Chapter 18

An Extended Cost-Effectiveness Analysis of Publicly Financed HPV Vaccination to Prevent Cervical Cancer in China

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INTRODUCTION

Disproportionate Burden of Disease

Cervical cancer is one of the 10 most common diseases affecting women in China. Although the average national estimates of the cervical cancer burden in China are low, the burden may be underestimated because the prevalence of the human papillomavirus (HPV) is high. Cervical cancer mortality is heterogeneous across geographic settings (Li, Kang, and Qiao 2011); it is highest among poor women living in Gansu, Shanxi, and Shaanxi, the least developed provinces in central and western China.

The low national cervical cancer estimates may be the result of the lack of a nationwide cancer registry. Most registries are located in urban areas, where the socioeconomic status of women is higher and the cancer disease burden is likely to be lower than in rural areas (Shi and others 2011). The HPV prevalence has been found to be similar in rural and urban regions, but cervical cancer mortality is significantly higher among women in rural areas. This disproportionate disease burden is likely attributable to the unequal availability and utilization of health services, such as screening and treatment.

Inadequate Screening Services

Screening in China is opportunistic in the absence of a national cervical cancer screening program. From 2009 to 2011, the national government initiated a program to provide free cervical cancer screening for 10 million rural women between ages 35 and 59 years; the program covered only 7 percent of women because of the shortages of gynecologists and cytologists and an overburdened health care system (Colombara and Wang 2013; Qiao 2010; *The Lancet* 2009). China has an estimated 500 million women in rural areas; scaling up preventive services constitutes a significant public health challenge (Li, Kang, and Qiao 2011), and national cervical cancer screening coverage remains low (Gakidou, Nordhagen, and Obermeier 2008; WHO 2012). Additional reasons for low screening coverage include weak health system infrastructure to support screening, diagnosis, and treatment; limited access to health services; and limited knowledge of cervical cancer among women in less developed regions (Jia and others 2013; Qiao and others 2008).

China's health care system has been evolving to respond to the pervasive inequity in access to health services. In 2009, China began to introduce

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universal health coverage (Yip and others 2012), reaching relatively high coverage in urban and rural areas with two government-sponsored schemes. Despite the high coverage, the benefits are minimal and reimbursement is limited to inpatient expenses. It is unclear how recent health insurance schemes and opportunistic screening programs have affected women's cervical cancer treatment rates, health outcomes, and costs. Recent studies that focused on prevention indicate that existing cancer prevention services do not reach women in poorer rural and urban areas (Jia and others 2013; Li, Kang, and Qiao 2011; Shi, Canfell, and others 2012). This trend is likely to continue until insurance schemes cover outpatient services, including treatment of precancer and early-stage cancer.

Although widespread screening with cytology has dramatically reduced the cervical cancer burden in high-income countries, low-resource settings have been unable to achieve similar cancer reductions. Newer screening technologies are cheaper and easier to implement and scale up than cytology and can reduce the cervical cancer burden among Chinese women, protecting them from the future costs and consequences of the disease. For example, a study of cervical cancer screening that evaluated strategies using cervical cytology and HPV DNA testing found that screening women three times in their lives (between the ages of 25 and 45 years) reduced the risk of cancer by 50 percent at a cost of US$150 per life-year saved (LYS). The most efficient strategy used a two-visit rapid HPV DNA test, with screening and diagnostic assessment at a county hospital and treatment provided during the second visit (Levin and others 2010; Li and others 2013; Shi, Canfell, and others 2012; Wang and others 2013; Zhang, Pan, and others 2013; Zhao and others 2013).

HPV Vaccination

In addition to screening, HPV vaccination presents a promising primary prevention strategy against cervical cancer. Several studies have concluded that screening women and vaccinating preadolescent girls against HPV are cost-effective interventions in reducing the burden of cervical cancer in China (Canfell and others 2011; Goldie and others 2008; Levin and others 2010; Shi and others 2011). Canfell and others (2011) showed that vaccination strategies were cost effective up to US$55 per vaccinated girl, with incremental cost-effectiveness ratios (ICERs) of US$2,746 per LYS when vaccination was combined with screening once in a lifetime; the ICER was up to US$5,963 per LYS when combined with five screenings in a lifetime. Goldie and others (2008) found an ICER of US$1,360 per LYS when total vaccine costs were US$25 per vaccinated girl. Chapter 4 in this volume (Denny and others 2015) provides a fuller description of the cost-effectiveness of cervical cancer prevention in China and other settings.

Extended Cost-Effectiveness Analysis

Recent attention to attaining the goal of universal health coverage provides a strong rationale for exploring mechanisms to expand access to the prevention and treatment of cervical cancer in China, without increasing the financial burden of the women seeking care and paying for services (WHO 2013b). We conducted an extended cost-effectiveness analysis (ECEA) to evaluate public financing of HPV vaccination to prevent cervical cancer. Importantly, the ECEA approach adds new dimensions to conventional cost-effectiveness analysis through a more explicit treatment of equity and impact on financial risk protection—prevention of medical impoverishment (Verguet and others 2015; Verguet, Laxminarayan, and Jamison 2015; Verguet and others 2013). Specifically, ECEA can evaluate publicly financed programs by measuring program impact along four main dimensions:

- Health benefits
- Household private expenditures averted (household cost savings)
- Financial risk protection provided to households
- Distributional consequences across the wealth strata of country populations.

As a result, ECEA enables the quantitative inclusion of information on equity and on how much financial risk protection is bought per dollar expenditure on health policy, in addition to how much health is bought (Verguet, Laxminarayan, and Jamison 2015; Verguet and others 2013).

As a consequence, the distribution of health and financial benefits resulting from health interventions—and, by extension, from the policy instruments that finance them—can be examined to answer the question of whether the interventions are pro-poor. In practice, the ECEA approach can also be used to examine the financial effects of interventions and policies on individuals or families by income group and in aggregate. Health policies and interventions typically involve costs to the public sector and to households. Even if a specific intervention is provided at no cost, users often incur time costs if they are required to travel or wait at health facilities to receive information, treatment, or test results; the value placed on these costs differs according to income level.

Publicly financed health interventions can help users to avoid future costs. For example, HPV vaccination and cancer screening programs reduce the risk of cervical cancer, which might otherwise lead to medical impoverishment, devastating health consequences (for example, the death of a mother increases the mortality risk for children), or both (for example, the death of the primary household income earner could impoverish the family).

The objective of this analysis is to evaluate the consequences of public finance of HPV vaccination in China, using the ECEA methodology. Public finance increases the uptake of the HPV vaccine, which can improve health, reduce household medical expenditures related to cervical cancer treatment, and prevent subsequent impoverishment. Finally, public finance can have differential impacts among populations of different income levels. We estimate the level and distribution across income groups of the cervical cancer deaths averted, the households' expenditures related to cervical cancer treatment averted and the costs needed to sustain the HPV program, and the financial risk protection that the program provides, using a combination of indicators.

MATERIALS AND METHODS

Model

We synthesized the available epidemiological, clinical, and economic data from China, using a previously described individual-based Monte Carlo simulation model of cervical cancer (Goldhaber-Fiebert and others 2007; Goldie and others 2007; Kim and others 2007). The model consists of health states representing important clinical stages of disease, including HPV infection, grade of precancerous lesions, and stage of invasive cancer. We evaluated vaccination and screening as a combined strategy in a single cohort, such that preadolescent girls who are vaccinated will also eventually receive screening.

Cervical cancer can be detected through symptoms or screening, and women with cancer survive according to stage-specific survival rates for local, regional, and metastatic disease. This model does not consider screening strategies alone for the current cohort of older women. Individual girls enter the model at age nine years, before sexual debut and free of HPV infection, and they transition between health states throughout their lifetimes. Each month, women face a risk of acquiring HPV infection; once infected, they can clear their infection or develop low- or high-grade lesions, categorized as cervical intraepithelial neoplasia, grade 1 (CIN 1) or grade 2,3 (CIN 2,3). Low-grade lesions can regress; CIN 2,3 can progress to invasive cancer. These transitions are determined by age, HPV type, and type-specific natural immunity after clearance of HPV infections. The natural history and model transitions have been well described elsewhere (Kim and Goldie 2008; Kim, Ortendahl, and Goldie 2009). For a more extensive discussion of the natural history of cervical cancer, see chapter 4 in this volume (Denny and others 2015).

All women are subject to mortality from the competing causes listed in the World Health Organization (WHO) life table estimates for China (WHO 2011). Our approach was to calibrate the model for the cervical cancer burden of the country as a whole and also for the HPV 16/18 type distribution in cervical cancer, which has been found in previous meta-analyses to be stable for 16/18 at 70 percent, regardless of country. De Sanjose and others (2010) found that more than 30 types of HPV are sexually transmitted and may lead to cervical cancer, most notably HPV 16 and 18, which together contribute to approximately 70 percent of cervical cancers worldwide. Accordingly, HPV is categorized as follows:

- High-risk type 16 (HR-16)
- High-risk type 18 (HR-18)
- Other high-risk types (HR-other), including 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, 68, 73, and 82
- Low-risk (LR) types, including 6, 11, 26, 32, 34, 40, 42, 44, 53, 54, 55, 57, 61, 62, 64, 67, 69, 70, 71, 72, 81, 83, and 84.

We initially established model parameters using the best available information on the natural history of HPV infection and cervical carcinogenesis. The model was adapted to the context in China using likelihood-based methods to fit the parameters to epidemiological data (figure 18A.1 in online annex 18A). Age-specific cervical cancer estimates were obtained from the GLOBOCAN (2008); data on HPV 16 and 18–type distribution in CIN 2,3 and cervical cancer were from a meta-analysis of primary data from Asia (Bao and others 2008) (figure 18A.2 in online annex 18A). The baseline natural history parameters were allowed to vary over plausible ranges. We identified sets of parameter values that achieved close fit to the empirical data and conducted the analysis using the parameter set with the maximum likelihood. Additional details of the model structure, calibration process, and calibration results are available online in annex 18A.

Strategies, Data, and Assumptions

To model the impact of cervical cancer prevention on distributional benefits and financial risk protection, we simulated screening with cytology and visual inspection with acetic acid (VIA) at five-year intervals, beginning at age 35 years, for a cohort of one million women in each of the income quintiles. We assumed that the screening frequency progressively increases with income; women in the lowest two quintiles would be screened once in a lifetime, those in the next two income quintiles would be screened three times in a lifetime, and those in the highest quintile would be screened five times in a lifetime. Consistent with assumptions made in previous analyses (Goldie and others 2001; Goldie and others 2005), cytology was assumed to occur in three visits: the initial screening (visit 1); colposcopy and possible biopsy for screen-positive women (visit 2); and treatment of precancerous lesions or invasive cancer (visit 3), including loop electrosurgical excision procedure (LEEP), cold knife conization, simple hysterectomy, or simple radiotherapy, depending on lesion size or cancer stage. The VIA screening incorporated same-day screening and treatment for all women with positive screening results as described in the Comprehensive Cervical Cancer Control guidelines (WHO 2006).

Vaccination was assumed to occur before age 12 (prior to sexual debut), with full adherence to the three doses, affording complete and lifelong protection against HPV 16 and 18. HPV vaccine coverage was assumed at 70 percent, based on current immunization rates of over 95 percent for childhood vaccines and recent evidence on the feasibility of reaching preadolescent girls with HPV vaccination using facility, school-based, and outreach strategies (La Montagne and others 2011; WHO 2013a). We used screening coverage estimates by quintile from the WHO Study of Global AGEing and Adult Health (WHO 2012). In the absence of patient health utilization data for screen-positive women, we assumed that loss to follow-up from screening to subsequent visits for diagnosis and treatment was inversely related to income, with loss to follow-up rates ranging from 62 to 5 percent from lowest to highest quintile, respectively. Recognizing that service utilization and loss to follow-up will be influenced by heterogeneity in health system, spatial, and socioeconomic factors across China's provinces, we conducted a sensitivity analysis on screening coverage rates and the loss to follow-up assumptions by quintile. Table 18.1 summarizes the point estimates for the model input parameters.

Using output data from the simulation model, we estimated the level and distribution of deaths averted by income quintile, comparing vaccination plus screening against screening at current coverage rates. We also estimated the reduction in cervical cancer, incremental costs to the government equal to HPV vaccination costs minus cervical cancer treatment costs averted, and patient cost savings, as well as the incremental government health care costs per death averted. Financial risk protection

Table 18.1 Summary of Parameters Used for Modeling the Impact and Costs of a Publicly Financed HPV Vaccination Policy in China

Parameter	Estimate
Screening with cytology: frequency[a] and coverage[b] (%)	
Quintile I: Once per lifetime	21
Quintile II: Once per lifetime	34
Quintile III: Three times per lifetime	43
Quintile IV: Three times per lifetime	47
Quintile V: Five times per lifetime	51
Loss to follow-up[c] (%)	
Quintile I	62
Quintile II	40
Quintile III	22
Quintile IV	13
Quintile V	5
Vaccine characteristics[c]	
Vaccination coverage (%)	70
HPV vaccine price per dose (US$)	13
Incremental vaccine program delivery cost per fully immunized girl (US$)	5
Vaccine cost per fully immunized girl, including wastage and handling (US$)	46
Income and wages[d]	
Average GDP per capita (US$)	3,749
Average GDP per capita[e] (US$)	
Quintile I	783
Quintile II	1,633
Quintile III	2,567
Quintile IV	3,888
Quintile V	7,896
Mean wage rate[f] (US$)	
Quintile I	3
Quintile II	6
Quintile III	10
Quintile IV	15
Quintile V	30

Note: Income quintiles are from lowest (I) to highest (V). Monetary values are in 2009 U.S. dollars. GDP = gross domestic product; HPV = human papillomavirus.

a. Frequency of screening was estimated at one time and five times per lifetime for all income quintiles in the sensitivity analysis.

b. Estimates from Gakidou, Nordhagen, and Obermeyer (2008) and WHO (2012).

c. Estimates are assumed values.

d. Estimates from WHO Global Health Observatory.

e. Estimates from WHO (2012) and WHO Global Health Observatory.

f. Estimates from WHO Global Health Observatory and Shi, Chen, and others (2012).

was estimated using a combination of indicators, including the number of women who would avoid cervical cancer treatment expenses and the average out-of-pocket expenses averted as a share of average per capita income, measured by gross domestic product (GDP). We present all results by income quintile.

Cost Data Sources

To estimate direct medical and nonmedical costs associated with screening, diagnosis, and treatment, we used published cost data from two studies conducted in China (Levin and others 2010; Shi, Chen, and others 2012), where all costs were expressed in 2009 U.S. dollars. Since these studies provided cost estimates by type of facility in urban and rural settings, we assumed an average health-seeking behavior by income quintile and geographic setting, where in the lowest three income quintiles rural and urban women were screened at the levels of township (primary health center) and county hospital, respectively, and all women in these lower quintiles received diagnosis and treatment at the county hospital. We assumed that in the highest two income quintiles, rural and urban women were screened and treated at prefecture or provincial level hospitals, respectively.

We then applied a weighted average unit cost for screening, diagnosis, and cancer treatment, based on urban and rural population proportions by income quintile. To estimate the consequences for household and government costs, we assumed that 35 percent of cancer screening and treatment costs are still privately financed in China (WHO Global Health Observatory), reflecting that many services, including outpatient services, are not covered, despite mandatory health insurance schemes. Direct nonmedical patient time costs for transportation and waiting were based on time estimates from Shi, Chen, and others (2012), using an updated national average wage rate in China ranging from US$3 to US$30 per day for the lowest to highest quintile, respectively. The average wage rate is equal to average per capita income divided by 255 workdays per year at eight hours per day (Shi, Chen, and others 2012). We obtained GDP data from the World Bank and used the consumer price index to deflate all costs to 2009 U.S. dollars. Per capita income for each quintile is the proportion of GDP accrued to each income quintile using estimates from the World Bank and PovCalNet, an online poverty analysis tool, divided by the total population per quintile (World Bank 2013a, 2013b).

Although Merck and GlaxoSmithKline's commercially available HPV vaccines are not yet approved in China, both are offered at low prices for public sector programs that range from less than US$5 for countries eligible for Gavi, the Vaccine Alliance, to US$13 for Pan American Health Organization (PAHO) countries (Gavi 2013). Given the likelihood that China could negotiate lower public sector prices (Colombara and Wang 2013), we assumed a public sector cost of US$46 per fully immunized girl, which includes the vaccine price (three doses at US$13 per dose), vaccine wastage (2 percent), freight (6 percent), and program administration cost (US$5). The program administration cost captures the average cost of new delivery strategies to reach preadolescent girls who fall outside existing routine immunization programs. The program administration costs are lower than the average incremental costs in recent studies in Latin America and the Caribbean and Sub-Saharan Africa, but they are likely to reflect economies of scale that are found in more densely populated Asian countries (Levin and others 2013). Tables 18A.2 and 18A.3, in online annex 18A, summarize the cost data by quintile.

Sensitivity Analysis

We performed a sensitivity analysis of the findings and evaluated the robustness of the results to changes in screening frequency per lifetime, screening coverage, loss to follow-up rates, and the cost per fully vaccinated girl. To accommodate the uncertainty around the uptake of the vaccine and vaccine delivery costs in the case of China, we conducted a sensitivity analysis and varied the cost between US$10 and US$100 per fully immunized girl to allow for either higher vaccine prices or higher service delivery costs. Table 18.2 provides the estimates or ranges used in the sensitivity analysis for these parameters and the way they varied by income quintile. Not shown are the estimates for cancer treatment costs, which were uniformly increased by 50 and 100 percent for all income quintiles.

RESULTS

We estimate that adding preadolescent HPV vaccination at 70 percent coverage to current screening will yield a 44 percent cancer reduction across all income quintiles, as shown in table 18.3. Although the relative cancer reduction is constant across income groups, the absolute numbers of cervical cancer deaths averted and the financial risk protection from HPV vaccination are highest among women in the lowest quintile; women in the bottom income quintiles received relatively higher benefits compared with those in the upper income quintiles. HPV vaccination averts 15 percent more detected cancer cases and 18 percent more deaths in the

Table 18.2 Sensitivity Analysis Parameter Estimates and Ranges for HPV Vaccine and Service Delivery Costs

(US$)

Parameter	Point estimate	Estimate or range
Screening with cytology: frequency[a,b] and coverage (%)		
Quintile I: Once per lifetime	21	21–70
Quintile II: Once per lifetime	34	34–70
Quintile III: Three times per lifetime	43	43–70
Quintile IV: Three times per lifetime	47	47–70
Quintile V: Five times per lifetime	51	51–70
Loss to follow-up[c] (%)		
Quintile I	62	15, 39
Quintile II	40	15, 24
Quintile III	22	15, 22
Quintile IV	13	15, 17
Quintile V	5	11, 15
Vaccine cost per fully immunized girl, including wastage and handling (US$)	46	10–100

Note: Income quintiles are from lowest (I) to highest (V). Monetary values are in 2009 U.S. dollars. HPV = human papillomavirus.
a. The frequency of screening is estimated at one time and five times per lifetime for all income quintiles in the sensitivity analysis.
b. Estimates from Gakidou, Nordhagen, and Obermeyer (2008) and WHO (2012).
c. Estimates are assumed.

lowest compared with the highest quintile. Although in absolute dollars patient savings were higher in the top income quintile compared with the lowest quintile (US$7,041,335 and US$1,633,160, respectively), the cost savings from HPV vaccination constituted a larger share of per capita income among women in the bottom income quintiles, ranging from 60 percent among the lowest income quintile to 30 percent among the highest quintile.

At a vaccine cost of US$46 per fully immunized girl and 70 percent coverage, the incremental cost is approximately US$160 million for a single cohort of five million girls. At the relatively low levels of cancer screening and treatment in China, government intervention costs do not vary by wealth strata, since these medical savings are offset by the publically financed HPV vaccination costs.

Given China's low reported rates of cervical cancer screening, the model results and relative relationships across income quintiles are robust to changes in assumptions about screening frequency, screening coverage, and loss to follow-up (table 18.4). As expected, changes in the cost per fully immunized girl do not have an impact on deaths averted, cancer reduction, or financial risk protection, assuming that 70 percent coverage is maintained. At US$10 per fully vaccinated girl, the cost per death averted ranges from US$2,161 for the lowest income quintile to US$2,608 for the highest income quintile. At US$100 per vaccinated girl, the cost per death averted increases to US$24,000 for the lowest income quintile to more than US$29,000 for the highest income quintile (table 18.4). Universal coverage of the HPV vaccination becomes even more favorable for individuals in the lower income quintiles and provides greater relative financial risk protection when treatment costs are increased by an additional 50 or 100 percent (table 18.5).

DISCUSSION

Despite worldwide progress in reducing the burden of cervical cancer, more than 270,000 women still die from the disease each year; the majority of these deaths occur

Table 18.3 Benefits and Costs of a Publicly Financed HPV Vaccination Policy in China

Benefit or cost	Quintile I	Quintile II	Quintile III	Quintile IV	Quintile V
Deaths averted per million women	2,877	2,854	2,667	2,604	2,362
Government cost per million women (incremental) (US$)	31,417,285	31,420,191	31,440,420	31,446,679	31,359,970
Government cost per death averted (US$)	3,540	3,511	3,312	3,256	2,999
Treatment-seeking cases of cancer averted per million women	3,540	3,511	3,312	3,256	2,999
Patient cost savings per million women (US$)	1,633,160	2,240,688	2,785,626	4,417,303	7,041,335
Savings as percentage of total income	59	39	33	35	30
Cancer reduction (%)	44	44	43	43	44

Note: Income quintiles are from lowest (I) to highest (V). Monetary values are in 2009 U.S. dollars. HPV = human papillomavirus.

Table 18.4 Results of Sensitivity Analysis for HPV Vaccination Costs at US$10, US$46, and US$100 per Fully Vaccinated Girl

	Quintile				
Result	**I**	**II**	**III**	**IV**	**V**
HPV vaccination at US$10 per fully vaccinated girl					
Deaths averted	2,877	2,854	2,667	2,604	2,362
Government cost (incremental) (US$)	6,217,285	6,220,191	6,240,420	6,246,679	6,159,970
Government cost per death averted (US$)	2,161	2,179	2,340	2,399	2,608
Treatment-seeking cases of cancer averted	3,540	3,511	3,312	3,256	2,999
Patient cost savings (US$)	1,633,160	2,240,688	2,785,626	4,417,303	7,041,335
Savings as percentage of income	59	39	33	35	30
Cancer reduction (%)	44	44	43	43	44
HPV vaccination at US$46 per fully vaccinated girl					
Deaths averted	2,877	2,854	2,667	2,604	2,362
Government cost (incremental) (US$)	31,417,285	31,420,191	31,440,420	31,446,679	31,359,970
Government cost per death averted (US$)	10,920	11,009	11,789	12,076	13,277
Treatment-seeking cases of cancer averted	3,540	3,511	3,312	3,256	2,999
Patient cost savings (US$)	1,633,160	2,240,688	2,785,626	4,417,303	7,041,335
Savings as percentage of income	59	39	33	35	30
Cancer reduction (%)	44	44	43	43	44
HPV vaccination at US$100 per fully vaccinated girl					
Deaths averted	2,877	2,854	2,667	2,604	2,362
Government cost (incremental) (US$)	69,217,285	69,220,191	69,240,420	69,246,679	69,159,970
Government cost per death averted (US$)	24,059	24,254	25,962	26,592	29,280
Treatment-seeking cases of cancer averted	3,540	3,511	3,312	3,256	2,999
Patient cost savings (US$)	1,633,160	2,240,688	2,785,626	4,417,303	7,041,335
Savings as percentage of income	59	39	33	35	30
Cancer reduction (%)	44	44	43	43	44

Note: Income quintiles are from lowest (I) to highest (V). Monetary values are in 2009 U.S. dollars. HPV = human papillomavirus.

in Asia, Latin America and the Caribbean, and Sub-Saharan Africa. China accounts for 12 percent of new cervical cancer cases each year (Ferlay and others 2013), with higher incidence and death rates in the country's poorest provinces. The factors contributing to the disproportionate distribution of cervical cancer disease include low coverage and poor quality of screening programs, differential access to services for screening and treatment, poverty, and lack of awareness. The availability of HPV vaccines can complement existing cervical cancer prevention efforts, accelerating the equity and health impacts by overcoming many of these barriers (Tsu and Levin 2008).

The HPV vaccine holds great promise for reducing the burden of cervical cancer, but the vaccine is not yet available in China. Delaying the introduction of the HPV vaccine will result in a lost opportunity to prevent cervical cancer cases and deaths. A national vaccination program from 2006 to 2012 of all girls ages 9–15 years could have prevented 381,000 cervical cancer cases and 212,000 related deaths in the coming decades (Colombara and Wang 2013). It is expected that China could negotiate HPV vaccine prices to cost-effective levels of approximately US$9 to US$13 per dose, but many Chinese women—at least 33 percent—are not willing to pay more than US$3 (Li and others 2009). A successful program is likely to depend on government financing.

We applied an ECEA approach to evaluate the impact of a publically financed policy for HPV vaccination in China on the distribution of health consequences and

Table 18.5 Results of Sensitivity Analysis Assuming Treatment Costs Increase by 50 Percent and 100 Percent Compared with Baseline

	Quintile				
Result	**I**	**II**	**III**	**IV**	**V**
Baseline strategy					
Deaths averted	2,877	2,854	2,667	2,604	2,362
Government cost (incremental) (US$)	31,417,285	31,420,191	31,440,420	31,446,679	31,359,970
Government cost per death averted (US$)	10,920	11,009	11,789	12,076	13,277
Treatment-seeking cases of cancer averted	3,540	3,511	3,312	3,256	2,999
Patient cost savings (US$)	1,633,160	2,240,688	2,785,626	4,417,303	7,041,335
Savings as percentage of income	59	39	33	35	30
Cancer reduction (%)	44	44	43	43	44
Treatment costs increased by 50%					
Deaths averted	2,877	2,854	2,667	2,604	2,362
Government cost (incremental) (US$)	31,035,156	31,057,311	31,085,113	31,103,101	30,939,508
Government cost per death averted (US$)	10,787	10,882	11,655	11,944	13,099
Treatment-seeking cases of cancer averted	3,540	3,511	3,312	3,256	2,999
Patient cost savings (US$)	1,899,093	2,506,089	3,040,532	4,714,290	7,310,555
Savings as percentage of income	69	44	36	37	31
Cancer reduction (%)	44	44	43	43	44
Treatment costs increased by 100%					
Deaths averted	2,877	2,854	2,667	2,604	2,362
Government cost (incremental) (US$)	30,647,484	30,682,085	30,728,534	30,760,469	30,550,290
Government cost per death averted (US$)	10,653	10,751	11,522	11,813	12,934
Treatment-seeking cases of cancer averted	3540	3511	3312	3256	2999
Patient cost savings (US$)	2,165,026	2,771,490	3,295,438	5,011,276	7,579,775
Savings as percentage of income	78	48	39	40	32
Cancer reduction (%)	44	44	43	43	44

Note: Income quintiles are from lowest (I) to highest (V). Monetary values are in 2009 U.S. dollars.

financial risk protection benefits across income levels. Our analysis showed that preadolescent HPV vaccination, added to current cervical cancer screening, could reduce cancer by over 40 percent across all income groups, while providing relatively higher financial protection to households in the bottom income quintiles. The low screening coverage rates reported for China affect the government and patient screening and treatment costs, but with differential results.

- From the governmental perspective, a publically financed HPV vaccination program would increase net costs, with little offset from averted cervical-related treatment costs, because of the low levels of screening.
- Although HPV vaccination led to patient cost savings that were small relative to the increase in government costs, all income groups experienced cost savings; importantly, there was a powerful equity effect, with higher financial risk protection in the poorest groups.
- Patient cost savings represent a large proportion of poor women's average per capita income, reaching 60 percent among women in the bottom income quintile and declining to 30 percent among women in the wealthiest quintile.

We also estimated standard cost-effectiveness ratios (results available from the authors) and, similar to previous studies conducted in China, found that HPV vaccination is cost effective across all income groups when the cost is less than US$50 per vaccinated girl.

Since the vaccine is not yet available in China, we assumed a cost of US$46 per vaccinated girl, using US$13 per dose, based on the manufacturers' offer price to PAHO for public vaccination programs in Latin America and the Caribbean. The financial cost of vaccinating 70 percent of China's current cohort of 6.6 million 10-year-old girls is US$213 million. This estimate, which accounts for less than 0.5 percent of projected health care spending of US$357 billion in 2011, would have a large financial impact on China's current Expanded Program for Immunization (EPI). The introduction of the HPV vaccine would require a change in policy to finance the vaccine publicly, through current health insurance schemes or inclusion in EPI, which provides free childhood vaccines for measles, diphtheria/tetanus/pertussis, Bacille Calmette–Guérin, polio, and hepatitis B. EPI manages non-EPI vaccines, such as those for Japanese encephalitis, mumps, and rubella, but patients pay for these vaccines via user fees. A third type of "optional" vaccines, such as hepatitis A, *Haemophilus* influenza type B, and rotavirus, are procured and delivered outside EPI and paid for by patients without government subsidies (Liu and others 2006).

Limitations of the Analysis

This analysis has several limitations:

- First, the analysis is an illustrative application of the ECEA method using the best available published data from selected provinces, which do not fully capture the heterogeneity in disease burden, health systems, socioeconomic development, and GDP per capita across China's provinces. For example, we used data from different regions in China to estimate the cervical cancer burden and costs for the whole country, leading to results that may not hold for a country as large as China. Accordingly, in this application, the results should be considered suggestive, rather than evidence based, but the estimates can be refined for specific subregions as improved data become available.
- Second, the ECEA method simulates the costs and impacts of HPV vaccination by income quintile; however, there are limited data on the variation of HPV incidence, mortality rates, loss to follow-up rates for screening, and out-of-pocket health expenses related to cancer prevention or treatment by wealth or income category.
- Third, there is limited information on health service utilization; screening and treatment costs; and the impact of mandatory health insurance by prefecture, province, and other geographic settings or across wealth strata. Our assumptions were based on aggregate national estimates of private expenses, which may be out of date, given the recent rapid growth in GDP per capita.
- Fourth, we estimated women's time using a wage rate derived from a national estimate of GDP per capita income, which may overestimate income in the lowest quintile, where some rural communities are likely to live on US$2 per day or less.
- Fifth, this analysis does not include women's transport costs in seeking screening, treatment, or vaccination; these costs are expected to be small components of patient costs based on previous analyses in China (Canfell and others 2011; Levin and others 2010; Shi, Chen, and others 2012).
- Sixth, we did not conduct an exhaustive evaluation of scenarios, including increasing screening to higher levels, since the objective of the analysis was to illustrate the potential of an HPV vaccination program to address equity and financial risk protection and not to identify optimal cervical cancer prevention approaches.

An ECEA approach yields new and essential information on a policy's ability to reduce inequity and catastrophic expenses. The approach complements information on value for money from traditional cost-effectiveness analyses. Future applications of this approach will benefit from improved information on public and private health financing, as well as from disaggregated data on disease burden and health service utilization by key socioeconomic, demographic, and geographic variables.

CONCLUSIONS

HPV vaccines have not yet been approved in China, and concern is growing that the use of HPV vaccines in the country is still a long way off (Lu 2013). A recent editorial recognizing the burden of cervical cancer in China, as well as its unequal impact among women in lower income groups, proposes a semi-mandatory HPV vaccination program in China targeted to low-income, high-risk women living in regions with historically high prevalence of cervical cancer (Zhang, Li, and others 2013). This illustrative application of the ECEA approach to a publicly financed HPV vaccination policy provides decision makers with the potential distributional consequences and financial risk protection of including cervical cancer in future health care reform investments to provide insight to policy debates in China. An ECEA can provide policy makers with additional evidence beyond evidence of effectiveness, costs, and cost-effectiveness for selective resource allocation to the populations and provinces most in need in the context of public financing and the strengthening of Chinese health reform.

Previous research has demonstrated that HPV vaccination in China can be cost-effective at a cost of US$50 per vaccinated girl. A targeted program may even be affordable, given China's plans for dramatically increasing health care spending in the near future (Le Deu and others 2012; Zhang, Li, and others 2013). Ensuring high and uniform HPV vaccine uptake will likely also contribute to more equitable gains with respect to the reduction of morbidity and mortality from cervical cancer and has the potential to protect women in poor households against catastrophic cervical cancer medical expenses.

NOTE

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World Bank Income Classifications as of July 2014 are as follows, based on estimates of gross national income (GNI) per capita for 2013:

- Low-income countries (LICs) = US$1,045 or less
- Middle-income countries (MICs) are subdivided:
  a) lower-middle-income = US$1,046 to US$4,125
  b) upper-middle-income (UMICs) = US$4,126 to US$12,745
- High-income countries (HICs) = US$12,746 or more.

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