



衛生防護中心
Centre for Health Protection

**Cancer Expert Working Group on
Cancer Prevention and Screening (CEWG)**

**Recommendations on Prevention and Screening for Cervical Cancer
For Health Professionals**

Local epidemiology

Cervical cancer was the seventh commonest cancer among women in Hong Kong in 2018. A total of 582 new cases of cervical cancer were recorded in the year, accounting for 3.4% of all new cancer cases in women.¹ The age-standardised incidence rate (ASIR) of cervical cancer was 8.4 per 100,000 standard population^a. The median age at diagnosis was 54 years old and the age-specific incidence rates generally increase with age. Being the eighth leading cause of cancer deaths among women in 2019, cervical cancer caused 162 deaths, accounting for 2.6% of all female cancer deaths.² The age-standardised mortality rate (ASMR) of cervical cancer was 2.1 per 100,000 standard population.^a



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^a Rates were standardised to the Segi's world standard population (Segi, 1960).

2. Both ASIR and ASMR of cervical cancer showed a downward trend over the past three decades. Comparing with Asian countries, the latest ASIR of cervical cancer for Hong Kong was lower than that of Japan, but slightly higher than those of Korea and Singapore. While the latest ASMR for Hong Kong was lower than those for Singapore and Japan, it was higher than those of Korea and a number of developed Western economies.^{1,2,3}

Risk factors

3. Cervical cancer is caused by persistent infection with high-risk human papillomavirus (HPV), with HPV-16 and 18 accounting for about 70% of cervical cancer cases. In Hong Kong, HPV-16, 18, 31, 33, 45, 52 and 58 accounted for about 90% of cases of cervical cancer.⁴ About 90% of HPV infections usually clear up within 2 years and a small proportion of persistent infections would progress to cervical cancer in 15 to 20 years in women with normal immune systems.⁵

4. Risk factors for HPV acquisition/persistence or cervical cancer include: ^{6,7,8,9,10,11,12,13}

- (a) early first sexual intercourse
- (b) multiple sexual partners
- (c) tobacco use
- (d) chronic immunosuppression, e.g. HIV-infected individuals, recipients of organ transplant
- (e) increasing parity
- (f) younger age at full term pregnancy
- (g) long term use of oral contraceptive pills for more than five years (the risk declined after use ceased, and by 10 or more years returned to that of never users)

- (h) co-infection with sexually-transmitted diseases (such as chlamydia infection)

5. There is no evidence on increased risk of cervical intraepithelial neoplasia (CIN) in women receiving cytotoxic chemotherapy for non-genital cancers, estrogen antagonists such as tamoxifen, long term biologic agents.¹⁰

Primary prevention

6. Primary prevention is an important strategy to lower the risk of developing cervical cancer. The World Health Organization (WHO) recommends the introduction of HPV vaccination to national immunisation programmes and prevention of cervical cancer is best achieved through immunisation of girls prior to sexual debut.¹⁴ In Hong Kong, eligible female primary school students of suitable ages have been provided with HPV vaccine under the Hong Kong Childhood Immunisation Programme (HKCIP) starting from the 2019/20 school year to prevent cervical cancer.¹⁵ However, since HPV vaccines do not treat pre-existing HPV infection, nor do they offer a 100% protection from cervical cancer, HPV vaccination does not replace cervical cancer screening.⁴

7. Other preventive measures to reduce the risk of HPV infection include the practice of safe sex (such as avoid having multiple sexual partners and use condoms) to reduce the chance of contracting HPV and other sexually transmitted diseases,^{16,17} as well as abstinence from tobacco smoking.¹⁸

Early detection

8. Early stage of cervical cancer and pre-cancerous cell changes may

produce no symptoms at all. Common signs and symptoms of cervical cancer include abnormal vaginal bleeding (for example, between periods, during or after sex, and after menopause), vaginal discharge with foul smell, and discomfort or pain during sex. Women should visit doctors promptly if suspicious symptoms develop.

Screening for general female population

9. Screening can prevent cervical cancer by detecting and treating pre-cancerous abnormalities of the cervix.

(a) Cervical cytology

10. Cervical cytology, conducted by either conventional cytology (also known as cervical smear or Pap smear) or liquid-based cytology (LBC), has been a primary screening strategy in Hong Kong. A systematic review conducted by the U.S. Preventive Services Task Force established that LBC does not differ from conventional cytology in sensitivity, specificity, or relative CIN detection.¹⁹

11. According to a collaborative study of screening programmes in eight countries performed by the International Agency for Research on Cancer, the percentage reduction in cumulative incidence in women aged 35-64, who have been screened before age 35, is 93.5% when the interval between cervical smears is 1 year, 92.5% at 2 years, 90.8% at 3 years, 83.6% at 5 years and 64.1% at 10 years, assuming 100% compliance. Screening every one to two years provides little additional protection compared with screening every three years.²⁰

(b) HPV testing

12. HPV testing should only target at high-risk HPV types (e.g. HPV-

16, 18, 31, 33, 45, 52 and 58) as testing for low-risk HPV types has no clinical role in cervical cancer screening. Moreover, only clinically validated HPV tests should be used since the performance characteristics vary among HPV tests. Laboratory standard operating procedures and quality assurance programmes should be in place for use of any HPV testing procedures.²¹

13. Studies have shown that HPV testing has superior sensitivity and slightly lower specificity when compared with cervical cytology in detecting CIN grade 2 or worse (CIN2+).²² There is also evidence suggesting that HPV testing for high-risk types detected cervical precancerous lesions earlier than cytology.^{23,24,25,26} A pooled analysis of four European randomised controlled trials (RCTs) indicated HPV-based screening as co-testing (i.e. both HPV testing and cytology) was associated with 40% lower risk of cervical cancer when compared with cytology.²⁷ In addition, studies found that extension of screening interval to 5 years for HPV-based screening is scientifically sound because a baseline HPV-negative status was associated with lower cumulative risk of CIN2+/CIN3+ over 2-3 rounds than baseline cytology-negative status, demonstrating an extended period of protection against CIN2+/CIN3+ lesions.^{28,29,30}

14. Locally, the University of Hong Kong (HKU) has embarked on a RCT to investigate the effectiveness of co-testing for cervical cancer screening as compared to cytology alone in a sample of over 15,000 local Chinese women aged 30-60. Published in 2020, the HKU study had findings consistent with overseas RCT results and demonstrated that co-testing led to earlier detection of clinically significant pre-invasive lesions.³¹ In the baseline screen, the CIN2+ detection was 2.5 times higher in the co-testing group compared to the cytology group. In the subsequent round 3 years later, there was a 77% reduction in CIN2+ lesions. The total CIN2+ detection over 2 rounds were higher in the co-testing group.

15. Screening with primary high-risk HPV testing as a stand-alone test or co-testing was associated with more false-positive results and higher colposcopy rates.^{31,32} However, if HPV-positive results were triaged with cytology, the false-positive rates and colposcopy referral rates were similar to that for cytology.^{32,33} A second triage test such as cytology or HPV16/18 genotyping should be done to better predict which of these women would have a high risk of developing CIN2+ and hence need referral for colposcopy.²¹

16. Moreover, studies have shown that women younger than 30 years of age screened with primary high-risk HPV testing or co-testing had higher referral rates for colposcopy than women screened with cytology (2.3-13.1% vs. 1.9-4.7%).³² A modelling study suggested switching from cytology to high-risk HPV testing at age 30 years yielded the most efficient harm to benefit ratio when compared with switching at other younger ages using colposcopy as a proxy for harms.³⁴ Of note, HPV testing offers another benefit through opening the feasibility of self-sampling.³⁵

17. In recent years, an increasing number of overseas countries like Australia, the Netherlands, U.K. and U.S. implement or recommend HPV testing as the main or one of the primary screening tests for cervical cancer.^{36,37,38,39,40} Economic analyses from Australia and the U.K. predicted that a switch from cytology to HPV testing would be cost-effective in terms of its ability in reducing cervical cancer incidence and mortality and is associated with substantially lower annual healthcare cost in both HPV-vaccinated and unvaccinated cohorts.^{41,42} Local study on the cost-effectiveness of HPV testing is underway.

Screening for women at increased risk

18. Some studies have shown that cervical cancer screening among

persons with increased risk, such as HIV-positive women and renal transplant recipients, was effective in reducing the risk of pre-cancerous lesions and cervical cancer mortality.^{43,44} On the other hand, there is concern about potential harms associated with detection of mild cervical abnormalities^{45,46} which are common in younger age group, as the majority of which can be cleared on their own naturally. Although evidence on the benefit of cervical cancer screening for the younger age group is limited and inconsistent,^{47,48} there may be merit to screen women aged 21-24 with risk factors, based on individual risk assessment by doctors.

Revised recommendations by CEWG

19. After taking into consideration the local epidemiology, emerging scientific evidence, local and overseas screening practices, the CEWG has formulated the revised recommendations on cervical cancer screening which were endorsed by the Cancer Coordinating Committee at its 16th meeting on 18 June 2021. The revised recommendations for the local female population are as follows-

- (i) Women **aged 25 to 64** who ever had sexual experience are recommended to have regular cervical cancer screening.
- (ii) For women **aged 30 to 64**, cervical cancer screening by cytology every three years, after two consecutive normal annual screenings, continues to be recommended. Owing to the potential higher sensitivity, earlier and increased detection of precancerous lesions, better reduction in incidence of precancerous lesions and longer screening intervals and feasibility of self-sampling, HPV-based screening, either in the form of stand-alone primary high-risk HPV testing or co-testing, for screening average-risk women aged 30 years or above can be adopted as an alternative to cytology testing. Re-screening of HPV-negative cases is recommended

to be every five years. Triage is necessary to limit the higher false-positive rate and colposcopy rate associated with HPV-based testing and the Guidelines for Cervical Cancer Prevention and Screening by the Hong Kong College of Obstetricians and Gynaecologists provides references on recommended means of triage.²¹

- (iii) For women **aged 25 to 29**, cervical cancer screening by cervical cytology every three years, after two consecutive normal annual screenings, continues to be recommended.
- (iv) HPV testing should only target at high-risk HPV types (e.g. HPV-16, 18, 31, 33, 45, 52 and 58).
- (v) Cost effectiveness of adopting primary high-risk HPV testing has been well demonstrated in overseas' programmes/studies. In view of absence of local data on cost-effectiveness, further local study on cost-effectiveness analysis is proposed.

Summary of Revised CEWG Recommendations on Cervical Cancer Screening (June 2021)

(a) For asymptomatic population at Average risk

<p>Women aged 25 to 29 who ever had sexual experience</p>	<ul style="list-style-type: none"> ● Women aged 25 to 29 who ever had sexual experience are recommended to have cervical cancer screening by cytology every three years after two consecutive normal annual screenings.
<p>Women aged 30 to 64 who ever had sexual experience</p>	<ul style="list-style-type: none"> ● Women aged 30 to 64 who ever had sexual experience are recommended to have cervical cancer screening by <ul style="list-style-type: none"> (i) cytology every three years after two consecutive normal annual screenings; or

	<p>(ii) primary HPV testing every five years; or</p> <p>(iii) co-testing every five years.</p> <p>* clinically validated high-risk HPV testing should detect high-risk HPV types (e.g. HPV- 16, 18, 31, 33, 45, 52 and 58) in samples taken from cervix.</p>
<p>Women aged 65 or above who ever had sexual experience</p>	<ul style="list-style-type: none"> ● Screening may be discontinued in women aged 65 or above if routine screening within 10 years are normal. ● Women at or above 65 years of age who have never had cervical cancer screening should be screened.

(b) For persons at Increased risk

<p>Women aged 21 to 24 who ever had sexual experience</p>	<ul style="list-style-type: none"> ● Women aged 21 to 24 years who ever had sexual experience and with risk factors for HPV acquisition/persistence or cervical cancer are considered at increased risk. They may be screened by cytology every three years after two consecutive normal annual screenings, depending on doctor's assessment.
<p>Others</p>	<ul style="list-style-type: none"> ● Other women at high risk of developing cervical cancer may require more frequent screens based on doctor's assessment.

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