Experiences in implementing Canada’s prostate screening guidelines.

James A Dickinson
MBBS PhD CCFP FRACGP FAFPHM(RACP)
Professor of Family Medicine and Community Health Sciences
University of Calgary
Former member: Canadian Task Force on Preventive Health Care
Disclaimers

I have not received support from any commercial source.

Canadian Task Force members are volunteers: supported by salaries from their institutions with travel and accommodation reimbursement only.

The presentation reflects my views only.
Outline

• Message
• Prostate Cancer in Canada
• Canadian Task Force methods
• Evidence review
• Recommendations
• Implementation in practice
• Challenges in Canada
Message

• PSA is a useful tumour marker, but poor screening test
• PSA screening may cure 1 per 1000 screened
• But harms large numbers 300, 30-50/1000
• It is beneficial to:
  – Companies that sell tests, devices or treatments
• Policies should limit PSA screening
  – Argue from position of men: not cost
  – Health care system
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• *Prostate Cancer in Canada*
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Canada: Age-standardised incidence and mortality rates, number of cases and deaths 1969-2013
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Background CTFPHC

- 1976-2005 – originally Canadian Task Force on Periodic Health Examination
- Recommendations and updates
- Re-established 2010 by Public Health Agency of Canada
- Recommendations on primary and secondary preventive interventions
- Target audience primary care professionals
Task Force

• Independent panel
  – Primary Care and prevention experts
  – Methodologists
  – *Not* topic experts
  – Unpaid volunteers, No conflicts of interest

• Uses evidence-based methods
  – Systematic synthesis of published evidence
  – GRADE
Analytical Framework

Population at risk of prostate cancer

1. No prostate cancer
2. Early detection of prostate cancer

Harms of screening

Screening

Surgery
Radiation therapy
Hormonal therapy
Cryotherapy
Ultrasonography
Watchful waiting
Active surveillance

Treatment

Reduced prostate cancer-specific and all-cause mortality

Harms of treatment
Process of development

Formal standardized process
• Writing group
• Analytic framework
• Systematic search and review
  – Evidence Review and Synthesis Centre
• Harms, Overdiagnosis included
• Recommendations linked from evidence
• External reviews: including content experts
• Paper to CMAJ (reviewers)
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What do the trials show?

6 Trials: 3 with severe risk of bias: disregarded

**PLCO (US)** trial. Annual screening,
- Substantial contamination of control group
- No effect

**ERSPC (European)** trial 2014 report: 13 year F/U. 7 countries
- Screening 2-4 years, threshold 3.5-2.
- Variable results between centres: 2 show benefit
- Overall benefit: Prostate Cancer relative risk 0.8 deaths
- Absolute reduction 12.8/10,000 men screened

**Gøteborg** trial. Overlaps with ERSPC, included in ERSPC.
## Harms of Screening

<table>
<thead>
<tr>
<th>Over-diagnosis</th>
<th>ERSPC modelling data, various sources</th>
<th>40-56% of cases diagnosed</th>
</tr>
</thead>
<tbody>
<tr>
<td>False Positives</td>
<td>ERSPC‡ Uncontrolled observational PSA&gt;3ng/ml cut-point biopsy referral</td>
<td>19.8% (11.5% to 28.1%) of men screened</td>
</tr>
<tr>
<td>Intervention arm of PLCO§ Uncontrolled observational PSA&gt;4.0ng/ml cut-point biopsy referral</td>
<td>11.3% (9.9% to 12.7%) of men screened</td>
<td></td>
</tr>
</tbody>
</table>

### Harms of Biopsy

- < 30 days
- Haematuria* Mean=30.9% (20.2% to 41.5%) of men who had a biopsy
- Infection* Mean=0.94% (0.01% to 1.86%) of men who had a biopsy
- Not requiring hospitalization
- Hospitalization=2.1% (1.6% to 2.5%) of men who had a biopsy
- Death = 0.17% (0.09% to 0.25%)
Findings: harms of treatment

Most common treatments
Radical prostatectomy, radiation therapy and androgen deprivation therapy (ADT)

Potential harms include
- urinary incontinence
- erectile dysfunction
- bowel dysfunction
Findings: harms of treatment

Most common treatments
Radical prostatectomy, radiation therapy and hormone androgen deprivation therapy (ADT)

Potential harms include
- urinary incontinence
- erectile dysfunction
- bowel dysfunction

Premature mortality
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 <30 days

Observational studies: VERY LOW QoE

• 53/11010  0.48 %; CI 95% (0.36-0.63)
• 1/280  0.36 %; CI 95% (0.02-2.3)
Harms of prostatectomy

Urinary incontinence
RCT: RR 3.22 (2.27 to 4.56)
• 178 more per 1000 (from 102 more to 286 more) HIGH QoE
Cohort: RR 3.68 (2.37 to 5.72)
• 167 more per 1000 (from 85 more to 293 more) MODERATE QoE

Erectile dysfunction
RCT: RR 1.39 (0.77 to 2.53)
• 221 more per 1000 (from 130 fewer to 867 more) LOW QoE
Cohort: RR 1.56 (1.33 to 1.83)
• 234 more per 1000 (from 138 more to 347 more) LOW QoE

Bowel dysfunction
RCT: RR 0.42 (0.04 to 4.14)
• 54 fewer per 1000 (from 90 fewer to 293 more) LOW QoE
Cohort: RR 0.69 (0.43 to 1.11)
• 15 fewer per 1000 (from 27 fewer to 5 more) VERY LOW QoE
Harms of Radiation Therapy

**Urinary incontinence**
RCT - RR 8.31 (1.1 to 62.63)
• 149 more per 1000 (from 2 more to 1000 more) MODERATE QoE
Cohort - RR 1.35 (0.9 to 2.02)
• 22 more per 1000 (from 6 fewer to 63 more) VERY LOW QoE

**Erectile dysfunction**
Cohort - RR 1.30 (1.17 to 1.43)
• 127 more per 1000 (from 72 more to 182 more) LOW QoE

**Bowel dysfunction**
Cohort - RR 1.65 (0.84 to 3.25)
• 31 more per 1000 (from 8 fewer to 106 more) VERY LOW QoE
Harms of hormone therapy (androgen deprivation)

**Urinary incontinence**
Observational studies: RR 1.32 (0.75 to 2.3)
- 19 more per 1000 (from 15 fewer to 76 more) VERY LOW QoE

**Erectile dysfunction**
Observational studies: RR 2.35 (1.53 to 3.59)
- 442 more per 1000 (from 174 more to 849 more) MODERATE QoE

**Bowel dysfunction**
Observational studies: RR 2.44 (0.24 to 24.4)
- 40 more per 1000 (from 21 fewer to 653 more) VERY LOW QoE
Higher risk populations

- Caribbean, African American
- Family history of prostate cancer

- No data on different benefits for “high risk” groups
- No data on harms
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Prostate cancer

2014
Recommendations on screening for prostate cancer with the prostate-specific antigen test

Canadian Task Force on Preventive Health Care

Box 2: Summary of recommendations for clinicians and policy-makers

The recommendations apply to all men without a previous diagnosis of prostate cancer.

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

- For men aged 55–69 years, we recommend not screening for prostate cancer with the PSA test. (Weak recommendation; moderate-quality evidence.)

- For men 70 years of age and older, we recommend not screening for prostate cancer with the PSA test. (Strong recommendation; low-quality evidence.)
Weak recommendation (against) indicates a values-driven, shared decision making approach between patient and physician, based on objective information on benefits and harms

Strong recommendation indicates clear advice against screening
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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 CTCRC recommend against PSA screening for prostate cancer?
   The CTCRC 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 biopsy, as described in the table. In addition, there is a risk that you will be diagnosed and treated for a non-existent cancer that would not result in 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 die as a result of 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.
  - False-positive result occurs when a man with a positive PSA result undergoes a biopsy, which can cause unnecessary biopsy to confirm they do not have prostate cancer.
  - 172 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 bleeding in the urethra or semen, rectal bleeding, infection, and in rare cases, death.
- 22 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 240 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 all of 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:
  - 116–214 will have short-term complications such as infections, additional surgery, and blood transfusions.
  - 127–33 will experience long-term erectile dysfunction.
  - 168 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 guidelines published in 2014 by the Canadian Task Force on Preventive Health Care.
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.
**Prostate Cancer**

**The Harms of Screening Greatly Outweigh the Benefits**

**Results of Screening 1,000 Men with the PSA Test**

- 1,000 men screened
- 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.
- 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.
- 720 men will have a negative PSA test

**What Are My Risks If I Don’t Get Screened?**
- Among men ages 55 to 69 who do not get screened, the risk of dying from prostate cancer is 6 in 1,000.
- With regular PSA screening, the risk of dying from prostate cancer among men aged 55 to 69 may be reduced to 5 in 1,000.
- In many cases, prostate cancer does not, and will not, pose a threat to a man’s life.

**Isn’t It Better to Get Screened Than to Do Nothing?**
- Screening with the PSA often leads to further testing, which comes with its own serious risks and problems.
- For example, a biopsy involves a number of potential harms such as infection, blood in the urine, or even death.
- Additionally, if testing leads to treatment, such as a prostatectomy (removal of the prostate gland), the chances of urinary incontinence and erectile dysfunction significantly increase. Other short-term post-surgical complications include infections, additional surgeries and blood transfusions and death.

**What Does the Canadian Task Force on Preventive Health Care Recommend?**
- Based on the lack of convincing evidence that PSA screening reduces prostate cancer mortality, and based on the consistent evidence that screening and active treatment does lead to harm, the CTFPHC recommends not using PSA testing to screen for prostate cancer.
- For more information on the Canadian Task Force on Preventive Health Care’s recommendations please visit: www.ctfphp.ca

**What Are the Benefits of Screening?**
- Reduced risk of dying from prostate cancer—1 out of every 1,000 men will escape death because he underwent PSA screening.
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.
WHAT ARE MY RISKS IF I DON’T GET SCREENED?

- Among men ages 55 to 69 who do not get screened, the risk of dying from prostate cancer is 6 in 1,000.
- With regular PSA screening, the risk of dying from prostate cancer among men aged 55 to 69 may be reduced to 5 in 1,000.
- In many cases prostate cancer does not, and will not, pose a threat to a man’s life.

ISN’T IT BETTER TO GET SCREENED THAN TO DO NOTHING?

- Screening with the PSA often leads to further testing, which carries with it its own serious risks and problems.
- For example, a biopsy involves a number of potential harms such as infection, blood in the urine, or even death.
- Additionally, if testing leads to treatment, such as a prostatectomy (removal of the prostate gland), the chances of urinary incontinence and erectile dysfunction significantly increase. Other short term post-surgical complications include infections, additional surgeries and blood transfusions and death.
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 37 men with prostate cancer.

<table>
<thead>
<tr>
<th>RESULTS OF SCREENING 1,000 MEN WITH THE PSA TEST</th>
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<tbody>
<tr>
<td>(ages 55-69 years, overall risk of 1.3% per person, and with PSA screening threshold of 3.0 ng/mL)</td>
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<table>
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<tr>
<th>Event</th>
<th>Percentage</th>
</tr>
</thead>
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<tr>
<td>PSA positive</td>
<td>720</td>
</tr>
<tr>
<td>Prostate cancer diagnosed</td>
<td>176</td>
</tr>
<tr>
<td>4 men will have a negative PSA test</td>
<td></td>
</tr>
<tr>
<td>102 men will be diagnosed with prostate cancer</td>
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</tr>
<tr>
<td>53 men will die from prostate cancer despite undergoing PSA screening</td>
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<td>1 man will escape death from prostate cancer because he underwent PSA screening</td>
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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 6 in 1,000.
- Among men who are not screened with the PSA test, the risk of dying from prostate cancer is 4 in 1,000.

Complications of treatment for prostate cancer

- For every 1,000 men who receive treatment for prostate cancer:
  - 154-316 men will have short-term complications such as infections, additional surgeries, and blood transfusions.
  - 178-442 men will experience longer-term complications such as erectile dysfunction and bladder incontinence.
  - 8-35 men will live with complications of prostate cancer treatment.

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

- 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.

Complications of treatment for prostate cancer

- 5 men will die from prostate cancer despite undergoing PSA screening
- 1 man will escape death from prostate cancer because he underwent PSA screening
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PROSTATE CANCER

Scrapping the PSA test is an injustice to men

ROCCO ROSSI
President and CEO
of Prostate Cancer Canada

The Canadian Task Force on Preventive Health Care released guidelines Monday recommending against using the prostate-specific antigen (PSA) test to screen for prostate cancer. Quite simply, those guidelines do not only create a disservice but also a great injustice to men and their loved ones.

Why is that? Early detection of prostate cancer saves lives. That’s especially important for a disease that often has no symptoms until it has advanced to a stage when there are fewer treatment options with better outcomes. The task force will say that the PSA test isn’t a perfect test, and we don’t disagree. But it currently is the best clinical indicator - a red flag - that something might be amiss and warrants further follow-up. That type of monitoring allows for the best possible outcomes.

The PSA test can and should be used to help determine an individual’s risk of prostate cancer. That baseline test value, considered along with other risk factors such as family history and age, will better inform the patient-physician conversation about appropriate follow-up.

That’s not just screening - that’s smart screening. We are not advocating for mass population screening, or annual PSA testing; instead, we propose tailored clinical follow-up appropriate for the individual. But if PSA testing is eliminated, men who are at high risk of prostate cancer with benefit from early detection; this includes men of black African or black Caribbean descent or men with a family history of prostate cancer.

And men have a right to know their risk. Men have a right to decide how they will use that information. The reality suggested by the task force harkens back to the not-so-distant past of paternalistic medicine, rather than informed decision-making.

The task force also notes that PSA testing will lead to over-treatment. Let me be clear: The PSA is one tool, really just the entry point to more specific diagnostics should there be any warning signs. One PSA test should never mean leaping into treatment. Perhaps, in the past, physicians were too quick to recommend treatment without determining whether the prostate cancer was low-risk or potentially aggressive. But the solution to that is more education about the appropriate interpretation of the test result, not a full-scale ban on using the test.

A recent study from the United States estimated what would happen if PSA testing was eliminated, as was recommended by the task force. It found that cases of metastatic disease would double, leading to a nearly seven-fold increase in prostate cancer-related deaths.

SUBMISSIONS: We welcome unsolicited articles. They should be about 650 words, argumentative and include your credentials.

If the article is accepted, you’ll be notified within three days.

E-mail comment@globeandmail.com
Arguments *for* screening

• Prostate cancer is rising: one in 6 men will get
• The mortality rate is dropping since PSA was introduced
• Over 90% of men survive prostate cancer
  – 5 yr survival 96%
  – Compared with 35% previously
• If we don’t screen, we will go back to the old days of presentation with advanced cancer

• Canadian urologists work differently from the US pattern of practice.
Have your baseline PSA blood test starting at 40 years old!

THE MAN VAN™
Free PSA test done here!
ProstateCancerCentre.ca

GET CHECKED

403-943-8888
The Drive to Eliminate Advanced Prostate Cancer
Prostate Cancer Canada

“In an age of informed healthcare, we believe the PSA test is one of the most powerful tools we have, early detection can be the difference between life and death”.

“Many individuals within the health care community agree with Prostate Cancer Canada and think it would be irresponsible to discontinue testing: ...”.

Press release from Prostate Cancer Canada, October 27, 2014
Canada: Age-standardised incidence and mortality rates, number of cases and deaths 1969-2013

Dickinson et al  CMAJ Open 2016 DOI: 10.9778/cmajo.20140079
Age-standardized incidence and Annual % Change
Age-standardized incidence and Annual % Change
Prostate cancer prevalence by age from autopsy studies

Bold: Unadjusted Model estimates
Interrupted: Final model estimates, adjusting for Gleason score

Changes in age-specific incidence rates

Incidence rate (per 100,000 population)
What else happened? Incidence

- From 1970s increasing TURP -> diagnosis
- 1994 Approved FDA for screening
- 1990s Increasing u/s guided prostate biopsies
- 1993 α-agonists, 5α-reductase inhibitors
- Modification to Gleason grading
Age-standardized mortality and Annual % Change

![Graph showing mortality rates over time with observed, modeled, and annual percentage changes for different periods.](graph.png)
What else happened? Mortality

• Increase prior to PSA
  – Artefact of more diagnosis? CT

• Changed
  – surgical approaches
    – anti-androgens, chemotherapy, radiation

• Decline >> effects of surgery in trials
Age-standardized mortality and Annual% Change
Changes in age-specific mortality rates

- Mortality rate (per 100,000 population)
- 85+
- 80-84
- 75-79
- 70-74
- 65-69
- 60-64
- 55-59
- 50-54
- 45-49

Changes in age-specific mortality rates
Replacing the PSA test is an injustice to men.
Prostate Canada

Safeway

DEPENDS

Janssen
Amgen
Astellas
Sanofi-Aventis
Heterogeneity of cancer progression

Message

• PSA is a useful tumour marker, but poor screening test
• PSA screening may cure 1 per 1000 screened
• But harms large numbers 300, 30-50/1000
• It is beneficial to:
  – Companies that sell tests, devices or treatments
  – Urologists and Oncologists in private practice
• Policies should limit PSA screening
  – Argue from position of men: not cost
  – Health care system
It is difficult to get a man to understand something if his income depends on him not understanding it

Upton Sinclair 1935