Effectiveness of Integrating HPV Vaccination into Adolescent Health Service Delivery in Low and Middle-income Countries: Protocol for a living systematic review

Protocol information

Version 1.0, 12/06/2026

Author list and CRediT

Name	Affiliation	Contribution	Conflict of interest
Britta Tendal Jeppesen	Future Evidence Foundation	Conceptualisation, methodology and supervision	None
Melissa Bond	EPPI Centre, UCL	Methodology, Writing - review and editing	None
Ailbhe Finnerty Mutlu	EPPI Centre, UCL	Methodology, Writing - review and editing	None
Mikey Rosato	Future Evidence Foundation	Writing and project administration	None
Firmaye Bogale	CESDA	Methodology, Writing - review and editing, Project administration	None
Sabit ababor	CESDA	Methodology, Writing - review and editing,Project administration	None
Zelalem Kebede	CESDA	Methodology, Writing - review and editing	None
Yordanos Tadesse	CESDA	Methodology, Writing - review and editing	None
Tadesse Dagget	CESDA	Methodology, Writing - review and editing	None

Shalu Jain	CESDA	Methodology advise	None
Greg Sheaf	CESDA	Searching of evidence and management	None
Mamuye Hadis	CESDA	Quality control (validation) and write up	None
Biruk Hailu	CESDA	Content expert input	None
Elaine Charurat	JHPIEGO	Writing - review and editing	None
Anissa Sidibe	JHPIEGO	Writing - review and editing	None
Dereje Bizuneh	WHO	Writing - review and editing	None
Rachel Belt	Consultant	Writing - review and editing	None
Mpheng Molapo	Lesotho Ministry of Education	Writing - review and editing	None
Katie Reynolds	Village Reach	Writing - review and editing	None
Julia Guerette	Village Reach	Writing - review and editing	None
Eva Muluve	Girl Effect	Writing - review and editing	None
Balkiss Abdelmoula	MENA Coalition for HPV Elimination	Writing - review and editing	None
Anju Malhotra	GFF	Writing - review and editing	None
Lauren Greenberg	EGPAF	Writing - review and editing	None
Lillian Chinyangana	EGPAF	Writing - review and editing	None
GebreMichael Molla	Africa CDC	Writing - review and editing	None
Lora Shimp	JSI	Writing - review and editing	None
Proma Paul	JSI	Writing - review and editing	None
Laura Nic Lochlainn	WHO	Writing - review and editing	None
Khin Devi Aung	UNICEF	Writing - review and editing	None

Funding

This work was supported by the Gates Foundation (INV-075762). The funders had no role in study design, data collection, analysis and interpretation of data, decision to publish, or preparation of the manuscript.

Correspondence

Britta Tendal Jeppesen britta@futureevidence.org

Note to tactical Group Members – common sections during reviewing the three LSRs

LSRs 6, 7, and 8 form part of a coordinated series of living systematic reviews evaluating different approaches to HPV vaccine delivery. To minimize duplication of effort during protocol review, please note that several sections are intentionally harmonized across the protocols and are identical or substantially similar.
The following sections are common across all three LSRs and generally only need to be reviewed once:
• Background and rationale relating to HPV vaccination and cervical cancer prevention (at least the first three paragraphs)
• Overall methodological approach
• Eligibility criteria relating to populations
    o Study types, Publication status, Participants, Geographical context, Language, Year
• Study designs eligible for inclusion
• Search methods and Screening
    o Study selection procedures
• Risk of bias/critical appraisal methods
• Data extraction procedures
• Analysis
• Certainty of evidence assessment
• Living review procedures and update processes

Note: we encourage focus on detailed review on the sections that differ across protocols, namely:

LSR 6 - Integrated Health Services and HPV Vaccination
- Key terms and concepts
- Eligibility criteria - concepts
- Outcomes

LSR 7- HPV Vaccination in Adolescent Health Service
- Key terms and concepts
- Description of the interventions
- Eligibility criteria - concepts
- Outcomes

LSR 8 - HPV Vaccination Through Routine EPI
- Key terms and concepts
- Eligibility criteria - concepts
- Outcomes

Introduction

This living systematic review (LSR) is being produced for the HPV Living Evidence and Knowledge Partnership.

The partnership includes:

- The Alive team at the Future Evidence Foundation. The goal of Alive is to build innovative evidence systems that empower decision-makers to solve society's most pressing challenges.
- The Center for Evidence-synthesis, Support & Development in Africa (CESDA), an Ethiopia-based organisation with expertise in systematic reviews, evidence synthesis, and knowledge translation. CESDA brings strong experience in systematic, rapid, qualitative, and mixed-methods reviews, supporting evidence-informed decision-making across health and development sectors in African contexts.
- UCL EPPI Centre. The EPPI Centre aims for better evidence for better decision-making: robust and responsive reviews informing policy and practice
- The HPV vaccine delivery community, represented through three structures: a Steering Group; a Tactical Group; and a Group of Advisors.

Background

Cervical cancer remains a major global public health problem despite being highly preventable. Globally, it was the fourth most common cancer among women worldwide in 2022, with an estimated 662,301 new cases and 350,000 deaths [1], [2]. However, this figure masks a profound geographic disparity where the disease disproportionately (94% of cervical cancer deaths) concentrates in low- and middle-income countries (LMICs), being the leading cause of cancer-related mortality among women across sub-Saharan Africa and parts of Southeast Asia [1], [2] .

These regional differences reflect disparities in access to vaccination, screening, and treatment services further influenced by broader social and economic determinants, including gender inequality and poverty [2], [3] .

More than 95% of cases are attributable to persistent infection with oncogenic HPV genotypes, particularly types 16 and 18. A causal relationship that renders cervical cancer, in principle, both preventable through vaccination and detectable through screening [1], [2] . Because prophylactic HPV vaccination can prevent the majority of HPV-attributable cervical cancers, it is a cornerstone of primary prevention and a critical component of global efforts to reduce the burden of disease [1], [3]

Recognizing both the preventability of cervical cancer and the disproportionate burden carried by poorer countries, the World Health Organization (WHO) launched the Global Strategy to Accelerate the Elimination of Cervical Cancer as a Public Health Problem. This strategy established the 90-70-90 targets to be achieved by 2030: 90% of girls fully vaccinated with the HPV vaccine by age 15 years, 70% of women screened with a high-performance test by ages 35 and 45 years, and 90% of women identified with cervical disease receiving appropriate treatment and care. Achieving these targets would place countries on the path toward eliminating cervical cancer as a public health problem [4].

Although HPV vaccination is central to this elimination agenda, implementation has lagged behind policy ambition. Global HPV vaccine coverage has improved, but it remains well below the 90% target, and progress has been uneven across settings. WHO reported that first-dose HPV vaccine coverage among girls increased from 27% in 2023 to 31% in 2024, while coverage in lower-income countries supported by Gavi reached 25% in 2024 [5], [6]. Although these gains are important, they remain far below the threshold required for elimination and point to persistent weaknesses in programme reach and continuity.

In many LMICs, suboptimal uptake and incomplete series completion have been linked to fragmented service delivery, weak adolescent health platforms, school absenteeism or exclusion, limited access for out-of-school girls, workforce constraints, insufficient community engagement, and financing or supply challenges[3]. These constraints create missed opportunities to reach adolescents through routine contacts with health and education systems and help explain why HPV vaccination often underperforms when delivered as a stand-alone intervention.
Integrating HPV vaccination into existing service delivery platforms has therefore emerged as a promising implementation strategy [7] . Potential platforms for integration include adolescent health services, school health services, child health days, among other platforms that help reach the target population. Integration may improve operational efficiency, reduce duplication of outreach and delivery costs, strengthen follow-up for subsequent doses where relevant, and create more equitable opportunities to reach girls who might otherwise be missed by vertical HPV programmes [3], [8], [9]. . This rationale is also consistent with Immunization Agenda 2030, which emphasizes people-centred, integrated, so that immunization is not confined to infancy alone[9], [10] .

Evidence on the integration of HPV vaccination into existing delivery platforms remains fragmented and difficult to apply in decision-making. Studies are dispersed across immunization, adolescent health, school health, implementation science, and health

systems literature, with considerable variation in terminology, delivery models, and outcome measures[11], [12], [13]. Evidence is also uneven across settings and populations, with limited synthesis focused on outcomes most relevant to LMIC policy and programme decisions, including effectiveness, acceptability, equity, costs, and unintended consequences [11], [12]. As a result, decision-makers often lack clear and consolidated evidence on which integration models are most feasible and beneficial in specific contexts [11].

A living systematic review (LSR) is needed to provide timely, policy-relevant evidence on whether embedding HPV vaccination into existing adolescent health services improves delivery outcomes relative to stand-alone approaches [3], [7], [8] . Accordingly, this review will synthesize evidence on the effects of integrating HPV vaccination into adolescent health services on key outcomes, including uptake, completion, acceptability, cost, and equity, compared with standalone school-based, outreach, routine EPI, or hybrid delivery models [12].

Why is it important to do this living systematic review?

Given the rapidly evolving and context-dependent nature of evidence-based practice, traditional static review would quickly become outdated.

This review is suitable for a living systematic review because the evidence base on HPV vaccine delivery is changing rapidly. Recent WHO guidance has expanded programmatic options, including single-dose or two-dose schedules for adolescents and young people, catch-up vaccination, co-administration with other vaccines, and delivery through schools, health facilities, outreach, and campaigns. These changes create new opportunities to embed HPV vaccination into adolescent health service delivery points but the effectiveness, equity, feasibility, cost, and acceptability of these approaches are still evolving, particularly in low- and middle-income countries.

An LSR provides an approach that can continually incorporate new evidence, track emerging patterns, and support timely decision-making for countries introducing or scaling up HPV vaccination. This is particularly important in LMIC settings, where programmes must often adapt to dynamic information environments, resource constraints, and varying sociocultural contexts [17]. We currently have funding to keep the review living until early 2027, but are exploring options for sustainability beyond that.

In this protocol, we have considered PRISMA guidance established for living systematic reviews [17]

Research questions

What is the effectiveness of embedding HPV vaccination into adolescent health service delivery compared with other delivery platforms on uptake, completion, timeliness, equity, cost, acceptability, and unintended effects in Low- and Middle-income countries (LMICs)?

Primary Research Question

1. What is the effect of integrating HPV vaccination into adolescent health service delivery on initiation (uptake)of HPV vaccine compared with stand-alone or other delivery platforms?
2. What is the effect of embedding HPV vaccination into adolescent health service delivery or on completion of the HPV vaccine series compared with stand-alone or other delivery platforms?
3. What is the effect of embedding HPV vaccination into adolescent health service delivery on timely receipt of doses according to recommended schedules?

Secondary Research Questions

1. How does integrating HPV vaccination into adolescent health service delivery points affect equity in vaccination outcomes (uptake, completion, timeliness) across population subgroups defined by PROGRESS-Plus characteristics?
2. What evidence exists on the programme cost, delivery cost, cost-effectiveness, and resource requirements of embedding HPV vaccination into adolescent health service delivery points compared with stand-alone or other delivery platforms?
3. How do health workers, caregivers, adolescents, and other stakeholders perceive the acceptability and feasibility of embedding HPV vaccination into adolescent health service delivery compared with stand-alone or other delivery platforms?
4. What unintended effects (positive or negative) are associated with integrating HPV vaccination into adolescent health service delivery, including impacts on health systems, service utilization, and equity?

Key terms and concepts

This section defines the key concepts used in this review to ensure consistent interpretation

Integrating HPV vaccination: refers to the intentional integration of HPV vaccination with existing adolescent health services rather than delivery as a stand-alone or vertically implemented activity. This review adopts a broad conceptualization that

includes integration occurring at multiple levels, including programmatic, service delivery, workforce, financing, information systems, supply chain, governance, and monitoring and evaluation processes.

Adolescent health service delivery: refer to scheduled and routine health service contacts for young people aged 9-19 years that may include screening, counselling, preventive care, and immunisation delivered through clinical, school-based, or community-based platforms or other service delivery platforms.

Non-integrated HPV vaccination delivery platforms: refer to stand-alone HPV vaccination approaches that are not integrated into broader health service delivery platforms, including routine immunisation-only delivery, campaign-based delivery, outreach programmes, and stand-alone school-based vaccination programmes.

PROGRESS Plus framework: P-Place of residence (urban/rural, region); R - Race/ethnicity/culture/language; O- Occupation; G - Gender/sex; R – Religion; E-Education; S-Socioeconomic status; S-Social capital, Personal characteristics (age and disability), and feature of relationship (schooling status) [14]

Low- and middle-income countries (LMICs): Countries classified as Low- and middle-income economies according to the World Bank country income classification at the time of the study.

Description of the interventions

This review will consider studies that evaluate the integration of HPV vaccination delivery, i.e., the intentional integration of HPV vaccination into adolescent health service points, rather than delivered as a standalone activity as an intervention. Adolescent health service delivery are defined as scheduled, routine, and regular checkups by healthcare providers designed to ensure the healthy growth, development, and well-being of young people aged 9 to 19 years (WHO). These services may include preventive, promotive, and clinical components such as screening, counselling, and immunisation, delivered through clinical, school-based, or community platforms as long as these platforms are routine and scheduled.

The review will compare the intervention (integrated HPV vaccination delivery approaches) with non-integrated HPV vaccination strategies as comparator. This includes stand-alone routine immunisation services, campaign-based delivery, outreach programmes, school-based vaccination programmes, or hybrid delivery approaches that are not integrated into broader health service platforms.

Engagement and reporting

The primary users of this LSR will be decision-makers and primarily their advisors in low- and middle-income countries (LMICs), involved in HPV vaccine delivery, including but not limited to: representatives from National and Regional Immunization Technical Advisory Groups (NITAGs), EPI teams, Ministries of Health, Ministries of Education, Ministries of Finance, technical partners, academia, researchers, implementing partners, and civil society. However, this LSR also has application to policy, program design, and implementation decisions for normative and financing institutions, technical and learning partners, and evidence intermediaries at global and regional levels.

This review is not intended to replace national decision-making processes. Rather, it aims to strengthen evidence-informed deliberation by providing decision-makers at all levels with a continuously updated and contextually relevant synthesis of the effectiveness of embedding HPV vaccine delivery service into adolescent health service delivery points, including its effects on uptake, completion, timeliness, equity, cost, acceptability, and unintended effects.

Alive as the partnership secretariat will facilitate and convene a community of users to engage with, support the dissemination of, and directly use evidence that emerges from this LSR. This community and engagement process will focus on collectively refining a rigorous body of evidence to ensure policy and practice questions are met with timely and context-specific answers.

The community will be engaged through three structures.

- Steering Group (SG) which provides stewardship to the development of the living HPV vaccine delivery evidence base. It provides strategic direction and ensures that the living evidence serves the needs of the broader research and delivery community and meets the needs of end users. See here for the involved individuals.
- Tactical Group (TG) which provides expert guidance and technical oversight to CESDA, UCL and Alive, the teams responsible for developing the LSR. Members of the TG will provide technical oversight to ensure the LSR is both methodologically sound and meets the needs of decision-makers. The TG will provide technical oversight to ensure the development of robust, high-quality living protocol, providing input on PICO frameworks, search strategies, and inclusion criteria.
- Advisory Group (AG): Provides technical input and systems insight to inform the SG's strategic decisions. The AG includes membership from global normative and financing institutions and regional technical and learning partners and evidence intermediaries

Methods

This study is an LSR and will be updated continually. An LSR is a high quality, up-to-date online synthesis of research that is updated as data from new relevant research that meets study inclusion criteria becomes available [19]. This means that, following an initial search up to September 2026, repeat searches will be re-run monthly, any new studies incorporated into the review, and updates will be regularly published. Based on current funding, we anticipate that the last update will be in February 2027, but options for sustainability beyond that are being explored. The protocol will be registered on PROSPERO. In this protocol, we have considered PRISMA guidance established for LSRs (Akl et al., 2024). All the data and analyses compiled and generated by the project will be stored at data.evidence-repository.org.

Eligibility criteria

Study types

Inclusion

- The review will include eligible studies using experimental and quasi-experimental study designs (randomized controlled trials, cluster RCTs, and controlled before-and-after studies) and observational studies (cohort, case-control, and cross-sectional).
- This review will also include Qualitative and mixed methods studies to capture implementation determinants (barriers and facilitators), feasibility and acceptability, and unintended consequences along with contextual, stakeholder perspectives related to integrating HPV vaccine delivery into the routine immunization services.

Exclusion

- The review will exclude Editorial comments, conference abstracts without full data, non-evaluative program reports, animal studies, reviews and text and opinion papers

Publication status

Inclusion

This review will consider

- Studies involving early adolescent and adolescent girls as the primary target population, defined as all girls aged 9-14 years, consistent with WHO priority recommendations for HPV vaccination.
- Studies involving secondary target populations will also be considered, including
    - Females aged 15 years and older (including women in catch-up cohorts), Boys and men
- Parents/caregivers
- Healthcare providers
- Teachers/school administrators
- Policymakers/program managers

Exclusion

- Adults above 45 years of age (the age limit applies only to the vaccine-recipient population, not to stakeholder respondents)
- Pregnant women
- Populations with existing HPV-related cancers

Concepts

Inclusion

This review will include studies that evaluate the concept of embedding HPV vaccination into existing adolescent health service delivery points and life-course immunisation milestones delivery platforms, specifically:

- HPV vaccination delivered as part of or alongside adolescent health service delivery, including routine, scheduled adolescent health services (clinical, school-based, or community-based platforms).
- Studies where HPV vaccination is intentionally integrated into broader health service encounters, rather than delivered as a stand-alone activity.
- Comparisons involving non-embedded HPV delivery platforms, such as routine immunisation programmes, campaign-based delivery, outreach strategies, school-only vaccination programmes, or hybrid stand-alone delivery approaches.

Exclusion

- HPV vaccination delivered solely as a stand-alone immunisation intervention without integration into broader adolescent health service delivery. Studies primarily evaluating the integration of other health services alongside HPV vaccination delivery will be excluded, as these integrations/interventions are addressed in LSR 6

Participants

Inclusion

This review will consider

- Studies involving early adolescent and adolescent girls as the primary target population, defined as all girls aged 9-14 years, consistent with WHO priority recommendations for HPV vaccination.
- Studies involving secondary target populations will also be considered, including
    - Females aged 15 years and older (including women in catch-up cohorts), boys and men
- Relevant stakeholders
    - Parents/caregivers
    - Healthcare providers
    - Teachers/school administrators
    - Policymakers/program managers

Exclusion

- Adults above 45 years of age (the age limit applies only to the vaccine-recipient population, not to stakeholder respondents)
- Pregnant women
- Populations with existing HPV-related cancers

Geographical context

Inclusion

- Studies conducted in low- and middle-income countries (LMICs).
- Multi-country studies will be eligible if data from LMIC settings can be extracted separately.

Exclusion

- Studies conducted exclusively in high-income countries (HICs) will be excluded.

Language

Inclusion

- Publications in any language will be eligible.
- Non-English records identified during the search will be screened for potential eligibility using automated translation tools (e.g., Google Translate) at the title and abstract stage. Where studies are deemed potentially relevant, full-text translation support will be sought where feasible to enable full-text review and inclusion.

Exclusion

- None; no language restrictions are applied
- Studies for which full-text translation is not possible or feasible will not be included in the review. These studies will be documented and their potential relevance will be noted, but they may be excluded from full-text review, data extraction and synthesis.

Year

Inclusion

- All studies/records with no date restriction

Exclusion

- None

Outcomes

This review will consider studies that include one or more of the following outcomes

Primary outcomes:

- **HPV vaccine uptake:** The proportion of the target population (e.g., eligible adolescents) that have received at least one dose of the HPV vaccine within a specified period [8].
- **HPV vaccine completion:** The proportion of individuals who finish the full recommended HPV vaccination schedule (e.g., all required doses) among those who initiated the vaccine. This will for instance include A one or two-dose schedule for girls aged 9-14; A one or two-dose schedule for girls and women aged 15-20; Two doses with a 6-month interval for women older than 21 [15]

- **HPV vaccine timeliness:** proportion completing the series within the recommended schedule window at recommended ages

The secondary outcomes are:

- **Equity:** the distribution of HPV vaccination outcomes (e.g., uptake, completion, timeliness) across population groups based on factors that create social disadvantage or vulnerability including place of residence (urban/rural, geographic location, region), disability, migration, race/ethnicity/language, occupation, gender/sex, religion, education, socioeconomic status, social capital [10].
- **Cost:** The total reported cost of integrated HPV vaccine service versus non-integrated HPV vaccine service alone.
- **HPV vaccine acceptability:** The willingness of individuals, parents, or communities to agree to receive or allow administration of the HPV vaccine, regardless of whether vaccination actually occurs
- **Unintended effects**: Any unintended outcomes resulting from embedding HPV into adolescent health service delivery points. These could include misinformation, changes in health-seeking behaviours, logistical strain on health systems, or increased awareness of other health services.

Search and screening

Search strategy

A comprehensive search strategy will be developed by the team which includes an information specialist with a background in evidence synthesis reviews. The search strategy will aim to locate both published and unpublished records studies including institutional reports with no time limit. Searches will be performed in the following electronic databases: CINAHL (Ebsco), Cochrane Library, Embase (Elsevier), MEDLINE (Ebsco), PsycInfo (Ebsco), and Web of Science (Clarivate). Grey literature will be searched through Google Scholar, OpenAlex, WHO IRIS, UNICEF, WHO's ICTRP, and Gavi repositories, and directly on the websites of relevant organizations if identified.

The search will combine controlled vocabulary as appropriate with title/abstract keywords to account for evolving terminology in integrating other health services with HPV vaccination research. The strategy will incorporate truncation, wildcards, and proximity operators where supported, and will be adapted for each database as appropriate. An example search strategy for MEDLINE is presented in *Appendix 1*.

Title and abstract screening

Following the search, all identified citations will be collated and uploaded into EPPI Reviewer, a web application that enables researchers to manage the entire lifecycle of a review in a single location [18], and duplicates removed. A pilot test will be done on titles and abstracts, which will be screened by two independent reviewers for assessment against the inclusion criteria for the review. Any disagreements will be resolved by a third reviewer or through team discussions. After achieving high agreement (80% and above), a further subset of references will be single screened with a 10% check in by the team lead.

The double screened references will be divided into 10% subsets . These subsets will be used to iteratively develop and test the use of Large Language Models (LLMs) for screening. Prompts will be developed using the inclusion and exclusion criteria for the review and run in EPPI Reviewer using the integrated OpenAI GPT-4.1 model on the first 10%. The performance of the LLM will be evaluated by comparing it to the gold standard human reviewer judgments to determine the accuracy of the model in correctly including and excluding citations. Once the prompt has been refined and evaluated to accurately achieve above .95 recall, it will be deployed on all remaining unscreened citations. A 10% random selection of records will then be screened by the team lead to calculate agreement with the LLM.

Full text screening

Reviewers will independently assess the full text of studies retained after title and abstract screening. Discrepancies will be resolved by a third reviewer, or through team discussions. Reasons for exclusion will be documented. The results of the search and the selection process will be illustrated on a PRISMA flow diagram.

Data extraction

Data will be extracted using a standardized data extraction form (see Appendix 2 for the data extraction form). For each study retained after full-text screening, one reviewer will extract the data and a second reviewer will verify the data for accuracy and completeness.

Using a subset of studies with data extraction verified by two reviewers, LLM prompts will be iteratively developed and tested for all items on the data extraction form using the integrated OpenAI GPT-4.1 model within EPPI Reviewer. The prompts will be applied to all studies included at full text with a 10% random subset double screened by a human reviewer. If agreement is above 95%, the LLM will extract the remaining studies and then verify by a human reviewer for accuracy and completeness.

The data extraction form will be used to systematically collect information on study characteristics, intervention and comparator details, and review outcomes. Extracted information will include the country in which the study was conducted, participant characteristics, sample size, study design and methods, study setting and context, and characteristics of the intervention and comparator(s). Data will also be extracted on all review outcomes, including primary outcomes (HPV vaccine uptake, completion, and timely receipt where applicable) and secondary outcomes (equity, feasibility, acceptability, cost, and unintended effects). Information on implementation barriers and facilitators reported by study authors will be captured and synthesized under the relevant outcome domains, particularly feasibility, acceptability, and unintended effects.

Risk of bias (RoB)

Two reviewers will independently conduct the appraisal using the JBI critical appraisal tool dedicated to study types, with any disagreements resolved through discussion or consultation with a third reviewer. All studies, regardless of the results of their methodological quality, will undergo data extraction and synthesis. For this LSR, RoB assessments will be updated as new studies are incorporated. The results will be presented in summary tables and will inform the interpretation of findings and the overall confidence placed in the body of evidence.

Analysis

Quantitative evidence will, where possible, be pooled in statistical meta-analysis using Eppi-Reviewer. Effect sizes for binary outcomes will be expressed as either odds ratios or risk ratios with 95% confidence intervals. Effect sizes for continuous outcomes will be expressed as weighted mean differences (WMD) or standardized mean differences (SMD) and with their 95% confidence intervals. Statistical heterogeneity will be assessed using the standard chi-squared and I squared tests. Heterogeneity will be considered significant if $p < 0.05$ or $I2 > 50\%$. A random-effects model will be used as the primary analysis in order to account for expected variations in healthcare delivery platforms across different national contexts. If sufficient data are available, subgroup analysis will be done based on the country of primary study, study design, context of intervention, context of implementation, age group of the target population, type of adolescent health services to which HPV vaccination is embedded, and year of primary study publication.

Sensitivity analyses will be conducted to test decisions made regarding the influence of one study over the other for quantitative study. A funnel plot will be generated to assess publication bias if there are 10 or more studies included in a meta-analysis. Statistical

tests for funnel plot asymmetry (Egger test, Begg test, Harbord test) will be performed where appropriate. Where meta-analysis is not possible, the findings will be presented in narrative form including tables and figures to aid in data presentation. Equity analysis will be done using the PROGRESS-Plus framework [14]. Data will be extracted and synthesized on differences in uptake, completion, and timeliness across population subgroups defined by place of residence, gender, socioeconomic status, and other relevant factors. Where quantitative data are available, differences between subgroups will be summarized descriptively. Where studies report differential effects of the intervention across subgroups, the direction of impact on equity will be categorized as reduced inequity, increased inequity, no difference, or unclear. Qualitative findings will be synthesized using thematic synthesis. Data will be analysed inductively and deductively using relevant domains from the Consolidated Framework for Implementation Research (CFIR) [20]. The CFIR will be used as an analytical lens to identify and interpret barriers and facilitators to implementation and to explain variations in intervention delivery and outcomes across contexts. Themes will be mapped to CFIR domains and constructs and synthesized narratively.

Certainty assessment

Certainty of the evidence of effect will be assessed using the GRADE (Grading of Recommendations Assessment, Development and Evaluation) approach. The GRADE approach offers a structured framework for assessing the certainty of a wide range of different evidence types and supporting healthcare decision-making (Neumann I, Schünemann H (Editors) 2024). GRADEpro GDT 2020 will be used to generate Summary of Findings (SoF) tables including pooled effect estimates, relative and absolute risks, and quality ratings based on directness, precision, heterogeneity, risk of bias, and risk of publication bias. For qualitative findings, confidence will be assessed using the GRADE-CERQual approach [16].

References

[1] WHO, “Cervical Cancer.” Accessed: May 20, 2026. [Online]. Available: https://www.who.int/news-room/fact-sheets/detail/cervical-cancer%0A

[2] 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(3):229–63.

[3] WHO, “Human papillomavirus vaccines. WHO position paper (2022 update),” 2022. [Online]. Available: https://www.who.int/publications/i/item/who-wer9750-645-672

[4] WHO, *Global strategy to accelerate the elimination of cervical cancer as a public health problem*. 2020. [Online]. Available: https://www.who.int/publications/i/item/9789240014107

[5] WHO, “Immunisation Coverage.” Accessed: May 20, 2026. [Online]. Available: https://www.who.int/news-room/fact-sheets/detail/immunization-coverage

[6] Gavi, “2024 global immunisation coverage estimates: understanding the picture in lower-income countries.” Accessed: May 20, 2026. [Online]. Available: https://www.gavi.org/news/media-room/2024-wuenic-immunisation-lower-income-countries

[7] C. Ndiaye *et al.*, “Integrating HPV vaccine service delivery with adolescent health programmes – Experiences and perspectives from selected countries in Africa,” *Vaccine*, vol. 42, pp. S45–S48, 2024, doi: https://doi.org/10.1016/j.vaccine.2023.10.022.

[8] A. Portnoy *et al.*, “Landscape report on the economics of integration of immunization and primary health care services in low- and middle-income countries,” *Gates Open Res. 2022 661*, vol. 6, no. May, p. 61, 2022, [Online]. Available: https://gatesopenresearch.org/documents/6-61

[9] A. S. Wallace *et al.*, “Leaving no one behind: Defining and implementing an integrated life course approach to vaccination across the next decade as part of the immunization Agenda 2030.,” *Vaccine*, vol. 42 Suppl 1, no. Suppl 1, pp. S54–S63, Apr. 2024, doi: 10.1016/j.vaccine.2022.11.039.

[10] WHO, “Immunization agenda 2030: A global strategy to leave no one behind.,” 2022. [Online]. Available: https://www.unicef.org/ghana/immunization

[11] E. N. Rosser, M. D. Wysong, J. G. Rosen, R. J. Limaye, and S. Park, “HPV Vaccine Delivery Strategies to Reach Out-of-School Girls in Low- and Middle-Income Countries: A Narrative Review,” *Vaccines*, vol. 13, no. 5, pp. 1–27, 2025, doi: 10.3390/vaccines13050433.

[12] M. C. Jennings *et al.*, “Realist review of low- to upper-middle-income country experiences on integration of HPV vaccination with other adolescent health services,” *Vaccine*, vol. 50, no. February, p. 126833, 2025, doi: 10.1016/j.vaccine.2025.126833.

[13] T. A. Holroyd *et al.*, “Designing a Pro-Equity HPV Vaccine Delivery Program for Girls Who Have Dropped Out of School: Community Perspectives From Uttar Pradesh, India.,” *Health Promot. Pract.*, vol. 23, no. 6, pp. 1039–1049, Nov. 2022, doi: 10.1177/15248399211046611.

[14] J. O’Neill *et al.*, “Applying an equity lens to interventions: using PROGRESS ensures consideration of socially stratifying factors to illuminate inequities in health.,” *J. Clin. Epidemiol.*, vol. 67, no. 1, pp. 56–64, Jan. 2014, doi: 10.1016/j.jclinepi.2013.08.005.

[15] WHO, “WHO updates recommendations on HPV vaccination schedule.” Accessed: Jun. 12, 2026. [Online]. Available: https://www.who.int/news/item/20-12-2022-WHO-updates-recommendations-on-HPV-vaccination-schedule

[16] S. Lewin *et al.*, “Applying GRADE-CERQual to qualitative evidence synthesis findings: Introduction to the series,” *Implement. Sci.*, vol. 13, no. Suppl 1, pp. 1–10, 2018, doi: 10.1186/s13012-017-0688-3.

[17] E. A. Akl *et al.*, “Extension of the PRISMA 2020 statement for living systematic reviews (PRISMA-LSR): checklist and explanation,” *BMJ*, vol. 387, p. e079183, Nov. 2024, doi: 10.1136/bmj-2024-079183.

[18] A. Thomas, J., Graziosi, S., Brunton, J., Ghouze, Z., O’Driscoll, P., & Bond, M. & Koryakina, “EPPI-Reviewer: advanced software for systematic reviews, maps and evidence synthesis. EPPI Centre, UCL Social Research Institute, University College London).” Accessed: May 21, 2026. [Online]. Available: https://eppi.ioe.ac.uk/cms/resources/tools/eppi-reviewer-introduction

[19] J. H. Elliott *et al.*, “Living Systematic Reviews: An Emerging Opportunity to Narrow the Evidence-Practice Gap,” *PLOS Med.*, vol. 11, no. 2, p. e1001603, Feb. 2014, [Online]. Available: https://doi.org/10.1371/journal.pmed.1001603

[20] C. M. Reardon *et al.*, “The Consolidated Framework for Implementation Research (CFIR) User Guide: a five-step guide for conducting implementation research using the framework.,” *Implement. Sci.*, vol. 20, no. 1, p. 39, Aug. 2025, doi: 10.1186/s13012-025-01450-7.

Appendices

Appendix 1. Example Search Strategy

MH – MeSH heading; XB – title/abstract; N2 – within two words (either order); * - stem plus 0 or more letters

((MH "Papillomavirus Vaccines+" AND MH "Immunization+") OR XB(((HPV* OR “Human Papilloma*”) N2 (immuni* OR vaccin*)) OR cecolin OR cervarix OR gardasil OR walrinvax))

AND

(MH "Adolescent Health Services" OR MH "Delivery of Health Care" OR MH "Delivery of Health Care, Integrated+" OR MH "Health Services Accessibility" OR MH "Immunization Programs" OR MH "Preventive Health Services” OR MH "Primary Health Care" OR MH "School Health Services" OR XB(anthelminthic OR "bed net*" OR bundle* OR combin* OR contracept* OR "condom us*" OR codeliver* OR coordinat* OR "co-implement*" OR “co-ordinat*” OR deliver* OR embed* OR EPI OR “expanded program*” OR “general practic*” OR “health check” OR "health education" OR "health system*" OR hybrid OR integrat* OR “life course” OR lifestyle* OR opportunistic OR packag* OR platform* OR "primary care" OR parallel* OR promot* OR routine OR "sanitary pad*" OR schedul* OR schistosomiasis OR school* OR "service delivery" OR "skills building" OR soap* OR "social behavio*" OR SBC* OR "vaccine delivery" OR "vitamin A"))

AND

(MH "Developing Countries" OR XB(((low* OR middle) N2 (income)) OR "LMIC" OR "LMICs" OR "third world" OR "central asia*" OR "north* asia*" OR "southeast* asia*" OR "south east* asia*" OR "western asia*" OR "east* europe*" OR africa* OR caribbean OR "south america*" OR "latin america*" OR "central america*" OR "global south" OR "middle east*" OR "south pacific" OR afghan* OR albania* OR algeria* OR angola* OR argentin* OR armenia* OR azerbaij* OR bangladesh* OR belarus* OR byelarus* OR belorus* OR byelorus* OR beliz* OR benin* OR dahomey* OR bhutan* OR bolivia* OR bosnia* OR herzegovina* OR botswana* OR bechuanaland* OR brazil* OR brasil* OR bulgaria* OR "burkina fas*" OR "upper volta*" OR burundi* OR urundi* OR "cabo verde*" OR "cape verde*" OR cambodia* OR kampuchea* OR khmer* OR cameroon* OR cameron* OR cameroun* OR "ubangi shari" OR chad* OR chile* OR china OR chinese OR colombia* OR comoro* OR mayotte* OR congo* OR zair* OR "costa rica*" OR "cote d’ivoire*" OR "ivory coast" OR cuba* OR djibouti* OR dominica* OR ecuador* OR egypt* OR "united arab republic" OR "el salvador*" OR eritrea* OR eswatini* OR ethiopia* OR fiji* OR gabon* OR gambia* OR georgia* OR ghana* OR "gold coast" OR grenada* OR guatemala* OR guinea* OR guyana* OR guiana* OR haiti* OR hispaniola* OR hondura* OR india* OR indonesia* OR iran* OR iraq* OR jamaica* OR jordan OR kazakh* OR kenya* OR "north korea*" OR "democratic people’s republic of korea" OR kosov* OR kyrgyz* OR kirgiz* OR kirghiz* OR lao* OR latvia* OR lebanon* OR lesoth* OR basutoland* OR liberia* OR libya* OR lithuania* OR macedonia* OR madagascar* OR malagas* OR malawi* OR nyasaland* OR malaysia* OR maldiv* OR mali* OR micronesia* OR kiribati OR "marshall island*" OR nauru*

OR palau OR tuvalu OR maurit* OR mexic* OR moldova* OR mongolia* OR montenegr* OR morocc* OR ifni OR mozambiqu* OR myanmar OR burm* OR namibia* OR nepal* OR "netherlands antill*" OR nicaragua* OR niger* OR pakistan* OR panam* OR paragu* OR peru* OR philippin* OR philipin* OR phillipin* OR phillippin* OR filipin* OR romania* OR russia* OR rwanda* OR ruanda* OR samoa* OR "pacific island*" OR polynesia* OR "sao tome*" OR senegal* OR serbia* OR seychell* OR "sierra leon*" OR melanesia* OR "solomon island*" OR "norfolk island*" OR somali* OR "sri lanka*" OR ceylon* OR "saint kitts" OR "st kitts" OR "saint lucia*" OR "st lucia*" OR "saint vincent*" OR "st vincent*" OR grenadine* OR sudan* OR surinam* OR syria* OR swaziland OR tajikistan OR tadjikistan OR tadzhik* OR tanzania* OR tanganyika* OR thai* OR siam* OR timor* OR togo* OR tonga* OR tunisia* OR turk* OR uganda* OR ukrain* OR uruguay* OR uzbek* OR vanuatu* OR "new hebride*" OR venezuela* OR vietnam* OR "viet nam*" OR "west bank" OR gaza* OR palestin* OR yemen* OR zambia* OR zimbabwe* OR rhodesia* OR magreb* OR maghrib* OR sahara*))

Appendix 2. Data Extraction Form

Draft Extraction tool: LSR 6,7,8