

Canadian **U**rological Association
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Association des **U**rologues du Canada
La voix de l'urologie au *Canada*

PSA Screening

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Speaker Disclosures | Ricardo Rendon

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Disclosure of Financial Support

Potential for conflict(s) of interest:

- Members of the SPC committee (Alan Bell, Peter Lin, and Arthur Kushner) received honorarium from the Canadian Urological Association.
- Ricardo Rendon received honorarium from the Canadian Urological Association at the start of the program.



Mitigating Potential Bias

The scientific planning committee of this program have complete control over the content of this program.

There has been no influence from the sponsors on the content.



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Learning Objectives

Upon completion of this program, participants will be able to:

- examine the rationale for prostate cancer screening
- interpret the current recommendations for the management of elevated PSA



Prostate Cancer Screening: When, Why and How?



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 (Numbers Needed to Screen 1410, Numbers Needed to Diagnose 48)



Screening for prostate cancer with the prostate specific antigen (PSA) test: Recommendations 2014

Canadian Task Force on Preventive Health Care

July 2014

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 not screening for prostate cancer with the PSA test.

(Weak recommendation; moderate quality evidence)

Basis of the recommendation

- The CTFPHC placed a relatively low value on a small and uncertain potential reduction in the risk of PCa mortality and a relatively higher value on the risk of false positive results, unnecessary biopsy and overdiagnosis, and harms of unnecessary treatment.
- The weak recommendation against screening implies that the harms of screening and subsequent testing/treatment probably outweigh benefits, but uncertainty exists.

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- 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
- **More men in the control arm had PSAs**
- **Younger men benefited from PSA screening**



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- 9 years (NNS 1410, NND 48)
- **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)
- 24% reduction in PCa mortality**



Men ages 55–69

- 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 → additional workup
 - Overdiagnosis
 - Overtreatment
 - Treatment complications
- **C Recommendation**

Men age 70 and older

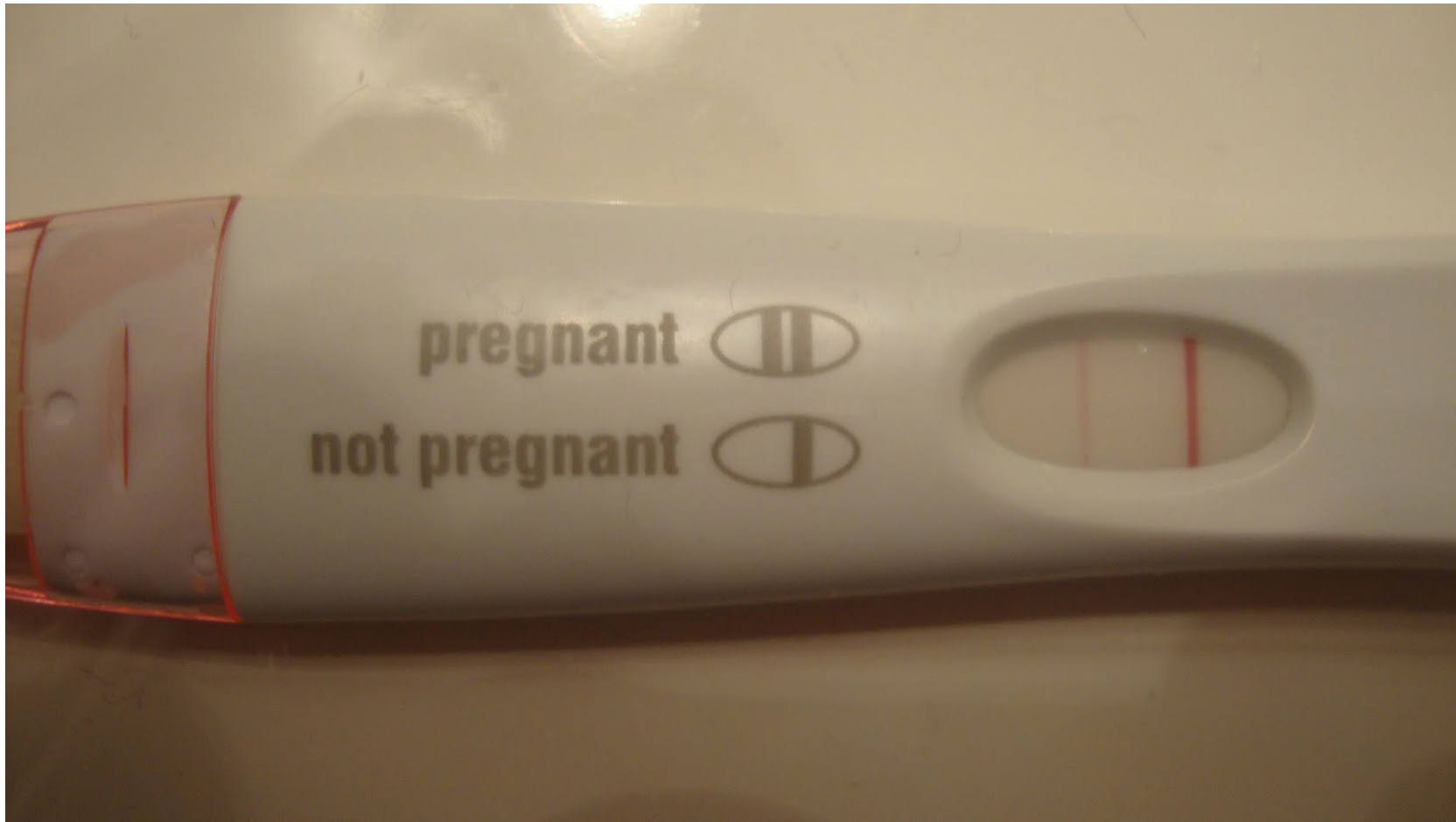
- The USPSTF recommends against PSA-based screening for prostate cancer in men age 70 years and older
- **D Recommendation**

Screening Principles

- Most men with low risk PCa will be followed by active surveillance
- 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 ng/mL

17-32

>10.0 ng/mL

43-67

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

40-49	0.7 ng/mL
50-59	0.9 ng/mL
60-69	1.2 ng/mL
70-79	1.5 ng/mL

A baseline PSA level \uparrow 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 ($\leq 1.2 \mu\text{g/L}$)

DRE

- 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



Canadian Urological Association Update – 2022 Recommendations on Prostate Cancer Screening and Early Diagnosis

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

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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



Frequency of screening

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

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



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- 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 with a **life expectancy less than 10 years**, discontinue PSA screening
- For all other men, discontinue PSA screening at **age 70-75**
- For men aged 60 with a PSA <1 ng/ml, **consider** discontinuing PSA screening



Adjunctive tests

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



Multiparametric MRI – *Endorsement of 2021 CCO recommendations*

For biopsy-naive patients at elevated risk of clinically significant (cs) PCa, mpMRI is recommended prior to biopsy

- If the mpMRI is positive:
mpMRI-targeted biopsy and TRUS-guided systematic biopsy
- If the mpMRI is negative:
consider forgoing any biopsy



Multiparametric MRI –

Endorsement of 2021 CCO recommendations

Prior negative TRUS-guided systematic biopsy and high risk of csPCa:

- mpMRI should be performed
- mpMRI is positive:
 - targeted biopsy - Concomitant TRUS-SB can be considered
- mpMRI is negative:
 - consider forgoing a TRUS-SB



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 PCa risk calculators exist to aid in the pre-biopsy 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

Caucasian

Age

55

PSA [ng/ml]

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?


Risk of prostate cancer if biopsy were to be performed

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

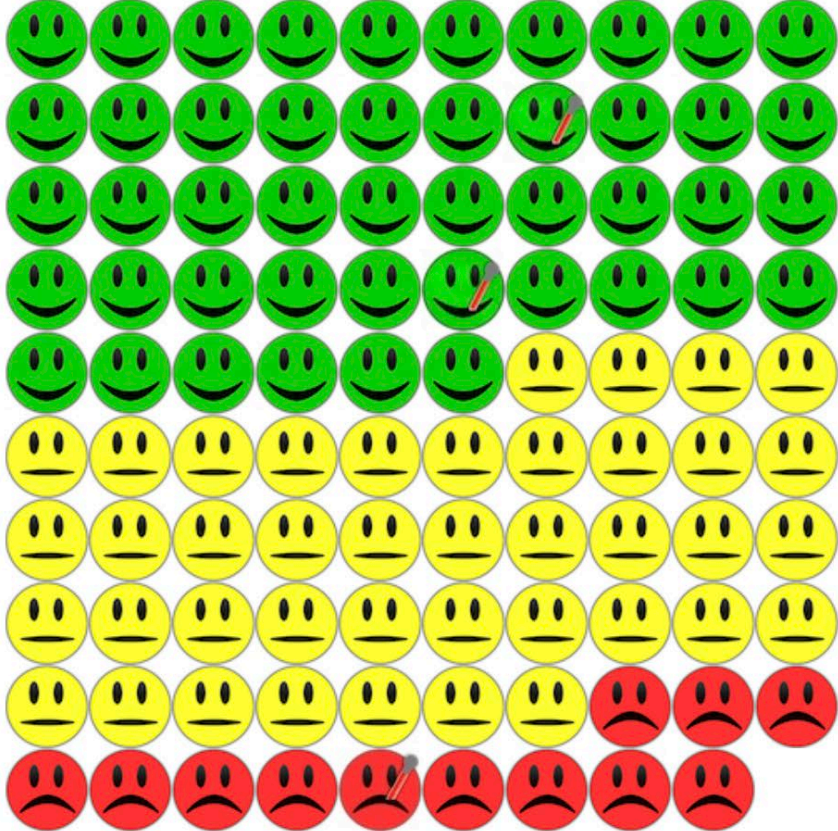
 12% chance of high-grade prostate cancer,

 41% chance of low-grade 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.



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).

Smarter Screening: Appropriate Patient Selection

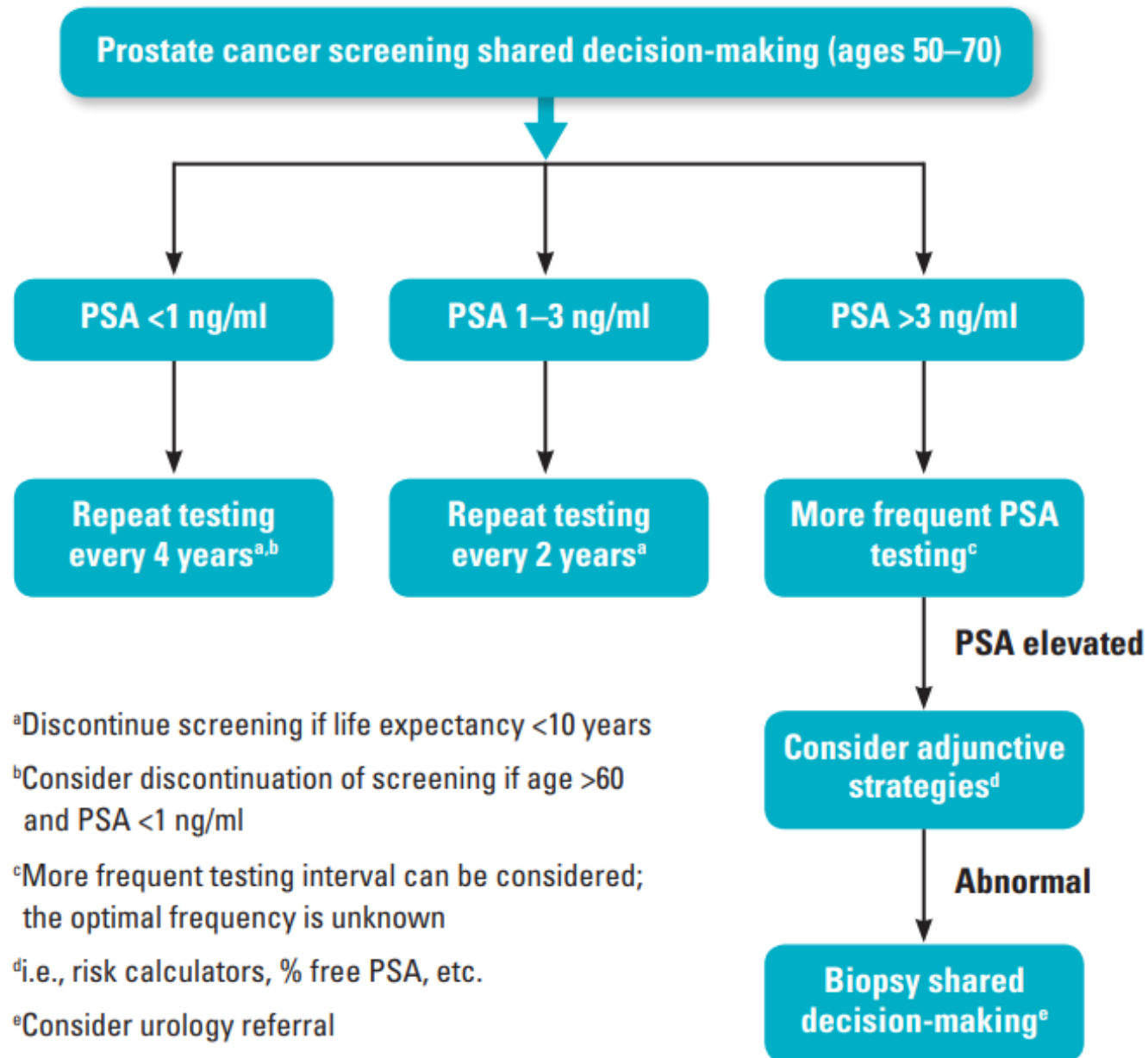
- 36% of men ages ≥ 85 years in worst health had PSA test (unlikely to benefit)
- Careful selection of men with long life expectancy is critical for screening and treatment

Walter et al. JAMA 2006; 296: 2336

Hugosson et al. Lancet Oncol 2010; 11: 725



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).

QUESTIONS?

