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The effect of hrHPV prevalence on cervical cancer screening strategies: a cost-effectiveness study of Bangladesh

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Abstract

Background Cervical cancer is the second most prominent cancer among women in Bangladesh, which is mainly caused by persistent infection with high-risk human papillomavirus (hrHPV). This study aims to evaluate impact of hrHPV prevalence on cost-effectiveness of screening with self-sampling hrHPV testing versus visual inspection with acetic acid (VIA) for cervical cancer screening in low- and middle-income countries with Bangladesh as an example.

Methods A micro-simulation Markov model was developed from a health system perspective in Bangladesh to evaluate the cost-effectiveness of screening with self-sampling hrHPV testing followed by VIA and VIA as primary screening method followed by colposcopy. We compared these strategies in optimal (70%) and realistic (8.7%) uptake scenarios, considering different hrHPV prevalence rates. Key indicators for cost-effectiveness were number of prevented cervical cancers cases and incremental cost-effectiveness ratio (ICER).

Results The number of cervical cancers cases prevented by screening and cost-effectiveness of screening strategies increased as hrHPV prevalence increased. In both optimal and realistic uptake scenarios, hrHPV test + VIA strategy prevented more cancers than VIA + colposcopy strategy in most instances. Regardless of the uptake, both screening strategies were cost-effective compared to no screening within a hrHPV prevalence range of 2–30%, and the hrHPV test-based strategy was cost-effective compared with VIA-based strategy. When the price of hrHPV test was estimated 50% lower (10 USD), the hrHPV test-based strategy gained more life years at nearly the same cost as the VIA-based strategy.

Conclusions Our study demonstrates that the hrHPV test + VIA strategy is cost-effective both compared to no screening and VIA + colposcopy screening strategy under the optimal (70%) and realistic (8.7%) uptake scenarios, with greater cost-effectiveness at higher hrHPV prevalence levels. While VIA-based strategy is cheaper, self-sampling hrHPV test-based strategy offers greater health benefits. Implementing hrHPV testing in national screening programs at lower hrHPV test prices is crucial for promoting health equity and accelerating cervical cancer elimination worldwide. In resource-constrained settings, screening with hrHPV testing should initially target high-prevalence populations.

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Keywords Human papillomavirus DNA tests, Prevalence, Cost-effectiveness analysis, Bangladesh

Introduction

Globally, cervical cancer is the fourth most frequently diagnosed cancer and the fourth leading cause of cancer death in women, with an estimated 604,000 new cases and 342,000 deaths worldwide in 2020 [1]. More than 80% of the disease burden occurs in low- and middle-income countries (LMICs), many of which have only recently initiated nationwide screening programs [2]. Despite an overall decline in incidence and mortality rates observed in most countries around the world for the past decades [3], cervical cancer is still the second most predominant type of cancer among women in Bangladesh, accounting for 12% of all female cancers [4]. According to the Bangladeshi Human Papillomavirus and Related Diseases Report from World Health Organization (WHO), there were over 8,000 new cases and about 5,000 cervical cancer deaths in 2020, yielding age-standardized incidence and mortality rates of 10.6 and 6.67 per 100,000 women per year, respectively [5].

Persistent infection of high-risk human papillomavirus (hrHPV) causes the development of cervical cancer [3]. While globally the lifetime risk of hrHPV infection for women is estimated at 80%, most infections resolve spontaneously [6]. Persistent infection with one or more hrHPV genotypes increases the risk of premalignant cervical intraepithelial neoplasia (CIN), and may eventually lead to cervical cancer [6]. Estimates for hrHPV prevalence vary widely within regions and countries. For example, in Bangladesh, a study reported hrHPV prevalence ranging from 0.5 to 7.1% in 16 regions [7], while a multicenter study across 14 regions of Bangladesh reported estimates near 20% [8]. Similarly, the neighboring country, India shows a similar regional heterogeneity in prevalence rates, with HPV prevalence differing a nearly 16 fold across various areas [9].

Besides vaccination, screening is part of the WHO strategy to reduce the high incidence and mortality of cervical cancer by early detection and treatment of precancerous lesions [10]. In the national screening program proposed by Bangladesh, all women between 30 and 60 years of age are invited for cervical cancer screening every 5 years. The primary screening test is visual inspection with acetic acid (VIA) and if positive women are referred for colposcopy [5]. However, the coverage of this national screening program is less than 9% in the past 5 years [11]. Instead of the combination of VIA and colposcopy, screening with hrHPV testing has been advocated as a prioritized approach by WHO [12]. The addition of this test to the screening flow has showed high sensitivity and specificity in detecting CIN grade two or higher (CIN2+) (96.1% and 90.7%) [13]. A major advantage is that all HPV-negative women do not need to undergo a gynecological examination. In addition, women can perform the hrHPV self-sampling tests, which is convenient, and give the test great potential to increase participation rates.

In the Prevention and Screening Innovation Project Toward Elimination of Cervical Cancer (PRESCRIP-TEC) project, the hrHPV testing approach for cervical cancer screening was implemented in Bangladesh as an effective way to strengthen cervical cancer screening [14]. This study evaluates the impact of hrHPV prevalence on the cost-effectiveness of screening with hrHPV testing versus VIA for cervical cancer screening in LMICs. For that, we simulated two strategies at an optimal (70%) and realistic (8.7%) uptake, inviting women between 30 and 60 years of age in cervical cancer screening every 5 years, where we used Bangladesh as an example. Given the wide range of estimates for the prevalence of hrHPV, we evaluated the impact of the hrHPV prevalence on the outcomes to provide scientific evidence for the selection of cervical cancer screening strategies in low- and middle-income countries, and specifically in Bangladesh.

Methods

Model and assumptions

This cost-effectiveness evaluation study was performed from a health care system perspective, to objectively account for all costs incurred by either the health care facility, the patients, as well as other funding sources [15]. The micro-simulation Markov model "SiMCerC was used in this study (Fig. 1) [16]. This model was originally developed to simulate the cervical cancer screening process for the Dutch population. The model simulated the life course of 100,000 women from birth to death. As in the natural history of hrHPV infection and cervical cancer [17], women may change states between hrHPV negative, hrHPV infection (positive), CIN 1, CIN 2, CIN 3, cervical cancer, cervical cancer death and all-cause mortality every year. We assumed that when a woman is infected with hrHPV, the state could progress to CIN1, CIN2, or CIN3, and from CIN1 to CIN2 or CIN3. Women with CIN3 status could regress to mild or moderate CIN lesion, and even hrHPV-positive state. Only women with CIN3 stage could progress to the cervical cancer state. We adapted the model to the Bangladeshi population by adjusting input parameters of hrHPV prevalence, cervical cancer staging, and cervical cancer survival.

The strategies and scenarios

The hrHPV test + VIA strategy was derived from the implementation of PRESCRIP-TEC project, which

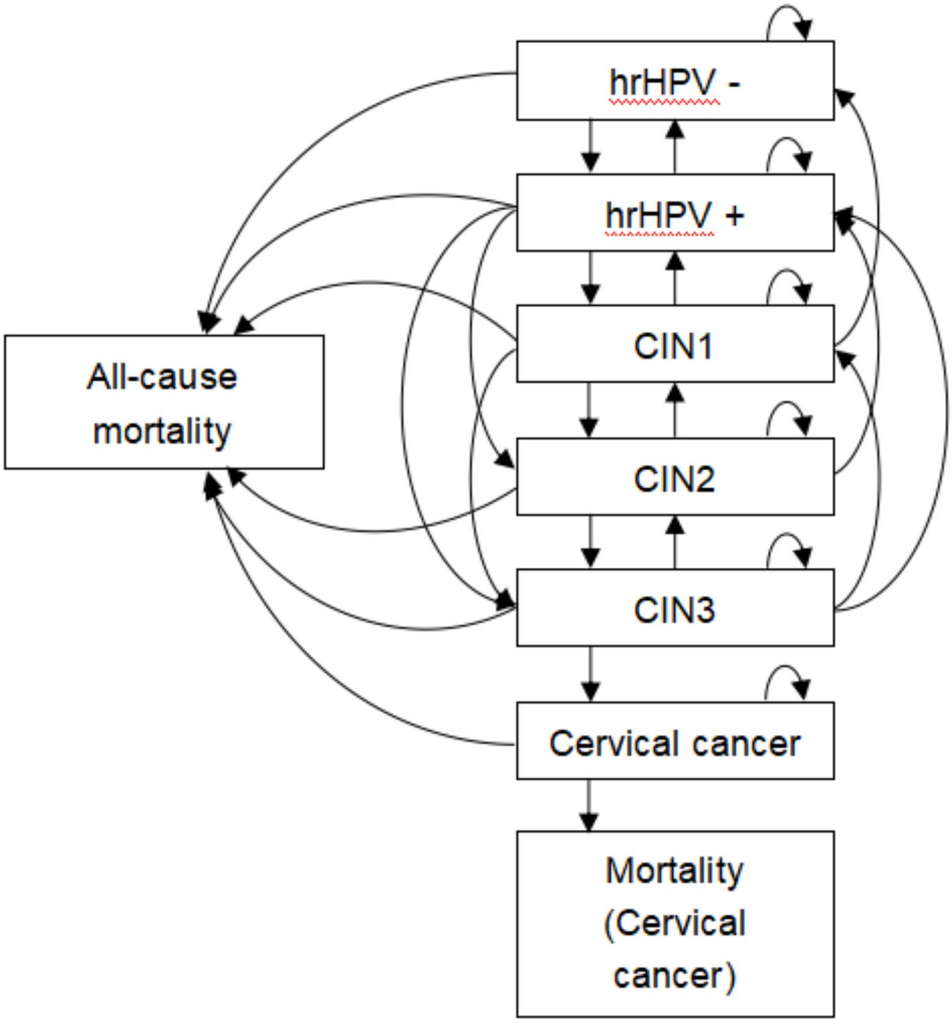

Fig. 1 SiMCerC Markov model
Note: Women's states are represented by rectangular boxes. The arrows represent yearly transition paths. hrHPV, High-risk Human papillomavirus; CIN, Cervical Intraepithelial Neoplasia

explored new strategies for cervical cancer screening in Bangladesh [14]. This strategy used self-sampling hrHPV test as the primary screening test. In case of a positive hrHPV result, women were invited for VIA triage. Women with pre-cancerous cervical lesions were treated with thermal ablation (TA) if eligible or Loop Electrosurgical Excision Procedure (LEEP) in case of bigger lesions. Regardless mode of treatment, women who tested positive for hrHPV were followed up after 12 months with a hrHPV test. In case of suspicion of cervical cancer, patients were referred to tertiary oncology centers for further treatment and withdrawn from the screening flow. Women who tested negative for hrHPV were re-invited for screening after 5 years.

The VIA + colposcopy strategy stemmed from the national screening strategy proposed by Bangladesh in 2017 [18]. Women who accepted the invitation were first screened by VIA. VIA-positive women received colposcopy triage and were treated according to diagnosis with TA or LEEP. Women receiving pre-cancer treatments would be followed up after one year by VIA. Women whose results were negative or CIN1 would be invited again after five years (Fig S1).

In this study we simulated the implementation of these two strategies under the optimal and realistic uptake scenarios, both compared with no screening as reference because the current cervical cancer screening program coverage was very low in most areas. For example, the number of VIA tests in the region of Sylhet was only 3.6% of the national screening [11]. In the optimal scenario, we assumed that the uptake of screening and loss to follow-up rate were close to common targets. The expectation of screening uptake was 70% according to the "Cervical Cancer Elimination Initiative" proposed by WHO [10]. In the realistic scenario, the two parameters were derived from actual world uptake of screening in Bangladesh. The

cost-effectiveness of screening versus no screening was compared. The VIA-based strategy was used as a reference to calculate the cost-effectiveness indicator of the hrHPV test-based strategy at the same uptake to compare the two screening strategies. In addition, we calculated the ICER after a 50% price reduction of hrHPV test.

Input parameters

Table S1 shows the input parameters of the model based on available published literature. Due to the variation in hrHPV prevalence across regions in Bangladesh [8, 19], we varied the hrHPV prevalence from 2 to 30% at 2% intervals in our model. The cost-effectiveness indicator was calculated separately. As women in Bangladesh are sexually active at a relatively early age, women in the model had the probability of being infected with hrHPV from the age of 13 [7]. The hrHPV prevalence was defined as the number of women aged 13–64 infected with hrHPV divided by the number of women aged 13–64. The transition probabilities between states in the natural history of cervical cancer were derived from literature [20–26]. The stage distribution of cervical cancer was obtained from a hospital based study in Bangladesh [27] according to International Federation of Gynecology and Obstetrics (FIGO). As no cohort study was available on cervical cancer in Bangladesh, stage-specific cervical cancer survival data were obtained from an Indian cohort study [28], considering comparable geographic locations and current health expenditures (CHE) per capita in 2020 [29]. Specific survival rates were shown in Fig S2. Although the HPV vaccine has been introduced in Bangladesh, it has not yet been rolled out nationwide [30]. Therefore it was assumed that participants in the screening simulation were not vaccinated.

Women in the generated cohort were invited to participate in cervical cancer screening between ages 30–60 with 5 years intervals, similar to the existing Bangladesh screening policy [18]. In the optimal uptake scenario, we assumed that 70% of eligible women participate in screening when invited every 5 years [10]. It was assumed that the uptake of triage, precancerous treatment and follow up would decrease by 15% for each additional step in screening [31]. In the realistic scenario, we assumed an uptake of the primary screening test (8.7%) and loss to follow-up (70.9%). These estimates were derived from the implementation of cervical cancer screening in Bangladesh [11, 32]. In all scenarios we assumed that 85% of cervical cancer patients were treated [31]. The clinical performance of self-sampling hrHPV test [33], VIA [34] and colposcopy [35] were obtained from systematic reviews. The proportion of pre-cancer therapies [32] and the cure rate of LEEP [36] were obtained the implementation of cervical cancer screening in Bangladesh. The cure rate for thermal ablation came from a meta-analysis of low- and middle-income countries [37].

Cost data were derived from a cost analysis study conducted in Bangladesh with Friendship (a non-Governmental Organization, NGO). The bottom-up micro costing approach was used to calculate the cost of self-sampling hrHPV test, VIA, colposcopy and TA. The gross-costing approach was used to estimate the cost of LEEP [38]. See Appendix S1 File for more details. Cervical cancer treatment cost was derived from a cost-effectiveness study in Bangladesh [39]. All costs were converted to 2022 United States Dollar (USD).

Model validation

We calculated the age-specific hrHPV prevalence from 13 years old, when a girl potentially become sexually active, to 64 years old and cervical cancer incidence rates per 100,000 women per year. The incidence rate of cervical cancer was standardized by using the 1966 Segi-Doll World standard population to ensure comparability with WHO data [40, 41]. Model validation was performed by comparing simulated results with observed data from literature as described above.

Outcomes

The outcomes were the number of cervical cancers cases prevented, life years gained (LYG), total cost, and incremental cost-effectiveness ratio (ICER) in 2022 USD. ICER was defined as the incremental cost per life year gained compared with the reference scenario at a particular hrHPV prevalence rate. The average results of 10 model runs were calculated to compensate for the probabilistic nature of the model and the simulation results. Based on a study of willing-to-pay (WTP) threshold for low- and middle-income countries [42], we applied the 4-51% of Bangladeshi gross domestic product (GDP) per capita ($2,657 in 2020) as the cost-effectiveness cut-off point (not cost-effective if ICER > 51% GDP per capita, cost-effective if ICER ≤ 51% GDP per capita, highly cost-effective if ICER ≤ 4% GDP per capita). All costs and health benefits were discounted at a rate of 3% per year from the start of the screening age [43].

Sensitivity analysis

We used one-way deterministic sensitivity analyses to examine the robustness of our model. The hrHPV prevalence was set to the same value as model validation. We varied each input value of both screening strategies by 95% confidence interval (CI) or ± 25% under the optimal scenario. Then the changes in ICERs were calculated compared with no screening.

Results

Model validation

The prevalence of hrHPV in different age groups of the simulated cohort was consistent with observed data [19] (Fig. S3). Also, the simulated age-standardized incidence rate of 10.78 (95%CI: 8.75–12.82) per 100,000 women per year was comparable with the estimation by WHO of 10.6 per 100,000 women per year in Bangladesh [5].

Scenario simulations

Compared with no screening, the number of cervical cancers cases prevented by screening increased as hrHPV prevalence increased (Table 1). At an hrHPV prevalence of 30%, the number of cervical cancer cases prevented was approximately 10 times higher than at a prevalence of 2%. In both scenarios, hrHPV test + VIA strategy prevented more cancers than VIA + colposcopy strategy in most instances. In the optimal scenario, uptake was elevated and the number of cancer cases prevented by hrHPV test + VIA strategy was about 1.4 times greater than that of VIA + colposcopy strategy.

As seen in Fig. 2, the discounted incremental costs per life years gained of the two screening strategies compared to no screening first decreased sharply as hrHPV prevalence increased, and at higher hrHPV prevalence rates plateaued. The largest decline was in the hrHPV test + VIA strategy in the optimal scenario. 93% reduction in ICER at hrHPV prevalence of 30% compared to hrHPV prevalence at 2%. Whereas at lower uptake, changes in hrHPV prevalence had less impact on ICER. Both screening strategies were cost-effective in both scenarios with optimal and realistic uptake. In the realistic uptake scenario, the VIA + colposcopy strategy was highly cost-effective regardless of how hrHPV prevalence changes, while hrHPV test + VIA strategy became highly cost-effective when hrHPV prevalence exceeded 2%. Under the optimal uptake scenario, the VIA-based strategy was highly cost-effective when hrHPV prevalence exceeded 2%, whereas hrHPV test-based strategy became highly cost-effective when hrHPV prevalence was greater than 10%.

Compared with VIA + colposcopy strategy, hrHPV test + VIA strategy was cost-effective under both uptake scenarios (Fig. 3). The discounted ICERs of hrHPV test-based strategy declined with the rising hrHPV prevalence. In the realistic uptake scenario, hrHPV test + VIA strategy was always highly cost-effective regardless of changes in hrHPV prevalence. As hrHPV prevalence increased, the costs of hrHPV test + VIA strategy dropped from 1.63 to 1.07 times the cost of VIA + colposcopy strategy, and incremental life years gained of hrHPV test + VIA strategy increased from 785.55 to 9160.20. In the optimal scenario, hrHPV test + VIA strategy became highly cost-effective when hrHPV prevalence exceeded 14%. Despite gaining more life years, hrHPV test + VIA strategy cost 1.66–2.85 times more than VIA + colposcopy strategy. Assuming a 50%(10.0 $) reduction in the price of self-sampling hrHPV test, the ICERs gradually declined as hrHPV prevalence grew. Although the ICERs approached zero, it was still greater than 0, in which case the hrHPV test + VIA strategy gained more life years at nearly the same cost as the VIA + colposcopy strategy.

Sensitivity analysis

Figure 4 shows the top 10 variables as a result of the univariate sensitivity analysis. ICERs of both screening strategy versus no screening were most sensitive to annual progression probability of hrHPV + to CIN3, the annual

Table 1 Number of cervical cancer cases prevented compared to a no screening scenario

hrHPV prevalence	Number of cervical cancer cases prevented					
	Realistic uptake scenario			Optimal uptake scenario		
	hrHPV test + VIA	VIA + colposcopy	Ratio	hrHPV test + VIA	VIA + colposcopy	Ratio
2%	7	2	3.50	237	172	1.38
4%	13	7	1.86	443	336	1.32
6%	15	10	1.50	627	469	1.34
8%	19	17	1.12	809	593	1.36
10%	20	20	1.00	991	743	1.33
12%	23	21	1.10	1157	874	1.32
14%	24	25	0.96	1319	996	1.32
16%	28	25	1.12	1478	1118	1.32
18%	31	29	1.07	1619	1210	1.34
20%	32	30	1.07	1758	1302	1.35
22%	37	28	1.32	1906	1409	1.35
24%	41	29	1.41	2027	1493	1.36
26%	42	30	1.40	2130	1573	1.35
28%	44	31	1.42	2251	1654	1.36
30%	46	34	1.35	2355	1723	1.37

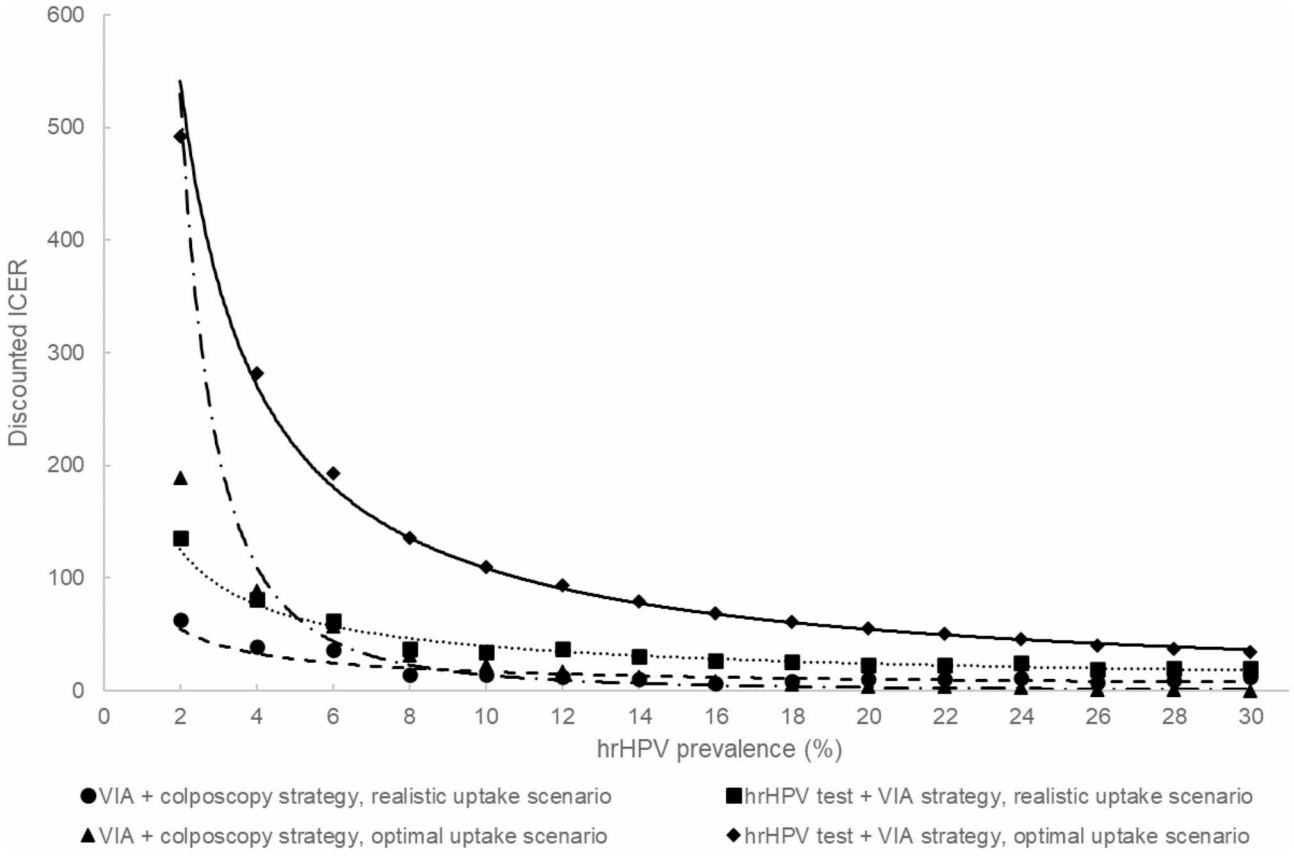

Fig. 2 Comparison of discounted ICERs as a function of hrHPV prevalence, with the no screening scenario as the reference
Note: Fitting trendlines using the power function

progression probability of CIN2 to CIN3 and the costs of primary screening test. Although we adjusted the input parameters in the sensitivity analysis, both screening strategies under the optimal uptake scenario were still cost-effective compared to no screening.

Discussion

This study found that implementing the self-sampling hrHPV test + VIA screening strategy can prevent more cases of cervical cancer than VIA + colposcopy screening strategy at the same level of uptake in almost all cases. This is because the hrHPV test has a higher sensitivity and specificity than the VIA test and can target high-risk populations more accurately [33, 34]. The higher the prevalence of hrHPV, the more cost-effective cervical cancer screening will be as more women will have a higher probability to develop cervical cancer. Countries and regions with high hrHPV prevalence should invest more to improve the coverage of cervical cancer screening, and the health achievement will be more considerable if hrHPV test + VIA strategy was practiced. Especially when hrHPV prevalence is higher than 14%, the hrHPV test + VIA strategy is highly cost-effective compared with VIA + colposcopy strategy. Although implementing hrHPV test + VIA screening is more costly than VIA + colposcopy screening strategy, there is still a lot of room for the price of hrHPV test to drop when large-scale centralized national procurement is introduced [44]. When the price of hrHPV test is reduced with 50%, the hrHPV test + VIA strategy will have similar costs compared to VIA + colposcopy strategy, making it more affordable for LMICs.

The potential impact of our findings on future research and clinical practice is that screening is crucial to achieve the goal of eliminating cervical cancer. As a low-cost tool, VIA is less sensitive than hrHPV testing but has advantages for low-resource countries, although the combination of hrHPV testing and VIA is more favorable for cervical cancer control. Further studies could explore innovative strategies to reduce the cost of hrHPV testing, such as optimizing the manufacturing process, developing more economical test materials, and implementing cost-effective screening protocols while also accounting for the HPV prevalence and genotype distribution. In addition, the SiMCerC model performed an established and validated model designed specifically for cervical cancer screening and prevention programs, which was used and validated in the Netherlands as well

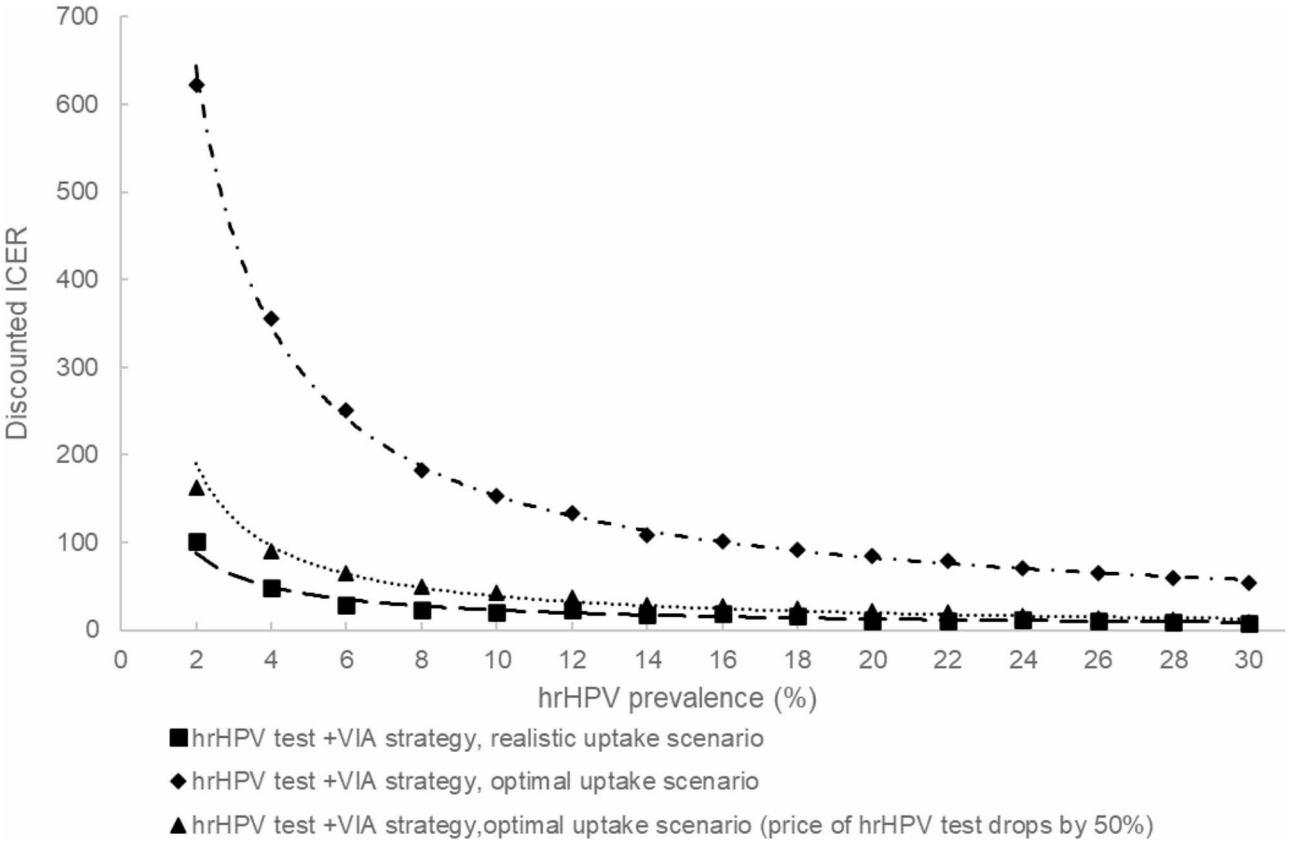

Fig. 3 Discounted ICERs for hrHPV test + VIA strategy in 2 scenarios at different hrHPV prevalence, with VIA + colposcopy strategy as the reference
Note: Fitting trendlines using the power function

as PRESCRIP-TEC related countries [45]. Its structure allows for the incorporation of country-specific parameters and the comparison of various screening strategies, which fits with the aims of this study.

VIA has undoubtedly achieved positive results for low- and middle-income countries [46]. However, the current participation rate of cervical cancer screening in Bangladesh is less than 9% [11]. Low priority setting and lack of funding are the main obstacles to achieve satisfactory coverage. Besides, the large target population, deficient infrastructure and organization make it hard to implement the VIA + colposcopy strategy [47]. The accuracy of VIA and colposcopy is highly dependent on the experience of the operator [48]. A Bangladeshi study reports that insufficient trained and experienced healthcare providers is the main reason that these colposcopy centers are unable to perform at full capacity [49]. Coverage is also an important factor in determining the effectiveness of cervical cancer screening programs. Self-sampling hrHPV tests offer unique advantage to achieve wider coverage [50]. A meta-analysis found a higher participation rate in the use of HPV self-sampling at screening compared with standard care in the control group, including pap smears, VIA, and clinician-sampling HPV tests (RR: 2.13, 95% CI 1.89 to 2.40) [51]. Another major advantage is that HPV-negative women do not need further gynecological examination. In this way, only women at high risk of cervical cancer will visit the clinic, which can reduce the burden on the healthcare system. What's more, considering the current situation of imbalance of healthcare resources and uneven hrHPV prevalence across regions in low- and middle-income countries [9, 11], coverage of cervical cancer screening can be further improved by the different primary screening options across regions.

In addition to find a relatively easy to implement, cost-effective screening program, LMICs should also focus on educational interventions to increase awareness of the importance and impact of cervical cancer prevention, including childhood HPV vaccination and cervical cancer screening for adult women. Many women in Bangladesh are typically reserved and feel uncomfortable discussing diseases of the reproductive system [52], which may cause hesitation to participate in cervical cancer screening. The key role of trained community health workers in local communities should be fully utilized to overcome cultural barriers [46]. It is also necessary to strengthen basic medical facilities. A study found that some tertiary and specialty hospitals in Bangladesh were ready

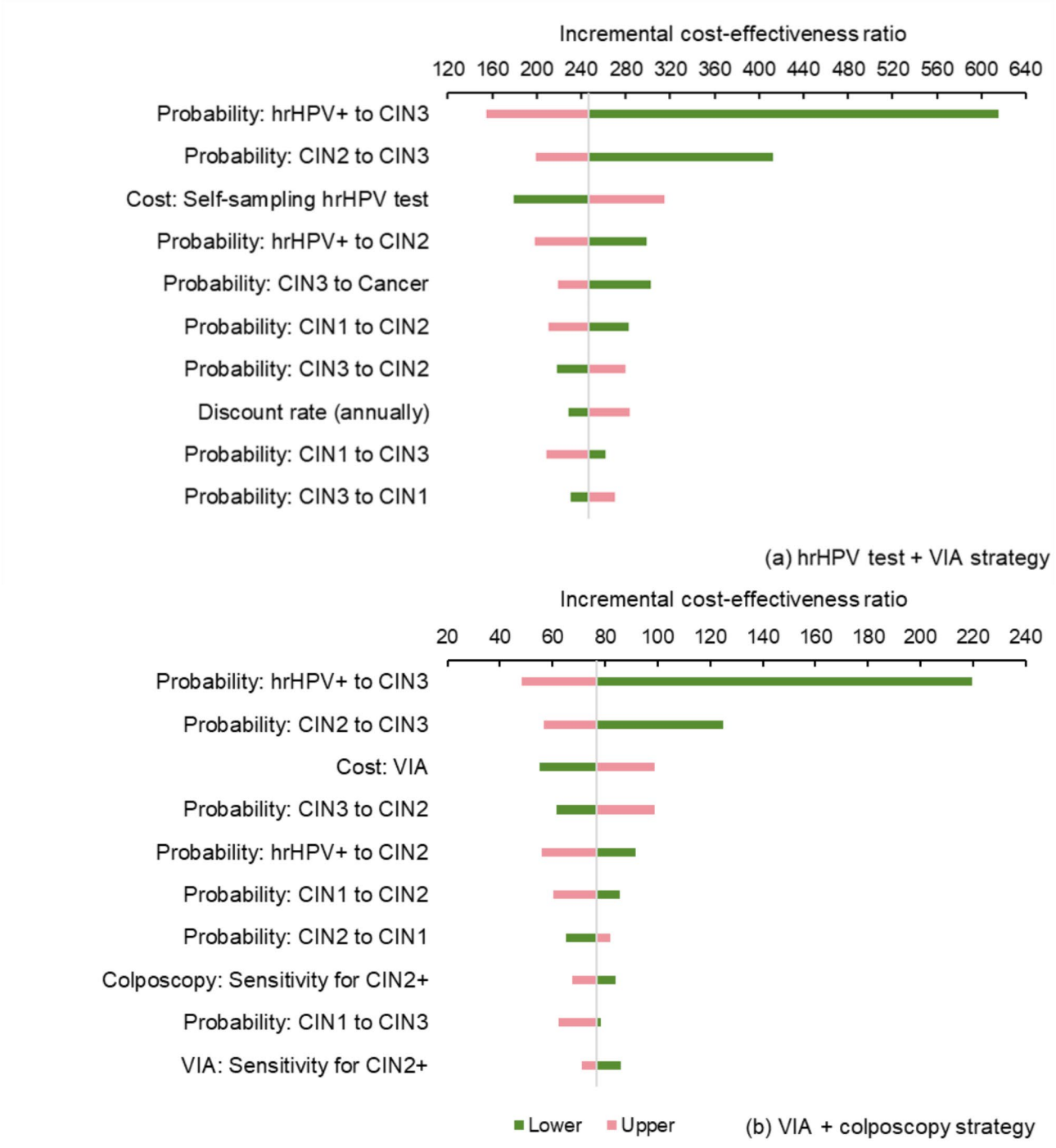

Fig. 4 Tornado diagram analysis of the sensitivity analysis for 2 strategies under optimal scenario

to manage cervical cancer [53]. However, the remaining health facilities were not prepared sufficiently to provide cervical cancer services [53]. Global population growth and ageing are also driving an increase in the absolute number of cervical cancer cases [54]. LMICs need to scale up preventive interventions, including screening and HPV vaccination, to achieve sustainable development goals.

This is the first cost-effectiveness study of cervical cancer screening in Bangladesh. The strength of this study is that we use Markov model to simulate scenarios that are difficult to observe in reality. We not only compared hrHPV test + VIA and VIA + colposcopy screening strategies with the consideration that hrHPV prevalence varies widely in different parts of the country, but also took into account two comparable screening uptake. This could

serve as a reference for low- and middle-income countries and for countries with different hrHPV prevalence across regions, to introduce hrHPV test first in areas with higher hrHPV prevalence such as urban areas. However, this study also has some limitations. Since subtype-specific hrHPV prevalence data for different regions of Bangladesh is currently limited [55], we cannot evaluate whether this interregional heterogeneity is due to differences in hrHPV genotypes. The model simplified the practice of screening, which did not include unanticipated consequences in screening. Implementation costs like program expansion costs were not considered in our model, which may lead to an overestimation of the cost-effectiveness in the optimal uptake scenario. Due to limited research in Bangladesh, the cervical cancer survival data were obtained from an Indian cohort study. But considering the similarities between India and Bangladesh in terms of geographic location and economic conditions, we think this will have limited impact on our results. Disability-adjusted life years (DALYs) and quality-adjusted life years (QALYs) are not used because there is currently no study to estimate the corresponding utility values for the Bangladeshi population.

Conclusions

Our study demonstrated that the hrHPV test + VIA strategy was cost-effective both compared to no screening and VIA + colposcopy screening strategy under the optimal (70%) and realistic (8.7%) uptake scenarios. The higher the prevalence of hrHPV, the greater the cost-effectiveness of cervical cancer screening. Although the cost of VIA-based strategy is lower, the hrHPV test-based strategy can achieve more health benefits. It is important to incorporate hrHPV testing into the national cervical cancer screening program. However, a lower hrHPV test price is crucial to make it more acceptable to low- and middle-income countries, which would help the health equity and accelerate the elimination of cervical cancer worldwide.

Abbreviations

hrHPV	high-risk human papillomavirus
VIA	visual inspection with acetic acid
ICER	incremental cost-effectiveness ratio
LMICs	low- and middle-income countries
WHO	World Health Organization
CIN	cervical intraepithelial neoplasia
CIN2+	cervical intraepithelial neoplasia grade two or higher
PRESCRIP-TEC	Prevention and Screening Innovation Project Toward Elimination of Cervical Cancer
TA	thermal ablation
LEEP	Loop Electrosurgical Excision Procedure
FIGO	International Federation of Gynecology and Obstetrics
CHE	current health expenditures
NGO	non-Governmental Organization
USD	United States Dollar
LYG	life years gained
WTP	willing-to-pay
GDP	gross domestic product
CI	confidence interval
RR	risk ratio
DALYs	disability-adjusted life years
QALYs	quality-adjusted life years
ICDDR, B	International Centre for Diarrheal Disease Research, Bangladesh

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12889-025-21756-x.

Supplementary Material 1

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Author contributions

F. Pan, G.H. de Bock, M.J.W. Greuter, J. van der Schans, and J.A.R. Koot contributed to the conceptualization, study design and original draft. N. Nazrul and J. van der Schans contributed to the collection of cost data. J. Beltman and N. Nazrul contributed to the review of model parameters and structure. M.J.W. Greuter and F. Pan contributed to the adaptation of the model code. 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 code files used in this analysis are available on the DataverseNL (https://doi.org/10.34894/LO4AA6), which are shared as part of the PRESCRIP-TEC project research data. Files relevant to this analysis have been labeled accordingly in their descriptions.

Declarations

Ethics approval and consent to participate

This study was conducted in accordance with the principles of the Declaration of Helsinki. The study received ethical clearance from the Institutional Review Board of International Centre for Diarrheal Disease Research, Bangladesh (ICDDR, B) (approval number 21029). The respondents provided written consent before data collection using an Informed Consent Form. Only information on hospital names was stated in the supplement to explain the calculation of costs. No further traceable information to individual patients was used.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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References

1. Singh D, Vignat J, Lorenzoni V, Eslahi M, Ginsburg O, Lauby-Secretan B, et al. Global estimates of incidence and mortality of cervical cancer in 2020: a baseline analysis of the WHO Global Cervical Cancer Elimination Initiative. Lancet Glob Health. 2023;11:e197–206.
2. Bhatla N, Singhal S. Primary HPV screening for cervical cancer. Best Pr Res Clin Obstet Gynaecol. 2020;65:98–108.
3. Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, et al. Global Cancer statistics 2020: GLOBOCAN estimates of incidence and Mortality Worldwide for 36 cancers in 185 countries. CA Cancer J Clin. 2021;71:209–49.
4. WHO. The Global Cancer Observatory - Bangladesh. 2021. https://gco.iarc.who.int/media/globocan/factsheets/populations/50-bangladesh-fact-sheet.pdf. Accessed 12 Apr 2024.
5. HPV INFORMATION CENTRE, Bangladesh. Human Papillomavirus and Related Diseases Report. 2023. https://hpvcentre.net/statistics/reports/BGD.pdf. Accessed 13 Apr 2024.
6. Snijders PJ, Steenbergen RD, Heideman DA, Meijer CJ. HPV-mediated cervical carcinogenesis: concepts and clinical implications. J Pathol. 2006;208:152–64.
7. Nessa A, Begum SA, Munshi SU, Begum F, Chowdhury A. Noor-E-Ferdous. High-risk human papillomavirus infection among Urban and Rural women in Bangladesh. Cancer Screen Prev. 2024;3:36–46.
8. Sharmin S, Sabikunnahar B, Aditya A, Khan MA-A-K, Nessa A, Ahsan CR, et al. Genotypic distribution and prevalence of human papillomavirus infection in an apparently healthy female population in Bangladesh. IJID Reg. 2021;1:130–4.
9. HPV INFORMATION CENTR. Human Papillomavirus and Related Disease Report: World. 2023. https://hpvcentre.net/statistics/reports/XWX.pdf. Accessed 12 Apr 2024.
10. WHO. Global strategy to accelerate the elimination of cervical cancer as a public health problem. 2020. https://iris.who.int/bitstream/handle/10665/336583/9789240014107-eng.pdf. Accessed 12 Apr 2024.
11. 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.
12. WHO. WHO recommends DNA testing as a first-choice screening method for cervical cancer prevention. 2021. https://www.who.int/europe/news/item/11-09-2021-who-recommends-dna-testing-as-a-first-choice-screening-method-for-cervical-cancer-prevention. Accessed 12 Apr 2024.
13. Cuzick J, Clavel C, Petry KU, Meijer CJ, Hoyer H, Ratnam S, et al. Overview of the European and north American studies on HPV testing in primary cervical cancer screening. Int J Cancer. 2006;119:1095–101.
14. Sultanov M, Zeeuw J, Koot J, der Schans JV, Beltman JJ, 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.
15. Kim DD, Silver MC, Kunst N, Cohen JT, Ollendorf DA, Neumann PJ. Perspective and costing in cost-effectiveness analysis, 1974–2018. PharmacoEconomics. 2020;38:1135–45.
16. Sultanov M, van der Schans J, Koot JA, Greuter MJ, de Zeeuw J, Nakisige C, et al. Early evaluation of a screen-and-treat strategy using high-risk HPV testing for Uganda: implications for screening coverage and treatment. J Glob Health. 2024;14:04157.
17. Schiffman M, Wentzensen N. Human papillomavirus infection and the multistage carcinogenesis of cervical cancer. Cancer Epidemiol Biomark Prev. 2013;22:553–60.
18. Directorate General of Health Services. National Strategy for Cervical Cancer Prevention and Control Bangladesh (2017–2022). 2017.
19. Nahar Q, Sultana F, Alam A, Islam JY, Rahman M, Khatun F, et al. Genital human papillomavirus infection among women in Bangladesh: findings from a Population-based survey. PLoS ONE. 2014;9:e107675.
20. Lazare C, Xiao S, Meng Y, Wang C, Li W, Wang Y et al. Evaluation of cervical intraepithelial neoplasia occurrence following the recorded onset of Persistent High-Risk Human Papillomavirus infection: a retrospective study on infection duration. Front Oncol. 2019;9.
21. Dick S, Kremer WW, De Strooper LMA, Lissenberg-Witte BI, Steenbergen RDM, Meijer CJLM, et al. Long-term CIN3 + risk of HPV positive women after triage with FAM19A4/miR124-2 methylation analysis. Gynecol Oncol. 2019;154:368–73.
22. Denise Zielinski G, Snijders PJF, Rozendaal L, Voorhorst FJ, Runsink AP, de Schipper FA, et al. High-risk HPV testing in women with borderline and mild dyskaryosis: long-term follow-up data and clinical relevance. J Pathol. 2001;195:300–6.
23. Nobbenhuis MA, Walboomers JM, Helmerhorst TJ, Rozendaal L, Remmink AJ, Risse EK, et al. Relation of human papilloma virus status to cervical lesions and consequences for cervical-cancer screening: a prospective study. Lancet. 1999;354:20–5.
24. Myers ER, McCrory DC, Nanda K, Bastian L, Matchar DB. Mathematical Model for the natural history of human papillomavirus infection and cervical carcinogenesis. Am J Epidemiol. 2000;151:1158–71.
25. Bulkmans NWJ, Berkhof J, Bulk S, Bleeker MCG, van Kemenade FJ, Rozendaal L, et al. High-risk HPV type-specific clearance rates in cervical screening. Br J Cancer. 2007;96:1419–24.
26. Motamedi M, Böhmer G, Neumann HH, von Wasielewski R. CIN III lesions and regression: retrospective analysis of 635 cases. BMC Infect Dis. 2015;15:541.
27. Banu PA, Rukhsana N, Yasmin J, Nahar L, Malik SR. Analysis on the incidence, staging and Treatment of Carcinoma Cervix at Delta Medical College and Hospital of Bangladesh. Delta Med Coll J. 2013;1:31–6.
28. Jayant K, Sankaranarayanan R, Thorat RV, Muwonge R, Hingmire SJ, Panse NS, et al. Improved survival of Cervical Cancer patients in a Screened Population in Rural India. Asian Pac J Cancer Prev APJCP. 2016;17:4837–44.
29. World Bank Open Data. World Bank Open Data. https://data.worldbank.org. Accessed 12 Apr 2024.
30. Makoni M. HPV vaccine roll-out in Nigeria and Bangladesh - The Lancet Oncology. https://www.thelancet.com/journals/lanonc/article/PIIS1470-2045(23)00571-5/fulltext. Accessed 13 Jan 2025.
31. Goldie SJ, Gaffikin L, Goldhaber-Fiebert JD, Gordillo-Tobar A, Levin C, Mahé C, et al. Cost-effectiveness of cervical-Cancer screening in five developing countries. N Engl J Med. 2005;353:2158–68.
32. Nessa A, Khanom Q, Ripa SZ, Khan KH, Azad AK, Kamal M. Present status of cervical cancer screening in Bangladesh. J Histopathol Cytopathol. 2019;3:45–52.
33. Arbyn M, Smith SB, Temin S, Sultana F, Castle P, Collaboration on S-S, et al. Detecting cervical precancer and reaching underscreened women by using HPV testing on self samples: updated meta-analyses. BMJ. 2018;363:k4823.
34. Smith SK, Nwosu O, Edwards A, Zerihun M, Chung MH, Suvada K, et al. Performance of screening tools for cervical neoplasia among women in low- and middle-income countries: a systematic review and meta-analysis. PLOS Glob Public Health. 2023;3:e0001598.
35. Qin D, Bai A, Xue P, Seery S, Wang J, Mendez MJG, et al. Colposcopic accuracy in diagnosing squamous intraepithelial lesions: a systematic review and meta-analysis of the International Federation of Cervical Pathology and Colposcopy 2011 terminology. BMC Cancer. 2023;23:187.
36. Basu P, Nessa A, Majid M, Rahman JN, Ahmed T. Evaluation of the National Cervical Cancer Screening Programme of Bangladesh and the formulation of quality assurance guidelines. BMJ Sex Reprod Health. 2010;36:131–4.
37. de Fouw M, Oosting RM, Rutgrink A, Dekkers OM, Peters AAW, Beltman JJ. A systematic review and meta-analysis of thermal coagulation compared with cryotherapy to treat precancerous cervical lesions in low- and middle-income countries. Int J Gynecol Obstet. 2019;147:4–18.
38. Health Economics Unit (HEU). Bangladesh National Health Accounts 1997–2015. http://oldweb.heu.gov.bd/pdf/bnha%201997-2007.pdf. Accessed 18 Sep 2024.
39. Mahumud RA, Gow J, Alam K, Keramat SA, Hossain MG, Sultana M, et al. Cost-effectiveness of the introduction of two-dose bi-valent (Cervarix) and quadrivalent (Gardasil) HPV vaccination for adolescent girls in Bangladesh. Vaccine. 2020;38:165–72.
40. Segi M, Fujisaku S. Cancer mortality for selected sites in 24 countries (1950–1957). Department of Public Health, Tohoku University School of Medicine; 1960.

41. Payne P, Waterhouse JA. Cancer Incidence in Five Continents: A Technical Report. International Union against Cancer; 1966.
42. Woods B, Revill P, Sculpher M, Claxton K. Country-Level cost-effectiveness thresholds: initial estimates and the need for further research. Value Health. 2016;19:929–35.
43. Haacker M, Hallett TB, Atun R. On discount rates for economic evaluations in global health. Health Policy Plan. 2020;35:107–14.
44. Inturrisi F, Berkhof J. Pricing of HPV tests in Italian tender-based settings. J Med Econ. 2022;25:762–8.
45. Sultanov M, Koot JAR, de Bock GH, Greuter MJW, Beltman JJ, de Fouw M, et al. High-risk human papillomavirus testing for cervical cancer screening in Uganda: considering potential harms and benefits in a low-resource setting. PLoS ONE. 2024;19:e0312295.
46. Sivaram S, Majumdar G, Perin D, Nessa A, Broeders M, Lynge E, et al. Population-based cancer screening programmes in low-income and middle-income countries: regional consultation of the International Cancer Screening Network in India. Lancet Oncol. 2018;19:e113–22.
47. Nessa A, Hussain MA, Rahman JN, Rashid MHU, Muwonge R, Sankaranarayanan R. Screening for cervical neoplasia in Bangladesh using visual inspection with acetic acid. Int J Gynecol Obstet. 2010;111:115–8.
48. Xue P, Ng MTA, Qiao Y. The challenges of colposcopy for cervical cancer screening in LMICs and solutions by artificial intelligence. BMC Med. 2020;18:169.
49. Bhatla N, Nessa A, Oswal K, Vashist S, Sebastian P, Basu P. Program organization rather than choice of test determines success of cervical cancer screening: case studies from Bangladesh and India. Int J Gynecol Obstet. 2021;152:40–7.
50. Lozar T, Nagvekar R, Rohrer C, Dube Mandishora RS, Ivanus U, Fitzpatrick MB. Cervical Cancer Screening Postpandemic: Self-Sampling opportunities to accelerate the elimination of Cervical Cancer. Int J Womens Health. 2021;13:841–59.
51. 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.
52. Qayum M, d O, Billah MM, Akhter R, Flora MS. Women's knowledge, attitude and practice on Cervical Cancer and its screening in Dhaka, Bangladesh. Asian Pac J Cancer Prev APJCP. 2021;22:3327–55.
53. Rakhshanda S, Dalal K, Chowdhury HA, Mayaboti CA, Paromita P, Rahman AKMF, et al. Assessing service availability and readiness to manage cervical cancer in Bangladesh. BMC Cancer. 2021;21:670.
54. Saraiya M, Senkomago V. A door-to-door approach to cervical cancer screening. Lancet Glob Health. 2015;3:e63–4.
55. Chakraborty S, Nessa A, Ferdous N-E, Rahman MM, Rashid MHU, Sonia AA, et al. Prevalence and genotypic distribution of high-risk human papillomavirus (HPV) among ever-married women in coastal regions of Bangladesh. PLoS ONE. 2024;19:e0313396.

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