RESEARCH COMMUNICATION

Cost-Effectiveness of HPV Vaccination in the Prevention of Cervical Cancer in Malaysia

Wan Puteh Sharifa Ezat [1]*, Syed Aljunid[2]

Abstract

Introduction: Cervical cancers (CC) demonstrate the second highest incidence of female cancers in Malaysia. The costs of chronic management have a high impact on nation's health cost and patient's quality of life that can be avoided by better screening and HPV vaccination. Methodology: Respondents were interviewed from six public Gynecology-Oncology hospitals. Methods include experts' panel discussions to estimate treatment costs by severity and direct interviews with respondents using costing and SF-36 quality of life (QOL) questionnaires. Three options were compared i.e. screening via Pap smear; quadrivalent HPV Vaccination and combined strategy (screening plus vaccination). Scenario based sensitivity analysis using screening population coverage (40-80%) and costs of vaccine (RM 300-400/dose) were calculated. Results: 502 cervical pre invasive and invasive cervical cancer (ICC) patients participated in the study. Mean age was 53.3 ± 11.21 years, educated till secondary level (39.39%), Malays (44.19%) and married for 27.73 ± 12.12 years. Life expectancy gained from vaccination is 13.04 years and average Quality Adjusted Life Years saved (QALYs) is 24.4 in vaccinated vs 6.29 in unvaccinated. Cost/QALYs for Pap smear at base case is RM 1,214.96/QALYs and RM 1,100.01 at increased screening coverage; for HPV Vaccination base case is at RM 35,346.79 and RM 46,530.08 when vaccination price is higher. In combined strategy, base case is RM 11,289.58; RM 7,712.74 at best case and RM 14,590.37 at worst case scenario. Incremental cost-effectiveness ratio (ICER) showed that screening at 70% coverage or higher is highly cost effective at RM 946.74 per QALYs saved and this is followed by combined strategy at RM 35,346.67 per QALYs saved. Conclusion: Vaccination increase life expectancy with better QOL of women when cancer can be avoided. Cost effective strategies will include increasing the Pap smear coverage to 70% or higher. Since feasibility and long term screening adherence is doubtful among Malaysian women, vaccination of young women is a more cost effective strategy against cervical cancers.

Key Words: HPV vaccination - Pap smear - cost-effectiveness - quality of life - cervical cancer

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Introduction

Cervical cancer (CC) was the second most common cancer after breast cancer in women globally until 1985, and ranked as the third most common cancer in 1990. Almost 80% of cervical cancer cases were diagnosed in developing countries, where it was the most common cancer in women. The Malaysian National Cancer Registry Report (2003) found that the most frequently occurring cancers in Malaysian women were cancers of the breast, cervix, colon, ovary, leukemia and lungs, in that order. CC contributed about 12.9% of all female cancers with an age standardized incidence rate of 19.7 per 100,000 in Malaysia, and thus higher compared to other Asian and Western countries and even global rates (National Cancer Registry, 2003). Deaths from CC are rare amongst young women but its incidence increased from age 30 onwards and peaked at 60-69 whereby 54.7% of cases in the age of 40-59. Incidence rates were in general, highest among Chinese women (28.8/100,000); Indians (22.4/100,000) and lowest amongst the Malays (10.5/100,000).

Based on Malaysia's Pap smear guidelines, women can be discharged from the screening program at the age of 65 if they have had two negative smears in the previous 10 years. Generally there has always been a low uptake of screening among Malaysian women and reasons include shame, lack of knowledge on the procedure (Jamsiah, 2008) and cancers, too busy with house works and husbands' lack of support (3rd National Health Morbidity Survey or 3rd NHMS, 2006). In the 3rd NHMS 2006, 43.7% of 18 years and above women (95% CI: 42.9-44.6) reported to have undergone Pap smear examination. This showed a positive increase in prevalence from only 26% of women undergoing Pap smear in the 2nd NHMS 1996. The increase in Pap smear coverage must be taken up with caution as not only that they must come forward for a screening, but they also have to come for follow ups for whatever cervical cells changes recognized or noted through the Bethesda system. This is where most women

*[1]Dept of Community Health, UKM Medical Centre, [2]United Nations University-International Institute for Global Health, Kuala Lumpur, Malaysia *For Correspondence: sh_ezat@yahoo.com*

become lost to follow ups.

The cervical cancer screening program was established in 1969, following the integration of family planning services into the Maternal and Child Health Program of the Ministry of Health Malaysia (Division of Family Health Development Malaysia 2004). The Pap smear screening program is planned, organized and evaluated by the Family Health Development Division, Ministry of Health Malaysia. A National Technical Committee comprising of members from other government agencies, NGOs, private sectors and universities is responsible in its implementation. Even though the program is targeted and offered to all sexually active women between the ages of 20 and 65 years, the screening interval recommended is three years following two initial consecutive negative smears taken one year apart. Since the 1995 Healthy Life Style Campaign themed 'Cancer', Pap smear screening was made available to all females aged between 20 and 65 years and reinforced through the promotion of a healthy family. In 1999, the Bethesda Classification System was introduced and was encouraged to be used by all health care providers for a standardized system of reporting. There are various agencies that provide Pap smear services such as the National Population and Family Development Board (Ministry of Women, Family and Community Development), Federation of Family Planning Association of Malaysia, private clinics and hospitals, university hospitals and army hospitals. One of the mechanisms to ensure good coverage of women having Pap smear done was setting a target for all providing agencies. The target given was based on their capabilities and available resources (Division of Family Health Development 2003). Majority of Pap smears taken in this country for screening are from the public health clinics, followed by private clinics and hospitals. The overall positive detection rate was 1.1% for year 2003. Three quality indicators reflects the activities involved in Pap smear screening, they are 'technically unsatisfactory smears' (not more than 5%), 'histo-cyto correlation' (a minimum of 65% agreement must be achieved in 100% colposcopic biopsy) and ' to minimize unnecessary colposcopy' (90% or more colposcopic biopsy should show evidence of CIN on histology).

Ironically, CC is probably the most preventable major form of cancer because of the availability of non invasive and in expensive screening methods. Voluntary and opportunistic cytological screening (Pap smear) programs have been demonstrated to be effective even though there will be issues on sensitivity, specificity and population uptake (Morantz, 2006) that are reported to be effective when they have reached 80% of women population (Mandelblatt et al., 2002). Cervical cytology is the most used method of screening (FIGO Committee on Gynecologic Oncology 2000). High Pap smear uptake in the developed countries and are responsible for the observed decline in the disease (Peto et al., 2004). Cervical cancer is an important reason for hospital admission and has put high cost burden on the overall health cost in a country. This is especially so if this catastrophic illness is borne out of the pocket of CC survivors that could even lead to bankruptcy and extreme poverty (Sharifa Ezat et al., 2008). There is also extreme reduction of quality of life among women inflicted with invasive cervical cancers (ICC) or its pre invasive diseases compared to normal women population especially in the physical components aspects compared to the mental components in Malaysia (Sharifa Ezat et al., 2009).

In 1995, the International Agency for Research on Cancer (IARC) ruled that HPV types 16 and 18 as carcinogenic. Since then, there has been further development as more clinical trials are made and published (Garland et al., 2007; Markowitz et al., 2007). With a clinically effective vaccine available (Goldie et al., 2004; Joura et al., 2007), more efforts are concentrated to the development of cost and the effectiveness of health screening and interventions programs. A detailed study on the potential health and economic impact of adding HPV vaccine to the current screening program of a developing country in the local setting is timely. This is done partly by deploying a costing approach to emerge with an economic model on cervical cancers cost of management in this country, that could be a useful decision-making tool when one is faced with the question of the viability of a nationwide mass HPV vaccination program as a major step in cervical cancer prevention. Before doing so, an economic burden of treating cervical cancer needs to be established.

Total cost of Pap smear screening in Malaysia (Nik Shamsidah 2005), through opportunity based conventional method amounted to a base cost of Ringgit Malaysia (RM) 22.6 millions (Range : RM 15.6 – 38 millions). From this amount, negative tests resulted in the largest proportion i.e. 94% of cost amounting to base cost of RM 21.1 millions (Range: RM 14.9 – 36.3 millions). The total percentage of inadequate samples from Pap smear was 4% of pap smear cost with the base cost of RM 903,539 (Range : RM 349,651-851,068). Abnormal pap smears cost 2 % of total cost with base cost of RM 496,946 (Range: RM 349,651- 851,068) (Nik Shamsidah 2005). The annual cost of cervical cancer screening and management in UK (Brown et al 2006), reflected the cost of screening was £ 104.3 millions and made up for 56.2% of management of cervical cancers. Another study demonstrated the fiscal burden of sustaining an effective screening programme costs £150 millions in UK alone (Balasubramani and Tidy 2006). Cost of managing pre-invasive stage made up 18.6% of total cost of cervical cancer management i.e. £ 34.5 millions. Cost of invasive cancer (new cases) made up of 17.9% of total management cost i.e. £ 33.3 millions. Cost of managing old existing cases was 7.3% of management cost i.e. £ 13.5 millions (Brown et al 2006). The main bulk in the management of cervical cancer was in its screening program and thus avoiding the higher impact of cervical cancer treatment and extensive management.

Goldie et al. (2004) model showed that the most cost effective strategy with incremental cost effective ratio of less than $60 000 per quality adjusted life year is to combine early vaccination with triennial conventional cytologic screening beginning at 25 years of age (Goldie et al., 2004). In a resource poor setting, incorporating visual cervix inspection or DNA testing for HPV in at

least one visit are cost effective alternatives (Mandelblatt et al., 2002; Goldie et al., 2005). In resource rich countries, further step of HPV DNA testing will improve health benefits compared with status quo screening policies (Kim et al., 2005).

There are data to show that HPV Infection is present in over 95% of patients with cervical cancer (Nurhayati et al 1994) with worldwide different proportions among global populations (Clifford et al., 2005). High risk HPV subtypes 16 and 18 are found in up to 70% of cervical cancers, so called the high risk groups, while the HPV 6 and 11 are categorized as low risk that plays a role into development of genital warts (Sherlaw-Johnson and Philips, 2004, Markowitz et al., 2007). Other co factors that increase the progression for cervical cancers in women include herpes simplex and Chlamydia infections (Hakama et al., 2000), smoking, low socioeconomic status, diet that is high in fat, increase sexual partners, impaired immune status such as seen in HIV positive individuals, persistent exposure to oral contraceptive pills (five or more years), in utero exposure to diethylstilbestrol and a positive family history of cervical cancers. Infection with such viral subtypes initially leads to pre-invasive changes within the cervical epithelium and with reduced immune response will later within 20 years of more, develop into invasive cervical cancers.

Transmission of HPV virus is relatively easy. Even if there are no visible warts or other symptoms, HPVs infected person can still pass on the virus to another person. Infection rate occurs at a reported rate of 1.2 to 1.3 percent per month. Cumulative lifetime risk is at least 80 percent (Morantz, 2006). It is passed through skin-to-skin contact with any HPV infected areas of the body, such as genital skin or anal area not covered by condoms. The epithelial cells abnormalities for squamous cells are called atypical squamous cells of undetermined significance (ASCUS), low grade squamous intraepithelial lesions (LSIL) and high grade intraepithelial lesions (HSIL) and these will later progress to squamous cell carcinoma. Low-grade SIL - refers to early changes in the size, shape, and number of cells that form the surface of the cervix. They may go away on their own or, with time may grow larger or become more abnormal, forming a high-grade lesion and more severe degree of cell dysplasia. As it becomes invasive, the tumour breaks through the basement membrane and invades the cervical stroma. Extension of the tumour in the cervix may ultimately manifest as ulceration, exophytic tumour, with infiltration of underlying tissue including bladder or rectum.

The precancerous low-grade lesions also called mild dysplasia or cervical intraepithelial neoplasia 1 (CIN 1). These early changes most often occur in women between the ages of 25 and 35, but can appear at any age (Balasubramani and Tidy, 2006). High-grade SIL correlates with large number of precancerous cells, and, like low-grade SIL, these precancerous changes involve only cells on the surface of the cervix. The cells often do not become cancerous for many months, perhaps years to come (Spitzer et al 2006). Longitudinal studies have shown that in untreated patients with in situ cervical cancer, as high as 30% to 70% will develop invasive carcinoma over a period of 10 to 12 years.

The need to study local scenario of cervical cancer burden was the main objective in this study. Specifically, this study aims to undertake cost analysis of management of cervical cancer cases in Malaysia by government health care providers and to estimate the economic burden of cervical cancer in Malaysian population. Obtaining input from the private sectors was not done as permission for costing data are not readily available from the private sectors. As method for national financing does not come from national health insurance or other form of national health coverage, data on costing was not easy to retrieve and are subjected to confidentiality from the private sectors. Furthermore, the main bulks of cost burden are shouldered upon the public sector and thus, would reflect the general cost burden of treatment in Malaysia.

Materials and Methods

This is a cross sectional study from November 2006 till December 2008 done in five tertiary hospitals based in West Malaysia and one teaching hospital in Klang Valley that provided gynae oncology services to public patients in Malaysia. Patients with cervical cancers and pre invasive diseases were universally selected in gynaecological and oncological inpatients wards and specialists out patients' clinics. Selection criteria's include aged 18 and above; diagnosed with cervical changes i.e. Atypical Squamous Cells of Undetermined Significance (ASCUS), pre invasive diseases such as LSIL (CIN 1) and HSIL (collectively for CIN 2 and CIN 3) or invasive squamous cell carcinoma (ICC) for at least six months prior seen at hospitals and willingness to participate.

Patients that have been admitted or seen at these tertiary hospitals were patients referred by primary or secondary districts hospitals, primary health centres or private general practitioners throughout the country. Gynae oncology services are received free of charge for patients that are covered through the fee exemptions mechanisms. These include ex-government servants, proven income below the national poverty income line of RM 660 and patients who are too ill to pay with no reliable family supports. While patients that are not covered through the fee exemption mechanisms will have to pay a nominal fee for admissions and procedures that are based on standardized Malaysia Medical Association's Fee Schedule 2003.

The costs components involved are the providers' costs i.e. direct and non direct medical cost that includes hospitalization, drugs, physician fees, laboratory tests and radiological procedures. Costing source of information for surgical procedures costs were gathered from the Medical Association's Fee Schedule of Malaysia year 2003. The cost on average inpatient days and outpatient clinic visit days was obtained from University Kebangsaan Malaysia Medical Centre (UKMMC) Case Mix Clinical Costing Software version 1.0. Costing on Pap smears for this country was obtained from secondary published costing study on Pap smear (Nik Shamsidah, 2005).

From the patient's point of view, costs covered were costs of lost productivities that were borne by the patients

during sick leave or carers' lost costs of productivities, cost borne during seeking treatment such as food and drinks, lodging, costs of transportations such as toll and petrol. The costs of lost productivities were calculated from the total number of sick leave days provided by health care provider and calculated by stage of disease. For the unemployed the cost of income was based on national income per capita in Ringgit Malaysia (RM) year 2005. Sensitivity analysis of base case and its ranges (minimum to maximum cost) were also calculated for all cost components.

Three alternative options were compared i.e. screening via opportunistic population based Pap smear screening; quadrivalent HPV Vaccination and the combined strategy (screening plus vaccination). The vaccination programme has not started in Malaysia's public sectors yet, although two types of HPV vaccinations i.e. the bivalent (also known as Cervarix by GSK) and quadrivalent vaccine (Gardasil by MSD), have been on the private market since FDA three years ago and Malaysia's Ministry of Health approvals. The Malaysian government has decided to implement mass HPV vaccination programme among 13 year old adolescents' girls back in September 2009. The programme is planned to run together with the school health programme and included in Malaysia's expanded scope programme for mass childhood immunizations.

In the combined strategy, HPV vaccinations programme is projected to run concurrently with screening of women population based on current clinical CPG recommendations in Malaysia. To determine the costs of three alternative programmes, secondary data for Pap smear programmes costs were taken and imputed in the model calculations.

Scenario based sensitivity analysis used these following assumptions. There are a 96% population screening coverage of 15 years old (ranges at 40% and 70%), a constant 70% population catch up period of 9-26 years old women and different costs of vaccination per dose at RM 300 or RM 400 per dose were calculated.

In the base case scenario, the current setting at status quo was taken into account whereby cost of vaccination per dose is at RM 300 and the screening coverage of women is estimated to be 40%. Best case scenario is when cost of vaccination per dose is maintained at RM 300 but the screening coverage is increased to 70% and worst case scenario is when the cost of vaccination is at RM 400 per dose but screening coverage is at 40% only.

Treatment costs of cervical cancers by stage has not been done in Malaysia thus a nominal group technique, so called an experts' group discussion has been done among 'experts' till a final decision and agreement has been reached for each stage of disease (ASCUS, LSIL and HSIL) and invasive cancers for squamous cell carcinoma only (stage 1 till 4). It is a written algorithm or framework for the expected management path for a certain disease or after a specific procedure (Herck et al., 2004; Mallock and Braithwaite, 2005). Once this agreement has been made based on treatment algorithms, activity based costing for that particular pathways are initiated. The results of this technique by treatment algorithm are too extensive to be included in this study and have been published elsewhere (Sharifa Ezat et al., 2008).

In calculation of quality of life (QOL), the locally validated (Azman et al. 2003 and 2005) tool i.e. the Short Form 36 (SF 36) was used to measure QOL among cervical pre invasive diseases and invasive cancer stages. There are eight main domains in the SF 36 output; however two main general outputs measured were Physical Composite Scores (PCS) and Mental Composite Scores (MCS). The PCS were used to measure the QALYs in this study as the physical aspects showed statistically significant variations by age and cervical lesions severity (Sharifa Ezat et al. 2009). Calculations of population quality adjusted life years saved were based on PCS multiplied by years of life living with the diseases according to age groups saved from respective interventions.

Cost per QALYs saved were costs of three alternative programs divided by total population QALYs saved. For estimation of life years that can be saved, i.e. they do not develop cervical cancers or its pre-invasive diseases, the respondents' were then estimated to live their full life based on the Malaysian populations' statistics. New life tables based on postulated life expectancies when they develop cancers by age groups were calculated based on United Kingdom 2005 cervical cancers mortality and morbidity data. The differences between them generated the amount of life years that could be saved if cancers or its' pre invasive diseases are avoided.

Results

Socio Demographic Profiles of Respondents

Five hundreds and two respondents participated in this study. Respondents came from Kuala Lumpur Hospital (30.9%), Seremban Hospital (25.7%), Alor Star Hospital (23.9%), UKMMC (13.1%), Kangar Hospital (4.0%) and Kuantan Hospital (2.4%) as in Table 1.

Mean age of respondents were 53.0 ± 11.23 years i.e. respondents are slightly older women. As much as 32.1% comes from the 45-54 years age group range, 27.5% from the 55-64 years age group, 18.3% from 35-44 years old, 16.9% from 65 years and above, 4.6% from 25-34 years old and only 0.6% from women age less than 25 years of age.

The combined ASCUS, HSIL and LSIL that makes up pre invasive diseases make a large proportion seen but invasive cervical cancers (ICC) is by far the highest portion by various stages in this study. From hereon, pre invasive diseases will cover the diseases mentioned above. From 502 respondents, majority of cases seen (in decreasing order) are from the pre invasive stages (33.0%), stage 2B-4A at 31.1%, followed by stage 1B-2A (29.0%), stage 1A1 (3.4%), stage 1A2 (2.2%) and lastly stage 4B (1.4%).

Majority of the respondents obtained education up till secondary school level (40.6%). This is followed by primary schools (36.9%), never schooled (20.5%) and tertiary level education (2%). By ethnicity most of the respondents are Malays (45.8%), followed by Chinese (37.3%), Indians (15.1%) and others (1.8%). These is a reflection the the normal distribution of the Malaysian population where Malays are the majority ethnic group,

Table 1. Socio-demographic Profiles of Respondents

Socio demographic Profiles		Percent (%)/ Mean	
Hospitals	Kuala Lumpur	30.9	
	Seremban	25.7	
	Alor Star	23.9	
	UKMMC	13.1	
	Kangar	4.0	
	Kuantan H	2.4	
Age Mean age	53.0 ± 11.23 years		
	<25 years old	0.6	
	25-34	4.6	
	35-44	18.3	
	45-54	32.1	
	55-64	27.5	
	=>65 years and above	16.9	
Stages of Pre invasive and ICC	Pre-Invasive Cancers		33.0
	Stage 1A1	3.4	
	Stage IA2	2.2	
	Stage 1B till 2A	29.0	
	Stage 2 B-4A	31.1	
	Stage 4B	1.4	
Education	Never Schooled	20.5	
	Primary	36.9	
	Secondary	40.6	
	Tertiary	2.0	
Ethnicity	Malays	45.8	
	Chinese	37.3	
	Indians	15.1	
	Others	1.8	
Marriage Status	Mean length of marriage	20.06 ± 16.1years	
	Married	73.3	
	Widowed	21.3	
	Divorced	4.2	
	Single	1.0	
	Cohabiting	0.2	
Employment Status	Unemployed	73.9	
	Employed Full Time	11.6	
	Employed Part Time	9.2	
	Self Employed	5.4	

followed by Chinese and Indians that seeks health services from the public sectors. Most of the respondents at 73.3% are currently married; 21.3% are widowed; 4.2% are divorced; 1.0% are single and unmarried while remaining 0.2% are seperated but cohabiting.

The mean ages by stages are as follows. In the pre-invasive stages, the mean age for ASCUS is 44.67 years ±11.08 years, 46.37 ± 12.02 years for LSIL and 47.85 ± 10.82 years for HSIL. For stage 1A1 mean age is 53.64 ± 9.56 years, stage 1A2 the mean age is 58.20 years ± 8.94, stage 1B -2A the mean age is 54.98 years ± 10.56, stage 2B-4A the mean age is 56.01years ± 10.16 and stage 4B the mean age is 55.60 years ± 7.91. These mean differences were statistically significant with ANOVA F=10.56 and p<0.0001.

The mean length of marriage is 20.06 ± 16.07 years. Most of the respondents are no longer working, retired or are full time housewives (73.9%). Thus formal income from work is not normally distributed. The income can come from own self or supported by spouse or family members. Only 11.6% are employed full time, 9.2% are employed on a part time basis, 4.8% are self employed and 0.6% are working on and off basis when health permits. Patient's income were not normally distributed, thus median income per month for 502 respondents per person is RM 300 (IQR 0.0-700). For women who have income n=318, the median self income value is RM 525 (IQR 300-1,000) per month.

By distribution of patients monthly income, majority of respondents at 62% received an income of RM 0-499. As much as 20.3% have a monthly income of RM 500-999, 10% received a monthly income of RM 1,000-1,499; 2.8% received RM 1,500-1,999, 2.6% received income of RM 2,000-2,499; 2% receive monthly income of RM 3000 and above and 0.4% receive income of RM 2,500-2,999.

Most of the respondents are still in marriage and are provided by their spouses. The median income of spouses is RM 500 (IQR 0-1,150). As high as 48.6% of respondents' spouses earned an income of less than RM 500 per month. 18.5% earned an income of RM 500-999 in a month; 11.4% earned between RM 1,000-1,499 in a month; 7.2% earned between RM 1,500-1,999; 6.4% earned between RM 2,000-2,499; 1.8% earned between RM 2,500-2,999 and 6.2% earned at least RM 3,000 and above in a month.

Household income per month is contribution from both, i.e. patients, their partners and members in the household that may contribute to the house income. Median household's income per month is RM 800 (IQR 400-1,525). Majority at 49.4% earned a monthly income of less than RM 500. In decreasing order, as much as 16.7% earned RM 500-999, 9.6% earned between RM 1,000-1,499; 7.8% earned RM 3,000 and above; 7.2% earned between RM 2,000-2,499, 7.0% earned between RM 1,500 – 1,999 and 2.4% earned between RM 2,500-2,999.

Health care expenditure shows that majority of respondents i.e. 86.5% does not spend any amount on health care such as buying vitamins, procuring preventive healthcare services or other health needs that are considered non critical. These patients largely will depend on free public provided health care facilities and services. 11.8% spent less than RM 250 per month. 1% spent between RM 250-499; 0.4% spent between RM 500-749 and the remaining 0.4% spent at least RM 750 and above per month on health care expenses.

Based on percentages spent on health care from total expenditure, the majority 90% of respondents spent less than 10% of their total expenditure on health care. The remaining 5% of respondents spent between 10-19%; 2.6% respondents spent between 20-29%; 0.6% spent between 30-39%; 0.2% respondents spent between 40-49% and 1.6% respondents also spent the maximum percentage on health care i.e. 50-59%.

Majority of 502 respondents received Pap smear screening before, i.e. n=415 (82.7%). However, still a small proportion has not received any Pap smear screening prior to this i.e. n=86 or 17.3%.

Respondents Quality of Life (QOL)

Patient's QOL is measured via the SF-36 that divides into two main domain outputs which are the physical and mental aspects and also eight subdomains. The two main outputs are termed the Physical Composite Score (PCS)

Table 2. Difference in QOL Scores between Cancer Patients and the General Female Population

Parameters	Cancer n=502		General n=1498	
	Mean	SD	Mean	SD
Physical functioning	51.79	33.98	84.52	18.52
Role limitation-physical	46.71	47.59	81.47	32.55
Bodily pain	61.9	21.06	68.96	17.56
General health	59.38	17.61	66.03	20.15
Vitality	59.56	16.46	65.1	17.54
Social functioning	70.89	21.63	82.94	19.6
Role limitation-emotional	50.4	47.83	76.9	37.25
Mental health	67.12	15.53	73.2	17.6

and Mental Composite Score (MCS). Mean PCS among our respondents are 39.7 (± 10.07), mean MCS is 47.4 (± 8.28). Table 2 shows a comparision of the scores of the eight domains between this study's respondents and normal women population (Azman et al 2003). There is a difference between the two groups however this differences can't be determined statistically.

Life Years Saved (Years)

Life years saved are the years that can be saved after an intervention or a preventive measure has been applied to a particular group. The more years saved from an intervention or a preventive measure, the better the intervention and more likely it is to be implemented as a health care modality. For life years saved, differences between general women population life expectancies and of cervical cancer survivors were calculated.

From the Malaysian Statistics Dept (2006), the life expectancy of normal population was obtained i.e. the years of a women (without any significant disease that can reduce life expectancy) from a certain age group are expected to live. The life expectancies of these women are assumed to be the life expectancies of women who have received HPV vaccination and thus protected against ICC. Using the life table and Age Standardised Death Rate of cervical cancer survivors in UK year 2006, life expectancies of cervical cancer women was calculated. The differences of life expectancies between normal women and cervical cancer survivors revealed the life years saved if cancer is avoided through vaccination.

The highest life expectancy is achieved if a women from a younger age group if they could avoid cancer, thus achieving the highest life years saved. In contrast if an elderly woman does develop cancer, the extra life expectancy gained is less compared to younger age of cancer detection. Example is of an 60-64 years old women and if cancer was detected, she has an extra 5 years more of life expectancies compared to a 20-24 years old woman that has a extra life expectacies of 45 years more. The mean life expectancy saved was 13.0 years.

QALYs Saved

The formula for Quality Adjusted Life years (QALYs) saved takes into account the composite scores for both the quantity and quality of life generated by health care interventions. The formula for QALYs i.e. the Life Years living with the disease x weighted Health Utility scores in our study the Physical Composite Scores.

Table 3. Life Expectancy (Years) in Normal Women and Those with Cervical Cancer by Age Group

Age (Years)	Life Expectancy (Years)		Life Years Saved
	Normal	Cancers	
20-24	56.96	44.79	12.18
25-29	52.09	39.81	12.28
30-34	47.22	34.83	12.39
35-39	42.38	29.85	12.53
40-44	37.58	24.89	12.69
45-49	32.87	19.92	12.95
50-54	28.29	14.95	13.34
55-59	23.85	9.98	13.87
60-64+	19.64	4.99	14.64
Mean Saved	28.04	15.00	13.04

If women without preinvasive or ICC, their QALYs would be higher than cervical cancer survivors. Normal populations' QALYs saved were obtained from the normal women's population life expectancies x utility values of normal women population in Malaysia (Azman et al. 2003). The average QALYs of normal women without preinvasive diseases or ICC was 24.40 ± 8.40 QALYs. The respondents mean QALYs saved was 6.29 ± 4.63. By cervical cancer stage, the highest QALYs saved is at pre invasive stages i.e. at 9.17 ± 5.54. This is followed by stage 1A1 with QALYs saved at 6.29 ± 4.17. Stage 4B and above has the lowest QALYs saved at 4.16 ± 3.06. By stage, differences in QALYs saved were significantly different at $F=19.49$ and $p<0.0001$. Intragroup differences in mean values using the post hoc test by Fisher's LSD analysis showed that differences of means for all disease stage groups were significant at $p<0.05$.

QALYs saved showed declining values with advancing age groups. The least score values are among the age of 65 years old and more (QALYs of 1.74 ± 0.48). This shows less physical activities and ability as age increases. The best scores are among the young women age less than 25 years i.e. QALYs of 18.32 ± 4.86. These different mean values are significant with $F=423.10$ at $p<0.0001$. The intra groups mean differences was tested using LSD post hoc analysis and results showed that all the age intra group differences are significant at $p<0.05$. Correlation analysis shows QALYs decreased significantly with age at $r = -0.874$ at $p<0.0001$. The older the age of respondents, there will be a decline in QALYs value. It showed a decrease in QALYs for every age gained.

Patients' Cost of Care

These cost will cover where the patients were seen, either as out-patients or in patient. These cost will be divided into direct and indirect cost of a patient per OPD visit or one day of inpatients stay. Direct costs are payment costs to providers such as to clinics, medications including traditional/ Chinese medications, for diagnostic procedures, laboratories investigations and payment of any operations. While indirect cost, consisted of patients and carere loss of productivity from work, payment of transportation, toll, food and drinks and extra equipments.

Out Patient Department (OPD)

OPD Direct Cost. Mean direct cost of patients from

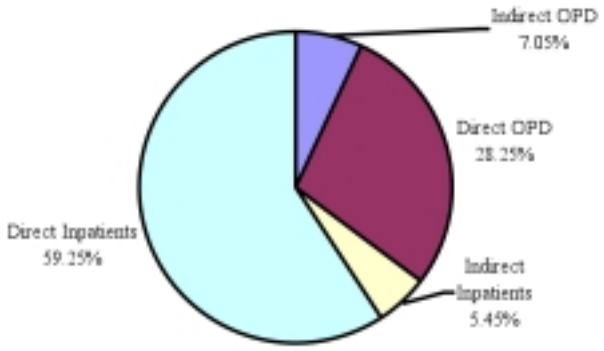

Figure 1. The Respondents Cost Components

OPD is RM 187.60. The data are not normally distributed as many of the respondents are not required to pay for consultation sessions. These can be due to mostly they were public servants who are subsidised even after retirement age and get free access and treatment for their diseases. They may also be subsidised by husband's or children's public servants status and need not pay for public hospitals treatments etc.

OPD Indirect Cost. Indirect cost components that goes into when the consumers received their OPD treatment is RM 41.10 (Range RM : 0.0-1,224.00). Loss of productivity of respondents and their carers are quite low i.e. mean RM 5.70 (range RM 1.0-215.0). These is because most of the women are not employed and does not have regular income. For the ones that are still employed, the hours spent when they go to the clinic for treatment is also quite low i.e. range of 1-4 hours maximum. They usually do not take leave or get full day MC from the clinics, instead they get time slips for short hours visits. Total indirect costs per patient for OPD visit is RM 46.80.

Inpatients Cost

The direct cost for inpatient treatment is higher that OPD visit. The mean cost is RM 393.40 (Range RM: 1.00-8,005.00). The indirect cost for inpatients treatment is less than OPD i.e. at RM 36.20 (Range RM: 1.00-732.00). The carers loss of productivity is RM 13.30 (Range RM: 1.00-220.00). From the percentages of cost components (Figure 1), inpatients direct cost makes the biggest percentage of cost components at 59.25 %, direct cost of OPD at 28.25 %, indirect cost of OPD at 7.05 % and indirect cost of inpatients care at 5.45%.

Cost/ QALYs saved for three options

Three programmes options defined in this study include women that undergo Pap smear screening only, HPV vaccinations only and combined strategy. The costs calculated are based at annual costs only at a certain point in time. Three scenarios cases are included in the sensitivity analysis are based on screening coverage's of women populations ranging from 40-70% and cost of HPV vaccination per dose ranging from RM 300-400 per dose.

Three situations are assumed in this study. The base case are assumed at status quo of screening at 40% coverage and cost of HPV vaccination is at RM 300/dose. The best case scenarios are when the screening coverage is increased to 80% and cost of HPV vaccination is at RM300/dose. While the worst case scenarios are when the screening is at 40% but the price of HPV vaccination is at RM 400/dose.

Costs of Pap smear is taken from secondary data and adjusted for inflation rates. The amount of women age 20-65 expected to perform and undergo Pap smear screening is from the Statistics Dept Malaysia year 2006.

The costs of vaccinations include 95% coverage of 15 years old girls adolescents across the country and a catch up program of quadrivalent HPV vaccination for 9-26 years old women but at 70% coverage of this population. Proportions of vaccine wastage per dose are expected to be around 0.05 only or 15 cents each. The prices of vaccinations differ by cost per dose ranging from RM 300-400. Vaccine efficacy is assumed at 95% efficacy and last a life time with no necessary booster needed. The side

Table 4. CEA of Three Programs at Different Coverage and Sensitivity Analysis

Cost of program (x 10^3)	Pap Smear		HPV Vaccination		Combined		
	(40%)	(70%)	(RM 300/dose)	(400/dose)	Base case	Best case	Worst case
1. Cost of Pap smear	41	72	-	-	133,463	211,462	133,463
2. Cost of HPV Vaccination	-	-	1,626,015	2,140,473	1,626,015	1,626,015	2,140,473
Total Cost	41	72	1,626,015	2,140,473	1,759,478	1,837,478	2,273,936
Cost of managing disease with intention to treat							
1. Cost for detected CC	74,211	129,869					
2. Cost for population	17,678	8,839					
Total Cost to manage	91,889	138,708					
Total Cost (Program and manage)	133,463	211,462					
Population QALYs saved							
1. QALYs saved from CC	109,850	192,237	8,243	8,243	109,850	192,237	109,850
2. QALYs saved from Vulva, Vagina CA and Genital Warts							
	-	-	37,759	37,759	46,002	46,002	46,002
Total QALYs saved	109,850	192,237	46,003	46,002	155,853	238,239	155,852
No of LYS	14,184	14,184	30,282	30,282	44,466	44,466	44,466
No of deaths averted	946	946	1,081	1,081	2,027	2,027	2,027
CEA Outcomes							
Cost/QALYs saved	1,215	1,100	35,347	46,530	11,290	7,713	14,590
Cost/LYS	7,002	11,093	39,955	52,595	29,443	30,748	38,052
Cost/Deaths Averted	105,006	166,375	1,119,096	1,473,141	645,929	674,551	834,779

Table 5. ICER Model for Three Methods of Strategy

Strategy	Cost (RM)	Effectiveness (QALYs)	Incremental Cost (RM)	Incremental Effectiveness (QALYs)	ICER (per QALYs avoided)
Pap smear program 40% coverage	133,463,219	109,850	_	_	_
Pap smear program 70% Coverage	211,462,910	192,237	77,999,691	82,387	947
Combined strategy best case	1,837,478,053	238,239	1,626,015,143	46,002	35,347

effects of vaccinations are assumed to be minimal and do not incur costs of deaths or admissions. Staffs costs of three administrations of vaccines are from secondary data at RM 16.21 per shot. An expected 70% fraction of women population CC can be avoided if HPV vaccinations against types 16 and 18 are administered. Each woman will save 13 years per person gained if CC could be avoided. All CC cases are assumed to meet deaths if they developed cancers. All costs and effects were discounted at 3% for next 10 years.

Cost of Managing Disease with Intention to Treat

The costs of managing disease are specific for Pap smear program. In Pap smear screening, the costs of detection of negative tests was RM 21,187,988 (min-max: RM 14,907,836-36,286,436), abnormal tests base cost was RM 496,946 (min-max: RM 349,651-851,068) and inadequate tests base costs was RM 903,539 (min-max: RM 349,651-851,068) (Nik Shamsidah 2005). 20.8% of women seen through screenings programs are expected to display LSIL changes, 11.2% LSIL and 2% ICC changes. Costs were imputed for percentage of women population that presents with these abnormalities and assumed everyone will get the chance for treatment. The rests of unscreened women population not screened though Pap smear would be expected to develop cervical cancer and invasive diseases from the national incidence of CC in this country i.e. 464 women only.

Total populations QALYs saved in screening program are for the whole women population. This is calculated based on average women with CC QALYs multiply the expected number of women population available in the country.

Costs for HPV vaccinations are calculated using the above assumptions. Although catch ups programs are utilized in the calculations, but since the coverage of vaccinations are only up to 70% only of women and adolescents populations, the unvaccinated populations' risks of developing new incidences of CC or pre invasive diseases are lower. Thus incidence of CC per annum was from among developed countries at 3.5/100,000 i.e. only 35 women developed ICC from 9-26 years old cohort that had not received the vaccinations. Total population QALYs saved are QALYs saved per person multiplied by number of women CC / pre invasive cervical diseases could be avoided. The total QALYs saved for the three different programs interventions are based on the number of women populations expected to benefit from those specific interventions. The combined strategy targeted towards both 9-26 years old girls and women at 70% coverage and screening for elderly women till age of 65 years old. Hereby after, screening does not provide any extra benefit against CC or its preinvasive diseases. The costs of three different programs and effects are as the tables below. Interventions that are cost effective are based on the Macroeconomics and Health Outcome WHO. Outcomes that are less three times the country's GDP as cost effective and if the cost per outcomes is less than country's GDP, then it is cost saving. Malaysia's country GDP per capita in year 2007 was RM 23,038 (Dept of Statistics Malaysia 2009).

Incremental Cost Effectiveness Ratio (ICER)

For ICER calculations, three different outcomes for different scenarios were compared. The Pap smear screening at status quo i.e. 40% population coverage was taken as reference base situation. Dominated consequences were eliminated from this table as its not cost effective. Once these strategies were eliminated from the table, the ICER were arranged again and recalculated. From the ICER table, only three options were left. They were reference scenario, Pap smear coverage at 70% and the combined strategy for best case scenario. The ICER for one QALYs saved was RM 947 and this is followed by the combined best case strategy at RM 35,347 per QALYs saved.

Discussion

Immunization, suitable with WHO recommendations are intended to reduce sufferings against disabilities, disease complications and even initiations of intended diseases such as seen in the HPV vaccinations programs (Preparing for the introduction of HPV vaccines UNFPA WHO, 2006). Young age of vaccinations are not only more easily incorporated but also at sexually naïve adolescents. The more extreme age of cervical cancer survivors were not suprising as it is a disease that mainly affects the middle to elderly women. The ethnicity in the study mainly comprised of Malays as this ethnic were the mainstay of patients that seeked public health provider especially for long staying and resource intense admissions. The majority of these patients were earning less than RM 500 per month and this falls below the poverty line income of Malaysia. This was very disturbing and it further proved the high level of care of the disease cant be afforded by many of these patients and the general population as well. Sunsidised care by the public sector have benefited our populations but the extent and durations of these subsidies will not sustainable in the long run. Cutting costs in treating these patients may jeoperdise the quality of care the patients received and have a general detrimental impact on cancers' survivors mortality and morbidity.

QOL by disease severity showed that mean PCS is highest in the pre invasive diseases, followed by stage 1, 2 and the least PCS scores are from stage 4B. These

differences is significant at all stages of PCS and between groups at $p<0.05$. The MCS however did not show the same results and p value was not significant. QOL by age showed declining values with advancing age. Lowest PCS values are among the 65 years and above while the highest PCS values are among the 25-34 years old. However, MCS values do not show the same pattern and was not significant ($p=0.22$).

It was noted that the scores by domains of our women are definitely lower compared to the healthy women population of Malaysia (Azman et al., 2003; 2005). This is distinctively seen among the physical domains that constitutes PCS composite score.that are significantly seen to be associated with age and disease severity. Higher scores, showed better perception on physical function. Examples of physical functions activities that were asked in our questionnaire were walking, carrying heavy load and other vigorous activities. The preinvasive diseases and early stage of cancer showed better perception and scoring of physical domains and PCS showed significant decline with increasing age and disease severity. From Sharifa Ezat et al., 2009, multiple linear regression showed that patients' age and income affected physical function perception scores of our women. Age showed decrease relationship with physical function but higher income had increment in physical functions scores perception. Patients' higher income is related with better logistics and availability of resources either for care or support. In comparison with the general women population of Malaysia, all domains showed that women affected with cancers had lower QOL at all domains. These differences are supposedly attributed to the disease presence in cervical cancer women and assuming all other sociodemographic variables are controlled. Our questionnaire was not able to show and evaluate depression, anxiety or sexual dysfunction that was commonly seen in cervical cancer survivors (Maissi et al., 2005; Reich et al. 2008). We also did not assess the social support of these women. However in this study, the MCS does not show any significant changes with age or increasing severity. Our cervical disease survivors came from different cultures and religious background. Studies have shown that long term survivors have adapted to cope with the disease and developed mental preparedness on its outcome and progress of disease (Greenwald et al., 2007).

Based on individual beliefs, respondents have high external locus of control, seeing themselves as pawns, thus leaving everything to faith. Mentally this allows them to accept, perpertuated high hopes and positive perception toward this deadly disease. Since most of our respondents are married and have children, these social factors would also have contributed to their mental preparations on the disease, hence not showing MCS changes with increasing age and disease severity. Linear regression analysis showed that percentage of income spent on health care significantly contributed to MCS (Sharifa Ezat et al., 2009), whereby as MCS reduced with increased burden of health care spent by out of pocket payment method. This method of payment increases risk of catastrophic poverty by increasing risk to the payer's household. Suprisingly patients and spouse income did not seem to influence or affect mental scores of patients. It seems that how much a person has to pay for health care affects the mental state of these women probably because of stress of worrying about income.

The mean life expectancy saved if women could avoid cancers was 13.04 years. The highest life expectancy is achieved if a women from a younger age group could avoid cancer thus achieving the highest life years saved. In contrast if an elderly women does develop cancer, the extra life expectancy gained is less compared to younger age of cancer detection. Example if a 60-64+ years old women and cancer was detected, she can only an extra 5 years more of life expectancy compared to a 20-24 years old woman that has a extra life expectacy of 45 years more.

Life expectancy for women without cancers, were based on the life expectancies by different age groups of normal women in Malaysia (Ministry of Health Malaysia 2005; Department of Statistics 2006; Cancer Research UK 2006). The mean age for normal women in this study was the ripe old age of 81.40 ± 2.66 years. However, with cervical cancers, their life expectancies were shortened due to the disease, subsequent management and complications, to the age of only 68.31 ± 3.83 years. From the differences between normal life expectancies compared with life expectancies when they develop cervical cancers, the mean life years saved was 13.06 years ± 3.2. This difference was significant at $p<0.0001$. If say, this data is measured in the population based term then the normal life expectancy of females in Malaysia year 2006 (Ministry of Health Annual Report, 2006) was 76.3 years. If this life expectancy is shortened by 13 years, then that makes the cervical cancer women population to live only to the age of 63.3 years.

Without cancers, these women would have lived to their full extent of the lives (Nik Ibrahim, 2005). However, with reduced life years secondary to cancer, its aggressive treatment or other non related causes (Baade et al., 2006) had shown that cancer survivors had an increased chance of earlier death compared to the normal population. The loss of years to cancer could have been avoided if the women comes early for screening, allowing detection of diseases and interventions hence improving survival outcomes (Sharifa Ezat et al., 2008).

The highest number of deaths that can be avoided is from the combined strategy. Not only the deaths from cancer averted through Pap smears can be detected (cancers caused by other other causes beside HPV infections), but also cancers averted through vaccinations that prevented cancers in the first place. In the Pap smear program, the cost per death averted in best case scenario is RM 223,631 /death averted; in base case scenario is RM 141,143 /death averted and in worst case scenario is RM 141,143 per death averted. It was most cost effective in base and worst cases scenario because of the lower cost of program implementation as it's assumed to cover only 40% of women population. In comparative the best case scenario is the less cost effective since cost of program is higher since there is a need to cover 80% of women population. In the HPV vaccination program, the CEA or cost/death averted in the base case scenario is when the

cost is RM 300/dose. The best case scenario is cost of vaccination at 70% coverage at RM 300/dose divided by number of deaths averted. Both base and best case scenarios gives CEA of cost/death averted at RM 1,503,468. The cost/death averted in the worst case scenario i.e. cost of vaccination at 40% coverage and at RM 400/dose divided by the number of deaths averted. This makes the cost/ death averted to be RM 1,979,153 per death averted in the worst case scenario. It was more cost effective in base and best cases scenario because of the lower cost of program implementation as one vaccination is assumed be RM 300 per dose. By comparison, the worst case scenario is the less cost effective since cost of program is higher as the cost per dose of HPV vaccination is at RM 400/dose. In the combined strategy program, the cost/death averted in base case scenario is RM 867,979 per death averted. In best case scenario the cost to avert a death is higher because the cost of vaccination and Pap smear is higher. In best case scenario, cost /death averted is RM 906,457/death averted. In worst case scenario, cost/death averted is RM 1,121,769.

It was most cost effective in base case scenario because of the lower cost of program implementation as it's assumed to cover only 40% of women population with RM 300 per vaccination dose. In comparison, the worst case scenario is the least cost effective due to higher cost of program since there is a need to cover 40% of women population but vaccination cost is RM 400 per dose. In best case scenario, the population coverage is high at 70% but the vaccination dose is still lower at RM 300 per dose.

The highest number of life years saved is also the highest from combined strategy compared with vaccinations or Pap smear programs. In Pap smear program, the cost/LYS in base case is RM 9,410/LYS and in best case is RM 14,909/LYS. The cost/LYS for worst case scenario is RM 9,410/LYS. It was most cost effective in base and worst cases scenario because of the lower cost of program implementation as screening covered only 40% of women population. In comparison, the best case scenario is the less cost effective since cost of program is higher to cover 70% of women population. Cost/LYS in HPV Vaccination program for base and best case scenario is RM 53,695/LYS and RM 70,684/LYS for worst case scenario. It was most cost effective in base and best cases scenario because of the lower cost of program implementation as one vaccination is assumed be RM 300 per dose. In comparative the worst case scenario is the less cost effective since cost of program is higher as cost per dose was RM 400/dose. In the combined strategy program, the cost/LYS in base case scenario is RM 39,569/ LYS; best case is RM 41,323/LYS and RM 51,139/LYS in worst case scenario. It was most cost effective in base case scenario because of the lower cost of program implementation as it's assumed to cover only 40% of women population with RM 300 per vaccination dose. In comparison, the worst case scenario is the least cost effective due to higher cost of program since there is a need to cover 40% of women population but vaccination cost is RM 400 per dose. In best case scenario, the population coverage is high at 70% but the vaccination dose is still lower at RM 300 per dose.

In Pap smear program, the total QALYs saved from cervical cancer will be based on the Pap smear coverage. Total QALYs saved for 70% population covered from Pap smear is 258,351 QALYs; 147,629 QALYs saved for 40% coverage and 295,258 QALYs saved for 80% coverage. The highest QALYs saved are from high Pap smear coverage at 70%. This is because of the higher number of women population covered through Pap smear screening and they will enjoy better quality of life for their life years that were saved. Cost per QALYs saved was RM 1,100 (Range : RM 1,081 - RM 1,215) i.e. more cost effective (lower cost per QALYs saved), if populations' Pap smear coverage is increased.

In the vaccination program, total QALYs combined saved against vulva, vaginal cancers and genital warts were 50,745 QALYs. Combined QALYs from cervical, vulva, vagina cancers and genital warts are 61,823 QALYs. Cost/ QALYs saved (if vaccination per dose is RM 300) are RM 35,347 (Range: RM 15,149 - 40,397). If vaccination cost per dose is increased to RM 400, then the cost/per QALYs saved increased to RM 46,530 (Range: RM 19,942 - 53,179). Thus this implies that costs per QALYs saved are more cost effective if the cost per dose of vaccination is at a lower (cheaper) cost. You have to pay more to gain the same amount of benefit.

In combined strategy, total QALYs saved was 320,174 (Range: 209,452 - 357,081). At vaccine cost of RM 300/ dose, cost per QALYs saved is RM 7,713 (Range: RM 7,013 - RM 11,289). When cost per vaccine dose is increased to RM 400/dose; cost per QALYs saved increased to RM 9,872 (Range: RM 9,872 - 14,590). This makes vaccination at higher cost/ dose less cost effective as evident from higher CEA ratios.

The highest QALYs saved are from the combined strategy but at a lower vaccination cost plus high Pap smear screening coverage. It showed the higher amount of utility values that were gained from this strategy. In the sense of cost effectiveness, the more cost effective option would be from the Pap smear program but at a higher population screening coverage.

Sensitivity analysis are based on the three scenarios which are the base case, best case and worst scenario. All costs and outcomes were post 3% discount rate for next 10 years. In the base and worst case scenario, cost/QALYs saved are the same at RM 1,215 for Pap smear program since in both cases, the coverage is assumed to be the same at 40% population coverage. The cost/QALYs saved for best case scenario showed lower cost/QALYs saved (more cost effective), since Pap smear coverage is higher at 70%, thus making it more cost effective to screen at higher population coverage.

Under the HPV vaccination program, cost/QALYs saved showed that in base and best case the cost/QALYs saved is lower (less cost effective) since the cost per dose is at RM 400. The best and base case scenarios that used RM 300/dose showed lower cost/QALYs saved that is more cost effective than in the worst case scenario.

Combined strategy program at best case scenario is definitely more cost effective since it covers higher population coverage of screening and lower cost of HPV

vaccination per dose. However the cost/LYS saved does not show the same similarity as the cost/LYS is highly dependent on program cost. In the best case scenario, the higher cost of Pap smear program is inevitable since in best case scenario the population coverage is the highest. This makes the cost /LYS and cost/deaths averted are more costly. The combined strategy in all setting shows the highest number of lives saved and also the highest number of averted deaths. Cost/LYS and cost/deaths averted under the vaccination and combined strategy programs are the least cost effective in the worst case scenario since vaccination cost is the most expensive at RM 400 per dose.

Since this is an expansive vaccine, establishing a comprehensive vaccination program in Malaysia (considered a high middle income country with high Human Development Index value), a program that encompasses catch up vaccinations of 9-26 years old women are highly unlikely. The funding among these age 9-26 years old group would be too substantial and can't be handled alone by the public sector. Since voluntary private and social health insurance are not establised in this country and health financing relies heavily on tax funded universal access to health care, government financing will be extremely stretched if universal mandatory vaccinations of 9-26 years old will be provided by the government.

The most likely less costly strategy would be establishing vaccinations among 13 years old for next 10 years as evidenced from a few other literatures (Goldie et al., 2004; 2005). A specific vaccination target in this age group ensure that long term sustainability and managiblity among health providers. The public school health team in Malaysia, mostly attended by nurses, has a long and successful immunization program. However it has been stretched to the limit and providing three doses in schools set ups among 13 years old will also be another challenge. Malaysia consists of a dichotomy of both private and private health providers, thus public and private primary care doctors in schools vicnicity can be incorporated as vaccinations centres that students, with their parents could come for vaccinations on their own time. Payment for these vaccinations should always come fron the government as to ensure public goods will be delivered in a standard and orderly forms. This approach encourages attendances by parents that may need to enquire related informations that could be provided by physicians. They could not obtain these precious informations and discussions had these vaccinations be done at schools' basis only because of the restricted attentions and time apportioned to students. Selecting which clinic to provide vaccinations services must come from governments' pre determined selections criterias and standards. A centrally defined guideline from a central committee must be in place for these mechanisms to run in order. Queries on culture conflicts, resistance and implementation issues must be dealt by advocacy groups from both private and public sectors. Even though existing mechanisms are already in place and incorporated in both public and private vaccinations services, these valuable resouces only reach a small proportions of the community and does not reach the ground level and the high at risks groups including men. A strong support by the male fraternity that may comprise of political figures and health advocaters are not well established in this country. This looks as if the women community are left to fend on their own of this disease that affects mainly women of elderly age groups (Othman et al., 2009).

From the ICER, the most cost effective strategy in cost/QALYs saved was from Pap smear programs however it must be done with a high screening coverages in the population. Achievement of high coverages are an imposible feat to achieve even after nearly 30 years of women advocacy and free screening services at public sectors. Thus vaccinating young women are a more reachable target. The next cost effective method of combatting CC was through the combined strategy, again with a high screening coverage and vaccinations at a lower cost per dose. Combined strategy also produced the highest number of life years and QALYs saved and number of deaths averted. However, governments roles in maintaining costs by mass supply and competitiveness of products, advocating vaccines among the community and teachers must be encouraged.

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