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Cost-effectiveness of organized versus opportunistic cervical cytology screening in Hong Kong

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Abstract

Background To assess the cost-effectiveness of alternative cervical cancer screening strategies to inform the design and implementation of a government-sponsored population-based screening programme in Hong Kong.

Methods Cost-effectiveness analysis using a computer-based model of cervical carcinogenesis was performed. Strategies included no screening, opportunistic screening (status quo), organized screening using either conventional or liquid-based cytology conducted at different frequencies. The main outcome measures were cancer incidence reduction, years of life saved (YLS), lifetime costs and incremental cost-effectiveness ratios. Data were from local hospitals and laboratories, clinical trials, prospective studies and other published literature.

Results Compared with no screening, a simulation of the current situation of opportunistic screening using cervical cytology produced a nearly 40 per cent reduction in the lifetime risk of cervical cancer. However, with organized screening every 3, 4 and 5 years, corresponding reductions with conventional (and liquid-based) cytology were 90.4 (92.9), 86.8 (90.2) and 83.2 per cent (87.3 per cent) compared with no screening. For all cytology-based screening strategies, opportunistic screening was more costly and less effective than an organized programme of screening every 3, 4 and 5 years. Every 3-, 4- and 5-year screening cost $12 300, $7100 and $800 per YLS, each compared with the next best alternative.

Conclusions Compared with the status quo of opportunistic screening, adopting a policy of organized, mass cervical screening in Hong Kong can substantially increase benefits and reduce costs.

Keywords: cervical cancer screening, cost-effectiveness analysis, Hong Kong

Introduction

Cervical cancer is the fourth leading cause of cancer death among women in Hong Kong, with an age-standardized incidence rate of 15.6 per 100 000.[1] Although the Hong Kong College of Obstetricians and Gynaecologists has recommended regular screening for all women from the time of commencing sexual activity until they reach the age of 65,[2] cervical cancer screening occurs haphazardly and opportunistically in Hong Kong. A report from the Health Services Research Committee estimated that as many as 45 per cent of women under the age of 60 have never been screened and that 20 per cent have had one or more screens but not at regular intervals.[3]

While previous studies have examined the relative costs and effectiveness of screening at different frequencies and at different ages,[4–11] there has been less emphasis on quantifying the comparative efficiency of an organized programme versus an opportunistic service in the context of middle- to high-income countries that can afford a screening programme but have not yet implemented one. Motivated by a government-sponsored initiative to provide effective cervical cancer screening coverage we sought to provide evidence on the cost-effectiveness of alternative cervical cancer screening strategies to inform the design and implementation of an organized screening programme in Hong Kong.

Methods

We used a computer-based Markov model to simulate the natural history of cervical cancer using a sequence of monthly transitions among health states. Health states were defined to reflect different levels of cervical intraepithelial neoplasia (CIN) and stages of invasive cancer (Fig. 1). Unique health states were defined to distinguish women with prior treatment for CIN and detected cervical disease (through symptoms or screening). Based on the mean age of onset of sexual activity in Hong Kong,[12] we assumed that a cohort of healthy females enter the

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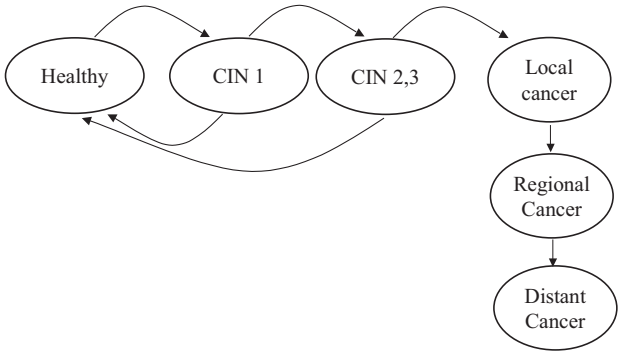

Fig. 1 Natural history model. Health states were defined using three categories of cervical health (normal, grade of CIN and stage of invasive cancer). Each month, women face an age-dependent risk of acquiring CIN 1. Women with established cervical lesions can regress to normal, or progress to higher-grade lesions or cervical cancer. Unique health states were defined to distinguish women with prior treatment for CIN and detected cervical disease (through symptoms or screening). Women at any age may die of a cervical cancer-related illness, or other causes.

model at age 15 and at each month face an age-dependent risk of developing CIN. Women with established CIN 1 or CIN 2,3 can regress to normal, or progress to higher-grade lesions or invasive cancer. Women at any age may die of a cervical cancer-related illness, or other causes.

Strategies included no screening, opportunistic screening (status quo), and organized screening using either conventional or liquid-based cytology conducted at different frequencies. While the conventional Pap smear is generally used in Hong Kong, the liquid-based Pap smear, a more costly test, is increasingly being used. Because of the uncertainty with respect to the relative performance of liquid-based versus conventional cytology we conducted all analyses using both types of cytology. Although we assumed that all cervical cancers are caused by human papillomavirus (HPV) this analysis did not evaluate primary HPV DNA testing.[13]

To simulate opportunistic screening we assumed that 45 per cent of all women are never screened, 13 per cent get one screen in their lifetime at age 30, 8 per cent get one screen at age 50, 2 per cent get screened every 3 years, 4 per cent get screened every 2 years, and 28 per cent get screened every 1 year. To simulate strategies within an organized programme we assumed that screening starts at age 21 and occurs at regular intervals (every 1, 2, 3, 4 and 5 years) in the absence of a cytological abnormality. We conservatively assumed there was no upper age limit for screening, but we evaluated the outcomes associated with an upper age limit of 65 and 55 in sensitivity analysis. We made the following additional assumptions: (1) colposcopy and biopsy are preformed for all cytological results of either LSIL or HSIL; (2) biopsy-confirmed cases of CIN 2,3 or invasive cancer are treated with either loop electrosurgical excision procedure (LEEP), conisation or hysterectomy; (3) women who have been successfully treated for precancerous lesions return to a healthy state but are still at risk for future disease.

We adopted a societal perspective and followed the recommendations of the Panel on Cost-Effectiveness in Health and Medicine.[14] Costs were converted from Hong Kong dollars (US$1 = HK$7.8) and inflated to US$2000 and clinical benefits were expressed as years of life saved (YLS) and reduction in the lifetime risk of cancer. Future costs and life years were discounted at an annual rate of 3 per cent. The performance of alternative screening strategies was measured using the incremental cost-effectiveness ratio, defined as the additional cost of a specific screening strategy, divided by its additional clinical benefit, compared with the next most expensive strategy. Strategies that were less effective and more costly than an alternative strategy (strongly dominated) and strategies that had a higher incremental cost-effectiveness ratio than a more effective alternative strategy (weakly dominated) were eliminated. Sensitivity analyses were conducted to assess the impact of parameter uncertainty and alternative assumptions on our results.

Data

Selected clinical data for the base case analysis and ranges used for sensitivity analysis are presented in Table 1.[15–39] The natural history parameters were obtained mainly from published literature although we used country-specific data where possible.[15–24] Estimates for test sensitivity and specificity for both types of cytology were obtained from the pathology laboratory at a tertiary academic medical centre.[25] Published comprehensive reviews of cytology performance were used to inform the plausible ranges for sensitivity analysis.[26–31]

Resource utilization and cost data were from fee schedules, regional health care organizations in Hong Kong, and the Hospital Authority (which manages all 44 public hospitals in Hong Kong accounting for >94 per cent of total bed-days and ~10 per cent of ambulatory visits).[32–39] Direct medical costs associated with screening included cost of test, office visit, and patient time and transportation costs. The cost values for the conventional and liquid-based cytology tests and office visits were obtained from two sources, namely the Hong Kong Family Planning Association (public sector)[34] and the AmMed Clinic and Quality Healthcare Asia Ltd (both are private for-profit managed care organizations).[38,39] While liquid-based cytology costs only $2 more than the conventional cytology in Hong Kong, there is a much smaller difference in cost than reported in the United States (corresponding price differential of $13).[40–42] The aggregate costs for colposcopy and biopsy, and for treating CIN 1 and CIN 2,3 were obtained from the Hospital Authority's Patient-Related Group (PRG) costing at the 1999/2000 level[32] and the publicly-operated Queen Mary Hospital.[33] The costs for the combination of LEEP, conisation and hysterectomy, and the stage-specific aggregate treatment costs for invasive cancer were derived as a proportion of each standard cost in the United States and thus were the same for both public and private sectors.

Patient time costs were assumed to be the same for public

Table 1 Model variables: baseline values and ranges used in sensitivity analysis*

Variable	Base case	Plausible range
Natural history15–23		
Normal to CIN 1	0.0007–0.0209†	0.0004–0.0418†
CIN 1 to CIN 2,3	0.0014–0.0049†	0.0007–0.0098†
CIN 2,3 to local invasive cancer	0.0040	0.0020–0.0080
Local invasive cancer to regional invasive cancer	0.0250	0.0100–0.0400
Regional invasive cancer to distant invasive cancer	0.0375	0.0250–0.0500
CIN 1 to normal	0.0068–0.0128†	0.0034–0.0256†
CIN 2,3 to normal	0.0029	0.0015–0.0058
Five-year cancer survival rate24		
Local invasive cancer	0.86	0.80–0.93
Regional invasive cancer	0.43	0.28–0.66
Distant invasive cancer	0.11	0.04–0.33
Annual probability of symptom detection24		
Local invasive cancer	0.19	0.10–0.66
Regional invasive cancer	0.60	0.36–0.84
Distant invasive cancer	0.90	0.68–0.99
Test characteristics25–31		
Sensitivity of ThinPrep™ cervical cytology (%)	70	50–100
Specificity of ThinPrep™ cervical cytology (%)	95	90–100
Sensitivity of conventional cervical cytology (%)	60	50–100
Specificity of conventional cervical cytology (%)	95	90–100
Direct medical costs (2000 US$)32–39		
ThinPrep™ cervical cytology	42	42–190
Test cost	12	12–100
Office visit	7	7–20
Time cost	17	17–50
Travel cost	6	6–20
Conventional cervical cytology	40	40–190
Test cost	10	10–100
Office visit	7	7–20
Time cost	17	17–50
Travel cost	6	6–20
Aggregate costs (2000 US$)‡[32,33]		
Colposcopy and biopsy	284	150–400
CIN 1	307	200–500
CIN 2,3	733	500–900
Local invasive cervical cancer	13 172	9500–22 000
Regional invasive cervical cancer	14 098	11 700–29 000
Distant invasive cervical cancer	22 580	12 670–81 550

*CIN, cervical intraepithelial neoplasia; LSIL, low-grade squamous intraepithelial lesion; HSIL, high-grade squamous intraepithelial lesion. Estimates are reported as monthly probabilities unless otherwise noted.
†Values are age-specific and are available from the authors upon request.
‡Aggregate costs reflect the sum of the procedure, office visit and woman's time.

and private clinic visits and were cited from the *Cost of Labours* survey by the Hong Kong Census and Statistics Department.[36] Travel costs were estimated for a woman who travelled from home to a clinic within the neighbourhood using public transportation.[43]

Results

Face validity of the model

The natural history model predicted a peak prevalence of 8.6 per cent for CIN1 and 1.9 per cent for CIN 2,3. Lifetime cancer incidence in the absence of screening was 2.7 per cent, with peak incidence of 81 cases per 100 000 women, similar to predicted values reported in other published cervical cancer screening models.[4–7,23]

Base case analysis

Results for the base case analysis are shown in Table 2. Since data for the relative performance of conventional and liquid-based cytology are increasingly reported to be uncertain, we conducted all analyses using conventional cytology and liquid-based cytology. Lifetime cervical cancer incidence was reduced

Table 2 Discounted costs, average life expectancy, and incremental cost-effectiveness of liquid-based and conventional cytology for different screening frequencies*

Screening strategy	Total average lifetime costs (US$)	Incremental costs (US$)†	Total average life-expectancy (years)	Cancer incidence reduction (%)	Cost-effectiveness ratio (US$/YLS)‡
No screening	207	–	28.1678	–	–
Conventional cytology					
Screen every 5 years	367	160	28.3663	83.2	800
Screen every 4 years	425	58	28.3770	86.8	5400
Screen every 3 years	525	100	28.3880	90.4	9000
Opportunistic screening§	553	(28)	28.2609	37.9	Dominated‖
Screen every 2 years	730	205	28.3990	93.8	18 600
Screen every 1 year	1351	622	28.4092	96.6	60 800
Liquid-based cytology					
Screen every 5 years	373	166	28.3795	87.3	800
Screen every 4 years	435	62	28.3881	90.2	7100
Screen every 3 years	540	105	28.3967	92.9	12 300
Opportunistic screening§	566	(26)	28.2640	39.0	Dominated‖
Screen every 2 years	754	214	28.4047	95.3	26 700
Screen every 1 year	1400	646	28.4117	97.2	92 400

*YLS indicates year of life saved.
†Incremental costs represent the difference between the strategy and the next best non-dominated strategy.
‡The difference in cost divided by the difference in life expectancy for each strategy compared with the next best strategy. All strategies are assumed to be equally available.
§Opportunistic screening strategy assumed the following screening pattern: 45 per cent never screened, 13 per cent one screen per lifetime at age 30, 8 per cent one screen per lifetime at age 50, 2 per cent screened every 3 years, 4 per cent screened every 2 years, 28 per cent screened every year.
‖Opportunistic screening cost more but was less effective than every 3- to every 5-year screening and was therefore dominated; conventional cytology strategies were more costly and either less effective or less cost-effective than liquid-based cytology strategies.

by 37.9 per cent with the status quo strategy of opportunistic screening using conventional cytology, compared with no screening. With every 3-, 4- and 5-year screening, cancer reduction with conventional smears was 90.4, 86.8 and 83.2 per cent, respectively, compared with no screening. When compared with no screening, every 5-year screening with conventional cytology cost $800 per YLS. Every 4-year screening, compared with every 5-year screening, resulted in an increase in life expectancy of 4 days and cost $5400 per YLS, and screening every 3 years cost $9000 per YLS, compared with every 4-year screening. The opportunistic screening strategy was more costly and less effective than every 3-, every 4- and every 5-year screening, and was therefore dominated by these strategies. Results for liquid-based cytology were similar.

We also compared the discounted lifetime costs and benefits of screening with both liquid-based and conventional cytology for all screening frequencies assuming both types of cytology were equally available (Fig. 2). The incremental cost-effectiveness ratio for each strategy is represented by the increase in costs divided by the gain in benefits (or, the reciprocal of the slope of the line between two strategies) compared with the next most expensive strategy. Strategies that lie on the efficiency curve are ones that are not dominated. In general, liquid-based cytology strategies had a more attractive cost-effectiveness ratio than the conventional cytology strategies, and therefore dominated them. These results were most sensitive to changes in the relative performance and costs of liquid-based and conventional cytology.

Provided the sensitivity of liquid-based Pap was at least 62 per cent and the specificity was $\geq$88 per cent, conventional cytology was less effective and cost-effective. On the other hand, if the sensitivity of conventional Pap improves to 69 per cent, every 5-year screening with conventional cytology was more cost-effective than liquid-based cytology. If the sensitivity of conventional cytology increases to 70 per cent, all strategies using liquid-based cytology were less efficient than conventional cytology. Unless the per-woman cost of liquid cytology doubled (to $34), these results were stable.

We evaluated the impact of an upper age limit of screening imposed at age 55 and 65 (Table 3). Although total costs, life years and cost-effectiveness ratios were lower when screening is terminated at earlier ages, the rank ordering of the strategies did not change from the base case results. Screening every 3 years or less with conventional cytology cost less than $10 000 per YLS under all three assumptions. As in the base case analysis, opportunistic screening was dominated, and screening every 1 or 2 years were less attractive strategies. Results were similar for liquid-based cytology.

Figure 3 depicts the total cost savings and years of life gained by switching from the current practice of opportunistic screening to an organized screening programme of every 3- to every 5-year screening for all women using liquid-based cytology.

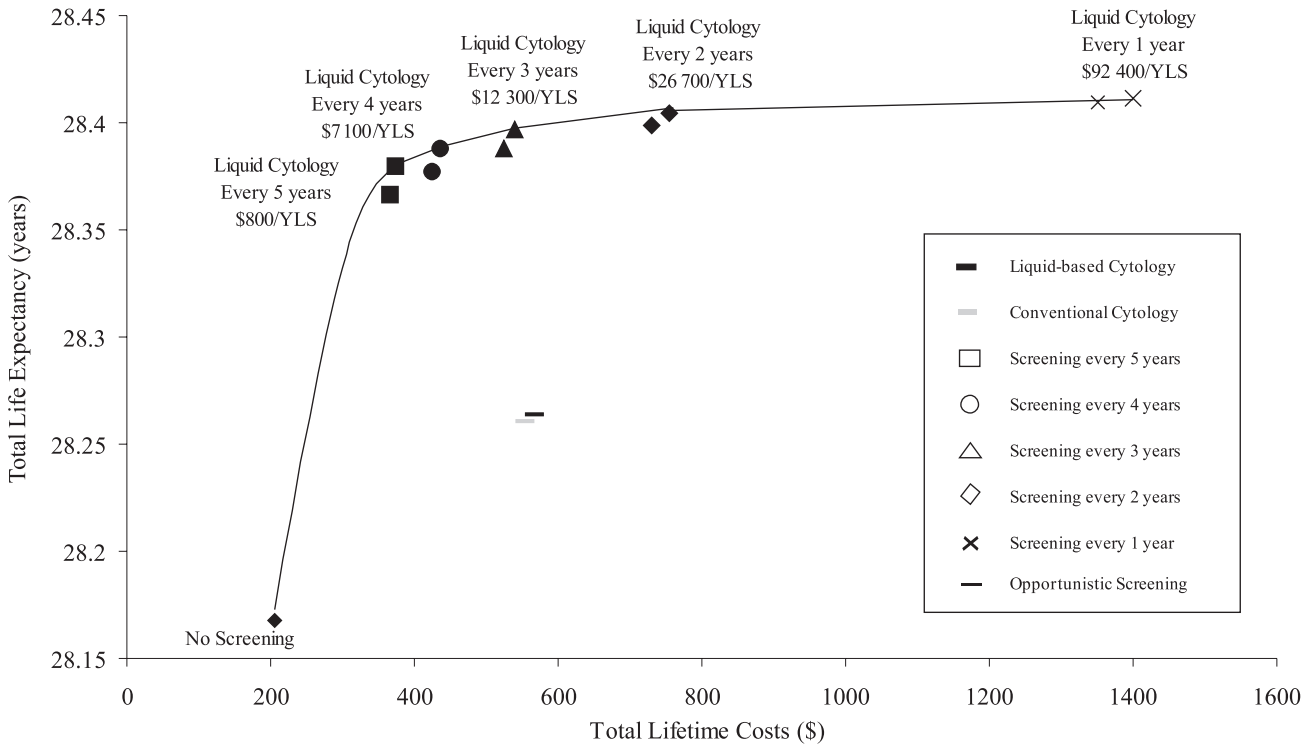

Fig. 2 Discounted costs and life expectancy for screening strategies for opportunistic (dash), every 1-year (cross), every 2-year (diamond), every 3-year (triangle), every 4-year (circle) and every 5-year (square) screening with liquid-based (blue) or conventional cytology (red). The cost-effectiveness ratio is the reciprocal of the slope of the line connecting the two screening strategies under comparison; this slope will be steeper when the net gain in life expectancy per dollar is greater. Strategies lying on the efficiency curve dominate those lying to the right of the curve because they are more effective, and either cost less or have a more attractive cost-effectiveness ratio, than the next best strategy. See Results for details.

Over the lifetime of a typical cohort of 20–24-year-old women in Hong Kong,[44] costs savings would exceed $43 million with every 5-year screening, $29 million with every 4-year screening and $6 million with every 3-year screening. Life expectancy gains would exceed 26 000 years with every 5-year screening, 28 000 years with every 4-year screening and 30 000 years with every 3-year screening.

Discussion

Our results show that, compared with the status quo of opportunistic screening, adopting a policy of an organized, population-based screening programme every 3–5 years for all women aged 21 and over in Hong Kong could substantially increase benefits and reduce costs. With organized screening every 3, 4 and 5 years, corresponding reductions in the lifetime risk of cervical cancer with conventional (and liquid-based) cytology are 90.4 (92.9), 86.8 (90.2) and 83.2 per cent (87.3 per cent) compared with an ~40 per cent reduction with the current situation of opportunistic screening. For all cytology-based screening strategies, regardless of whether conventional or liquid-based cytology is used, opportunistic screening was more costly and less effective than an organized programme of screening every 3, 4 and 5 years.

While there is no consensus on what is an acceptable cost per year of life gained (otherwise known as a threshold cost-effectiveness ratio) incremental cost-effectiveness ratios for particular settings are often placed in context by interventions that are widely mandated in that same region of interest. In the United States, adoption of medical technologies that are below $100 000 per YLS is quite common.[45,46] It is not clear what the willingness-to-pay threshold (i.e. cost-effectiveness threshold) is for preventive programmes in Hong Kong. If this threshold is $15 000 per YLS, the optimal screening frequency with liquid-based cytology would be every 3 years; if the threshold is $10 000 per YLS, the optimal screening frequency would be every 4 years; and if the threshold is $1000 per YLS, the optimal screening frequency would be every 5 years. Using cost-effectiveness analysis to inform public policy does not mean necessarily that less money should be spent, but rather that the use of resources might be more efficient. It is plausible that the resources saved by investing in organized cervical cancer screening every 3–5 years (compared with more frequent annual screening) could be invested in another intervention (e.g.

Table 3 Cost-effectiveness ratios for every 3-, 4- and 5-year screening with upper age limit

	No age limit (base case) ($ per YLS)	Stop screen at age 65 ($ per YLS)	Stop screen at age 55 ($ per YLS)
Conventional cytology			
Every 5 years	800	700	500
Every 4 years	5400	5200	4100
Every 3 years	9000	7600	6900
Opportunistic	Dominated	Dominated	Dominated
Every 2 years	18 600	16 600	14 400
Every 1 year	60 800	53 500	47 100
Liquid-based cytology			
Every 5 years	800	600	500
Every 4 years	7100	6700	5400
Every 3 years	12 300	10 400	9400
Opportunistic	Dominated	Dominated	Dominated
Every 2 years	26 700	23 600	20 500
Every 1 year	92 400	81 300	71 800

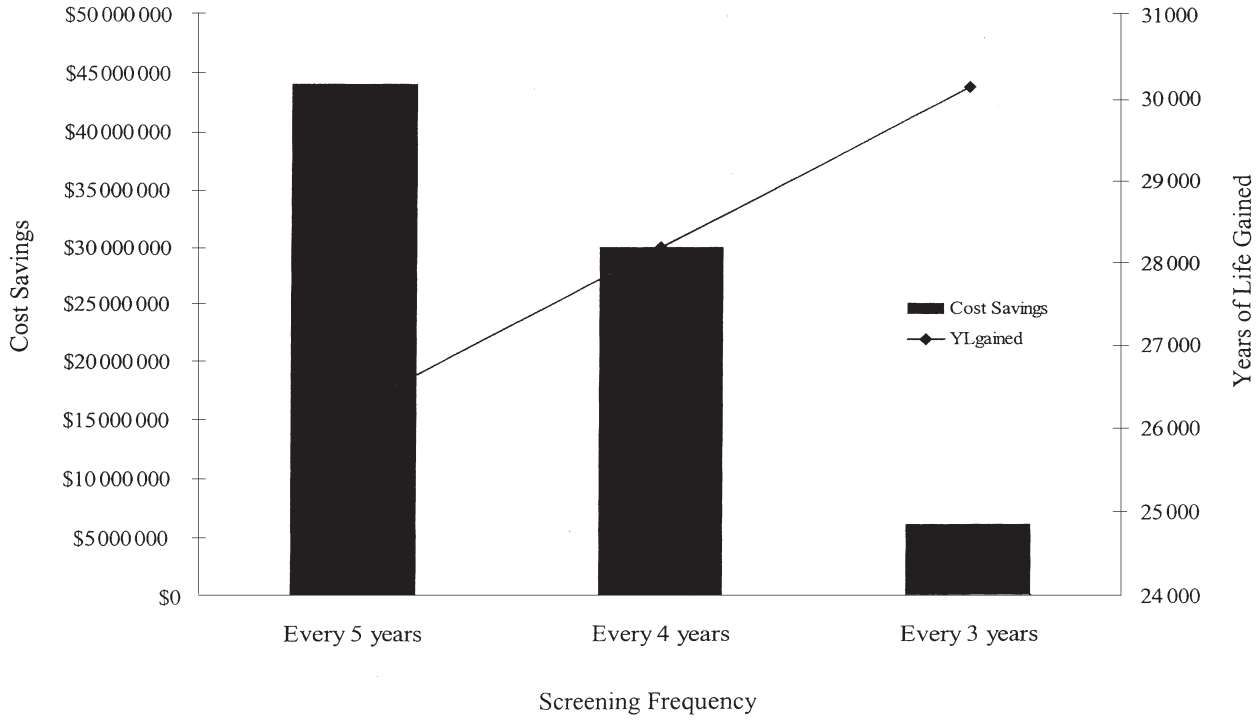

Fig. 3 Cost savings and years of life gained of organized screening compared with opportunistic screening.

mammography screening for breast cancer) that would produce greater gains in life expectancy than those obtained by increasing the frequency of cervical cancer screening. Regardless of the particular cost-effectiveness threshold, and across all screening frequencies evaluated, shifting from the status quo to organized screening would decrease costs while providing more benefit than current screening practice.

Our analysis has several limitations. First, we did not incorporate HPV DNA testing into our model. Instead, we focused on quantifying the additional benefits and cost savings that could occur with modest changes to an organized screening programme assuming no new technology. Secondly, our analysis was intended to broadly inform population-based screening policy and the model does not comprehensively capture the heterogeneous behaviour of clinicians and women; for example, there is evidence suggesting that women at higher risk for cervical cancer may be less likely to get screened, while women at lower risk are more likely to get screened.[3] If this is true, we may

have underestimated the gains in life expectancy and economic cost savings if Hong Kong were to shift from the status quo to organized mass screening. Thirdly, there is a great deal of uncertainty with respect to the relative performance and costs of liquid-based and conventional cytology. However, our results were robust regardless if we evaluated conventional cytology alone, liquid-based cytology alone, or if we assumed they were both equally available. There is a trade-off between using the best available published data versus country-specific data of lesser quality. To the extent possible, we used data from Hong Kong for the stage distribution and lifetime risk of cancer, direct medical costs and the costs of women's time.

The results of this analysis can be utilized as the first evidence-based study to inform a government-sponsored population-screening programme in Hong Kong. Our results demonstrate the potential for large additional gains in life expectancy and cost savings if Hong Kong shifts from the haphazard status quo to an organized approach. A programme of organized screening of every 3–5 years is more effective in reducing cancer incidence and increasing life expectancy, and is more cost-effective than the current practice of screening opportunistically. This message is particularly relevant for other rapidly developing or developed east Asian countries, such as China, Japan, Singapore, South Korea and Taiwan, where there are still no systematic screening programmes despite both the widespread availability of cytological tests and the economic means to afford such.

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