



Cancer Expert Working Group on Cancer Prevention and Screening

Recommendations on Prevention and Screening for Cervical Cancer For Health Professionals

Local epidemiology

1. Cervical cancer was the 8th commonest cancer among females in Hong Kong in 2014. There were 472 new cases of cervical cancer, accounting for 3.3% of all new cancer cases in the female population. The age-standardised incidence rate (ASIR) was 8.1 per 100,000 standard population. The median age at diagnosis was 52.5 years old.¹
2. Cervical cancer was the 8th leading cause of female cancer death in 2015. There were 169 deaths caused by cervical cancer, accounting for 2.8% of all cancer deaths in the female population. The age-standardised mortality rate (ASMR) was 2.5 per 100,000 standard population.² Over the past two decades, the age-standardised incidence and mortality rates of cervical cancer in Hong Kong showed a downward trend. More information on cervical cancer statistics can be found at the Centre for Health Protection (CHP) website: www.chp.gov.hk/en/content/9/25/56.html.
3. Comparing with Asian countries with organised cervical screening programmes such as the Republic of Korea, Japan and Singapore, Hong Kong had lower ASIR and ASMR for cervical cancer. Compared with those of Western countries such as United Kingdom, and United States, the ASIR was higher while the ASMR was comparable.

Risk factors

4. Cervical cancer is caused by persistent infection with high-risk human papillomavirus (HPV), with HPV 16 and HPV 18 accounting for about 70% of cervical cancer cases. It takes 15 to 20 years for cervical cancer to develop in women with normal immune systems.³

5. Risk factors for HPV acquisition/persistence or cervical cancer include:
- (a) early first sexual intercourse⁴
 - (b) multiple sexual partners⁵
 - (c) tobacco use⁶
 - (d) chronic immunosuppression, e.g. HIV-infected individuals,⁷ recipients of organ transplant⁸
 - (e) increasing parity⁹
 - (f) younger age at full term pregnancy¹⁰
 - (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)¹⁰
 - (h) co-infection with sexually-transmitted diseases (such as chlamydia infection)¹¹
- However, the most commonly neglected risk factor is failure to get a regular cervical cancer screen.

6. 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.⁸

Primary prevention

7. Primary prevention is an important strategy in lowering the risk of developing cervical cancer. Some preventive measures can help reduce the HPV infection and the progression from persistent HPV infection to cervical cancer:

- (a) Practise safer sex (such as avoid having multiple sexual partners and use condoms) to reduce the chance of HPV infection and to protect against sexually transmitted diseases
- (b) Do not smoke
- (c) Get HPV vaccination before initiation of sexual activity

Apart from the measures highlighted above, cervical cancer screening offers women additional protection.

8. HPV vaccines cannot offer a 100% full protection from cervical cancer. HPV vaccination does not replace the cervical cancer screening.¹² For details, please refer to the document “Consensus Statement on the use of Human Papillomavirus (HPV) Vaccine in prevention of cervical cancer” at CHP website: www.chp.gov.hk/en/sas1/101/110/102.html.

Early detection

9. 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. Individuals with these signs and symptoms should seek medical assessment and investigation.

Screening

10. Screening can prevent cervical cancer by detecting and treating pre-cancerous abnormalities of the cervix. World Health Organization recommends cervical cytology, HPV testing and visual inspection with acetic acid (VIA) as the screening tests for cervical cancer. Decision on the screening approach should be based on the cost-effectiveness and infrastructure of the local context.¹³

Cervical cytology

11. Currently, cervical cytology is a primary screening strategy for reducing cervical cancer mortality in Hong Kong. There are two methods to conduct cervical cytology – conventional cervical smear (also known as Pap smear) or liquid-based cytology (LBC) and both of them are acceptable.

12. 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 smear 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.¹⁴

13. Recent systematic review conducted by the U.S. Preventive Services Task Force also supported the use of conventional cytology or LBC for cervical cancer screening and both of them can reduce cervical successfully.¹⁵

HPV testing

14. Worldwide, HPV16 and HPV18 are the most frequent high-risk HPV genotypes, amounting to an estimated 53.5% and 17.2% of all cervical cancers respectively.¹⁶ HPV

testing for high-risk HPV types has been introduced as an alternative screening tool. HPV testing generally has higher sensitivity and can be done at longer intervals than cytology alone. However, HPV testing has lower specificity than cervical cytology in detecting cervical intraepithelial neoplasia II (CIN2) and CIN3. False-positive rates are higher among women younger than age 30 because of higher prevalence of transient HPV infection.¹⁵

15. The value of HPV testing can be three-fold:

- (a) as a triage of Atypical Squamous Cells of Undetermined Significance (ASCUS) cases for colposcopy ;
- (b) as primary screening either as a co-test with cytology or as a stand-alone test ;
- (c) as test of cure following treatment of CIN

16. Although HPV testing has been increasingly applied in primary screening either as a co-test with cytology or as a stand-alone test in some countries such as the United States,^{17,18} and Australia¹⁹, the efficacy and cost-effectiveness vary in different clinical and social-economical settings. Therefore, while more local data and cost-benefit analysis are needed to assess the applicability of HPV testing in Hong Kong, cervical cytology remains the most effective screening tool for population-based cervical cancer screening in Hong Kong.²⁰

Effectiveness of cervical cancer screening for women at increased risk

17. 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.^{21,22} On the other hand, there is concern about potential harms associated with detection of mild cervical abnormalities^{23,24} 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,^{25,26} there may be merit to recommend screening to women aged 21-24 with risk factors (such as those stated in para 5 above), based on individual risk assessment by doctors.

18. After taking into consideration local epidemiology, emerging scientific evidence, local and overseas screening practices, the Cancer Expert Working Group on Cancer Prevention and Screening (CEWG) has fine-tuned the recommendations on cervical cancer screening in June 2016 as follows:

<i>For asymptomatic population at average risk</i>	
1.	Women aged 25 to 64 who ever had sexual experience are recommended to have cervical cancer screening by cytology every three years after 2 consecutive normal annual smears.
2.	Screening may be discontinued in women aged 65 or above if three previous consecutive smears within 10 years are normal.
3.	Women at or above 65 years of age who have never had a cervical smear should have the test.
<i>For persons at increased risk</i>	
4.	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 2 consecutive normal annual smears, depending on doctor's assessment.
5.	Other women at high risk of developing cervical cancer may require more frequent screens based on doctor's assessment.

Cervical Screening Programme

19. The Government of Hong Kong Special Administrative Region launched the territory-wide Cervical Screening Programme (CSP) on 8 March 2004 in collaboration with healthcare professionals in the public, private and non-governmental sectors to facilitate and encourage women aged 25 to 64 who ever had sexual experience to receive regular cervical cancer screening by cytology every three years after two consecutive normal screens. The screening policy adopted by the CSP is in line with the CEWG's recommendation.

20. A computerised central registry, the Cervical Screening Information System (CSIS), has been established for storing all the data related to CSP, including participants' personal identification data, smear results and date of next smear recommended by healthcare professionals. Registrants of CSP can login to the CSIS to view their cervical smear records and will receive reminder letter before the next smear is due. Healthcare professionals who have registered with the CSP can view the past smear records upon authorisation by the registrants so as to provide better continual health care. For details, please visit the CSP website: www.cervicalscreening.gov.hk.

**Cancer Expert Working Group on Cancer Prevention and Screening
May 2018**

The copyright of this paper belongs to the Cancer Expert Working Group on Cancer Prevention and Screening, the Government of Hong Kong Special Administrative Region. Contents of the paper may be freely quoted for educational, training and non-commercial uses provided that acknowledgement be made to the Working Group. No part of this paper may be used, modified or reproduced for purposes other than those stated above without prior permission obtained from the Working Group.

References

- ¹ Hong Kong Cancer Registry, Hospital Authority. Cervical Cancer in 2014. Available from: https://www3.ha.org.hk/cancereg/pdf/factsheet/2014/cx_2014.pdf.
- ² Department of Health and Census and Statistics Department, HKSAR. Mortality Statistics, 2015.
- ³ World Health Organization. Fact sheet on Human papillomavirus (HPV) and cervical cancer. June 2016. Available from: <http://www.who.int/mediacentre/factsheets/fs380/en/>.
- ⁴ Plummer M, Peto J, Franceschi S, International Collaboration of Epidemiological Studies of Cervical Cancer. Time since first sexual intercourse and the risk of cervical cancer. *Int J Cancer*. 2012;130(11):2638-2644.
- ⁵ International Collaboration of Epidemiological Studies of Cervical Cancer. Cervical Carcinoma and Sexual Behavior: Collaborative Reanalysis of Individual Data on 15,461 Women with Cervical Carcinoma and 29,164 Women without Cervical Carcinoma from 21 Epidemiological Studies. *Cancer Epidemiol Biomarkers Prev*. 2009;18:1060-1069.
- ⁶ International Collaboration of Epidemiological Studies of Cervical Cancer. Carcinoma of the cervix and tobacco smoking: Collaborative reanalysis of individual data on 13,541 women with carcinoma of the cervix and 23,017 women without carcinoma of the cervix from 23 epidemiological studies. *International Journal of Cancer*. 2006;118(6):1481-1495.
- ⁷ Ellerbrock TV, Chiasson M, Bush TJ, et al. Incidence of cervical squamous intraepithelial lesions in HIV-infected women. *JAMA*. 2000;283(8):1031-1037.
- ⁸ Public Health England. NHS Cervical Screening Programme. *Colposcopy and Programme Management*. Third Edition. March 2016. Available from: https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/515817/NHSCSP_colposcopy_management.pdf.
- ⁹ International Collaboration of Epidemiological Studies of Cervical Cancer. Cervical carcinoma and reproductive factors: Collaborative reanalysis of individual data on 16,563 women with cervical carcinoma and 33,542 women without cervical carcinoma from 25 epidemiological studies. *International Journal of Cancer*. 2006;119(5):1108-1124.
- ¹⁰ International Collaboration of Epidemiological Studies of Cervical Cancer. Cervical cancer and hormonal contraceptives: collaborative reanalysis of individual data for 16 573 women with cervical cancer and 35 509 women without cervical cancer from 24 epidemiological studies. *The Lancet*. 2007;370(9599):1609-1621.
- ¹¹ Ault KA. Epidemiology and Natural History of Human Papillomavirus Infections in the Female Genital Tract. *Infectious Diseases in Obstetrics and Gynecology*. 2006;2006:40470.
- ¹² Centre for Health Protection, Department of Health, Hong Kong SAR. Scientific Committee on Vaccine Preventable Diseases and Scientific Committee on AIDS and STI. Consensus Statement on the use of Human Papillomavirus (HPV) Vaccine in prevention of

-
- cervical cancer. September 2016. Available from: http://www.chp.gov.hk/files/pdf/consensus_statement_on_the_use_of_hpv_vaccine_in_prevention_of_cervical_cancer.pdf.
- ¹³ World Health Organization (WHO). *Comprehensive Cervical Cancer Control A guide to essential practice – Second Edition*. Australia: WHO; 2014.
- ¹⁴ IARC Working Group on Evaluation of Cervical Cancer Screening Programmes. Screening for squamous cervical cancer: duration of low risk after negative results of cervical cytology and its implication for screening policies. *British Medical Journal*. 1986;293:659-664.
- ¹⁵ Whitlock EP, Vesco KK, Eder M, et al. Liquid-based cytology and human papillomavirus testing to screen for cervical cancer: A systematic review for the U.S. Preventive Services Task Force. *Annals of Internal Medicine*. 2011;155:687-697.
- ¹⁶ Castellsague X. Natural history and epidemiology of HPV infection and cervical cancer. *Gynecol Oncol*. 2008 Sep;110(3 Suppl 2):S4-7.
- ¹⁷ Screening for Cervical Cancer: U.S. Preventive Services Task Force (USPSTF) Recommendation Statement. March 2012. Available from: <http://www.uspreventiveservicestaskforce.org/Page/Topic/recommendation-summary/cervical-cancer-screening>.
- ¹⁸ Saslow D, and ACS-ASCCP-ASCP Cervical Cancer Guideline Committee (2012) et al. American Cancer Society, American Society for Colposcopy and Cervical Pathology, and American Society for Clinical Pathology screening guidelines for the prevention and early detection of cervical cancer. *CA: A Cancer Journal for Clinicians*, 62: 147–172.
- ¹⁹ Webpage on Australian Government National Cervical Screening Program. <http://www.cancerscreening.gov.au/internet/screening/publishing.nsf/Content/cervical-screening-1>.
- ²⁰ The Hong Kong College of Obstetricians and Gynaecologists (HKCOG), *Guidelines for cervical cancer prevention and screening*. Revised November 2016. Available from: http://www.hkcog.org.hk/hkcog/Download/Cervical_Cancer_Prevention_and_Screening_revised_November_2016.pdf.
- ²¹ Kuhn L, Wang C, Tsai WY, Wright TC, Denny L. Efficacy of human papillomavirus-based screen-and-treat for cervical cancer prevention among HIV-infected women. *AIDS*. 2010 Oct 23;24(16):2553-61.
- ²² Wong G, Howard K, Webster A, Chapman JR, Craig JC. The Health and Economic Impact of Cervical Cancer Screening and Human Papillomavirus Vaccination in Kidney Transplant Recipients. *Transplantation*. 2009;87(7):1078-1091.
- ²³ Arbyn M, Kyrgiou M, Simoens C, et al. Perinatal mortality and other severe adverse pregnancy outcomes associated with treatment of cervical intraepithelial neoplasia: meta-analysis. *BMJ*. 2008-09-18 11:24:04 2008;337.

-
- ²⁴ Watson LF, Rayner JA, King J, et al. Intracervical procedures and the risk of subsequent very preterm birth: a case–control study. *Acta Obstet Gynecol Scand.* 2012;91:204–10.
- ²⁵ Andrae B, Kemetli L, Sparen P, Silfverdal L, Strander B, Ryd W, et al. Screening-preventable cervical cancer risks: evidence from a nationwide audit in Sweden. *J Natl Cancer Inst* 2008;100:622-9.
- ²⁶ Sasieni P, Castanon A, Cuzick J. Effectiveness of cervical screening with age: population based case-control study of prospectively recorded data. *BMJ.* 2009;339:b2968.