

# Preventing avoidable death: the case of cervical cancer in Hong Kong

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**Cervical cancer remains an important cause of avoidable morbidity and mortality in Hong Kong. This paper briefly reviews the epidemiology of cervical cancer and explores the evidence on the effectiveness of screening. The essential components of a successful cervical cancer screening programme, based on international experience, are discussed. The present situation in Hong Kong is then examined and the options outlined for the way ahead.**

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## Introduction

Interest in the evaluation of disease screening has grown in recent years and the importance of considering both the scientific validity and overall benefits of screening, as well as establishing cost-effective, ethical and equitable policies for population screening is increasingly being recognised. Although insufficient evidence is available to support the provision of most screening procedures at a population level, a few have been shown to be highly effective and are now well established in many countries. Screening for cervical cancer using the Papanicolaou (Pap) smear is one such example, where the evidence supporting its effectiveness is so strong that death from the disease among women under the age of 65 years is considered to be avoidable.<sup>1</sup> This issue is topical and of increasing public interest in Hong Kong, as reflected by some recent articles in both the Chinese and English daily press.<sup>2-7</sup>

## Natural history and epidemiology of cervical cancer

Long-term studies have demonstrated that invasive disease arises as a consequence of progression from mild dysplasia through severe dysplasia to carcinoma in situ.<sup>8</sup> Richart introduced the commonly used classi-

fication system for these pre-invasive lesions as different grades of cervical intraepithelial neoplasia (CIN I to III).<sup>9</sup> Although mild dysplasia (CIN I) frequently regresses to normal, CIN III, once established, rarely exhibits spontaneous regression.<sup>10</sup> Therefore, for every patient with invasive cervical cancer there are approximately four patients with carcinoma in situ and more than 10 patients with low grade CIN.<sup>11</sup> Overall, up to three quarters of cases of CIN I or II progress to CIN III and 10% to 16% eventually progress to invasive cancer.<sup>12</sup>

Over the past few decades, overall mortality from cervical cancer has been falling in most countries, although the rate has increased in the younger age groups in some populations.<sup>13</sup> It remains a significant cause of morbidity and mortality, being the second most common form of cancer in women worldwide.<sup>14</sup> There is wide variation in the reported incidence of invasive disease between populations, ranging from 7% in one generation of women in Colombia, to 0.35% for the same generation in the non-Jewish population of Israel.<sup>15</sup> Apart from differences in diagnostic and reporting patterns, the two major factors contributing to this variation are considered to be differences in sexual practice, and differences in access to organised cervical cancer screening programmes. There is good evidence that sexual behaviour patterns such as age at first intercourse and the number of lifetime sexual partners of the woman and of her husband play an important role in the aetiology of cervical cancer. These practices determine the woman's risk of acquiring a sexually transmitted disease, and customs vary over

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time and between population groups. Thus, certain population subgroups, such as nuns and groups with strict practices of abstinence and monogamy, have long been noted to have very low rates of cervical cancer.<sup>8</sup> In contrast, populations with higher rates of sexually transmitted diseases, reflecting a greater level of extramarital sexual activity, have higher mortality rates from cervical cancer.<sup>16</sup>

The incidence of cervical cancer increases with age, starting to rise in women between the ages of 30 and 35 years in most countries, and reaching a peak at about 50 to 60 years. Apart from age, the other main factors which are strongly associated with invasive cancer include the following:

#### ***Infection with human papillomavirus***

Both epidemiological and molecular studies provide support for human papillomavirus (HPV), particularly HPV 16, 18, 45 and 56, as a primary aetiological factor in cervical cancer.<sup>17,18</sup> However, since exposure to HPV in young sexually active women is very common and infection with oncogenic viral types exceeds the number of cases of invasive cancer, other cofactors must play a part in cervical carcinogenesis.

#### ***The lifetime number of sexual partners***

Women who report three or more lifetime sexual partners have a two- to three-fold increased risk of developing cervical cancer, compared with those who report only one partner. The risk increases to nine-fold for women reporting 10 or more partners.<sup>19</sup>

#### ***Use of oral contraceptives***

Several studies have documented an association between the duration of oral contraceptive use and both CIN and cervical cancer.<sup>20</sup> The risk is increased in those who start using oral contraception before the age of 25 or who use it for 7 or more years.

#### ***Smoking***

Several observational studies have shown an association between smoking and cervical cancer, with an estimated two-fold increased risk for current smokers.<sup>21</sup> The risk increases with the amount and duration of smoking. The association persists after adjusting for sexual practice as a potential confounder, but is weakened after adjusting for infection with HPV.<sup>22</sup>

#### **Screening for cervical cancer**

Primary prevention of cervical cancer is not possible in the foreseeable future. However, several features of the disease make it an ideal target for a screening pro-

gramme. It has a long pre-invasive phase that may extend from 10 to 15 years. A safe, widely acceptable and inexpensive test, the Pap smear, is available to detect early-stage disease, and effective treatment of early-stage lesions can be accomplished with minimally invasive techniques.

Evidence for the effectiveness of screening comes from descriptive studies, which show a decline in both the incidence and mortality from invasive cervical cancer following the introduction of organised screening programmes.<sup>8,23,24</sup> Finland, Iceland and Sweden have implemented nationwide 'population-based organised' screening programmes since the 1960s. In these countries, the protective effect of two or more smears is clearly demonstrated<sup>25</sup> and the number of deaths from cervical cancer have been reduced by 80%.<sup>26</sup> There have also been several case-control studies documenting a reduction in the relative risk for invasive disease in women who have undergone Pap smear screening.<sup>27-29</sup> Most of these studies show a 90% reduction in the risk of invasive disease with screening intervals of up to 3 years.

The extent of risk reduction is partly dependent on the screening interval. Data from large screening programmes in European and North American centres have been analysed by the working group of the International Agency for Research on Cancer and used to quantify the reduction in the probability of developing cervical cancer with varying screening intervals (Table).<sup>30</sup> The data shows that after one negative Pap smear, screening every 3 years accomplishes about the same effect as screening annually. Furthermore, even screening once every 10 years can reduce the incidence of invasive cancer by almost two thirds. Hence, at a population level the achievement of adequate coverage of women at risk is a more significant determinant of risk reduction than the frequency of screening.<sup>31</sup> Targeting women who have never had a Pap smear

**Table. Reduction in cumulative rate of invasive cervical cancer in 35- to 64-year-old women screened at different frequencies\***

Interval between screenings (years)	Reduction in cumulative incidence (%)	Number of tests
1	93.5	30
2	92.5	15
3	90.8	10
5	83.6	6
10	64.1	3

\*Assuming the woman has had at least one previous screen

will have a much larger impact on reducing disease incidence and mortality, than screening more frequently those who have already been screened. In practice, despite the success of some screening programmes, others such as the early ones implemented in the United Kingdom and Norway have not been successful.<sup>32</sup> The main reasons cited for such failures are poor programme coordination and non-implementation of policy. In the United Kingdom, resources were concentrated on more frequent screening of younger women, rather than trying to achieve regular coverage for the entire population.<sup>33</sup> In Norway, only a small proportion of the population was covered by an organised programme.

### Effective cervical screening programmes

The essential elements of an effective cervical cancer screening programme, including organisation, accountability and commitment, are well documented.<sup>31,32,34</sup> Cases of invasive cervical cancer arising as a result of administrative and procedural failures thus cannot be justified in any developed country. The success of screening is dependent on factors which include the provision of adequate resources and the adoption of quality control measures. Ensuring that smears are promptly examined and the results fed back accurately requires considerable resources, both in terms of laboratories and human resources. Among screening smears, more than 90% of samples are expected to be normal, and some positive cases are likely to be missed. In order to minimise such false negative results, independent rescreening and quality assessment must be an integral part of the programme.<sup>33</sup>

Once abnormalities are detected, agreed guidelines for follow-up and clear lines of responsibility for doing this are essential. Several studies have highlighted inadequate follow-up as a problem which is more common than the problem of false negatives, and is responsible for a proportion of cases of invasive cervical cancer.<sup>35</sup> In one study, omission by clinicians and administrative errors accounted for more than 90% of cases of documented inadequate follow-up, and only a small proportion of cases were attributable to the patients themselves.<sup>36</sup> Furthermore there is increasing evidence that in women who have had conservative treatment for cervical intraepithelial neoplasia, regular and long-term follow-up is necessary, as the risk of invasive cancer remains high.<sup>37</sup>

Although financial and technical considerations are important, the main difference between effective programmes and those which fail is in their level of or-

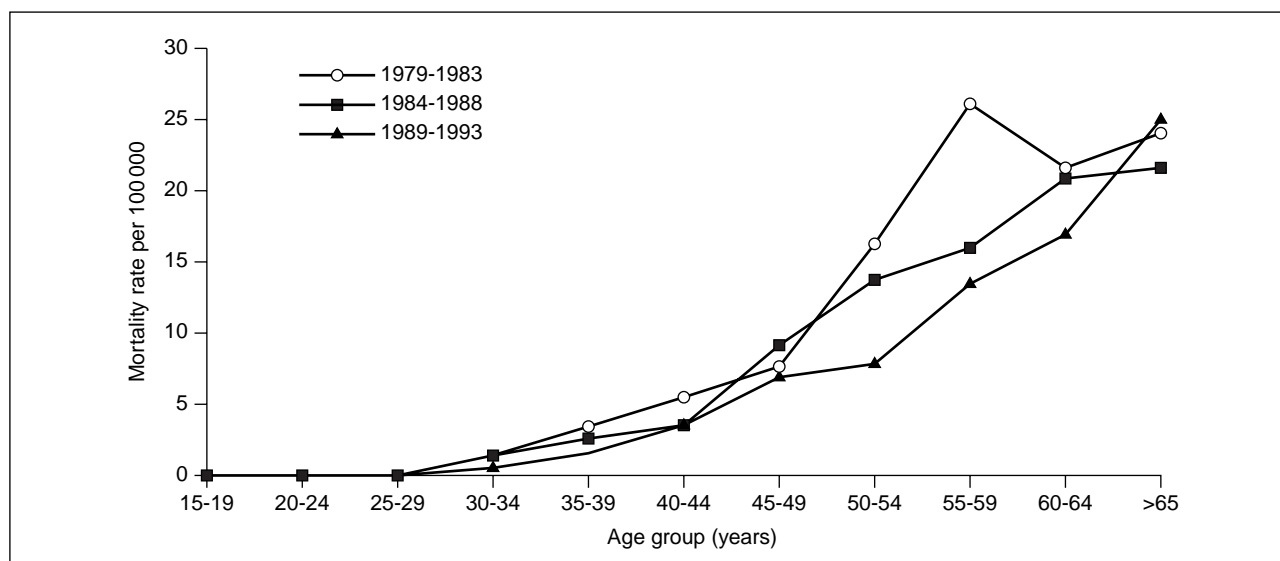
ganisation and management.<sup>32</sup> The recognition by the World Health Organization that poor management and the implementation of inappropriate policies are responsible for the failure of some screening programmes has prompted the Western Pacific Regional Office to adopt managerial guidelines.<sup>38</sup> The purpose of these is to assist in the planning, development, management, and monitoring of programmes for the early detection of cervical cancer.

An organised screening programme is more likely to target women at high risk compared to one where screening is opportunistic, and it can reduce the incidence of invasive cancer by up to 90%.<sup>39</sup> There is in fact a strong correlation between the organisation of screening and changes in disease incidence.<sup>40,41</sup> A well-managed programme also has several other advantages. Internationally there is evidence that older women and those with low socio-economic status have a higher than average risk for cervical cancer and are less likely to take up preventive health services.<sup>42</sup> Increasing coverage by targeting will tend to attract these women more, and can therefore contribute to a reduction in health inequalities.<sup>43</sup> Furthermore, if most women attending screening are those at lower risk, more false positives are likely to arise, resulting in additional medical work, unnecessary anxiety, and possibly iatrogenic disease. This also wastes resources and reduces the cost-effectiveness of screening.<sup>44,45</sup>

### Cervical cancer in Hong Kong

Cervical cancer is an important public health problem in Hong Kong. Compared to other industrialised countries, Hong Kong has a moderately high mortality rate for cervical cancer,<sup>46</sup> and is cited as a high-risk area for this by the International Agency for Cancer Research.<sup>15</sup> In contrast, Hong Kong women are at lower risk of other common cancers, such as those of the breast and lung, compared with their counterparts in most western countries. The incidence of clinical cancer increases with age and, reaches a peak in the 60 to 65 years age group (Fig 1). It is the fourth most common newly diagnosed cancer in local women,<sup>47</sup> in contrast to being ranked eighth in the UK in 1988.<sup>31</sup> Of 159 deaths from the disease in 1995,<sup>48</sup> one half occurred in the 15 to 64 years age group, where it should have been avoidable.

There has been a slow overall decline in incidence and mortality from cervical cancer in Hong Kong over the past 15 years (Fig 2). The decreasing tendency is more apparent in middle-age rather than in the elderly (Fig 1), and is less marked than the downward trend



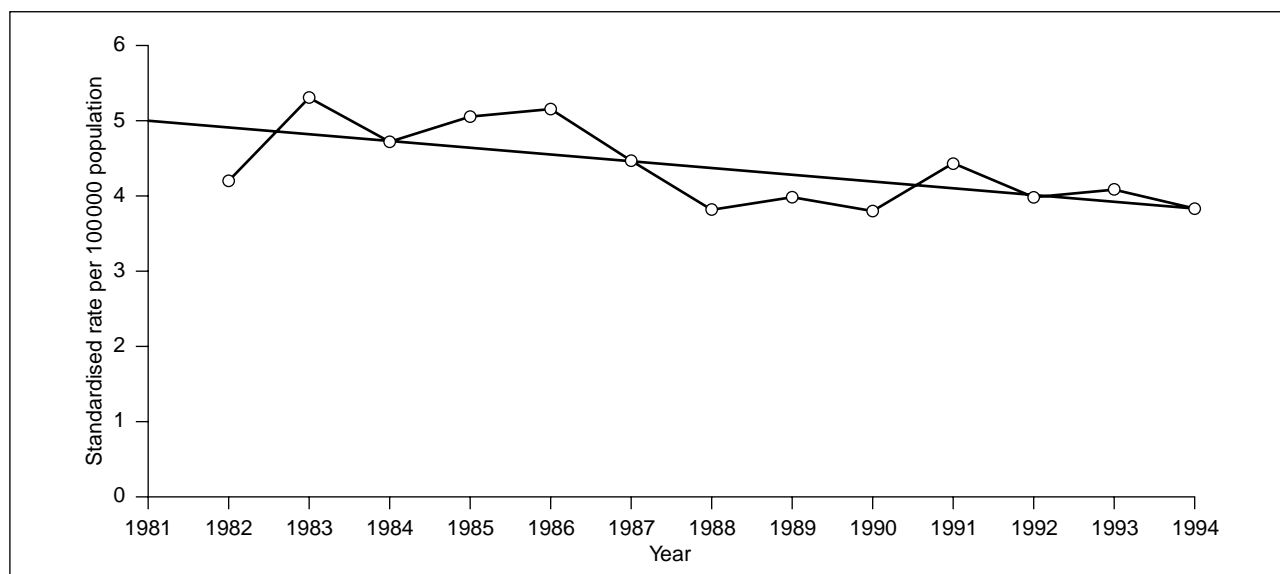
**Fig 1. Trends in cervical cancer mortality rate by age group**

seen in areas where there are well-organised screening programmes. The unexplained increase in mortality among younger women, which is seen in some countries, is not yet apparent in Hong Kong.

At present there is no centrally organised, systematic, population-based cervical screening programme. Most screening activity is either opportunistic or offered as a part of a general well woman check up by various health care providers, each with their own agenda. It is estimated that about two thirds of Pap smears are carried out by the Family Planning Association and the Department of Health, while the rest are done in the private sector. There is no locally developed policy on screen-

ing, and as yet there are no guidelines from the major local medical organisations such as the Hong Kong Medical Association or the Hong Kong College of Obstetricians and Gynaecologists.

Health surveys by the Family Planning Association of Hong Kong in 1992 found that the 1 year coverage of screening among women under the age of 60 years is around 30%.<sup>49,50</sup> The highest coverage was among the 30- to 49-year-olds, while women over the age of 50 years, who are at higher risk, had the lowest coverage (20%). However, there remain many unanswered questions. We do not know what the frequency of screening is among those who are currently



Source: Director of Health Annual Reports, 1981/82 - 1994/95; standardised to world standard population, linear trend line fitted

**Fig 2. Age-standardised mortality rates for cervical cancer in Hong Kong, 1981-1994**

screened, nor whether they are the women with other risk factors. More research is needed to assess the technical and quality control aspects of screening. There is no local information on the acceptability of the present arrangements for screening. Most important in terms of minimising the population impact of the disease is the need to consider the most effective means of achieving high coverage of the population at risk. This is a major challenge, because of the heterogeneous nature of Hong Kong's mixed medical economy.

## The way forward

While more local research is needed, we should also take heed of what has been learned the hard way in other countries. We need a local policy with clear objectives which define the target groups and screening arrangements, and which is linked to a continuing evaluation programme. In the absence of a centralised population register, various approaches for the implementation of such a policy need to be considered. These may include educational approaches that are aimed at both the public and health professionals, or the use of incentives, such as service payments. If there are professional or financial obstacles to the achievement of coverage through current health care providers, then new managed care contracts should be considered to provide cervical screening. Adequate resources for health promotion to target at-risk women, and facilities for the prompt examination and reporting of smears should be made available. Finally, locally developed guidelines that are linked to an audit programme should be disseminated to ensure that standardised methods are used for taking, analysing and reporting smears, and that adequate quality control arrangements are in place. A coordinated, population-wide approach to screening is the only way to prevent further avoidable deaths from cervical cancer.

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