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Systematic Literature Review

Mathematical Models for Evaluating Effectiveness and Cost-Effectiveness of Cervical Cancer Control Policies in Populations Including Women Living With Human Immunodeficiency Virus: A Scoping Review

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ABSTRACT

Objectives: Mathematical modeling is increasingly used to inform cervical cancer control policies, and model-based evaluations of such policies in women living with human immunodeficiency virus (HIV) are an emerging research area. We did a scoping review of published literature to identify research gaps and inform future work in this field.

Methods: We systematically searched literature up to April 2022 and included mathematical modeling studies evaluating the effectiveness or cost-effectiveness of cervical cancer prevention strategies in populations including women living with HIV. We extracted information on prevention strategies and modeling approaches.

Results: We screened 1504 records and included 22 studies, almost half of which focused on South Africa. We found substantial between-study heterogeneity in terms of strategies assessed and modeling approaches used. Fourteen studies evaluated cervical cancer screening strategies, 7 studies assessed human papillomavirus vaccination (with or without screening), and 1 study evaluated the impact of HIV control measures on cervical cancer incidence and mortality. Thirteen conducted cost-effectiveness analyses. Markov cohort state-transition models were used most commonly (n = 12). Most studies (n = 17) modeled the effect of HIV by creating HIV-related health states. Thirteen studies performed model calibration, but 11 did not report the calibration methods used. Only 1 study stated that model code was available upon request.

Conclusions: Few model-based evaluations of cervical cancer control strategies have specifically considered women living with HIV. Improvements in model transparency, by sharing information and making model code publicly available, could facilitate the utility of these evaluations for other high disease-burden countries, where they are needed for assisting policy makers.

Keywords: cervical cancer, comparative effectiveness, cost-effectiveness, HIV, HPV, modeling, prevention, screening, vaccination.

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Introduction

Cervical cancer is preventable through vaccination against oncogenic high-risk human papillomavirus (HPV), its underlying cause, and screening for and treatment of precancerous cervical lesions. Nevertheless, it remains the fourth most common cause of cancer-related mortality among women worldwide.[1,2] Most cervical cancer cases occur in low- and middle-income countries, where cervical cancer screening coverage is generally low.[3] In 2020, the World Health Organization (WHO) released a strategy to eliminate cervical cancer as a public health problem.[4] The report highlights that a combined scale-up of HPV vaccination (primary prevention) and screening for and treatment of cervical precancer (secondary prevention) is needed to achieve that goal. Nevertheless, there are many different possible cervical cancer prevention strategies, and the optimal combination of interventions in a given setting and population remains unclear.

The highest cervical cancer incidence rates are observed in sub-Saharan Africa, particularly in Southern African countries with high human immunodeficiency virus (HIV) infection prevalence.[1,5] Women living with HIV are disproportionally affected by cervical cancer because of an increased risk of persistent HPV infection, progression to cervical cancer, and precancer treatment failure.[6-8] In countries with high HIV prevalence, greater efforts with tailored prevention approaches for women living with HIV may be required to achieve elimination. The 2021 WHO cervical cancer screening guidelines recommend HPV testing as the primary screening method for all women, with an earlier starting age (25 vs 30 years) and shorter intervals (every 3-5 vs 5-10 years) for women living with HIV.[9] Furthermore, because HPV prevalence is

high in women living with HIV, a triage test is required to make treatment decisions in those who test positive for HPV.

Mathematical models help evaluate the effectiveness and cost-effectiveness of different cervical cancer prevention approaches, so they provide crucial information for policy makers.[10] A systematic review identified 153 model-based cervical cancer screening evaluations published by 2013.[11] Nevertheless, only 33 evaluations focused on cervical cancer control in low- and middle-income countries, and the review did not specifically consider women living with HIV.

We performed a scoping review to systematically map the published modeling work evaluating cervical cancer prevention strategies in populations that include women living with HIV and identify gaps to inform future work in this field.

Methods

The reporting of the scoping review followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension for Scoping Reviews checklist.[12]

Eligibility Criteria

We included mathematical modeling studies assessing the effectiveness or cost-effectiveness of cervical cancer prevention strategies in populations explicitly including women living with HIV. Studies reporting on models assessing outcomes related to cervical cancer or precancer and models assessing both clinical and economic outcomes were eligible. We included studies examining any form of cervical cancer prevention strategy such as HPV vaccination or different screening modalities such as cervical cytology, HPV testing, or visual inspection with acetic acid (VIA). We excluded posters and abstracts without full-text publications.

Literature Search

We systematically searched Embase.com, MEDLINE, Web of Science, Cochrane Central Register of Controlled Trials, and EconLit until April 27, 2022, without restrictions on language or the year of publication. The search strategy combined keywords for the clinical conditions of interest (cervical cancer and precancer, HPV infection, and HIV/AIDS) and cervical cancer prevention strategies (screening and vaccination), with terms related to mathematical modeling and economic evaluations (Appendix Box 1 in Supplemental Materials found at https://doi.org/10.1016/j.vhri.2022.07.001). The search strategy was developed in collaboration with an experienced information specialist (W.M.B.).

Two reviewers (R.I. and E.R.) independently screened the deduplicated records for eligibility based on their titles and abstracts. Where eligibility could not be determined from titles and abstracts, we retrieved and assessed the full texts. Disagreements concerning eligibility were resolved by discussion.

Data Charting and Analysis

We developed a standardized electronic data charting form using the Research Electronic Data Capture (REDCap) web application.[13] Given the anticipated variability in the types and features of models and their associated analyses among the included studies, the data charting form underwent extensive pilot testing and was adapted accordingly. We charted information on study characteristics, target population, cervical cancer prevention strategies assessed, and effectiveness and cost-effectiveness results reported. Studies were categorized into those modeling a hypothetical cohort and studies using population-based or clinic-based models. A hypothetical cohort refers to a cohort of individuals representing an average person in the target population. A population-based model focuses on a cohort comprising all individuals in the target population, who are stratified by demographic attributes, and reflects the actual size of the target population. A clinic-based model follows a well-defined group of individuals attending a clinic over an analytical period. We also captured data on the modeling approach, including the type of model used, assumptions made, calibration, validation, sensitivity analyses, and model transparency. Two reviewers (R.I. and E.R.) independently charted data from eligible studies. Discrepancies in charted data between the 2 reviewers were resolved by discussion. We used narrative synthesis and descriptive statistics to summarize the characteristics, cervical cancer prevention strategies, model building and testing, and results of the included studies. We used Stata 15 (StataCorp LLC, College Station, TX, USA) for descriptive statistical analyses.

Results

Study Selection and Characteristics

Our literature searches identified 2256 records. After removing duplicates, we screened titles and abstracts of 1504 records for eligibility and retrieved 162 full-text reports for an in-depth assessment (Fig. 1). The most common reason for exclusion was that HIV was not considered in the model (n = 98). Twenty-two reports met the inclusion criteria.[14-35]

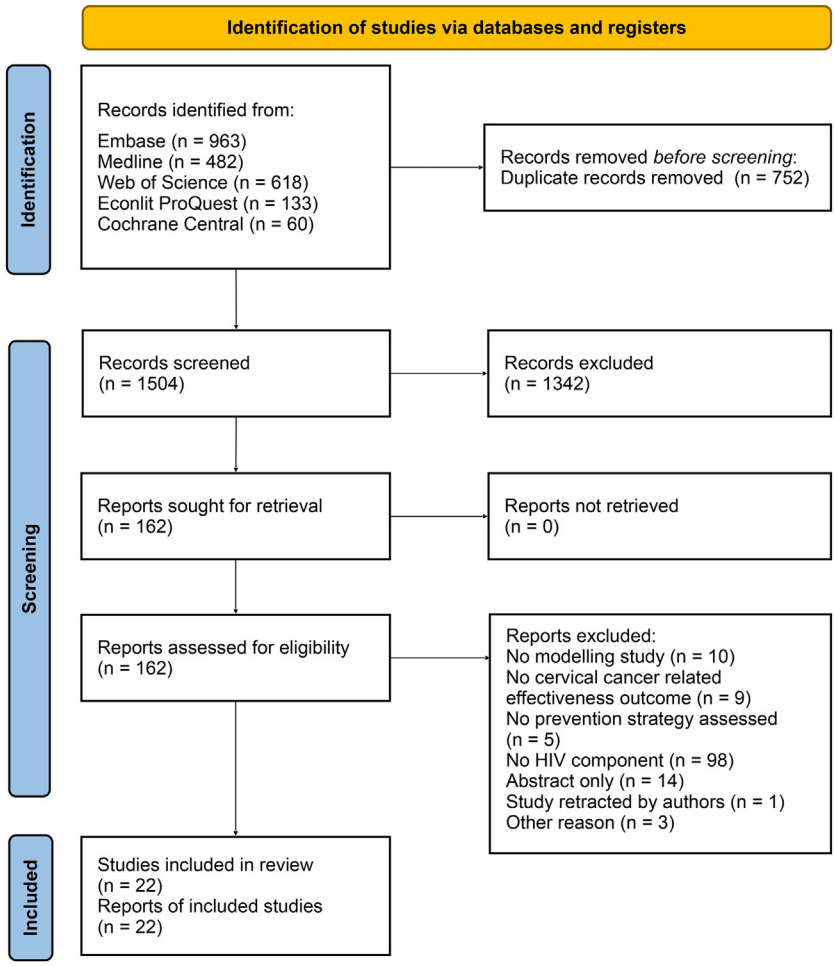
The 22 included studies are summarized in Table 1.[14-35] Thirteen studies (59%) conducted cost-effectiveness analyses (CEAs), and 9 (41%) examined the effectiveness of different prevention strategies on cervical cancer incidence or mortality. Fourteen studies (64%) were based on adaptations of previous modeling work: of these, 9 studies[15,16,18,25,28,30-33] built on published HIV, HPV, or cervical cancer models and 5 studies[14,22,24,27,35] were adaptations of already included models.[19,20,23,31] Most studies compared cervical cancer prevention strategies in 1 country; 18 (82%) focused on African countries (Fig. 2), including 10 on South Africa. One study evaluated the cost-effectiveness of screening across India, Kenya, Peru, South Africa, and Thailand.

Seven studies (32%) modeled hypothetical cohorts, 10 (45%) were population based, and 2 (9%) were clinic based (Table 1[14-35]). The other 3 studies (14%) did not specify the modeled population. Most studies (n = 15, 68%) focused on women; 7 studies (32%) included both men and women. Fourteen studies (64%) modeled individuals with and without HIV, whereas 8 studies (36%) modeled women living with HIV only.

Cervical Cancer Prevention Strategies

The number of strategies compared ranged from 2 to 27 per study; for 1 study, it was unclear. Most studies assessed the effectiveness and cost-effectiveness of cervical cancer screening strategies (n = 14, 72%; see Appendix Table 1 in Supplemental Materials found at https://doi.org/10.1016/j.vhri.2022.07.001 for details). Four studies (4%) evaluated both cervical cancer screening and HPV vaccination strategies; 3 studies (14%) focused on HPV vaccination only. The most common screening modality was cervical cytology (n = 15), followed by HPV testing (n = 14) and VIA (n = 7). One study assessed the effects of general HIV treatment and control measures, including antiretroviral therapy (ART), male circumcision, and pre-exposure prophylaxis, on cervical cancer incidence and mortality.[23] Of the studies that evaluated cervical cancer screening strategies or HPV vaccination, 2 studies also examined ART[14] or male circumcision.[16]

Figure 1. Flow diagram of study selection.



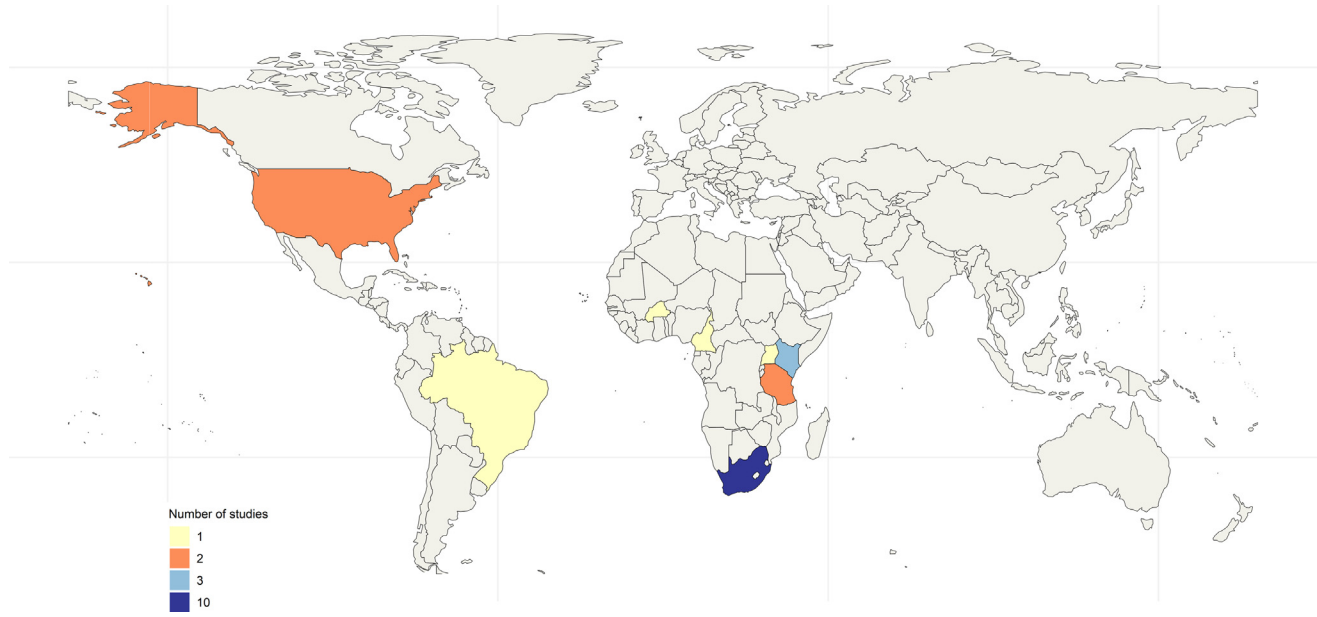
Modeling Approaches

Markov cohort state-transition models were used most commonly (n = 12, 55%). Four studies (18%) used differential equation models and 3 studies (14%) used microsimulation (Table 2). More than half of the studies applied a lifetime time horizon (n = 13, 59%). Four focused on cytological or histological detection of precancerous lesions as outcomes. They applied shorter time horizons of up to 2 screening cycles.[17,18,26,29]

Seventeen studies (77%) modeled the effect of HIV by creating HIV-related health states. Five studies (23%) considered HIV in a different way: 2 modified model parameters (eg, weighting them according to HIV prevalence),[16,18] and 3 of these studies were restricted to women living with HIV.[17,26,29] Five studies modeled HIV transmission.[23,24,27,31,33] HIV disease progression was typically characterized by CD4 cell counts (n = 9) or WHO clinical stage of HIV/AIDS (n = 1). Five studies did not model HIV disease progression but included HIV-related mortality in the model. Twelve studies considered the effect of ART, through (1) reductions in HIV-related mortality based on age at ART initiation, CD4 category at ART initiation, or time on ART, (2) adaptation of the transition probabilities between HIV-related health states without creating separate health states for ART, (3) inclusion of ART specific health states (untreated and treated with or without viral suppression), (4) cost of HIV care, or (5) assumptions on the risk of progression and regression of HPV and precancerous lesions. For 1 study,[35] we could not determine whether ART was considered.

Sixteen studies (73%) modeled the HPV dynamics; 11 of those (62%) modeled different HPV genotypes, including individual high-risk HPV genotypes or low-risk versus high-risk categorizations. Six studies modeled HPV transmission between men and women.[16,23,24,27,31,33] All but 2 study[17,26] incorporated precancerous progression in their models, using the cervical intraepithelial neoplasia classification (n = 13) or Bethesda system (n = 6) of low-grade intraepithelial lesions or high-grade lesions. One study incorporated progression, no change, and regression as arms in a decision tree model.[29] Among the 20 studies that modeled precancer progression, 13 (65%) allowed progression rates to vary by HIV status. For 1 study, it was unclear whether rates differed between women with and without HIV.[16] Most studies (n = 19, 86%) modeled different stages of cervical cancer, often using categories of localized, regional, and distant cancer (n = 11) or International Federation of Gynecology and Obstetrics stages I to IV (n = 5). Two studies[18,25] used broad categories such as cancer (any stage), cured cancer, or cancer-related death. For 1 study,[28] the cancer staging remained unclear. Only 4 studies assumed that cervical cancer progression varied by HIV status.

Figure 2. Number of single-country studies based on geographic location.



Model Estimation, Validation, Analyses, and Transparency

Model calibration was performed in 13 studies (59%), mainly for parameters related to HPV dynamics (n = 8, 36%) and cervical precancer and cancer development (n = 10, 45%). Most studies did not describe calibration approaches (Table 2). Nine studies (41%) validated models against external data. Six studies (27%) conducted parameter uncertainty analysis, using either Monte Carlo sampling to propagate parameter uncertainty (n = 4)[25,27,29,32] or the 50 best fitting parameter sets from a calibration result (n = 1).[15] No study estimated the value of conducting further studies to reduce uncertainty (value of information analyses).

Among the 13 CEA studies, 6 (46%) chose a societal perspective, 5 (38%) a healthcare perspective, and 2 (17%) both perspectives. All CEA studies reported the costing years. Five CEA studies (38%) included quality of life using quality-adjusted life-years as effectiveness measures,[19,21,25,30,34] and 10 (77%) provided the results in an incremental cost-effectiveness ratio (ICER) table.[15,17,19-21,25,26,30,32,34] One study[29] reported the average cost-effectiveness ratios but no incremental analysis. Ten CEA studies did not report a willingness-to-pay threshold.[17,19-22,26,29,30,34,35] The remainders used per capita gross domestic product as the benchmark for willingness-to-pay thresholds.[15,25,32] One study used the opportunity cost of providing HIV care as a proxy for the threshold.[15]

Most studies (n = 20, 91%) examined the sensitivity of results to variation in key parameters. All publications provided details on parameter values, and 16 (73%) included a diagram of the model structure. Supplemental material was available for 13 studies (59%), giving additional information on model estimation and validation, model structure, or results. Sixteen articles (73%) were open access publications, but only 1 study[28] made the model code available upon request.

Results of Included Studies

Early US-based modeling work examined the utility of cervical cancer screening among women living with HIV, given the high competing HIV-related mortality in the 1990s.[19,21] Cytology-based cervical cancer screening offered quality-adjusted life expectancy gains among women living with HIV,[19] and using HPV testing for risk stratification was cost-effective.[21] The authors expanded their work to low- and middle-income countries. Strategies such as VIA or HPV testing were cost-effective alternatives to cytology-based cervical cancer screening in these countries.[20,22] These results were confirmed by others.[15,17,18,26,32,34] Strategies combining HPV vaccination and primary HPV testing are predicted to be particularly effective in preventing cervical cancer.[24,33] A South African study compared cervical cell collection devices for cytology-based screening and found that the more expensive plastic brush would yield lower costs per woman screened than the wooden spatula because fewer smears would have to be repeated.[29] In a study on women living with HIV in Kenya, conventional VIA and HPV testing similarly reduced the number of cervical cancer cases and deaths because the effect of better diagnostic performance of HPV testing was balanced by minimized losses to follow-up through same-day treatment for VIA-positive women.[28] Screening benefits could be improved further through the use of digital imaging devices for VIA or point-of-care HPV testing.[28] Another Kenyan study suggested that preventive cryotherapy without previous screening was the most cost-effective cervical cancer prevention strategy in women living with HIV,[35] but the authors highlighted the ethical concerns regarding this approach.

In South Africa, adding the bivalent HPV vaccine to the cytology-based screening programs was cost-effective based on quality-adjusted life-years gained,[25,30] but because of HIV-related mortality cost-effectiveness might be lower in women living with HIV than the general female population.[25] A more recent study suggested that compared with no HPV vaccination, a single-dose nonavalent HPV vaccination (with an assumed 80% lifelong vaccine efficacy) among preadolescent South African girls would lead to a similar reduction in cervical cancer incidence and mortality among all female subpopulations, irrespective of HIV status, CD4 cell count, or ART status.[31] A Kenyan study found that catch-up HPV vaccinations for women at the age of 15 to 24 years will help in reducing the cervical cancer burden substantially faster and earlier.[27]

Table 1. Modeled populations and prevention strategies of included studies.

Author (year)	Country	Type of population	People with HIV only	Women only	Cost-effectiveness analysis	Prevention strategies modeled	Number of strategies
Atashili et al (2011)[14]	Cameroon	Hypothetical cohort	Yes	Yes	No	Screening, ART	4
Campos et al (2018)[15]	South Africa	Hypothetical cohort	No	Yes	Yes	Screening	19
Davis et al (2021)[16]	Uganda	Population based	No	No	No	Screening, HPV vaccination, male circumcision	8
Devine et al (2021)[17]	Burkina Faso	Hypothetical cohort	Yes	Yes	Yes	Screening	12
Dreyer et al (2019)[18]	South Africa	Population based	No	Yes	No	Screening	2
Goldie (1999)[19]	USA	Hypothetical cohort	Yes	Yes	Yes	Screening	7
Goldie et al (2001)[20]	South Africa	Hypothetical cohort	No	Yes	Yes	Screening	> 16*
Goldie et al (2001)[21]	Probably USA	Unclear	Yes	Yes	Yes	Screening	10
Goldie et al (2005)[22]	India, Kenya, Peru, South Africa, and Thailand	Unclear	No	Yes	Yes	Screening	25
Hall et al (2020)[23]	Tanzania	Population based	No	No	No	Male circumcision, ART, PrEP	5
Hall et al (2021)[24]	Tanzania	Population based	No	No	No	Screening, HPV vaccination, cervical cancer treatment	8
Li et al (2015)[25]	South Africa	Population based	No	Yes	Yes	Screening, HPV vaccination	2
Lince-Deroche et al (2015)[26]	South Africa	Clinic based	Yes	Yes	Yes	Screening	5
Liu et al (2022)[27]	Kenya	Population based	No	No	No	HPV vaccination	6
Perez-Guzman et al (2020)[28]	Kenya	Population based	No	No	No	Screening	5
Schnippel et al (2015)[29]	South Africa	Population based	Yes	Yes	Yes	Screening	4
Sinanovic et al (2009)[30]	South Africa	Hypothetical cohort	No	Yes	Yes	Screening, HPV vaccination	2
Tan et al (2018)[31]	South Africa	Population based	No	No	No	HPV vaccination	2
Vanni et al (2012)[32]	Brazil	Unclear	No	Yes	Yes	Screening	27
van Schalkwyk et al (2021)[33]	South Africa	Population based	No	No	No	Screening, HPV vaccination	16
Vijayaraghavan et al (2009)[34]	South Africa	Hypothetical cohort	No	Yes	Yes	Screening	6
Zimmermann et al (2017)[35]	Kenya	Clinic based	Yes	Yes	Yes	Screening	7

ART indicates antiretroviral therapy; HIV, human immunodeficiency virus; HPV, human papillomavirus; PrEP, pre-exposure prophylaxis.
*Exact number of prevention strategies assessed is unclear.

Several studies examined the effect of HIV interventions on cervical cancer-related outcomes. Providing ART for women living with HIV in Cameroon without offering cervical cancer screening doubled cervical cancer-related mortality due to increased life expectancy.[14] Adding a once-in-a-lifetime screening at age 35 years reduced cervical cancer-related mortality from 47 to 42 per 1000 women on ART.[14] Two modeling studies from Uganda and Tanzania found that HIV control measures substantially reduce cervical cancer incidence and mortality. The Tanzanian study predicted that maintaining a high male circumcision coverage of

Table 2. Modeling characteristics and calibration of the 22 included studies.

Modeling characteristics	Number of studies, n (%)
Type of model	
Markov cohort state-transition model	12 (55)
Deterministic differential equations	4 (18)
Microsimulation	3 (14)
Decision tree	1 (5)
Algebraic formula	2 (9)
Time step for model updating	
1 month	8 (36)
2 months	2 (9)
3 months	2 (9)
6 months	1 (5)
12 months	2 (9)
Unclear/not applicable	7 (32)
Randomness	
Stochastic	15 (68)
Deterministic	4 (18)
Unclear/not applicable	3 (14)
Unit of analysis	
Individual	4 (18)
Compartment	17 (77)
Unclear	1 (5)
Interaction between individuals modeled	
Yes	6 (27)
No	16 (73)
Model calibration	
HIV-related parameters	4 (18)
HPV-related parameters	8 (36)
Cervical (pre)cancer-related parameters	10 (45)
Not performed	9 (41)
Calibration method among studies using calibration (n = 13)	
Likelihood based approach	1 (8)
Random search algorithm	1 (8)
Unclear/not reported	11 (85)
Goodness-of-fit criteria* among studies using calibration (n = 13)	
Likelihood score	3 (23)
Chi-squared test	1 (8)
Trust region reflective algorithm	1 (8)
Visual comparison	1 (8)
Unclear/not reported	8 (62)

HIV indicates human immunodeficiency virus; HPV, human papillomavirus.
*One study used more than 1 criterion.

80% by 2070 would reduce cervical cancer incidence rates by 28%, with ART lowering the cervical cancer incidence rates by an additional 7%, relative to a scenario without ART.[23] Scaling up male circumcision in Uganda was particularly beneficial where the rollout and uptake of HPV vaccination had been slow.[16]

Discussion

We found 22 modeling studies that assessed the effectiveness or cost-effectiveness of cervical cancer control policies in populations including women living with HIV. Most studies used Markov cohort state-transition models, and almost half focused on South Africa. There was substantial heterogeneity regarding cervical cancer control policies, type of population modeled, and modeling approaches, including the calibration and validation of the model or sensitivity analyses.

Our scoping review shows that few model-based evaluations of cervical cancer control strategies specifically considered women living with HIV in their analyses. A systematic review[11] identified 153 model-based cervical cancer screening evaluations published by 2013, 6 of which are also included in our scoping review.[19-22,32,34] Nevertheless, the review did not report whether studies incorporated HIV in their models. This finding is in line with a consensus statement and quality framework for modeled evaluations of HPV-related cancer control (HPV-FRAME) published in 2019, which identified model-based evaluations in individuals living with HIV as an emerging research topic.[36]

The HPV-FRAME consensus statement recommends that differences in HPV pathogenesis and HPV-associated cancer mortality by HIV status should be captured in the model. The importance of adapting disease state-transition probabilities for women living with HIV who have consistently high HPV prevalence was also highlighted in a 2021 publication proposing a new generation of microsimulation models for cervical cancer control evaluation.[37] We found that more than half of the reviewed studies modeled the effect of HIV on HPV disease progression and regression, but only 4 studies also varied the cervical cancer progression and mortality rates by HIV status. Authors frequently acknowledged a lack of empirical data on HPV and cervical disease dynamics among women living with HIV as a limitation of their studies. In general, models considered HIV in different ways depending on the policy question examined. Only 5 studies modeled HIV transmission—1 because it focused on the effectiveness of HIV control strategies on cervical cancer incidence and mortality,[23] and the other studies extended HIV and HPV transmission models to assess the impact of cervical prevention strategies.[24,27,31,33] If HIV disease progression was incorporated, this was mostly done by including CD4 cell count stages in the model, yet CD4 cell categories varied across studies.

The ISPOR Task Force on Good Research Practices on Modeling Studies provides generic guidance on mathematical modeling for economic evaluations of pharmaceuticals and other healthcare technologies.[38] Good modeling principles stipulate that the model types fit the policy question and are built as parsimoniously as possible in structure and parameterization. For example, static models may be suitable for the evaluation of cervical cancer screening strategies. In contrast, dynamic models that include transmission are recommended in the context of HPV vaccination to capture herd effects.[36] We found that 2 of 7 models that evaluated HPV vaccination were static and did not consider HPV incidence and prevalence changes over time. Static models may be appropriate to obtain a worst-case estimate, that is, ignoring the effect of herd immunity, or if among the compared strategies, only 1 leads to herd effects.[36] The studies included in our scoping review generally did not clarify their rationale for their selected modeling approach. Markov models[39] were likely chosen for their parsimonious structure and, hence, the limited amount of data needed for estimating the model parameters. Nevertheless, unlike individual-based models, cohort models cannot capture patterns arising from complex dynamics. They cannot track individual trajectories, and the number of model states can become impractically large when numerous individual characteristics are modeled.

The increasing role of mathematical models to inform public health decisions makes rigorous testing of such models and the transparency and reproducibility of the modeling studies more critical than ever. For estimating model parameters whose data were not available (eg, not directly observable or measurable), most studies used a statistical calibration approach (model

calibration). We found that, in general, the studies did not provide technical information on calibration. Few studies indicated their calibration approaches and the criteria by which the estimates were deemed sufficiently accurate (goodness of fit). Moreover, while acknowledging the lack of data (by using model calibration), only 6 studies evaluated the effect of uncertainty in the parameter estimates on model outcomes. Among these 6 studies, none quantified the value of collecting more data to reduce decisional uncertainty.[40] More than half of the studies in our review did not report whether they examined the concordance between their model outputs and external sources (external validation).

More than a decade ago, the participants of a workshop on HPV modeling noted that scientific journal articles' content and word limitations do not allow for a sufficiently detailed description of model-based evaluations.[41] They suggested that comprehensive appendices should be published and that model code should be made available online. Many studies included in our scoping review provided supplemental materials with additional information on model structure, estimation, validation, or analytical results. Nevertheless, only 1 study in our review stated that their computer codes could be accessed online upon request.[28]

Specific best practice guidelines for CEA studies were set forth by the first and second panels on cost-effectiveness in health and medicine.[42] In line with these guidelines, most of the reviewed CEAs adopted a societal perspective to capture health- and nonhealth-related consequences, reported the costing years, and summarized the results in ICER table. One study[29] did not use the proper metric for demonstrating the cost-effectiveness of a health intervention (ie, ICER).[43] It calculated the average cost-effectiveness ratios but no incremental analysis, failing to capture the opportunity cost of the next best use of resources. Several studies did not specify a willingness-to-pay threshold for an additional gain in outcome. Such information is useful for ensuring the comparability of the cost-effectiveness estimates with other studies. In addition, many studies did not consider the quality of life in their outcome measures. The omission of this critical dimension was most likely driven by the lack of data on utility weights, particularly for low- and middle-income settings.[30]

The strengths of our scoping review lie in the comprehensive literature search performed, the in-depth assessment of the included studies, and the identification of gaps in model-based evaluations for cervical cancer prevention among women living with HIV. Nevertheless, some limitations need to be acknowledged. We identified only 22 eligible studies, and there was substantial between-study heterogeneity in terms of cervical cancer control policies assessed and modeling approaches used. Therefore, it was difficult to summarize the study results beyond a narrative synthesis of the individual study results and to compare the modeling approaches and parameterizations directly. Depending on the study question of a given model-based evaluation, different model types, parameters, and data sources for parameterization may be appropriate. We were also not able to perform meta-regression analyses and assess the impact of specific modeling aspects on the effectiveness and cost-effectiveness results obtained. Furthermore, we did not provide an in-depth critical appraisal of the studies but rather highlighted areas where model reporting and transparency could be improved.

Conclusions

Although mathematical modeling for the evaluation of cervical cancer control strategies is a rapidly growing field and women living with HIV are disproportionally affected by cervical cancer, few model-based evaluations have specifically considered the impact of HIV. Moreover, almost half of the identified studies focused on South Africa, and evaluations in other settings with high HIV and cervical cancer burden are lacking. Country-specific models may not be directly transferable to different settings. Improving transparency by sharing detailed information on model structure, parameters, and assumptions and making model code available online could facilitate the expansion of model-based evaluations to other high disease-burden countries, where they are needed to guide policy making.

Supplemental Material

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