The Cost-Effectiveness of Visual Triage of Human Papillomavirus-Positive Women in Three Low- and Middle-Income Countries

Nicole G. Campos1, Jose Jeronimo2, Vivien Tsu2, Philip E. Castle3,4, Mercy Mvundura5, and Jane J. Kim1

Abstract

Background: World Health Organization guidelines support human papillomavirus (HPV) testing alone (followed by treatment with cryotherapy) or in conjunction with visual inspection with acetic acid (VIA) triage testing. Our objective was to determine the cost-effectiveness of VIA triage for HPV-positive women in low-resource settings.

Methods: We calibrated mathematical simulation models of HPV infection and cervical cancer to epidemiologic data from India, Nicaragua, and Uganda. Using cost and test performance data from the START-UP demonstration projects, we assumed screening took place either once or three times in a lifetime between ages 30 and 40 years. Strategies included (i) HPV alone, followed by cryotherapy for all eligible HPV-positive women; and (ii) HPV testing with VIA triage for HPV-positive women, followed by cryotherapy for eligible women who were also VIA-positive (HPV-VIA). Model outcomes included lifetime risk of cervical cancer and incremental cost-effectiveness ratios (ICERS; international dollars/year of life saved).

Results: In all three countries, HPV alone was more effective than HPV-VIA. In Nicaragua and Uganda, HPV alone was also less costly than HPV-VIA; ICERS associated with screening three times in a lifetime (HPV alone) were below per capita GDP. In India, both HPV alone and HPV-VIA had ICERS below per capita GDP.

Conclusions: VIA triage of HPV-positive women is not likely to be cost-effective in settings with high cervical cancer burden. HPV alone followed by treatment may achieve greater health benefits and value for public health dollars.

Impact: This study provides early evidence on the cost-effectiveness of HPV testing followed by VIA triage versus an HPV screen-and-treat strategy. Cancer Epidemiol Biomarkers Prev; 26(10); 1500–10. ©2017 AACR.

Introduction

Cervical cancer is a leading cause of cancer-related death among women worldwide (1), despite the potential for prevention through organized screening programs that detect and treat precancerous lesions. While routine screening with Pap smear testing has reduced the burden of cervical cancer in the United States and other high-income countries (2), the implementation of Pap-based screening programs has not been feasible in low-resource settings due to a lack of health care delivery infrastructure and limited health budgets. Consequently, nearly 90% of cervical cancer-related deaths worldwide occur in the developing world (1).

The knowledge that cervical cancer is caused by persistent cervical infection with one or more oncogenic human papillomavirus (HPV) types (3) has led to advances in screening technology, including HPV DNA tests (4). HPV testing is more sensitive and reliable for detection of precancer and cancer than Pap testing (5–10). This increased sensitivity for detection of cervical intraepithelial neoplasia grade 3 and higher (≥CIN3) translates into two important benefits: (i) earlier detection of CIN3 lesions that, if treated, results in reduced cervical cancer incidence and mortality (11, 12); and (ii) sustained lower risk of cancer following a negative HPV test result, permitting safe extension of screening intervals (11–14). Thus, when HPV testing is used as the primary screening test, women only need one to several screens in their lifetimes to significantly reduce the burden of cervical cancer (15). Where resources are available, the World Health Organization (WHO) thus recommends screening with HPV testing in a "screen-and-treat" strategy for women ages 30 to 49 years, and treating eligible HPV-positive women with timely cryotherapy (16).

One drawback of HPV testing is that only a small proportion of women who test positive for oncogenic HPV have, or would develop, precancer or invasive cervical cancer in the future, as the vast majority of infections clear spontaneously within one year (17). The high prevalence of oncogenic HPV infections coupled with the relatively low prevalence of precursor leads to a high "false positive rate" with current HPV DNA testing. Consequently, potentially high rates of overtreatment and its associated economic costs may burden health care systems in low-resource settings.
settings. For countries with sufficient resources to implement a sequence of tests, the WHO recommends that women with positive HPV test results may receive a triage test such as visual inspection with acetic acid (VIA; ref 16), with treatment provided only to women who also test positive on the triage test. Women who are HPV-positive but VIA-negative are recommended for rescreening in one year. Although there are few studies that have evaluated the diagnostic accuracy or health outcomes associated with HPV testing followed by VIA triage, countries in the early stages of implementing HPV-based screening are employing this strategy (18).

As cervical cancer screening programs are implemented and scaled in low-resource settings, decision-makers need information on the long-term health and economic consequences of screening algorithms to develop evidence-based guidelines. Our objective was to determine the cost-effectiveness of VIA triage for HPV-positive women in resource-limited settings with different epidemiologic profiles.

Materials and Methods

Analytic overview

We used an existing individual-based Monte Carlo simulation model of the natural history of HPV and cervical cancer to estimate the lifetime health and economic outcomes associated with screening with either careHPV testing alone or careHPV testing followed by VIA triage of HPV-positive women. The model was calibrated to epidemiologic data from India, Nicaragua, and Uganda (19). Test performance for careHPV and cost data were drawn from the START-UP multisite demonstration project conducted in India (Hyderabad), Nicaragua (Masaya Province), and Uganda (Kampala); a fourth site in India was not included in this evaluation (refs 7, 20; the model parameterization process for each setting, including calibration and costing data, is available at: http://www.sciencedirect.com/science/article/pii/S240585211500004X). Model-projected outcomes included health benefits, in terms of reductions in lifetime risk of cervical cancer and gains in life expectancy, and lifetime costs [in 2011 international dollars (I$)]. Cost-effectiveness ratios were expressed using incremental cost-effectiveness ratios (ICERs), defined as the additional cost of a particular strategy divided by its additional health benefit, compared with the next most costly strategy. Dominated strategies (defined as more costly and less effective, or having higher ICERs than more effective options) were eliminated. While there is no universal criterion that defines a threshold cost-effectiveness ratio, we considered per capita GDP as a benchmark; an intervention with an ICER less than the country’s per-capita GDP would be "cost-effective," and less than three times per capita GDP would be "cost-effective" (21). Consistent with guidelines for cost-effectiveness analysis (22–24), we adopted a societal perspective, including costs irrespective of the payer, and discounted future costs and life-years at a rate of 3% per year to account for time preferences.

Mathematical simulation model

The natural history model of cervical carcinogenesis comprises mutually exclusive health states, including type-specific HPV infection status, grade of precancer [i.e., CIN grade 2 (CIN2) or CIN3], and stage of invasive cancer (19, 25). Individual girls enter the model at age 9 years with a healthy cervix and transition between health states on a monthly basis until death. Transition probabilities may vary by age, HPV type, duration of infection or precancerous lesion status, and prior HPV infection. Cancer detection can occur through symptoms or via screening. Death from all-cause mortality can occur from any health state, and excess stage-dependent mortality can occur from cervical cancer after its onset. The model tracks disease progression and regression, clinical events, and economic outcomes over the lifetime for each individual woman, which are then aggregated for analysis. The model parameterization process, including calibration and model fit to epidemiologic data, has been described previously (19, 25–27). Briefly, we established baseline parameter values for the natural history component of the model using longitudinal data from a variety of settings, including age- and type-specific HPV incidence data and time-dependent rates of HPV clearance and progression by genotype (17, 28–31). To reflect heterogeneity in age- and type-specific HPV incidence between settings, as well as natural immunity following initial infection and uncertainty in progression and regression of precancer, we set plausible ranges around these input parameter values. Repeated model simulations in the absence of any intervention selected a single random value from the plausible range for each uncertain parameter, creating a unique natural history input parameter set. We then computed a goodness-of-fit score by summing the log-likelihood of model-projected outcomes for each unique parameter set to represent the quality of fit to country-specific epidemiologic data on age-specific HPV prevalence and cancer incidence (i.e., calibration targets). For each country, we selected the top 50 input parameter sets that produced good fit to the epidemiologic data to use in analyses as a form of probabilistic sensitivity analysis (19, 25, 27, 32). We report results as the mean of outcomes across these top 50 parameter sets.

Strategies

We assumed screening took place once in a woman’s lifetime at age 35 years or three times in a lifetime at ages 30, 35, and 40 years, with 80% coverage of the target population. We compared the following strategies, which are outlined in Figs. 1 and 2: (i) screening with 2-visit HPV testing (hereafter referred to as "HPV alone"), in which a provider administered the careHPV test at an initial clinic visit; women who complied with recommended follow-up returned for a second visit to receive results and, if HPV-positive and eligible, immediate cryotherapy (Fig. 1), and (ii) screening with 2-visit HPV testing at the clinic with VIA triage for HPV-positive women at the subsequent results visit (referred to as "HPV-VIA"), followed by same-day cryotherapy for eligible women who were both HPV-positive and VIA-positive (Fig. 2). In the HPV-VIA strategy, women who were HPV-positive but VIA-negative in a given screening episode were assumed to be referred to repeat screening with careHPV in one year; we assumed 80% of women complied with follow-up screening, with HPV-positive women sent to cryotherapy (if eligible) or to further diagnostic testing (if ineligible for immediate cryotherapy) and HPV-negative women returning to routine screening intervals. For both the HPV alone and HPV-VIA strategies, we assumed that all eligible women complied with the referral to same-day cryotherapy, and that women who were ineligible for cryotherapy were referred to colposcopy and, if necessary, further treatment for women with a histologic diagnosis of cervical intraepithelial neoplasia grade 1 or more severe (CIN1+), with compliance rates of 85% for each clinical contact after screening (i.e., visits for receiving screening results, colposcopy, and treatment following colposcopy). The test performance of careHPV was based on the
The performance of VIA in known HPV-positive women was not evaluated in START-UP. Therefore, sensitivity and specificity of VIA as a triage test for HPV-positive women (Table 1) were informed from the published literature. To bias the analysis in favor of the strategy of interest, we optimistically assumed that VIA sensitivity to detect cervical intraepithelial neoplasia grade 2 or more severe diagnoses (CIN2+) was 0.70 in women known to be HPV-positive. On the basis of the available literature, we assumed that VIA specificity was 0.85. Model input parameters are summarized in Table 2.

Cost data

Cost data have been published elsewhere (19, 20) but are summarized in Table 2. Direct medical costs of screening, diagnosis, and treatment of precancerous lesions were drawn from the START-UP study sites, and included staff time, clinical supplies, drugs, clinical equipment, laboratory staff time, laboratory supplies, and laboratory equipment. We converted local currency units to 2011 $, a hypothetical currency that provides a means of translating and comparing costs among countries, taking into account differences in purchasing power. We assumed the careHPV test kit was a tradable good valued at US$5 per test. Transportation costs and the cost of women’s time spent traveling to, waiting for, and receiving care were dependent upon the facility level and were derived from START-UP data and the published literature, as described previously (7, 20, 26, 33, 34). With the HPV-VIA strategy, women who tested HPV-positive incurred the direct medical costs associated with the VIA test, but we assumed that women’s time spent waiting for and receiving VIA (following receipt of HPV results) was minimal. Thus, women did not incur additional time costs associated with triage testing, but women who screened positive on VIA in the HPV-VIA strategy or positive on the HPV alone strategy did incur additional waiting and procedure time for cryotherapy. Costs associated with cancer care by stage included direct medical costs, women’s time costs, and transportation costs.

Figure 1.
Screening algorithm for the 2-visit HPV (HPV alone) strategy. We assumed screening took place either once in a woman’s lifetime at age 35 or three times in a lifetime at ages 30, 35, and 40 years, with screening coverage of the target population at 80%. In the HPV-alone strategy, a provider administered the careHPV test at an initial clinic visit. Women who complied with recommended follow-up returned for a second visit to receive results and, if HPV-positive and eligible, same-day cryotherapy. We assumed that all eligible women complied with the referral to same-day cryotherapy, and that women who were ineligible for cryotherapy were referred to colposcopy and, if necessary, further treatment for women with a histologic diagnosis of CIN1+. Each clinical contact for receiving results, colposcopy, or treatment (for women ineligible for cryotherapy) was associated with compliance rates of 85%.
Scenario analysis

To explore the impact of uncertainty in cost, test performance, and treatment parameters, we evaluated the following scenarios: (i) alternative sensitivity/specificity pairs of VIA performance in HPV-positive women; (ii) a lower compliance rate per visit; (iii) HPV self-collection (as opposed to provider collection) at the clinic; (iv) decreased direct medical costs of cryotherapy; (v) elimination of the direct medical cost of VIA triage test in HPV-positive women; (vi) elimination of repeat HPV testing in 1 year for HPV-positive VIA-negative women; (vii) simultaneously decreased eligibility for same-day cryotherapy and increased direct medical and women’s time costs for treatment of ineligible women (i.e., cryotherapy following histological confirmation in India; LEEP procedures in Nicaragua and Uganda; ref. 35). To derive alternative sensitivity/specificity pairs for VIA performance in HPV-positive women, we considered the inherent tradeoff between sensitivity and specificity by computing Youden J index values (sensitivity + specificity – 1). Assuming the highest Youden J index value suggested by the literature on VIA triage was a ceiling (36), we derived sensitivity/specificity pairs with Youden J index values between this maximum index and indices found in the remaining studies identified by our literature review. The following pairs were selected because they also explore less optimistic sensitivity values than the base case, while also varying specificity across the reasonable ranges suggested by the literature: 0.70/0.75; 0.60/0.85; 0.50/0.90.

Results

Reduction in cervical cancer risk

Reduction in cervical cancer risk is presented, for each country, in Table 3. In all three countries, HPV alone reduced the lifetime risk of cervical cancer more than HPV-VIA, as more women with CIN2+ and HPV infections destined to progress to CIN2+
Table 1. Literature review on the performance of HPV DNA testing with VIA triage

<table>
<thead>
<tr>
<th>Study (setting)</th>
<th>Performance of sequential HPV, VIA testing system</th>
<th>Sensitivity (95% CI)</th>
<th>Specificity (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Joshi et al. (India; ref. 43)</td>
<td>0.80 (0.67–0.90)</td>
<td>0.96 (0.95–0.97)</td>
<td></td>
</tr>
<tr>
<td>Kamal et al. (Egypt; ref. 44)</td>
<td>0.59 (CIN2), 0.75 (CIN3)</td>
<td>0.98 (CIN2), 0.99 (CIN3)</td>
<td></td>
</tr>
<tr>
<td>Tebeu et al. (Cameroon; ref. 38)</td>
<td>0.33 (0.15–0.58)</td>
<td>0.97 (0.95–0.98)</td>
<td></td>
</tr>
<tr>
<td>Performance of VIA in HPV-positive women</td>
<td>0.25 (0.07–0.59)</td>
<td>0.74 (0.64–0.82)</td>
<td></td>
</tr>
<tr>
<td>Bignon et al. (Cameroon; ref. 37)</td>
<td>0.67 (0.30–0.90)</td>
<td>0.86 (0.77–0.92)</td>
<td></td>
</tr>
<tr>
<td>Catarino et al. (Madagascar; ref. 36)</td>
<td>0.36 (0.15–0.64)</td>
<td>0.87 (0.79–0.95)</td>
<td></td>
</tr>
<tr>
<td>Muwonge et al. (India; ref. 39)</td>
<td>0.82 (0.77–0.86)</td>
<td>0.87 (0.85–0.90)</td>
<td></td>
</tr>
<tr>
<td>Qiao et al. (China; ref. 45)</td>
<td>0.46 (0.37–0.56)</td>
<td>0.87 (0.85–0.90)</td>
<td></td>
</tr>
</tbody>
</table>

Model inputs for performance of VIA in HPV-positive women

<table>
<thead>
<tr>
<th>Sensitivity/specificity</th>
<th>0.70/0.85</th>
</tr>
</thead>
<tbody>
<tr>
<td>Scenario analysis</td>
<td>0.70/0.75, 0.60/0.95, 0.85/0.90, 0.90/0.90</td>
</tr>
</tbody>
</table>

NOTE: The table presents data stratified on whether the reported test performance describes the testing system (i.e., HPV testing followed by VIA) or the performance of VIA in HPV-positive women.

The model inputs reflect the performance of VIA in care-HPV-positive women, with HPV positivity determined by site-specific START-UP care HPV test performance (provider or self-collection; see Table 2). Because the base case test performance parameters assumed optimistically high VIA sensitivity, we explored alternative combinations of sensitivity and specificity in scenario analyses. To reflect the inherent tradeoff between sensitivity and specificity, we assumed the study with the highest value of Youden J index (sensitivity + specificity – 1; Catarino et al.; ref. 36) represented a maximum Youden J index for VIA performance in HPV-positive women. We then explored several sensitivity and specificity pairs with Youden J index values between the maximum index and the indices found in the remaining studies.

received treatment; this finding held true whether screening occurred once or three times in a woman's lifetime. HPV alone once in a lifetime at age 35 years reduced cancer risk by 24.2% (India), 27.2% (Nicaragua), and 28.5% (Uganda). Screening three times in a lifetime at age 35 years reduced cancer risk by 27.0% (India), 24.2% (Nicaragua), and 28.5% (Uganda). Screening once in a lifetime with HPV-VIA cost I$770 per YLS, while screening three times in a lifetime with HPV alone was the most effective strategy considered and cost I$840 per YLS. Thus, screening three times in a lifetime with either HPV alone or HPV-VIA would be considered “very cost-effective” in India, with ICERs considerably less than India’s per capita GDP of I$5,750; while the ICER for HPV-VIA was slightly lower (i.e., more attractive) than for HPV alone, HPV alone reduced cancer risk by an additional 4.2%.

Unlike India, where HPV-VIA was less costly than HPV alone, the HPV-VIA strategy was both more costly and less effective than (i.e., dominated by) HPV alone in Nicaragua. Because cancer incidence and the cost of cancer treatment are high in Nicaragua, HPV-VIA was associated with higher costs than HPV alone due to the cost of missing HPV infections and precancers that will eventually progress to cancer. We found that screening with HPV testing alone once in a lifetime was cost-saving, while HPV testing alone three times in a lifetime cost I$200 per YLS, well below Nicaragua’s per capita GDP of I$4,960.

In Uganda, as in Nicaragua, HPV-VIA was more costly and less effective than (i.e., dominated by) HPV testing alone, whether screening occurred once or three times in a lifetime. Screening once in a lifetime with HPV alone cost I$130 per YLS, while screening three times in a lifetime with HPV alone cost I$410 per YLS. Both strategies with HPV alone would be considered "very cost-effective" in Uganda, with ICERs well below the per capita GDP of I$1,690.

Scenario analysis

Cost-effectiveness results for scenario analyses in India are presented in Table 4: results from scenario analyses in Nicaragua and Uganda, where HPV alone consistently dominated HPV-VIA as baseline assumptions were varied, are presented in Supplementary Tables S1 and S2.

In India (Table 4), ICERs were fairly stable as VIA test sensitivity and specificity were varied relative to baseline assumptions. When VIA specificity was reduced to 0.75 (base case: 0.85) while sensitivity was held constant, ICERs remained stable as both the lifetime costs and life expectancy associated with HPV-VIA increased slightly (due to more women receiving immediate treatment with cryotherapy). When VIA sensitivity was reduced to 0.60 (base case: 0.70) and specificity held constant, screening three times in a lifetime with HPV-VIA was no longer an efficient strategy; the ICERs associated with HPV alone declined from I$460 per YLS to I$400 per YLS for once in a lifetime screening, and from I$840 per YLS to I$780 per YLS for screening three times in a lifetime. When VIA sensitivity was further reduced to 0.50 (base case: 0.70) and specificity increased to 0.90 (base case:...
The prevalence of CIN1 among women with HPV infections in the START-UP studies.

LEEP at a secondary facility. In Uganda, we assumed that, upon a histologic diagnosis of CIN1, women received cryotherapy at a secondary facility; a histologic and availability of and preferences for treatment options. In India, we assumed that, upon a histologic diagnosis of CIN1, CIN2, or CIN3, women received

Eligibility for cryotherapy (26)

No lesion or CIN1

100% 100% 100%

CIN2

85% 85% 85%

CIN3

75% 75% 75%

Cancer

10% 10% 10%

Effectiveness of cryotherapy (26, 40, 47) 92% 92% 92%

Effectiveness of cryotherapy/LEEP following colposcopy (26, 47) 96% 96% 96%

Direct medical costs by procedure (7, 20)

careHPV (provider collection)

9.24 15.61 8.78

careHPV (self-collection at the clinic)

8.90 13.48 8.48

VIA

3.55 9.61 2.90

Colposcopy

9.86 15.25 7.08

Colposcopy and biopsy

31.06 39.48 32.90

Cryotherapy

38.13 33.04 13.49

LEEP

NA 133.64 139.54

Cytopathy (follow-up post-treatment)

15.15 13.71 12.25

Direct nonmedical costs

Transportation (round-trip, clinic; refs. 26, 33, 34)

0.08 0.69 4.46

Transportation (round-trip, secondary facility; refs. 26, 33, 34)

15.29 2.75 10.87

Women’s time (per hour; ref. 48)

1.14 1.41 0.68

Treatment of local cervical cancer (FIGO stages Ia–Ia; refs. 26, 33, 34)

1.621 3.322 888

Treatment of regional/distant cervical cancer (FIGO stages IIA–IVb; refs. 26, 33, 34)

2.652 4.268 1.776

a FIGO, International Federation of Gynecology and Obstetrics; LEEP, loop electrosurgical excision procedure.

b We considered complication rates for cryotherapy or LEEP, as treatment complications were very rare in the START-UP demonstration projects.

f All cervical cancer costs presented include the value of women’s time spent pursuing care and transportation to health facilities.

The proportion of colposcopies that were accompanied by a biopsy was drawn from START-UP data as follows: 93.1% (India); 95.6% (Uganda); and 99.5% (Nicaragua), in the absence of data from actual practice in low-resource settings.

m All costs are in 2011 international dollars (I$). In the START-UP study, procedures were performed at secondary or tertiary facilities, and costs may over- or under-estimate costs at primary health facilities due to differences in volume of procedures and overhead costs. Further details on costs are published elsewhere (19).

p This includes the cost of the careHPV test, which was assumed to be I$5. Self-collection was assumed to occur at the clinic, and the difference in costs is attributable to personnel time.

q The proportion of colposcopies that were accompanied by a biopsy was drawn from START-UP data as follows: 93.1% (India); 95.6% (Uganda); and 99.5% (Nicaragua), in the absence of data from actual practice in low-resource settings.

r We considered complication rates for cryotherapy or LEEP, as treatment complications were very rare in the START-UP demonstration projects.

s Provisions for follow-up after treatment varied by country, and are published elsewhere (19).

Table 2. Baseline values for model parameters

<table>
<thead>
<tr>
<th>Variable (Reference)</th>
<th>India</th>
<th>Nicaragua</th>
<th>Uganda</th>
</tr>
</thead>
<tbody>
<tr>
<td>Population coverage of screening program</td>
<td>80%</td>
<td>80%</td>
<td>80%</td>
</tr>
<tr>
<td>Compliance rate per visit</td>
<td>85%</td>
<td>85%</td>
<td>85%</td>
</tr>
<tr>
<td>Proportion of eligible women receiving immediate cryotherapy following positive careHPV result</td>
<td>100%</td>
<td>100%</td>
<td>100%</td>
</tr>
<tr>
<td>careHPV (provider collection) sensitivity/specificity for CIN2+ (5)</td>
<td>0.89/0.95</td>
<td>0.79/0.89</td>
<td>0.89/0.80</td>
</tr>
<tr>
<td>careHPV (self-collection) sensitivity/specificity for CIN2+ (5)</td>
<td>0.75/0.95</td>
<td>0.67/0.87</td>
<td>0.76/0.80</td>
</tr>
<tr>
<td>VIA sensitivity/specificity for CIN2+ in HPV-positive women (36, 39)</td>
<td>0.70/0.85</td>
<td>0.70/0.85</td>
<td>0.70/0.85</td>
</tr>
<tr>
<td>Test sensitivity/specificity for CIN1+, colposcopy</td>
<td>0.50/0.96</td>
<td>0.95/0.68</td>
<td>0.95/0.51</td>
</tr>
<tr>
<td>Eligibility for cryotherapy (26)</td>
<td>100%</td>
<td>100%</td>
<td>100%</td>
</tr>
<tr>
<td>No lesion or CIN1</td>
<td>100%</td>
<td>100%</td>
<td>100%</td>
</tr>
<tr>
<td>CIN2</td>
<td>85%</td>
<td>85%</td>
<td>85%</td>
</tr>
<tr>
<td>CIN3</td>
<td>75%</td>
<td>75%</td>
<td>75%</td>
</tr>
<tr>
<td>Cancer</td>
<td>10%</td>
<td>10%</td>
<td>10%</td>
</tr>
<tr>
<td>Effectiveness of cryotherapy</td>
<td>92%</td>
<td>92%</td>
<td>92%</td>
</tr>
<tr>
<td>Effectiveness of cryotherapy/LEEP following colposcopy</td>
<td>96%</td>
<td>96%</td>
<td>96%</td>
</tr>
<tr>
<td>Direct medical costs by procedure (7, 20)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>careHPV (provider collection)</td>
<td>9.24</td>
<td>15.61</td>
<td>8.78</td>
</tr>
<tr>
<td>careHPV (self-collection at the clinic)</td>
<td>8.90</td>
<td>13.48</td>
<td>8.48</td>
</tr>
<tr>
<td>VIA</td>
<td>3.55</td>
<td>9.61</td>
<td>2.90</td>
</tr>
<tr>
<td>Colposcopy</td>
<td>9.86</td>
<td>15.25</td>
<td>7.08</td>
</tr>
<tr>
<td>Colposcopy and biopsy</td>
<td>31.06</td>
<td>39.48</td>
<td>32.90</td>
</tr>
<tr>
<td>Cryotherapy</td>
<td>38.13</td>
<td>33.04</td>
<td>13.49</td>
</tr>
<tr>
<td>LEEP</td>
<td>NA</td>
<td>133.64</td>
<td>139.54</td>
</tr>
<tr>
<td>Cytopathy (follow-up post-treatment)</td>
<td>15.15</td>
<td>13.71</td>
<td>12.25</td>
</tr>
<tr>
<td>Direct nonmedical costs</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Transportation (round-trip, clinic; refs. 26, 33, 34)</td>
<td>0.08</td>
<td>0.69</td>
<td>4.46</td>
</tr>
<tr>
<td>Transportation (round-trip, secondary facility; refs. 26, 33, 34)</td>
<td>15.29</td>
<td>2.75</td>
<td>10.87</td>
</tr>
<tr>
<td>Women’s time (per hour; ref. 48)</td>
<td>1.14</td>
<td>1.41</td>
<td>0.68</td>
</tr>
<tr>
<td>Treatment of local cervical cancer (FIGO stages Ia–Ia; refs. 26, 33, 34)</td>
<td>1.621</td>
<td>3.322</td>
<td>888</td>
</tr>
<tr>
<td>Treatment of regional/distant cervical cancer (FIGO stages IIA–IVb; refs. 26, 33, 34)</td>
<td>2.652</td>
<td>4.268</td>
<td>1.776</td>
</tr>
</tbody>
</table>

PROSTATE CANCER TRENDS AND OUTCOMES FOR HISPANIC/LATINO MEN: COMPARISONS TO NONHISPANIC WHITE MEN ON THE ATTACHMENT TO 5- AND 10-YEAR SURVIVAL FOLLOW-UP

When we assumed that HPV test sensitivity was reduced due to self-collection (base case: provider collection) at the clinic, HPV-VIA remained less costly and also less effective than HPV alone in India, but had a slightly higher ICER than HPV alone, and was thus not an efficient strategy.
Cancer incidence reduction for each strategy reflects percentage reduction in lifetime risk of cervical cancer compared with no screening. Cancer incidence reduction, discounted lifetime cost per woman, and discounted life expectancy represent the mean values across 50 input parameter sets. Dominated strategies are defined as those that are either more costly and less effective or have higher ICERs than more effective options.

### Discussion

This study represents one of the first cost-effectiveness analyses of HPV testing followed by visual triage in low-resource settings. We found that using VIA as a triage test to determine which HPV-positive women receive immediate treatment with cryotherapy is less effective at reducing cervical cancer than sending all HPV-positive women to treatment in India, Nicaragua, and Uganda. We found that HPV with VIA triage was consistently more costly and less effective than (i.e., dominated by) HPV alone in Nicaragua and Uganda, due to the costs of repeating HPV screen-and-treat in one year and the costs of missing some precancers that are destined to progress. In India, where the burden of HPV and cervical cancer is lower and the specificity of HPV testing in the START-UP study was high, HPV-VIA was an efficient strategy under baseline assumptions. Even in India, however, screening with HPV alone was a more effective strategy, and very cost-effective with an ICER well below India’s per capita GDP. In both Nicaragua and Uganda, findings from scenario analyses indicated that HPV alone robustly dominated HPV-VIA whether we assumed altered VIA test performance, reduced visit compliance, HPV self-collection at the clinic, reduced direct medical costs of cryotherapy, elimination of the additional cost of the VIA triage test, or elimination of repeat HPV testing at one year for HPV-positive/VIA-negative women. Similar scenario analyses in India found that while both the HPV-VIA and HPV alone strategies would be very cost-effective if specificity of VIA was reduced or the direct medical cost of VIA was eliminated, HPV alone consistently remained the more effective strategy. When VIA test sensitivity was reduced or when the direct medical cost of cryotherapy was reduced by 50%, HPV-VIA three times in a lifetime was no longer an efficient strategy. Under circumstances when visit compliance was reduced, HPV specimens were self-collected, or when there was no repeat HPV testing in one year for HPV-positive/VIA-negative women, HPV-VIA was not an efficient strategy in India.

There were several limitations to this analysis. Data on the performance of VIA in HPV-positive women were limited, but indicate its high variability based on setting. As the START-UP demonstration projects did not evaluate VIA as a triage test for HPV-positive women, we based VIA performance characteristics on available literature. Our review of the literature found that VIA sensitivity to detect CIN2+ in HPV-positive women was as low as 25% in Cameroon (37, 38). The highest VIA sensitivity in HPV-positive women was 82% in a study from India (39), but this was considerably higher than the next highest sensitivity rate of 67% in Madagascar (36). We set VIA sensitivity in HPV-positive women at

<table>
<thead>
<tr>
<th>Strategya</th>
<th>Reduction in cervical cancer risk, %c</th>
<th>Discounted lifetime cost per womand</th>
<th>Discounted life expectancy, meand</th>
<th>ICER ($/YLS), meand</th>
</tr>
</thead>
<tbody>
<tr>
<td>India (GDP per capita: $5,750)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No screening</td>
<td>—</td>
<td>8.87</td>
<td>27.78559</td>
<td>—</td>
</tr>
<tr>
<td>HPV-VIA 1x</td>
<td>24.2</td>
<td>10.09</td>
<td>27.80300</td>
<td>$240</td>
</tr>
<tr>
<td>HPV 1x</td>
<td>27.0</td>
<td>13.66</td>
<td>27.80429</td>
<td>$460</td>
</tr>
<tr>
<td>HPV 3x</td>
<td>44.2</td>
<td>23.48</td>
<td>27.81695</td>
<td>$770</td>
</tr>
<tr>
<td>HPV-VIA 3x</td>
<td>48.4</td>
<td>25.23</td>
<td>27.81903</td>
<td>$840</td>
</tr>
<tr>
<td>Nicaragua (GDP per capita: $4,960)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No screening</td>
<td>—</td>
<td>42.67</td>
<td>25.58210</td>
<td>—</td>
</tr>
<tr>
<td>HPV 1x</td>
<td>29.8</td>
<td>40.67</td>
<td>28.64935</td>
<td>CS</td>
</tr>
<tr>
<td>HPV-VIA 1x</td>
<td>27.2</td>
<td>42.12</td>
<td>28.64933</td>
<td>Dom</td>
</tr>
<tr>
<td>HPV 3x</td>
<td>51.3</td>
<td>51.15</td>
<td>28.70094</td>
<td>$200</td>
</tr>
<tr>
<td>HPV-VIA 3x</td>
<td>48.6</td>
<td>53.24</td>
<td>28.69458</td>
<td>Dom</td>
</tr>
<tr>
<td>Uganda (GDP per capita: $1,690)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No screening</td>
<td>—</td>
<td>12.42</td>
<td>25.20221</td>
<td>—</td>
</tr>
<tr>
<td>HPV 1x</td>
<td>30.5</td>
<td>20.08</td>
<td>25.26293</td>
<td>$130</td>
</tr>
<tr>
<td>HPV-VIA 1x</td>
<td>28.5</td>
<td>20.54</td>
<td>25.25940</td>
<td>Dom</td>
</tr>
<tr>
<td>HPV 3x</td>
<td>52.3</td>
<td>38.37</td>
<td>25.30774</td>
<td>$410</td>
</tr>
<tr>
<td>HPV-VIA 3x</td>
<td>50.0</td>
<td>39.04</td>
<td>25.30357</td>
<td>Dom</td>
</tr>
</tbody>
</table>

aDom, dominated strategy; 1x, screening once in a lifetime at age 35; 3x, screening three times in a lifetime at ages 30, 35, and 40 years.
bScreening strategies are listed in order of increasing cost.
cCancer incidence reduction for each strategy reflects percentage reduction in lifetime risk of cervical cancer compared with no screening. Cancer incidence reduction, discounted lifetime cost per woman, and discounted life expectancy represent the mean values across 50 input parameter sets. Dominated strategies are defined as those that are either more costly and less effective or have higher ICERs than more effective options.
dMedical cost of the VIA triage test, the ICERs associated with HPV-VIA in India fell dramatically as women with persistent HPV infections did not treat in one year and the costs of missing some precancers that are destined to progress. In India, where the burden of HPV and cervical cancer is lower and the specificity of HPV testing in the START-UP study was high, HPV-VIA was an efficient strategy under baseline assumptions. Even in India, however, screening with HPV alone was a more effective strategy, and very cost-effective with an ICER well below India’s per capita GDP. In both Nicaragua and Uganda, findings from scenario analyses indicated that HPV alone robustly dominated HPV-VIA whether we assumed altered VIA test performance, reduced visit compliance, HPV self-collection at the clinic, reduced direct medical costs of cryotherapy, elimination of the additional cost of the VIA triage test, or elimination of repeat HPV testing at one year for HPV-positive/VIA-negative women. Similar scenario analyses in India found that while both the HPV-VIA and HPV alone strategies would be very cost-effective if specificity of VIA was reduced or the direct medical cost of VIA was eliminated, HPV alone consistently remained the more effective strategy. When VIA test sensitivity was reduced or when the direct medical cost of cryotherapy was reduced by 50%, HPV-VIA three times in a lifetime was no longer an efficient strategy. Under circumstances when visit compliance was reduced, HPV specimens were self-collected, or when there was no repeat HPV testing in one year for HPV-positive/VIA-negative women, HPV-VIA was not an efficient strategy in India.

There were several limitations to this analysis. Data on the performance of VIA in HPV-positive women were limited, but indicate its high variability based on setting. As the START-UP demonstration projects did not evaluate VIA as a triage test for HPV-positive women, we based VIA performance characteristics on available literature. Our review of the literature found that VIA sensitivity to detect CIN2+ in HPV-positive women was as low as 25% in Cameroon (37, 38). The highest VIA sensitivity in HPV-positive women was 82% in a study from India (39), but this was considerably higher than the next highest sensitivity rate of 67% in Madagascar (36). We set VIA sensitivity in HPV-positive women at

As we reduced the direct medical cost of cryotherapy by 50% in India, the ICER associated with HPV-VIA once in a lifetime and HPV alone once or three times in a lifetime remained stable, but HPV-VIA three times in a lifetime was inefficient (i.e., was less effective and had a higher ICER) than HPV-VIA. When we assumed there would be no repeat HPV testing in one year for HPV-positive/VIA-negative women, HPV-VIA was no longer an efficient strategy, and the ICERs for HPV-VIA in India fell dramatically as women with persistent HPV infections did not treat in one year and the costs of missing some precancers that are destined to progress. In India, where the burden of HPV and cervical cancer is lower and the specificity of HPV testing in the START-UP study was high, HPV-VIA was an efficient strategy under baseline assumptions. Even in India, however, screening with HPV alone was a more effective strategy, and very cost-effective with an ICER well below India’s per capita GDP. In both Nicaragua and Uganda, findings from scenario analyses indicated that HPV alone robustly dominated HPV-VIA whether we assumed altered VIA test performance, reduced visit compliance, HPV self-collection at the clinic, reduced direct medical costs of cryotherapy, elimination of the additional cost of the VIA triage test, or elimination of repeat HPV testing at one year for HPV-positive/VIA-negative women. Similar scenario analyses in India found that while both the HPV-VIA and HPV alone strategies would be very cost-effective if specificity of VIA was reduced or the direct medical cost of VIA was eliminated, HPV alone consistently remained the more effective strategy. When VIA test sensitivity was reduced or when the direct medical cost of cryotherapy was reduced by 50%, HPV-VIA three times in a lifetime was no longer an efficient strategy. Under circumstances when visit compliance was reduced, HPV specimens were self-collected, or when there was no repeat HPV testing in one year for HPV-positive/VIA-negative women, HPV-VIA was not an efficient strategy in India.

There were several limitations to this analysis. Data on the performance of VIA in HPV-positive women were limited, but indicate its high variability based on setting. As the START-UP demonstration projects did not evaluate VIA as a triage test for HPV-positive women, we based VIA performance characteristics on available literature. Our review of the literature found that VIA sensitivity to detect CIN2+ in HPV-positive women was as low as 25% in Cameroon (37, 38). The highest VIA sensitivity in HPV-positive women was 82% in a study from India (39), but this was considerably higher than the next highest sensitivity rate of 67% in Madagascar (36). We set VIA sensitivity in HPV-positive women at...
70% to observe outcomes under a scenario of high performance. Even under these optimal conditions, HPV with VIA triage was less effective than HPV testing alone in all three countries, and was only a potentially efficient strategy in India.

While the START-UP demonstration projects did not evaluate VIA as a triage strategy, we analyzed the site-specific data to determine the proportion of care HPV-positive women with CIN2+ that were also positive on VIA (i.e., the proportion that might theoretically be referred to cryotherapy with VIA triage of HPV-positive women). We found that, at the START-UP sites, 56% (57%), 63% (64%), and 71% (76%) of women with CIN2+ who were HPV-positive with provider (self)-collection in Hyderabad, Nicaragua, and Uganda, respectively, also screened positive on VIA. These data support our assertion that VIA sensitivity to detect CIN2+ in HPV-positive women is indeed optimistic at 70%.

### Table 4. Scenario analyses for 2-visit HPV alone versus 2-visit HPV-VIA in India (GDP per capita: I$5,750)

<table>
<thead>
<tr>
<th>Strategyb</th>
<th>Cancer incidence reduction, %c</th>
<th>Discounted lifetime cost per womanc</th>
<th>Discounted life expectancy, meana</th>
<th>ICER (I$/YLS), meana</th>
</tr>
</thead>
<tbody>
<tr>
<td>Base case</td>
<td>—</td>
<td>8.87</td>
<td>27.8539</td>
<td>—</td>
</tr>
<tr>
<td>HPV-VIA 1x</td>
<td>24.2</td>
<td>13.09</td>
<td>27.80300</td>
<td>240</td>
</tr>
<tr>
<td>HPV 1x</td>
<td>27.0</td>
<td>13.66</td>
<td>27.80425</td>
<td>460</td>
</tr>
<tr>
<td>HPV-VIA 3x</td>
<td>44.2</td>
<td>23.48</td>
<td>27.81695</td>
<td>770</td>
</tr>
<tr>
<td>HPV 3x</td>
<td>48.4</td>
<td>25.23</td>
<td>27.81903</td>
<td>840</td>
</tr>
</tbody>
</table>

VIA test sensitivity/specificity in HPV-positive women: 0.70/0.75 (Youden J index: 0.45)

| No screening | 8.87 | 27.8539 | — |
| HPV-VIA 1x   | 24.6 | 13.96   | 27.80376 | 240 |
| HPV 1x       | 27.0 | 13.66   | 27.80425 | 460 |
| HPV-VIA 3x   | 44.7 | 23.71   | 27.81717 | 780 |
| HPV 3x       | 48.4 | 25.23   | 27.81903 | 820 |

VIA test sensitivity/specificity in HPV-positive women: 0.60/0.85 (Youden J index: 0.45)

| No screening | 8.87 | 27.8539 | — |
| HPV-VIA 1x   | 24.0 | 13.10   | 27.80286 | 240 |
| HPV 1x       | 27.0 | 13.66   | 27.80425 | 400 |
| HPV-VIA 3x   | 43.9 | 23.50   | 27.81669 | Dom |
| HPV 3x       | 48.4 | 25.23   | 27.81903 | 780 |

VIA test sensitivity/specificity in HPV-positive women: 0.50/0.90 (Youden J index: 0.40)

| No screening | 8.87 | 27.8539 | — |
| HPV-VIA 1x   | 23.6 | 13.98   | 27.80257 | 250 |
| HPV 1x       | 27.0 | 13.66   | 27.80425 | 340 |
| HPV-VIA 3x   | 43.4 | 23.39   | 27.81630 | Dom |
| HPV 3x       | 48.4 | 25.23   | 27.81903 | 780 |

Compliance rate per visit: 60%

| No screening | 8.87 | 27.8539 | — |
| HPV-VIA 1x   | 16.1 | 13.23   | 27.79646 | Dom |
| HPV 1x       | 18.4 | 13.53   | 27.79769 | 380 |
| HPV-VIA 3x   | 34.8 | 22.87   | 27.80907 | Dom |
| HPV 3x       | 38.9 | 23.82   | 27.81149 | 750 |

| HPV self-collectiona | — | 8.87 | 27.8539 | — |
| HPV-VIA 1x          | 20.0 | 13.23 | 27.79987 | Dom |
| HPV 1x              | 23.9 | 13.75 | 27.80185 | 300 |
| HPV-VIA 3x          | 40.2 | 23.29 | 27.81381 | Dom |
| HPV 3x              | 45.7 | 24.98 | 27.81679 | 750 |

Direct medical cost of cryotherapy: reduced by 50%

| No screening | 8.87 | 27.8539 | — |
| HPV-VIA 1x   | 24.2 | 12.90   | 27.80300 | 250 |
| HPV 1x       | 27.0 | 13.27   | 27.80425 | 300 |
| HPV-VIA 3x   | 44.2 | 23.00   | 27.81695 | Dom |
| HPV 3x       | 48.4 | 24.25   | 27.81903 | 740 |

Direct medical cost of VIA: I$0

| No screening | 8.87 | 27.8539 | — |
| HPV-VIA 1x   | 24.2 | 13.01   | 27.80300 | 240 |
| HPV 1x       | 27.0 | 13.66   | 27.80425 | 520 |
| HPV-VIA 3x   | 44.2 | 23.29   | 27.81695 | 760 |
| HPV 3x       | 48.4 | 25.23   | 27.81903 | 930 |

No repeat HPV testing in 1 year for HPV+ VIA- women

| No screening | 8.87 | 27.8539 | — |
| HPV-VIA 1x   | 14.7 | 13.38   | 27.79671 | Dom |
| HPV 1x       | 27.0 | 13.66   | 27.80425 | 250 |
| HPV-VIA 3x   | 36.8 | 22.64   | 27.81208 | Dom |
| HPV 3x       | 48.4 | 25.23   | 27.81903 | 780 |

(Continued on the following page)
We did not consider the quality-of-life implications of rare adverse events associated with treatment, and we assumed only a small proportion of women (who were ineligible for cryotherapy and had histologically confirmed CIN2+ in Nicaragua; 20% of confirmed CIN2+ in Uganda) received LEEP. While cryotherapy is generally a safe procedure, LEEP may be accompanied by complications such as infection, bleeding, cervical stenosis, and risk of infertility, preterm birth (40, 41); the risk of these outcomes may be higher in low-resource settings, where LEEP is performed infrequently. Where the burden of HPV is high, even a slight risk of serious adverse events among the relatively small proportion of women referred to LEEP for CIN2+ may lead to a substantial number of cases at the population level, particularly if eligibility for cryotherapy is low. In our scenario analysis of reduced eligibility for same-day cryotherapy and increased costs of either LEEP (in Nicaragua and Uganda) or cryotherapy following histologic confirmation (in India, where LEEP was assumed to be unavailable), HPV alone three times in a lifetime remained the most effective strategy with an ICER below per capita GDP in all resource settings, countries will need to design screening algorithms based on many factors in addition to the cost-effectiveness profile of a screening strategy, including acceptability, feasibility, existing infrastructure, anticipated gains relative to competing healthcare priorities, and affordability. The chronic shortage of health care workers in low-resource settings is a potential barrier to scale-up of HPV-based screening programs that recommend treatment for all HPV-positive women. Furthermore, gas-based cryotherapy relies on consistent resupply of gas, which is expensive to transport and not always available. We found that HPV followed by VIA triage may reduce the number of cryotherapy procedures by approximately 34% to 50%, but due to the low sensitivity of VIA and imperfect follow-up of HPV-positive/VIA-negative women, there is a corresponding decline in health benefits as fewer women with persistent HPV infection and precancer receive treatment. In Nicaragua and Uganda, the cost savings associated with fewer cryotherapy procedures were outweighed by increased costs of cancer treatment. Our findings in all three countries also indicate that, when HPV-positive/VIA-negative women did not attend recommended follow-up at one year, the health benefits associated with screening were markedly reduced. In low-resource settings where clinic visits may require substantial time and travel over long distances, compliance with follow-up screening in one year’s time may be low, but the consequences of not receiving recommended follow-up may be serious for these women at high risk of precancer. Of note, both HPV alone and HPV-VIA may have less than the reported impact on cancer risk if cryotherapy is considerably less effective than we assume here.

While HPV testing alone may be a more effective and efficient strategy than HPV-VIA in many settings, the costs and feasibility of facilitating widespread access to cryotherapy in primary health centers may reduce the real-world effectiveness of this strategy. New treatment technologies may lessen the burden of treating all HPV-positive women, if feasibility and cost-effectiveness can be demonstrated. New ablative technologies currently undergoing testing are smaller, portable, and do not require gas. Thermal coagulation has been used as part of a “screen-and-treat” program in Malawi (42), and for treatment of HIV-infected women in India (43), with interim cure rates comparable with cryotherapy (40).

The World Health Organization recommends HPV testing for countries with sufficient resources (16). HPV testing with VIA triage has received consideration as a screening algorithm to reduce the costs and logistical demands of cryotherapy in low-resource settings. We found that HPV testing followed by VIA triage is not necessarily less costly than HPV testing alone in...
settings with a high burden of HPV and cervical cancer, despite reductions in the number of immediate cryotherapy procedures. In addition, HPV testing followed by VIA triage is less effective than HPV testing alone, as fewer women with precancer or HPV infections that would progress to precancer receive treatment, even with an optimistically sensitive VIA triage test. This analysis highlights the need for more accessible treatment options for women in low-resource settings with a high burden of HPV, only when treatment is widely available to HPV-positive women will an HPV screen-and-treat strategy be feasible. Our findings also demonstrate that, if program planners opt to use a triage strategy to reduce the number of women referred to treatment, there is a need for improved genotype restriction, biomarkers, and triage tests with better ability to predict cervical cancer risk that are also adaptable to low-resource settings. On the basis of current data on the performance of VIA as a triage test for HPV-positive women, this screening and triage algorithm is not likely to be cost-effective in settings with a high burden of cervical cancer.

Disclosure of Potential Conflicts of Interest

J. Jeronimo was the co-owner and Deputy Manager of Onco Prev International, a Peruvian company, from 2012 through March 2017. Onco Prev offers cervical cancer screening services. No potential conflicts of interest were disclosed by the other authors.

Disclaimer

The findings and conclusions contained within are those of the authors and do not necessarily reflect positions or policies of the Bill & Melinda Gates Foundation. The funders had no role in study design, data collection, analysis, and interpretation; preparation of the manuscript; or decision to submit the article for publication.

Authors’ Contributions

Conception and design: N.G. Campos, J. Jeronimo, V. Tsu, J.J. Kim
Development of methodology: N.G. Campos, J. Kim
Acquisition of data (provided animals, acquired and managed patients, provided facilities, etc.): N.G. Campos, J. Jeronimo, M. Mvundura
Analysis and interpretation of data (e.g., statistical analysis, biostatistics, computational analysis): N.G. Campos, J. Jeronimo, V. Tsu, P.E. Castle, M. Mvundura, J.J. Kim
Writing, review, and/or revision of the manuscript: N.G. Campos, J. Jeronimo, V. Tsu, P.E. Castle, M. Mvundura, J.J. Kim
Administrative, technical, or material support (i.e., reporting or organizing data, constructing databases): N.G. Campos
Study supervision: N.G. Campos, J.J. Kim

Acknowledgments

The authors thank all investigators and field workers that participated in the START-UP demonstration projects, and the cervical cancer modeling team at the Center for Health Decision Science, Harvard T.H. Chan School of Public Health, for their research contributions.

Grant Support

This work was based on research funded in part by the Bill & Melinda Gates Foundation OPP1053342. The costs of publication of this article were defrayed in part by the payment of page charges. This article must therefore be hereby marked advertisement in accordance with 18 U.S.C. Section 1734 solely to indicate this fact.

Received October 12, 2016; revised May 11, 2017; accepted July 5, 2017. Published online First July 14, 2017.

www.aacbjournals.org

Cancer Epidemiol Biomarkers Prev; 26(10) October 2017

References


Received October 12, 2016; revised May 11, 2017; accepted July 5, 2017. Published online First July 14, 2017.
Macroeconomics and Health. Geneva, Switzerland: World Health Organiza-
22. Jamison DT, Breman JG, Measham AR, Alleyne G, Claeson M, Evans DB,
An updated natural history model of cervical cancer: derivation of model
database: Incidence - SEER 18 Regs Research Data
County Attributes
gov/data/seerstat/nov2011/.
comparative and cost-effectiveness of HPV-based cervical cancer screening
28. Munoz N, Mendez F, Popos H, Molano M, van den Brule AJ, Ronderos M,
et al. Incidence, duration, and determinants of cervical human papillo-
mavirus infection in a cohort of Colombian women with normal cytologi-
et al. Rationale and design of a community-based double-blind random-
ized clinical trial of an HPV 16 and 18 vaccine in Guanacaste, Costa Rica.
Vaccine 2008;26:4795–808.
JG, et al. Cancer survival in Africa, Asia, and Central America: a populatio-
31. Surveillance Epidemiology and End Results (SEER) Program. SEER’Stat
Database: Incidence - SEER 18 Regs Research Data + Hurricane Katrina
Impacted Louisiana Cases Nov 2011 Sub (1973–2009 varying) – Linked to
gov/data/seerstat/nov2011/.
32. Goldhaber-Fiebert JD, Stout NK, Orteindahl J, Kuntz KM, Goldie SJ, Salomon
JA. Modeling human papillomavirus and cervical cancer in the United States
33. Goldie SJ, Gaffikin L, Goldhaber-Fiebert JD, Gordillo-Tobar A, Levin C,
Mahe C, et al. Cost-effectiveness of cervical cancer screening in five devel-
Health and economic impact of HPV 16/18 vaccination and cervical cancer
Treatability by cryotherapy in a screen-and-treat strategy. J Low Genit Tract
Hamme U, Ricardo-Gauthier D, et al. Smartphone use for cervical cancer
screening in low-resource countries: a pilot study conducted in Madagas-
37. Bigoni J, Gundur M, Tebeu PM, Bongoe A, Schafer S, Fokom-Domgou J,
et al. Cervical cancer screening in sub-Saharan Africa: a randomized trial of
VIA versus cytology for triage of HPV-positive women. Int J Cancer
2015;137:127–34.
Effectiveness of a two-stage strategy with HPV testing followed by visual
inspection with acetic acid for cervical cancer screening in a low-income
Evaluation of cytology and visual triage of human papillomavirus-positive
women in cervical cancer prevention in India. Int J Cancer 2014;134:
2902–9.
40. Sauvaget C, Muwonge R, Sankaranarayanan R. Meta-analysis of the effec-
tiveness of cryotherapy in the treatment of cervical intraepithelial neopla-
Systematic reviews and meta-analyses of benefits and harms of cryother-
rapy, LEEP, and cold knife conization to treat cervical intraepithelial
The use of thermo-coagulation as an alternative treatment modality in a 'screen
and treat' programme of cervical screening in rural Malawi. Int J Cancer
43. Joshi S, Sankaranarayanan R, Muwonge R, Kulkarni V, Somanathan T,
Divate U. Screening of cervical neoplasia in HIV-infected women in India.
44. Kamal EM, EL Sayed GA, EL Behery MM, EL Shennawy GA. HPV detection in
a self-collected vaginal swab combined with VIA for cervical cancer screen-
ing with correlation to histologically confirmed CIN. Arch Gynecol Obstet
cost strategies for triage of human papillomavirus DNA-positive women.
versus visual inspection with acetic acid among women treated previously
with cryotherapy in a low-resource setting. Int J Gynaecol Obstet 2010;111:
249–52.
47. Chirenje ZM, Rusakankiko S, Kirmundi I, Ngwalle EW, Makulta-Tlebere P,
Kagwa S, et al. Situation analysis for cervical cancer diagnosis and
management in east, central and southern African countries. Bull World
Health Organ 2001;79:127–32.
48. United Nations Development Programme. International Human Develop-
The Cost-Effectiveness of Visual Triage of Human Papillomavirus—Positive Women in Three Low- and Middle-Income Countries

Nicole G. Campos, Jose Jeronimo, Vivien Tsu, et al.


Updated version Access the most recent version of this article at: doi:10.1158/1055-9965.EPI-16-0787

Supplementary Material Access the most recent supplemental material at: http://cebp.aacrjournals.org/content/suppl/2017/07/14/1055-9965.EPI-16-0787.DC1

Cited articles This article cites 40 articles, 2 of which you can access for free at: http://cebp.aacrjournals.org/content/26/10/1500.full#ref-list-1

E-mail alerts Sign up to receive free email-alerts related to this article or journal.

Reprints and Subscriptions To order reprints of this article or to subscribe to the journal, contact the AACR Publications Department at pubs@aacr.org.

Permissions To request permission to re-use all or part of this article, contact the AACR Publications Department at permissions@aacr.org.