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Cost-effectiveness analysis of cervical cancer prevention based on a rapid human papillomavirus screening test in a high-risk region of China

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This study assessed the cost-effectiveness of a new, rapid human papillomavirus (HPV)-DNA screening test for cervical cancer prevention in the high-risk region of Shanxi, China. Using micro-costing methods, we estimated the resources needed to implement preventive strategies using cervical cytology or HPV-DNA testing, including the Hybrid Capture 2 (hc2) test (QIAGEN Corp., Gaithersburg, MD) and the rapid HPV-DNA *care*HPV™ test (QIAGEN). Data were used in a previously published model and empirically calibrated to country-specific epidemiological data. Strategies differed by initial test, targeted age, frequency of screening, number of clinic visits required (1, 2 or 3) and service delivery setting (national, county and township levels). Outcomes included lifetime risk of cancer, years of life saved (YLS), lifetime costs and incremental cost-effectiveness ratios (cost per YLS). For all screening frequencies, the most efficient strategy used 2-visit rapid HPV-DNA testing at the county level, including screening and diagnostics in the first visit, and treatment in the second visit. Screening at ages 35, 40 and 45 reduced cancer risk by 50% among women compliant with all 3 screening rounds, and was US$ 150 per YLS, compared with this same strategy applied twice per lifetime. This would be considered very cost-effective evaluated against China's per-capita gross domestic product (US$ 1,702). By enhancing the linkage between screening and treatment through a reduced number of visits, rapid HPV-DNA testing 3 times per lifetime is more effective than traditional cytology, and is likely to be cost-effective in high-risk regions of China.

Cervical cancer affects millions of individuals worldwide and is a leading cause of cancer death among women in developing countries.[1] Although China registers a low average incidence of cervical cancer compared to many other regions of the world, the overall burden is large due to the size of the country's population. Moreover, there is considerable heterogeneity in terms of risk, with cervical cancer mortality rates in poor provinces such as Shanxi and Gansu exceeding 30 cases per 100,000.[2] Data available from one survey indicate that the prevalence of carcinogenic types of human papillomavirus (HPV) is 20.8% among 35- to 50-year-old women.[3] Since a national cervical cancer prevention program does not exist, most women have not been screened.[2]

Cervical cancer has been reduced in countries able to implement organized secondary prevention programs that screen women with cytology at regular closely spaced intervals.[4] Unfortunately, the requirement for high-quality laboratory and cytotechnologist support, coupled with the need for multiple visits, has proven difficult to implement in low-resource settings. Screening approaches that use HPV-DNA testing may prove more practical when incorporated into strategies less dependent on existing laboratory infrastructure and requiring fewer visits.[5,6] Most recently, a randomized trial in Osmanabad district in India demonstrated a single round of HPV-DNA testing among enrolled women between the ages of 30 and 59 years, was associated with a significant reduction in the number of advanced cancers and deaths

Key words: cervical cancer, screening, cost-effectiveness, HPV, modeling

Abbreviations: CICAMS: Chinese Academy of Medical Sciences; CIN: cervical intraepithelial neoplasia; DNA: deoxyribonucleic acid; GDP: gross domestic product; hc2: Hybrid Capture 2 test; HPV: human papillomavirus; LBC: liquid-based cytology; LEEP: loop electrosurgical excision procedure; YLS: years of life saved

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compared with a control group; no significant reductions in cervical cancer cases or deaths were found with a single round of conventional cytologic testing.[7,8]

We previously reported, in an analysis conducted in 5 developing countries that strategies that enhance the linkage between screening and treatment—thereby delivering the secondary prevention strategy in 1 or 2 visits—are the most effective and cost-effective.[6] A single-visit HPV-DNA testing strategy requires screening sites to run the test on the day the sample is received, allowing for treatment of cervical precancer during the same visit. The hc2 test is the HPV-DNA test that is currently available; it takes at least 6 hr to process, making a single-visit approach impossible. The new, rapid HPV-DNA *care*HPV™ test has a 2-hr processing time, permitting a same-day diagnostic evaluation, with treatment in a second visit, or even screening and treatment in the same day.[9,10]

To quantify the potential impact of integrating rapid HPV-DNA testing into cervical cancer screening, we adapted a previously published disease model to epidemiological data from Shanxi and assessed the reduction in lifetime risk of cancer with different strategies. Using micro-costing methods, we estimated the resources needed to implement preventive strategies that used cervical cytology or HPV-DNA testing. These data were used in the empirically calibrated model to assess the incremental cost-effectiveness of rapid HPV-DNA testing compared with other screening approaches.

Material and Methods

Overview

We modified a previously developed computer-based model to synthesize the best available data in a high-risk region of China and simulate the natural history of HPV infection and cervical cancer as well as strategies for screening, diagnosis and treatment. We compared alternative strategies by calculating the incremental cost-effectiveness ratio, defined as the additional cost of a specific strategy, divided by its additional clinical benefit, compared with the next most costly strategy. We followed recommendations of several published guidelines for economic evaluations intended to inform resource allocation in that we adopted a societal perspective and included all costs and benefits without any regard to whom they accrue, incorporated patient time costs, and discounted future costs and life years by 3% annually.[11–14]

Natural history model

We adapted a previously published model to the specific epidemiologic setting of Shanxi, China by integrating primary data (prevalence of cervical intraepithelial neoplasia (CIN) 1, CIN2, CIN3, cancer, and cancer mortality from Xiangyuan and Yangcheng counties of Shanxi Province) and data drawn from published literature. Calibration methods ensure that the age-specific cervical cancer incidence predicted by the model approximates the best available country-specific data. In the calibration process, progression and regression parameters, including type-specific rates of acquisition and clearance of HPV, probabilities of progressing to or regressing from a cervical lesion, and the probability of developing cancer, are informed by country- or region-specific population-based estimates of disease epidemiology. Because of data limitations and inconsistency between country- *versus* region-specific datasets, the model was calibrated to primary data from the Shanxi region. Details of the model are reported elsewhere.[6]

Screening strategies

We differentiated screening strategies by initial screening test, number of clinical visits, screening frequency in a lifetime, procedure locations and targeted ages. We assume that screening, diagnostic and treatment services may occur at a variety of facility levels, including the township, county and national levels, but that the location of the test did not affect accuracy. Tests include conventional cervical cytology using a Papanicolaou smear, liquid-based cytology (LBC), HPV-DNA testing using the currently available hc2 test (requiring at least 6 hr for samples to be processed), and HPV-DNA testing using the new, rapid *care*HPV test, with results available in 2 hr.[8–10] Treatment options for precancerous lesions include cryotherapy, loop electrosurgical excision procedure (LEEP), cold knife conization, or simple hysterectomy, depending upon lesion size, location on the cervix, and type.[15] However, it is rare to find cryotherapy used in China, given technological advances in LEEP, as well as logistical challenges in obtaining gas tanks for cryotherapy.

China does not have an established nationwide cervical cancer screening program at this time. The qualified conventional Pap smear, LBC and HPV DNA tests are available for opportunistic screening in urban areas only. Therefore, strategies selected for the base case were based on in-country expert opinion reflecting cervical cancer screening recommendations at a consensus meeting organized by the Cancer Foundation of China and the Ministry of Health in 2005[16] that considered acceptability, availability and cultural preferences. Accordingly, the base-case strategies included HPV-DNA testing and cytology, and omitted strategies that provided same-day test and treatment without confirmation by biopsy, as these were not considered acceptable by local experts. Three-visit strategies include an initial screening test, colposcopy/biopsy for positive screening results and treatment in a third visit. For example, women may be screened at the township level with HPV-DNA testing, return for diagnostic testing, and if necessary are referred for treatment at the county level; those screened with cytology or LBC are referred to the county or national level, respectively, for diagnostic testing and treatment. All women screened at the national level return to the national-level facility for diagnostic testing, and again for treatment. Two-visit strategies incorporate initial screening coupled with colposcopy/biopsy for positive results, with treatment occurring in a second visit. For example, in a 2-visit rapid HPV-DNA strategy, screening

Table 1. Test characteristics

Variable	Base case	Plausible range[1]
Cytology		
Sensitivity of liquid-based cytology (%)[2]	87.2	50–100
Specificity of liquid-based cytology (%)[2]	93.5	60–100
Sensitivity of conventional cytology (%)	63	50–100
Specificity of conventional cytology (%)	94	60–100
HPV-DNA testing		
Sensitivity of rapid test (%)	89.7	50–100
Specificity of rapid test (%)	84.2	50–100
Sensitivity of Hybrid Capture 2 (%)[2]	95.2	50–100
Specificity of Hybrid Capture 2 (%)[2]	85.9	50–100

[1]Range used in sensitivity analyses. HPV, human papillomavirus; DNA, deoxyribonucleic acid. [2]Base case test characteristics for liquid-based cytology and Hybrid Capture 2 varied in sensitivity analysis.[1,19–21]

and diagnostic testing occur at the county-level health facility. Women return to the county-level facility to retrieve their biopsy results, and if positive, receive treatment. Single-visit strategies, incorporating same-day screening and treatment in screen-positive women, were also considered as potential future strategies because these have been shown in previous analyses to be cost-effective under certain circumstances.[6] For example, a single-visit rapid HPV-DNA strategy performed at the county level was evaluated in sensitivity analysis.

Model input parameters were based on previous analyses, primary data and published literature[6,10,17,18] (Table 1). Loss to follow-up between each visit was assumed to be 15% for strategies that occur at the national hospital; for visits at county-level or township-level health facilities, there is assumed to be a 20% loss to follow-up per visit.

Costs

Costs are presented in 2005 U.S. dollars (Table 2). Using a societal perspective, costs were categorized into direct medical costs (*e.g.*, staff, disposable supplies, equipment and specimen transport), women's time costs (time spent traveling, waiting and receiving care), transportation costs and programmatic costs.

Average unit costs for screening using cytology, diagnosis, treatment of precancerous lesions and treatment of different states of cancer were based on primary data collected between January and June 2005 from the Tumor Hospital of the Chinese Academy of Medical Sciences (CICAMS) in Beijing and from a convenience sample of facilities in Shanxi Province. The selected hospitals were illustrative of the range of public health care institutions and the expected quality of care and costs found in the public health system in Shanxi Province. The estimated cost for HPV-DNA testing is based on a targeted price by the manufacturer for the rapid *care*HPV quoted by Qiagen at less than $5 per assay for bulk procurements for large-scale screening programs

Table 2. Cost data[1]

	Base case[2] Setting		
Variable	Township	County	National
Direct medical costs			
Hybrid Capture 2 HPV-DNA test	$45.89	$45.89	$45.89
Liquid-based cytology	$22.34	$22.34	$22.34
Conventional cytology	$5.43	$5.43	$5.43
Rapid HPV-DNA test	$3.52	$3.52	$8.22
Colposcopy	–	$8.21	$12.68
Biopsy	–	$15.46	$7.85
LEEP	–	$87.58	$144.93
Cold knife conization	–	$87.13	$144.93
Simple hysterectomy	–	$354.24	$1,167.48
Local cancer	–	$387.31	$1,360.71
Regional/distant cancer	–	$1,739.30	$1,739.30
Direct non-medical costs			
Woman hourly wage[3]	$0.42	$0.42	$0.42
Transportation	$0.24	$0.48	$0.36
Time waiting	15	15	20
Time of screen	13	14.5	16
Time of colposcopy and biopsy	–	36	57
Time of LEEP	–	47.5	73
Time of cold knife conization	–	65.5	76
Time of hysterectomy	–	225	488
Time for transport	30	40	60

[1]HPV, human papillomavirus; DNA, deoxyribonucleic acid; LEEP, loop electrosurgical excision procedure. [2]All costs reported are in 2005 US Dollars, all times reported in minutes. [3]Woman hourly wage drawn from National Bureau of Statistics of China.

supported by the public sector in low-resource settings (personal communication, Qiagen, 10/01/09).Direct medical and nonmedical costs were collected in RMB and converted to 2005 US dollars using the exchange rate at the time of US$ 1 = 8.28 RMB.

Cost data for the direct medical costs were collected using an ingredients-based costing methodology based on guidelines recommended by the World Health Organization.[22] Resource use for each stage of cancer was based on clinical protocols from national and regional hospitals and interviews with hospital personnel. Project staff interviewed health care providers and hospital administrators to obtain information on staff time, salaries, clinical consumable supplies, laboratory supplies, clinical and laboratory equipment, and indirect costs directly involved in all cervical cancer screening, diagnostic and treatment services. When feasible, a visual inspection of the procedure and surgical room, as well as laboratory

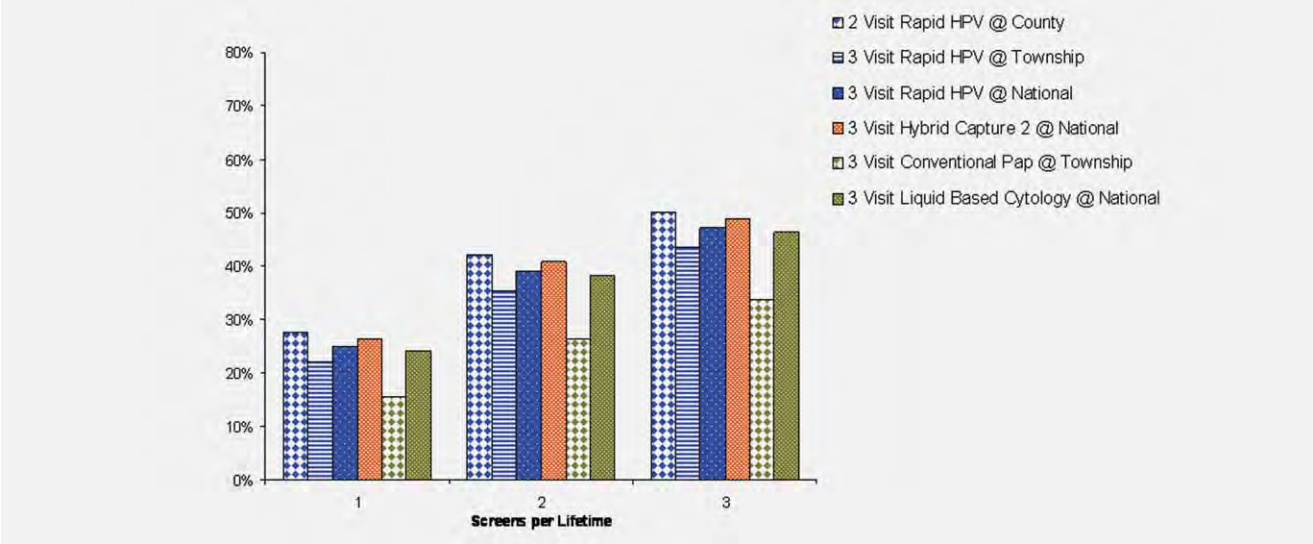

Figure 1. Reduction in the lifetime risk of cancer among women screened. [Color figure can be viewed in the online issue, which is available at www.interscience.wiley.com.]

facilities, was used to create an inventory of supplies and equipment. Supplementary budgetary data and expenditure records were used to provide information on salaries of non-clinical staff and indirect costs that comprise facility overhead costs. Cost estimates were supplemented with national and international data sources.[14,18,23] Additional details are available in the Supporting Information Appendix.

To generate an estimate of women's wages, we utilized the average woman's annual earnings of 11,320 RMB for women in urban settings, 4,630 RMB for women in rural settings and converted this to US dollars using the exchange rate, to estimate an average wage per minute, assuming women work an average of 50 weeks a year, at 40 hr per week.[14,18] We calculated the percent of Shanxi province that is rural *versus* urban, and took a weighted average of the annual income of urban residents and rural residents. For transportation costs, we used primary data regarding transportation time to each facility level, and transportation costs (2, 4 and 3 RMB for transportation to and from local, county, and national health facilities, respectively, incorporating the value of a woman's time to travel to the facility as well as the actual cost of taking transportation). Waiting time does not vary by procedure, but does vary by the location of the facility. For the amount of a woman's time required by each procedure, we aggregated data on the amount of direct service time of the medical staff and assumed women were present for all parts of a visit (registration, sample collection and labeling), but not for the room preparation. Care was taken, however, to assume that the time of a procedure was no longer than the recorded time for the combined medical staff.

We estimated programmatic costs differing by strategy, and their varying resource requirements for laboratory equipment and supplies, specimen transport costs, and training and supervision of particular techniques, assuming capacity utilization of 80%. We assumed that activities related to administration would increase the total medical costs by an additional 25%, and varied this from 10 to 75% in sensitivity analysis.

Results

Cancer reduction

Among women who are screened once in a lifetime at age 35, the lifetime risk of cancer is reduced from 15 to 28% depending on the specific strategy. Screening twice in a lifetime (at ages 35 and 40) or 3 times per lifetime (at ages 35, 40 and 45) provides additional benefits (Fig. 1). Cytology-based strategies requiring multiple visits are the least effective.

Both 2- and 3-visit rapid HPV-DNA testing strategies were more effective than cytology because of enhanced sensitivity, and in the case of the 2-visit approach, a lower loss to follow-up. Among women screened with HPV-DNA testing, cancer reduction was 21–47% (3-visit) and 26–50% (2-visit) depending on whether screening was once, twice, or three times per lifetime.

Cost-effectiveness

Figure 2 shows the lifetime costs and life expectancy of different strategies performed once, twice, or three times per lifetime. Total discounted costs for the base-case screening strategies (2-visit rapid HPV-DNA testing, 3-visit HPV-DNA testing with hc2, and 3-visit cytology) are generally lowest at the county and township levels and highest at the national level.

The cost-effectiveness of moving from one screening strategy to a costlier alternative is represented by the difference in cost divided by the difference in life expectancy associated with competing strategies. Strategies lying on the "efficiency curve" shown in Figure 2 "dominate" those lying to the right of the curve because they are more effective, and either cost

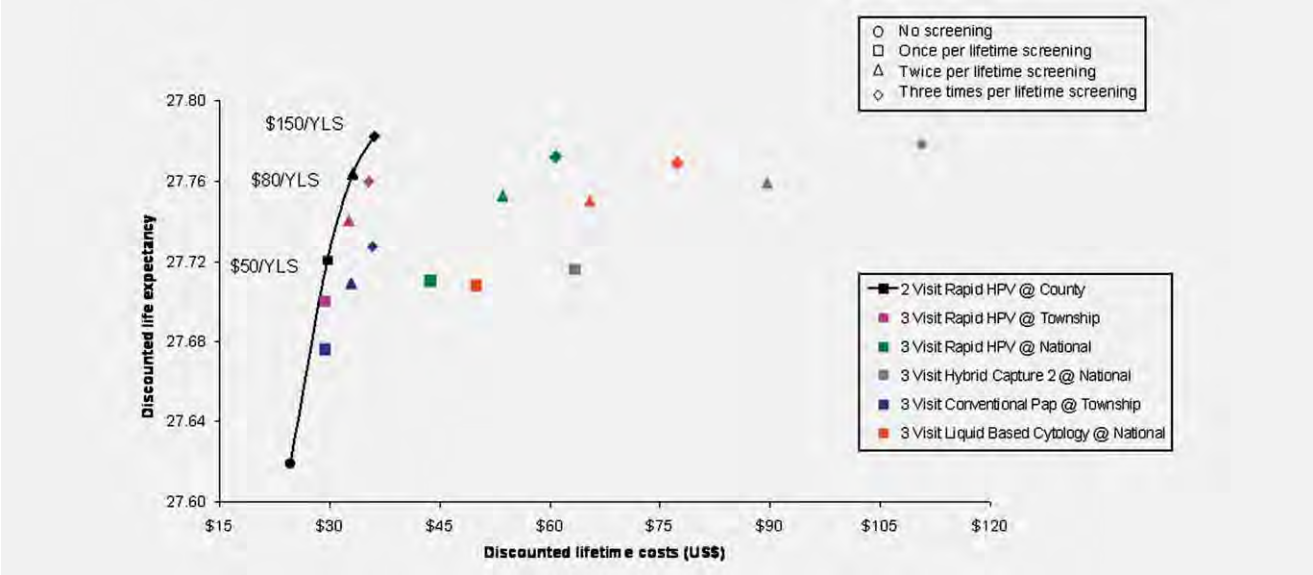

Figure 2. Cost-effectiveness of screening strategies. [Color figure can be viewed in the online issue, which is available at www.interscience.wiley.com.]

less or have a more attractive cost-effectiveness ratio, than the next-best strategy. The cost per years of life saved (YLS) for a single lifetime screening, using rapid HPV-DNA testing at the county level is US$ 50 per YLS compared with no screening (Table 3). Screening twice or three times per lifetime with this same strategy is US$ 80 and US$ 150 per YLS, respectively compared with the next-best strategy.

Although rapid HPV-DNA testing at the county level was the most efficient strategy in the base case, 3-visit rapid HPV-DNA testing at the township level had very similar costs and benefits; accordingly, this strategy is shown just adjacent to the efficiency curve. In contrast, strategies lying to the far right of the efficiency curve—including 3-visit HPV-DNA testing with hc2, 3-visit rapid HPV-DNA testing, and 3-visit LBC, all at the national level—are consistently unattractive because they cost more, but are no more effective, than the analogous strategies delivered at the county or township level.

Although no consensus exists on a universal threshold below which an intervention would be considered "cost-effective," benchmarks can be useful to generally compare the relative value provided by different interventions to improve health. For example, the Commission on Macroeconomics and Health[24] has suggested that an incremental cost-effectiveness ratio less than a country's annual per capita gross domestic product (GDP) (China, U.S. $1,702) represents a very cost-effective intervention. Using this criterion, rapid HPV-DNA testing 3 times per lifetime would unarguably provide good value for money.

Sensitivity analyses

The rank ordering of strategies, in terms of cost-effectiveness, was robust across plausible changes in the base-case parameters and assumptions. The cost-effectiveness results were only moderately sensitive to the costs associated with invasive cancer, treatment of precancerous lesions and screening test costs. When the costs associated with invasive cancer were doubled, the cost-effectiveness ratios associated with rapid HPV-DNA testing increased to US$ 90, US$ 120 and US$ 200 per YLS for once, twice, and three times per lifetime. Doubling the costs associated with treatment of precancerous lesions had a greater impact, since this change affected more women-cost-effectiveness ratios associated with rapid HPV-DNA testing increased to US$ 130, US$ 160 and US$ 250 per YLS for once, twice, and three times per lifetime. Importantly, since these ratios are still only a fraction of the GDP per capita, rapid HPV-DNA testing would still be considered very cost-effective.

The values used in the base-case analysis for sensitivity and specificity of HPV-DNA testing and LBC are similar to those recently reported from China[25]; plausible ranges were explored in sensitivity analyses.[1,17,19–21] We repeated the base-case analysis using values reported by Li *et al.*,[25] in which the sensitivity of HPV-DNA testing was reduced from 95.2 (base case) to 90.4% and the specificity of LBC was reduced from 93.5 (base case) to 85.4%. The rank ordering of strategies was unchanged and the cost-effectiveness results were unaffected. As specificity of rapid HPV-DNA testing was varied from 60 to 99% (base case 87.5%), the cost-effectiveness ratio varied from US$ 190 to US$ 130 per YLS, remaining a fraction of the per capita GDP. As sensitivity of rapid HPV-DNA testing was varied from 60 to 95% (base case 83.8%), the cost-effectiveness ratios varied by less than 10%.

We considered 2 additional strategies at the county level: a single-visit rapid HPV-DNA test and a 2-visit hc2 HPV-DNA test (Supporting Information Appendix). Both of these assume that a positive screen is followed by a colposcopy, and precancer is treated without verification by biopsy. Consistently, the most cost-effective strategies incorporated rapid

Table 3. Cost-effectiveness of selected cervical cancer screening strategies[1]

Screening strategy[2]					
Screening test	Location	Number of visits	Screens per lifetime	Discounted lifetime costs (US$)	Cost-effectiveness ratio (US$/YLS)[3]
No Screen				24.60	
Conventional cytology	Township	3	1	29.31	4
Rapid HPV test	Township	3	1	29.28	4
Liquid-based cytology	National	3	1	49.89	4
Conventional cytology	Township	3	2	32.85	4
Rapid HPV-DNA test	National	3	1	43.56	4
Hybrid Capture 2 test	National	3	1	63.25	4
Rapid HPV-DNA test	County	2	1	29.70	$50
Conventional cytology	Township	3	3	35.74	4
Rapid HPV-DNA test	Township	3	2	32.59	4
Liquid-based cytology	National	3	2	65.51	4
Rapid HPV-DNA test	National	3	2	53.62	4
Hybrid Capture 2 test	National	3	2	89.65	4
Rapid HPV-DNA test	Township	3	3	35.26	4
Rapid HPV-DNA test	County	2	2	33.18	$80
Liquid-based cytology	National	3	3	77.39	4
Rapid HPV-DNA test	National	3	3	60.76	4
Hybrid Capture 2 test	National	3	3	110.58	4
Rapid HPV-DNA test	County	2	3	36.01	$150

[1]Costs reported in 2005 US dollars. HPV, human papillomavirus testing; YLS, years of life saved; ICER, incremental cost-effectiveness ratio.
[2]Strategies indicate the location of screening (township, county or national level), the frequency of screening (once, twice or three times per lifetime), and the number of visits required (one, two or three visits). Screening women once per lifetime occurs at age 35; twice per lifetime occurs at ages 35 and 40; three times per lifetime occurs at ages 35, 40 and 45. [3]All screening tests are assumed to be equally available, and therefore the cost-effectiveness ratios shown are calculated by comparing the incremental costs (2005 US$) and benefits (life expectancy gains) of each strategy compared with the next best strategy.[4]Strategies shown either cost more but are less effective (strongly dominated), or cost more and are less cost-effective (weakly dominated), than an alternative strategy.

HPV-DNA testing 3 times per lifetime; cost-effectiveness ratios remained less than 10% of the GDP per capita. If rapid testing was unavailable, the cost-effectiveness ratio for a 2-visit hc2 strategy at the township level, provided 1, 2 or 3 times per lifetime, had ratios that were 23, 36 and 65% of the GDP per capita.

Discussion

The most effective and cost-effective strategies in this high-risk region of China enhance linkages between screening and treatment, either through a reduced number of visits or improved follow-up, and rely on less laboratory infrastructure than conventional cytology. Screening women 3 times per lifetime, between ages 35 and 45, would reduce the lifetime risk of cervical cancer by 34–50%. These findings are consistent with a previous study of the cost-effectiveness of cervical cancer prevention in 5 countries.[6]

The novel contribution of the present analysis is the evaluation of a rapid affordable alternative to existing HPV-DNA tests, and the inclusion of strategies—and their costs—which deliver the screening intervention at different levels of the health system. We considered cost differences in various screening tests, the technical requirements of tests, the laboratory infrastructure required, and the program feasibility for the given setting of China, specifically the high-risk province of Shanxi. We considered 3 levels of preventive health care (township, county and national). Not surprisingly, the costs of screening with 2-visit rapid HPV-DNA testing, 3-visit HPV-DNA testing with hc2, and 3-visit cytology, are lowest at the county and township level and highest at the national level. Since we assumed that test performance did not differ by setting, for any specific strategy screening at the county and township level was always more cost-effective.

Given the base-case assumptions, rapid HPV-DNA testing at the county level was the most efficient strategy. The rapid HPV-DNA, with its lower cost per test and greater sensitivity than conventional cytology dominated other screening methods. In addition, the results reflect the additional costs and benefits associated with fewer visits, reduced medical, time, and transportation costs, and reduced loss to follow-up. With a cost-effectiveness ratio less than the GDP per capita (US$ 1,702 in China), a commonly cited threshold for a "very cost-

effective" intervention, a rapid HPV-DNA test-based strategy clearly provides good value for the resources invested.[24]

With the availability of an effective vaccine against HPV types 16 and 18, there has been enthusiasm for vaccination of young adolescent girls.[26–28] However, it is imperative that the efforts of the last decade to develop feasible options for cervical cancer screening in poor countries do not stall.[29] Although preadolescent vaccination offers great hope for future generations, there exist a number of uncertainties that will persist for the next decade, and a number of challenges that will take time to solve—including, but not limited to, the need for drastically lower vaccine prices and creative sources of sustainable financing to support new vaccine introduction costs, and reaching young adolescents through new delivery channels, such as schools. Moreover, for older women, the primary avenue and best option to reduce deaths from this disease will be effective secondary prevention.[29–32] Our study finds that rapid HPV-DNA testing, 3 times per lifetime, has excellent potential to be an effective and cost-effective strategy in China; the rapid provision of test results allows for the construction of screening strategies at lower levels of the health system, thereby enhancing access and the probability of high coverage, lower costs and reduced loss to follow-up. An optimal cervical cancer prevention strategy of vaccination targeting young adolescent girls, and screening and treatment of older women can address the social, economic and political disadvantages that contribute to disparities in cervical cancer incidence and mortality in the developing world.[33]

Our analysis has several limitations. Data were combined from multiple sources with varied study designs, and many parameters are uncertain. Primary cost data were collected at the national cancer hospital in Beijing and in representative hospital settings in Shanxi Province, and therefore may not be representative of cost structures and costs in other parts of China. In this analysis, we used an estimate of the cost of the hc2 HPV-DNA test to the public health sector, including any mark-ups imposed through China's public sector procurement system. For the rapid HPV-DNA test, we included a best estimate of the cost of the rapid HPV-DNA test; however, it is difficult to estimate what the final price in China's public health sector will be since the test is not yet commercially available.

This analysis has demonstrated the potential cost-effectiveness of a single-visit screening followed by same-day treatment of precancer with cryotherapy. Administering treatment without histologic confirmation of precancer is not currently acceptable to Chinese medical experts. Likewise, cryotherapy is not acceptable as treatment for precancer, limiting the treatment options to excisional methods such as LEEP, cold knife conization, and hysterectomy, generally provided by large-capacity hospitals located in urban or peri-urban centers. Given available treatment options, all strategies currently require at least 2 visits. In this case, it is even more imperative to reduce the number of visits to 2 rather than 3 by using a rapid HPV-DNA test, especially in rural areas, where access to screening and treatment services is limited. An additional possibility for primary screening based on HPV-DNA testing is the use of vaginal specimens obtained by the women themselves or providers. We did not model this strategy, but it is anticipated that despite the approximate 10% loss in sensitivity compared to the use of cervical specimens, use of vaginal sampling may have advantages such as increasing coverage and acceptability while decreasing costs.[9,10,19]

In addition to cost-effectiveness, the optimal mix of cervical cancer prevention options will depend on a number of factors. The availability of quality health care services, including laboratory infrastructure supporting pathology and histology services, is more concentrated in China's cities, compared to rural areas, and may favor certain screening tests over others. Socio-economic access to services is increasingly constrained among low-income households.[34] User fees may also affect women's demand for screening services by reducing their willingness and ability to return for results and treatment, if needed. The most cost-effective strategies may be unaffordable in the poorest parts of the country without new financing incentives to increase the overall level of medical resources through the private and public health sectors.

Implementing the most effective and cost-effective choices for cervical cancer prevention, whether vaccination or screening, will require affordable technologies, new sources of financing, political support, and programs to both strengthen existing services and effectively deliver new interventions. A rapid HPV-DNA test, priced at a fraction of currently available HPV-DNA diagnostics and able to provide expedient results allowing the elimination of at least one return visit, offers great promise to the reduction of mortality from cervical cancer.

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