Canadian Urological Association

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Association des Urologues du Canada La voix de l'urologie au Canada

PSA Screening

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By the end of this presentation, participants will:

- gain insight into the rationale for prostate cancer screening
- review the current recommendations for the management of elevated PSA



Prostate Cancer Screening: When, Why and How

CUA GUIDELINE

Canadian Urological Association recommendations on prostate cancer screening and early diagnosis

Ricardo A. Rendon, MD¹; Ross J. Mason, MD²; Karim Marzouk, MD³; Antonio Finelli, MD⁴; Fred Saad, MD⁵; Alan So, MD⁶; Philippe D. Violette, MD^{7,8}; Rodney H. Breau, MD⁹



The Main Problem:

- High prevalence
- High biologic variability
- Over detection
- Overtreatment
- Morbidity associated with PSA testing
 - Diagnosis
 - Treatment



U.S. PLCO (Prostate, Lung, Colorectal, and Ovarian) Cancer Screening Trial

- 76,685 men aged 55-74 years
- annual screening for 6 years or "usual care"
- median f/u of 13 years by 2009
- The cumulative incidence rate for PCa was slightly higher in the screened group with no difference in PCa mortality



ERSPC (European Randomized Study of Screening for Prostate Cancer)

- 162 243 men aged 55 to 69 years
- PSA screening once q1-4 years or an unscreened control group
- Median f/u 11 years
- The cumulative incidence of PCa was 8.2% in the screened group vs 4.8%
- PCa death was reduced by 21% and 29% after adjustment for noncompliance
- 9 years (NNS 1410, NND 48)



Canadian Task Force on Preventive Health Care

CTEPHC Evidence Evidence Evidence

Putting Prevention into Practice

Canadian Task Force on Preventive Health Care Groupe d'étude canadien sur les soins de santé préventifs



Summary of the recommendations for clinicians and policy makers

For men aged 55-69 years, we recommend <u>not screening</u> for prostate cancer with the PSA test.

(Weak recommendation; moderate quality evidence)

Implies that: Harms of screening and subsequent testing/treatment probably outweigh benefits, but uncertainty exists

Basis of the recommendation

- small and uncertain potential reduction in the risk of PCa mortality
- risk of false positive results, unnecessary biopsy and overdiagnosis, and harms of unnecessary treatment



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- median f/u of 13 years by 2009
- The cumulative incidence rate for PCa was slightly higher in the screened group with no difference in PCa mortality
- More men in the control arm had PSAs
- Younger men benefited from PSA screening



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- 11 years (NNS 979, NND 35)
- 13 years (NNS 781, NND 27)
- 16 years (NNS 570, NND 18)



Prostate Cancer Screening Meta-analysis

- 8 trials
- Findings:
 - Increased PCa detection
 - Stage migration (lower stage)
- When excluded trials with:
 - High PSA-contamination at baseline (> 33.3%)
 - Short follow-up (< 8 years)

\rightarrow 24% reduction in PCa mortality





- The decision to screen for PCa should be an individual one
- The USPSTF recommends that clinicians inform men ages 55 to 69 years about the potential benefits and harms of PSA-based screening for PCa
- Screening offers a small potential benefit of reducing the chance of dying of PCa
- Potential harms:
 - False-positive results \rightarrow additional workup
 - Overdiagnosis
 - Overtreatment
 - Treatment complications

C Recommendation



Men age 70 and older



- The USPSTF recommends against PSA-based screening for prostate cancer in men age 70 years and older
- D Recommendation



Screening Principles

- Many men with PCa can be followed by AS
- A diagnosis of PCa is information used to help make decisions ...not an indication for immediate treatment
- There is a balance between the harms and benefits of screening
 - Focus on men at the highest risk for life-threatening PCa
 - Younger, Family history, African descent
- Screening applies to men expected to live at least 10 years



PSA Reflects Risk Continuously





PSA Provides a Spectrum of Risk

Prostate Cancer Prevention Trial- empiric biopsies at PSA<4

PSA	% Prostate Cancer Detection	High Grade Ca
≤0.5	6.6%	12.5%
0.6-1.0	10.1%	
1.1-2.0	17%	
2.1-3.0	23.9%	25%
3.1-4.0	26.9%	

No PSA below which cancer can be definitively excluded



Serum PSA % Probability of cancer 4.0–10.0 17-32 ng/mL 43-67



As a reference, age-specific, median PSA values are:

0.7 ng/mL 0.9 ng/mL 1.2 ng/mL 1.5 ng/mL

A baseline PSA level I median for age is a stronger predictor of future risk of prostate cancer than family history or race

PSA at age 60 has a strong association with the risk of death from prostate cancer by age 85 (AUC 0.90) with extremely low risk (\leq 0.2%) in men with PSA below the median (\leq 1.2 µg/L).





- PSA is the best single test for early PCa detection
- DRE can also identify men with the disease
- Combining PSA & DRE improves overall rate of PCa detection when compared to either test alone 🗆 3 uncontrolled studies
- TRUS adds no additional information to the combination of PSA & DRE as screening tests



CUA GUIDELINES



Canadian Urological Association Recommendations on Prostate Cancer Screening and Early Diagnosis

Ricardo A. Rendon; Ross J. Mason; Karim Marzouk; Antonio Finelli; Fred Saad; Alan So; Rodney H. Breau

> Originally published in *Can Urol Assoc J* 2017;11(10):298-309. http://dx.doi.org/10.5489/cuaj.4888



PSA Screening:



PSA screening

The CUA recommends **offering** PSA screening to men with a life expectancy greater than 10 years. The decision of whether or not to pursue PSA screening should be based on **shared decision-making** after the potential benefits and harms associated with screening have been discussed.





Age to begin screening

For men electing to undergo PSA screening:

Begin PSA testing at age 50 in most men

OR

• Age 45 in men at an increased risk of prostate cancer



For men electing to undergo PSA screening, the **intervals between testing should be individualized** based on previous PSA levels.



Frequency of screening

For men with PSA <1 ng/ml, repeat PSA testing every 4 years

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Frequency of screening

- For men with **PSA <1 ng/ml**, repeat PSA testing every 4 years
- For men with **PSA 1–3 ng/ml**, repeat PSA testing every 2 years
- For men with PSA >3 ng/ml, consider more frequent PSA testing intervals or adjunctive testing strategies



When to discontinue screening

- For men aged 60 with a PSA <1 ng/ml, consider discontinuing PSA screening
- For all other men, discontinue PSA screening at age 70
- For men with a life expectancy less than 10 years, discontinue PSA screening





Adjunctive tests

- Multiparametric MRI
- PSA kinetics
- PSA density
- Free-to-total PSA
- 4K/PHI/PCA3
- Prostate cancer risk calculators



Adjunct strategies for PCa early diagnosis:



Multiparametric MRI – CCO recommendation

In patients with an elevated risk of clinically significant prostate cancer (according to PSA levels and/or nomograms) who are **biopsy-naive**, mpMRI followed by targeted biopsy (biopsy directed at cancer-suspicious foci detected with mpMRI) should **not be considered the standard of care**.





Multiparametric Magnetic Resonance Imaging in the Diagnosis of Clinically Significant Prostate Cancer

M.A. Haider, J. Brown, J. Chin, A. Loblaw, N. Perlis, N. Schieda, and the MPMRI in the Diagnosis of Clinically Significant Prostate Cancer Guideline Development Group

Report Date: February 11, 2021

Recommendation 1 (Recommendation to use the diagnostic tool)

For biopsy-naïve patients at elevated risk of CSPCa:

- MPMRI is recommended prior to biopsy in patients who are candidates for curative management with suspected clinically localized prostate cancer.
 - <u>If the MPMRI is positive</u>, MPMRI-TB and TRUS-SB should be performed together to maximize detection of CSPCa.
 - If the MPMRI is negative, consider forgoing any biopsy after discussion of the risks and benefits with the patient as part of shared decision making and ongoing follow-up.



Multiparametric MRI – CCO recommendation

In men who had a prior negative TRUS-guided systematic biopsy who demonstrate an increasing risk of having clinically significant prostate cancer since prior biopsy (e.g., continued rise in PSA and/or change in findings from digital rectal examination), mpMRI followed by targeted biopsy may be considered to help in detecting more clinically significant prostate cancer patients compared with repeated TRUS-guided systematic biopsy.





PSA velocity

The CUA does not recommend using PSAV alone for clinical decision making in men undergoing routine screening. However, **PSAV can provide additional information** about a patient's risk of prostate cancer.

PSA density

The use of PSAD alone for clinical decision-making is discouraged. However, use PSAD can be considered in men with known prostate volumes.



Biomarkers and PSA isoforms:

- Currently available biomarkers (4K score, the Prostate Health Index, and the PCA3 score) can be offered to interested men as secondary tests to further estimate the risk of harboring clinically significant prostate cancer
- Routine use in all men with suspected prostate cancer is not currently recommended

(Level of evidence: 2a, Grade of recommendation: B)



Prostate Risk Calculators

- Several prostate cancer risk calculators exist to aid in the prebiopsy risk stratification of men with an elevated PSA
- The most widely utilized calculators include the PCPT calculator and the ERSPC calculator
- Moderate discriminatory ability for predicting clinically significant PCa compared with PSA alone



Characteristics

Race

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3.8

Family History of Prostate Cancer

No

Digital rectal examination

Normal

Prior biopsy

Never had a prior biopsy

Percent free PSA available?

Percent free PSA

10

PCA3 available?

T2:ERG available?



Based on the provided risk factors a prostate biopsy performed would have a:



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2% chance of high-grade prostate cancer,





46% chance that the biopsy is negative for cancer.

About 2 to 4% of men undergoing biopsy will have an infection that may require hospitalization.

Please consult your physician concerning these results.

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If you are Caucasian, click here for a new update to the PCPTRC that incorporates detailed family history into a risk of prostate cancer calculation.

If you are Caucasian, click here for a research calculator that allows the incorporation of up to five single-nucleotide polymorphisms (SNP).



ERSPC Risk Calculator App

- Available for PDAs
- Inputs: PSA, DRE, prior biopsy, prostate volume if available, Prostate Health Index (phi)
- Output: risk of detectable and significant prostate cancer on biopsy





ERSPC Risk Calculator A

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Risk Calculator 🔿				
Prostate volu	40			
Outcome of T	Normal			
Phi available?	Yes			
How much is your Phi?				
	56	í		
🛞 Clear	[Done 🧭		
1	2 ABC	3 DEF		
4 GHI	5 JKL	6 ^{MNO}		
7 PQRS	8 TUV	9 wxyz		
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Smarter Screening: Appropriate Patient Selection

- 36% of men ages ≥ 85 years in worst health had PSA test (unlikely to benefit)
- Careful selection of men with long life expectancy is critical for screening and treatment





The CUA Prostate Cancer Screening Pathway



The age at which to discontinue PSA screening should be based on current PSA level and life expectancy.

- For men aged 60 with a PSA <1 ng/ml, consider discontinuing PSA screening (LoE, 2; GoR, C).
- For all other men, discontinue PSA screening at age 70 (LoE, 2; GoR, C).
- For men with a life expectancy <10 years, discontinue PSA screening (LoE, 4; GoR, C).

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