PSA SCREENING
REVIEW OF CANADIAN TASK FORCE RECOMMENDATIONS
PROPOSAL FOR LOCAL EXPERT OPINION

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CANADIAN TASK FORCE ON THE PREVENTATIVE HEALTH CARE

As you are likely aware, the Canadian Task Force on the Preventive Health Care (CTFPHC) (formerly the Canadian Task Force on the Periodic Health Examination, CTFPHE) has recently produced a guideline on prostate-specific antigen (PSA) screening. Their recommendations, directed at clinicians and policy-makers, apply to all men without a previous diagnosis of prostate cancer. They are as follows:

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

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

3. For men 70 years and older, they recommend not screening for prostate cancer with the PSA test. (Strong recommendation; low-quality evidence.)

CANADIAN UROLOGY ASSOCIATION CONCERNS

1. The Task Force comments that the randomized trials do not show a decrease in overall mortality. This is misleading to the reader because none of the screening trials were powered to demonstrate a decrease on overall mortality. For example, a trial designed to have 80% power to detect a 50% decrease in cancer mortality at 10 years, from 1 to 0.5%, in a population with an overall 20% mortality at 10 years, would have less than 10% power to detect a difference in all-cause death. Thus the lack of an overall mortality reduction should not be considered a criticism.

2. The document acknowledges that two of the higher quality trials found a reduction in prostate cancer-specific mortality, whereas four lower quality trials found no difference between the screening and control groups. The contamination in the PLCO trial, which has been reported to be as high as 85%, among other flaws, means that PLCO should not be considered equivalent to the ERSPC study. In other words, the Task Force observed that the strongest evidence revealed a reduction in prostate cancer death; however, the recommendation states there is "conflicting evidence suggesting a small and uncertain potential reduction in prostate cancer mortality." The statement acknowledging a mortality reduction from screening observed in the robust trials is at odds with the statement in the final recommendation that there is no clear evidence of a mortality reduction.

3. The review understates the benefit of screening, which it states as 1.28 deaths avoided per 1000 men screened. The published report from the Goteborg randomized trial is that with 14 years of follow–up, the number needed to diagnose for each death avoided is 12,[4] and in an analysis of healthy screened patients in PLCO, it is 5. The adjusted mortality reduction (corrected for non- compliance) in ERSPC was 27% at 13 years, while the Task Force quoted the unadjusted rate of 21%.

CANADIAN UROLOGY ASSOCIATION CONCERNS

4. Evidence for a decrease in metastatic disease is also important to patients and was not included.[5] Further, the mortality curves in ERSPC and Goteborg continue to diverge with longer follow-up. While a well-founded expectation of more benefit being demonstrated with longer follow-up should not drive current recommendations, it is reasonable that it influences the strength of these recommendations.

5. The unsubstantiated claim that the reduction in mortality is unlikely due to screening and more likely due to advances in treatment is contrary to published evidence. Epidemiological modelling studies consistently ascribe 40% to 75% of the reduction in mortality to screening,[6] and only 20% to 33% to changes in treatment.

6. Active surveillance has been widely adopted in Canada. This was not mentioned in the document. Clearly the widespread use of surveillance for low-grade disease in Canada is relevant.

CANADIAN UROLOGY ASSOCIATION CONCERNS

In conclusion, the best trials available to date, which are still in progress, have demonstrated that screening reduces prostate cancer death by 21% to 44%. To recommend against screening because “Available evidence does not conclusively demonstrate that screening with the PSA test will reduce mortality from prostate cancer” is misleading and reflects errors of fact, omission, interpretation, and statistics.

CANADIAN UROLOGY ASSOCIATION RESPONSE

PSA screening has had a major impact on prostate cancer mortality, but carries with it the risk of harm to patients who are unlikely to benefit. In our view, the following recommendations are more appropriate for a Canadian population.

1. Avoid PSA testing in men with little to gain. After appreciating the potential risks and benefits, those men who do decide to have a PSA and have a low value (<1.0 at baseline) should be tested infrequently, about every 5 years. Men with less than a 15-year life expectancy (typically over age 70) should not be screened unless they had a high PSA previously. Men whose PSA is above the median for their age but below the biopsy threshold should be counselled for more regular screening and risk assessment.

2. Digital rectal exam (DRE) has value for the detection of many anal and rectal problems, as well as prostatic abnormalities in addition to prostate cancer. DRE should continue to be performed as a routine part of the periodic health exam.

3. Do not treat men with low-risk prostate cancer, or older men with intermediate- risk prostate cancer, who are not likely to benefit from treatment.

EVIDENCE: RANDOMIZED CONTROLLED TRIALS

Table 1: Evidence of benefit of screening for prostate cancer with PSA testing

Study (country)	Study characteristics	PSA threshold, ng/mL	Contamination (rate of screening in control group), %	Prostate cancer mortality, RR (95% CI)	All-cause mortality, RR (95% CI)	Absolute effect	GRADE quality of evidence*
PLCO[21] (United States)	RCT; 76 693 men aged 55–74 yr; annual PSA screening for 6 yr and digital rectal examination annually for 4 yr; 14-yr follow-up	4	52	1.09 (0.87–1.36)	0.96 (0.93–1.00)	No effect	Moderate
ERSPC[19] (Finland, Sweden, Italy, the Netherlands, Belgium, Spain and Switzerland)	RCT; 162 243 men aged 50–74 yr (core group 55–69 yr); PSA screening every 4 yr; 13-yr follow-up	3.0 at most sites	20	Core group: 0.79 (0.69–0.91) All ages: 0.83 (0.73–0.94)	Core group: 1.00 (0.98–1.02) All ages: 1.00 (0.98–1.02)	12.8 fewer deaths per 10 000 men screened	Moderate

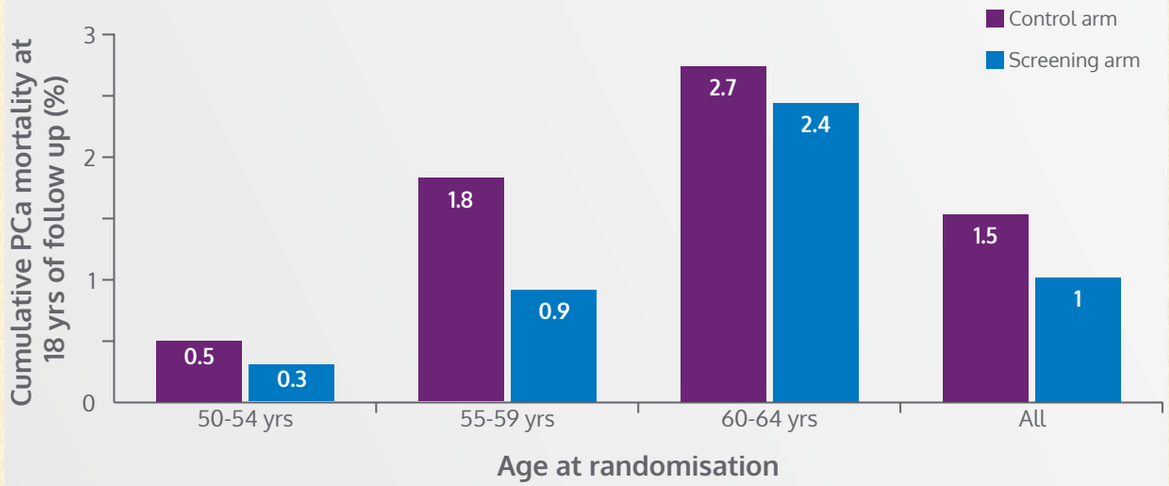
Note: CI = confidence interval, ERSPC = European Randomized Study of Screening for Prostate Cancer, PLCO = Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial, PSA = prostate-specific antigen, RCT = randomized controlled trial, RR = relative risk.
*GRADE (Grading of Recommendations, Assessment, Development and Evaluation)[15] rates the continuum of quality of evidence in 4 categories of high, moderate, low or very low; see evidence review for complete assessment of study quality.[13]

EVIDENCE: RANDOMIZED CONTROLLED TRIALS

This recent randomized screening study from Goteborg, which had considerably longer median follow up (14 years) than other screening studies, estimated the mortality reduction with prostate-specific antigen (PSA) screening at 50%. With this longer follow-up, the benefits of screening were greater with one life saved for every 12 patients treated.

Organised screening results in a significant decrease in prostate cancer mortality, but overdiagnosis remains a major problem.[2]

Figure 1: Prostate cancer mortality in the Göteborg trial at a median follow-up of 18 years



Adapted from Hugosson J *et al,* 2014.[2]

LOCAL OPINION

- All patients who wish screening for prostate cancer should have a discussion about screening risks and benefits.
- There should be no restriction of access to PSA testing in Newfoundland
- Patients over 70 or younger patients with life expectancy less than 15 years should not be screened
- At risk populations should have first screening at age 40
- Non at risk populations screening between 55-69
- Any abnormal DRE should have a confirmatory PSA
- A prostate biopsy is not without risk and physicians recommending it should confirm an abnormal PSA with clinical findings, repeat PSA levels and risk stratification
- Patients found to have very low risk prostate cancer (< or = 2 cores, <50% Gleason 6) should be treated with active surveillance thereby decreasing treatment side effects of screened population.