

RESEARCH COMMUNICATION

Health and Economic Burden of HPV-related Diseases in Singapore

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Abstract

Objective: To assess the health and economic burden of human papillomavirus (HPV)-related diseases (cervical cancer, cervical intraepithelial neoplasia (CIN) 1/2/3, and genital warts) in Singapore over a period of 25 years beginning in 2008. **Methods:** Incidence-based modeling was used to estimate the incidence cases and associated economic burden, with the assumption that age-stratified incidence rates will remain the same throughout the period of 25 years. The incidence rates in 2008 were projected based on data obtained from the National Cancer Registry for cervical cancer, and from a combination of published data and hospital registry review for CIN1/2/3 and genital warts. The population growth rate was factored into the projection of incidence cases over time. Direct cost data per cervical cancer and per CIN1/2/3 case were obtained from the financial database of large local hospitals while cost data for genital warts were obtained from the National Skin Center; these costs were multiplied by the number of incidence cases to produce an aggregate estimate of the economic burden over the 25-year period (in 2008 Singapore dollars) using a 3% discount rate. **Results:** The total number of incidence cases of HPV-disease over 25 years beginning in 2008 was estimated to be 60,183, including 8,078 for cervical cancer, 11,685 for CIN 2/3, 8,849 for CIN1, and 31,572 for genital warts. The estimated total direct cost was 83.2 million Singapore Dollars over 25 years: 57.6 million attributable to cervical cancer, 13.0 million to CIN2/3, 6.83 million to CIN1, and 5.70 million to genital warts. **Conclusion:** HPV-related diseases are expected to impose significant health and economic burden on the Singapore healthcare resources in the next 25 years.

Keywords: Human papillomavirus - cost of illness - Singapore

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Introduction

Human papillomavirus (HPV) infection is the most common sexually transmitted infection (STI) (Ebrahim et al., 2005), and it is associated with substantial clinical, social, and economic burdens. Because the infection is often asymptomatic and may not have obvious signs, the risk of unwitting transmission is high. Although the majority of infections are self-limited, acquisition of specific types of HPV can cause genital warts, cervical intraepithelial neoplasia (CIN), and invasive cervical cancer, all of which produce significant morbidity and, in the case of cervical cancer, mortality. (Wiley and Masongsong, 2006) In fact, cervical cancer is the second most common cancer in women worldwide, with 492,800 incident cases and 274,000 deaths annually. (Parkin and Bray, 2006) Because infection with HPV is a necessary cause of cervical cancer, virtually all cases of cervical cancers, and thus all the deaths resulting from those cases,

can be attributed to HPV (Walboomers et al., 1999).

HPV-related diseases incur substantial economic burdens in many countries. Among the HPV-related diseases, cervical cancer and cervical dysplasias are the most costly, and are estimated to account for direct medical costs of \$4.6 billion (in 2005 US dollars) annually in the United States (Lipsy, 2008). If the costs of anogenital warts and other cancers associated with oncogenic HPV are also included, the total economic burden of HPV-related diseases can rise to \$5 billion (in 2006 US dollars) per year (Lipsy, 2008). In Belgium, the annual direct medical costs of cervical cancer, cervical dysplasia, and genital warts combined were estimated at approximately €11 million, with around 60% and 20% of the costs spent on cervical cancer and CIN management, respectively (Annemans et al., 2008).

In Singapore, cervical cancer is the 6th most common cancer in women while the genital warts incidence rate is ranked 6th highest among STIs (Ministry of Health,

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Singapore, 2009). In spite of the prevalence of these conditions, the present study is the first to conduct a burden of illness (BOI) study to analyze both the health and economic burden of HPV-related diseases in Singapore. The present study aimed to estimate the incidence cases and associated economic burden of HPV-related diseases in Singapore, focusing on cervical cancer, cervical dysplasia, and genital warts, over a period of 25 years beginning in 2008. The results of this BOI study could be used to evaluate the potential benefits of new medical technologies for preventing, diagnosing, or treating HPV-related diseases, including HPV vaccines (Paavonen et al., 2009; Dillner et al., 2010) and HPV DNA testing. (Kulasingam et al., 2002) Furthermore, the study could aid the development of health policies to optimize healthcare resource allocation.

Materials and Methods

Study design

The incidence-based approach was used to estimate the incidence and economic burden of cervical cancer, cervical dysplasia, and genital warts in Singapore, with the assumption that age-stratified incidence rates remain the same throughout a period of 25 years.

Incidence estimation

The incidence rate of cervical cancer and genital warts in Singapore residents was estimated by the most recent data found in published reports of the National Registry and the National Skin Center (NSC), respectively (Singapore Cancer Registry, 2004; National Skin Center, 2006). Among the genital wart cases treated by the NSC, 80% of the cases were assumed to be Singapore residents. Published reports and hospital disease registry databases of three large hospitals that have an obstetrics and gynaecology department were used to provide information on the number of patients per year who were newly diagnosed with CIN1/2/3 and treated in these hospitals. Altogether, the three hospitals were assumed to treat 75% of the total cases of CIN1/2/3 in Singapore residents. The estimated annual incidence rate was subsequently multiplied by the resident population size of a given year to obtain the number of incidence cases in the corresponding year beginning in 2008. A 1.7% annual population growth rate was used in the projection (Wong, 2008).

Economic burden estimation

In order to estimate the management cost per case for cervical cancer and CIN, billing data were obtained from two of the hospitals where the incidence data were retrieved. The lifetime direct medical cost of management incurred in each hospital was summed for each case, and an average was calculated, weighted by the number of incidence cases in each hospital and the number of patients at various disease stages. The resource use and costs associated with the treatment of genital warts was obtained from the NSC financial database; an average management cost was calculated by multiplying the mean resource use estimates with the unit cost for the corresponding item of resource use. Management costs included all direct medical

Table 1. Annual Incidence Rate of HPV-Related Diseases in 2008

Age group (years old)	Cervical cancer (/100,000)	CIN 1 (/1000)	CIN 2/3 (/1000)	Genital warts (/1000)
0-19	0.04	N.A.*	N.A.*	0.04
20-39	4.92			0.63
40-59	24.19			0.2
60+	37.76			0.1
Total	12.61	0.16	0.21	0.28

*Age-group specific CIN1/2/3 data were not available.

costs associated with screening, diagnosis and treatment of the disease that were incurred from the time of diagnosis to cure or death. All retrieved cost data were adjusted for inflation to year 2008 Singapore dollars (SGD) using the health care component of the Singapore Consumer Price Index. In the estimation of the total economic burden over 25 years beginning in 2008, future costs were discounted by 3% annually. The discounted lifetime direct medical cost per case of each of the three examined diseases was multiplied by the estimated number of incidence cases of the respective disease that occurred in the corresponding year. The resulting estimates were then summed up for the three diseases to estimate the total economic burden of HPV-related diseases for a given year.

Sensitivity analysis

Multiple one-way analyses were conducted to assess the influence of varying a few key parameter estimates on the predicted economic burden: the discount rate (0% and 5%), the incidence rate of cervical cancer (decreased to 11.2/100,000 based on the interim report of cancer trends in Singapore 2002-2006), the incidence rate of CIN1/2/3 (increased by 20% due to the expected increase in Pap smear screening rate), and the incidence rate of genital warts (increased by 118% to match with the male-female incidence ratio in Taiwan) (National Health Insurance Research Database, 2009). In the NSC database, the male to female ratio of patients with genital warts was considered skewed (male : female = 4.2:1) with the number of female patients significantly underestimated because most female patients with genital warts were likely to be treated by gynecologists. As such, in the sensitivity analysis on the incidence rate of genital warts, the male-to-female ratio reported in Taiwan (male : female = 1:1.7) was used to increase the estimate of the number of female incidence cases.

Results

The age-stratified annual incidence rates of HPV-related diseases in 2008 in Singapore are presented in Table 1. The estimated rates of cervical cancer, CIN1, CIN2/3, and genital warts were 12.61 per 100,000 people, 0.16 per 1,000 people, 0.21 per 1,000 people, and 0.28 per 1,000 people, respectively. Assuming unchanged incidence rates and a 1.7% annual population growth, the total number of incidence cases of HPV-disease over 25 years beginning in 2008 was estimated to be 60,183 cases, distributed as 8,078 cases of cervical cancer, 11,685 of CIN 2/3, 8,849 of CIN1, and 31,572 of genital warts

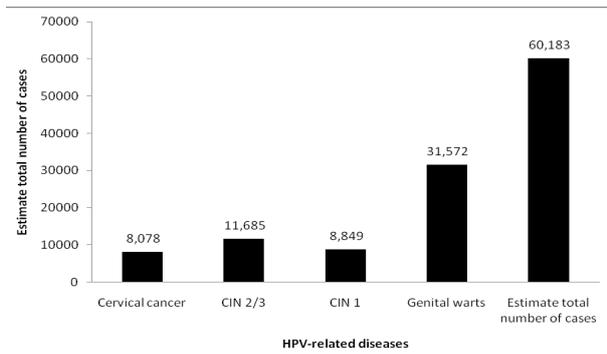


Figure 1. Incidence of HPV-Related Diseases Over 25 Years Beginning in 2008

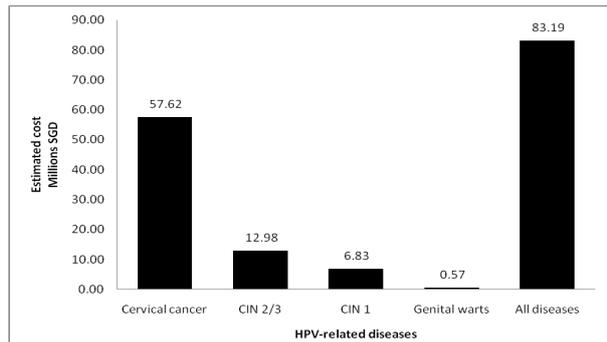


Figure 2. Total Direct Cost of HPV-Related Diseases Over 25 Years Beginning in 2008

Table 2. Sensitivity Analysis Results

Input variables	Economic burden (million SGD in 2008)	% change
Base-case scenario	83.19	
Cervical cancer crude incidence rate decreased to 11.2/100,000	76.81	-7.67
CIN 1/2/3 incidence rate increased by 20%	87.15	4.76
Genital warts incidence F/M ratio increased to the Taiwan ratio	88.85	6.8
Discount rate 0%	118.99	43.03
Discount rate 5%	67.53	-18.82

(Figure 1).

The direct costs per case of cervical cancer, CIN1/2, CIN3, and genital warts were estimated at 10,204, 1,104, 1,589, and 260 SGD, respectively. Using an incidence-based approach, the economic burden (expressed in 2008 SGD) associated with HPV-related diseases occurring in Singapore residents was estimated to be 83.19 million over 25 years; 57.62 million (69.2%) was attributable to cervical cancer, 12.98 million (15.6%) to CIN2/3, 6.83 million (8.2%) to CIN1, and 5.70 million (6.9%) to genital warts (Figure 2). The results of multiple one-way sensitivity analyses are shown in Table 2. Discount rate was found to be the predominant factor that drove the estimates.

Discussion

In this BOI study, we adopted the incidence-based approach, which is commonly used in the literature to examine the economic burden associated with the HPV-

related diseases (Insinga et al., 2005). We estimated the direct medical costs of cervical cancer, cervical dysplasia, and genital warts in Singapore residents to be 83.19 million SGD over 25 years. With the emergence of new technologies for HPV prevention and treatment, such as quadrivalent and bivalent prophylactic HPV vaccines (Koutsky and Harper, 2006), most incidences of HPV-related diseases and their associated costs may be prevented. The results of this study can serve as a basis for future cost-effectiveness analyses and budget impact analyses. In addition, the findings can be compared with national estimates of the health and economic burden associated with other medical conditions, despite the dearth of such estimates in Singapore, in order to aid priority-setting in healthcare and research.

This study has quantified the overall economic magnitude and also the relative contribution of the three most costly HPV-related diseases. Although the figures reported are approximate estimates at best, this study provides significant insight into and highlights the importance of preventing the health and economic burden imposed by HPV-related diseases. The study results are consistent with previous studies in that cervical cancer is responsible for the majority of the cost burden associated with HPV-related diseases, followed by CIN; together, these two diseases contribute to 80-90% of overall costs estimated. (Annemans et al., 2008; Lipsy, 2008)

There are several limitations to our study. First, sources of cost data were limited to several large hospitals and may not be representative of all health institutions that treat patients with HPV-related diseases. Second, due to the unavailability of data break-down, micro-costing was not feasible. Instead, the average cost-per-case estimates were used to estimate the total economic burden, and no differentiation in disease stages or differentiation between prevention/screening and treatment was made for cost estimates. Third, the economic burden estimated by this study is conservative because we did not include the medical costs associated with the noncervical cancers that are etiologically related to HPV-infection, such as cancers of the anus, oropharynx, penis, vagina, and vulva. (Chaturvedi, 2010) We excluded the costs associated with these cancers because the proportion of these cancers that may be attributable to HPV infection has not been well established, particularly in Asian populations. In addition, our estimates would have been much higher if indirect and nonmedical costs had been included because these costs could be several times greater than direct medical costs. (Max et al., 2003; Insinga, 2006)

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