First do no harm? The importance of communicating overdiagnosis in guideline recommendations: Approach of the Canadian Task Force on Preventive Health Care

Wilson BJ, Bell NR, Grad R, Groulx S, Moore A, Tonelli M, on behalf of the Canadian Task Force on Preventive Health Care
The presentation reflects the views of Task Force members
1. Describe when and how the CTFPHC emphasizes overdiagnosis in its guidelines

2. Illustrate its use of evidence-based knowledge translation (KT) tools to help patients and clinicians understand this

3. Discuss strategies for supporting professionals in discussing overdiagnosis as part of shared decision making
Background CTFPHC

- 1976-2005 – originally Canadian Task Force on Periodic Health Examination
- Recommendations and updates until 1994
- Re-established 2010 by Public Health Agency of Canada
- Independent panel of clinicians and methodologists, non-remunerated
- Recommendations on primary and secondary preventive interventions
- Target audience primary care professionals
Guidelines since 2010

- Breast cancer
- Cervical cancer
- Cognitive impairment
- Colorectal cancer
- Depression
- Developmental delay
- Diabetes, type 2
- Hepatitis C
- Hypertension
- Lung cancer
- Obesity in adults
- Obesity in children
- Pelvic examination
- Prostate cancer
- Tobacco smoking in children and adolescents
CTFPHC methods

Standardized approach
• rigorous systematic review
• application of the GRADE methodology
• consensus about the direction and strength of each recommendation
• overdiagnosis explicitly considered
• consensus process
Supporting guideline implementation

- KT group (St Michael’s Hospital/University of Toronto) provides support
- KT tools for practitioners and patients use evidence based methodologies
- TF evaluates the reach and self-reported use of these KT tools in practice conducted each year
  - No systematic data on effectiveness in communicating about overdiagnosis
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- No systematic data on effectiveness in communicating about overdiagnosis
Prostate cancer is the most commonly diagnosed non-skin cancer in men and the second leading cause of cancer-related death among men in Canada. The current estimated lifetime risk of diagnosis is 14%, whereas the lifetime risk of death from prostate cancer is 3.8%. The prevalence of undiagnosed prostate cancer at autopsy is high and increases with age (0-45% among men aged 40-49 yr to >70% among men aged 80-89 yr). Most cases of diagnosed prostate cancer have a good prognosis; the 10-year estimated relative survival rates is now 99%, the highest among all cancers in men.

In Canada, the age-standardized rate of death from prostate cancer rose from 1950 to 1991, followed by a decline of 25.5% from 1992 to 2008, at an annual rate of 2.6% per year (Figure 1). In 1990, the estimated age-standardized mortality was 30 cases per 100,000 and in 2010 it was just below 20 per 100,000. However, over the same period, the number of men and the age-standardized incidence of prostate cancer both increased. Subsequent to the introduction and adoption of prostate-specific antigen (PSA) testing, the incidence of prostate cancer increased rapidly from 1990 to a peak in 1993 and a second, less pronounced peak in 2001 (Figure 1). Much of the excess incidence represents overdiagnosis,3 that is, the detection of cancers that would not progress to cause symptoms or death.

There is no conclusive evidence to determine what proportion of the decline in prostate cancer mortality is due to screening, worse impaired treatment, or other factors. It is likely that both screening and treatment have contributed.1 If PSA screening were the primary reason for the decrease in mortality, the steep increase in incidence due to early case detection would have been followed by a sharp decline in mortality. Instead, the reduction in prostate cancer mortality over time has been relatively steady and began soon after the test’s introduction to be attributed mainly to PSA screening.4-13

This guideline provides recommendations on screening for prostate cancer using the PSA test with or without digital rectal examination in men in the general population. The guideline updates a prior guideline by the task force that was last published in 1992.14

Methods

The Canadian Task Force on Preventive Health Care is an independent panel of volunteer clinicians and methodologists that makes recommendations about clinical interventions aimed at primary and secondary prevention (www.canruralhealth.ca). Work on each set of recommendations is led by a workgroup of two to six members of the task force. Each workgroup establishes the research questions and analytical frameworks for the guideline. More information about the task force’s methods can be found elsewhere5,10 and on the task force website (http://canadianpreventiverisknetwork.ca)

The development of these recommendations was led by a workgroup of six members of the task force and scientific staff at the Public Health Agency of Canada. Guidelines development was based on an analytical framework (Appendix I, Key Points).

Key Points

- The prevalence of undiagnosed prostate cancer in autopsy is high and increases with age (45-70% among men aged 45-70 yr to 70-99% among men aged 90-99 yr).
- Only a small proportion of men with prostate cancer have symptoms or die from the disease, most prostate cancers are detected by PSA screening.
- Screening with the PSA test may lead to a normal reduction in prostate cancer mortality but not a reduction in mortality.
- The finding of PSA less than 4 ng/mL is not sufficient for screening, however a test result below 4 ng/mL increases the probability of a biopsy result that returns negative, and no threshold completely eliminates prostate cancer.
- Only 1 in 100 men with PSA screening has a biopsy, so the value of the test is low.
- The PSA test should not be used for screening without a detailed discussion with the patient, and the use of decision aids to facilitate comprehension.
• based on update of two previous systematic reviews

• summary evidence presented on overdiagnosis and overtreatment
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.
KT Tools

Led by a KT working group

• Patient FAQs
• Physician FAQs
• Summary infographic
• ‘1,000 person’ harms and benefits diagram
Patient FAQ

**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 conditions such as an enlarged prostate (also known as benign prostate hyperplasia or BPH) or inflammation of the prostate gland (also known as prostatitis) due to an infection or other cause.

2. **Why does the CTFHC recommend against PSA screening for prostate cancer?**
   The CTFHC 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 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.

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**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 biopsy, which may result in unnecessary biopsy to confirm they do not have prostate cancer.
  - 7.3 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**
  - 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.

- **Overdiagnosis**
  - Overdiagnosis is the detection of cancers that grow so slowly they would not have caused illness or death during the man’s lifetime. Nearly 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 100 men who receive treatment for prostate cancer:
    - 11–21% will have short-term complications such as infections, additional surgery, and blood transfusions.
    - 1.7–6% will experience long-term erectile dysfunction.
    - up to 17% will experience long-term urinary incontinence.
    - 4 or 5 will die from complications of prostate cancer surgery.

[Sources related to benefits and harms are calculated from the European Randomized Study of Screening for Prostate Cancer (ERSPC) and the prostate cancer screening guidelines 2014 prostate cancer systematic review.]
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 conditions such as prostatitis or certain medications. It is important to note that a high PSA level does not always mean cancer.

Benefits
- Lower risk of dying from prostate cancer: 1 in every 1,000 men will die of prostate cancer because they were screened with PSA.

False-positive results:
- Most men who have a positive PSA result may not have prostate cancer. It is estimated that about 1 in 4 men who have a positive PSA test will have a negative biopsy. This can be a source of anxiety and psychological distress.

Complications of prostate biopsy:
- Each biopsy causes a number of complications, including bleeding, infection, and/or pain. The biopsy procedure can also cause some men to experience erectile dysfunction for a short period of time.

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.

2. Why does the CTFHC recommend against PSA screening for prostate cancer?
   The CTFHC recommends against PSA screening because it is not cost-effective and does not improve survival. PSA testing can lead to unnecessary treatments and procedures, such as biopsies and surgeries, which can cause significant harm.

3. Are there any other tests that can detect prostate cancer?
   Yes, there are several other tests available for detecting prostate cancer. These include digital rectal exam (DRE), transrectal ultrasound (TRUS), and prostate-specific antigen levels (PSA).

4. Why are there harms with PSA screening? Isn’t it a simple blood test?
   The PSA test is a relatively simple blood test, but it has several potential harms associated with it. These include:
   - Psychological distress: A positive PSA test can cause anxiety and stress.
   - Biopsy complications: A biopsy can cause bleeding, infection, and other serious complications.
   - False-positives: A positive PSA test does not always indicate cancer.

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.

Statistics related to benefits and harms were calculated from the European Randomised Study of Screening for Prostate Cancer (ERSPC) and the prostate cancer screening guidelines of the US Preventive Services Task Force.
Prostate Cancer

The harms of screening greatly outweigh the benefits

Results of screening 1,000 men with the PSA test:

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

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 test 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 CTPHC 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.canadiantruthsite.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.

1,000 MEN SCREENED

720 MEN WILL HAVE A NEGATIVE PSA TEST

178 MEN WITH A POSITIVE PSA IN WHOM FOLLOW-UP TESTING DOES NOT IDENTIFY PROSTATE CANCER

33 MEN WITH 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

4 MEN WILL EXPERIENCE BIOPSY COMPLICATIONS SUCH AS INFECTION AND BLEEDING SEVERE ENOUGH TO REQUIRE HOSPITALIZATION.

*Age 55-69 years, screened over a 15-year period, and with a PSA screening threshold of 3.0 ng/mL

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

THE HARMS OF SCREENING GREATLY OUTWEIGHT THE BENEFITS

RESULTS OF 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.

1,000 MEN SCREENED

178

MEN WITH A POSITIVE PSA IN WHOM FOLLOW-UP TESTING DOES NOT IDENTIFY PRESENT CANCER

720

MEN WILL HAVE A NEGATIVE PSA TEST

4

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

As if I Don’t Get Screened?

If you are aged 55 to 69 who do not get screened, your lifetime risk of prostate cancer is 1 in 1000. Screening increases your risk of dying from prostate cancer by 2%. PSA testing does not identify prostate cancer that does not, and will not, cause you harm.

What gets Screened Than

PSA testing often leads to further testing, which is not without serious risks and problems. Further testing may involve a number of potential complications such as pain, bleeding in the urine, or even death. Further testing also increases the risk of treatment side effects such as incontinence and erectile dysfunction. Other short term 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.canadian Taskforce.ca

What are the Benefits of Screening?

• Reduced risk of dying from prostate cancer—4 out of every 1000 men will escape death because he underwent PSA screening.
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 57 men with prostate cancer.

#### RESULTS OF SCREENING 1,000 MEN WITH THE PSA TEST

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<thead>
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<th>Test Positive</th>
<th>Test Negative</th>
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<tr>
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#### What are my risks if I don’t get screened?

- Among men who get 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 require treatment for prostate cancer:
  - 154.5 will have short-term complications such as infections, additional surgeries, and delayed recovery.
  - 157.4 will experience long-term complications such as incontinence, stool difficulties, and erectile dysfunction.
  - 178.5 will experience urinary incontinence.
  - 2.5 will die from complications of prostate cancer treatment.
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

5 men will die from prostate cancer despite undergoing PSA screening

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

Complications of treatment for prostate cancer
The prevalence of undiagnosed prostate cancer at autopsy is higher than 40%.

Only a small proportion of prostate cancer causes symptomatic disease or death whereas the majority are asymptomatic.

Screening with PSA may lead to a small reduction in prostate-specific mortality.

PSA thresholds of 2.5ng/ml to 4.0ng/ml are commonly used for prostate with lower risk.

Harms (such as bleeding, infection, urinary incontinence, false positives and overdiagnosis) are common following PSA screening.
Media analysis

- >800 media stories in outlets nationwide
- Majority focused on TF recommendations, evidence and overall rationale
- Some articles included comments from critics - not prominent, often mentioned at the end of article
- Some critics responded with op-eds, the impact of which formed small percentage of the overall coverage
- Suggested that these would have the effect of further raising profile of the issue and driving dialogue between men and their physicians
Media analysis

André Picard’s column “Evidence, not emotion, should drive prostate cancer screening”

...So let’s focus on one key issue: Mortality,... according to the data, for every man who benefits from PSA testing, 27 are harmed by unnecessary treatment – complications such as impotence, incontinence and higher risk of heart disease and osteoporosis (because many men get a hormonal treatment that deprives their body of androgens).
Discussion

- Overdiagnosis evidence can be systematically incorporated into a guideline development process and KT tools.
- However, no evidence about impact on actual patient decision making or physician advice.
- Evidence based materials, or credibility of guideline developer, no guarantee of change in patient or physician understanding or behaviour.
- Concept of overdiagnosis is difficult for professionals as well as patients.
Discussion

• New TF initiatives include clinical prevention leaders pilot study
• How do other agencies and groups handle this?
• Is there merit in aligning efforts across major guideline development groups? For example,
  – Operationalize how overdiagnosis is specifically quantified
  – Share best practices
  – Develop collaborative research proposals to identify effective dissemination and implementation strategies
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