High-risk human papillomavirus testing for underscreened populations: cost-effectiveness and affordability in three country settings

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Abstract

Background The high-risk human papillomavirus (hrHPV)-based screening recommended by the World Health Organization is expected to lead to worldwide reduction of the cervical cancer burden, but the countries burdened most by cervical cancer also struggle with the costs of transitioning to this approach. Country-specific evaluations are needed to inform policymakers on implementation of hrHPV-based screening for their setting. Following initial implementation in Uganda, Bangladesh and Slovakia focused on underscreened women in the PRESCRIP-TEC project, we investigated the potential cost-effectiveness and affordability of hrHPV-based screening strategies.

Methods Country-specific model-based cost-effectiveness and budget impact analyses were conducted for the three countries, comparing the PRESCRIP-TEC strategy with the existing screening strategy in each setting. Data from initial project implementation informed the relevant model parameters.

Results The PRESCRIP-TEC strategy resulted in disability-adjusted life year (DALY) gains in all three countries. The cervical cancer incidence rate was reduced by a third for Uganda, 15% for Bangladesh and 11% for Slovakia. The incremental cost-effectiveness ratios were UGX 0.56 million per DALY for Uganda (I$ 475), BDT 76 thousand per DALY for Bangladesh (I$ 1698) and EUR 1782 (I$ 3637) per DALY for Slovakia. Substantial additional funding will be required to enable implementation, particularly in relation to the initial start-up costs.

Conclusions The provided estimates can serve to inform policymakers and researchers in the context of implementing hrHPV-based screening in diverse settings.

Keywords Cervical cancer, Screening, Cost-effectiveness, Budget impact, High-risk human papillomavirus, Economic evaluation

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Background

The global burden of cervical cancer remains high, with estimated 660 thousand new cases and 350 thousand deaths annually [1]. While its burden has been substantially reduced in high-income countries through organized cytology-based screening, many low- and middle-income countries (LMICs) struggle with cervical cancer prevention due to high costs of implementing organized screening [2]. This has resulted in large numbers of underscreened women (i.e. women who have not been screened with the recommended frequency according to the WHO guidelines), subjected to higher risks of developing cervical cancer. Most LMICs rely on visual inspection with acetic acid (VIA) for screening [3], the accuracy of which can be subject to high degree of variability in practice. VIA screening is often provided opportunistically without systematically organized screening programs in place. Meanwhile, even in high-income countries, substantial gaps in cervical cancer screening coverage still remain for marginalized population subgroups, such as ethnic minorities, women with migrant backgrounds and sex workers [4, 5].

In light of these issues, the World Health Organization (WHO) has adopted high-risk human papillomavirus (hrHPV) testing as the recommended primary screening method for cervical cancer as part of the global strategy of cervical cancer elimination [6]. The self-sampling option can increase uptake among underscreened populations [7, 8]. In addition, compared to cytology or VIA, hrHPV testing offers higher sensitivity and specificity [9]. Countries with VIA-based programs are especially urged to transition to hrHPV testing. However, before initiating national implementation of a novel screening strategy, governments must consider the associated costs and potential health impact first. Various factors can influence the economic value of cervical cancer screening [10], including epidemiological factors related to prevalence of HPV and cervical cancer, quality of existing screening policies in place, and the programmatic costs of implementing and sustaining a screening strategy, achieving sufficient uptake of screening and adherence to follow-up. These context-specific factors require consideration of how the screening strategy will be implemented in each country's setting.

As part of the PREvention and SCReening Innovation Project Toward Elimination of Cervical Cancer (PRESCRIP-TEC), the feasibility of the WHO-recommended hrHPV self-sampling was investigated in several countries with a focus on underscreened populations [11]. Following the initial implementation of hrHPV-based screening in Bangladesh, Uganda and Slovak Republic, the aim of this work was to investigate the cost-effectiveness and affordability of the hrHPV-based screening strategies.

Methods

Analysis setup

Model-based country-specific cost-effectiveness analyses and budget impact analyses were conducted for Uganda, Bangladesh and Slovak Republic. The disease model of cervical cancer progression was based on a previous microsimulation model [12]. The analyses were conducted from the healthcare system/payer perspective, comparing the country-specific hrHPV-based screening strategy (hereinafter referred to as "PRESCRIP-TEC" strategy) against the country-specific existing screening practice/policy ("business-as-usual" (BAU) strategy). The evaluated strategies were based on the WHO's recommendations for general female populations, excluding women living with human immunodeficiency virus, for whom separate guidelines have been produced.

The cost-effectiveness analysis setup is summarized in Table 1, and the strategies for each country are visualized in the appendix (Figures S1-S6). The formulation of country-specific screening strategies in the PRESCRIP-TEC project was informed by the WHO recommendations and adhered to the national guidelines specifying age eligibility in each country setting. In the case of Slovak Republic, in accordance with advice from the Ministry of Health, a lower starting age of eligibility was used for the PRESCRIP-TEC strategy compared to the existing screening policy due to the lower average of marriage in the target population. In addition, while ablative treatment was not used in Slovak Republic in the PRESCRIP-TEC or BAU strategy in the project implementation, we chose to include it in the modelled strategies similarly to Uganda and Bangladesh, considering that it is recommended as part of WHO guidelines and could be implemented in the future.

The main outcomes of the cost-effectiveness analyses were the projected population health impact, expressed as disability-adjusted life years (DALYs), and costs. We note that disability weights were only applied for the cervical cancer model state due to the asymptomatic nature of pre-cancer states. Therefore, the DALYs in this study were calculated and interpreted as incremental life years (life years gained) adjusted for disability incurred by cervical cancer, representing health gains in terms of life expectancy. This is in contrast to the more commonly reported indicator of DALYs averted, which instead represents the reduction of disease burden.

Costs were expressed in national currency units of each country, as well as 2022 international dollars (I$), which represents a hypothetical currency unit adjusted for purchasing power differences between countries. The results from the cost-effectiveness analyses were used to estimate the 5-year budget impact for defined target populations in each country (more details on the estimation are provided in Tables S5-S6 in the appendix). The budget

Table 1 Country-specific screening strategies compared in cost-effectiveness analysis

			Countries		
		Strategies compared	**Bangladesh**	**Uganda**	**Slovak Republic**
Population		Hypothetical cohorts of 100 000 women, subject to country-specific all-cause mortality, modeled from birth to death			
Intervention	Primary screening test	PRESCRIP-TEC	hrHPV (self-sampled or provider-collected)		
		BAU	VIA	VIA	Cytology
	Eligible ages (years)	PRESCRIP-TEC	30-60	25-50	19-64
		BAU			23-64
	Triage test	PRESCRIP-TEC	VIA	None	Cytology
		BAU	None		None
	Treatment options	Ablative treatment (cryotherapy, thermal ablation), excisional treatment (LEEP)			
	Method to determine treatment option	PRESCRIP-TEC	VIA (visual assessment for treatment)	VIA (visual assessment for treatment)	Colposcopy
		BAU			
	Interval (years)	PRESCRIP-TEC	5	5	5
		BAU		3	1-1-3[a]
	Follow-up screening (years)	1			
Comparison		PRESCRIP-TEC vs BAU			
Outcomes		Incremental disability-adjusted life years per woman, incremental costs per woman			

[a]Two negative results in two years required to switch to three-year interval

Abbreviations: *BAU* business-as-usual, *VIA* visual inspection with acetic acid, *LEEP* loop electrosurgical excision procedure

impact was interpreted as the impact of implementing the PRESCRIP-TEC strategy from 2024 for the target populations, including the community mobilization campaigns required to achieve improved uptake of screening compared to existing screening policy in each setting.

The PRESCRIP-TEC project aimed to include vulnerable populations in the countries, which were selected to provide a geographically and culturally diverse mix of implementation settings. In consultation with local NGOs implementing screening, these populations were selected for the project due to their reduced access to healthcare facilities and lack of participation in a national screening program. In the context of the present evaluation study, these target populations were also defined as the target populations for the budget impact calculation. This contrasts with defining all women of eligible ages in each country as the target population, since the project-based outcomes would potentially be less applicable for such national implementation. For Uganda, the target population was the rural female population of eligible ages. For Bangladesh, two different target populations were defined: (1) women of eligible ages in catchment areas of the partner institution (Friendship), representing an expanded implementation of PRESCRIP-TEC strategy to the maximum reach of the institution, and (2) women of eligible ages living in slums and floating dwellings based on national demographic data. For Slovak Republic, the eligible population was defined as female Roma population of eligible ages.

Model parameters

The disease model contained a total of 7 states (Fig. 1). The probabilities of transitioning between model states at 1-year cycles were informed by relevant literature [12], and were calibrated separately to each country's hrHPV prevalence, cervical cancer incidence rates and survival rates (details on the disease model and adaptation are provided in the Appendix). For the cost-effectiveness analysis, a lifetime horizon was used in the model, with each individual simulated from age 0 until death. In contrast, the budget impact was estimated for a 5-year time horizon, using average 5-year cost results from the cost-effectiveness analysis.

The parameters related to screening strategies and cost-effectiveness were based on project data, relevant literature, and expert opinions. Parameter uncertainty was explored via one-way probabilistic sensitivity analysis. The full list of parameters is provided in Table S3. Specifically, data from the project implementation informed the parameters of screening uptake and adherence to treatment of pre-cancer. The screening uptake parameter was informed by the project data both for the PRESCRIP-TEC strategy (proportion of women accepting the hrHPV test out of all women were offered the hrHPV test) and BAU strategy (proportion of women reporting ever having ever been tested for cervical cancer in the control area), adjusted for the number of lifetime screening rounds. The adherence to treatment parameter was also informed by project data (proportion of women treated out of all women who were tested positive at the

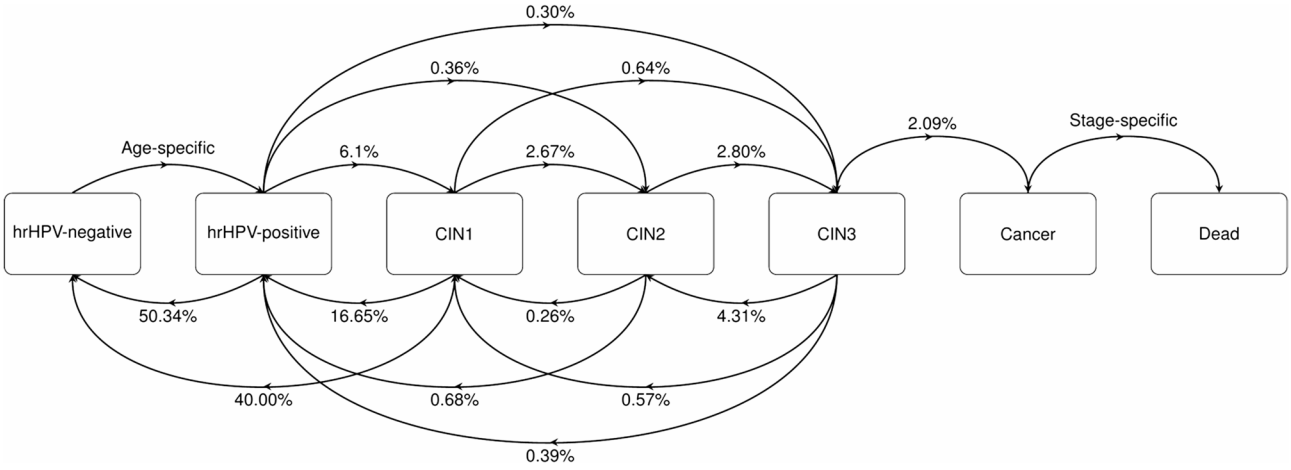

Fig. 1 Disease model structure. The 1-year transition probabilities between health states are represented by arrows from states (placed above the state) and to states (placed below the state). HrHPV - high-risk human papillomavirus, CIN - cervical intraepithelial neoplasia

previous step in the screening flow and were offered treatment), with the exception of Slovak Republic, where the colposcopy and treatment steps of the screening flow were combined into a single treatment visit in practice. Thus, for Slovak Republic this parameter was expressed in the adherence to colposcopy parameter instead.

In terms of cost parameters, the study used financial costs, focusing on the potential fiscal burden on the healthcare system in the budget impact analysis, and not economic (opportunity) costs, estimating which was not considered feasible. In the absence of national guidelines for cost-effectiveness thresholds, we adopted a strict willingness-to-pay (WTP) threshold of 10% of the national gross domestic product (GDP) per capita, which was further explored via cost-effectiveness acceptability curves. We decided not to apply the commonly used 1–3 times GDP per capita thresholds due to potential issues associated with their use in LMICs [13]. Previous attempts at informing more relevant country-specific thresholds have suggested considerably lower values specifically for low-income countries [14, 15]. Differential discounting was applied with a 3% annual rate for costs and zero discounting for health effects, similarly to the approach used in the updated WHO-CHOICE methods [16]. The cost parameters were informed by project-based costs, including a preliminary costing study conducted in Bangladesh and Uganda [17], supplemented by estimates from local partners and relevant literature.

Results

Cost-effectiveness analysis

The PRESCRIP-TEC strategy produced health gains for all three countries compared to BAU, with the highest potential increase estimated in Uganda (0.17 mean incremental DALYs per woman). The cervical cancer incidence rate was reduced by approximately a third for Uganda, 38% for Bangladesh and 11% for Slovak Republic. The incremental cost-effectiveness ratios were UGX 0.56 million per DALY gained for Uganda (I$ 475), BDT 47.12 thousand per DALY gained for Bangladesh (I$ 1698) and EUR 1.78 thousand per DALY gained (I$ 3637) for Slovak Republic. The results are summarized in Table 2. Visualizations in the form of cost-effectiveness planes are presented in the appendix (Figures S7-S9).

Most simulations for the countries saved DALYs while adding costs from the healthcare system perspective and were therefore located in the "North-East" region of the cost-effectiveness plane (Figures S7-S9). To explore the impact of the strict WTP threshold on the evaluated PRESCRIP-TEC strategy, the proportions of these results under different WTP thresholds are presented in the form of cost-effectiveness acceptability curves (Figs. 2, 3 and 4). "Acceptability" in this context is interpreted as the probability of the strategy being cost-effective, dependent on the "decision rule" (WTP threshold).

For Uganda, raising the WTP threshold from 10 to 20% GDP per capita would increase the acceptability of the PRESCRIP-TEC strategy from 8 to 66%, reaching almost 90% acceptability at the WTP threshold of 60% GDP per capita. In contrast, the acceptability for Bangladesh was lower, starting at only 15% at the 0.1 GDP per capita WTP used in the base case analysis, and peaking at 76% at 0.7. For Slovak Republic, the 10% threshold resulted in 65% acceptability, which peaked at 74% at the 30% WTP threshold.

Sensitivity analysis

Simple one-way probabilistic sensitivity analysis was conducted for the screening-related parameters. Tornado plots are provided in the appendix for the Bangladesh model (Figures S10-S11) for illustration. The model was generally robust to variation in the parameters in terms

Table 2 Country-specific cost-effectiveness analyses results

Outcome	Country	PRESCRIP-TEC	BAU	Incremental
Mean costs per woman (SD) – national currency units	Uganda	UGX 117 788.57 (488.27)	UGX 20 633.65 (486.42)	UGX 97 154.92 (669.36)
	Bangladesh	BDT 4 206.12 (29.92)	BDT 821.04 (45.22)	BDT 3 385.08 (57.21)
	Slovak Republic	EUR 100.52 (0.15)	7.87 (0.13)	92.65 (0.22)
Mean costs per woman (SD) – I$	Uganda	I$ 99.96	I$ 17.51	I$ 82.45
	Bangladesh	I$ 151.57 (1.08)	I$ 29.59 (1.63)	I$ 121.98 (2.06)
	Slovak Republic	I$ 205.14	I$ 16.06	I$ 189.09
Mean total DALYs per woman (SD)	Uganda	68.90 (0.08)	68.72 (0.07)	0.17 (0.09)
	Bangladesh	74.51 (0.07)	74.44 (0.06)	0.07 (0.08)
	Slovak Republic	79.34 (0.04)	79.29 (0.04)	0.05 (0.06)
Mean cervical cancer incidence rate per 100 000 woman-years at risk (SD)	Uganda	20.25 (0.54)	30.76 (0.63)	0.66[a]
	Bangladesh	4.47 (0.20)	7.21 (0.32)	0.62[a]
	Slovak Republic	22.70 (0.53)	25.63 (0.51)	0.89[a]
Mean incremental cost-effectiveness ratio – national currency units	Uganda		UGX 559 689.63	
	Bangladesh		BDT 47 121.89	
	Slovak Republic		EUR 1 782.04	
Mean incremental cost-effectiveness ratio – I$	Uganda		I$ 474.97	
	Bangladesh		I$ 1 698.09	
	Slovak Republic		I$ 3 636.83	

[a]Rate ratio

Abbreviations: *SD* standard deviation, *BAU* business-as-usual, *UGX* Ugandan shilling, *BDT* Bangladeshi taka, *EUR* euro, *I$* 2022 international dollar

of their impact on the health outcomes, without any of parameters resulting in much larger variation than others, while the incremental costs were subject to slightly larger variation from the coverage parameter. Compared to the range of incremental DALYs in the cost-effectiveness analysis (−0.09-0.28), the values across the sensitivity analysis results ranged from −0.22 to 0.32. Incremental costs per woman in the sensitivity analysis were also relatively stable, ranging between BDT 2927 and BDT 3856 (I$ 105–139), compared to BDT 3211–3496 (I$ 116–126).

Budget impact

The budget impact analysis results are presented in Table 3 (more details are presented in Tables S5-S6 in the appendix). For Uganda, where the scenario included all eligible rural women, the 5-year budget impact was estimated at over UGX 115 billion, corresponding to approximately I$ 142.31 million. For Bangladesh, the impact of implementing the strategy at maximum reach of the partner institution (Friendship) was estimated at BDT 77.70 million (I$ 2.80 million), while targeting all eligible women living in slums and floating dwellings would require over BDT 413 million (I$ 14.89 million). For the female Roma population in Slovakia, the impact was estimated at EUR 1.25 million. It is important to note that these impact estimates represent the total 5-year cost of offering screening to women of eligible ages in the target population once (in 2024), which results from the 5-year interval between hrHPV-based screenings, including the associated screening and treatment costs from the healthcare system perspective. The budget impact of continued screening for eligible women in subsequent years will depend on coverage and follow-up rates achieved in practice for different age groups, and will need to be assessed accordingly.

Discussion

Our model-based analysis suggests that the recommended hrHPV-based approach as implemented in PRESCRIP-TEC could be effective in reducing cervical cancer incidence in the three country settings (Uganda, Bangladesh, and Slovak Republic). The screening strategies were estimated to produce health gains for all three countries in terms of life years, with the highest increase observed in Uganda, as well as substantial reductions in cervical cancer incidence. In general, the acceptability curves indicated that either lowering the overall costs of the screening strategy or increasing the WTP thresholds (at least above 0.2 GDP per capita) would be needed for the strategy to be considered cost-effective in Bangladesh and Uganda from the healthcare system perspective. Due to Slovakia's high GDP per capita, the strategy was estimated to be cost-effective even at 0.1 GDP per capita threshold.

Interpretation of results

In case of Uganda, the relatively high DALY gain can be explained by the very low existing screening coverage and relatively high burden of hrHPV and cervical cancer. However, even with this improvement, approximately 40% overall reduction of costs would be needed to meet the strict 0.1 GDP per capita WTP threshold. The strategy could still be considered cost-effective in Uganda while remaining under 1 GDP per capita WTP threshold (reaching over 90% "acceptability) in line with

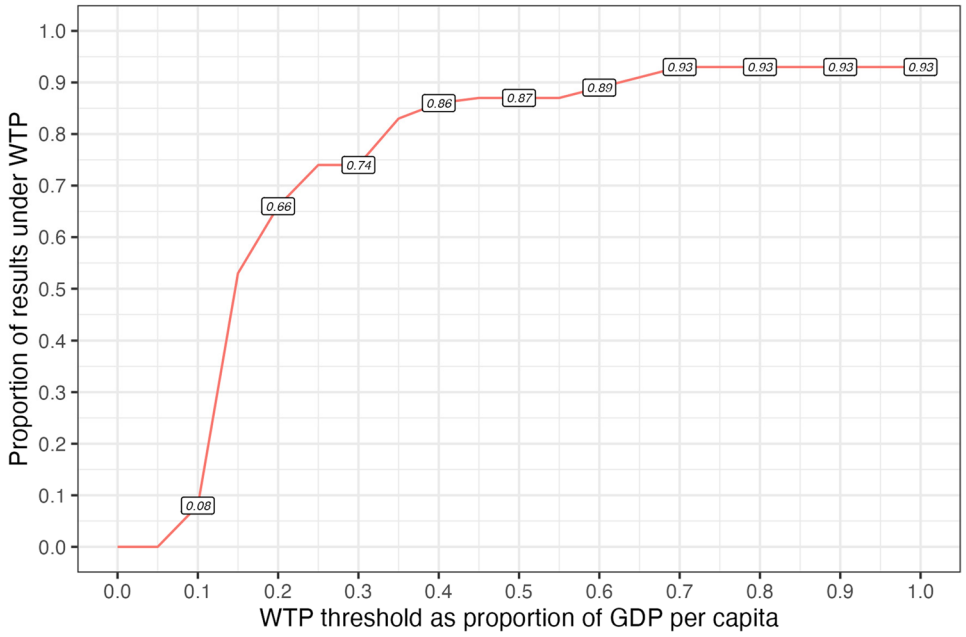

Fig. 2 Cost-effectiveness acceptability curve - Uganda. The plotted curve represents the proportion of simulations with positive incremental DALYs and costs under each WTP threshold level (expressed as proportions of GDP per capita in 10% increments). WTP - willingness-to-pay, GDP - gross domestic product

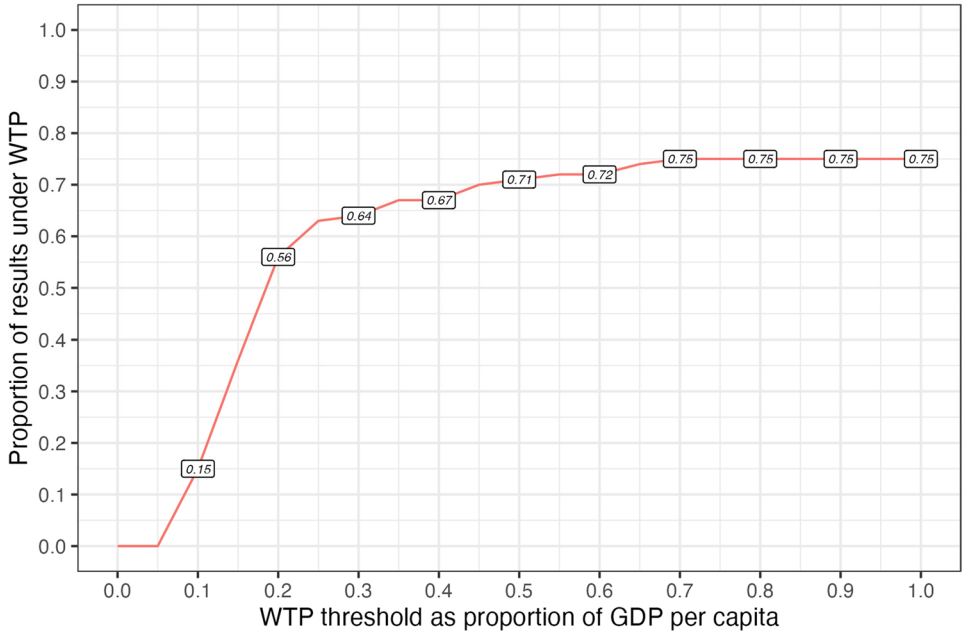

Fig. 3 Cost-effectiveness acceptability curve - Bangladesh. The plotted curve represents the proportion of simulations with positive incremental DALYs and costs under each WTP threshold level (expressed as proportions of GDP per capita in 10% increments). WTP - willingness-to-pay, GDP - gross domestic product

the WTP thresholds of 1-3 times GDP per capita commonly used in cost-effectiveness evaluations [13], in which case being under 1 times GDP per capita would be interpreted as "very cost-effective". However, when considering affordability from the budget impact perspective, due to Uganda's target population including all women of eligible ages living in rural areas, its estimated 5-year budget impact (over I$ 142 million) was not only considerably higher than in Bangladesh or Slovak Republic in absolute numbers, but also in the context of health expenditure, constituting around 9.8% of the total annual domestic general governmental health expenditure in the

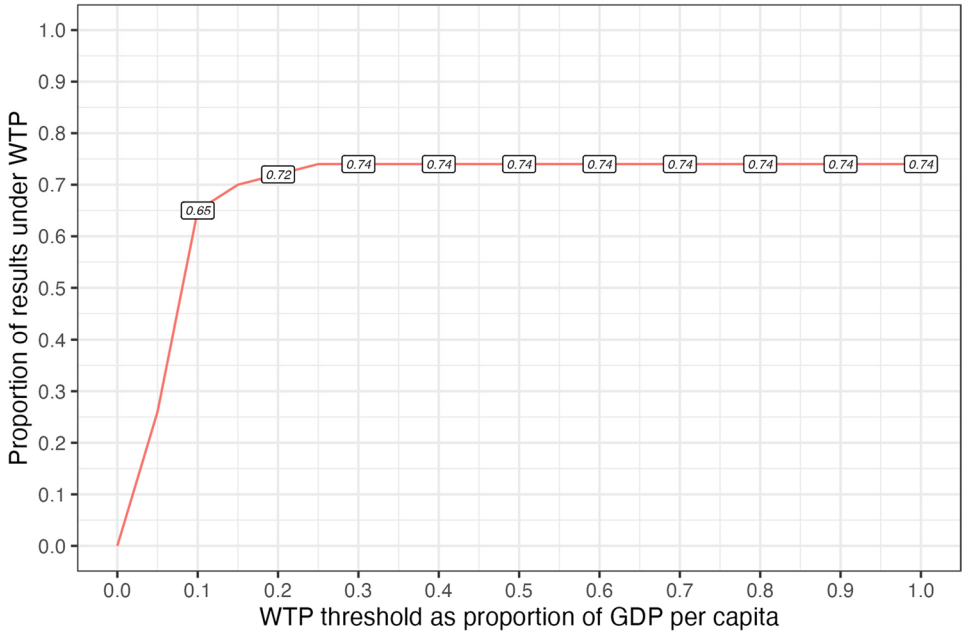

Fig. 4 Cost-effectiveness acceptability curve – Slovak Republic. The plotted curve represents the proportion of simulations with positive incremental DALYs and costs under each WTP threshold level (expressed as proportions of GDP per capita in 10% increments). WTP - willingness-to-pay, GDP - gross domestic product

Table 3 Country-specific budget impact analyses results

Estimate	Uganda	Bangladesh		Slovak Republic
Target population size	5 074 560 (rural)	49 760 (catchment area of Friendship)	264 537 (slums and floating dwellings)	43 674 (Roma)
Mean 5-year incremental costs per target woman – local currency units	UGX 11 782.87	BDT 227.28		EUR 6.59
Mean 5-year incremental costs per target woman – I$	I$ 10.00	I$ 8.19		I$ 13.44
Unit cost per target woman – local currency units	UGX 33 045.85	BDT 1561.45		EUR 28.55
Unit cost per target woman – I$	I$ 28.04	I$ 56.27		I$ 58.26
5-year budget impact of implementing in 2024 for the target population – local currency units	UGX 115 171 510 742	BDT 77 697 510	BDT 413 060 012	EUR 1 246 762
5-year budget impact of implementing in 2024 for the target population – I$	I$ 142 309 436	I$ 2 799 910	I$ 14 885 046	I$ 2 544 412

Abbrevations: *UGX* Ugandan shilling, *BDT* Bangladeshi taka, *EUR* euro, *I$* 2022 international dollar

country (UGX 1.72 trillion (I$ 1.46 billion)) [18]. In this context, it is important to note that the cost parameters based on a preliminary costing study in a limited number of facilities were also subject to considerable uncertainty, and will need to be validated in the future. In particular, the cost estimate of excisional treatment in Uganda was quoted as a gross cost of procedure by the provider facility, likely including a substantial markup, which we were not able to verify. It should also be noted that the number of facilities available to perform the procedure is limited in practice in this setting, meaning that a similar cost may still apply in the case of expanded or national implementation, particularly if costs of additional training and infrastructure to expand the capacity are not considered. More detailed microcosting will need be conducted in Uganda to ascertain more reliable cost estimates of treatment procedures, so that budget impact of hrHPV testing can be estimated more accurately.

In contrast, for Bangladesh, where the existing screening coverage was estimated to be slightly higher (in the areas involved in PRESCRIP-TEC) and the burden of hrHPV and cervical cancer was lower compared to Uganda, the health gain was estimated to be more modest, requiring approximately an 85% cost reduction to reach the same threshold. The potential gain in life years, while lower relative to Uganda, is still an important outcome, considering that the existing coverage (the BUA strategy) may be even lower in other areas of the country. Due to the population size of Bangladesh, in terms of budget impact, the two target population scenarios

constituted less than a percent (0.0013 and 0.0067) relative to reported total annual governmental health expenditure (BDT 61.53 billion (I$ 2.70 billion)) [18]. However, when considered on a per-capita basis, the modeled per-woman impact accounted for 31.49% of the country's total health expenditure per capita (I$ 178.71) and was almost 5 times the governmental health expenditure per capita (I$ 11.58). In this context, it should be noted that the relative share of the community mobilization campaign costs as part of total budget impact was higher for Bangladesh, for which the unit cost increased almost seven-fold through inclusion of community mobilization costs. While this was to be expected given the accessibility of rural areas involved, future community mobilization efforts could be integrated more closely with other national health initiatives to leverage existing infrastructure and reduce such costs. Whether the smaller, more specific target populations defined for the budget impact analysis in Bangladesh are relevant for national implementation efforts will need to be considered by the country's policymakers. Additionally, as previously discussed, the preliminary costs estimated through the costing study are subject to high uncertainty, in particular with regards to treatment costs, whereby the excisional treatment cost for Bangladesh was estimated to be considerably lower than in Uganda and Slovak Republic (I$ 177 versus I$ 849 and I$ 1020 for Uganda and Slovak Republic respectively). These costs will need to be examined further in these settings across a larger and more representative number of facilities.

Finally, Slovakia's status as a high-income country presents a different case to consider from a policy perspective. The focus of the strategy was on a specific underserved population group (Roma), as opposed to more broadly defined rural, hard-to-reach populations in Uganda and Bangladesh. We therefore note that the results for this setting are less applicable for a national program for general population, but more relevant for a scaled-up implementation of hrHPV testing targeting Roma communities throughout the country. The estimated health gain (0.05 DALYs) was smaller on average than in Bangladesh and Uganda. Nevertheless, due to the country's high GDP level, it was sufficient to be cost-effective on average even under the strict 0.1 GDP per capita threshold. The estimated 5-year budget impact (EUR 1.25 million (I$ 2.54 million) for the small target population would be a miniscule proportion of the country's total annual governmental health expenditure (approximately EUR 6.77 billion (I$ 13.81 billion) [18], and would represent only 1.84% of the per-capita total health expenditure (I$ 3168.87). Priority-setting at the regional level in the country will need to be informed by initial implementation results from the underserved Roma community for targeted implementation efforts to succeed in the future.

Policy implications

In the context of potential affordability of hrHPV-based screening in these countries, it is important to consider the policymakers' perspective. The health expenditures of the countries constitute less than 10% of their GDP (2.39% for Bangladesh, 4.39% for Uganda and 7.73% for Slovak Republic) [19]. In low-resource settings, the initial costs of required equipment, infrastructure and training will certainly require substantial additional funding. The recent financial commitments to increased funding for cervical cancer prevention [20] will need to be supported further in this context.

The potential effect of upscaling on the cost structure of screening could play an important role in affordability of hrHPV testing and reducing the costs. There are various barriers to scale-up of coverage in low-resource settings at multiple levels, including health system policies and general public sector policies, requiring tailoring the intervention to country settings [21]. In case of hrHPV-based screening, there are both fixed and variable costs that need to be considered for scale-up. The prices of required supplies, such as hrHPV test kits, can vary with volume, and thus depend on the scale-up strategy and planning. Some fixed costs, such as costs of establishing and maintaining a health facility in a low-density area, would be reduced with scale-up through reaching more people, when considered on a cost-per-person basis at a local level. Achieving high coverage at a national level will require considering these costs and their relationship with scale, which may often be non-linear [22].

It should also noted that the cost-effectiveness of screening, which is a long-term outcome, is often less of a priority for policymakers than the immediate costs of delivery of screening and treatment services [23]. While upscaling screening coverage can provide leverage for negotiating test prices by increasing the potential volume of tests purchased [24], it is not an immediate consideration for countries that are still at early stages of planning and introducing hrHPV testing, faced with upfront costs of establishing laboratory facilities and staff capacity [25]. Global procurement strategies, similar to those for vaccines, as well as improved coordination of overlapping efforts, are needed to ensure access to screening in countries suffering the majority of global cervical cancer burden [26]. A recent example of lowered costs of tuberculosis tests by Cepheid, the manufacturer of one of the hrHPV assays currently on the market, for countries with high burden of tuberculosis [27] highlights the need for continued advocacy and pressure to reduce prices. Similar challenges with financing and capacity, in particular related to resources required to deliver the intervention, have been highlighted for scale-up of HPV vaccination in LMICs [28]. In this context, our estimated budget impact results could serve as starting points for decision-makers

in planning the implementation, including the potential costs of community mobilization needed to ensure uptake of screening, but will require continued assessment with scale-up. Further investigation into the impact of upscaling on the cost structure of screening may be needed in these settings to facilitate planning.

We note that our analysis relied on screening uptake and follow-up adherence levels observed in the project implementation, which may not translate directly into practice when implementation is expanded. Linkage to follow-up and treatment is particularly important to ensure the cost-effectiveness of screening [29]. In particular, the high screening uptake among the target population achieved through community mobilization efforts in PRESCRIP-TEC will be difficult to sustain when turned into routine activity. In this context, it is important to ensure sufficient monitoring and surveillance efforts to support effective implementation [30]. Other existing electronic systems in these settings, such as District Health Information System in Bangladesh [31] and Kampala cancer registry in Uganda [32], will need to be strengthened to provide data for decision-makers on the real-world cost-effectiveness of hrHPV screening.

Moreover, in the context of cost-effectiveness results, it is important to remember that GDP-based WTP thresholds are often misused [33]. The commonly used 1-3 times GDP per capita thresholds based on WHO-CHOICE recommendations are arguably too high for most LMICs [34], and do not take into account health system constraints. However, the countries in this study also lack defined health economic decision-making policies at the healthcare system level, making it difficult to identify a relevant WTP threshold rule. If we were to apply more commonly used 1-3 times GDP per capita WTP thresholds instead, the evaluated strategies would be considered cost-effective, as evidenced by the acceptability curves. It should also be noted that purchasing power parity conversion rates for I$ were based on GDP conversion rates, and the actual purchasing power may be different for each country's healthcare sector (in relation to GDP). Therefore, the presented budget impact and cost-effectiveness results expressed in I$, while useful for initial comparisons between the settings, should be interpreted with caution.

Strengths and limitations

While previous international evaluations have supported the WHO's recommendation of hrHPV testing as a generally cost-effective strategy [35], we focused our evaluation on the implementation context. Our analysis setup benefitted from using implementation-based data, and adapted country-specific cost-effectiveness and budget impact models with considerations of countries' resource constraints and existing screening situations. However, there are notable limitations to our study. The simplified model did not include women living with human immunodeficiency virus, for which the WHO has produced dedicated recommendations. HPV vaccination was not considered in the analysis, given that the vaccination programs are either new or yet to be introduced in the chosen settings. Future decisions regarding implementation of vaccination in these settings will affect the cost-effectiveness of screening, and as a result will require re-evaluation. Moreover, we limited our analysis to comparison of the PRESCRIP-TEC strategy, which followed the WHO recommendations, to existing screening situation only, and did not consider alternative or parallel implementation strategies. Given the focus of the study, we also did not further consider the specific cost components of community mobilization separately, or alternative upscaling scenarios, which could change considerably if implementation is expanded. In general, the chosen evaluation perspective (payer / healthcare system rather than societal) and the related use of financial rather than economic costs in the analysis limit the interpretation of the results in terms of the broader "value" of the intervention, which should be explored in future evaluations. In addition, while the cost parameters were informed by available country-specific estimates, including a preliminary costing study in Uganda and Bangladesh, the uncertainty of estimates also limits the generalizability of results, and future projects will need to include more rigorous costing as part of the process to produce national cost estimates for use in economic evaluations.

Conclusions

In conclusion, our study presented data in support of the WHO's strategy for global elimination of cervical cancer and the countries' efforts to commit to corresponding recommendations, following successful initial local implementation of recommended screening strategies in diverse settings. Our study highlights that the affordability of hrHPV screening is dependent on the current burden of hrHPV and cervical cancer, existing screening coverage, as well as the country-specific perspective on what is considered to be cost-effective (i.e. the WTP threshold). The combined multi-country evaluation provides useful insights into the economic aspects of implementing hrHPV-based screening programs for policymakers and researchers.

Abbreviations

BAU	business-as-usual
BDT	Bangladeshi takka
CIN	cervical intraepithelial neoplasia
DALY	disability-adjusted life year
EUR	euro
HrHPV	high-risk human papillomavirus
LEEP	loop electrosurgical excision procedure
I$	2022 international dollars

LMIC	low- and middle-income country
PRESCRIP-TEC	PREvention and SCReening Innovation Project Toward Elimination of Cervical Cancer
UGX	Ugandan shilling
VIA	visual inspection with acetic acid
WHO	World Health Organization

Supplementary Information

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Supplementary Material 1.

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Authors' contributions
MS, GHDB, JARK, JS1, JVDS contributed to initial conceptualization and design of the study. MS, FP contributed to data preparation and presentation. MJWG, MS, GHDB, JVDS contributed to modeling and analysis. CN, NN, MUK, AR, JK, EA, MM, JM, JS2, JJB, MDF contributed to validation and interpretation of results. NN, AR, MUK, EA, CN contributed to data collection and validation. MS, GHDB, JARK, JVDS contributed to initial manuscript preparation. All authors contributed to manuscript revisions. All authors reviewed the manuscript and approved the final version for publication.

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Data availability
The model-related files used for the analysis will be made available on the DataverseNL open research data repository (https://doi.org/10.34894/LO4AA6), shared as part of the PRESCRIP-TEC project's research data.

Declarations

Ethics approval and consent to participate
Not applicable.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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References

1. Bray F, Laversanne M, Sung H, Ferlay J, Siegel RL, Soerjomataram I, et al. Global cancer statistics 2022: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin. 2024;74:229–63.
2. Bruni L, Serrano B, Roura E, Alemany L, Cowan M, Herrero R, et al. Cervical cancer screening programmes and age-specific coverage estimates for 202 countries and territories worldwide: a review and synthetic analysis. Lancet Glob Health. 2022;10:e1115–27.
3. Allanson E, Schmeler K. Cervical cancer prevention in low and middle income countries. Clin Obstet Gynecol. 2021;64:501–18.
4. Mallafré-Larrosa M, Ritchie D, Papi G, Mosquera I, Mensah K, Lucas E, et al. Survey of current policies towards widening cervical screening coverage among vulnerable women in 22 European countries. Eur J Public Health. 2023;33:502–8.
5. Descamps P, Dixon S, Bosch Jose FX, Kyrgiou M, Monsonego J, Neisingh O, et al. Turning the tide—Recommendations to increase cervical cancer screening among women who are underscreened. Int J Gynecol Obstet. 2024;166:3–21.
6. World Health Organization. WHO guideline for screening and treatment of cervical pre-cancer lesions for cervical cancer prevention. 2021. https://www.who.int/publications/i/item/9789240030824. Accessed 15 Sep 2021.
7. Serrano B, Ibáñez R, Robles C, Peremiquel-Trillas P, de Sanjosé S, Bruni L. Worldwide use of HPV self-sampling for cervical cancer screening. Prev Med. 2022;154:106900.
8. Yeh PT, Kennedy CE, de Vuyst H, Narasimhan M. Self-sampling for human papillomavirus (HPV) testing: a systematic review and meta-analysis. BMJ Glob Health. 2019;4:e001351.
9. Rayner M, Welp A, Stoler MH, Cantrell LA. Cervical Cancer screening recommendations: now and for the future. Healthcare. 2023;11:2273.
10. Okeah BO, Ridyard CH. Factors influencing the Cost-Effectiveness outcomes of HPV vaccination and screening interventions in Low-to-Middle-Income countries (LMICs): A systematic review. Appl Health Econ Health Policy. 2020;18:641–54.
11. Sultanov M, de Zeeuw J, Koot J, der Schans J, Beltman JJ, de Fouw M, et al. Investigating feasibility of 2021 WHO protocol for cervical cancer screening in underscreened populations: prevention and screening innovation project toward elimination of cervical Cancer (PRESCRIP-TEC). BMC Public Health. 2022;22:1356.
12. Castañeda KM, Vermeulen KM, van Asselt ADI, Schuuring E, Wisman GBA, Greuter MJW, de Bock GH. Molecular testing as triage in cervical Cancer screening: economic evaluation using headroom analysis. Cancers. 2025;17(4):612. https://doi.org/10.3390/cancers17040612.
13. Robinson LA, Hammitt JK, Chang AY, Resch S. Understanding and improving the one and three times GDP per capita cost-effectiveness thresholds. Health Policy Plan. 2017;32(1):141–5. https://doi.org/10.1093/heapol/czw096.
14. Woods B, Revill P, Sculpher M, Claxton K. Country-Level Cost-Effectiveness thresholds: initial estimates and the need for further research. Value Health. 2016;19(8):929–35. https://doi.org/10.1016/j.jval.2016.02.017.
15. Ochalek J, Wang H, Gu Y, Lomas J, Cutler H, Jin C. Informing a Cost-Effectiveness threshold for health technology assessment in china: A marginal productivity approach. PharmacoEconomics. 2020;38(12):1319–31. https://doi.org/10.1007/s40273-020-00954-y.
16. Bertram MY, Lauer JA, Stenberg K, Edejer TTT. Methods for the economic evaluation of health care interventions for priority setting in the health system: an update from WHO CHOICE. Int J Health Policy Manag. 2021;10(11):673–7. https://doi.org/10.34172/ijhpm.2020.244. Published 2021 Nov 1.

17. Sultanov M, Koot JAR, de Bock GH, Pan F, Stekelenburg J, Twardowski PK, Naheed N, Rahman A, Kabukye J, Nakisige C, de Zeeuw J, van der Schans J. Costing of cervical cancer screening and treatment pathways case studies in Bangladesh and Uganda [Unpublished manuscript in review]; 2025.
18. World Health Organization. Global Health Expenditure Database. https://apps.who.int/nha/database. Accessed 20 Jun 2025.
19. World Bank. World Bank Open Data. https://data.worldbank.org/. Accessed 20 Jun 2025.
20. WHO Media Team. Wave of new commitments marks historic step towards the elimination of cervical cancer. World Health Organization. 2024. https://www.who.int/news/item/05-03-2024-wave-of-new-commitments-marks-historic-step-towards-the-elimination-of-cervical-cancer. Accessed 30 Oct 2024.
21. Mangham LJ, Hanson K. Scaling up in international health: what are the key issues? Health Policy Plan. 2010;25:85–96.
22. Adawiyah Ral, Saweri OPM, Boettiger DC, Applegate TL, Probandari A, Guy R, et al. The costs of scaling up HIV and syphilis testing in low- and middle-income countries: a systematic review. Health Policy Plan. 2021;36:939–54.
23. Holme F, Kapambwe S, Nessa A, Basu P, Murillo R, Jeronimo J. Scaling up proven innovative cervical cancer screening strategies: challenges and opportunities in implementation at the population level in low- and lower-middle-income countries. Int J Gynecol Obstet. 2017;138:63–8.
24. Tsu VD, Njama-Meya D, Lim J, Murray M, de Sanjose S. Opportunities and challenges for introducing HPV testing for cervical cancer screening in sub-Saharan Africa. Prev Med. 2018;114:205–8.
25. Rol ML, Picconi MA, Ferrera A, Sánchez GI, Hernández M, de la L, Lineros J, et al. Implementing HPV testing in 9 Latin American countries: the laboratory perspective as observed in the ESTAMPA study. Front Med. 2022;9:1006038.
26. Kundrod KA, Jeronimo J, Vetter B, Maza M, Murenzi G, Phoolcharoen N, et al. Toward 70% cervical cancer screening coverage: technical challenges and opportunities to increase access to human papillomavirus (HPV) testing. PLOS Glob Public Health. 2023;3:e0001982.
27. The Global Fund, Global Fund STB, Partnership. and USAID Announce New Collaboration with Danaher to Reduce Price and Increase Access to Cepheid's TB Test. 2023. https://www.theglobalfund.org/en/news/2023/2023-09-19-global-fund-stop-tb-partnership-and-usaid-announce-new-collaboration-with-danaher-to-reduce-price-and-increase-access-to-cepheids-tb-test/. Accessed 31 Oct 2024.
28. Guillaume D, Waheed D-N, Schleiff M, Muralidharan KK, Vorsters A, Limaye RJ. Global perspectives of determinants influencing HPV vaccine introduction and scale-up in low- and middle-income countries. PLoS ONE. 2024;19:e0291990.
29. Campos NG, Tsu V, Jeronimo J, Mvundura M, Kim JJ. Estimating the value of point-of-care HPV testing in three low- and middle-income countries: a modeling study. BMC Cancer. 2017;17:791.
30. Brotherton JML, Wheeler CM, Clifford GM, Elfström M, Saville M, Kaldor J, et al. Surveillance systems for monitoring cervical cancer elimination efforts: focus on HPV infection, cervical dysplasia, cervical screening and treatment. Prev Med. 2021;144:106293.
31. Nessa A, Hossain MS, Uddin SMN, Islam MR, Khan MAH, Azad AK. Electronic aggregated data collection on cervical cancer screening in Bangladesh since 2014: what the data tells us? BMC Public Health. 2024;24:270.
32. Nakaganda A, Spencer A, Orem J, Mpamani C, Wabinga H, Nambooze S, et al. Estimating cancer incidence in uganda: a feasibility study for periodic cancer surveillance research in resource limited settings. BMC Cancer. 2023;23:772.
33. Kazibwe J, Gheorghe A, Wilson D, Ruiz F, Chalkidou K, Chi Y-L. The use of Cost-Effectiveness thresholds for evaluating health interventions in Low- and Middle-Income countries from 2015 to 2020: A review. Value Health. 2022;25:385–9.
34. Leech AA, Kim DD, Cohen JT, Neumann PJ. Use and misuse of Cost-Effectiveness analysis thresholds in Low- and Middle-Income countries: trends in Cost-per-DALY studies. Value Health. 2018;21:759–61.
35. Simms KT, Keane A, Nguyen DTN, Caruana M, Hall MT, Lui G, et al. Benefits, harms and cost-effectiveness of cervical screening, triage and treatment strategies for women in the general population. Nat Med. 2023;29:3050–8.

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