAU making different recommendations Conclude that evidence shows early detection of prostate cancer reduces prostate cancer mortality and incidence of advanced and metastatic prostate cancer Multivariable clinical risk-prediction tools needed and new serum or urinary biomarkers or genetic markers might be used to improve risk prediction in the future.	47 references Authors state that they used "EBM principles" but not shown in the publication Reviewed 5 RCTS for mortality: ERSPC (2012) & Goteborg (2010) showed reduced mortality and form the basis of the statement Goteborg study used for other outcomes also Reviewed observational studies for risk-based testing in younger men; and data from ERSPC and Malmo Preventive Project for screening intervals in younger men.

ORGANISATION (YEAR) TITLE (INTENDED AUDIENCE)	MAIN ADVICE	OTHER BACKGROUND/DISCUSSION INCLUDED IN THE DOCUMENT	EVIDENCE USED
CANADA			
Canadian Task Force on Preventive Health Care (2014) Recommendations on screening for prostate cancer with the prostate-specific antigen test (mainly for healthcare providers with online support for men) CMAJ 2014;186:1225-1234	Recommend not screening for prostate cancer with the PSA test for men aged <55, 55-69 and 70+ years Recommendations only apply to screening not following diagnosis Small and uncertain potential reduction in prostate cancer mortality for men aged 55-69 years outweighed by risks of false positives, unnecessary biopsies, overdiagnosis and overtreatment Discussion with men in 55-69 year age group useful as some may place greater value on small reduction in mortality than the risks Task Force recognises that men may be interested in screening. Informed decision-making facilitated by online decision aids/tools – www.canadiantaskforce.ca No evidence that DRE adds value to PSA test	Based on evidence of risks from screening outweighing benefits Patients values and preferences important to consider Clinicians may wish to discuss benefits and harms of screening with men at increased risk Future research on: alternatives to PSA test; MRI and clinical decision tools as means to improving risk/benefit ratio; identifying men with clinically relevant disease; altering PSA thresholds; AS to improve risk/benefit ratio; RCT in high risk groups	68 references Systematic review of all available evidence To assess benefits of screening, 6 RCTs identified but 3 excluded due to bias (none of these showed benefit) ERSPC results given more weight in recommendation than PLCO to assess benefit due to high rates of opportunistic screening in PLCO RCTs and observational studies used to assess harms of screening and benefits and harms of treatment
Canadian Urological Association (CUA) (2011) Prostate cancer screening: Canadian guidelines 2011 (for urologists & other health professionals) CUAJ 2011;5:235-240	Do not recommend population screening Offer screening to all men 50 years of age with at least 10 years life expectancy; initial test PSA and DRE Probably discontinue screening after age 75 years Men must be fully informed of benefits and harms Higher risk men should be offered screening at 40 years Screening interval not clear –has been annually but studies suggest 2-4 years may be more beneficial It may be beneficial to offer a baseline PSA at 40 years for risk-based screening Base decisions about biopsy on more than one PSA test There is no PSA cut-off level for all men – continuous risk increases; also take other factors into account AS a reasonable option for men with favourable risk, screen-detected prostate cancer.	Authors noted these are guidelines to facilitate discussion with patients, not a standard of care for all patients; should not over-ride clinical judgement DRE and PSA first-line prostate cancer screening tests PSA velocity and density, free to total PSA ratio, PCA3 discussed but not recommended yet Evidence for testing in men 40 years not robust and risk of further testing and therapy with this approach Await results from the "START" trial for better evidence on benefits/risks of AS	68 references Systematic literature search ERSCP and PLCO (2009) and Goteborg (2010) reviewed as Level 1 evidence for mortality benefit from screening