

# Prostate-Specific Antigen (PSA)–Based Population Screening for Prostate Cancer: OHTAC Recommendation

HEALTH QUALITY ONTARIO

## ONTARIO HEALTH TECHNOLOGY ADVISORY COMMITTEE RECOMMENDATION

OHTAC recommends against the introduction of a formal, population-based PSA screening program for prostate cancer in Ontario.

### BACKGROUND

Prostate cancer (PC) is the most commonly diagnosed non-cutaneous cancer in men and their second or third most common cause of cancer-related deaths. Prostate cancer is a heterogeneous disease with a variable natural history ranging from low-risk tumours (unlikely to threaten men's quality or length of life) to highly aggressive forms. The etiology of PC is largely unknown and the established risk factors—older age, ethnicity, and family history—explain only a fraction of variation in disease occurrence. The wide geographic variation in internationally reported rates of PC reflects differences in detection or diagnostic practices, treatments, lifestyle, and genetic factors.

In Canada, the incidence of PC has gradually increased over time. The age-standardized incidence rate was 53.8 per 100,000 in 1970 and 124.7 per 100,000 in 2007 and has grown much more than for lung (59.3 to 67.8) or colorectal (47.8 to 60.4) cancers. In Ontario, the number of incident cases diagnosed in 2009 was 9,300, representing 28% of all incident male cancers. Also in 2009, the age-standardized mortality rate for PC in Ontario was 19 per 100,000, and the number of PC deaths in Ontario was 1,400 or 10.2% (1,400/13,700) of all male cancer deaths. The 5-year (96%) and 10-year (95%) relative survival rates for prostate cancer in Canada are the highest for any cancer. The prevalence rate for PC, which is a function of both detection and survival, represents 42% of the total cancer prevalence burden in Canada.

Population-based screening programs aim to reduce disease-specific mortality and/or morbidity by identifying disease at an early stage when it is more likely to be curable. Prostate-specific antigen (PSA) testing for PC has been common practice for years and the prevalence of self-reported PSA testing in Canadian men is 48%. Screen-detected cases must account for a substantial proportion of disability or death from disease. It is not entirely clear with PC to what extent the early forms of the disease progress to or are associated with high-risk or potentially lethal disease. In addition to diagnostic efficacy, the early treatment must be effective to reduce mortality. The management of PC has been changing over time, and the optimal therapeutic approaches for the various stages of PC are far from certain.

Health Quality Ontario conducted an evidence-based analysis (1) to answer the following research question: What is the evidence that PSA-based population screening of asymptomatic,

average-risk males reduces prostate cancer mortality or overall mortality, increases the detection of prostate cancer, or decreases the rate of aggressive or metastatic cancers?

A systematic search of trials published between 2008 and 2013, specifically systematic reviews and randomized controlled trials (RCT) of PSA-based population screening programs, identified 11 reports, including 5 systematic reviews and 6 RCTs.

Health Quality Ontario also conducted an economic literature review and primary economic evaluation (2) to answer these additional research questions:

- What is known from published economic evaluations of population-based PSA screening programs for prostate cancer?
- How much is currently being spent on opportunistic PSA screening of men in Ontario?
- How much would it cost to introduce a population-based PSA screening program for men aged 50 to 74 years in Ontario?

## REVIEW OF THE EVIDENCE

### Research Questions

- What is the efficacy of PSA-based population screening programs in asymptomatic males of average risk to reduce prostate-specific cancer mortality or overall mortality, to increase detection of prostate cancer, or to decrease rates of aggressive or metastatic cancers?
- What are the harms of PSA screening for prostate cancer?
- What is known from published economic evaluations of population-based PSA screening programs for prostate cancer?
- How much is currently being spent on opportunistic PSA screening of men in Ontario?
- How much would it cost to introduce a population-based PSA screening program for men aged 50 to 74 years in Ontario?

### Main Findings

None of the systematic reviews of the RCT screening trials for PC found a statistically significant reduction in relative risk of PC mortality or overall mortality with PSA-based population screening programs. The evidence from the primary screening trials on the benefit of PSA-based population screening programs for PC mortality was conflicting and found to vary by country, by screening program, and by age of men at study entry.

PSA screening programs in some but not all of the countries participating in the European Randomized Study of Screening for Prostate Cancer (ERSPC) found a statistically significant reduction in relative risk of PC mortality for some age groups, although the absolute risk reduction was small. The American Prostate, Lung, Colorectal, and Ovarian Cancer (PLCO) Screening Trial found a non-statistically significant increase in relative risk for PC mortality. Both trials, however, had methodological limitations potentially influencing their results: differential treatment of trial groups in the ERSPC trial and high rates of PSA screening in the usual-care group in the PLCO trial.

The primary PSA-based screening trials were consistent in that none demonstrated a reduction in relative risk of all-cause mortality and all found a statistically significant increase in the detection of PCs in the screening arm, with the majority of cancers being low risk and organ

confined. The detection of intermediate-risk tumours was similar in the study groups and, although the detection of high-grade tumours declined with subsequent screening, the progression of PC to metastasis during follow-up did not decline, potentially limiting the effectiveness of screening programs. Overall, although the probability of having a PC detected increased significantly through screening, men's risk of dying from PC was low and their risk of dying from other causes was much higher.

There are major harms (unnecessary risks) associated with screening for prostate cancer including the risks of biopsy and overdiagnosis that can result in unnecessary invasive treatments (e.g. prostatectomy) having potential major complications such as infection, incontinence, and impotence. There are also minor harms associated with screening for prostate cancer including the risks of the PSA test itself such as high false positive rates resulting in anxiety and unnecessary biopsies.

## **OHTAC DELIBERATIONS**

HQO has developed a decision-making framework to help guide deliberation and support the development of OHTAC recommendations regarding the uptake, diffusion, distribution, or removal of health interventions in Ontario. A summary of the decision determinants for this recommendation is provided below.

## DECISION DETERMINANTS

**Table 1: Decision Determinants for PSA-Based Population Screening for Prostate Cancer**

Decision Criteria	Subcriteria	Decision Determinants Considerations
<b>Overall clinical benefit</b> How likely is the health technology/intervention to result in high, moderate, or low overall benefit?	<b>Effectiveness</b> How effective is the health technology/intervention likely to be (taking into account any variability)?	PSA screening is not effective in reducing prostate cancer mortality or all-cause mortality.
	<b>Safety</b> How safe is the health technology/intervention likely to be?	There are no major safety issues with the screening test itself; however, there are significant unnecessary risks associated with biopsy, overdiagnosis, and overtreatment of men who would otherwise have no clinical symptoms during their lifetimes.
	<b>Burden of illness</b> What is the likely size of the burden of illness pertaining to this health technology/intervention?	Prostate cancer is the most common cancer in men and is the third most common cause of cancer deaths.
	<b>Need</b> How large is the need for this health technology/intervention?	There is a need to adequately identify which prostate cancers are more likely to become clinically significant.
<b>Consistency with expected societal and ethical values<sup>a</sup></b> How likely is adoption of the health technology/intervention to be congruent with societal and ethical values?	<b>Societal values</b> How likely is the adoption of the health technology/intervention to be congruent with expected societal values?	Men and their physicians are supportive of screening practices for PC.
	<b>Ethical values</b> How likely is the adoption of the health technology/intervention to be congruent with expected ethical values?	None known.
<b>Value for money</b> How efficient is the health technology likely to be?	<b>Economic evaluation</b> How efficient is the health technology/intervention likely to be?	Diagnosis and treatment costs associated with PSA-based population screening are high. Depending on the uptake, a population screening program could cost at least \$30 million to implement.
<b>Feasibility of adoption into health system</b> How feasible is it to adopt the health technology/intervention into the Ontario health care system?	<b>Economic feasibility</b> How economically feasible is the health technology/intervention?	The implementation of a formal screening program would have significant resource implications.
	<b>Organizational feasibility</b> How organizationally feasible is it to implement the health technology/intervention?	

Abbreviations: PC, prostate cancer; PSA, prostate-specific antigen.

<sup>a</sup>The anticipated or assumed common ethical and societal values held in regard to the target condition, target population, and/or treatment options. Unless there is evidence from scientific sources to corroborate the true nature of the ethical and societal values, the expected values are considered.

## REFERENCES

(1) Pron G. Prostate-specific antigen (PSA)–based population screening for prostate cancer: an evidence-based analysis. *Ont Health Technol Assess Ser* [Internet]. 2015 May;15(10):1–64. Available from: <http://www.hqontario.ca/evidence/publications-and-ohtac-recommendations/ontario-health-technology-assessment-series/prostate-cancer-screening-eba>.

(2) Tawfik A. Prostate-specific antigen (PSA)–based population screening for prostate cancer: an economic analysis. *Ont Health Technol Assess Ser* [Internet]. 2015 May;15(11):1–37. Available from: <http://www.hqontario.ca/en/documents/eds/2015/prostate-cancer-screening-econ>.

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