

Cancer Expert Working Group on Cancer Prevention and Screening

Recommendations on Prevention and Screening for Prostate Cancer For Health Professionals

Local epidemiology

1. Prostate cancer was the 3rd commonest cancer among males in Hong Kong in 2014. There were 1709 new cases of prostate cancer, accounting for 11.3% of all new cancer cases in the male population. The age-standardised incidence rate (ASIR) was 28.0 per 100,000 standard population. The median age at diagnosis was 71 years old.¹
2. Prostate cancer was the 5th leading cause of male cancer death in 2015. There were 404 deaths caused by prostate cancer, accounting for 4.8% of all cancer deaths in the male population. The age-standardised mortality rate (ASMR) was 5.5 per 100,000 standard population.² After adjusting for population ageing, the ASIR increased significantly whereas the ASMR increased slightly over the past two decades. More information on prostate cancer statistics can be found at the Centre for Health Protection (CHP) website: www.chp.gov.hk/en/content/9/25/5781.html.
3. Despite the increase in the ASIR and ASMR of prostate cancer in Hong Kong, the rates remained substantially lower comparing with overseas data available as of 2012.³

Risk factors

4. Prostate cancer is associated with increasing age and is more common in men of black ethnicity than men of white ethnicity or Asian men.⁴ The lifetime risk of being diagnosed with prostate cancer is 1 in 4 for men of black ethnicity compared to 1 in 8 for men of white ethnicity.⁵ The UK PROCESS (Prostate Cancer in Ethnic Subgroups) Study showed that men of black ethnicity present about 5 years younger and are more likely to have higher PSA on presentation, compared to men of white ethnicity.⁶ Indeed, African American men have the highest incidence and mortality from prostate cancer in the world.⁷

5. Aside from age and race, the only well-established risk factor for all stages of prostate cancer is a family history of the disease.⁸ The risk for first-degree relatives of men with prostate cancer is approximately twice of that for men in the general population.^{9,10} This lifetime risk increases up to about fourfold if there are 2 first-degree relatives with prostate cancer. Age at diagnosis of first-degree relatives is also important, because the lifetime risk is increased around threefold if the relative was 60 years of age or younger when diagnosed.¹¹ A 50% higher risk in monozygotic twins than in dizygotic twins^{12,13,14} and the higher incidence in African Americans (and lower rate in Americans of Asian ancestry) supports genetic factors as an important determinant of the variation in risk at the population level.¹⁵

6. About 35% of the familial risk of prostate cancer is explained by known genes.^{16,17,18} Two of these are breast cancer susceptibility genes *BRCA1* and *BRCA2* genes.¹⁹ The relative risk of developing prostate cancer by 65 years of age is estimated at 1.8-fold to 4.5-fold for *BRCA1* carriers^{20,21} and at 2.5-fold to 8.6-fold for *BRCA2* carriers.^{22,23,24} Mutations in other genes such as *HOXB13*, *NBS1*, and *CHEK2* genes²⁵ are also reported to be associated with an increased risk of prostate cancer.

Early detection

7. Early prostate cancer may have no symptoms, so they often go unnoticed. Common symptoms of prostate cancer include difficulty or delay in urination, slow or weak stream of urine, need to pass urine more often and especially at night, blood in the urine, and pain in the lower back, pelvis and hips. The earlier prostate cancer is detected, the higher the chance of cure. However, most of these symptoms are also found in men suffering from benign prostatic hyperplasia (BPH). Therefore, all men are advised to be aware of prostate health. Individuals with these symptoms should consult their doctors for assessment and investigation.

Screening

8. The purpose of prostate cancer screening is to identify men with abnormalities suggestive of prostate cancer before they develop symptoms, so that prompt definitive diagnostic investigation and treatment can be offered. Prostate-specific antigen (PSA) test is the most commonly used biomarker for prostate cancer; though with limitations such as low sensitivity and specificity, as well as the potential harms of over-diagnosis and over-treatment.²⁶ Although it has been believed that digital rectal examination (DRE) may identify prostate cancer that would not necessarily be picked up on PSA alone,²⁷ the European Randomized Study of Screening for Prostate Cancer (ERSPC) showed that a DRE

did not provide any additive information beyond PSA.²⁸ The positive predictive value of the DRE would increase as the PSA increases.^{29,30}

9. Current efforts are underway to identify new biomarkers that can supplement or replace PSA as a screening test for prostate cancer. One promising test is the Prostate Health Index (PHI), which combines all 3 known isoforms of PSA (total PSA, free PSA, and [-2]proPSA) into a single score and has greater specificity for distinguishing prostate cancer on biopsy compared with PSA or percentage free PSA.³¹ Another promising test is the 4 Kallikrein (4K) Score Test.³² Nevertheless, their utility still needs to be validated in large prospective trials.²⁶

Effectiveness of prostate cancer screening for men

10. Evidence from the Prostate, Lung, Colorectal and Ovary screening study (PLCO)³³ and the ERSPC³⁴ are insufficient to support universal PSA screening to the general population, although ERSPC data with follow-up to 13 years showed continued improvement in risk reduction of prostate cancer mortality, and decline in the number needed to screen and treat to prevent one prostate cancer death.³⁵ The main scientific challenge is to differentiate between men who will benefit from screening and men who will not, reducing over-diagnosis and over-treatment while achieving mortality reduction. Indeed, there is international consensus of insufficient evidence for universal population-based prostate cancer screening by PSA.^{36,37}

11. However, there is currently no international consensus on targeting screening on men at increased risk.¹⁹ Among the limited number of studies of screening in men at increased risk of prostate cancer, quite a few supported the use of targeted screening in high risk families and/or race. However, methodological differences make it difficult to draw conclusions from these data.

12. The IMPACT study (Identification of Men with a genetic predisposition to Prostate Cancer: Targeted screening in *BRCA1/2* mutation carriers and controls) is an international, multicentre study evaluating the role of targeted PSA screening in men aged 40 to 69 years with *BRCA1/2* mutations. The first screening round of IMPACT demonstrated that targeted screening for prostate cancer in men with a genetic predisposition detects clinically significant disease. Using a PSA threshold of 3 ng/ml resulted in a low biopsy rate (8.0%) and a high positive predictive value, particularly in *BRCA2* carriers, for the detection of intermediate- and high-risk disease. The preliminary results supported the use of PSA screening for *BRCA2* carriers.²⁰

13. Taking into account the emerging scientific evidence, international practice, local epidemiology and relative ease of risk stratification, the Cancer Expert Working Group on Cancer Prevention and Screening (CEWG) has fine-tuned the recommendations on prostate cancer screening in June 2016 as follows:

<i>For asymptomatic population at average risk</i>	
1.	There is insufficient scientific evidence to recommend for or against population-based prostate cancer screening in asymptomatic men by Prostate Specific Antigen (PSA) and/or Digital Rectal Examination (DRE).
2.	For asymptomatic men considering prostate cancer screening, CEWG encourages them to discuss with their doctor about individual circumstances and make informed decision on whether or not to go for prostate cancer screening.
<i>For persons at increased risk</i>	
3.	Men at increased risk, namely African American men or those with one or more first-degree relatives diagnosed with prostate cancer before age 65, should consider seeking advice from doctors regarding the need for and approach of screening. While the screening blood test to be considered is PSA, the DRE may also be done as part of screening. The PSA screening should start at an age not earlier than 45 until age 70, and the interval should not be more frequent than once every two years.

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