Screening for Prostate Cancer with the Prostate Specific Antigen (PSA) Test: Recommendations 2014

Canadian Task Force on Preventive Health Care

October 2014

Putting Prevention into Practice

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

CTFPHC Prostate Cancer Screening
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Background

- Prostate cancer is the most commonly diagnosed non-skin cancer among Canadian men.
- Long term survival with prostate cancer is now >90% in Canada.
- 1 in 7 men will be detected as having prostate cancer (at current levels of screening).
- The PSA test was introduced in Canada in 1986, but its use for screening did not become widespread until 1996.

Global Rates of Prostate Cancer Mortality

- 25 fold variation in prostate cancer mortality worldwide.
- Early reduction in prostate cancer mortality is probably due to improvements in treatment with surgery, radiation and hormone therapy.

- For example, in the UK:
  - Low rates of screening but reduction in mortality rates for prostate cancer are still seen[‡].

[‡]Melissa Center, Ahmedin Jemal, Joanne Loret-Tieulent, Elizabeth Ward, Jacques Ferlay, Otis Brawley, Freddie Bray. International variation in prostate cancer incidence and mortality rates. Eur Urol 2012;61:1079-92.

Objectives of the 2014 Guideline

- To update the 1994 guideline by the CTFPHC on screening for prostate cancer.
- To review the latest evidence on the benefits and harms of screening for prostate cancer with PSA.
- To provide recommendations on screening for prostate cancer using PSA with or without digital rectal examination (DRE) for men in the general population.

Screening for Prostate Cancer with PSA

METHODS

Methods of the CTFPHC

- Independent panel of:
  - clinicians and methodologists
  - expertise in prevention, primary care, literature synthesis, and critical appraisal
  - application of evidence to practice and policy

- Prostate Cancer Screening Working Group
  - 6 Task Force members
  - establish research questions and analytical framework

Methods of the CTFPHC (continued)

- Evidence Review and Synthesis Centre (ERSC)
  - Undertakes a systematic review of the literature based on the analytical framework
  - Prepares a systematic review of the evidence with GRADE tables
  - Participates in working group and task force meetings
  - Obtain expert opinions (i.e. urologist)

CTFPHC Review Process

- Internal review process involving guideline working group, Task Force, scientific officers and ERSC staff
- External review process involving key stakeholders
  - Generalist and disease specific stakeholders
  - Federal and P/T stakeholders
- CMAJ undertakes an independent peer review journal process to review guidelines

External Reviewers for Prostate Cancer

Disease Specific Stakeholders

- Canadian Urological Association (4 reviewers)
- Prostate Cancer Canada (2 reviewers)
- Canadian Cancer Society (1 reviewer)

Generalist Organizations

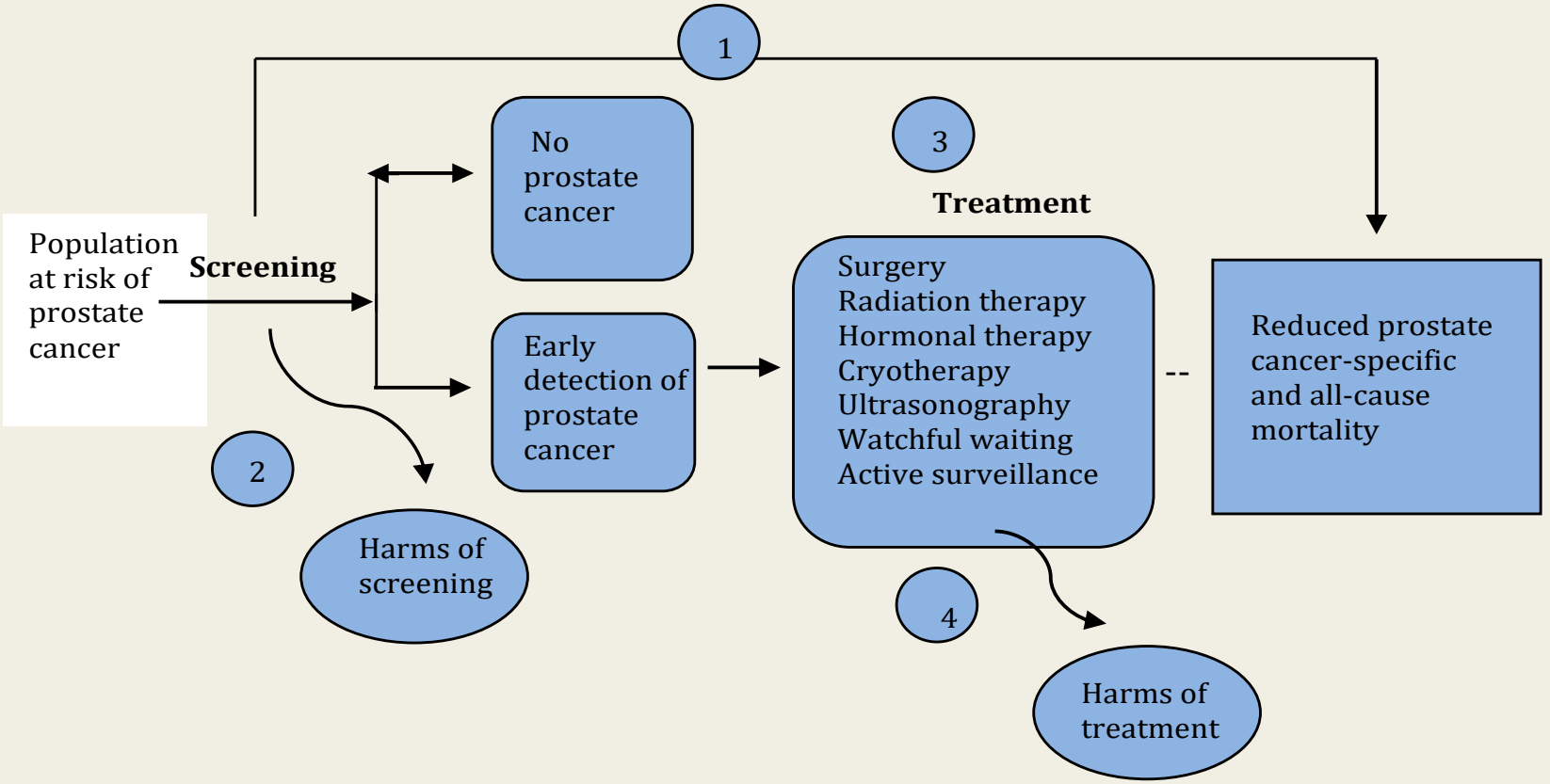
- College of Family Physicians of Canada (1 reviewer)

Federal and P/T Stakeholders

- Public Health Agency of Canada (2 reviewers)
- Health Canada (1 reviewer)
- Canadian Institutes of Health Research (1 reviewer)
- Council of Chief Medical Officers of Health (1 reviewer)

Anonymous reviewers from CMAJ (5)

Analytical Framework



Key Research Questions

KQ1a. What is the direct evidence that screening for prostate cancer with prostate-specific antigen (PSA), as a single-threshold test or as a function of multiple tests over time, decreases morbidity and/or prostate cancer-specific and all-cause mortality?

KQ1b. Is there evidence to support differential screening based on individual risk factors for prostate cancer such as age, black race/ethnicity, family history of prostate cancer or previously assessed increased PSA values – either absolute values or increased PSA measures over time?

KQ2. What are the harms of PSA-based screening for prostate cancer?

Key Research Questions (continued)

KQ3. What are the benefits of treatment of early-stage or screen-detected prostate cancer?

KQ4. Is there evidence that tailoring the method of following up abnormal screening results to patient characteristics lead to clinically important differences in the harms and benefits of screening with PSA?

KQ5. What are the harms of treatment of early-stage or screen-detected prostate cancer?

Contextual Questions

Stage one: Assist in making a decision about the direction of the recommendation:

1. What are the patient values and preferences for PSA screening for prostate cancer?

Stage 2: If evidence is sufficient to recommend screening:

1. What process and outcome performance measures or indicators have been identified in the literature to measure and monitor the impact of PSA screening for prostate cancer?

Contextual Questions (continued)

Stage 2: If evidence is sufficient to recommend screening:

2. What is the optimal screening interval for PSA screening for prostate cancer and should this interval vary based on risk level (e.g., age, prior PSA levels, or other measures such as Gleason score)?

3. What are the most effective (accurate and reliable) risk assessment tools to identify: a) risk of prostate cancer and b) risk of poor outcomes after PSA testing and biopsy?

4. What is the cost-effectiveness of PSA screening for asymptomatic adults for prostate cancer? Costs to the system and to patients will be included if found.

Eligible Study Types

Population: This recommendation applies to men in the general population. This includes men with lower urinary tract symptoms (nocturia, urgency, frequency and poor stream) or with benign prostatic hyperplasia (BPH).

- **Effectiveness of screening on preselected outcomes*:***
  - Systematic reviews, randomized controlled trials
- **Harms of screening:**
  - Studies of any design
- **Contextual questions:**
  - Studies of any design

How is Evidence Graded?

The "**GRADE**" System:

- **G**rading of **R**ecommendations, **A**ssessment, **D**evelopment & **E**valuation

What are we grading?

- **1. Quality of Evidence**
  - confidence or certainty in estimate of effects
  - high, moderate, low, very low
- **2. Strength of Recommendation**
  - strong and weak

1. How is the Quality of Evidence Determined?

The quality of the evidence is graded as:

- **High** confidence that the true effect lies close to the estimate of effect
- **Moderate** confidence that the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
- **Low** confidence that the true effect is close to the estimate of the effect. The true effect may be substantially different from the estimate of the effect
- **Very Low** – Any estimate of effect is very uncertain

1. How is the Quality of Evidence Determined? (continued)

- RCT Studies - start as high quality evidence
- Observational Studies – start as low quality evidence
- Both can be downgraded or upgraded based on various study characteristics

2. How is the Strength of Recommendations Determined?

The strength of the recommendations (strong or weak) are based on four factors:

- **Quality** of supporting evidence
- Certainty about the **balance between desirable and undesirable** effects
- Certainty / variability in **values and preferences** of individuals
- Certainty about whether the intervention represents a **wise use of resources**

Interpretations of the Recommendations

Implications	Strong Recommendation	Weak Recommendations
For patients	• Most individuals would want the recommended course of action; • only a small proportion would not.	• The majority of individuals in this situation would want the suggested course of action but many would not.
For clinicians	• Most individuals should receive the intervention.	• Recognize that different choices will be appropriate for individual patients; • Clinicians must help patients make management decisions consistent with values and preferences.
For policy makers	• The recommendation can be adapted as policy in most situations.	• Policy making will require substantial debate and involvement of various stakeholders.

Screening for Prostate Cancer with PSA

RECOMMENDATIONS

Summary of the Recommendations

Clinicians and Policy Makers

For men aged less than 55 years of age, we recommend <u>not screening</u> for prostate cancer with the prostate-specific antigen test.
(Strong recommendation; low quality evidence)

Basis of the recommendation

- The CTFPHC based this recommendation on the low incidence of prostate cancer and prostate cancer mortality, and the lack of evidence for benefit of screening in this age group, as well as the evidence of harms.
- The strong recommendation implies that the CTFPHC is confident the harms of screening and subsequent testing/treatment outweigh the benefits.

Summary of the Recommendations
Clinicians and Policy Makers

For men aged 55-69 years, we recommend not screening for prostate cancer with the prostate specific antigen 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 prostate cancer mortality and a relatively higher value on the risk of harms associated with diagnosis and treatment due to false positive results and overdiagnosis.
- The weak recommendation against screening implies that the harms of screening and subsequent testing/treatment probably outweigh benefits, but uncertainty exists.

Summary of the Recommendations

Clinicians and Policy Makers

For men aged 70 years and older, we recommend <u>not screening</u> for prostate cancer with the prostate-specific antigen test.
(Strong recommendation; low quality evidence)

Basis of the recommendation

- The CTFPHC based this recommendation on the lower life expectancy and the lack of evidence for benefits of screening in this age group, as well as the evidence of harms.
- The strong recommendation implies that the CTFPHC is confident the harms of screening and subsequent testing/treatment outweigh the benefits.

Summary of the Recommendations

Clinicians and Policy Makers

- These recommendations apply to all men who have not been previously diagnosed with prostate cancer.
- This includes men with lower urinary tract symptoms (nocturia, urgency, frequency and poor stream) or with benign prostatic hyperplasia (BPH).
- These recommendations do not apply to the use of the PSA test for surveillance after diagnosis or treatment for prostate cancer.

Findings: Benefits of Screening with PSA

Moderate Quality of Evidence

The evidence review identified 6 RCTs of varying quality:

- Of these 6 trials, 3 had a low risk of bias (RoB).
  - 1 low RoB trial (Goteborg) was a report from a site within a larger multi-centre trial (ERSPC*). In formulating the recommendation, all sites from the ERSPC were considered together.
  - This resulted in 2 low RoB trials that formed the basis of the recommendation: 1 found a positive effect of screening on prostate cancer-specific mortality, while 1 found no effect.
- A small absolute reduction in mortality from prostate cancer was found in one trial.
- There was no reduction in all cause mortality.

* European Randomized Study of Screening for Prostate Cancer

Findings: Benefits of Screening with PSA

Study (country)	Study Characteristics	PSA Threshold	Contamination (rate of screening in control group)	Prostate cancer mortality Relative Risk (95% C.I.)	All-Cause Mortality Relative Risk (95% C.I.)	Absolute Effect (per 1000 men screened)	GRADE Quality of Evidence *
PLCO† U.S. population	RCT 76,693 men age 55-74, annual PSA screening for six years and DRE annually for four years 14 year follow-up	4 ng/ml	52%	1.09 (0.87-1.36)	0.96 (0.93 - 1.00)	No effect	moderate
ERSPC‡ (Finland, Sweden, Italy, Netherlands, Belgium, Switzerland and Spain)	RCT 162,243 men Age 50-74 (core group 55-69) PSA every 4 years 13 year follow-up	Most sites 3.0 ng/ml	20%	Core gp: 0.79 (0.69-0.91) All ages: 0.83 (0.73-0.94)	Core gp: 1.00 (0.98 - 1.02) All ages: 1.00 (0.98 – 1.02)	1.28 fewer deaths per 1,000 men screened	moderate

*Grading of Recommendations, Assessment, Development and Evaluation (GRADE) rates the continuum of quality of evidence in four categories of high, moderate, low or very low – see evidence review for complete assessment of study quality

†Prostate, Lung, Colorectal and Ovarian Screening Study

‡European Randomized Study for Screening for Prostate Cancer (published online August 7, 2014)

Findings: Harms of Screening with PSA

The main harms of screening identified were:

- Harms of biopsy
- Harms of overdiagnosis
- False positives

* European Randomized Study of Screening for Prostate Cancer

Findings: Harms of Biopsy

Harm	Study type	Study characteristics	Proportions (proportion % with 95% CI)	GRADE Quality of Evidence*
Harms of Biopsy		< 30 days	Haematuria* Mean=30.86% (20.18% to 41.51%) of men who had a biopsy Infection* Mean=0.94% (0.01% to 1.86%) of men who had a biopsy Not requiring hospitalization	Very low
			Hospitalization=2.07% (1.59% to 2.54%) of men who had a biopsy	Very low
			Death = 0.17% (0.09% to 0.25%)	Very Low

Grading of Recommendations, Assessment, Development and Evaluation (GRADE) rates the continuum of quality of evidence in four categories of high, moderate, low or very low – see evidence review for complete assessment of study quality

Findings: Additional Harms of Screening

Harm	Study type	Study characteristics	Proportions (proportion % with 95% CI)	GRADE Quality of Evidence*
Overdiagnosis	ERSPC‡ modelling data, various sources		40-56% of cases diagnosed	Very low

- Definition: Overdiagnosis occurs when cancer is detected correctly, but would not cause symptoms or death during the patient's lifetime.

‡ All data can be found in Dunfield L, Usman A, Fitzpatrick-Lewis D, Shane A, eds. Screening for prostate cancer with prostate specific antigen (PSA) and treatment of early-stage or screen-detected prostate cancer: A systematic review of the clinical benefits and harms. Ottawa: Canadian Task Force; 2013.

Findings: Additional Harms of Screening

Harm	Study type	Study characteristics	Proportions (proportion % with 95% CI)	GRADE Quality of Evidence*
False Positives	ERSPC‡‡ observational	PSA>3ng/ml cut-point biopsy referral	17.8% of men screened at least once had one or more false positive (all centres)	Very low

- Not all men who screened above threshold had a biopsy
- Some men who screen positive on the first round could be diagnosed with prostate cancer on a subsequent round
- Some men will have multiple biopsies

‡ ‡ Kilpelainen TP, Tammela TL, Roobol M, et al. False-positive screening results in the European Randomized Study of Screening for Prostate Cancer. Eur J Cancer 2011;47:2698-705.

Treatments of Prostate Cancer

The primary treatments reviewed:

- Radical Prostatectomy
- Radiation Therapy
- Androgen Deprivation Therapy (ADT)
- Combination Therapy

Findings: Benefits of Treatment

Some treatments were found to reduce the risk of **prostate cancer-specific mortality**, although the quality of evidence was variable.

- Prostatectomy was the only treatment with high QoE
- Hormone therapy alone was found to produce an increased risk of prostate cancer-specific mortality.

Very limited and low QoE to support a reduction in the risk of **all-cause mortality** for the following treatments:

- Prostatectomy
- Radiation Therapy
- Combination Therapy (Radiation and Hormone Therapy)

Findings: Benefits of Treatment

Treatment	Findings	Study Type	Prostate cancer-specific mortality (RR)	All-cause morality (RR)	GRADE Quality of Evidence*
Prostatectomy	The risk of prostate cancer-specific mortality was reduced. Inconclusive results on all-cause mortality: some trials reported no effect, while cohort studies showed an effect.	RCT	0.68 (o.52 to 0.89) 50 fewer per 1000 (from 17 fewer to 75 fewer)	0.92 (o.83 to 1.02) 46 fewer per 1000 (from 97 fewer to 11 more)	-High QoE for prostate-specific mortality -Moderate QoE for all-cause mortality
		Cohort	0.42 (0.33 to 0.53) 33 fewer per 1000 (from 27 fewer to 38 fewer)	0.38 (0.32 to 0.47) 221 fewer per 1000 (from 189 fewer to 242 fewer)	- Low QoE for both prostate-specific and all-cause mortality
Radiation Therapy	The risk of both prostate cancer-specific and all-cause mortality were reduced.	Cohort	0.74 (0.57 to 0.96) 18 fewer per 1000 (from 3 fewer to 31 fewer)	0.69 (0.62 to 0.77) 137 fewer per 1000 (from 101 fewer to 168 fewer)	-Low QoE for prostate-specific and all-cause mortality
Hormone Therapy	There was an increased risk of prostate-specific mortality. No effect on all-cause mortality.	Cohort	1.62 (1.16 to 2.26) 43 more per 1000 (from 11 more to 88 more)	1.13 (1 to 1.27) 69 more per 1000 (from 0 to 144 more)	-Low QoE for prostate-specific and all-cause mortality
Combination Radiation and Hormone Therapy	The combined hormonal and radiation therapies decrease both prostate-specific and all-cause mortality.	Observational	0.52 (0.29 to 0.93) 56 fewer per 1000 (from 9 fewer to 83 fewer)	0.44 (0.32 to 0.59) 289 fewer per 1000 (from 211 fewer to 347 fewer)	- Low QoE for prostate-specific and all-cause mortality

Findings: Harms of Treatment

Radical prostatectomy, radiation therapy and ADT are the most common treatments for prostate cancer and are associated with potential harms that include:

- Urinary incontinence
- Erectile dysfunction
- Bowel dysfunction

Findings: Harms of Treatment

Harms of Treatment	Study Type	Relative Risk (RR)	GRADE Quality of Evidence*
Urinary Incontinence	RCT	3.22 (2.27 to 4.56) 178 more per 1000 (from 102 more to 286 more) 8.31 (1.1 to 62.63) 149 more per 1000 (from 2 more to 1000 more)	High QoE Moderate QoE
	Cohort	3.68 (2.37 to 5.72) 167 more per 1000 (from 85 more to 293 more) 1.35 (0.9 to 2.02) 22 more per 1000 (from 6 fewer to 63 more)	Moderate QoE Very low QOE
	Observational	1.32 (0.75 to 2.3)19 more per 1000 (from 15 fewer to 76 more)	Very low QoE
Erectile Dysfunction	RCT	1.39 (0.77 to 2.53) 221 more per 1000 (from 130 fewer to 867 more)	Low QoE
	Cohort	1.56 (1.33 to 1.83) 234 more per 1000 (from 138 more to 347 more) 1.30 (1.17 to 1.43) 127 more per 1000 (from 72 more to 182 more)	Low QoE Low QoE
	Observational	2.35 (1.53 to 3.59) 442 more per 1000 (from 174 more to 849 more)	Moderate QoE
Bowel Dysfunction	RCT	0.42 (0.04 to 4.14) 54 fewer per 1000 (from 90 fewer to 293 more)	Low QoE
	Cohort	0.69 (0.43 to 1.11)15 fewer per 1000 (from 27 fewer to 5 more) 1.65 (0.84 to 3.25) 31 more per 1000 (from 8 fewer to 106 more)	Very low QoE Very low QoE
	Observational	2.44 (0.24 to 24.4) 40 more per 1000 (from 21 fewer to 653 more)	Very low QoE

Prostatectomy and Post-Surgical Harms

- **ANY <30 days**
  - Observational studies: VERY LOW QoE
    - 2246/11010 20%; CI 95% (19.7-21.2)*
    - 247/1243 20%; CI 95% (17.8-22.2)*
    - 395/3458 11.4%; CI 95% (10.4-12.5)*
    - 60/280 21.4%; CI 95% (17.0-26.8)*

- **Mortality <30days**
  - Observational studies: VERY LOW QoE
    - 53/11,010 0.48 %; CI 95% (0.36-0.63)*
    - 1/280 0.36 %; CI 95% (0.02-2.3)*

Grading of Recommendations, Assessment, Development and Evaluation (GRADE) rates the continuum of quality of evidence in four categories of high, moderate, low or very low – see evidence review for complete assessment of study quality

Additional Findings

Evidence on patient preferences and values:

- Men with perceived self-vulnerability to the disease and physician recommendation are associated with patient request for screening.
- High quality evidence is lacking about the best way to facilitate informed decision making about screening.
- Practitioners should distinguish between benefits and harms of screening, subsequent investigation and treatment.
- Discussions should include overview of diagnostic and therapeutic options in the event PSA test results are abnormal.

Additional Findings

Evidence on resource implications:

- The CTFPHC did not consider the costs of screening or treatment of prostate cancer when formulating these recommendations.

Balancing the Benefits and Harms of Screening

- There is conflicting evidence of a small and very uncertain potential reduction in prostate cancer mortality in men 55-69 years (1 death avoided per 1,000 invited for screening).
  - If you screen 5 of 1000 men die of prostate cancer
  - If you don't screen 6 of 1000 men die of prostate cancer
  - For one death avoided from prostate cancer 27 or 28 additional men will be diagnosed with prostate cancer
- There is no convincing evidence of a reduction in prostate cancer mortality for any other age group.

Balancing the Benefits and Harms of Screening (continued)

- There is consistent evidence that screening and active treatment lead to harm.

- Therefore, the potential small benefit from screening is outweighed by the potential significant harms and the CTFPHC recommends not screening for prostate cancer with the PSA test.

Considerations for the Implementation of Weak Recommendations

- The implication of the weak recommendation for men aged 55-69 years is that clinicians who believe a patient places a high value on the small potential benefit of screening and may not be concerned about harms, may wish to discuss the benefits/harms of screening with men in this age group.
- A weak recommendation implies that most people would want the recommended course of action, but some would not.

Considerations for the Implementation of Strong Recommendations

- The implication of the strong recommendation for men <55 and 70 years and older is that clinicians should not routinely discuss screening with men in these age groups, unless the topic is raised by the patient.
- A strong recommendation implies that most men will be best served by the recommended course of action.

Considerations for High Risk Populations

High risk populations include men of black ethnicity or men with a family history of prostate cancer.

- Men of black ethnicity were included in the USA studies, however, the results are not broken down by risk level or risk factor. Instead, the studies provide results for the male population as a whole.
- Therefore, there is currently no trial data to suggest that men at high risk should be screened differently from men in the general population.
- Clinicians may wish to discuss the benefits and harms of screening in men at high risk, with explicit consideration of their values and preferences.

Comparison to Previous CTFPHC and International Guidelines

The 2014 CTFPHC recommendation is consistent with recommendations issued by other industrialized countries, including:

- The USPSTF (2012)
- The Cancer Council Australia (2010)
- The National Health Service UK (2013)

However, there are other guidelines available providing conflicting recommendations.

Screening for Prostate Cancer with PSA

CONCLUSIONS

Conclusions

- Among men aged 55-69 years, the harms of screening probably outweigh the benefits, but uncertainty exists.

- Therefore, the CTFPHC made a weak recommendation to not screen for prostate cancer with the PSA test in this age group.

- The implication of the weak recommendation is that clinicians should discuss the benefits and harms of screening so they can make an informed decision in line with their values and preferences.

Conclusions (continued)

- Among men younger than 55 years and 70 years and older, there is a lack of evidence for benefit of screening and clear evidence of harms. There is certainty that the harms of screening outweigh the benefits.

- Therefore, the CTFPHC made a strong recommendation to not screen for prostate cancer with the PSA test in these age groups.

- The implication of the strong recommendations is that clinicians should not routinely discuss screening with men unless the topic is raised.

Evidence Review Reference

For more information on the details of this guideline please see:

- Canadian Task Force for Preventive Health Care website: http://canadiantaskforce.ca/?content=pcp
- Dunfield L, Usman A, Fitzpatrick-Lewis D, Shane A, eds. Screening for prostate cancer with prostate specific antigen (PSA) and treatment of early-stage or screen-detected prostate cancer: A systematic review of the clinical benefits and harms. Ottawa: Canadian Task Force; 2014.

Screening for Prostate Cancer with PSA

KT TOOLS

Prostate Cancer Screening Recommendations 2014

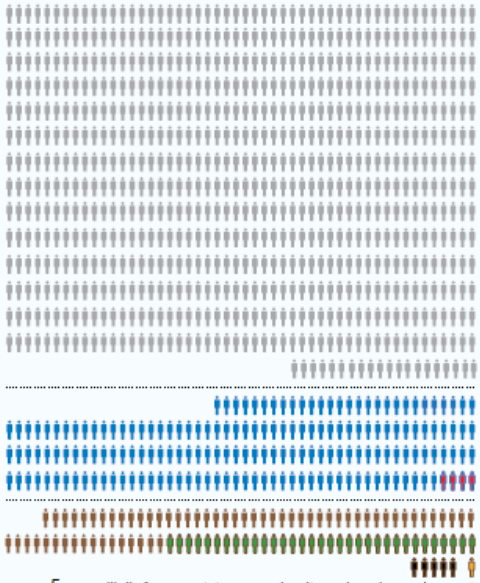
Canadian Task Force on Preventive Health Care

Benefits and Harms of PSA Screening

The Canadian Task Force on Preventive Health Care recommends against screening for prostate cancer with the PSA test

- The CTFPHC found that the potential small benefit from PSA screening is outweighed by the potential significant harms of the screening and associated follow-up treatment.
- Men should understand that PSA screening may result in additional testing if the PSA level is raised.
- To save one life we would need to diagnose an additional 27 men with prostate cancer

RESULTS OF SCREENING 1,000 MEN WITH THE PSA TEST
(age 55–69 years, screened over a 13-year period, and with a PSA screening threshold of 3.0 ng/ml)



720 men will have a negative PSA test

178 men with a positive PSA in whom follow-up testing does not identify prostate cancer

4 of these 178 will experience biopsy complications such as infection and bleeding severe enough to require hospitalization

102 men will be diagnosed with prostate cancer

33 of these 102 prostate cancers would not have caused illness or death
Because of uncertainty about whether their cancer will progress, most men will choose treatment and may experience complications of treatment

5 men will die from prostate cancer despite undergoing PSA screening

1 man will escape death from prostate cancer because he underwent PSA screening

What are my risks if I don't get screened?

- Among men who *are screened* with the PSA test, the risk of dying from prostate cancer is 5 in 1,000
- Among men who *are not screened* with the PSA test, the risk of dying from prostate cancer is 6 in 1,000

Complications of treatment for prostate cancer

For every 1,000 men who receive treatment for prostate cancer:
- 114–214 will have short-term complications such as infections, additional surgeries, and blood transfusions
- 127–442 will experience long-term erectile dysfunction
- up to 178 will experience urinary incontinence
- 4–5 will die from complications of prostate cancer treatment

Statistics for benefits and harms were calculated from the European Randomized Study of Screening for Prostate Cancer (ERSPC).

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Prostate Cancer Screening Recommendations 2014

Canadian Task Force on Preventive Health Care

PSA Screening: Patient FAQ

1. What is the PSA test?

   The PSA test is a blood test that is commonly used to detect possible prostate cancer. Elevated PSA levels may indicate the presence of prostate cancer, but can also be caused by other common non-cancer related conditions such as an enlarged prostate (also known as benign prostatic hyperplasia or BPH) or inflammation of the prostate gland (also known as prostatitis) due to an infection or other cause.

2. Why does the CTFPHC recommend against PSA screening for prostate cancer?

   The CTFPHC recommends against PSA screening because they found that the potential harms of screening outweigh the benefits.

3. Are there any other tests that can detect prostate cancer?

   Currently no other screening tests have been proven to accurately identify prostate cancer. Several tests are being developed to improve the accuracy of PSA screening. However, right now there is not enough evidence to tell us whether or not they are accurate.

4. Why are there harms with PSA screening? Isn't it a simple blood test?

   The PSA test is a simple blood test, but if the result is positive, men are likely to then undergo further tests such as a biopsy. There are several harms associated with biopsies, as described in the table. In addition, there is a risk that you will be diagnosed and treated for a slow-growing cancer that would not have caused any trouble in your lifetime.

5. What if I still want the PSA test?

   Because of recent efforts to encourage screening for prostate cancer, some men may still be interested in the test. Talk to your doctor about the benefits and harms of PSA screening.

BENEFITS

LOWER RISK OF DYING FROM PROSTATE CANCER

- 1 out of every 1,000 men will escape death from prostate cancer because they were screened with PSA.

HARMS

FALSE-POSITIVE RESULTS

- Most men who have a positive PSA result will undergo a prostate biopsy.
- A false-positive result occurs when a man with a positive PSA result undergoes a biopsy, with the biopsy showing that he does not have prostate cancer.

178 out of every 1,000 men screened with the PSA test will have an unnecessary biopsy to confirm they do not have prostate cancer.

COMPLICATIONS OF PROSTATE BIOPSY

- Prostate biopsy carries a number of complications, including blood in the urine or semen, rectal bleeding, infection and in rare cases, death.

21 out of every 1,000 men who undergo prostate biopsy will have complications severe enough to require hospitalization.

2 out of every 1,000 men who undergo prostate biopsy will die within 120 days of the biopsy, because of complications.

OVERDIAGNOSIS

- Overdiagnosis is the detection of cancers that grow so slowly they would not have caused illness or death during the man's lifetime.

Almost half of all the cancers detected through PSA screening would NOT have caused illness or death in the man's lifetime. However, because of uncertainty about whether their cancer would progress, most men will choose treatment and may experience complications of treatment.

HARMS OF TREATMENT

For every 1,000 men who receive treatment for prostate cancer:

- 114–214 will have short-term complications such as infections, additional surgeries, and blood transfusions
- 127–442 will experience long-term erectile dysfunction
- up to 178 will experience long-term urinary incontinence
- 4 or 5 will die from complications of prostate cancer surgery

Statistics related to benefits and harms were calculated from the European Randomized Study of Screening for Prostate Cancer (ERSPC) and the prostate cancer screening review (http://canadiantaskforce.ca/ctfphc-guidelines/2014-prostate-cancer/systematic-review/)

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Prostate Cancer Screening
Recommendations 2014

Canadian Task Force
on Preventive Health Care

PSA Screening: Primary Care Practitioner FAQ

The recommendations apply to all men not previously diagnosed with prostate cancer

- For men aged less than 55 years, we recommend not screening for prostate cancer with the prostate-specific antigen test.
  (Strong recommendation; low quality evidence)*
- For men aged 55-69 years, we recommend not screening for prostate cancer with the prostate-specific antigen test.
  (Weak recommendation; moderate quality evidence)
- For men 70 years of age and older, we recommend not screening for prostate cancer with the prostate-specific antigen test.
  (Strong recommendation; low quality evidence).

1. Why are there different recommendations for different age groups?

   There is no evidence that PSA screening reduces overall mortality for men of any age and consistent evidence that screening and active treatment lead to harm. However there is conflicting evidence suggesting a small and very uncertain potential reduction in prostate cancer mortality in men aged 55-69 years and no convincing evidence of a reduction in prostate cancer mortality for any other age group.

2. Do these guidelines include high-risk groups such as those of black race/ancestry or those with a family history of prostate cancer?

   Yes. There was no evidence indicating that men of black race/ancestry or those with a family history of prostate cancer (one or more affected first-degree relatives) should be screened differently from the average-risk population.

3. Does this guideline include screening with digital rectal examination (DRE)?

   This guideline recommends not screening with the PSA test, regardless of whether DRE is performed. Although DRE has been used in clinical practice to screen for prostate cancer, there was no evidence showing that DRE reduces prostate cancer mortality when used on its own or with the PSA test.

4. Is it necessary for primary care practitioners to discuss the benefits and harms of screening with their patients?

   If patients raise the issue of PSA screening, physicians should discuss the benefits and harms associated with screening. Men should understand that undergoing a PSA test can lead to additional testing if the PSA level is raised. Tools outlining the harms and benefits of screening are available at www.canadiantaskforce.ca

5. Why does the CTFPHC recommend against prostate cancer screening when the death rate has fallen since the introduction of the PSA test?

   There is no conclusive evidence to indicate what proportion of the decline in prostate cancer mortality is due to screening, improved treatment, or other factors; it is likely that both screening and treatment have contributed.

   However, the CTFPHC found that the potential small benefit that can result from PSA screening is outweighed by potential significant harms of PSA screening and associated follow-up treatment.

KEY POINTS

- The prevalence of undiagnosed prostate cancer at autopsy is high and increases with age (over 40% in men aged 40-49 years to over 70% in men aged 70 to 79 years).
- Only a small proportion of prostate cancer causes symptomatic disease or death whereas the majority is slowly progressive and not life threatening.
- Screening with PSA may lead to a small reduction in prostate cancer mortality but does not reduce overall mortality.
- PSA thresholds of 2.5ng/ml to 4.0ng/ml are commonly used for screening, with lower thresholds increasing the probability of false positive results and overdiagnosis, but no value completely excludes prostate cancer.
- Harms (such as bleeding, infection, urinary incontinence, false positives and overdiagnosis) are common following PSA screening.
- PSA should not be used for screening without prior informed discussion, ideally using decision aids to facilitate comprehension.

**Recommendations are graded according to the Grading of Recommendations Assessment, Development and Evaluation (GRADE) system. For explanation of GRADE recommendations, please see: www.canadiantaskforce.ca/methods/grade/*

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Questions & Answers

Thank you