Topical Health Report
No. 4

Prevention and Screening of
Cervical Cancer

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Foreword

At the end of 2003, the population of Hong Kong was 6.8 million and more than 50% of the population (3.5 million) were females. The life expectancy of women at birth has been increasing over the past two decades, reaching 84.3 years in 2003.

Cancer is a major public health problem in Hong Kong. In 2001, there were 9 531 new cases of cancer in women, giving an age-standardized incidence rate of 216 per 100 000 women. Cancer is also the leading cause of deaths among females in Hong Kong, accounting for 4 306 deaths in 2001. Cervical cancer is the fifth most common cancer and the eighth leading cause of cancer deaths among women in Hong Kong, registering 438 new cases and 128 deaths in 2001.

Cervical cancer may be prevented primarily by controlling the causes and risk factors of the disease such as practising safer sex, avoiding smoking and adopting healthy lifestyle. It has also been shown that a population-based cervical screening programme is effective in reducing cervical cancer mortality and morbidity. Pre-cancerous lesions can be readily detected by cervical screening and early treatment may prevent the development of cervical cancer. However, cervical screening is currently performed on an opportunistic basis and coverage of at-risk women is rather low in Hong Kong.

This Report highlights the importance of primary prevention for cervical cancer and the role of regular cervical screening in the prevention of the disease. It aims to provide information for the health care professionals. Women's groups, non-governmental organizations as well as the general public will also find the information in the Report useful.

The Government is committed to improving women's health. The Chief Executive's Policy Address in 2001 pledged to launch a territory-wide Cervical Screening Programme for women, with a view to increasing the coverage of women having cervical smears and ultimately to achieving a reduction in the incidence and mortality of cervical cancer in Hong Kong. The Department of Health has launched the Cervical Screening Programme on 8 March 2004. We look forward to working in partnership with health care providers in the public and private sectors to achieve our common goal of improving women's quality of life.

Dr P Y LAM
Director of Health

This report is part of a series of

Topical Health Reports issued regularly

by the Surveillance and Epidemiology Branch,

Centre for Health Protection, Department of Health

Contents

Report Highlights

Disease Burden and Risk Factors of Cervical Cancer

➢ Cervical cancer is the second most common cancer among females and is a leading cause of cancer deaths in females worldwide.

➢ In Hong Kong, cervical cancer is the fifth most common cancer and the eighth leading cause of cancer death in females in 2001.

➢ Cervical cancer is affecting women of relatively young age. The median age at diagnosis is 52 years old, compared to 65 years old for all cancers in women in 2001.

➢ The age-standardized incidence and mortality rates of cervical cancer had decreased substantially over the period 1971-2001.

➢ Although the burden of cervical cancer in Hong Kong has been decreasing, its incidence and mortality rank high when compared to those in many developed countries where organized screening programmes have been established.

➢ Human papillomavirus (HPV) infection has been established as a cause of cervical cancer and its precursor lesions.

➢ Smoking is an independent risk factor for development of cervical cancer even after adjusting for the effect of HPV infection.

➢ Other established risk factors associated with cervical cancer include early age at first intercourse, having multiple sexual partners or a partner with multiple sexual partners, high parity, low intake of vegetables and fruits, long-term use of oral contraceptives, history of genital tract infections, increasing age and low socio-economic status.

Pre-malignant and Malignant Disease of the Cervix

➢ Cervical cancer arises as a consequence of progression from mild dysplasia through severe dysplasia to carcinoma-in-situ and carcinoma.

➢ Majority of low-grade cervical intraepithelial neoplasia (CIN) will revert to normal spontaneously over 2 years. About 5%–10% of high-grade CIN may progress to cervical cancer over months to years.

➢ Majority of the CIN lesions are asymptomatic and can only be detected by cervical screening.

➢ Treatment of CIN includes loop electro-surgical excision procedure (LEEP), cryosurgery, laser vaporization, cold coagulation and electrocoagulation diathermy.

➢ Treatment of the premalignant lesions may reduce the risk of cervical cancer by 95%.

➢ 90% of cervical carcinoma are of squamous cell origin and majority arise from the squamous-columnar junction.

➢ Early symptoms of cervical cancer include irregular vaginal bleeding, post-coital bleeding and foul vaginal discharge.

➢ The mainstay of treatment for cervical cancer is radiotherapy followed by surgery and chemotherapy.

Primary Prevention of Cervical Cancer

➢ Primary prevention of cervical cancer aims at reducing the incidence of cervical cancer by controlling the causes and risk factors.

➢ Condom use has been associated with lower rate of cervical cancer.

➢ Limiting the number of sexual partners reduces the risk of cervical cancer.

➢ Avoiding or quitting smoking and minimizing exposure to environmental tobacco smoke can reduce the risk of cervical cancer.

➢ Diet rich in fresh vegetables and fruits may help reduce the risk of cervical cancer.

➤ Health promotion activities on sexual health, smoking cessations and healthy diet organised by Government and non-government organisations in Hong Kong contribute to the prevention of cervical cancer.

➤ Vaccines against HPV, both for prophylactic and therapeutic use, are still under development.

Secondary Prevention of Cervical Cancer

➤ Most women who develop cervical cancer are not screened.

➤ The largest gain in reducing cervical cancer incidence and mortality could be attained by increasing the coverage of women who are currently unscreened or screened only infrequently.

➤ Cervical cytology is the only test known to reduce cervical cancer incidence and mortality, particularly with organized screening programmes.

➤ Both the conventional and the liquid-based cytology methods for smear examination are acceptable.

➤ HPV test is not recommended as a screening tool for asymptomatic women in view of its low positive predictive value and low specificity.

➤ Visual inspection of the cervix with acetic acid wash and cervicography have low sensitivity and specificity and are not recommended as screening tests.

Local Situation on Cervical Screening

➤ Currently cervical screening is performed on an opportunistic basis.

➤ The coverage of the current cervical screening is low, around 45%. The better educated and health-conscious women are more likely to receive screening. A systematic and organized screening programme should be more equitable and cost-effective.

➤ Facilitators to cervical screening for women include support from family and friends, practitioner's advice and communication skill, female practitioner, information and publicity, higher accessibility and affordability of service.

- Barriers to cervical screening for women include embarrassment, anxiety, lack of knowledge, perceived no need, high cost, inconvenient time and place.

- Smear-taker should be adequately trained to ensure proper techniques in smear taking and preparation.

- Accreditation of cytology laboratories would help improve the diagnostic and reporting standards.

Cervical Screening Programme in Hong Kong

- A Cervical Screening Programme (CSP) was launched by the Department of Health in collaboration with health care providers in the public and private sectors on 8 March 2004.

- Women aged 25-64 years who have ever had sex should receive regular cervical screening.

- If the first two yearly smears show no abnormality, women should be re-screened every three years till 64 years old.

- Invitation letters and mass publicity campaigns help recruit women for cervical screening.

- Quality management guidelines and performance indicators have been developed to ensure quality of service providers and laboratories.

- The Cervical Screening Information System (CSIS) serves as a central registry for cervical smear results. The effectiveness of CSIS depends on complete and accurate data submitted by health care professionals, laboratories and women.

- Collaboration between the public and private sectors in the planning, implementation and continuous improvement of the programme would contribute to the success of CSP.

Chapter 1 Introduction

1.1   Global Burden of Disease

Cervical cancer is the second most common cancer among women worldwide, with 470 000 new cases diagnosed each year.[1]   Although the incidence and mortality of cervical cancer have declined substantially over the last four decades, cervical cancer continues to be one of the leading causes of cancer deaths in women,[2] with about 230 000 deaths every year.[1]   About 80% of all cervical cancer cases and deaths occur in developing countries, including those of Latin America, sub-Saharan Africa and Southeast Asia.[2]   This disproportionate burden of cervical cancer is probably due to the absence of well-organized screening programmes in these countries.

1.2   Local Burden of Disease

1.2.1   Incidence

In Hong Kong, cervical cancer is the fifth most common cancer among females (ranked after breast cancer, lung cancer, colon cancer and rectal cancer). A total of 438 cases of cervical cancer were diagnosed in 2001.[3]   Cervical cancer accounts for 4.6% of all new cancers in females.   The age-standardized incidence rate[*] was 10.1 per 100 000 women.

1.2.2   Mortality

Cervical cancer ranked eighth as a cause of cancer deaths among females (after lung cancer, breast cancer, colon cancer, liver cancer, stomach cancer, rectal cancer and pancreatic cancer) in Hong Kong in 2001.   A total of 128 deaths were due to cervical cancer in 2001.[4]   It accounts for 3.0% of all cancer deaths in females.   The age-standardized mortality rate* was 2.8 per 100 000 standard population.   The potential years of life lost (PYLL) before 75 years of age due to cervical cancer is 1 713 accounting for 4.4% of total PYLL before 75 years from all cancers among females.

1.2.3   Age distribution

Cervical cancer is affecting relatively young women.   In 2001, the median age at diagnosis of cervical cancer was 52 years which is 13 years earlier than the median age at diagnosis of 65 years for all cancers in females.[3]

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[*] *Standardization is according to 1997-99 World Health Statistics Annual*

In general, the burden of cervical cancer increases with age. The average age-specific incidence and mortality rates of cervical cancer based on pooling of data for the 5-year period 1997-2001 are presented in Figure 1.1. Both incidence and mortality rates are very low before 25 years of age, but rise sharply afterwards. The peak incidence rate is at the age group 75-79 years while the peak mortality rate is at the age group 80-84 years.

1.2.4   Trends of incidence and mortality

Figure 1.1   Average Age-specific Incidence and Mortality Rates* of Malignant Neoplasm of Cervix Uteri, 1997-2001
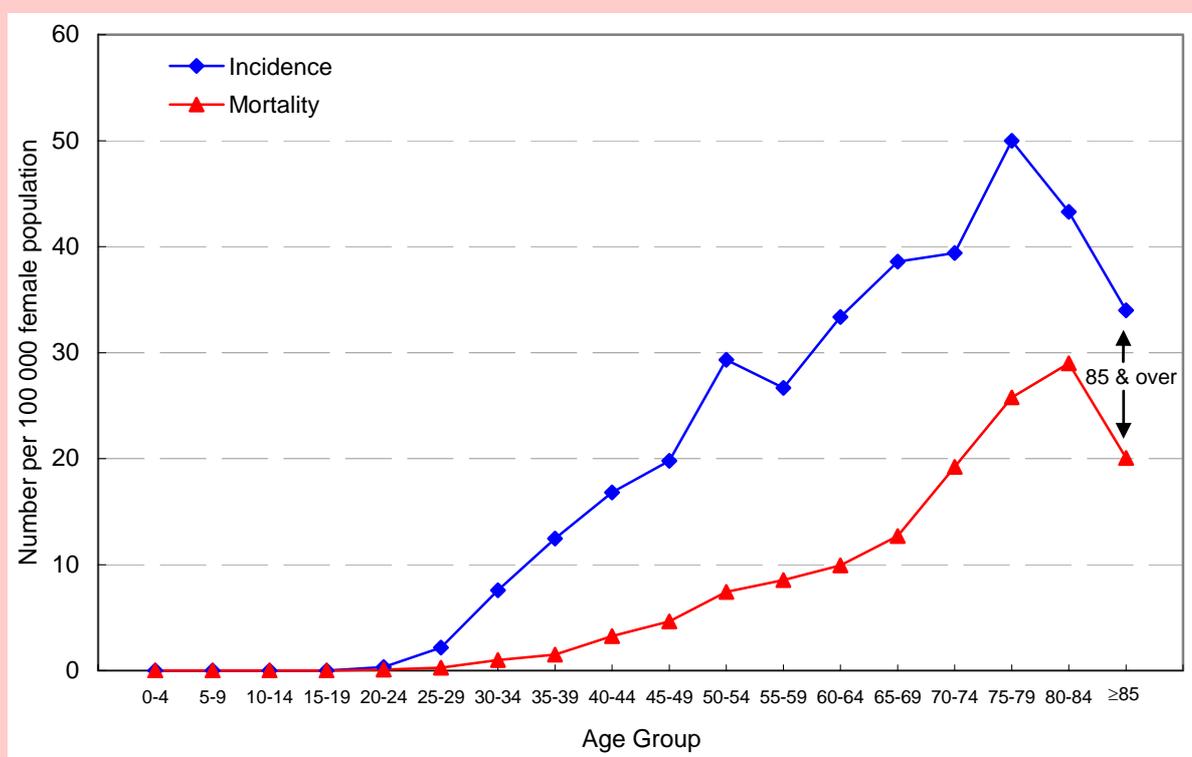
Notes:

*   The average age-specific rates are based on pooling of data for 5 years to remove random fluctuations in individual year. The rates are computed as the average number of new cases (deaths) over the 5-year period divided by the mid-period female population in each age group.

Sources: Hong Kong Cancer Registry, Hospital Authority
Department of Health, Hong Kong SAR
Census and Statistics Department, Government of Hong Kong SAR

Since 1977, the number of new cases of cervical cancer has been decreasing slowly but the number of deaths has been relatively stable (Figure 1.2). Although the actual numbers are stable, both the age-standardized incidence and mortality rates have decreased substantially over the years (Figure 1.3). The

average annual percent changes[*] in the age-standardized incidence and mortality rates, after removing fluctuation in individual years, were -4.3% and -3.0% per annum respectively during the years 1983-2001.

Factors contributing to these decreasing trends include increased screening among women in middle age groups where this downward trend is the most significant, as shown in Figure 1.4.   In 1983-2001, the age-specific incidence rates of cervical cancer decreased by 70.4% for women aged 40-64 years.[3]

Figure 1.2   **Number of Registered Deaths and Number of New Cases of Malignant Neoplasm of Cervix Uteri, 1971-2002**

Note :   Figure for new cases in 2002 not available

Sources: Hong Kong Cancer Registry, Hospital Authority
Department of Health, Government of Hong Kong SAR
Census and Statistics Department, Hong Kong SAR

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[*]   The average annual percent change is calculated by fitting a linear regression model to the age-standardized rates against time after logarithmic transformation assuming a constant rate of change in the rates.   It is standardized to the World Standard Population published in the 1997-99 World Health Statistics Annual.

Figure 1.3   Age-standardized Death Rate and Age-standardized Incidence Rate* of Malignant Neoplasm of Cervix Uteri, 1971-2002
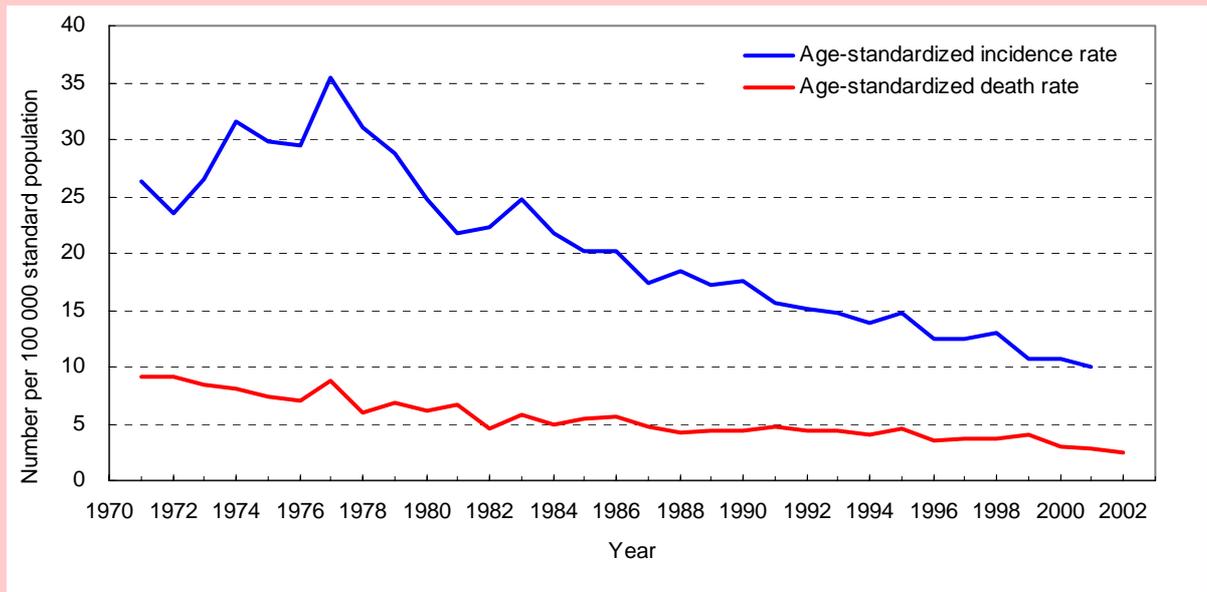
Notes:

*   The age-standardized incidence and death rates are standardized to the World Standard Population published in the 1997-99 World Health Statistics Annual.

Figure for age-standardized incidence rate in 2002 not available.

Sources: Hong Kong Cancer Registry, Hospital Authority
Department of Health, Government of Hong Kong SAR
Census and Statistics Department, Hong Kong SAR

Figure 1.4   Trend of Average Age-specific Incidence Rates* of Malignant Neoplasm of Cervix Uteri, 1983-2001

Notes:

*   The average age-specific rates are based on pooling of data for 5 years to remove random fluctuations in individual year. The rates are computed as the average number of new cases over the 5-year period divided by the mid-period female population in each age group.
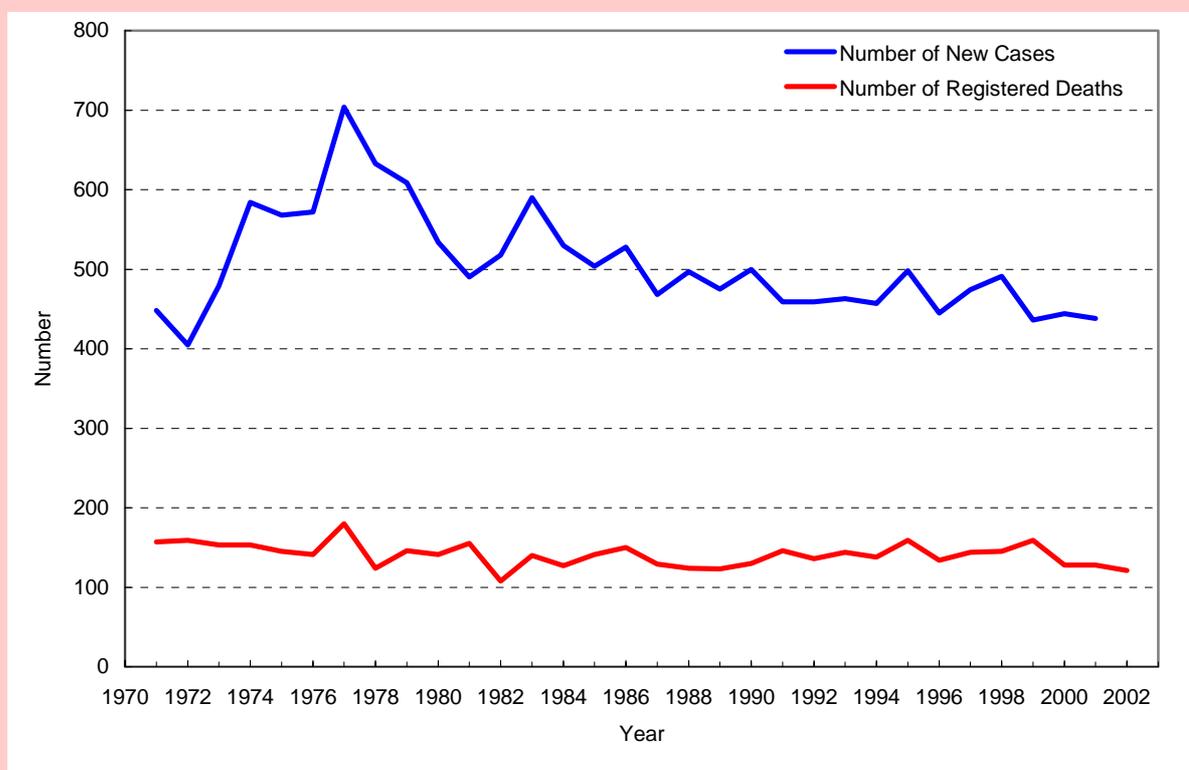
Sources: Hong Kong Cancer Registry, Hospital Authority
Department of Health, Hong Kong SAR
Census and Statistics Department, Government of Hong Kong SAR

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1.2.5　　Morbidity

Hospitalization of women with cervical cancer decreased slightly in the 1990's. The number of in-patient discharges and deaths from the disease was around 2 500 per year in the first half of 1990's and decreased by over 20% to 1 901 in year 2001 (Figure 1.5).[5] During the decade, the number of in-patient discharges and deaths from the private sector remained relatively stable at around 200 per year. The rate of in-patient discharges and deaths decreased by one-third in the past 10 years. This can be explained by the growing population and the decreasing number of patients.

Figure 1.5　Number and Rate of In-patient Discharges and Deaths from Malignant Neoplasm of Cervix Uteri, 1992–2001
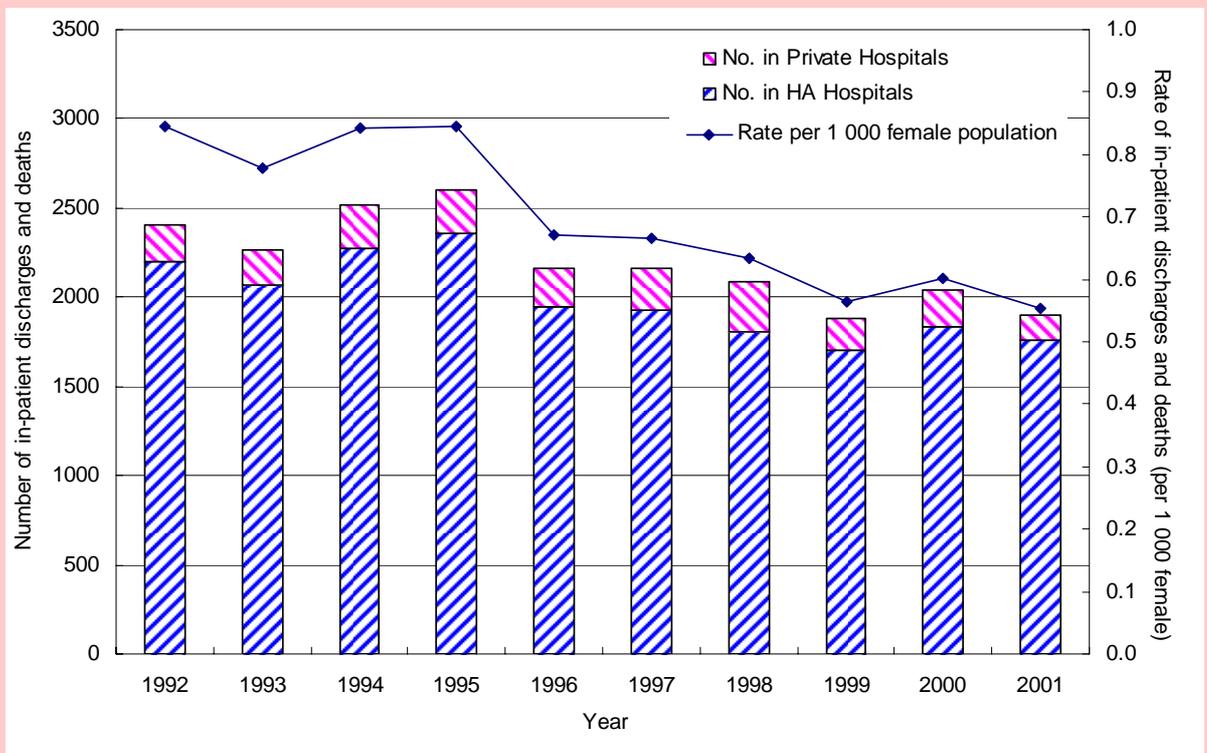
Sources:　Hospital Authority, Hong Kong SAR
Department of Health, Government of Hong Kong SAR
Census and Statistics Department, Hong Kong SAR

1.2.6   The local burden of cervical cancer is summarized in Table 1.1.

Table 1.1   Some Facts on Cervical Cancer in 2001

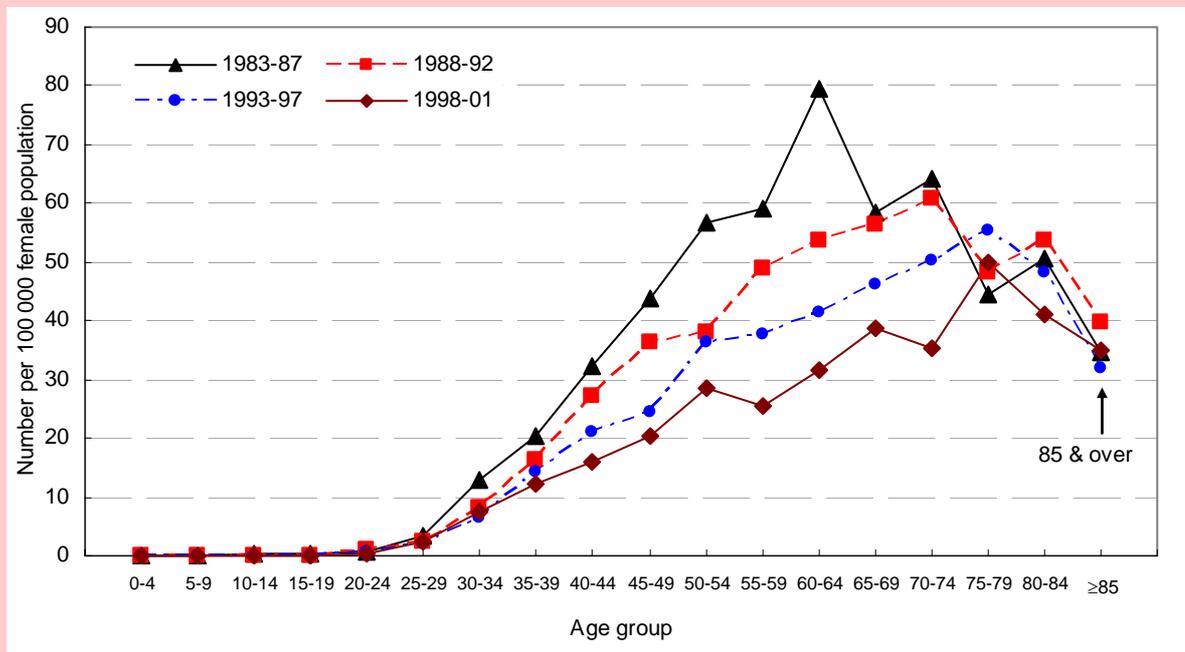| **New cases**	
Number of new cases	438
Ranking of cervical cancer in female cancers	5
Incidence rate (per 100 000 female population)	12.7
Age-standardized incidence rate* (per 100 000 female standard population)	10.1
Incidence trends (1983-2001)[†]	-4.3% p.a.
% of all female cancer new cases[‡]	4.6
Cumulative lifetime risk (0-74 years)[‡§]	1 in 104
Median age at diagnosis (years)[‡]	52
Death	
Number of deaths	128
Ranking of cervical cancer in female cancers	8
Mortality rate (per 100 000 female population)	3.7
Age-standardized mortality rate* (per 100 000 female standard population)	2.8
Mortality trends (1983-2001)[†]	-3.0% p.a.
Potential years of life lost (0-74 years)	1 713 (4.4% in females)
% of all female cancer deaths[‡]	3.0
Cumulative lifetime risk (0-74 years)[‡§]	1 in 349
Median age at death (years)[‡]	66

*   The age-standardized incidence and mortality rates are standardized to The World Standard Population published in the 1997-99 World Health Statistics Annual.

[†]   The incidence and mortality trends are the average annual percent change (AAPC) in the age-standardized incidence and mortality rates respectively. The AAPC is calculated by assuming a constant rate of change in the age-standardized rates after logarithmic transformation.

[‡]   Source: Hong Kong Cancer Registry.

[§]   The cumulative lifetime risk (0-74 years) is a measure of the risk of an individual who would have been developing (or dying from) a particular cancer during his/her whole life span, usually taken as 0-74 years.

1.3 International Comparison

Although the burden of cervical cancer in Hong Kong is falling, its incidence and mortality rank high when compared to those in developed countries where organized screening programmes have been established (Figure 1.6).

In terms of cancer incidence, the rate in Hong Kong is higher than that in all selected countries except Singapore. For instances, in 1999, the age-standardized incidence rates of cervical cancer in the United Kingdom, Canada, Australia and Finland ranged from 3.8-7.5 per 100 000 women which are 23%-61% below the corresponding rate in Hong Kong. On the other hand, the age-standardized mortality rates in these countries ranged from 1.3-2.3 per 100 000 women, which are again substantially below the rate in Hong Kong.

Moreover, the reduction of the age-standardized incidence rate for cervical cancer over the years is below that in developed countries where screening programmes have been well organized. For example, the age-standardized incidence and mortality rates in Finland had been reduced by 80% from 1963 to 1990[6] and in British Columbia, Canada, by 70-80% from 1955 to 1985,[7] as compared to only 50% in Hong Kong from early 1980's to 1999.

Figure 1.6   International Comparison of Age-standardized Incidence and Mortality Rates of Malignant Neoplasm of Cervix Uteri (ICD9: 180/ICD10: C53)

Age-standardized incidence rates

Country	Rate
Singapore (1993-1997)[1]	14.2
Hong Kong (2000)[2]	9.7
Ireland (1998)[3]	9.5
Germany (1998)[3]	9.4
US(SEER) - Black (1996-2000)[4]	9.4
Norway (2000)[5]	9.3
New Zealand (1999)[6]	9.2
European Union (1998)[3]	8.1
England (1999)[7]	7.5
Sweden (2000)[8]	7.0
Canada (1999)[9]	6.7
The Netherlands (1998)[10]	6.5
US(SEER) - White (1996-2000)[4]	6.4
Australia (1999)[11]	6.3
Finland (1999)[12]	3.8

Rates (per 100 000 standard population)

Age-standardized mortality rates

Country	Rate
US - Black (1996-2000)[4]	4.2
Singapore (1998)[13]	4.1
Ireland (1998)[3]	3.5
Norway (1997)[13]	3.2
European Union (1998)[3]	2.8
New Zealand (1999)[6]	2.7
Hong Kong (2000)[2]	2.6
Germany (1999)[13]	2.6
England and Wales (2001)[14]	2.3
US - White (1996-2000)[4]	2.0
Sweden (2000)[15]	1.9
Canada (1997)[13]	1.9
The Netherlands (1999)[13]	1.8
Australia (1999)[11]	1.6
Finland (1999)[12]	1.3

Rates (per 100 000 standard population)

Notes

1.   All age-standardized incidence and mortality rates were standardized to the World Standard Population published in the 1996 World Health Statistics Annual.

2.   Incidence and mortality rates under US (SEER) represented the rates reported by the US Surveillance, Epidemiology and End Results (SEER) Programme, based within the Cancer Surveillance Research Programme at the National Cancer Institute (NCI).

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1.4 Risk Factors

1.4.1 Human papillomavirus infection

The causal link between some types of human papillomavirus (HPV) infection and cervical cancer has been established.[8] Epidemiological studies that evaluated risk factors of squamous intraepithelial lesions (SIL) and cervical malignancy demonstrated conclusively a sexual mode of transmission of a carcinogen. It is now widely accepted that HPV is strongly implicated epidemiologically as the primary aetiologic infectious agent.[9]

The finding of HPV viral DNA integrated in the majority of cellular genomes of cervical carcinomas supported the epidemiological evidence that linked this agent to cervical cancer. Epidemiological evidences of different polymerase chain reaction protocols found that the prevalence of HPV DNA in cervical tumours is over 90%[10] in studies using the most sensitive HPV detection methods, which supports the claim that HPV is the causative agent.[11-13] The presence of HPV DNA in virtually all cases of cervical intraepithelial neoplasia (CIN) has also been shown.[12]

Studies have shown that up to 70% of all sexually active women have been infected by HPV, although most of them do not develop cervical cancer.[14] There are over 100 distinct types of HPV identified and approximately 40 of them are known to infect the human genital tract. Epidemiological studies suggest that at least 14 of these, called oncogenic or high-risk types, are significantly associated with progression to cervical cancer.[15] The high oncogenic risk group includes HPV 16, 18, 45 and 56, the intermediate group includes HPV 31, 33, 35, 52 and 58 and the low-risk group includes 6, 11, 42, 43 and 44.[1]

In a meta-analysis of worldwide prevalence of HPV types, two-thirds of cervical cancer cases were associated with HPV-16 (51%) or HPV-18 (16%) infection.[14] More than 16 other HPV types were also associated with cervical cancer and collectively accounted for 18.3% of cases. Prevalence of specific HPV types varies with geographical region. In Asia, HPV-58 and HPV-52 are more prevalent and are found in nearly 10% of all cervical cancer cases, compared to less than 1% in North America and Australia or 3.4% worldwide.[14]

Based on the recent International Agency for Research on Cancer (IARC) multicentric study, an estimate of the pooled odds ratio for cervical cancer associated with the presence of any HPV was 158.2 (95% CI: 113.4 to 220.6).[16] The corresponding risk estimates for HPV16 and HPV18 were 434.5 (95% CI: 278.2 to 678.7) and 248.1 (95% CI: 138.1 to 445.8) respectively.

1.4.2   Number of sexual partners

The lifetime number of sexual partners has been found to be associated with increased risk of both squamous cell carcinoma and adenocarcinoma of the cervix.[9,17] There has been evidence from case-control studies that women with cervical cancer more frequently reported multiple sexual partners than controls. Moreover, the risk appears to increase directly with the reported number of sexual partners.[9] The risk associated with 10 or more partners has been reported to be nearly three times higher than that associated with one or a few partners.

The effect of increasing lifetime number of sexual partners is found to be stronger for squamous cell carcinoma than for adenocarcinoma.[17] For women reporting five or more partners compared to those with one partner, the odds ratio for squamous cell carcinoma is 4.09 (95% CI: 2.75-6.08), whereas the odds ratio for adenocarcinoma is 1.98 (95% CI: 1.21-3.26).

In addition, the role of the male in the causation of cervical cancer had also been examined by comparing the sexual characteristics of husbands of cervical cancer cases with husbands of women free of the disease. In most studies, the husbands of cases reported significantly more sexual partners than husbands of controls.[9]

1.4.3   Age at first sexual intercourse

Women having sexual intercourse at early age are at higher risk of cervical cancer than women who have sexual experience later in life.[9,17,18] Several case-control studies have shown that women with first sexual experience before the age of 16 have about twice the risk compared to women who start sexual intercourse after the age of 20.[9] The risk of cervical cancer associated with earlier age at first intercourse is higher for both squamous cell carcinoma and adenocarcinoma, with odds ratio of 2.70 (95% CI: 1.78-4.11) and 2.01 (95% CI: 1.23-3.30) respectively.[17]

1.4.4 Presence of other sexually-transmitted diseases

History of having sexually-transmitted diseases (STD) is associated with an increased risk of cervical cancer.[9,18] Multiple STD have been found to be a risk factor for cervical cancer even after adjustment for HPV infection suggesting that non-HPV STD may act as HPV cofactors.[19] Sexually-transmitted pathogens other than HPV and cervical inflammation may influence the natural history of HPV infection along the pathways of persistence, progression or regression.[20]

A case-control study found that, among oncogenic HPV-infected women, antibodies to *Chlamydia trachomatis* were associated with a two-fold increased risk of cervical cancer.[21] However, because of poor adjustment for HPV, the conclusion for this study was difficult to interpret. Another recent multicentric case-control study had provided strong evidence for herpes simplex virus type 2 infection as an HPV cofactor.[22] Although there is strong evidence that these STD increase the risk of cervical cancer, further studies are required to confirm whether infections by these STD are surrogates for high risk behaviour that increases exposure to HPV.

Human Immunodeficiency Virus (HIV) damages the immune system and causes the Acquired Immunodeficiency Syndrome (AIDS). Women with HIV infections are significantly at higher risk of cervical cancer than women not infected with HIV.[23]

1.4.5 Cigarette smoking

Cigarette smoking has long been found associated with an increased risk for squamous cell carcinoma of the cervix.[24] The effect of smoking is not diminished by the adjustment for HPV or analysis restricted to cases and controls both positive for HPV. There is now sufficient evidence to establish a causal association of squamous cell cervical carcinoma with smoking.[25]

From a pooled analysis of multi-centric case-control studies conducted by the IARC[24], the risk of cervical cancer for ever smoking among HPV-positive women was increased by more than 100% (OR=2.17 95% CI: 1.46-3.22). The risk for cervical neoplasia increased with longer duration and intensity of smoking and exposure to environmental tobacco smoke. Ex-smokers, women who smoked less than one pack of cigarettes per day, and women who smoked one or more packs per day had crude relative risks for CIN III or cervical cancer of 2.1 (95% CI: 1.1 to 3.9), 2.2 (95% CI: 1.2 to 4.2) and 2.9 (95% CI: 1.5 to 5.6) respectively, compared with never smokers.[26]

A prospective study demonstrated that smokers had cervical HPV infections of longer duration and lower chance of clearing an oncogenic infection than women who never smoked.[27] There is also association between smoking and lower levels of plasma β-carotene, folate and vitamin C.[28-31] Moreover, mutagens in cervical mucus are found in smokers but not in non-smokers.[32] The significant association found between the extent of smoking reduction and the reduction in lesion size in an intervention study of smoking cessation among women with lower-grade lesions further strengthened the possible role of tobacco smoking in HPV carcinogenesis.[33]

1.4.6   Diet

There is yet no convincing evidence that any dietary factors modify the risk of cervical cancer, nor evidence of any probable causal relationship with diet.[34] Nevertheless, both case-control and prospective studies demonstrated that diets rich in vegetables and fruits, and higher intake of carotenoids, vitamin C and vitamin E, found in foods of plant origin, are possibly protective for cervical cancer and its pre-cancerous lesion.[34] There are methodological limitations when examining the association between cervical cancer risk and dietary intake, and serologic measures of nutrient concentrations. Moreover, the presence of other potential confounding factors, such as smoking and use of oral contraceptives further complicates the interpretation of nutrient studies.

1.4.7   Oral contraceptives

A recent systematic study pooling results from 28 case-control and cohort studies found that increased risk of cervical cancer was associated with use of oral contraceptives (OC) for 5 years or more among HPV positive women and the risk increased with duration of use.[35,36] The odds ratio for use of OC was 1.3 (95% CI: 1.0-1.9) for 5-9 years of use, and 2.5 (95% CI: 1.6-3.9) for 10 or more years of use. However, the risk of cervical cancer may decrease after use of OC has ceased.[36]

Use of OC has been found to be associated with cervical cancer in many epidemiological studies that adjusted for HPV status, suggesting the role of OC use as cofactor in HPV carcinogenesis.[36-37] Hormone-related mechanisms may influence the progression from pre-malignant to malignant cervical lesions by promoting integration of HPV DNA into the host genome.[38]

1.4.8   Parity

High parity has consistently been found in most case-control studies to be associated with both cervical cancer and carcinoma in-situ.[37] Major studies limiting the analysis to HPV-positive women also reported an increased risk of high-grade SIL or cervical cancer with increase in the number of pregnancies. In an IARC pooled analysis, the odds ratio for squamous-cell cervical cancer in HPV-positive women with seven or more full-term pregnancies was 3.8 (95% CI: 2.7-5.5) compared with nulliparous women, and 2.3 (95% CI: 1.6-3.2) compared with women who had one or two full-term pregnancies.[39] The risk increased linearly with increasing number of pregnancies. However, there was no significant association between risk of adenocarcinoma or adenosquamous carcinoma of cervix and number of full-term pregnancies.

It has been postulated that high parity may increase the risk of cervical cancer by maintaining the transformation zone on the ectocervix for many years, facilitating the direct exposure to HPV and, possibly, to other cofactors. Hormonal changes induced by pregnancy may also modulate the immune response to HPV and influence the risk of persistence or progression.[37]

1.4.9   Age

     Older women are at higher risk and the peak incidence of cervical cancer in Hong Kong is found in the age group of 75-79.   Although screening for cervical cancer reduces the risk of developing the disease, the coverage of screening in women aged 65 years or above is less than 10% in Hong Kong.[40]   Women in this age group are less willing to seek medical care or go for screening.

1.4.10   Socio-economic status

     Low socio-economic status is also a risk factor for cervical cancer.   Many women with low incomes do not have ready access to adequate health care services, including cervical smear and treatment of pre-cancerous cervical disease.   These women may also be under-nourished and under-nutrition may play a role in increasing the risk of developing cervical cancer.

1.5   Summary

     Cervical cancer is a public health problem with significant local health burden. Although the age-standardized mortality and incidence rates are decreasing, the reduction is below those countries where cervical screening programmes are organized. Risk factors of cervical cancer include human papillomavirus infection, smoking, multiple sexual partners, sexually-transmitted diseases, early age at sexual intercourse, high parity, low intake of vegetables and fruits, long-term use of oral contraceptives, increasing age and low socio-economic status.

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Chapter 2   Pre-Malignant and Malignant Disease of the Cervix

2.1   Natural History of Cervical Cancer [1-5]

Studies have demonstrated that cervical cancer arises as a consequence of progression from mild dysplasia through severe dysplasia to carcinoma-in-situ and carcinoma.   Richart introduced the commonly used classification system for the pre-invasive lesions as different grades of cervical intraepithelial neoplasia (CIN I to III).   CIN I refers to mild dysplasia limited to the basal layers of the epithelium. When changes involve two-thirds of the total thickness of the epithelium, the lesion is referred to as CIN II.   When they involve the whole thickness of the epithelium, it is referred to as CIN III.

Table 2.1 shows the proportion of different grades of CIN (I, II and III) regressing or progressing to other grades of lesions.   The majority of low-grade lesions (CIN I) will regress in two years without treatment and about 10% may progress to higher-grade lesions (CIN III).   About 5% to 10% of high-grade CIN (CIN II and III) may progress to cervical cancer over months to years.   The risk of progression from CIN III to invasive disease is about 12% over 10 years.

Table 2.1   Proportion of CIN Lesions Regressing or Progressing to CIN III or Cancer

	CIN I	CIN II	CIN III
Regression	60%	40%	33%
Progression to CIN III	10%	20%	---
Progression to cancer	1%	5 %	12%

2.2   Cervical Intraepithelial Neoplasia (CIN) and Squamous Intraepithelial Lesions (SIL)

2.2.1   Grading of severity of cervical pre-malignant lesions

Severity of cervical pre-malignant lesions has been described by different classification systems used in cytology reports (Table 2.2).   The Bethesda System

has replaced the Papanicolaou Classification in which cytological findings were designated Class I (normal) through to Class V (conclusive for malignancy). The Bethesda System also covers the CIN classification of pre-invasive lesions. In the Bethesda System, the lesions that are called Low-grade Squamous Intraepithelial Lesion (LSIL) encompass CIN I and human papillomavirus (HPV) lesions while High-grade Squamous Intraepithelial Lesion (HSIL) includes CIN II and III lesions as well as carcinoma-in-situ.[6] In the Atypical Squamous Cells of Undetermined Significance (ASCUS) category, the cellular changes are not clear-cut and a more specific diagnosis cannot be made.

Table 2.2   Squamous Cell Abnormalities and the Different Nomenclatures[7]

Description	CIN grades	Bethesda System	Papanicolaou classes
Normal	Normal	Within normal limits	Class I
Atypia: reactive or neoplastic	Atypia	ASCUS	Class II
HPV	HPV	LSIL	Class II
Mild dysplasia	CIN I	LSIL	Class II
Moderate dysplasia	CIN II	HSIL	Class III
Severe dysplasia	CIN III	HSIL	Class III
Carcinoma-in-situ	CIS	HSIL	Class IV
Invasive carcinoma	Invasive carcinoma	Invasive carcinoma	Class V

HPV = Human papillomavirus
ASCUS = Atypical squamous cells of undetermined significance
LSIL = Low-grade squamous intraepithelial lesion
HSIL = High-grade squamous intraepithelial lesion
CIN = Cervical intraepithelial neoplasia
CIS = Carcinoma-in-situ

2.2.2   Reporting system for cervical smear

Most of the CIN lesions are asymptomatic and can only be detected by cervical screening. The cervical smear test can detect the vast majority of cytological abnormalities. The Bethesda System for reporting cervical cytology is the outcome of two workshops at the National Cancer Institute (Bethesda, Maryland) in 1988 and 1991.[8] It was created as a standardized framework for laboratory reports that included a descriptive diagnosis and an evaluation of specimen adequacy. It is recommended by the Hong Kong College of Obstetricians and Gynaecologists (HKCOG) and is used by most laboratories in Hong Kong for reporting of cervical smear. The system promotes effective communication of cervical cytology results from laboratory to clinicians. The major elements of the Bethesda system are shown in Table 2.3.

Table 2.3   Major Elements of the Bethesda System for Reporting Cervical Smears

Specimen adequacy
Satisfactory for evaluation Satisfactory for evaluation but has limitations (eg. limited by excess blood, drying artefact) Unsatisfactory (e.g. lack of cells)
General categorization
Within normal limits, benign cellular changes, epithelial cell abnormalities
Descriptive diagnosis
Benign cellular changes, including: a.   Infections, or b.   Reactive changes not associated with any increased risk of CIN or cancer
Epithelial cellular abnormalities
a.   Squamous: ASCUS, LSIL, HSIL, invasive cancer b.   Glandular: AGUS (atypical glandular cells of undetermined significance), AIS (adenocarcinoma-in-situ), adenocarcinoma

2.2.3   Management of abnormal cervical smears

The HKCOG has published guidelines on management of abnormal smears in 2002.[9] Table 2.4 summarizes the suggested actions for different cytological abnormalities.

Table 2.4   Suggested Actions for Different Cytological Abnormalities

Cervical Smear	Significance	Suggested Actions
Normal (± inflammation)	0.1% CIN II-III	Normal screening programme (Once every 3 years after 2 normal annual smears)
ASC-US	5-17% CIN II-III 0.1-0.2% invasive	Repeat smear in 4-6 months. Refer for colposcopy if abnormality persists
ASC-H	24-94% CIN II-III	Refer for colposcopy and biopsy
Low-grade squamous intraepithelial lesion (LSIL)	15-30% CIN II-III 0.1% invasive	Refer for colposcopy and biopsy
High-grade squamous intraepithelial lesion (HSIL)	70-75% CIN II-III 1-2% invasive	Refer for colposcopy and biopsy
HSIL-cannot exclude invasion		Early referral for colposcopy and biopsy
Invasive cancer	53.8% invasive	Biopsy if frank growth, otherwise early referral for colposcopy and biopsy
Abnormal glandular cells (AGC-endocervical/endometrial*)		Refer for colposcopy and biopsy, endocervical sampling, cone biopsy and endometrial sampling may be required
AGC-NOS	9-41% CIN II-III, AIS, Ca	
AGC-favour neoplasia	27-96% CIN II-III, AIS, Ca	
AIS	48-69% AIS 38% Adenocarcinoma	*for AGC - endometrial cells - endometrial sampling first
Endometrial cells on smear in		
a. women after menopause	28% benign pathology, 12% significant pathology (hyperplasia, endometrial carcinoma, sarcoma)	Investigation recommended
b. women greater or equal to 40 years of age		Interpret the smear result together with the clinical findings to determine the management
c. women <40 years of age		Treat as normal

Source : Hong Kong College of Obstetricians and Gynaecologists
Abbreviations : ASC-US - Atypical squamous cells of undetermined significance
ASC-H - Atypical squamous cells - cannot exclude HSIL
AGC-NOS - Atypical glandular cells - not otherwise specified
AIS – Adenocarcinoma-in-situ
Ca - Carcinoma

2.2.4   Treatment of CIN[9]

Treatment of pre-cancerous lesion is simple, safe, often non-destructive and usually curative.[6]   Treatment is indicated if CIN I involves more than two quadrants of cervix or if the patient is unable or unwilling to return for follow-up, or if the lesion persists for more than two years.   CIN II or CIN III should be treated.

Treatment options include loop electro-surgical excision procedure (LEEP), cryosurgery, laser vaporization, cold coagulation and electrocoagulation diathermy.   LEEP is recommended by HKCOG as it provides a tissue specimen for histological exclusion of occult invasion.

After treatment, patients should be followed-up by cervical cytology for three times at 4-6 months intervals, then annually for 5 years, and then every 3 years.

2.2.5   Prognosis after treatment

There has been consensus that the widespread and adequate removal of pre-malignant lesions prevents the subsequent development of most invasive carcinomas and leads to a significant reduction in incidence and mortality due to cervical cancer.[10]   Early detection and treatment of cervical pre-malignant changes have been the main contributing factor for cervical cancer to fall from the second to the sixth commonest cancer in the UK and USA.[11]   A recent analysis of long-term studies of follow-up conservative treatment of the pre-malignant stage has shown a reduction in the risk of cervical cancer by 95% for at least 8 years.[12]

2.3   Cervical Cancer[13-15]

2.3.1   Pathology

Carcinoma arising from the ectocervix is five times more common than from the endocervix. 90% are squamous cell carcinoma, mostly arising from the squamous-columnar junction and 10% are adenocarcinoma, mostly arising from the endocervix.

2.3.2   Route of metastasis

There are three routes of metastasis. Local metastasis involves vaginal wall, urinary bladder, parametrium, pelvic wall, uterosacral ligaments, and uncommonly to uterine body.   Lymphatic metastasis involves the external iliac, internal iliac and obturator nodes, then to the common iliac and para-aortic nodes. Hematogenous metastasis involves the lung, liver, bone and bowel.

2.3.3   Symptoms of cervical cancer

Local symptoms
- Irregular bleeding may be brought by coitus (post-coital bleeding), micturition or defecation in the early stage. Later, bleeding may become continuous with variable quantity
- Foul-smelling discharge (thin, watery, bloody) may be present

Symptoms from involvement of adjacent organs
- Ureters: ureteric obstruction, renal failure
- Urinary bladder: frequency, dysuria, haematuria, incontinence
- Rectum: tenesmus, diarrhoea and rectal bleeding
- lymphatics: lower limb lymphoedema
- Vertebrae: back pain
- Lumbrosacral plexus, pelvic wall: pelvic pain
- Abdominal swelling

Systemic symptoms
- anorexia, anaemia and uraemic symptoms

2.3.4   Physical signs of cervical cancer

Ectocervical carcinoma
- Nodule, small ulcer or diffuse patch, with contact bleeding may be seen early
- Later, crater-shaped ulcer with high, everted edge or friable warty mass may be seen. Bleeding is heavier and offensive discharge may be present

Endocervical carcinoma
- Difficult to recognize in early stage but may be discovered when curettage is performed for irregular bleeding
- The cervix becomes larger, hard and barrel-shaped later. Deep excavation with indurated edges may be felt when the growth has broken through the cervical surface

Carcinoma involving the parametrium
- Mobility of the cervix may be reduced
- Rectal examination may detect parametrial tissues, utero-sacral ligaments and pelvic sidewall involvement

2.3.5   Common causes of death
- Uraemia (due to bilateral ureteric blockade), haemorrhage and sepsis

2.3.6   Investigations for cervical cancer
For diagnosis: cervical biopsy for histological study
For staging: vaginal and rectal examinations, cystoscopy, proctoscopy, intravenous urography, lung and skeletal radiographs, lymphangiography, computed tomography (CT) abdomen

2.3.7   Staging of cervical cancer by International Federation of Gynaecologists and Obstetricians (FIGO)

Stage 0: carcinoma-in-situ or CIN III
Stage 1 (tumour confined to cervix)
    1A – microinvasion, where the tumour invades to 5 mm deep
    1B – invasion extends beyond 5 mm but is confined to cervix
Stage 2 (extended beyond the cervix)
    2A – spreading to upper third of vagina
    2B – parametrial involvement
Stage 3 (spread to pelvic wall and/or lower third of vagina)
    3A – involving lower third of vagina
    3B – extension to the pelvic wall and hydronephrosis or
        non-functioning kidney
Stage 4 (extended to adjacent organs or extrapelvic spread)
    4A – spreading to bladder or rectum
    4B – spreading to distant organs beyond the pelvic area, such as
        the lungs

2.3.8   Treatment of cervical cancer

Treatment modalities depend on the staging and options include radiotherapy, surgery, chemotherapy or a combination of these.

2.3.9   Prognosis

The prognosis depends more on the extent of the growth at the time of diagnosis than on the histological type and varies greatly among the reported series of cases, depending on the method of treatment chosen, and the experience of the radiotherapist or surgeon. In general, the 5-year survival rates are:
    Stage 1: >85%
    Stage 2: 50%
    Stage 3: 25%
    Stage 4: 5%

For recurrence of cervical cancer, it occurs within 1 year in 50% of patients, 2 years in 75% of patients and 5 years in 90% of patients.

2.4   Summary

Majority of pre-malignant lesions regress spontaneously whereas the risk of progression from CIN III to invasive disease is about 12% over 10 years. Pre-malignant lesions can readily be detected in the latent phase by cervical smears. Proper management of abnormal smears and early treatment give good prognosis and prevent the development of cervical cancer.

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Chapter 3 Primary Prevention of Cervical Cancer

3.1 Primary Prevention of Cervical Cancer

Primary prevention aims to limit or reduce the incidence of disease by controlling the causes and risk factors, hence it reduces the disease burden to the society. In the primary prevention of cervical cancer, some of the risk factors (such as risky sexual behaviours that can lead to human papillomavirus (HPV) or human immunodeficiency virus (HIV) infection, oral contraceptives, smoking and poor nutrition) can be avoided or changed, but some cannot, such as age. By modifying the avoidable risks, women can reduce their chances of getting cervical cancer.

3.2 Sexual Behaviours

One of the most important risk factor for cervical cancer is the HPV infection.[1] Women who have more lifetime sexual partners have increased risk of developing cervical cancer, compared to those who have only one partner. Early age of first intercourse and high parity are also factors associated with higher risk of cervical cancer.[1-4] Women with HIV infections are significantly at higher risk of developing cervical cancer than women not infected.[5]

3.2.1 Safer sex

Safer sex is the most effective way to prevent HPV infection, as well as other sexually-transmitted diseases (STD). Safer sex behaviours mean taking precautions, when participating in sexual relationships, that decrease the potential for transmitting or acquiring STD. Abstinence is the only completely effective method of preventing STD but it is not practical. A monogamous sexual relationship with an individual free of any STD is probably the most acceptable preventive measures that people can take. Other measures like limiting the number of sexual partners and being aware of partners' sexual history help towards minimizing the risk of developing cervical cancer. While available scientific evidence suggests that the effect of condoms in preventing HPV infection is unknown, condom use has been associated with lower rate of cervical cancer.[6-9] In order to promote safer sex practice and to reduce the risk of HPV-related illnesses and cervical cancer, women should be informed about the potential benefit of safer sex in the protection against cervical cancer.[10]

A systematic review had been conducted to determine the effectiveness of health education interventions to promote safer sex amongst women in order to reduce transmission of HPV.[11] The reviewers concluded that educational interventions, targeting socially and economically disadvantaged women, in which

information provision is complemented by sexual negotiation skill development, can encourage at least short-term sexual risk reduction behaviour. Educational interventions which effectively reduce risk have the potential to reduce the transmission of HPV, therefore possibly reduce the incidence of cervical cancer.

3.2.2   Local sex education programmes

Local sex education programmes are organized by the Government, non-governmental organizations, voluntary associations and community groups. There are a variety of focuses in the promotion of sexual health to various target groups. With promotion of safer sex, changes in sexual behaviour with regard to the number of sexual partners, the age of first intercourse and the use of barrier contraception (e.g. condoms) can prevent cervical cancer by reducing the chance of contracting STD.

Topics on sex-education are wide-ranged and may include prevention of STD and HIV infection, family planning, contraception, teenage pregnancy, sex development and marriage life. Mode of delivery of sex-education programmes, depending on the topics and audience, include educational activities, mass publicity campaigns and train-the-trainers course for school teachers.

3.3   HPV Vaccines

The recognition of HPV infection as a major cause of cervical cancer by the IARC and World Health Organization (WHO) has paved the way for immunization as one of the strategies for primary prevention.[12]

3.3.1   Types of vaccines and their uses

Two types of vaccines against the infection with some types of HPV are being developed and are in different phases of clinical trials.[13-15] Prophylactic vaccines should elicit strong anti-tumour response to protect against HPV infection and render the recipient immune to HPV. Therapeutic vaccines, based on the induction of cellular immunity directed against cells expressing viral proteins, could help women who are infected with HPV. The potential use of these vaccines is to induce regression of HPV associated lesions, eliminate the residual cancer, as well as prevent infection.[16]

Some criteria must be met so that HPV vaccine is developed into a safe and effective means of preventing and controlling diseases.[13] Firstly, it must be effective against the common high-risk types of HPV associated with cervical cancer; secondly, it must offer a long-lasting protection against HPV and preferably without booster shots; and thirdly, economic production cost is also a main factor in determining wide-spread use. Preliminary trials of the vaccines have shown some success.

3.3.2   HPV vaccination combined with HPV screening

Although prevention of infection with HPV type 16 by a prophylactic vaccine has been established,[17] the efficacy of immunizing HPV negative women against this virus needs further research before screening programme using HPV testing as screening tools could be implemented.

HPV vaccination in combination with HPV screening test can be a cost effective intervention, however, it depends on maintaining effectiveness during the ages of peak oncogenic HPV incidence.   Identifying the optimal age for vaccination should be a research priority.[18]   The advantage of a HPV vaccine is not only to prevent HPV infection, but also to prevent the causative agent from residing in the genital tract where it can infect new sexual partners.[19]

3.4   Oral Contraceptives

In women who are positive for cervical HPV DNA, long-term use of oral contraceptives (OC) could be a cofactor that increases the risk of developing cervical cancer.[20,21]   The public health implications of these findings depend largely on the extent to which the observed associations remain long after use of hormonal contraceptives has ceased.   Further research could give more information on whether the risk of cervical cancer associated with oral contraceptive use would decline after cessation of use.

In general, benefits of oral contraceptives, including prevention of pregnancy and cancers of the ovary and corpus uteri, outweigh the risk of cervical cancer. Instead of discouraging the use of OC, extra efforts should be made to encourage long-term users of oral contraceptives to have regular cervical screening. Women who have persistent HPV infection may have to balance benefits of oral contraceptives against risk of long term use.

3.5   Smoking

The exposure to tobacco is another modifiable risk factor for cervical cancer.   Many case-control and cohort studies found that cancer of the cervix is associated with cigarette smoking.[22-24]   The crude relative risk of developing CIN III or cervical cancer in women who smoked is two to three times of those who never smoked.[25]

3.5.1   Anti-smoking policies

At the 56th World Health Assembly in 2003, member states of WHO adopted the world's first public health treaty, the WHO Framework Convention on Tobacco Control.   This new treaty is the first legal instrument designed to reduce tobacco-related deaths and disease around the world.   Among its many measures, the treaty requires countries to impose restrictions on tobacco advertising, sponsorship and promotion; set standard for new packaging and labelling of tobacco

products; establish clean indoor air controls; and strengthen legislation to clamp down on tobacco smuggling.[26]

3.5.2   Local anti-smoking programmes

The Government's policy on anti-smoking is determined to promote a smoke-free culture so as to safeguard the health of the community.   Although there is a gradual downtrend of the overall smoking prevalence in Hong Kong for the past 20 years, prevalence of smoking among women has been gradually increasing in recent years, especially in the age group of 15-39.   Female non-smokers should be advised to avoid smoking and smokers are recommended to stop smoking in order to reduce the risk of having cervical and other cancers.   As environmental tobacco smoke may cause cervical cancer, avoiding exposure to passive smoking at home, at schools, in workplace and other public places may reduce the risks of cervical cancer.   Effective anti-smoking actions include banning cigarette advertisements, taxation on tobacco products and setting of public smoke-free areas.   Programmes that raise awareness of environmental tobacco smoke, smoking cessation service and other anti-smoking programmes have been delivered by the Government and non-governmental organizations such as the Hong Kong Council on Smoking and Health (COSH) and Action on Smoking or Health Limited (ASH).

3.6   Diet

Studies have demonstrated that dietary intake of dark green and yellow vegetables and other foods rich in β-carotene, folic acid, vitamins C and vitamin E reduces the risk for CIN III and carcinoma-in-situ.[27]   Vitamin A has been proposed as a chemo-prophylactic agent for cancer.[27-28]

3.6.1   Healthy dietary practices

As recommended by the World Cancer Research Fund and the American Institute for Cancer Research, intake of carotenoids, vitamins C and E is possibly protective against cervical cancer.   Fruits and vegetables are the richest source of vitamin C and other vitamins.   Other major micronutrients such as carotenoids and folic acid are found in fresh green leafy vegetables which possibly reduce the risk of cervical cancer.[29]   Examples include carrots, tomatoes, cruciferous vegetables (broccoli and spinach), peaches, oranges, and cantaloupes.

3.6.2   Local programmes on healthy diet

Promoting healthy diet is a priority area in Hong Kong.   Through health education activities and campaigns organized by the Government, non-governmental organizations and the community, promotion of healthy dietary practices is reinforced as part of healthy lifestyle promulgated in different settings such as the schools and families.   The Health Eating Movements in schools and the territory-wide Healthy Living Campaign are examples of concerted efforts of the Government, community groups and the media in promoting healthy eating.

3.7 *Summary*

Primary prevention of cervical cancer focuses at modifying the avoidable risks to reduce women's chances of getting cervical cancer.   The main strategies are organized programmes to promote safer sex, anti-smoking and healthy diet.

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Chapter 4   Secondary Prevention of Cervical Cancer

4.1   *Secondary Prevention of Cervical Cancer*

Secondary prevention aims at lowering the occurrence of the later and more severe stages of the disease, often by identifying the disease at an early and curable stage, as in screening, therefore reducing the prevalence of the disease through treatment.[1]

4.2   *Cytology Screening*

Cervical cancer is preventable because it has a long latent stage. A histological analysis of invasive cases in Iceland showed that screening affected mainly the rate of squamous-cell carcinoma but not that of adenocarcinoma and adenosquamous carcinomas. The latter two cancers are not easily detected by screening because of their location higher in the endocervix.[2] The National Institute for Clinical Excellence (NICE) of United Kingdom reported that approximately 10% of cervical cancers are adenocarcinomas which are frequently undetected by screening.[3]

4.2.1   Cervical smear

George Papanicolaou introduced cervical cytology into clinical practice in 1940. Cervical smear (Pap smear) is a simple test that can detect early abnormal changes in the cells of the cervix. Smear collection instruments include the wooden or plastic Ayre's spatula and the broom type. Early detection followed by appropriate treatment can achieve a very high cure and survival rate.   Women with pre-invasive lesions have a five-year survival rate of nearly 100% after treatment.[4] The results of meta-analysis of studies suggest that the sensitivity of cytological screening has a wide range of 30-87%.[5] Sensitivity of cervical smear for detection of high-grade squamous intraepithelial lesion (SIL) is in the range of 70-80%. Specificity of cervical smear has been reported to be higher than 90%.[6]   Factors that limit test sensitivity include small size of the lesion, inaccessible location of the lesion, the lesion not being sampled or the presence of inflammation and/or blood obscuring cell visualization.[4]

Techniques for taking cervical smears are important in obtaining satisfactory specimens for cytological examination. Some of the reasons for unsatisfactory cervical smear are as follows:[7,8]
- Cervix not visualized adequately.
- Transformation zone not adequately scraped.
- Material incompletely transferred to the slide.
- Sample poorly spread, too thick or too thin.

- Smear allowed to dry before fixation or fixation is inadequate.
- Smear consisting mainly of blood or inflammatory cells.
- Contamination of the smear with lubricant, vaginal cream or spermicide.

4.2.2   Limitations of cervical cytology

The limitations of cervical cytology in screening for cervical cancer include the following:[9]

- The test is difficult to comprehend in many cultures.
- The test is potentially embarrassing.
- Trained personnel are required.
- Smear adequacy is not intrinsically obvious.
- It is necessary to recall women for further tests where indicated.
- The test has only moderate sensitivity.
- Cytology is unable to distinguish progressive disease from those regressed.

4.2.3   False-positive and false-negative smears

The cervical smear test, just like many screening tests, is not a perfect test. It may have false-positive and false-negative results. False-positive result is defined as a cytology report of a high grade or invasive lesion, when followed within 6 months by a biopsy, gives a normal histological diagnosis. It is usually due to normal cells being mistaken as abnormal cells or lesions may have regressed to normal and are no longer detected by repeat smears. In one study of over 300 laboratories given slides with known cytologic diagnoses, false-positive diagnoses were made in 8.9% of smears with no more than benign atypia.[10] A false-positive result causes needless anxiety and unnecessary clinical follow-up with colposcopy, biopsy or other tests to the woman who does not have the disease.

False-negative cervical smear result is defined as a negative report, when followed within 6 months by a biopsy, gives a histological diagnosis of a high-grade or invasive lesion. A false-negative result may be due to failure to obtain cells representative of a lesion or failure to recognize or diagnose abnormal cells present. Sampling error can be due to small lesion size, a lesion at an inaccessible site in the cervix or improper sampling technique. Estimations of the false-negative rate of cervical smears vary substantially among studies. Based on studies in which the cervical smear was performed under optimal conditions, an estimate of the false-negative rate ranged from zero to 29.7%.[11]

One way to reduce the false-negative rate is to optimize the smear specimen by using new types of samplers and liquid-based cytology techniques.[12] Another way is to repeat smears at regular intervals.

4.2.4   Liquid-based cytology (LBC)

The liquid-based methods are designed to improve smear preparation, thus enhancing the quality of the specimen and reducing sampling error.   Examples of liquid-based monolayer systems include the ThinPrep Pap test and AutoCyte.

ThinPrep Pap Test

In 1996, US Food and Drug Administration (FDA) approved the ThinPrep Pap Test for clinical use.   The ThinPrep Pap test employs a liquid collection medium into which the specimen obtained with either a brush or broom device is placed.   The liquid medium is sent to the laboratory where an instrument disperses the cells in the solution and then places them in a thin, uniform layer on a special microscope slide. Advantages of ThinPrep include:[13]

- A uniform, reproducible and statistically representative sample is obtained.
- Blood and mucus are removed to decrease cellular obscuration.
- Cellular preservation is improved.
- Only a portion of the sample is used, permitting testing for HPV later if indicated.

Additional positive features of ThinPrep technology include increased job satisfaction among cytotechnologists, a 20% increase in productivity and a reduction of turnaround time from 12 to 6 days.[14]

AutoCyte Prep

AutoCyte Prep was approved by the US FDA in 1999.   A cervical sample is obtained in a routine manner and is immediately placed in a vial containing fixative solution.   Because all the cells on the sampling device are placed in the vial, there is a marked improvement in sample quality.   Direct-to-vial use of AutoCyte Prep improves the specificity of cervical cytology screening.[15]   In the AutoCyte system, cells in fixative are separated on a gradient by centrifugation and allowed to sediment on a microscope slide forming a thin layer of cells.[16] AutoCyte Prep stains the cells and the thin-layer slide shows a uniform distribution and density of cells across a 13 mm-diameter circle.[17]

The NICE reported a meta-analysis of 14 studies comparing the sensitivity of LBC and the cervical smear in the detection of abnormalities of low-grade SIL (LSIL) or higher.   It demonstrated that sensitivity might be up to 12% higher with LBC compared with that of the conventional cervical smear.   In this study, there was a statistically significant decrease in the number of inadequate samples from 9.1% with Pap slides to an average of 1.6% with LBC.   NICE has recommended that LBC be used as the primary means of processing samples in the cervical screening programme in England and Wales.[3]

Benefits and cost

Although these new technologies have been developed to improve the detection of cervical cancer and its precursors, not all the studies show positive findings. A French study found that monolayer testing is less reliable than conventional cervical smear testing.[18]

The United States Preventive Services Task Force (USPSTF) could not determine whether the potential benefits of new screening technology such as LBC relative to conventional smear tests are sufficient to justify a possible increase in potential harms or costs.[19]

Most studies have shown improved sensitivity for LBC compared to conventional smears. However, screening with LBC at an interval same as the conventional cytology will likely lead to significant increase in the detection of atypical squamous cells and low-grade abnormalities, with subsequent increase in referral of women for colposcopy unnecessarily, risking the potential for over-treatment and increased health care costs.[4]

4.3   Organized Cervical Screening Programme

4.3.1   Experience from overseas cervical screening programmes

Although cervical cancer screening has not been evaluated by a randomized trial, its effect has been evaluated by non-experimental cohort and case-control studies as well as by the observed changes in incidence and mortality rates before and after the launching of screening programme. Finland started a nation-wide screening programme for cervical cancer in 1963. By early 1990's, both the age-standardized incidence and mortality rates of cervical cancer had recorded a decrease of 80%.[20] Similar declines have been observed in Iceland, where incidence and mortality rates had decreased by 70% and 62% respectively from 1966-1970 to 1981-1985.[2] In countries where screening programmes are not so well organized, such as Denmark and Norway, age-standardized mortality rates have declined by 35% and 18% respectively over the same period.

Most of the cervical cancer diagnosed in Iceland during the period 1978 to 1991 were diagnosed among women who had never attended screening or had not attended screening during the three years prior to diagnosis of invasive disease.[2] The majority of cervical cancer in the United States occur in women who have never been screened or who have not been screened within the past 5 years and additional cases occur in women who do not receive appropriate follow-up after an abnormal cervical smear. [4,21]

4.3.2   Effective cervical screening programmes

Mass screening programmes in which women have cervical smear tests at least once every three to five years have proven to be effective in reducing cervical cancer mortality and morbidity rates. The factors that determine the success of

cervical cancer screening are coverage of the population at risk through organized screening and quality assurance in the collection and interpretation of cervical smears.[7] Essential elements for a successful cytology screening programme are summarized as follows:[9]

- Training of health care professionals including smear-takers, cytotechnologists, cytopathologists and colposcopists.
- An agreed decision on the priority age group to be screened.
- Adequately taken and fixed smears.
- High quality laboratory services.
- A mechanism to inform women of the test results in an understandable form.
- A mechanism to ensure that women with an abnormal test result attend for management and treatment.
- An accepted definition of an abnormality to be treated.
- A mechanism to follow-up treated women.
- A decision on the frequency of subsequent screens.
- A mechanism to invite women with negative smears for subsequent smears.

4.3.3   Screening frequency

The International Agency for Research on Cancer (IARC) conducted a collaborative study of screening programmes in eight countries which showed that little was gained by screening every year compared to screening every two or three years. The percentage reduction in cumulative incidence among women aged 35-64 years who had a second negative smear at the age of 35 was 93.5% when the interval between cervical smears was one year, 92.5% at 2-year interval, 90.8% at 3-year interval and 83.6% at 5-year interval.[22]

A cohort study in Denmark found that women with two-to-four previous normal cytology results had a negligible risk of developing cancer within two years. Repeat screening at regular intervals compensates for the limitations in the sensitivity of the technique.   While more frequent screening increases sensitivity, it also increases harm and costs in patients.[4]

4.4   Human Papillomavirus (HPV) Testing

Persistent detection of high-risk HPV types is a strong predictor of development of cervical cancer.   Compared with cervical smear, HPV DNA testing is significantly more sensitive, but less specific in the detection of CIN III or higher lesions.   Limiting HPV testing to women aged 30 to 50 years may result in improved specificity.[23]   The sensitivity of HPV testing is significantly higher than that of cytology for all grades of SIL. For high-grade SIL (HSIL), the sensitivity and specificity of HPV test are around 90% and 51% respectively.[24]

HPV DNA testing has been found to be more cost effective than other management strategies including repeat cervical cytology or immediate colposcopy for women diagnosed as having atypical squamous cells of undetermined significance (ASCUS).[25] Since around half of ASCUS has high risk HPV, HPV typing in triaging women with ASCUS is an alternative to repeat cytology at 6 months for deciding whether colposcopy referral is needed.[26,27] On the other hand, HPV typing has limited advantage in triaging patients with LSIL for colposcopy because over 80% of LSIL has high risk HPV.[26,28]

A positive HPV DNA test result is not an absolute indicator that high-grade lesions exist or will develop; the prognostic value of a positive test result, especially in the absence of a cytological abnormality, has not been fully validated in prospective studies.[4] Harms of HPV testing may include anxiety or stigmatization among infected women and impact on relationships with sexual partners.[29]

The reported positive predictive value of a HPV test for HSIL and carcinoma is less than 10%. The suitability of HPV typing for routine screening in asymptomatic women is limited by its poor predictive value and uncertain natural history. Moreover, due to the absence of an effective treatment, there is a lack of evidence that screening affects clinical outcomes.[30]

Although there is evidence to suggest that HPV testing in conjunction with cytology may improve the screening efficacy of cytology alone, more evidence is required to confirm whether the benefit outweighs the high cost of HPV testing.

4.5   Alternative Methods of Cervical Screening

Cervical cancer is an important public health problem among adult women in developing countries such as South and Central America, sub-Saharan Africa and South and South-east Asia.[5] About 80% of cervical cancers occur in less developed countries, mainly due to the lack of well-organized screening programmes.[31] Substantial costs are involved in providing the infrastructure, manpower, consumables, follow-up and surveillance for both organized and opportunistic screening programmes for cervical cancer. Owing to their limited health care resources, developing countries cannot afford to screen women frequently.[5]

Acetic acid denatures nuclear proteins and dehydrates cellular cytoplasm causing tissues with increased nuclear cytoplasmic ratios to reflect projected white light and appear white. Naked-eye visual inspection of the cervix with acetic acid wash (VIA) or cervicography has been used as an alternative to cytology for cervical cancer screening in places lacking resources.[32]

4.5.1   Visual inspection of the cervix with acetic acid wash (VIA)

The sensitivity of VIA for LSIL and HSIL is 57.7% and 76.9% respectively with a specificity of 65.4%.[31]   Although the negative predictive value of VIA is consistently reported at 96% or greater,[33] it is associated with high rate of false-positive results.[32]

Besides its high sensitivity and low cost, VIA is a simple procedure that can be carried out by trained nurses. A study in Thailand found that VIA with immediate treatment using cryotherapy was safe, acceptable and feasible.   It is a potentially efficient method of cervical cancer prevention in rural settings.   This single-visit approach has the advantage of avoiding loss to follow-up when women have to return or travel long distances for diagnosis and/or treatment.[33]

4.5.2   Cervicography

Cervicography is said to help improve the sensitivity of cervical screening, but its accuracy and technical requirements are suboptimal.   With cervicography, a photograph of the cervix is examined for atypical lesions.   This test has a sensitivity of 60%, which is comparable to that of the cervical smear but has a much lower specificity of about 50%.

The reported positive predictive value in most studies is only 1-26%. Moreover, about 10-15% of cervicograms are unsatisfactory.[4]   Cervicography gives a sensitivity of 54.6% in women younger than 50 years of age and around 27% in women 50 years of age and older. Cervicography is not effective in postmenopausal women.[34]   Moreover, cervicography is less sensitive and less specific than cervical cytology.   The false-positive rate of cervicography is higher than that of cytology. Therefore, cervicography is not recommended as an alternative to cytology for cervical screening.[35]

4.6   Summary

Cervical cytology, having sensitivity of around 70%-80% and specificity of about 90%, is the proven screening method for cervical cancer.   Liquid-based cytology may reduce false-negatives of cervical smear.   Potential benefits of HPV testing alone or combined with cytology in the prediction of cervical cancer await further study.   Visual inspection of the cervix with acetic acid wash and cervicography are less sensitive and specific than cervical cytology.   They are not recommended for cervical screening.

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Chapter 5 Local Situation on Cervical Screening

5.1 Background of Cervical Screening in Hong Kong

Cervical screening service first became available at the Aberdeen Maternal and Child Health Centre under the Family Health Service of the then Medical and Health Department in April 1970. Since then, many more Maternal and Child Health Centres started to provide cervical screening service. The Family Planning Association of Hong Kong started to provide cervical screening service since 1990's.

Until recently, there was no centrally organized, systematic, population-based cervical screening programme in Hong Kong. Most cervical screening is performed opportunistically or as part of check-up package provided by various health care providers. Currently, the main providers of screening services are:

- Private sector: general practitioners and gynaecologists

- Non-governmental organizations such as Family Planning Association of Hong Kong (FPA)

- Department of Health (DH)

- Hospital Authority (HA)

A local study showed that about 60% of cervical smears are carried out by the FPA, DH and HA and 40% are done in the private sector (Table 5.1)[1].

Table 5.1   The Frequency of Service Utilization of Different Service Providers

Service Provider	Number of women (%)
Public	
Department of Health	89 (11.1%)
Public hospitals	143 (18.0%)
Well Women Clinic in Hospital Authority	25 (3.1%)
Family Planning Association of Hong Kong	168 (21.1%)
Private	
Private practitioners	254 (32.0%)
Private hospitals	71 (8.9%)
Others	25 (3.1%)
Overseas	20 (2.5%)
Total	**795 (100%)**

Note: Percentages do not add up to one hundred percent due to rounding of decimals.

The commonly chosen service provider for cervical screening was from the private sector. Most screened women had the test as part of a woman's check-up package (52.3%), or other health package (17%) rather than as cervical smear alone (30.7%).[1]

Factors influencing the choice of service provider include the competence of the practitioner, both in technical skills and interpersonal skills, attitude of practitioners as well as location and convenience of opening times. The practitioner's use of opportunistic screening, for example, during consultation for contraceptive advice also influences where the women attend for screening.[2]

5.2   Coverage of Cervical Screening

According to data from Hong Kong Population Census 2001, there were about 2.02 million females aged between 25 and 64 in Hong Kong[3] and they are the target group for cervical screening.

A study on knowledge, attitude and practice (KAP) of around 1 500 randomly selected married women aged between 15 and 49 done in 1997 by FPA revealed that about 10% of the respondents had never heard of the test whereas the rate was 20% in 1992. A total of 52% of respondents had taken cervical smear in the previous 3 years, 61% had ever taken the test and 28.3% had heard of but never

taken the test. For the age group of 45-49, nearly half had not taken the test. These suggested a very unsatisfactory coverage rate.[4] Figure 5.1 shows the knowledge and practice about cervical smear among respondents by age group in this study.

Figure 5.1   Prevalence of Knowledge and Practice of Cervical Smear Test by Age, 1997
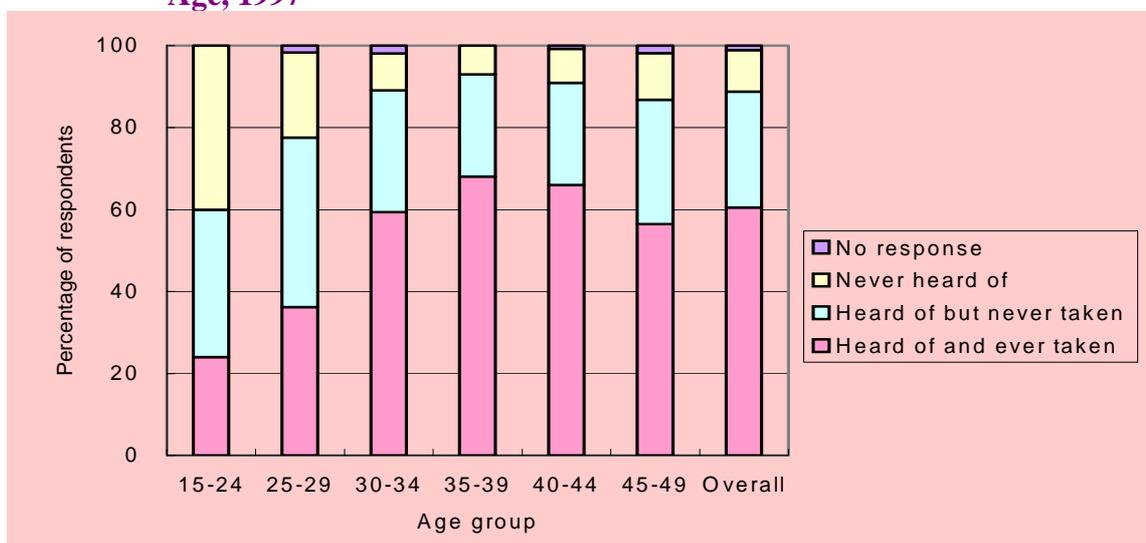
Source : Family Planning Association of Hong Kong

A study in 1998 found that 44% of at risk women over the age of 20 had ever had a smear test and one third had at least two screening tests. Screening coverage was lowest in the oldest age group – 59% for age group 20-30, 57% for age group 40-59 and 20% for age group 60 and above.[5]   One quarter of all women attended for screening regularly, and among these, the majority attended at least once per year. The current screening practice in Hong Kong is therefore inequitable, consumes resources, and may result in cervical cancer cases that could be preventable. Moreover, over-screening women at lower risk may also cause unnecessary harm.[6]

5.3   *Factors Influencing Participation in Cervical Screening*

5.3.1   Facilitators

Local studies found the following facilitators for attending cervical screening:[1,2,7]
- Family and friends are particularly important in encouraging women to attend for screening.
- Women who are married are more likely to have screening than women who are single.
- Opportunistic advice of practitioners is important to maximize attendance rates.
- Female practitioner is preferred for smear-taking service.
- Sexually active women in 25-34 and 50-64 age groups are more likely to have cervical screening.

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- Women who are more health-conscious have higher uptake.
- TV is seen as one of the most important source of information for women of all age groups. Other sources of information include health talks, health care practitioner and the internet. Early evening TV is seen as the most effective method of publicity. Outreach health education sessions and workshops held in the community are also considered important. Government is viewed as a credible body to publicize the programme.
- Information on the need for screening, in particular knowledge about the preventive nature of cervical screening, availability and cost of screening service is considered important.
- Reminders about future smears in the form of letter are welcomed by majority of screened women.

In some local studies, women described that caring attitude, expertise in decreasing fear and pain, teaching and communication and the experience of the practitioner, rather than the type of professional discipline, played an important role in influencing women's level of satisfaction with the procedure.[8-10]

A questionnaire survey of 430 women who attended a well-women clinic found that the major reasons of choosing screening services were: belief in 'prevention is better than cure', experience of previous gynecological screening, support from family and friends, recommendation by other users, convenience, low price and perceived risk of cancer.[11] Use of screening services was also associated with positive health behaviors including low fat-diet, physical exercise and absence of smoking habits. Staff manner was reported as the most important factor for future participation. Other factors include privacy and financial issues.

5.3.2   Barriers

A focus group study and other studies identified the following barriers for attending cervical screening:[1,2,7,11-16]

- Embarrassment, especially if the practitioner is a male.
- Lack of knowledge
  Although many women know the risk factors associated with cervical cancer, they do not consider 'no cervical screening' as a risk factor. Women describe themselves not at risk because they have "a stable sexual relationship". Women lack knowledge about the nature of disease, the need for regular screening, frequency of screening, availability of service, the need to screen even if there is no symptom.
- Cost
  6% of respondents gave 'too expensive' as a reason for not having 'vaginal check-ups'.
- Smear taker
  Lack of skills of the practitioners in carrying out screening, with respect to communication and technical competence. Lack of female practitioners.
- Fear of the procedure, pain or abnormal result.

- Lack of time to attend.
- Lack of publicity.
- Misbelief
  Have the impression that cancer cells exist in everyone's body and it can't be prevented.
- Notification of result.
  Fear generated by a phone call.
  Concern that notification letter of result may go astray.

Lack of knowledge about screening is an important barrier. If a health information package can be developed in an easily comprehensible and culturally acceptable way, pilot tested, and delivered through efficient dissemination routes, the acceptance of screening services would be increased.[17]

5.3.3   The facilitators and barriers to the uptake of cervical screening service are summarized in Table 5.2.

Table 5.2 Internal and External Facilitators and Barriers for Attending Cervical Screening

	Facilitators	Barriers
Internal factors	- Marriage - History of childbirth - Sexually active - Self-care practice, health consciousness (non-smoker, low-fat diet, regular exercise) - Perceived risk of cervical cancer - Belief of 'prevention is better than cure' - Previous cervical smear - Younger age - Higher socio-economic class	- Embarrassment - Anxiety, fear of pain, discomfort, humiliation or fear of abnormal result - Perceived no need because had been sexually inactive for some time. - Perceived no need for screening, absence of symptoms - Lack of time - Belief of 'cancer cannot be prevented' - Inappropriate association of promiscuity with cervical cancer - Older age
External factors	- Information: publicity (mass media, pamphlets), friends/ relatives, health care workers - Female practitioner - Preference for doctor to nurse - Staff manner - Advice from doctors - Interpersonal and communication skill of practitioner	- Lack of information about disease nature, need for screening, service provision and frequency of screening - Unfamiliar doctor - Male doctor - Too expensive - Lack of child care - Poor communication skill

	• Reminder letter • Reducing cost • Increasing accessibility, convenient time and place • Improved test attribute	or experience of practitioner

5.4   Quality of Cytology Screening

5.4.1   Detection of abnormal smears

During 1986 to 1988, about 90% out of a total of 108 388 smears sent to the Public Health Laboratory of DH in Lek Yuen Health Centre came from women in the reproductive age group of 30-39 years.   About 4 800 (4.4%) were reported as abnormal.   These abnormalities included 3 (0.003%) invasive carcinoma, 129 CIN, 54 condylomatous lesions, 414 atypia and 4 156 inflammatory changes.   The incidence of cervical cancer detected was much lower than the 0.02% detected by the FPA in the same period.   This discrepancy of the detected rates is believed to be due to the difference in the age distribution.[17]

A study to evaluate the cytohistological correlation of 283 cervical smears was done in private laboratories in 1996-1997.   Among the 34,570 cervical smears reported, 0.52% were classified as 'unsatisfactory'.   Among the 283 matching cases between the cytological and histological records, the overall absolute concordance rate was 51.2%.   The concordance rates within the diagnostic category were 63.9% and 74.6% for LSIL and HSIL respectively.   The overall sensitivity of the test was 91.7% with a positive predictive value of 93.5%. 10% of the error rate was attributed to laboratory error; 90% was attributed to sampling error and unsatisfactory smear preparation. 45% of cases of atypical squamous cells of undetermined significance (ASCUS) showed evidence of CIN on subsequent biopsy. Follow-up biopsies of LSIL also showed as many lesions from CIN I as from CIN II & III.   The overall false-negative rate of 8.3% is comparable with those reported in the literature, which are at least 5%, even in the best laboratories.[18]

5.4.2   Improving the quality of cervical smear

The ability of the cervical smear to detect a lesion is greatly influenced by the quality of the specimen.   Even when the most advanced technology is used in the laboratory to examine smears, a lesion will remain undetected if the smear is of inferior quality.   Laboratories have a responsibility to indicate the adequacy of a cervical smear in their report and to request a further smear if a suboptimal one has been provided.   In the widely used Bethesda System for reporting cervical smears, specimen adequacy is stated in the report.[19]

Quality of test specimen may be improved by using newer broom-type plastic cell sampler e.g. Cervex brush, usually in conjunction with liquid-based cytology.   It is shown that this sampler produces less cell trapping on the sampler and hence higher yield of cells when compared with conventional wooden spatula.   Liquid-based cytology allows cells to be spread as monolayer on glass slide, hence allowing more accurate microscopic examination.

Accuracy and efficiency of laboratory diagnosis of cervical smears may be improved by using computer-assisted microscopy which helps prevent overlooking areas on the slide by the screener when the microscope is used for slide interpretation.   An automated cervical screening device consisting of a high resolution scanner and a high speed microscope helps identify areas containing abnormal cells for further confirmation by cytologist.

5.4.3   Quality performance of laboratories

The Basic Criteria for a Cervical Cytology Screening Laboratory composed by the Hong Kong College of Pathologists defined the basic requirements, performance standards and reporting guidelines for cervical cytology. Apart from laying down the staff structure, physical facilities and reporting system, the quality assurance measures, information system and laboratory safety are also specified.   The performance measures and indicators include screening workload, report turnaround time, proportion for re-screening and cytology-histology correlation.

A laboratory is accredited when it possesses a system that allows high quality laboratory work to be performed.   The potential benefits of accreditation for laboratories include improving the diagnostic and reporting standards, being recognized as a quality-focused organization and increased opportunity of collaborative work.[19]

5.4.4   Guidelines on Cervical Screening

In 1999, the Hong Kong College of Obstetricians and Gynaecologists (HKCOG) published guidelines on smear taking procedures, interval for cervical screening and management of an abnormal cervical smear.[20]   The Hong Kong Society of Cytology has published the Cervical Cytology Practice Guidelines.

5.4.5   Training for professionals

On-job or refresher training courses on smear-taking and management of abnormal smears aim at professional development and upgrading of smear-takers. There are training programmes on smear-taking offered by the Hong Kong Society for Colposcopy and Cervical Pathology, the Hong Kong Medical Association, the Hospital Authority and the universities.   There are also training course in diagnostic cytopathology organized by the Hong Kong College of Pathologists in partnership with the university.

5.5 Summary

In the current opportunistic cervical screening, the coverage of women in the target group is rather low, especially the at-risk women. The local situation calls for the establishment of an organized cervical screening programme.

Various facilitators and barriers to the use of cervical screening service have been identified, which highlight the importance of procedural, interpersonal, and culturally sensitive skills, particularly in respect to information giving and interaction with women. In order to encourage screening, enhancing information delivery about the benefits of screening as well as increasing health awareness are important.

New technology, quality performance of laboratories, guidelines for cervical screening and training of smear-takers and laboratory professionals all contribute to improving the quality of cytology screening.

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Chapter 6 Cervical Screening Programme in Hong Kong

6.1 Planning of Cervical Screening Programme

The Government's 2001 Policy Address pledged to launch a Cervical Screening Programme (CSP) for women.   The objectives of the CSP are:

- To increase the population coverage rates of cervical screening among women.
- To reduce the incidence of cervical cancer in Hong Kong.
- To reduce the mortality of cervical cancer in Hong Kong.

In December 2001, a Cervical Screening Task Force (CSTF) chaired by the Director of Health was established to oversee the planning and implementation of the CSP.   Members of the Task Force included representatives from professional colleges, university experts, service providers from both the public and private sectors, non-government organizations and women groups.   Three Working Groups were formed under the CSTF.   They are Working Group on Recruitment and Education, Working Group on Quality Management, and Working Group on Information System.

The CSP was launched on 8 March 2004 by the Department of Health (DH) in collaboration with other health care providers.   Benefits of the CSP include:
- Improved overall coverage of the target population not achievable by opportunistic screening alone.
- More equitable and efficient screening across the target population.
- Better quality management in screening service, including smear-taking, cytological examination, referrals and follow-up management.
- Better support and collaboration between the public and private sectors in providing cervical screening.
- The establishment of a central registry, i.e., the Cervical Screening Information System (CSIS), to monitor the quality and effectiveness of the screening programme.

6.2 Screening Policy

6.2.1 Target group

Cervical cancer is exceedingly rare in women aged less than 25.[1]   In 2001, there were 438 new cases in Hong Kong.   Of these, no case was below age 25. There were five cases in the age group of 25-29, 21 cases in the age group of 30-34, 55 cases in age group of 35-39 and 357 cases above the age of 40.[2]

The number of women needed to screen to prevent a case of cervical cancer is considerably higher in women with age below 25.   Moreover, there is a comparatively high incidence of cervical cytological abnormalities that would spontaneously regress among women below age 25.   Screening before this age on a population-wide basis therefore could cause undue anxiety and result in a considerable number of unnecessary interventions.

There is evidence that the incidence of cervical cancer in older women is almost entirely confined to the unscreened or under-screened.   Screening in the unscreened population can reduce morbidity and mortality from cervical cancer.   It was reported that low rates of LSIL and HSIL were observed in women aged 65 and over and had at least one previous normal cytology result within the last three years.[3]

The United States Preventive Services Task Force recommends against routinely screening women above age 64 for cervical cancer if they have had adequate recent screening with normal smear results.   The yield of screening is low in previously screened women older than 64 and there is fair evidence of increased risk for potential harms including false-positive results and invasive procedures during follow-up.[4]

Based on the above findings, the screening policy is formulated.   The target population includes women starting from age 25 until they reach 65 years of age.   The CSTF recommends an interim target coverage rate of 60% among women aged 25-64 years to be achieved three years after programme launch.   In the long term, the coverage rate should reach levels of international best models, around 80-85%.   According to overseas experience, it usually takes many years for an organized cervical screening programme to reach such levels of coverage.

The CSTF noted the global trend of women commencing sexual activity at a younger age.   A potential effect to watch for is an age-shift of onset in cervical cancer towards younger women, which will have bearing on the recommended target population for screening.

6.2.2   Screening interval

The CSTF recommends cervical smear screening at 3-yearly intervals for women aged 25-64 after two consecutive normal annual smears have been obtained. Screening may be discontinued in women aged 65 or above if three previous consecutive smears within 10 years are normal.   Women at or over 65 years of age and who have never had a smear should be offered the test.   Women aged below 25 years with high-risk profile may be screened, based on the doctor's professional assessment. Women who have never had sex or who have total hysterectomy need not receive cervical screening.   For women at high risk of developing cervical cancer, for example, immuno-compromised women, annual screening is advised.

The above recommendation has taken into consideration the epidemiology of cervical cancer in Hong Kong, local professional guidelines, and experience from overseas programmes. It is also in line with the Hong Kong College of Obstetricians and Gynaecologists (HKCOG) Guidelines.[5]

The CSTF noted that the marginal yield of the initial two annual smears in detecting cervical cancers is small and the sensitivity of cervical smears depends crucially on the performance of smear takers and cytology laboratories. With the lack of elaborate quality assurance mechanisms, it is prudent therefore to recommend two consecutive normal annual smears before having screening at 3-year intervals. The screening interval will be reviewed when more information about smear quality and laboratory performance is available through the CSIS.

6.3 Recruitment and Education

A coordinated recruitment and education strategy is needed to recruit women in the target population into the programme and ensure that they understand the reasons for screening, the procedures involved, the meaning of result, and treatment options. The CSTF has made the following recommendations:

- Address both the general public, service providers and laboratories in recruitment and education efforts.
- Give particular attention to women who have never received screening.
- Send invitation letters to encourage screening and reminder letters to women when the next smears are due.
- Conduct mass media campaigns to promote cervical screening to the target population.
- Collaborate with community organizations to promote cervical screening, particularly to access certain high-risk groups of women who are hard to reach otherwise.
- Develop education and publicity materials for the general public.
- Collaborate actively with the service providers in the public and private sectors in providing cervical screening services. This may take the form of providing data on cervical screening, sending reminder letters to recall clients due for screening, providing education materials on cervical screening, setting up an enquiry system for cervical smear and biopsy results and developing a website.

6.4 Quality Management

Quality assurance standards and performance indicators that are pragmatic, achievable and comparable with international acceptable standards should be set to monitor the reliability and consistency in performance.

The HKCOG guideline is recommended as the standard protocol for management of abnormal smears. The Basic Criteria for a Cervical Cytology Screening Laboratory composed by the Hong Kong College of Pathologists is

adopted as reference quality assurance and laboratory standards. The Colposcopy Service Provision and Standards developed jointly by the Hong Kong Society for Colposcopy and Cervical Pathology and HKCOG are also adopted as the reference quality assurance standards.

All registered medical practitioners may take cervical smears. Nurses may also take smears if they have undergone a proper training course and taken adequate satisfactory smears under supervision.

With regard to smear-taking, reporting and management of abnormal smears, the CSTF has made the following recommendations:

- Both the conventional and liquid-based methods are acceptable for smear taking and cytological examination.
- The Bethesda System is the recommended cytology reporting system
- The SNOMED system is the preferred reporting system for histology results of cervical biopsies.
- Professional education and training should include both technical skills in smear taking and communication skills, such as counselling women with abnormal smear results.
- Women should be informed of both positive and negative smear results.
- All women with abnormal smear results should be called back for further management.

6.5   Cervical Screening Information System (CSIS)

The CSIS, established and maintained by the DH, serves as a central registry of the smear results and personal data of all women. Effectiveness in achieving the aims of CSIS depends on regular and accurate data submission from participating women, service providers and laboratory professionals to the CSP.

6.5.1   Data transfer

Women who present to their health care providers for cervical smears are invited to register and give consent to have their personal data and smear results transferred to the CSIS. Besides smear data, biopsy results and referrals will also be collected from service providers to ascertain the outcome of those women with abnormal smears.

Before signing the consent form, women are requested to read the Personal Information Collection Statement which clearly states the purpose of data collection and how it will be used in the CSIS. While making efforts to ensure that personal data privacy and confidentiality are maintained, the CSIS should serve the following purposes:

- To maintain information on screening history and results.
- To track utilization of cervical screening service and follow-up events

of clients.

- To facilitate record linkage across service providers.
- To link cervical smear data to biopsy results for analysis of cytology-biopsy correlation.
- To support quality assurance, evaluation, monitoring and research.

6.5.2   Functions of the CSIS

Recruitment and screening
- Recruit women in the target population for screening.
- Record results of cervical smears detected on screening.
- Identify women due for screening and send them reminders.

Diagnosis and treatment
- Facilitate record linkage of smear results and other information (upon woman's consent) to allow sharing of information among registered service providers for better patient care.
- Provide data to assist follow-up and management plan.

Evaluation and monitoring
- Evaluate individual compliance with screening and overall programme coverage.
- Generate statistics and reports for quality assurance, monitoring and research.

6.5.3   Output of the CSIS

The data users of the CSIS include women as well as service providers and laboratories in the public and private sectors. Subject to the Personal Data (Privacy) Ordinance, the CSIS will provide users with the following services:

Doctors
- Online secure interface to register for themselves and for women.
- Online secure interface to update women's information and smear and biopsy results.
- Online secure enquiry service to access smear records necessary for patient management.
- Reminder list to recall patients who are due for smears. Doctors may choose to send reminder letters to their own clients themselves.
- Quality performance report.

Laboratories
- Online secure interface for laboratories to register for themselves.
- Online secure interface for laboratories to record cytology and histology results.

- Online secure enquiry service to access smear records necessary for smear examination and reporting.
- Feedback on cytology and histology correlation.

- Quality performance report.

Women
- Viewing past smear results kept in CSIS.
- Reminder letters received before the next due date for screening.
- Continual health care from service providers who have access to women's previous smear result upon women's consent.

In essence, the CSIS plays a pivotal role in monitoring the quality assurance standards, through collection and analysis of data, and generation of a range of monitoring and evaluation indicators for the CSP. Continuous development in areas of data interface and screen workflow should enhance public/private sector communication and provide support to patient management.

6.6   Collaboration Between Public and Private Sectors

Private-public collaboration among public and private service providers and laboratories is crucial to the success of the CSP. Members from both the public and private sectors contributed to planning and implementation of the CSP. Through the CSIS, the CSP supports public and private doctors and pathologists by providing search for cervical smear and biopsy results, on-line enquiries, and feedback about quality indicators. The CSIS could provide the necessary data to support the monitoring of quality performance of cytology laboratories. The CSP will issue reminder letters for doctors to recall clients due for cervical screening.

The CSP has produced professional training kits which are distributed free to public and private service providers and laboratories. Refresher courses will be organized for private doctors in conjunction with professional training institutions. The private sector will also receive support in mass publicity and education campaigns to promote cervical screening.

6.7   Evaluation and Monitoring

The DH will evaluate and measure the effectiveness of the CSP, including coverage, performance indicators for quality control, public awareness, incidence and mortality of cervical cancer. Effort should be focused on increasing the coverage and having more women, including women of the older age group and those in the ethnic minority to go for smears, rather than repeating annual smears to those who already participated. Feedback from doctors as well as future research on the knowledge, attitude and practice of women on cervical cancer prevention are important in guiding continual development of the CSP.

6.8 *Summary*

In Hong Kong, the DH launched a territory-wide CSP on 8 March 2004 in collaboration with other health care providers. It aims to increase the coverage and better utilize resources. The ultimate goal is to reduce the morbidity and mortality of cervical cancer, hence bring better quality of life to women. The pillars of the cervical screening programme are recruitment and education, quality management, establishment of cervical screening information system and close collaboration between the public and private sectors.

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Chapter 7   Conclusions

Cervical cancer is a public health problem. It remains a major preventable cause of morbidity and mortality among women in Hong Kong.   With regard to primary prevention, strategies in safe sex, anti-smoking and healthy eating should contribute to health benefits to women.

An organized cervical screening programme is a proven effective strategy to combat the disease.   The Cervical Screening Programme (CSP) of Hong Kong aims at increasing the coverage rate of cervical screening, thereby decreasing the incidence and mortality of cervical cancer and ultimately improving the quality of life of women in Hong Kong.

There will be successive phases of publicity for the CSP to promote equitable screening and achieve high coverage rate.   Quality management on areas of smear taking, cytology reporting and colposcopy is essential to assure the quality of the CSP.   Use of information technology has a crucial role in collating and analyzing the relevant data and generating meaningful reports to continuously improve the CSP.

Maintaining and improving the CSP is an on-going challenge.   Success in prevention of cervical cancer entails the coordinated efforts and inter-sectoral collaboration of different parties, including medical and health services, professional and academic bodies, non-governmental organizations, and the community.

Resources

1. Department of Health
   http://www.info.gov.hk/dh/index.htm

2. Centre for Health Protection, Department of Health
   http://www.chp.gov.hk/

3. Cervical Screening Programme, Department of Health
   http://www.cervicalscreening.gov.hk

4. Central Health Education Unit, Department of Health
   http://www.cheu.gov.hk/

5. Hong Kong College of Obstetricians and Gynaecologists
   http://www.hkcog.org.hk

   (a) Management of Abnormal Cervical Smear Revised (2002) - Hong Kong College of Obstetricians and Gynaecologists

   http://hkcog.obg.cuhk.edu.hk/docs/college_guidelines/Management of Abnormal Cervical Smear Revised_2002.pdf

   (b) Colposcopy Service Provision and Standard - Hong Kong College of Obstetricians and Gynaecologists and the Hong Kong Society for Colposcopy and Cervical Pathology

   http://www.hkcog.org.hk/docs/training/colposcopy/co1.pdf

6. National Cancer Institute (United States)
   http://www.nci.nih.gov/

7. U.S. Preventive Services Task Force
   http://www.ahcpr.gov/clinic/uspstf/uspscerv.htm

8. NHS Cancer Screening Programmes (United Kingdom)
   http://www.cancerscreening.nhs.uk/cervical/index.html

9. National Cervical Screening Program (Australia)
   http://www.cervicalscreen.health.gov.au/home/index.html

10. Canadian Task Force on Preventive Health Care
    http://www.ctfphc.org/

Appendix

Report Evaluation Questionnaire

We hope that this report has provided you and your organization with useful information on cervical screening in Hong Kong. Your feedback will enable us to improve future issues of the Topical Health Report. Please let us have your opinion concerning the following:

What information do you find most useful in this report?

_____

_____

What additional information would you like to include in future editions of the report?

_____

_____

Do you have any further suggestions or comments of this report?

_____

_____

What is the name of your organization and your main work activity?

_____

_____

Any other comments?

_____

_____

Thank you for taking the time to complete the report evaluation questionnaire.

Please return by mail or fax (Fax No: 2575 4110) to
    Cervical Screening Programme
    Surveillance and Epidemiology Branch
    Centre for Health Protection
    Department of Health
    18/F Wu Chung House
    213 Queen's Road East
    Wan Chai,
    Hong Kong