Towards the elimination of cervical cancer in low-income and lower-middle-income countries: modelled evaluation of the effectiveness and cost-effectiveness of point-of-care HPV self-collected screening and treatment in Papua New Guinea

Diep Thi Ngoc Nguyen, Kate T Simms, Adam Keane, Glen Mola, John Walpe Bolnga, Joseph Kuk, Pamela J Toliman, Steven G Badman, Marion Saville, John Kaldor, Andrew Valley, Karen Canfell

ABSTRACT

Introduction WHO has launched updated cervical screening guidelines, including provisions for primary HPV screen-and-treat. Papua New Guinea (PNG) has a high burden of cervical cancer, but no national cervical screening programme. We recently completed the first field trials of a screen-and-treat algorithm using point-of-care self-collected HPV and same-day treatment (hereafter self-collected HPV S&T) and showed this had superior clinical performance and acceptability to visual inspection of the cervix with acetic acid (VA). We, therefore, evaluated the effectiveness, cost-effectiveness and resource implications of a national cervical screening programme using self-collected HPV S&T compared with VA in PNG.

Methods An extensively validated platform (‘Policy1-Cervix’) was calibrated to PNG. A total of 38 strategies were selected for investigation, and these incorporated variations in age ranges and screening frequencies and allowed for the identification of the optimal strategy across a wide range of possibilities. A selection of strategies that were identified as being the most effective and cost-effective were then selected for further investigation for longer-term outcomes and budget impact estimation. In the base case, we assumed primary HPV testing has a sensitivity to cervical intraepithelial neoplasia 2 (CIN2+) of 81.8% and primary VA of 51.5% based on our earlier field evaluation combined with evidence from the literature. We conservatively assumed HPV sampling and testing would cost US$18. Costs were estimated from a service provider perspective based on data from local field trials and local consultation.

Results Self-collected HPV S&T was more effective and more cost-effective than VA. Either twice or thrice lifetime self-collected HPV S&T would be cost-effective at 0.5× gross domestic product (GDP) per capita (incremental cost-effectiveness ratio: US$460–US$656/life-years saved; 10Dper-capita: US$2829 or PGK9446 (year 2019)) and could prevent 33,000–42,000 cases and 23,000–29,000 deaths in PNG over the next 50 years, if scale-up reached 70% coverage from 2023.

Conclusion Self-collected HPV S&T was effective and cost-effective in the high-burden, low-resource setting of PNG, and, if scaled up rapidly, could prevent over 20,000 deaths over the next 50 years. VIA screening was not effective or cost-effective. These findings support, at a country level, WHO updated cervical screening guidelines and indicate that similar approaches could be appropriate for other low-resource settings.
INTRODUCTION

Cervical cancer is the second most common cancer among women in low- and lower-middle income countries with a population-weighted average age-standardised incidence rate (ASR) of 17.8 new cases per 100,000 women in 2018.1 Papua New Guinea (PNG) has a high estimated burden of cervical cancer with an ASR incidence rate of 29.1/100,000 in 2018,1 which is 1.6 times the average incidence rate among 1005 women in PNG, and the evaluation of the ‘screen and treat’ approach using visual inspection of the cervix with acetic acid (VIA), followed by cervical cryotherapy if lesions were identified, which was based on the 2014 WHO cervical cancer screening guidelines.4 5 A subsequent evaluation found the sensitivity of VIA to detect high-grade precancerous lesions in PNG was 51.5% and specificity 81.4%.6 We recently conducted the first field trials to evaluate a new screening model comprising point-of-care (PoC) HPV testing (GeneXpert; Cepheid, Sunnyvale, California, USA) using self-collected vaginal specimens followed by same-day curative treatment using a new, battery-operated, portable, thermal ablation device (WISAP Medical Technology).6–11 In our first trial among 1005 women in PNG (2013–2015), we showed that (1) HPV testing of self-collected vaginal specimens had comparable sensitivity (91.7%) and specificity (87.0%) to clinician-collected cervical specimens for the detection of cervical pre-cancer using the GeneXpert platform;6 7 12 (2) VIA alone, or VIA in combination with HPV testing had poor performance for the detection of underlying High-Grade Squamous Intraepithelial Lesions (HSIL) or worse (sensitivity 51.5% and 45.5%, respectively) compared with HPV testing alone (sensitivity 91.7%);6 and (3) with suitable training and support, PoC HPV self-collected screen and treat (thereafter self-collected HPV S&T) can be provided routinely in primary care facilities.7 The poor performance of VIA in this trial is similar to the findings reported in India and Rwanda.13 14 In a second field trial among 4000 women in PNG (2017–2020), we confirmed the clinical performance of our self-collected HPV S&T modality for the detection and treatment of cervical pre-cancer, and its high acceptability among women and health providers.15

In May 2018, the Director-General of the WHO announced a global call to action towards achieving the elimination of cervical cancer as a public health problem. In November 2020, WHO launched the global elimination strategy16 that included the ‘90-70-40’ triple intervention targets to be met by 2030: (1) 90% of girls fully vaccinated with the HPV vaccine by age 15; (2) 70% of women screened with a high-precision HPV test by age 35 and 45 years of age; and (3) 90% of women with cervical precancer treated, and 90% of women with invasive cancer managed and treated appropriately. Achieving the triple-intervention targets in the next decade would put countries on the path to achieving elimination in the next century, reducing cervical cancer mortality by 99% and saving more than 62 million women’s lives over the next century.5 To support elimination efforts, WHO has recently released updated cervical screening guidelines which recommend primary HPV screen-and-treat
or primary HPV screen-triage-and-treat for women aged 30–49 years.\textsuperscript{17}

To make progress towards elimination, it will be essential for countries to implement locally appropriate, context-specific intervention strategies. In this paper, we evaluated new WHO screen-and-treat approach informed by local data from a field trial of self-collected HPV S&T modality to identify the optimal cervical screening strategy for PNG. Here, we reported on the estimated effectiveness and cost-effectiveness of national roll-out of self-collected HPV S&T in PNG, the long-term impact on cervical cancer incidence and mortality, and the resource implications of scaling up such an algorithm.

\textbf{METHODS}

\textbf{Model platform}

A validated dynamic individual-based microsimulation model (‘Policy1-Cervix’) of HPV transmission, type-specific natural history of cervical intraepithelial neoplasia (CIN) and invasive cancer staging, and cervical screening, diagnosis, and treatment was used. This model platform has been used to evaluate the effectiveness and cost-effectiveness of cervical cancer screening for both vaccinated and unvaccinated cohorts across different settings, including the renewal of the cervical screening programme in Australia,\textsuperscript{18,19} the impact of HPV testing using self-collected samples in Australia,\textsuperscript{20} the impact of primary HPV testing in New Zealand,\textsuperscript{21} England\textsuperscript{22} and China\textsuperscript{23–25} and vaccine evaluations in Japan.\textsuperscript{26} Most recently, this model was also used to evaluate the timeline to cervical cancer elimination for 78-low-income and lower-middle income countries (LMICs), in Australia, USA and globally\textsuperscript{27–30} and is also being used to inform development of updated WHO screening guidelines.\textsuperscript{17}

(online supplemental figure A1. More details of the model platform present in the online supplemental appendix, p1-2 and via Policy1-Cervix website https://www.policy1.org/models/cervix/documentation).

\textbf{Model calibration}

We calibrated the model to the cervical cancer incidence rate in PNG using age-specific GLOBOCAN 2018 data\textsuperscript{1} (ASR=28.4/100 000 women (0–84 years)) as shown in online supplemental figure A2 (A)). Additionally, the model was also calibrated to the age-specific high-risk HPV prevalence among women aged 18–54 years, based on data from a local HPV prevalence survey\textsuperscript{31} (online supplemental figures A2 (C) and A3).

\textbf{Background hysterectomy rates}

Although there is some hysterectomy being done on benign conditions, this information is not well documented or there is paucity of information, we assumed there was no background hysterectomy for benign conditions.

\textbf{Screening and management pathways}

We considered two screening and management pathways. The first is the same pathway as in the field project, utilising self-collected HPV S&T (figure 1A). In this pathway, women who are positive at primary HPV testing are treated with thermocoagulation of the transformation zone of the cervix. For the second pathway, we considered screening with VIA (figure 1B). In both screening pathways, women who have a cervical lesion at visual assessment, but are not suspected of harbouring a cancer, are immediately treated with ablation and that women whose lesions are large or suspicious for cancer are referred to a specialist for further assessment. For both pathways, we assumed that women who were referred for diagnosis with suspicion of cancer, but found to have CIN3, would be treated with hysterectomy or conisation depending on patient individual clinical circumstances (based on local expert opinion). We assumed that women who are negative may return for screening at a set time, depending on the screening frequency, and that women who received treatment for precancer for a ‘test of cure’ using the same test as the primary test.

\textbf{Screening ages and frequencies}

Although initial field trials focused on women aged 30–59 years, in the modelled analysis we considered various screening frequencies (once, twice, thrice lifetime and 5 yearly) at different initiating ages (30 years, 35 years and 40 years).

For this analysis, we considered two overall steps. In the first step (step 1), a total of 38 screening strategies were assessed to identify the optimal screening strategies for PNG, considering both ‘self-collected HPV S&T’ and VIA approaches and varying screening ages and frequencies. Single cohort modelling approaches were used for this step to identify the lifetime impacts of each screening strategy and cost-effective screening strategies. In step 2, strategies that appeared on the cost-effectiveness frontier from step 1 were selected to assess the long-term impact of scaling-up screening on ASR cancer incidence and mortality, cases and deaths, resource utilisation and projected financial costs nationwide (table 1). In addition to the scenarios that appeared at the cost-effectiveness frontier, we also included the WHO elimination strategy (twice per lifetime at ages 35, 45)\textsuperscript{17} in step 2.

\textbf{Screening compliance assumptions}

We assumed 10% of women never attend screening in their lifetime for all scenarios. We assumed that 70% of women will attend routine screening at each invitation, selected from 90% of the population of ever-screeners. Given that treatment with ablation is performed on the same day, we assumed 5% lost to follow-up for ablation as this is consistent with experiences on-the-ground in PNG.\textsuperscript{17}

These assumptions on compliance with routine attendance were similar to the assumptions used in the modelling to support WHO’s updated cervical screening guidelines. However, for women referred to diagnostic services and for women who received treatment and need to attend post-treatment follow-up at 12 months,
we assumed 50% lost to follow-up, based on local experience. For women who were referred for diagnostic evaluation for suspicion of cancer, we assumed a 30% lost to follow-up, due to limited facilities and difficulties in travel, particularly for rural women (see figure 1A,B).

**Screening test characteristics**

The test characteristics for primary self-collected HPV testing were obtained from an international systematic review on the sensitivity and specificity of PCR-based HPV testing using self-collected samples as well as from the local trial of PoC HPV self-collected testing in PNG. The international systematic review has found that PCR self-collected HPV testing was as sensitive as clinician-collected HPV testing to detect CIN2+ (pooled relative ratio 0.99 (95% CI 0.97 to 1.02). Based on a local trial in PNG, Toliman et al found that self-collected HPV testing had sensitivity of 91.7% to detect high-grade lesions. Therefore, in this study, we took a conservative approach and assumed that HPV had sensitivity to CIN2+ of 91.7% and specificity of 89.8%.

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**Figure 1** Screening management pathway. (A) Point-of-care (PoC) HPV self-collected screen and treat (self-collected HPV S&T), (B) VIA screening.
in the base case, which is slightly lower than performance reported for clinician-collected HPV samples. We also considered 89.1% (lower bound) and 95.3% (upper bound) sensitivity to CIN2+ in sensitivity analysis. VIA test characteristics estimated from a screening trial in PNG was used in the base case analysis.6 The VIA screening trial in PNG involved ~1000 women and identified 51.5% sensitivity and 81.4% specificity to detect CIN2+ and this test performance was assumed in the model.6 This performance assumption for VIA is consistent with studies from India13 and Rwanda14 and consistent with the outcomes of large population-based experiences of VIA in India, in which VIA testing of 70,000 women over 12 years did not reduce the incident cancer, and only reduced mortality rates through stage-shifting.33 A more favourable sensitivity (70% sensitivity to CIN2+) of VIA testing inferred from international systematic review was also used in sensitivity analysis34 35 (table 2).

**Vaccination assumptions**

Although the PNG government is committed to HPV vaccine introduction and pilot HPV vaccine projects were completed in some provinces for schoolgirls some years ago,36 at this point a national HPV vaccination programme has not been recommended in PNG. In the first couple of decades after vaccination, most women over 30 years, and thus eligible for screening, will not be vaccinated. Therefore, in this analysis, we assumed that cervical screening strategies were conducted in women who have not received the HPV vaccine.

### Table 1 Screening strategies

<table>
<thead>
<tr>
<th>Strategy no</th>
<th>Step 1: Strategies included, varying ages and frequencies for both primary HPV and VIA approaches</th>
<th>Step 2: Strategies assessed to predict impact on health outcomes, resource utilisation and budget impact</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>No intervention</td>
<td>No intervention</td>
</tr>
<tr>
<td>1</td>
<td>1X-lifetime screening</td>
<td>Once lifetime at age 35 (1X)</td>
</tr>
<tr>
<td>1.1</td>
<td>Once lifetime at age 30 (1X)</td>
<td>Once lifetime at age 35 (1X)</td>
</tr>
<tr>
<td>1.2</td>
<td>Once lifetime at age 35 (1X)</td>
<td>Twice lifetime at age 35, 40 (2X)</td>
</tr>
<tr>
<td>1.3</td>
<td>Once lifetime at age 40 (1X)</td>
<td>Twice lifetime at age 35, 40 (2X)</td>
</tr>
<tr>
<td>1.4</td>
<td>Once lifetime at age 45 (1X)</td>
<td>Twice lifetime at age 35, 40 (2X)</td>
</tr>
<tr>
<td>1.5</td>
<td>Once lifetime at age 50 (1X)</td>
<td>Twice lifetime at age 35, 40 (2X)</td>
</tr>
<tr>
<td>2</td>
<td>2X-lifetime screening</td>
<td>Twice lifetime at age 35, 40 (2X)</td>
</tr>
<tr>
<td>2.1</td>
<td>Twice lifetime at age 30, 35 (2X)</td>
<td>Twice lifetime at age 35, 40 (2X)</td>
</tr>
<tr>
<td>2.2</td>
<td>Twice lifetime at age 35, 40 (2X)</td>
<td>Twice lifetime at age 35, 40 (2X)</td>
</tr>
<tr>
<td>2.3</td>
<td>Twice lifetime at age 40, 45 (2X)</td>
<td>Twice lifetime at age 35, 40 (2X)</td>
</tr>
<tr>
<td>2.4</td>
<td>Twice lifetime at age 45, 50 (2X)</td>
<td>Twice lifetime at age 35, 40 (2X)</td>
</tr>
<tr>
<td>2.5</td>
<td>Twice lifetime at age 30, 40 (2X)</td>
<td>Twice lifetime at age 35, 40 (2X)</td>
</tr>
<tr>
<td>2.6</td>
<td>Twice lifetime at age 35, 45 (2X)—WHO global elimination strategy and 2021 WHO guideline’s recommended strategy</td>
<td>Twice lifetime at age 35, 45 (2X)—WHO global elimination strategy and 2021 WHO guideline’s recommended strategy</td>
</tr>
<tr>
<td>2.7</td>
<td>Twice lifetime at age 40, 50 (2X)</td>
<td>Twice lifetime at age 35, 40 (2X)</td>
</tr>
<tr>
<td>2.8</td>
<td>Twice lifetime at age 45, 55 (2X)</td>
<td>Twice lifetime at age 35, 40 (2X)</td>
</tr>
<tr>
<td>3</td>
<td>3X-lifetime screening</td>
<td>Twice lifetime at age 35, 40 (3X)</td>
</tr>
<tr>
<td>3.1</td>
<td>Thrice lifetime at age 30, 35, 40 (3X)</td>
<td>Thrice lifetime at age 30, 35, 40 (3X)</td>
</tr>
<tr>
<td>3.2</td>
<td>Thrice lifetime at age 35, 40, 45 (3X)</td>
<td>Thrice lifetime at age 35, 40, 45 (3X)</td>
</tr>
<tr>
<td>3.3</td>
<td>Thrice lifetime at age 40, 45, 50 (3X)</td>
<td>Thrice lifetime at age 35, 40, 45 (3X)</td>
</tr>
<tr>
<td>3.4</td>
<td>Thrice lifetime at age 30, 40, 50 (3X)-2021 WHO guideline’s recommended strategy</td>
<td>Thrice lifetime at age 30, 40, 50 (3X)-2021 WHO guideline’s recommended strategy</td>
</tr>
<tr>
<td>3.5</td>
<td>Thrice lifetime at age 35, 45, 50 (3X)</td>
<td>Thrice lifetime at age 30, 40, 50 (3X)</td>
</tr>
<tr>
<td>4</td>
<td>5-yearly screening 30–55</td>
<td>5-yearly screening 30–55</td>
</tr>
<tr>
<td>4.1</td>
<td>5-yearly at age 30–55 (6X)</td>
<td>5-yearly at age 30–55 (6X)</td>
</tr>
<tr>
<td>Total</td>
<td>38 screening strategies</td>
<td>Total: 5 screening strategies plus WHO elimination strategy</td>
</tr>
</tbody>
</table>

S&T, screen and treat; VIA, visual inspection with acetic acid.
Table 2  Summary of model parameters for screening, diagnosis, and treatment procedures, and ranges for sensitivity analysis

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Baseline value</th>
<th>Range for sensitivity analysis (lower bound and upper bound)</th>
<th>Sources</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preintervention burden of disease</td>
<td></td>
<td></td>
<td>GLOBOCAN, 2018⁷</td>
</tr>
<tr>
<td>Incidence</td>
<td>ASR-W (0–84)=28.4/100 000</td>
<td>N/A</td>
<td></td>
</tr>
<tr>
<td>Mortality</td>
<td>ASR-W (0–74)=18.6/100 000</td>
<td>N/A</td>
<td></td>
</tr>
<tr>
<td>Screening participation and compliance</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Screening participation rate</td>
<td>90% of women ever screen; 70% return for their next scheduled routine visit (selected from the 90% ever-screeners)</td>
<td>50%–90%</td>
<td>Based on WHO elimination targets by 2030⁸</td>
</tr>
<tr>
<td>Rate of lost to follow-up for same-day treatment with thermal ablation</td>
<td>5%</td>
<td>NA</td>
<td>Assumption based on the trial outcomes</td>
</tr>
<tr>
<td>Rate of loss to follow-up (LTFU) of referral for treatment of larger lesions or suspicious cancer investigation</td>
<td>30% for self-collected HPV S&amp;T; 30% for VIA</td>
<td>Lower bound: 10% for self-collected HPV S&amp;T and 10% for VIA screening</td>
<td>Based on limited health facilities that can offer cancer diagnosis and treatment, as well as the limited access for rural women. (Personal communication with local experts)</td>
</tr>
<tr>
<td>LTFU of women after ablative treatment for precancer at 12 m follow-up visit</td>
<td>50% for self-collected HPV S&amp;T; 50% for VIA</td>
<td>Lower bound: 10% for self-collected HPV S&amp;T and 10% for VIA screening</td>
<td>Base case: based on limited health facilities and as well as the limited access for rural women. Lower bound: based on the experience of the field trial in PNG.</td>
</tr>
<tr>
<td>Screening test characteristics</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>self-collected HPV</td>
<td>Sensitivity of 91.7% and specificity of 89.8% to detect CIN2+.⁹</td>
<td>Sensitivity: 89.1%–95.3% and Specificity: 88.6%–90.6% to detect CIN2+</td>
<td>Arbyn et al⁴⁰ 32; Toliman et al⁵</td>
</tr>
<tr>
<td>Primary VIA</td>
<td>Sensitivity of 51.5% and specificity of 81.4% for CIN2+.⁹</td>
<td>Upper bound: Sensitivity of 70% and specificity of 78% for CIN2+</td>
<td>Base case: based on the upper 95% CI of VIA test performance Toliman et al⁶ and a systematic review on VIA test performance categorised for high quality studies.⁸⁹</td>
</tr>
<tr>
<td>Ablation treatment success rate</td>
<td>84.3%–92.4% for CIN1-3; 0% for cancer</td>
<td></td>
<td>Randall et al⁴⁹</td>
</tr>
<tr>
<td>Cancer treatment</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>% Cancer treatment uptake for symptomatically detected cancers</td>
<td>20% treatment access rate overall. (Detailed assumptions in the Methods section and online supplemental appendix)</td>
<td>Lower bound: 8%; Upper bound: 90% treatment access overall</td>
<td>Base case: Only a few health facilities can offer cancer diagnosis and treatment, which is limited to radical hysterectomy (Based on personal communication with local experts). Lower bound: Based on access rate to radiotherapy estimated by Datta et al.⁴⁷ Upper bound: Based on WHO cancer treatment target for cervical cancer elimination.⁶⁶</td>
</tr>
<tr>
<td>5-year survival by FIGO stage (%)</td>
<td>FIGO I: 0.64; FIGO II: 0.52; FIGO III: 0.12; FIGO IV: 0.01 (online supplemental table A1)</td>
<td>Lower bound: FIGO I: 0.625; FIGO II: 0.48; FIGO III: 0.101; FIGO IV: 0.011 Upper bound: FIGO I: 0.869; FIGO II: 0.774; FIGO III: 0.599; FIGO IV: 0.117 (online supplemental table A1)</td>
<td>Base case: Informed by stage-specific survival rates for countries with ~20% cancer treatment access to radiotherapy,¹ assuming the survival benefits are mostly targeted to Stage 1 and 2, and further adjusted to fit to GLOBOCAN2018 mortality rates. Lower bound: We assumed the same survival rates estimated for PNG as reported in Canfell et al.⁴⁷ Upper bound: We assumed the same survival rates estimated for countries with 90% treatment access rate across all stages as reported in Canfell et al.⁴⁷</td>
</tr>
<tr>
<td>Costs † (US$) and other health economic parameters</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>self-collected HPV test cost ‡</td>
<td>US$18</td>
<td>US$8</td>
<td>Base case costs were estimated based on the current screening trial in PNG. Lower cost of HPV test in sensitivity analysis was assumed based on discussions with experts regarding future reduction in HPV test costs.</td>
</tr>
<tr>
<td>VIA test cost ‡</td>
<td>US6</td>
<td>NA</td>
<td></td>
</tr>
<tr>
<td>Biopsy</td>
<td>US$59</td>
<td>NA</td>
<td></td>
</tr>
<tr>
<td>Ablation</td>
<td>US$15</td>
<td>NA</td>
<td></td>
</tr>
<tr>
<td>Cancer treatment costs</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Cancer treatment assumptions

The current infrastructure for cancer treatment in PNG is very limited, based on consultation with local experts. Only one radiotherapy treatment unit has been established, which was reported to be non-functional since 2015. We therefore assumed that radiotherapy access is limited and unreliable. We assumed that only radical hysterectomy (available in a few hospitals) was used for women with early-stage cancers. Given this situation, at base case analysis we assumed that 80% of cervical cancer diagnosed at International Federation of Gynaecology and Obstetrics (FIGO) stage I, 20% of those diagnosed at FIGO II would be treated with radical hysterectomy, those diagnosed at FIGO III and IV were not treated, and that these treatment rates did not vary for screen-detected or symptomatically detected cancers. The modelled distribution of cervical cancer stage in PNG was 14%, 55%, 27% and 3% for FIGO I, II, III and IV, respectively. Assuming 80% of FIGO I and 20% of FIGO II cancers receive treatment resulted in 80×14%+20×55%+0×27%+0×3%=20% of any diagnosed cancer would be treated in base case analysis, and therefore costs of cancer for these stages were adjusted accordingly. Our survival inputs produced similar mortality rates to those reported in GLOBOCAN2018 for PNG (online supplemental figure A2 (B)). We also considered lower (8%) and higher (90%) cancer treatment access rates in sensitivity analysis. (more details in online supplemental appendix 1, part 3. Cancer treatment access rate and survival assumptions)

Costs

Costs were estimated from a service provider perspective. Direct medical costs were considered only. Costs were originally assessed in the field in PGK (PNG currency) and were converted to US$, using the 2019 exchange rate (PGK1=US$0.3, 17 October 2019, Commonwealth Bank, Australia). Costs associated with cervical cancer screening and thermal ablation were estimated from our screening trials in PNG. Based on financial expenditures on personnel, equipment, consumables, and the number of women screened during the trial period, we estimated unit costs of HPV testing, VIA testing, visual assessment for ablation and thermal ablative treatment (table 2). The number of screened women was based on the actual number of women who were screened and treated each day in the ongoing trials in PNG. Using this method, the cost of HPV testing (including costs associated with test and test delivery) was US$18 per test as currently estimated. In the context of expected mass HPV testing in the next decade, we conservatively assumed a unit test cost for HPV testing of US$18 in the base case. However, it is possible the HPV test cost would be decreased in the context of a national screening programme as higher volumes could result in more competitive test prices. Therefore, we considered a lower HPV test cost (US$8) in sensitivity analysis. The cost of VIA as a primary or as an assessment for same-day treatment was estimated to be US$6 per test. The unit cost of thermal ablation was estimated to be US$15. Other unit costs, including costs of biopsy and treatment for lesions ineligible for ablation and for early-stage cancers with full course of treatment with hysterectomy

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Baseline value</th>
<th>Range for sensitivity analysis (lower bound and upper bound)</th>
<th>Sources</th>
</tr>
</thead>
<tbody>
<tr>
<td>FIGO I</td>
<td>US$1614 (applied to 80% of FIGO I diagnosed cases)</td>
<td><strong>Upper bound:</strong> US$1937</td>
<td><strong>Base case:</strong> costs were estimated based on personal communication with local experts. <strong>Upper bound:</strong> Cancer treatment cost for FIGO I and II was assumed 20% higher than base case. In a sensitivity analysis considering a 90% cancer treatment access, we assumed some treatment options for advanced cancer stages would be available in PNG. We assumed cancer treatment costs for FIGO III were 40% higher than treatment cost for FIGO I and cost for FIGO IV was equal to cost for FIGO I treatment. These factors were derived from previous study, (see online supplemental tables A2 and A3)</td>
</tr>
<tr>
<td>FIGO II</td>
<td>US$1614 (applied to 20% of FIGO II diagnosed cases)</td>
<td><strong>Upper bound:</strong> US$1937</td>
<td><strong>Base case:</strong> costs were estimated based on personal communication with local experts. <strong>Upper bound:</strong> Cancer treatment cost for FIGO I and II was assumed 20% higher than base case. In a sensitivity analysis considering a 90% cancer treatment access, we assumed some treatment options for advanced cancer stages would be available in PNG. We assumed cancer treatment costs for FIGO III were 40% higher than treatment cost for FIGO I and cost for FIGO IV was equal to cost for FIGO I treatment. These factors were derived from previous study, (see online supplemental tables A2 and A3)</td>
</tr>
<tr>
<td>FIGO III</td>
<td>0</td>
<td><strong>Upper bound:</strong> 0</td>
<td></td>
</tr>
<tr>
<td>FIGO IV</td>
<td>0</td>
<td><strong>Upper bound:</strong> 0</td>
<td></td>
</tr>
<tr>
<td>Threshold for willingness-to-pay</td>
<td>0.5X PNG GDP per capita, US$1415 (PGK4723)</td>
<td>1X PNG GDP per capita, US$2829 (PGK9446)</td>
<td>WHO-CHOICE cost-effectiveness analysis guideline.</td>
</tr>
<tr>
<td>Effects</td>
<td>3%</td>
<td>0%</td>
<td>WHO-CHOICE cost-effectiveness analysis guideline.</td>
</tr>
<tr>
<td>Costs</td>
<td>3%</td>
<td>3%</td>
<td>WHO-CHOICE cost-effectiveness analysis guideline.</td>
</tr>
</tbody>
</table>

We assumed the test performance for HSIL are equivalent for CIN2+. Costs were collected in PGK currency and converted to US$, using exchange rate of PGK1=US$0.3, 17 October 2019, Commonwealth Bank, Australia. The Toliman et al study reported test performance of PoC HPV self-collected testing and VIA testing for HSIL. Costs were estimated from service provider's perspective, considering direct medical costs that associated with each screening, diagnostic tests or treatment procedures. Including costs of test and test delivery. ASR, age-standardised rate; CIN, cervical intraepithelial neoplasia; FIGO, International Federation of Gynaecology and Obstetrics; GDP, gross domestic product; HSIL, high-grade squamous intraepithelial lesions; PNG, Papua New Guinea; PoC, point-of-care; S&T, screen and treat; VIA, visual inspection with acetic acid.
(that are currently available in PNG) were estimated based on consultation with local experts. In consultation with local experts, the costs of biopsy and cancer treatment for FIGO I and FIGO II were estimated to be US$59 and US$1614, respectively. At present, treatments for stage III and stage IV cancers and for palliative care are not available in PNG, therefore no treatment cost was assumed to be incurred for cancer at these stages in base case analysis. However, in sensitivity analysis considering a 90% treatment access rate, we assumed that treatment for advanced-stage cancers would be available. (Details in online supplemental appendix, part 4. Cost estimations) Based on the analysis of the cost profile by different cost components, which show substantial proportions of screening costs and cancer treatment costs (which mainly were treatment costs for early-stage cancers), we checked for the robustness of the results by considering variations in these costs in sensitivity analysis.

Outcomes assessed

For step 1, we report on outcomes over the lifetime of unvaccinated women who would turn 30 in 2023, the first cohort to be fully impacted by scale-up of cervical screening in PNG. Outcomes assessed include ASR of cervical cancer incidence and mortality, and cost-effectiveness. For step 2, we selected the strategies that appeared on the cost-effectiveness frontier from step 1 as well as the WHO elimination strategy, and further assessed the longer-term outcomes of scaling-up screening to reach 70% coverage from 2023 onwards and reported on the ASR of cervical cancer incidence and mortality out to 2072, and total cancer cases and deaths predicted. We also estimated the total undiscounted financial budget impact of a national screening programme over a 5-year (2023–2027) and 10-year (2023–2032) horizon. We did not account for inflation in this budget impact analysis. This financial cost projection was estimated at service provider perspective, including direct medical costs associated with cervical cancer screening, precancer treatment, cancer diagnosis and treatment for PNG; however, they do not include overhead costs of the programme, including administrative costs and capital costs of existing buildings, equipment, vehicles, that allocated to these services. These costs also do not include start-up costs associated with the establishment of a national screening programme, including costs of screening registry system, training for health staff and community mobilisation that usually occur at a configuration stage of a national cervical screening programme. For step 2, we also estimated the annual number of HPV tests, annual number of women diagnosed with precancerous lesions and eligible for ablation, annual number of women diagnosed with precancerous lesions but ineligible for ablation, and the number with symptomatic cancer and screen-detected cancer. The annual resource utilisation numbers were calculated as an average over the first 5 years of a potential national cervical screening programme in PNG.

The cost-effectiveness analysis (CEA) was conducted from the service provider perspective for cervical cancer prevention. A single cohort CEA over the lifetime of the cohort was performed across 38 screening strategies assuming a 3% discount rate for effects and costs (starting at age 12), based on WHO recommendations. A 0% discount for effects and 3% discount for costs was considered in sensitivity analysis. In CEA, the incremental cost-effectiveness ratios (ICERs) were used to compare to willingness-to-pay (WTP) threshold. Half of the gross domestic product (GDP) per capita for PNG (0.5GDPc (US$1415 or PGK4723, World Bank 2019)) was used as the indicative WTP threshold for the evaluation. We also considered a WTP threshold of 1GDPc (1GDPpc=US$2829 or PGK9446).

Sensitivity analysis

Univariate sensitivity analysis was performed on key model assumptions to evaluate the robustness of the results. Key parameters were considered, including PoC HPV self-collected test accuracy (best sensitivity (95.3%) and worst sensitivity (89.1%) vs 91.7% at base case) of HPV and VIA screening, lower costs of HPV tests (US$8/test vs US$18/test at base case), higher cancer treatment costs (20% higher vs costs at base case), variation in screening coverage (50% and 90% vs 70% at base case), lower loss to follow-up rates at post-treatment follow-up (10% vs 50%), lower and upper cancer treatment access rate (8% and 90% vs 20% at base case), and lower discount rates for effects (0% vs 3% at base case) (table 2).

Patient involvement

This modelling study has been done as part of a programme ‘Prospective cohort study to evaluate PoC HPV-DNA self-collected testing for the early detection and treatment of cervical pre-cancer in high-burden, low resource settings’ funded by the National Health and Medical Research Council (NHMRC) Australia Project Grant 1104938. The modelling assumptions have been informed by data/information regarding screening management pathways, PoC HPV self-collected test performance, VIA test performance, costing data from past and ongoing field trials in PNG in collaboration with local investigators, who directly working with patients and understand the local context.

As many other field trials, patient involvement concept has been integrated through different study stages. The previous VIA and ongoing self-collected HPV S&T field trials were designed in partnership with national and provincial health authorities, expert groups (PNG OBGYN Society, Technical working group on cervical cancer)—whose works are focused on improving population health in general and women health in particular, and civil society groups (PNG Cancer Foundation)—where including patient representatives/cancer survivors. The design of the field trials had been informed by findings of a qualitative study, in which we engaged women and their families at community level to explore
understandings around cervical cancer causation, stigma, women’s health priorities. As a result, the self-collected HPV S&T modality was designed to create the most convenient environment for women to get screened and reduced waiting time.

At recruitment and implementation stage of screening trials, women were provided general information about the screening trials, including key study objectives and procedures; eligibility and inclusion/exclusion criteria; and the benefits and potential risks of study participation. Women can choose to participate or not in the study based on formal informed consent procedures.

Six-monthly newsletters have been prepared for study participants, local stakeholders and clinical staff at study sites documenting progress with each stage of the trial, emerging issues, upcoming events and new staffing. These newsletters have been disseminated to study sites and key local and national stakeholders including community leaders, national and provincial health departments, and other relevant organisations. Cancer survivors who participated in the trials have been invited to talk about her experience of being early diagnosed and treated cervical cancer.

RESULTS

Effectiveness outcomes

Assuming no further intervention in PNG (‘no intervention’), the ASR of cervical cancer incidence was predicted to remain at 29.7 per 100,000 women (0–84 years) and mortality at 20.8 per 100,000 women (0–84 years) for the next 50 years, and generate 1085 new cases and 737 deaths in the year 2020 alone (figure 2 and online supplemental figure A4). Screening either two or three times in a lifetime for women aged 30, 40 years and 30, 35, and 40 years, respectively, using self-collected HPV S&T reduced the ASR of cervical cancer incidence to 15.6–18.6 per 100,000 (35%–48% reduction) and reduced ASR mortality to 10.6–12.7 per 100,000 women (39%–49% reduction) over the longer term. In contrast, either two or three times screening with VIA in a lifetime reduced the ASR of cervical cancer incidence by 17%–24%, and the ASR of mortality by 18%–25% over a lifetime. With a favourable sensitivity of VIA for CIN2/3 (70% sensitivity), two or three times in a lifetime reduced the ASR of cervical cancer incidence by 19%–30% and reduced mortality by 20%–32%, and therefore, remained less effective than self-collected HPV S&T even in this favourable scenario (online supplemental figure A5).

Cost-effectiveness outcomes (step 1)

Once lifetime (age 35 years, 1X), twice lifetime (30&40 years and 35, 40 years, 2X) and thrice lifetime (age 30, 35 and &40 years, 3X) screening strategies with self-collected HPV S&T were on the cost-effectiveness frontier (figure 3). The ICERs of these strategies were US$311/life-years saved (LYS), US$460/LYS, US$568/LYS, US$656/LYS, respectively, and therefore, these strategies were considered as cost-effective at the 0.5GDP per capita threshold (US$1415). At 1GDPpc (US$2829), once, twice and thrice lifetime screening, and even 5-yearly
screening were cost-effective. When assuming 70% VIA sensitivity for CIN2/3, once, twice and thrice lifetime self-collected HPV S&T remained cost-effective at either 0.5GDP or 1GDP per capita thresholds, and therefore primary VIA screening was not cost-effective even under these favourable assumptions around test performance (online supplemental figure A6).

**Figure 3** Cost-effectiveness analysis. The performance of VIA screening test (51% sensitivity) was derived from VIA screening trial in PNG reported in Toliman et al. The cost-effectiveness analysis included current situation (no screening) and 38 self-collected HPV S&T and VIA screening scenarios. The gross domestic product (GDP) per capita for PNG (0.5GDPpc (US$1415 or PGK4723, world bank 2019) was used as the indicative willingness-to-pay (WTP) threshold for the evaluation. We also secondarily considered a WTP threshold of 1GDPpc (1GDPpc=US$2829 or PGK9446). LYS, life-years saved; PNG, Papua New Guinea; S&T, screen and treat; VIA, visual inspection with acetic acid.

**Table 3** Cumulative cases and deaths over 50 years (2023–2072) of the strategies which were the most cost-effective as identified in step 1 in PNG

<table>
<thead>
<tr>
<th>Scenarios</th>
<th>No intervention</th>
<th>1X at age 35 self-collected HPV S&amp;T</th>
<th>2X at age 30, 40 self-collected HPV S&amp;T</th>
<th>2X at age 35, 40 self-collected HPV S&amp;T</th>
<th>2X at age 35, 40 self-collected HPV S&amp;T*</th>
<th>3X at age 30, 35, 40 self-collected HPV S&amp;T</th>
<th>5-yearly (6X) 30–55 self-collected HPV S&amp;T</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Incidence</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cumulative cases over 2023–2072</td>
<td>108204</td>
<td>88509</td>
<td>74623</td>
<td>75323</td>
<td>77183</td>
<td>65852</td>
<td>52158</td>
</tr>
<tr>
<td>Cases averted (2023–2072)</td>
<td>–</td>
<td>19695</td>
<td>33581</td>
<td>32881</td>
<td>31021</td>
<td>42352</td>
<td>56047</td>
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<tr>
<td><strong>Mortality</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Cumulative deaths over 2023–2072</td>
<td>75731</td>
<td>61716</td>
<td>52247</td>
<td>52789</td>
<td>53899</td>
<td>46378</td>
<td>37487</td>
</tr>
<tr>
<td>Deaths averted (2023–2072)</td>
<td>–</td>
<td>14015</td>
<td>23484</td>
<td>22942</td>
<td>21833</td>
<td>29353</td>
<td>38244</td>
</tr>
</tbody>
</table>

*WHO recommendation of cervical screening for cervical cancer elimination was added.
PNG, Papua New Guinea; S&T, screen and treat.
Table 4  Estimated resource utilisation and budget required for a national screening programme of the most cost-effective strategies in PNG. (A) Average annual resources§ required for a national screening program in PNG estimated over the first 5 years of implementation (2023–2027). (B) Estimated total budget* (US$) over the first 5-year and 10-year periods †.

### (A) Annual resource utilisation§

<table>
<thead>
<tr>
<th>No of HPV tests</th>
<th>No of women diagnosed with precancerous lesions and eligible for ablation</th>
<th>No of women diagnosed with cervical cancer through symptomatic presentation</th>
<th>No of women diagnosed with cervical cancer through screening</th>
<th>No of women diagnosed with precancerous lesions but ineligible for ablation</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>42,500</td>
<td>5,892</td>
<td>974</td>
<td>53</td>
<td>58</td>
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<td>78,200</td>
<td>8,802</td>
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<td>83,800</td>
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<td>88</td>
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<td>71,400</td>
<td>8,186</td>
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<tr>
<td>197,400</td>
<td>20,484</td>
<td>726</td>
<td>193</td>
<td>182</td>
</tr>
</tbody>
</table>

### (B) Budget *

<table>
<thead>
<tr>
<th>No of HPV tests</th>
<th>No of women diagnosed with precancerous lesions and eligible for ablation</th>
<th>No of women diagnosed with cervical cancer through symptomatic presentation</th>
<th>No of women diagnosed with cervical cancer through screening</th>
<th>No of women diagnosed with precancerous lesions but ineligible for ablation</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
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<tr>
<td>300</td>
<td>500</td>
<td>78</td>
<td>88</td>
<td>110</td>
</tr>
<tr>
<td>2,000</td>
<td>2,800</td>
<td>288</td>
<td>234</td>
<td>213</td>
</tr>
<tr>
<td>8,000</td>
<td>11,300</td>
<td>1,408</td>
<td>1,204</td>
<td>1,213</td>
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<td>16,000</td>
<td>21,900</td>
<td>2,940</td>
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<td>24,000</td>
<td>31,800</td>
<td>3,850</td>
<td>2,404</td>
<td>2,431</td>
</tr>
</tbody>
</table>

*5-year and 10-year budgets were calculated as the financial costs (US$, 2019) associated with cervical cancer screening, diagnosis, and treatment over the first 5 years (2023–2027) and 10 years (2023–2032) of implementation. This budget is a broad estimate of that required for a future national cervical cancer screening programme in PNG (inflation was not considered).
†We used UN population structure estimated for PNG (year 2020) and assumed this population structure remained over 2023–2032 to estimate budget and resources.
‡WHO recommendation for cervical screening for cervical cancer elimination.
§Annual resources for a national cervical screening program in PNG were estimated as an average of the resources required over the first 5 years of implementation (2023–2027).
programme is scaled-up nationally in PNG to reach 70% coverage from 2023 onwards. We found that once lifetime self-collected HPV S&T would require 42 500 HPV tests per year. As expected, more frequent screening strategies would require more HPV tests (71 400–83 800 for twice lifetime, depending on screening ages, up to 124 900 for thrice lifetime and 197 400 for 5-yearly screening). Similarly, more frequent screening strategies would require a higher number of ablative treatments, ranging from an annual number of 5892 ablative treatment with once lifetime screening to 20 484 ablative treatments with 5-yearly screening (table 4A). Without screening, on average 1085 women would be diagnosed with cervical cancer through symptomatic presentation annually over the next 5 years. With 70% scale up of the screening programme using self-collected HPV S&T in 2023, on average annually over the next 5 years 1028 women would be diagnosed with cervical cancer (of which 53 cases are screen detected) for once lifetime screening or 919 cases for 5-yearly screening (of which 193 cases are screen detected). The number of women with lesions ineligible for ablation (and therefore referred for more advanced treatment) was predicted to range from 58 cases in once lifetime screening to 182 cases in 5-yearly screening (table 4A).

Budget impact and profile of financial costs associated with screening, diagnosis and treatment using self-collected HPV S&T modality

Without a cervical screening programme, it was estimated that total 5-year and 10-year undiscounted financial costs of ~US$1.9 million and US$3.8 million, respectively would be spent on diagnosis and treatment of cervical cancer, due to the limited amount of treatment available for cervical cancer (table 4B). If a national cervical screening programme were to be implemented, there would be additional costs incurred for HPV testing, visual assessment for ablation, and precancer treatment and cancer treatment. We estimated that the total undiscounted 5-year financial costs (2023–2027) for cervical cancer screening, diagnosis and treatment would range from ~US$6.9 million (once lifetime screening) to US$24.8 million (5-yearly (6X lifetime) screening) (table 4B). For the WHO’s ‘elimination strategy’ (twice lifetime screening at age 35 and 45 years), the total 5-year cost would be about US$10.2 million, which averages to US$2.1 million per annum. The cost of the HPV test alone contributed the largest amount to the total 5-year cost, ranging from ~US$3.7 million (53% of total cost, once lifetime) to ~US$17.4 million (70% of total cost, 5-yearly (6X) screening) (figure 4A.B). The costs of treatment for lesions ineligible for ablation and early-stage cancer contributed the second largest cost category, which ranged from US$2.7 million (38% of the total cost, once lifetime) to US$4.9 million (20% of the total cost, 5-yearly (6X) screening). The 10-year budget was approximately double that of the 5-year budget, noting slight differences generated because of the impact of screening as it is introduced over time. On average, estimated undiscounted financial costs over a lifetime per women screened ranged from US$25 per woman (5-yearly screening) to US$40/woman (once lifetime) (data not shown).

Sensitivity analysis

Assumptions around screening coverage and loss to follow-up rates after treatment are the most influential factors on the ASR incidence rates (online supplemental figure A7). In terms of CEA, 0% discount rate for effect, lower self-collected HPV S&T test cost (US$8/test), lower screening coverage, and lower (8%) cancer treatment access rate generally result in reduced ICERs compared with the base case. In contrast, higher screening coverage, higher cancer treatment costs, and a higher assumed cancer treatment access rate (90%) resulted in higher ICERs in almost all strategies (online supplemental table A4). It should be noted that under the (currently counter factual) 90% cancer treatment access assumption, 5-yearly (6X) self-collected HPV S&T screening would not be considered cost-effective at either 1GDPpc or 0.5GDPpc in PNG, however, thrice lifetime screening remained cost-effective at both thresholds in this high cancer treatment scenario.

DISCUSSION

We evaluated the long-term impact of national scale-up of self-collected HPV S&T modality using local field data and found that self-collected HPV S&T was highly effective and cost-effective in PNG when screening up to thrice in a lifetime from age 30 years. Rapid scale-up twice or thrice per lifetime self-collected HPV S&T strategies were cost-effective and could prevent tens of thousands of deaths over the next 50 years. In contrast, primary VIA screening was substantially less effective and was not cost-effective, even when assuming favourable assumptions about test performance for VIA. Our findings were consistent with our modelled evaluations that informed WHO’s updated cervical screening guidelines, which found that primary HPV testing was cost-effective at an average across 78 LMICs. These findings were also consistent with previous published literature on the effectiveness and cost-effectiveness of PoC HPV screen and treat modality in a modelling study on HPV screening in LMICs: Based on data from demonstration projects in Nicaragua, India and Uganda, a modelling study using the Harvard model found that PoC-HPV screen and treat modality would be value-for-money in settings with high lost to follow-up rates and the same day-treatment availability. Our findings about the efficacy of HPV screening in this setting are consistent with results from other modelled evaluations considering HPV self-collection, based on data from ASPIRE and START-UP trials in Uganda. In our study, we found that twice lifetime screening at age 35 and 45 (the WHO screening age and frequency recommendation for cervical cancer elimination) with self-collected HPV S&T can prevent over...
20,000 deaths after 50 years of achieving 70% screening coverage in PNG. In comparison, previous work has shown that twice lifetime screening at age 35 and 45 in addition to 90% HPV vaccination coverage in adolescent females and 90% cancer treatment access (the triple-intervention strategy recommended by WHO) would avert twice as many deaths (42,000) after 50 years in PNG, mostly due to the additional benefits of scaled-up access to cervical cancer treatment.2

We showed that once a national screening programme was established in PNG, a population of under 10 million people, its average annual costs of HPV screening (for thrice lifetime screening) over the first 5 years would be US$3.3 million per annum, including the costs of HPV screening and precancer and cancer treatment. In terms of preparedness for the national HPV screening programme, PNG needs to secure more than 100,000 HPV tests (for thrice lifetime screening) annually over the first 5 years of scaling-up to 70% coverage across the whole population of age-eligible women. In preparation for the full-scale programme roll-out, the health system also needs to improve capacity to provide adequate colposcopy, biopsy and cancer treatment services for more than 1,000 women annually who would be diagnosed with cervical cancer and would therefore require cancer treatment and care. Additionally, PNG also needs to provide up to 16,000 ablative treatment (for thrice lifetime screening) annually for women who would be detected with eligible cervical precancerous lesions. These estimates will support major new implementation effort in the Western Pacific to scale up HPV vaccination, screen-and-treat, and cancer treatment services towards achieving cervical cancer elimination in PNG and more broadly in the region (ECCWP), a collaboration between C4 and the Minderoo foundation.45

In this study, we found that cost of HPV testing accounted for over 50% of the total costs associated with screening, diagnosis and treatment. The current cost of HPV screening used in this model were based on a field trial of self-collected HPV S&T in PNG, and we
made the assumption that this cost would be the same (US$18/test) under national roll-out. However, this cost may reduce for a national screening programme, due to HPV test market shaping and pricing negotiations and lower programme costs when the screening is integrated in the existing health system, which would improve cost-effectiveness as shown in our sensitivity analysis. Given the limited facilities in PNG for cancer diagnosis and treatment, lost to follow-up rates at diagnosis were high and we assumed that late-stage cancers were not treated in the base case. If cancer treatment services for women can be scaled-up in line with the WHO targets for increasing cancer treatment and care, for instance, by increasing radiotherapy services, costs associated with cancer treatment will increase, and deaths associated with cervical cancer would decline. In this case, our sensitivity analysis showed that self-collected HPV S&T remained cost-effective.

There are several limitations to this study. Data sources on the burden of disease for PNG is limited. Cervical cancer incidence and mortality assumptions were based on GLOBOCAN2018 estimates. Because a population-based cancer registry has not been established in PNG, the GLOBOCAN’s estimate utilised data from neighbouring countries in the region. For cancer treatment access rates, we incorporated local expert information on the availability of hysterectomy for early-stage cancers (table 2) and mortality rates were compared well against GLOBOCAN2018 estimates (online supplemental figure A2 (B)). We also assumed that screening could be scaled up rapidly to reach 70% coverage nationally. There will be many challenges to scale-up screening rapidly in lower-resource settings, particularly challenges for scaling-up screening in hard-to-reach rural areas.

This study has many strengths. First, the Policy1-Cervix model has been extensively validated across a range of settings and used to evaluate various cervical screening strategies for many countries. It has been explicitly used to evaluate policy questions for some high-income countries19 21 and was the sole model to be used to evaluate the benefits, harms, and cost-effectiveness of cervical screening algorithms to inform WHO updated 2021 cervical screening guidelines.17 The model was one of three models used by the CCEMC to assess the impacts of cervical cancer elimination strategies on cervical cancer incidence and mortality to inform the WHO global strategy towards cervical cancer elimination.22 25 This model incorporated data on cervical cancer incidence and mortality from GLOBOCAN 2018 and local data on age-specific and type-specific HPV prevalence was used. Second, key model inputs, including loss-to follow-up rates and costing data were derived from the self-collected HPV S&T trial that are currently being conducted in PNG. Third, the ‘screen and treat’ management pathway was consistent with new 2021 WHO cervical screening recommendations and we evaluated it in context of data from local field screening experience and consultation with local experts.

Findings of our study support the WHO strategy for cervical cancer elimination that investing in interventions to meet the 90-70-90 targets offers immense economic and societal benefits. These findings will support major new implementation effort in the Western Pacific to scale up HPV vaccination, screen- and-treat, and cancer treatment services towards achieving cervical cancer elimination in PNG and more broadly in the region (ECCWP).45 However, given the limitations on human resource and infrastructure of the existing health system in PNG, particularly for cervical cancer screening, diagnosis and treatment, in order to scale up cervical screening nationwide, the country would need to develop a cervical screening programme and integrate this screening with the existing primary healthcare services. More importantly, investment in infrastructure and human resource for radiotherapy is needed, which would improve survival across all cancers and not just cervical cancer. A range of practical steps to implement cervical cancer screening and precancer treatment have been developed by WHO.47 The understanding of social, cultural, and religious barriers are crucial to establish referral systems that connect all screening, diagnosis and treatment services, as recommended by the WHO.16

In the 2014 WHO cervical cancer screening guidelines, primary HPV testing was recommended and VIA testing was recommended as an alternative for low-resource settings.3 The recently updated 2021 WHO guidelines now recommend all countries consider primary HPV testing.17 The local experience of self-collected HPV S&T modality has shown that primary HPV testing is feasible and acceptable in PNG, and here we demonstrated that it is also more effective and cost-effective than primary VIA screening; together these findings support the updated 2021 WHO cervical screening guidelines. Our findings are highly relevant for other low-income countries considering screen-and-treat modalities for primary HPV screening.

Author affiliations
1Daffodil Centre, The University of Sydney, Sydney, New South Wales, Australia
2Department of Reproductive Health, Obstetrics and Gynaecology, School of Medicine and Health Sciences, University of Papua New Guinea, Port Moresby, CND, Papua New Guinea
3Department of Obstetrics and Gynaecology, Port Moresby General Hospital, Port Moresby, Papua New Guinea
4Department of Obstetrics and Gynaecology, Modillon Hospital, Mango, Madang, Papua New Guinea
5Department of Obstetrics and Gynaecology, Mt Hagen Provincial Hospital, Mt Hagen, Western Highlands Province, Papua New Guinea
6Kirby Institute, University of New South Wales, Sydney, New South Wales, Australia
7Papua New Guinea Institute of Medical Research, Goroka, Papua New Guinea
8Australian Centre for the Prevention of Cervical Cancer, Melbourne, Victoria, Australia

Twitter Diep Thi Ngoc Nguyen @DiepN99

Contributors DTNN: reviewed literature and field data for model inputs; calibrated the model; performed model simulations and data analyses; drafted and revised the manuscripts. KTS: reviewed data for model inputs; guided for modelling outcomes; reviewed and commented for model outcomes; reviewed and revised manuscripts. AK: provided technical support for the model and reviewed the
manuscripts. GM: provided insights on local context; provided local information that has been used for model assumptions, reviewed and commented on the manuscripts. JW: provided insights on local context; provided local information that has been used for model assumptions, reviewed and commented on the manuscripts. JC: provided insights on local context; provided local information that has been used for model assumptions, reviewed and commented on the manuscripts. PJT: provided local information that has been used for model assumptions, reviewed and commented on the manuscripts. SGB: provided support for field screening trials in PNG, reviewed and comments on the manuscripts. MS: provided support for field screening trials in PNG, reviewed and comments on the manuscripts. AV: conceptualised the field screening trials in PNG, worked closely with local collaborators and gathered very important data from field screening trials in PNG and provided insights on the local context that have been used for model inputs, reviewed and commented on the manuscripts. KC: responsible for the overall content of the manuscript and controlled the decision to publish; conceptualised the modelling study as part of the grant; oversaw the modelling steps and outcomes; reviewed and commented for the data analysis; reviewed and commented on the final version of the manuscript.

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Competing interests MS is Executive Director at VCS Foundation which has developed the canSCREEN digital health platform used in Project ROSE, which is a partnership between the University of Malaya and VCS Foundation. VCS Foundation is a not-for-profit organisation that offers services to implement, support, monitor and manage population health programs. KC and MS are co-PIs of an investigator-initiated trial of cytology and primary HPV screening (Compass; ACRN1261300127707 and NCT023228872), which is conducted and funded by the VCS Foundation (VCS), a government-funded health promotion charity. KC is also an investigator of Compass New Zealand (ACRNT12614000714684), which was conducted and funded by Diagnostic Medlab (DML), now Auckland District Health Board. The VCS Foundation received equipment and a funding contribution from Roche Molecular Systems and Ventana USA and DML received equipment and a funding contribution for Compass from Roche Molecular Systems. However, neither KC nor her institution on her behalf (Daffodil Centre) receives direct funding from industry for this trial or any other project.

Patient consent for publication Not applicable.

Provenance and peer review Not commissioned; externally peer reviewed.

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ORCID iDs
Diep Thi Ngoc Nguyen http://orcid.org/0000-0002-7103-7877
John Walpe Bolinga http://orcid.org/0000-0003-1214-9617

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Supplementary material

Manuscript title: Towards the elimination of cervical cancer in low- and middle-income countries: Effectiveness and cost-effectiveness of point-of-care HPV self-collected testing and treatment in Papua New Guinea

1. Model platform - Policy1-Cervix

A dynamic multicohort model of HPV transmission, HPV vaccination, cervical precancer, cancer survival, screening, diagnosis and treatment (‘Policy1-Cervix’) was used for the evaluation. The model has been used for a wide range of evaluations, including recently being used to predict the timeline to elimination of cervical cancer for 181 countries\(^1\), for 78 low-and lower-middle income countries [Canfell/Brisson], for USA [Burger,JNIC2020] and for Australia\(^2\). It has been used for a range of government-commissioned on behalf of national cervical screening programs in Australia, New Zealand and England; some specific examples of this include: the effectiveness modelling and economic evaluation of cervical screening for both unvaccinated cohorts and cohorts offered vaccination, as part of the Renewal of the cervical screening program in Australia\(^3\), as well as similar screening policy evaluations for New Zealand\(^4\) and England\(^5\). It has also been used to inform provide estimates of resource utilization and disease impacts during the transition from cytology to HPV screening in Australia and New Zealand\(^6-8\) and to inform clinical management guidelines in Australia\(^9\). It has previously been extensively validated and used to evaluate changes to the cervical cancer screening interval in Australia and the United Kingdom\(^10,11\), the role of alternative technologies for screening in Australia, New Zealand and England\(^12-15\), the role of HPV triage testing for women with low-grade cytology in Australia and New Zealand\(^16\), the role of HPV testing for the follow-up management of women treated for cervical abnormalities\(^17\) and the cost-effectiveness of alternative screening strategies and combined screening and vaccination approaches in China\(^18,19\). The model has also been used to evaluate female vaccination\(^20\) and the incremental impact of vaccinating males in Australia\(^21\), the impact of the nonavalent HPV vaccine in four developed countries\(^22\) and to assess the cost-effectiveness of the nonavalent HPV vaccine in Australia\(^23\).

Predictions from the dynamic HPV transmission and vaccination model have also been validated against observed declines in HPV prevalence in women aged 18-24 years after the introduction of the quadrivalent vaccine\(^24\). Model predictions of age-specific cervical cancer incidence and mortality, the rate of histologically confirmed high-grade lesions per 1,000 women screened and overall screening participation rates have been previously validated against national data from Australia, England and New Zealand\(^25-27\) after taking into account local age-specific screening behaviour obtained via analysis of screening registry data. Policy1-Cervix has also been used in conjunction with a model of fertility to estimate the impact of vaccination and screening changes on adverse pregnancy outcomes\(^28\), and with a model of HIV to estimate the impact of HIV control on future cervical cancer\(^29\). Ethnicity-specific models have been developed for New Zealand\(^30\).

The model simulates HPV infection which can persist and/or progress to cervical intraepithelial neoplasia grades I, II and III (CIN1, CIN2, CIN3); CIN 3 can then progress to invasive cervical cancer. Progression and regression rates between states are modelled separately for HPV 16, HPV 18 types, other high-risk nonavalent-included types (31/33/45/52/58), and other non-nonavalent-included high risk types (Appendix Figure 1). The model platform captures the increased risk of CIN2+ recurrence in successfully treated women (compared to the baseline risk of CIN2+ in the population), as previously described\(^28\) (see Figure A1).

For further information, please visit the Policy1-Cervix website
Figure A1: Model structure – Policy-1 Cervix

- **DYNAMIC TRANSMISSION MODEL OF HPV INFECTION, TRANSMISSION AND VACCINATION**
  - Susceptible
  - HPV infection
  - Naturally acquired immunity
  - Vaccine acquired immunity

- **COHORT MODEL OF NATURAL HISTORY OF CERVICAL PRE-CANCER**
  - CIN1
  - CIN2
  - CIN 3

- **COHORT MODEL OF INVASIVE CERVICAL CANCER**
  - 5 and 10 year survival outcomes by stage at diagnosis
  - Cancer incidence and mortality

- **CERVICAL CANCER SCREENING, DIAGNOSIS AND TREATMENT MODEL**
  - Test probability matrix to define screening and diagnostic test outcomes for each underlying health state
  - Management according to potential strategies, taking into account screening history and test outcome
  - Women eligible for ablation treated immediately; Women ineligible for ablation referred; Efficacy of treatment depends on treatment modality.
  - Post-treatment natural history module (incorporating systematic review on probability of recurrence) and HPV test-of-cure according to management strategies

From all health states, age-specific rates for other-cause mortality and for hysterectomy for indications unrelated to cervical cancer are applied.

HPV: Human Papillomavirus; CIN: Cervical Intraepithelial Neoplasia; NS: Non-symptomatic; S: Symptomatic
2. Model calibration:

When adapting the existing Policy1-Cervix model platform to PNG setting, natural history of progression and regression from HPV infection to CIN1, CIN2, CIN3 and from CIN3 to invasive cancer remained unchanged, except for the HPV infection rates. The age-specific HPV infection rates for HPV16, HPV18, high-risk HPV types and other high-risk HPV types were adjusted, depending on the age-specific and type-specific HPV prevalence reported for PNG\textsuperscript{29} to fit to the age-specific cervical cancer incidence rates that reported for PNG\textsuperscript{30}. Additionally, survival rates were also adjusted to fit to age-specific mortality rate\textsuperscript{30}.

Results of model calibration show in figures below:

Figure A2: Model calibration to cervical cancer incidence (A), mortality (B) and HPV prevalence (C) in PNG
3. Cancer treatment access rate and survival assumptions:

The model used 5-year and 10-year stage-specific survival rates for PNG, that have previously published31, but based on advice from local experts on country-specific treatment access rates, we further adjusted to match the cancer mortality estimated by GLOBOCAN 2018.30 Based on consultation with local experts on cancer treatment access rates, treatment capacity was only available for early-stage cancer and not for advanced cervical cancer. Therefore, in base case analysis we assumed 80% of FIGO I cancer and 20% of FIGO II cancer would be treated with hysterectomy and 0% FIGO III and IV cancer were treated. The modelled distribution of cervical cancer stage in PNG was 14%, 55%, 27% and 3% for FIGO stages I, II, III, and IV, respectively. Assuming 80% of FIGO I and 20% of FIGO II cancers receives treatment resulted in 80*14% + 20*55% + 0*27% + 0*3% = 20% of any diagnosed cancer would be treated in base case analysis. This assumption is higher than the treatment access rate assumed in the global analysis by Canfell et al, 2020, which was the estimated access rate to radiotherapy.32 Survival rates were informed by stage-specific survival rates for countries with ~20% cancer treatment access to radiotherapy31 and further adjusted to fit to GLOBOCAN2018 mortality rates. (Table A1, Appendix)

In sensitivity analysis, based on comments from local collaborators that the treatment access was even lower in PNG, we assumed 8% overall cancer treat access rate as previously estimated based on radiotherapy in PNG33 which we assumed a similar survival rates that estimated for PNG as reported by Canfell et al, 2020.31 We also assumed an upper bound of treatment access rate, using WHO 90% target for precancer and cancer treatment for cervical cancer elimination and we assumed survival rates estimated for countries with high treatment access (90%) to radiotherapy as reported by Cancel et al, 2020.31 (Table A1, Appendix)
Table A1: Assumption on 5-year and 10-year survival rates of symptomatic cervical cancer by FIGO stages

<table>
<thead>
<tr>
<th>Cancer stage</th>
<th>5-year (10-year) survival rate at (20% treatment access) - base case analysis</th>
<th>5-year (10-year) survival rate at 8% treatment access - sensitivity analysis (lower bound)*</th>
<th>5-year (10-year) survival rate at 90% treatment access - sensitivity analysis (upper bound)†</th>
</tr>
</thead>
<tbody>
<tr>
<td>FIGO 1</td>
<td>0.640 (0.300)</td>
<td>0.625 (0.073)</td>
<td>0.870 (0.783)</td>
</tr>
<tr>
<td>FIGO 2</td>
<td>0.520 (0.270)</td>
<td>0.480 (0.065)</td>
<td>0.774 (0.693)</td>
</tr>
<tr>
<td>FIGO 3</td>
<td>0.120 (0.060)</td>
<td>0.101 (0.049)</td>
<td>0.599 (0.522)</td>
</tr>
<tr>
<td>FIGO 4</td>
<td>0.010 (0.008)</td>
<td>0.011 (0.008)</td>
<td>0.117 (0.081)</td>
</tr>
</tbody>
</table>

(-) Survival rates at base case (20% treatment access rate) were informed by the survival rates estimated for countries with treatment access rates of ~20% to radiotherapy as reported in Canfell et al., 2020. We further adjusted to fit to GLOBOCAN2018 mortality rates.

(*) Survival rates at sensitivity analysis for lower treatment access rate (8%) were similar the survival rates estimated for PNG with 8.4% treatment access rates to radiotherapy as reported in Canfell et al., 2020.

(†) Survival rates at sensitivity analysis for upper treatment access rates (90%) were similar survival rates estimated for countries with 90% treatment access rate to radiotherapy as reported in Canfell et al., 2020.

4. Cost estimates

For costs of point-of-care self-collected HPV testing, VIA testing/visual assessment for ablative treatment, and thermal ablative treatment, we estimated costs based on financial expenditure from field screening trials in PNG. First, total financial expenses associated with point-of-care self-collected HPV testing, VIA testing, and thermal ablative treatment were calculated, based on financial expenditure on personnel, equipment, and consumables in the screening trial in PNG. We estimated expenditure on staff salaries and clinic equipment (including examination table, examination light, speculums,) used for each participating clinic. These costs were shared among either point-of-care HPV self-collected screening or visual inspection with acetic acid (VIA) and thermal ablation treatment which were provided in each clinic. Besides the above shared costs, there were additionally costs required for specific tests or treatment. For HPV testing, we considered expenditure for point-of-care Xpert HPV test cartridges, sample collection kits and barcode specimen labels. For VIA screening or visual assessment for ablative treatment, the cost of acetic acid was added. For thermal ablative treatment, we considered the cost for thermal ablation equipment (WISAP C3 portable thermal coagulator, battery pack). Secondly, based on clinic records we estimated the total number of women that could be screened per year in each clinic. The final estimated unit costs of point-of-care HPV self-collected test, VIA/visual assessment for ablative treatment, and thermal ablative treatment were US$18, US$6, and US$15, respectively.

Regarding costs associated with cervical cancer diagnosis and treatment, unit costs of two available services – biopsy (US$59) and hysterectomy (US$1614) were estimated in consultation with local collaborators. In consultation with local collaborators, we assumed hysterectomy would be used to treat 80% of FIGO I cases and 20% of FIGO II in base case analysis and in sensitivity analysis scenarios, except for the scenario of a 90% cancer treatment access rate. In the sensitivity analysis considering this high treatment access rate, we assumed PNG would provide cancer treatment for 90% cancer cases across all stages. Therefore, we estimated cancer treatment costs for FIGO III and IV from cancer treatment costs of FIGO I by using multiplication factors of 1.4 and 1.0 respectively. These factors were derived from average stage-specific cancer treatment costs estimated for 21 lower-middle-income countries including PNG reported in Campos et al., 2017. Treatment cost for regional-stage cancers was 40% higher than treatment cost for local cancers and treatment cost for distant-stage cancers was about equal to the cost for local-stage cancers. We simply assumed treatment costs for FIGO III and IV would be equal to costs for regional cancer and distant cancer, respectively. We also assumed treatment costs for FIGO I and II would be equal to treatment cost for local cancer. (Table A2 and Table A3)
Table A2: Factors of cancer treatment costs among cancer stages

<table>
<thead>
<tr>
<th></th>
<th>Local stage</th>
<th>Regional stage</th>
<th>Distant stage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment costs</td>
<td>1765</td>
<td>2494</td>
<td>1689</td>
</tr>
<tr>
<td>Factors</td>
<td>1</td>
<td>1.4</td>
<td>1</td>
</tr>
</tbody>
</table>

Source: Campos et al., 2017

Table A3: Estimated cancer treatment costs for PNG that used in sensitivity analysis considering high cancer treatment access rate

<table>
<thead>
<tr>
<th>FIGO I</th>
<th>FIGO II</th>
<th>FIGO III</th>
<th>FIGO IV</th>
</tr>
</thead>
<tbody>
<tr>
<td>US$1614</td>
<td>US$1614</td>
<td>US$2260</td>
<td>US$1614</td>
</tr>
</tbody>
</table>

5. HPV self-collected testing

In the point-of care HPV self-collected screen and treat (self-collected HPV S&T) trial in PNG, women who come to participating Well women clinics were assessed for eligibility to participate in the trial of point-of-care HPV test using a self-collected vaginal cytobrush specimen. For women who agreed to participate, clinic staff used a laminated pictorial guide to help them explain the correct way to collect vaginal specimens for testing. During the explanation, staff indicated how samples are to be collected using a specimen collection kit reserved for this purpose, and encourage women to use cytobrushes, and to review the pictorial guide themselves. Women were asked to collect her specimens in a private room or the clinic toilet. Self-collected specimens were returned to clinic staff and immediately placed in 20 ml ThinPrep PreservCyt (Hologic, Marlborough, MA) prior to testing for hrHPV on the GeneXpert platform which were conducted in accordance with manufacturer’s instructions and study’s specific SOPs.
6. Supplementary results

6.1. Health outcomes from a single cohort analysis of 38 scenarios

Figure A4: Predicted impacts of screening strategies on cervical cancer incidence and mortality – Base case – 51% sensitivity

![Graph showing predicted impacts of screening strategies on cervical cancer incidence and mortality.]

Note: The performance of VIA screening tests was derived from Toliman et al, 2018. Range of bar charts represents the variation of ASR incidence and mortality by screening ages.

Figure A5: Predicted impacts of screening strategies on cervical cancer incidence and mortality – upper bound – 70% VIA sensitivity

![Graph showing predicted impacts of screening strategies on cervical cancer incidence and mortality.]

Note: The performance of VIA screening tests was derived from systematic reviews. Range of bar charts represents the variation of reduction in ASR incidence and mortality by screening ages.
6.2 Cost-effectiveness analysis

Figure A6: Cost-effectiveness analysis for cervical screening, if favourable (70%) sensitivity of VIA testing were achieved - Sensitivity analysis

Note: The performance of VIA screening tests was based on systematic reviews that reported favourable VIA test performance (70%).

The cost-effectiveness analysis included current situation (no screening) and 38 self-collected HPV S&T and VIA screening scenarios. Incremental Cost-effectiveness Ratios (ICERs) were calculated in US$, 2019. The gross domestic product (GDP) per capita for PNG (0.5GDPpc (US$ 1415 or PGK 4723, World Bank 2019) was used as the indicative willingness-to-pay (WTP) threshold for the evaluation. We also secondarily considered a WTP threshold of 1GDPpc (1GDPpc = US$ 2829 or PGK 9446).
7. Sensitivity analysis

Figure A7: Sensitivity analysis: Impact on cervical cancer incidence
The cost-effectiveness analysis included current situation (no screening) and 38 self-collected HPV S&T and VIA screening scenarios. Incremental Cost-effectiveness Ratios (ICERs) were calculated in US$, 2019. The gross domestic product (GDP) per capita for PNG (0.5GDPpc (US$ 1415 or PGK 4723, World Bank 2019) was used as the indicative willingness-to-pay (WTP) threshold for the evaluation. We also secondarily considered a WTP threshold of 1GDPpc (1GDPpc = US$ 2829 or PGK 9446)

The cost-effectiveness analysis included current situation (no screening) and 38 self-collected HPV S&T and VIA screening scenarios. Incremental Cost-effectiveness Ratios (ICERs) were calculated in US$, 2019. The gross domestic product (GDP) per capita for PNG (0.5GDPpc (US$ 1415 or PGK 4723, World Bank 2019) was used as the indicative willingness-to-pay (WTP) threshold for the evaluation. We also secondarily considered a WTP threshold of 1GDPpc (1GDPpc = US$ 2829 or PGK 9446).
The cost-effectiveness analysis included current situation (no screening) and 38 self-collected HPV S&T and VIA screening scenarios. Incremental Cost-effectiveness Ratios (iCERs) were calculated in US$, 2019. The gross domestic product (GDP) per capita for PNG (0.5GDPpc (US$ 1415 or PGK 4723, World Bank 2019) was used as the indicative willingness-to-pay (WTP) threshold for the evaluation. We also secondarily considered a WTP threshold of 1GDPpc (1GDPpc = US$ 2829 or PGK 9446)

Figure A10: Cost-effectiveness analysis of cervical screening, if best HPV-DNA test sensitivity were achieved - Sensitivity analysis

Figure A11: Cost-effectiveness analysis of cervical screening, if a worst HPV-DNA test sensitivity were achieved - Sensitivity analysis
Figure A12: Cost-effectiveness analysis of cervical screening, if a lower HPV-DNA test cost (US$8) were achieved - Sensitivity analysis

The cost-effectiveness analysis included current situation (no screening) and 38 self-collected HPV S&T and VIA screening scenarios. Incremental Cost-effectiveness Ratios (ICERs) were calculated in US$, 2019. The gross domestic product (GDP) per capita for PNG (0.5GDPpc (US$ 1415 or PGK 4723, World Bank 2019) was used as the indicative willingness-to-pay (WTP) threshold for the evaluation. We also secondarily considered a WTP threshold of 1GDPpc (1GDPpc = US$ 2829 or PGK 9446)

Figure A13: Cost-effectiveness analysis of cervical screening, if a 90% screening coverage were achieved – Sensitivity analysis

The cost-effectiveness analysis included current situation (no screening) and 38 self-collected HPV S&T and VIA screening scenarios. Incremental Cost-effectiveness Ratios (ICERs) were calculated in US$, 2019. The gross domestic product (GDP) per capita for PNG (0.5GDPpc (US$ 1415 or PGK 4723, World Bank 2019) was used as the indicative willingness-to-pay (WTP) threshold for the evaluation. We also secondarily considered a WTP threshold of 1GDPpc (1GDPpc = US$ 2829 or PGK 9446)
Figure A14: Cost-effectiveness analysis of cervical screening, if a 50% screening coverage were achieved – sensitivity analysis

The cost-effectiveness analysis included current situation (no screening) and 38 self-collected HPV S&T and VIA screening scenarios. Incremental Cost-effectiveness Ratios (ICERs) were calculated in US$, 2019. The gross domestic product (GDP) per capita for PNG (0.5GDPpc ($US 1415 or PGK 4723, World Bank 2019) was used as the indicative willingness-to-pay (WTP) threshold for the evaluation. We also secondarily considered a WTP threshold of 1GDPpc (1GDPpc = $US 2829 or PGK 9446).

Figure A15: Cost-effectiveness analysis of cervical screening, if a 0% discount rate for effect were considered – sensitivity analysis

The cost-effectiveness analysis included current situation (no screening) and 38 self-collected HPV S&T and VIA screening scenarios. Incremental Cost-effectiveness Ratios (ICERs) were calculated in US$, 2019. The gross domestic product (GDP) per capita for PNG (0.5GDPpc ($US 1415 or PGK 4723, World Bank 2019) was used as the indicative willingness-to-pay (WTP) threshold for the evaluation. We also secondarily considered a WTP threshold of 1GDPpc (1GDPpc = $US 2829 or PGK 9446).
Figure A16: Cost-effectiveness analysis of cervical screening, if a low loss-to-follow-up (10%) at post-ablative treatment of eligible precancers at 12 months were considered – sensitivity analysis

The cost-effectiveness analysis included current situation (no screening) and 38 self-collected HPV S&T and VIA screening scenarios. Incremental Cost-effectiveness Ratios (ICERs) were calculated in US$, 2019. The gross domestic product (GDP) per capita for PNG (0.5GDPpc (US$ 1415 or PGK 4723, World Bank 2019) was used as the indicative willingness-to-pay (WTP) threshold for the evaluation. We also secondarily considered a WTP threshold of 1GDPpc (1GDPpc = US$ 2829 or PGK 9446)

Figure A17: Cost-effectiveness analysis of cervical screening, if higher cancer treat costs (+20% of that costs at base case) were considered – sensitivity analysis

The cost-effectiveness analysis included current situation (no screening) and 38 self-collected HPV S&T and VIA screening scenarios. Incremental Cost-effectiveness Ratios (ICERs) were calculated in US$, 2019. The gross domestic product (GDP) per capita for PNG (0.5GDPpc (US$ 1415 or PGK 4723, World Bank 2019) was used as the indicative willingness-to-pay (WTP) threshold for the evaluation. We also secondarily considered a WTP threshold of 1GDPpc (1GDPpc = US$ 2829 or PGK 9446)
Table A4: Summary of impact on ICERs in sensitivity analyses** - for strategies that appeared on the cost-effectiveness frontier in the base case (arrows compare to base case ICER)

<table>
<thead>
<tr>
<th>Screening strategies</th>
<th>1X age 40 self-collected HPV S&amp;T</th>
<th>1X age 35 self-collected HPV S&amp;T</th>
<th>2X age 35, 40 self-collected HPV S&amp;T</th>
<th>2X age 30,40 self-collected HPV S&amp;T</th>
<th>3X age 30, 35,40 self-collected HPV S&amp;T</th>
<th>5-yearly 30-55 self-collected HPV S&amp;T</th>
<th>2X age 35,45 self-collected HPV S&amp;T</th>
<th>1X VIA age 40 *</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Base case</strong></td>
<td>Dominated</td>
<td>$311</td>
<td>$460</td>
<td>$568</td>
<td>$656</td>
<td>$1659</td>
<td>Dominated</td>
<td>Dominated</td>
</tr>
<tr>
<td>Best sensitivity of HPV test (95.3% for CIN2+)</td>
<td>Dominated</td>
<td>$295</td>
<td>$495</td>
<td>$569</td>
<td>$589</td>
<td>$1679</td>
<td>Dominated</td>
<td>Dominated</td>
</tr>
<tr>
<td>Worst sensitivity of HPV test (89.1% for CIN2+)</td>
<td>Dominated</td>
<td>$299</td>
<td>Dominated</td>
<td>$530</td>
<td>$709</td>
<td>$1403</td>
<td>Dominated</td>
<td>Dominated</td>
</tr>
<tr>
<td>Higher screening coverage (90%)</td>
<td>$303</td>
<td>$464</td>
<td>Dominated</td>
<td>$468</td>
<td>$812</td>
<td>$1764</td>
<td>Dominated</td>
<td>$300</td>
</tr>
<tr>
<td>Lower screening coverage (50%)</td>
<td>Dominated</td>
<td>$283</td>
<td>Dominated</td>
<td>$420</td>
<td>$771</td>
<td>$1654</td>
<td>Dominated</td>
<td>Dominated</td>
</tr>
<tr>
<td>Lower loss to follow-up rates (10%) at post-treatment follow-up at 12 months</td>
<td>$295</td>
<td>$334</td>
<td>Dominated</td>
<td>$600</td>
<td>$673</td>
<td>$1605</td>
<td>$439</td>
<td>Dominated</td>
</tr>
<tr>
<td>Lower HPV-DNA test cost (US$8)</td>
<td>Dominated</td>
<td>$178</td>
<td>$255</td>
<td>$401</td>
<td>$362</td>
<td>$843</td>
<td>Dominated</td>
<td>Dominated</td>
</tr>
<tr>
<td>Higher cancer treatment costs (+ 20%)</td>
<td>Dominated</td>
<td>$314</td>
<td>$469</td>
<td>$585</td>
<td>$661</td>
<td>$1672</td>
<td>Dominated</td>
<td>Dominated</td>
</tr>
<tr>
<td>Discounted rate for effect at 0%</td>
<td>$60</td>
<td>$79</td>
<td>$90</td>
<td>$145</td>
<td>$258</td>
<td>$59</td>
<td>Dominated</td>
<td>Dominated</td>
</tr>
<tr>
<td>Lower treatment access (8%)</td>
<td>Dominated</td>
<td>$288</td>
<td>$409</td>
<td>$446</td>
<td>$592</td>
<td>$1516</td>
<td>Dominated</td>
<td>Dominated</td>
</tr>
<tr>
<td>High end assumption cancer treatment access and survival (90%)</td>
<td>$420</td>
<td>$424</td>
<td>Dominated</td>
<td>$959</td>
<td>$992</td>
<td>$4016</td>
<td>$710</td>
<td>$369</td>
</tr>
</tbody>
</table>

Incremental Cost-effectiveness Ratios (ICERs) were calculated in US$, 2019
The gross domestic product (GDP) per capita for PNG (0.5GDPpc (US$ 1415 or PGK 4723, World Bank 2019) was used as the indicative willingness-to-pay (WTP) threshold for the evaluation. We also secondarily considered a WTP threshold of 1GDPpc (1GDPpc = US$ 2829 or PGK 9446)
(#) WHO cervical screening recommendation for cervical cancer elimination was added for comparison
(*) VIA cervical screening strategy appeared in some sensitivity analysis scenarios
(**) Please see cost-effectiveness plan figures in the main manuscript and in appendix for detail of cost-effective scenarios and ICERs presented in this table.

Appendix References


