Costs, Performance and Value for Money of HPV Vaccine Delivery Strategies in Low- and Middle-Income Countries: Living systematic reviews protocol (LSRs 3 & 4)

Protocol information

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Key Abbreviations

Abbreviations	Full Meaning
CHEERS	Consolidated Health Economic Evaluation Reporting Standards
CINAHL	Cumulative Index to Nursing and Allied Health Literature
CEA/CUA/CBAs	CEA (Cost-Effectiveness Analysis), CUA (Cost-Utility Analysis), and CBA (Cost-Benefit Analysis)
DALYs	Disability-Adjusted Life Years
ECOBIAS	Economic Evaluation Bias Checklist
EconLit	Economics Literature
EMBASE	Excerpta Medica dataBASE
EPI	Routine Expanded Programme on Immunization
EPPI-Reviewer	Evidence for Policy and Practice Information Reviewer (systematic review software)
GAVI	Gavi, the Vaccine Alliance
GRADE	Grading of Recommendations Assessment, Development and Evaluation
GRADE CERQual	Confidence in the Evidence from Reviews of Qualitative Research
HPV	Human papillomavirus vaccine
ICERs	Incremental cost-effectiveness ratios
LLM	Large Language Model
LMIC	Low- and middle-income countries
LSR 3	Cost of HPV Vaccine Delivery (Living Systematic Review 3)
LSR 4	Performance and Value for Money of HPV Vaccine Delivery (Living systematic review 4)
LSRs	Living systematic reviews
Medline	Medical Literature Analysis and Retrieval System Online
MMAT	Mixed-Methods Appraisal Tool
PICO	Population, Intervention, Comparator, Outcome
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
PROSPERO	International Prospective Register of Systematic Reviews
QALYs	Quality-Adjusted Life Years
RCTs	Randomised Controlled Trials
RoB	Risk of Bias
ROBINS-I	Risk Of Bias In Non-randomised Studies of Interventions
UNICEF	United Nations Children’s Fund
WAFERs	West African Institute for Applied Health Research and Socio-Economic Development
WHO	World Health Organization

Introduction

These two living systematic reviews (LSRs) on cost, performance and value for money of HPV Vaccine Delivery Strategies in LMICs are being produced for the HPV Living Evidence and Knowledge Partnership, read more about the partnership here.

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.
- WAFERs, the team commissioned to produce this review, is a mission-driven research organisation dedicated to generating and translating high-quality evidence into policies and practices that improve health, wellbeing, and socio-economic outcomes across West Africa.
- 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.

Why is it important to do this living systematic review?

Given the rapidly evolving and context-dependent nature of human papillomavirus (HPV) vaccine delivery and its associated costs, a traditional static review summarising costs and cost-effectiveness of delivery strategies would quickly become outdated. 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 low- and middle-income countries (LMICs) settings, where programmes must often adapt to dynamic information environments, resource constraints, and variances. We currently have funding to keep the review living until early 2027, but are exploring options for sustainability beyond that.

Existing traditional systematic reviews on HPV vaccine delivery costs (e.g. Slavkovsky et al. 2024; Akumbom et al. 2022; Vaughan et al. 2019) provide valuable insights into the costs of delivering HPV vaccination programmes across LMICs. However, these reviews are not conducted as LSRs and therefore may not adequately reflect the rapidly evolving evidence base, including new delivery strategies, changing vaccine schedules, and programme scale-up experiences. Emergence of new primary studies in this field

further underscore the need for an updated and continuously maintained synthesis of evidence.

In addition, previous systematic reviews have yet to integrate cost data and real-world effectiveness or cost-effectiveness outcomes (Slavkovsky et al. 2024; Gervais et al. 2017; Vaughan et al. 2019; Fesenfeld et al. 2013). As a result, the current evidence base provides limited support for estimating costs at scale, or assessing trade-offs when expanding vaccination to harder-to-reach populations.

There remains a gap in synthesising evidence on value for money, which is central to policy decision-making. In this review, value for money is defined as the extent to which HPV vaccination programmes achieve desired health and programme outcomes relative to the resources invested. This encompasses multiple dimensions, including cost-effectiveness, cost-utility, and cost-benefit; technical and allocative efficiency; affordability and budget impact; equity implications; and the extent to which programmes achieve their intended coverage and health objectives.

Since the publication of earlier reviews, the evidence base has expanded, but remains fragmented across delivery phases (introduction versus routine), delivery platforms (e.g. school-based, community outreach, facility-based), and analytical approaches (costing studies versus economic evaluations) (Table 1). Furthermore, much of the existing evidence is not systematically updated as new delivery models emerge, including integrated delivery approaches, single-dose schedules, and strategies targeting out-of-school populations (Akumbom et al. 2022). This creates a persistent “decision gap” for policymakers who require timely, comparable, and policy-relevant evidence to guide programme design and scale-up.

LSR3 and LSR4 are designed to address these gaps by providing a continuously updated, comprehensive, and policy-oriented synthesis of evidence. Specifically, these reviews will:

1. Synthesize delivery costs across implementation stages, from introduction to routine and scale-up, enabling a better understanding of cost dynamics.
2. Expand the evidence base by incorporating grey literature and multi-language sources, thereby capturing real-world programme experience that is often missed in traditional reviews.

3. Integrate cost, performance, and economic evaluation evidence, linking delivery costs with coverage, uptake, and cost-effectiveness outcomes to enable assessment of value for money across delivery strategies.
4. Address policy-relevant questions, including comparative performance of delivery strategies, and trade-offs in reaching underserved populations.
5. Explicitly map evidence gaps and uncertainty, supporting priority-setting for future research and improved investment decisions.

By maintaining the evidence base as a Living Systematic Review, LSR3 and LSR4 will ensure that new data are rapidly identified, synthesised, and translated into actionable insights. Together, these reviews will directly support global, national, and sub-national decision-making on HPV vaccination programme design, delivery strategy selection, scale-up pathways, and long-term sustainability.

Table 1: Summary of existing evidence base and policy relevant gaps

Policy relevant issues (informed by discussion with TG)	**Current Evidence (based on existing SRs)**	**LSRs 3 & 4 Potential Contribution**
What will HPV vaccine delivery cost at scale?	Evidence is based on small datasets and largely from pilot phases, with wide cost variation and limited routine programme data (Slavkovsky et al. 2024; Akumbom et al. 2022)	Updated synthesis of costs across implementation stages (introduction and routine)
How can HPV vaccine delivery model(s) be optimised to yield better coverage, uptake and broader public health impact?	Very limited comparative evidence on delivery strategies vs cost/outcomes, with reviews highlighting lack of integration of costs and cost effectiveness data (Akumbom et al. 2022)	Structured mapping of delivery approaches and comparisons across contexts
How and for whom should expand coverage be prioritised?	Cost-effectiveness evidence is largely model-based and not linked to delivery choices (Gervais et al. 2017; Ekwunife et al. 2017, Fesenfeld et al. 2013).	Integrated synthesis of cost and available cost-effectiveness evidence, with gap maps

Where should research/pilots focus next?	Evidence gaps acknowledged but not systematically mapped across reviews (Vaughan et al. 2019)	Living SR, structured gap analysis (by geography, delivery strategy, platforms and population)

In this protocol, we have considered PRISMA guidance established for living systematic reviews (Akl et al. 2024). Strategically, this document serves as a single, joint protocol for two linked LSRs systematic reviews: LSR 3 (focusing on vaccine delivery cost components and comparisons) and LSR 4 (focusing on policy relevant outcomes of different delivery strategies) across LMICs settings. While LSR 3 & LSR 4 are very distinct economic reviews, they are highly complementary in nature. This single shared protocol creates a unified framework, complementary workflows, and efficiency across the two economic reviews. A distinct 'triage point' is indicated in the methods section to indicate where the reviews are formally partitioned into costing and cost comparisons (LSR 3) or HPV vaccine delivery outcomes evaluation (LSR 4).

Primary Research Questions

1. What are the costs of HPV vaccine delivery during introduction, routine and or catch-up implementation in LMICs, and what contextual, operational, and health-system factors influence cost variation across different delivery strategies? (**LSR 3**)

2. What is the evidence on the performance of HPV vaccine delivery strategies in LMICs in terms of reach, uptake, coverage, equity, health impact and or broader public health outcomes? (**LSR 4**)

3. What is the value for money of HPV vaccine delivery strategies in LMICs, considering costs, in relation to health outcomes, programme performance, equity, and broader public health impact? (**LSR 3 and 4**)

This review adopts an approach, where cost evidence (LSR 3) and outcome/ programme performance evidence (LSR 4) are identified and analysed separately, and subsequently integrated qualitatively to assess value for money across HPV vaccine delivery strategies. Secondary research questions for each LSR are highlighted:

Secondary Research Questions

HPV vaccine delivery costs (LSR 3)

a. What are the total and unit costs of HPV vaccine delivery across different delivery strategies (e.g., school/facility-based targeting, routine immunization, campaign/outreach, integrated service)?
b. What costing approaches are used (economic vs financial cost, ingredients vs top-down)
c. What are the key cost components associated with different HPV vaccine delivery strategies (e.g., salaries and wages, trainer fees, cold chain equipment, transport, IEC materials) and how are these costs distributed?
d. How do costs differ across delivery strategies and between introduction vs routine delivery phases?
e. What are the contextual drivers of cost variation (e.g., country income level, scale, delivery design, geography) and how do these factors influence cost differences?
f. What differences exist between empirical (retrospective) costing studies and budget/financial estimates (prospective costing)?

HPV vaccine delivery strategies outcomes (LSR 4)

a. What is the reach, uptake (e.g., identification/initiation, completion) and level of vaccination coverage across different HPV vaccine delivery strategies?
b. How do different delivery platforms (at school, facility, mobile units or campaign sites) influence reach, uptake, coverage?
c. How do HPV vaccination delivery strategies differ in their ability to achieve uptake, coverage, reach, and equitable access, particularly among underserved populations?
d. What factors (e.g., community engagement, doses, timing, integration with other services) influence outcome of HPV vaccine delivery strategies?
e. How does integration of HPV vaccination with other health or school-based services influence costs, efficiency, programme performance, and value for money?

Definition of key concepts

To ensure conceptual clarity and consistency in this study, we define key concepts related to HPV vaccine delivery costs (LSR 3), delivery performance and value for

money (LSR 4), and their integration (Table 2). These definitions are informed by the Immunization Delivery Cost Catalogue, WHO and Gavi delivery frameworks, and health economic principles.

Table 2: Definition of Key Concepts for HPV Delivery Costs and Value for Money

A: HPV Delivery Cost Concepts (LSR 3)

Concept	**Definition**	**Interpretation for analysis and policy**
HPV Vaccine Delivery Programme	Organised system of activities to deliver HPV vaccines program	Defines scope and comparability
Delivery Strategy	Operational framework used to administer HPV vaccines to a targeted demographic	Compare resource intensity
Delivery Platform	The specific infrastructure, setting, or operational mechanism utilized to distribute and administer the vaccine to the target population	Helps explain structural variation
Programme Phase	Stage of implementation	Shows cost evolution
Cost	The total resource implications required to execute the vaccination program	Overall resource requirement
Financial Cost	Direct monetary outlays or actual expenditures spent on purchasing goods and services	Budget planning
Economic Cost	Financial outlays plus opportunity costs of health worker time and any donated items	True resource comparison
Delivery Cost	Operational and logistical expenses required to get the vaccine from the central storage to the recipient,	Core efficiency metric

	excluding the physical cost of the vaccine	
Vaccine Acquisition Cost	Actual price paid to purchase the vaccine from the manufacturer or distributor	Total costing
Total Programme Cost	Defines the comprehensive financial and economic resources required for procurement the vaccine antigens and execute the entire delivery strategy across the target population Sum of costs	Fiscal footprint
Unit Cost	Total expense required to procure, deliver, and administer the vaccine to a single target individual	Compare efficiency
Incremental Cost	Additional cost incurred by adding the vaccine program on top of existing healthcare operations	Policy trade-offs
Cost Components	Input categories, i.e. investment and recurrent costs	Identify drivers
Programme Activities	Actions undertaken	Explain cost structure
Cost Drivers	Drivers of variation	Explain differences
Resource Use	Input quantities	Interpret efficiency
Costing Perspective	Analytical viewpoint	Comparability
Time Horizon	Period of cost	Policy relevance
Currency and Price Year	Reporting standard	Enable comparison
Budget Impact	Financial implications	Planning decisions
Scale-up Costs	Expansion costs	Sustainability
Integration	Delivery with other services	Efficiency modifier

B: HPV Delivery Performance and Value for Money Concepts (LSR 4)

Concept	Definition	Interpretation for analysis and policy
Delivery Strategy	Approach used to deliver vaccines	Compare effectiveness
Delivery Platform	Where vaccination occurs	Identify best platforms
Programme Phase	Stage of implementation	Track performance change
Reach	Proportion accessed	Accessibility
Uptake	Initiation of vaccination	Demand effectiveness
Completion	Completion rate	Adherence
Coverage	Fully vaccinated proportion	Programme success
Equity	Distribution of access	Fairness
Programme Performance	Overall effectiveness	Outcome synthesis
Acceptability	Acceptance by users/providers	Sustainability
Feasibility	Practicality	Scalability
Sustainability	Long-term viability	Programme continuation
Integration	Combined delivery	Outcome improvement
Value for Money	Outcomes vs resources	Policy choice
Efficiency	Measures how well resources are used to maximize the health benefits of the program i.e., Input-output relation	Performance comparison
Cost per Outcome	Evaluates the financial resources required to achieve a specific health result i.e, Cost per vaccinated	Bridge metric
Cost-effectiveness	A measure of its economic value - i.e. cost vs outcomes	Supporting evidence
Incremental Cost-Effectiveness Ratio (ICER)	Metric used to determine if introducing or expanding the vaccine program is a	Comparison where available

	financially efficient use of public health funds compared to alternative strategies	
Trade-offs	Balance cost vs outcomes	Policy priorities
Affordability	Budget feasibility	Adoption decision
Equity-adjusted Value	Metric to calculate the broader societal and social justice impacts of the program	Inclusive policy

Description of the interventions

For the purpose of these reviews (LSR 3 and 4), the intervention of interest are strategies or approaches used to organise and implement HPV vaccination, particularly those targeting adolescent populations in diverse LMICs settings. HPV vaccine delivery strategies (e.g., routine immunisation, campaign delivery, school-based roll-out, facility-based targeting of adolescents, outreach to reach rural populations and integrated delivery with other services) may involve use of multiple platforms (e.g., school, health/religious facilities).

Reflecting on existing systematic review evidence and expert experience (Tactical group) that delivery approaches vary substantially in their resource intensity and cost drivers; for both LSRs 3 and 4, particular attention will be given to components of HPV delivery strategies aimed at increasing HPV vaccination coverage, demand generation and uptake, such as expanding service delivery platforms, education, social mobilisation/community engagement, reminder systems, and behavioural nudges). These interventions may influence cost structure, resource requirements such as logistics, and training).

Engagement and reporting

The primary users of LSRs 3 & 4 will be decision-makers and primarily their advisors in 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, these LSRs also have 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 HPV vaccines delivery costs.

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 these LSRs. 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 WAFERs, UCL and Alive, the teams responsible for developing the LSRs. Members of the TG will provide technical oversight to ensure the LSRs are both methodologically sound and meet 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.
- Group of Advisors (AG) which provides technical input and systems insight to inform the SG's strategic decisions.

Methods

The systematic reviews described in this protocol are both LSRs and will be updated continually. An LSR is a high quality, up-to-date online synthesis of health research that is updated as data from new relevant research that meets study inclusion criteria becomes available (Elliott et al. 2014). This means that, following an initial search from 2000 (GAVI Strategy 1.0) to June 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

Eligibility criteria for LSR 3 (cost of HPV vaccine delivery) and LSR 4 (policy relevant outcomes of HPV vaccine delivery) are drafted in a way to ensure comprehensive identification of relevant economic evidence, while maintaining transparency and reproducibility in line with PRISMA-LSR (Akl et al. 2024) and Consolidated Health Economic Evaluation Reporting Standards (CHEERS) guidance (Husereau et al. 2022). Appendix 2 presents a summary of eligibility criteria detailed below:

Study Population

Inclusion

Eligible populations include individuals targeted by HPV vaccination programmes, primarily adolescents (male and, or female depending on programme scope), as well as relevant high-risk groups within LMIC settings. Studies must relate to vaccination delivered within recognised programme contexts, including introduction, pilot, or routine implementation phases.

Exclusion

Studies not linked to HPV vaccine delivery programmes or irrelevant population groups will be excluded.

Concepts & Outcomes

Inclusion

The reviews will focus on costs, performance and economic aspects of HPV vaccine delivery.

- For LSR 3, eligible studies must report financial and/or economic costs of HPV vaccine delivery, including unit costs (e.g. cost per dose, cost per fully vaccinated

individual), cost components, and cost drivers across different delivery platforms, strategy and implementation phases.

- For LSR 4, eligible studies must report at least one or combination of HPV vaccine delivery performance outcomes such as reach, uptake, coverage, completion rates, equity indicators, and programme effectiveness (non-clinical) relevant for policy making. Studies reporting performance of delivery strategies with or without economic analysis will be eligible for inclusion. Where available, studies cost-effectiveness outcomes, including incremental cost-effectiveness ratios (ICERs), cost per DALY or QALY averted, or other relevant value-for-money metrics will be included.

Exclusion

Studies focusing solely on vaccine efficacy, immunogenicity, or vaccine manufacturing, procurement pricing alone, without delivery context will be excluded. Also studies or reports focusing on non-HPV vaccination programmes will be excluded.

Study types

Inclusion

- For LSR 3, we will include primary costing studies (including ingredient-based, top-down, bottom-up, or mixed approaches), prospective costing/budget studies, cost analyses embedded in programme or implementation evaluations reporting disaggregated cost data. Studies could be trial-based or observational design.
- For LSR 4, we will include programme evaluations and implementation studies, observational studies (cross-sectional, cohort) and policy relevant documents. If available we will include cost-effectiveness, cost-utility, and cost-benefit analyses, from trial-based studies relevant to HPV vaccine delivery strategies.

Studies identified for inclusion in LSR 3 and LSR 4 will not be required to report both cost and outcome data. Instead, evidence from each LSR will be integrated where appropriate at the synthesis stage by comparing cost estimates across delivery strategies (LSR 3) with corresponding evidence on reach, uptake, coverage, equity, and programme performance (LSR 4) to derive an overall assessment of value for money. Across both reviews, we will include studies that provide extractable economic outputs relevant to HPV vaccine delivery strategies and platforms.

Exclusion

We will exclude editorials, commentaries, and opinion pieces without primary or modelled economic data; studies reporting only clinical outcomes; and studies where HPV vaccine delivery-specific cost or outcomes data cannot be extracted. Studies conducted exclusively in high-income settings will also be excluded.

Publication status

Inclusion

We will include peer-reviewed journal articles, preprints with methodological detail, and relevant grey literature, including government reports, programme evaluations, and documents produced by international organisations (e.g. WHO, UNICEF, GAVI).

Exclusion

Conference abstracts will be excluded unless sufficient data are available for extraction and methodological appraisal. Reports lacking adequate transparency in methods or outcomes will also be excluded.

Geographical context

Inclusion

The reviews will include studies conducted in LMICs, as defined by the World Bank classification at the time of the study's data collection. Multi-country studies will be included where LMIC-specific data can be disaggregated or clearly attributed.

Exclusion

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

Language

Inclusion

No language restrictions will be applied. Studies published in languages other than English will be included where feasible translation can be achieved through the review

team, established collaborative networks and or artificial intelligence verified by bilingual researcher(s) or native speaker.

Exclusion

Studies for which translation is not feasible or where data cannot be reliably interpreted will be excluded.

Publication date (Year)

Inclusion

Studies published from 1 January 2000 onwards will be eligible for inclusion. This date reflects the period corresponding to the establishment and early implementation phase of Gavi, the Vaccine Alliance, and the subsequent expansion of global immunisation financing and HPV vaccine delivery strategies in LMICs. Restricting inclusion to studies published from 2000 onwards ensures that the evidence base reflects modern immunisation systems, delivery platforms, and financing mechanisms, including those supported through GAVI and related global initiatives. Earlier studies are unlikely to be comparable due to differences in vaccine availability, delivery infrastructure, and economic evaluation approaches.

No upper date limit will be applied, and searches will be updated continuously in line with the living systematic review model to ensure incorporation of the most recent evidence.

Exclusion

Studies and/or programme reports published before 2000 will be excluded.

Search and screening

Search strategy

A search strategy is being developed by TS (information specialist) in collaboration with the wider team and with input from the Tactical group. The search strategy will aim to locate both published and unpublished studies from 2000 onwards, representing the year when the HPV vaccine was introduced. Searches will be performed in the following electronic databases: Medline (Ovid), Embase (Ovid), Cumulative Index to Nursing and

Allied Health Literature (CINAHL; EBSCO), Global Index Medicus, Web of Science Core Collection (Web of Science), EconLit (EBSCO). Grey literature will be searched for through the World Health Organisation repositories, TechNet 21, Immunization Delivery Cost Catalogue, NITAG Resource Centre, International Cancer Control Partnership and the World Bank Open Research Working Papers, in addition to government and health ministry reports via respective national government websites. Additionally, discussions will be held with collaborators (e.g. deep-dive consultants) on the project to explore other existing papers that the team are aware of. The search will combine controlled vocabulary (e.g. MeSH terms in Medline) with free-text keywords related to HPV vaccinations costs and outcomes. As a sensitive approach will be taken, terms related to LMICs will not be included in the search. The strategy will incorporate truncation, wildcards, and proximity operators where supported, and will be adapted for each database. The search for Medline (Ovid) 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 (Thomas et al, 2023), and duplicates will be removed. A pilot test will be done on titles and abstracts which will be screened by paired independent reviewers for assessment against the inclusion criteria for the review. Any disagreements will be resolved by a third reviewer and 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 (OB) or senior research fellow (OA).

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 judgements 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 OB or SA to calculate agreement with the LLM. This will continue to be done on an ongoing basis during each living evidence update cycle.

Full text screening

Paired reviewers (EO, ST, DO, EA, SM) will independently assess each of 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.

Triage point (LSR 3 & 4 partitioning)

Given the integrated scope of cost evidence, implementation performance, and value for money, an explicit triage point will be implemented to allocate studies to LSR 3, LSR 4, or both. The triage classification will occur at the end of full-text eligibility assessment, once studies have been confirmed as meeting the overarching inclusion criteria for evidence on HPV vaccine delivery in LMICs. At this stage, each included study will be formally classified into one of the following categories:

1. LSR 3 eligible (Costs and cost determinants): studies reporting primary costing evidence related to HPV vaccine delivery, including:
    - Financial or economic costs (e.g. cost per dose, cost per fully vaccinated individual, total programme costs)
    - Disaggregated cost components (e.g. service delivery, logistics, training, social mobilisation)
    - Cost drivers and determinants of variation across delivery strategies, platforms, or contexts
    - Prospective or retrospective costing studies
2. LSR 4 eligible (Delivery performance and implementation outcomes): studies reporting evidence on performance of HPV vaccine delivery strategies, including:
    - Reach (e.g. proportion of target population accessed)
    - HPV vaccine uptake and completion rates
    - Coverage levels
    - Equity metrics (e.g. differences by geography, gender, socio-economic status, or marginalised groups)
    - Broader public health or programme outcomes (e.g. acceptability, feasibility, sustainability where reported alongside delivery performance)
3. Dual eligibility (LSR 3 & LSR 4: integrated evidence on value for money): Studies that link cost evidence with delivery performance or outcomes, including:
    - Reports of both cost data and implementation outcomes (e.g. cost per vaccinated individual alongside coverage or uptake)

- Comparative studies of delivery strategies including both resource use and programme performance metrics
- Model-based or empirical studies that combine cost inputs and delivery outcomes, even if not framed as formal economic evaluations

These studies contribute to Research Question 3 and (value for money) and will be included in both LSRs, with data extracted under separate but coordinated frameworks.

NB: Formal economic evaluations (e.g. cost-effectiveness analyses) will not be used as a primary classification criterion, but will be captured where they contribute cost data to LSR 3, delivery or outcome evidence to LSR 4), or integrate both dimensions (dual eligibility), informing value-for-money synthesis.

4. Exclude at triage: Studies that meet general inclusion criteria but do not report primary cost data, cost determinants, or delivery performance outcomes, and do not allow meaningful contribution to cost, performance, or value-for-money synthesis will be excluded or retained as background/contextual material, with reasons documented.

Operationalisation of triage decisions

To ensure consistency and transparency:

- A standardised triage decision rule set will be applied (Appendix 3 - Triage checklist) with definitions aligned to costing studies (primary resource use and cost estimation) or implementation/performance studies (delivery outcomes such as reach, uptake, equity);
- An initial calibration exercise (e.g. double screening of a sample of studies) will be undertaken to ensure consistent interpretation of classification criteria across reviewers;
- All triage decisions will be logged in EPPI reviewer, including brief justification of classification where ambiguity exists;
- Studies classified as dual-eligible will be flagged to enable coordinated data extraction and support integration during value for money synthesis.

The use of a unified screening workflow with a formal triage point reflects the interdependence of cost and implementation evidence in informing policy relevant decisions. Specifically, we acknowledge that cost evidence alone does not indicate

programme effectiveness, implementation outcomes alone do not indicate efficiency. This triage approach ensures that:

- all relevant evidence is identified through a single, efficient screening process;
- duplication of screening effort across LSRs is minimised;
- classification of studies is systematic, transparent, and reproducible; and
- cross-linkages between LSR 3 & LSR 4 are preserved to support integrated synthesis and interpretation.

This approach is particularly important within a living systematic review context, where continuous surveillance and updating require a scalable and auditable workflow for identifying and categorising emerging evidence.

Data extraction

The data extraction framework for LSRs 3 & 4 is designed to ensure transparency, comparability across studies, and alignment with PRISMA 2020 and CHEERS 2022 reporting standards (Page et al. 2020, Husereau et al 2022) , while supporting ongoing updates within a living review model. A customised data extraction proforma will be developed, informed by CHEERS checklist, the Immunization Delivery Cost Catalogue (ICAN 2019) and expert input from the Tactical group (see Appendix 4 for data extraction proforma to be embedded in EPPI reviewer). The form will be pre-piloted and standardized prior to the data extraction process. 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 using the integrated OpenAI GPT-4.1 model within EPPI Reviewer. Prompts will be tested across data extraction items. A 10% random subset will then be double-extracted by human reviewers. Agreement will be assessed at the item level by comparing LLM and human-extracted data, with a ≥95% agreement threshold required. If this threshold is achieved, the LLM will extract the remaining studies, followed by human verification for accuracy and completeness. If agreement is <95%, prompts will be refined and re-tested until the threshold is met before scaling to full extraction.

A common core data extraction structure will be used across both LSRs to ensure comparability and facilitate integrated synthesis:

A. Study descriptors (i.e. author(s), year of publication, and publication type (peer-reviewed or grey literature), study design (e.g. observational, trial-based, modelling), dosing schedule, sample size (where applicable)
B. Context and settings such as country, geographic setting (urban/rural; sub-national/national), and target population (girls only; girls and boys; age range)
C. Delivery strategy classification to include delivery platform(s) (e.g., school, facility, outreach, campaign, hybrid); HPV vaccine delivery strategy components, activities and co-interventions such as demand generation, reminders, community engagement, social mobilisation, training ; and integration with other services (if reported)
D. Delivery phase for example introduction, pilot, routine implementation

Specifically for LSR 3, data extraction will focus on costs of HPV vaccine delivery and drivers of costs variation. Data items will include:

E. Costing methods and perspective i.e. economic perspective (provider/programme, health-system level, societal), costing approach (ingredient-based, top-down, bottom-up, mixed), time horizon and costing year, currency, price year, and any adjustments (e.g. inflation, currency conversion, purchasing power parity where reported). Financial and economic costs will be delineated.
F. Cost Outcomes i.e. unit costs (e.g. cost per dose delivered, cost per fully vaccinated individual); total and incremental costs (total programme costs, incremental costs across delivery strategies); disaggregated cost components (e.g. personnel, supervision administration), activities (e.g. training, social mobilisation/ demand generation, logistics, cold chain, waste management), and start-up /recurrent costs, where reported. NB: Given that costs are usually temporally and geographically volatile, we will review technical appendices of included studies for disaggregated cost components to capture available records of ingredient quantities as well as unit and total costs where reported.
G. Cost drivers and contextual factors i.e. reported drivers of cost variation (e.g. scale and coverage levels, delivery modality and platforms, integration with other services), geographic and contextual factors
H. health-system constraints (e.g. workforce, infrastructure) or enablers (e.g. existing delivery platforms) that may be influencing costs and
I. Comparative cost evidence across strategies or contexts

All cost data will be extracted verbatim as reported and synthesised, with documentation of assumptions to support interpretation and comparability across settings.

For LSR 4, data extraction will focus on how well delivery strategies perform, rather than formal economic evaluation. In addition to shared core data, the following data items will be extracted:

J. Delivery performance outcomes i.e. reach (target population accessed), (uptake/utilisation (initiation / completion rates), and coverage (population-level vaccination rates)
K. Equity outcomes to enable exploration of variation by geography (rural vs urban), socio-economic status, marginalised populations, gender where relevant
L. Implementation and programme outcomes such as acceptability (community, providers), feasibility and operational challenges, implementation success/failure factors, sustainability and scale-up potential (where linked to delivery performance)
M. Comparative effectiveness of delivery strategies i.e. performance differences across delivery platforms, components (co-interventions) of HPV vaccine delivery strategies, mixed/hybrid delivery approaches
N. Health system outcomes for example sustainability of delivery strategy, and strengthening of immunisation systems (i.e., vaccine supply chain, workforce, capacity, data systems and monitoring),

To address primary research question 3 above, data will be extracted to support integration of cost and performance evidence e.g., cost per outcome (cost per vaccinated individual, cost per person reached); strategy-level comparators linking resource use, HPV vaccine implementation program performance, cost data and delivery outcomes. Where formal economic evaluations (e.g. CEAs) are found and included, we will extract cost data (LSR 3), outcome/performance data (LSR 4) and summary metrics (e.g. ICERs) as contextual evidence, not primary classification basis. Across both LSRs, extracted data will be stored in a shared, version-controlled data environment (EPPI reviewer), enabling efficient updating as new studies emerge. New dual-eligible studies will be flagged for coordinated extraction and integrated synthesis; cost inputs from LSR 3 will be mapped to delivery strategies in LSR 4 and used to support value-for-money interpretation. Updates in the living review will prioritise integration of newly identified cost evidence and revised assumptions reflecting evolving delivery strategies and or shifts in HPV vaccination programme performance.

Risk of bias (RoB)

Risk of bias in included studies will be assessed using a design-appropriate, domain-based approach, reflecting the diverse nature of evidence included across LSR 3 (costs and cost determinants) and LSR 4 (delivery performance and implementation outcomes). Depending on study design, appropriate tools will be used (e.g., Cochrane RoB tool for RCTs (Sterne et al. 2019); ROBINS-I (Sterne et al. 2016) for observational intervention studies, and the Mixed-Methods Appraisal Tool - MMAT (Hong et al. 2018) for mixed-methods studies).

For studies contributing cost data (LSR 3), risk of bias will be assessed in relation to costing methods and data quality drawing on principles from the ECOBIAS checklist (Adarkwah et al. 2016). Key domains will include:

- definition and transparency of costing perspective
- appropriateness of costing approach (e.g. ingredient-based vs top-down)
- completeness of cost component identification
- accuracy and transparency of resource measurement and valuation
- handling of uncertainty and assumptions (where applicable)

This approach ensures that bias in cost estimation and reporting is systematically captured, even where formal economic evaluations are not conducted.

For studies contributing to LSR 4, risk of bias assessment will focus on:

- selection bias (e.g. representativeness of the study population)
- measurement bias (e.g. validity and consistency of coverage, uptake, or reach measures)
- confounding (e.g. differences between delivery strategies or contexts)
- completeness and reliability of outcome reporting
- contextual limitations affecting generalisability

Where relevant, we will explore risk of bias in relation to comparability of delivery strategies and consistency of outcome definitions (e.g. coverage vs uptake). Studies contributing to both LSR 3 and LSR 4 will receive an integrated appraisal, recognising their role in informing value-for-money synthesis. Risk of bias will therefore be assessed across both cost and performance domains with limitations in either domain explicitly documented.

Where formal economic evaluations (e.g. cost-effectiveness analyses) are included, the ECOBIAS checklist will be used to assess model structure and assumptions, quality of data (both costs and outcomes), internal consistency and transparency. In addition, the CHEERS 2022 reporting standards (Husereau et al. 2022) will be applied to assess quality of reporting of economic evaluations.

Two reviewers will independently assess risk of bias for each included study. Disagreements will be resolved through discussion or consultation with a third reviewer. Calibration exercises will be conducted at the outset to ensure consistency across reviewers. Studies will not be excluded from the LSRs based on their RoB assessment, however, RoB will be used to inform interpretation of findings, explore heterogeneity in results and identify evidence gaps and research priorities. RoB assessments will contribute to grading the overall certainty of evidence using Grading of Recommendations Assessment, Development and Evaluation - GRADE (Guyatt et al. 2008).

Two reviewers will independently assess risk of bias for each included study, with any disagreements resolved through discussion or consultation with a third reviewer. Calibration exercises will be conducted at the outset to ensure consistency across reviewers. Risk of bias assessments will be summarised in domain-level tables and cross-study summary figures. In line with the LSR framework, RoB assessments will be updated as new studies are incorporated and any changes in overall evidence certainty will be documented transparently.

Analysis and Synthesis

The analysis and synthesis will be structured to address each of the specific objectives of LSR 3 (costs and cost determinants), LSR 4 (delivery performance and implementation outcomes), and their integration to inform value for money. In three stages, a mixed-methods, narrative-led synthesis approach will be adopted, consistent with Cochrane guidance for complex and living systematic reviews (Booker et al. 2019). Given the high level of methodological and contextual heterogeneity anticipated across studies, synthesis will prioritise structured descriptive approaches, with quantitative methods applied only where assumptions of comparability are met.

Stage 1: Data structuring and standardisation (cross - LSR 3 and 4)

Extracted data will first be organised into a harmonised analytic dataset, including i) study design and context, ii) delivery platform and strategy classification, iii) economic perspective and costing scope, and iv) outcome definitions (costs and delivery performance metrics).

Cost data (LSR 3) will be standardised using a transparent, pre-specified hierarchy, including currency conversion and price year alignment, adjustment for inflation and purchasing power parity (where feasible), and harmonisation of unit cost metrics (e.g. cost per dose; cost per fully vaccinated individual). Where comparable standardisation is not feasible, results will be reported as study-specific estimates with clear annotation of assumptions.

Stage 2a : To address research question 1, LSR 3 synthesis will be conducted across three integrated analytical components:

i) Costs across delivery strategies and implementation phases: summary tables of cost per dose delivered, cost per fully vaccinated individual and total and incremental programme costs, stratified by delivery platform, implementation phase (introduction, pilot, routine) and economic perspective. Given variability in reporting, synthesis will prioritise structured descriptive summaries such as median and interquartile ranges (where ≥3 comparable studies exist). Formal meta-analysis will be conducted only where studies are sufficiently homogeneous in metric, context, and methods.

ii) Cross-platform cost comparison and cost drivers: studies will be mapped into i) a standard delivery platform taxonomy and ii) a cost component framework (e.g. personnel costs, overheads/logistics, cold chain equipment, social mobilisation materials and resources). Outputs will include cross HPV delivery platform comparison tables, identification of dominant cost components by platform and phase and structured synthesis of cost drivers. Cost drivers will be classified as modifiable (e.g. delivery strategy design, integration) or non-modifiable (e.g. geography, structural constraints). A cost driver evidence table will summarise direction of effect, context and strength of evidence.

iii). Contextual moderation and transferability: Evidence will be synthesised across key contextual domains including scale and coverage, geography (rural vs urban), and workforce models (cold chain capacity, integration with other services). Where feasible and appropriate, subgroup comparisons will be conducted, and exploratory meta-regression may be undertaken considering transferability to policy contexts and interpretation for real-world decision-making. Sensitivity analyses will include step wise

exclusion of studies with unclear cost scope, separation of financial vs economic costs and distinction between start-up and recurrent costs

Stage 2b: to address research question 2, LSR 4 synthesis will focus on how delivery strategies perform, rather than formal economic evaluation metrics. Evidence will be synthesised across reach, uptake/initiation, completion rates, and coverage. Structured summary tables will be used to present outcome ranges, variation by delivery strategy and key contextual influences. Subsequently, equity-sensitive synthesis will assess differences in geographic access, socio-economic status, and marginalised populations. We will identify patterns of inequity and strategies associated with improved equity. Importantly, evidence will be synthesised on acceptability, feasibility, barriers and facilitators, sustainability and scale-up. Comparative synthesis will aim to identify which delivery strategies perform better under what conditions and which/how mechanisms drive differences in performance

Stage 3: to address research question 3, value for money will be assessed through integration of cost (LSR 3) and performance (LSR 4) evidence. Firstly, we will attempt linking cost and performance evidence using a structured integration to identify cost per outcome (e.g. cost per vaccinated individual), resource use and linked delivery performance, and strategy-level comparisons combining cost and outcome data. Secondly, evidence will be synthesised across delivery strategies to assess:

- Relative efficiency
- Trade-offs between cost and coverage/performance
- Conditions under which strategies represent better value

Findings will be presented as decision-focused summaries, and realist informed policy relevant statements on “What works, at what cost, and under what conditions”

Lastly, a combined driver matrix will summarise drivers, effect on cost, effect on performance and implication for value. Drivers may include context, resource and infrastructural factors such as scale, coverage levels, delivery platform and integration opportunities. Formal economic evaluations (e.g. CEAs) will be included as supporting evidence (deconstructed into cost inputs and outcome assumptions). ICERs and other metrics will be reported descriptively without forcing comparability across heterogeneous models.

To ensure coherence, LSR 3 cost estimates will inform interpretation of HPV vaccine delivery strategies in LSR 4 as well as assumptions in economic evaluations. LSR 4 will

explicitly highlight where performance evidence aligns with cost evidence and existing gaps between cost and outcome data. Given expected heterogeneity, synthesis will be narrative, structured, and transparent. Quantitative pooling will be limited to comparable subsets and sources of variation will be explicitly documented. Specifically, for LSR 4, attention will be given to variability in outcome definitions and implementation contexts. Across both LSRs 3 and 4, uncertainty and sensitivity analyses will be summarised and implications for decision-making under uncertainty will be highlighted. Evidence will be synthesised to identify equity-relevant gaps and implications for underserved populations. Within the living review framework, new evidence will be continuously integrated into synthesis, mapped against existing findings. Furthermore, changes in cost estimates, delivery performance, and value-for-money interpretations will be tracked and reported transparently.

Certainty assessment

The certainty of the evidence will be assessed using an adapted GRADE (Grading of Recommendations Assessment, Development and Evaluation) approach (Guyatt et al. 2008), tailored to reflect the diverse evidence base across LSR 3 (costs and cost determinants); LSR 4: (delivery performance and implementation outcomes) and integrated analysis: value-for-money synthesis. Certainty of the evidence will be evaluated across the following standard domains: risk of bias, inconsistency (variability in results across studies), indirectness (applicability to LMIC delivery contexts and populations), imprecision (uncertainty in estimates or small sample sizes), publication bias / dissemination bias. Where applicable, certainty ratings may also be upgraded based on large magnitude of effect, dose–response relationships (e.g. scale effects on cost or coverage), consistency of findings across diverse contexts, Certainty will be categorised as high, moderate, low, very low (Neumann et al. 2024).

For LSR 3, GRADE will be applied at the level of cost outcomes (e.g. cost per dose, cost per fully vaccinated individual) and cost drivers and determinants (where sufficient evidence exists). Additional considerations specific to cost evidence will include:

- Completeness and transparency of cost reporting
- Consistency of costing methods and assumptions across studies
- Variability in cost estimates due to context and implementation phase

Given the observational nature of most costing studies, initial certainty will typically be low, with possible upgrading where evidence is consistent across settings and strong explanatory patterns (e.g. economies of scale) are observed.

For LSR 4, GRADE will be applied across key programme/implementation outcome domains (i.e. reach, uptake/initiation, completion rates, coverage and equity outcomes - where sufficient data exist). Additional considerations will include consistency of outcome definitions, measurement validity and comparability across studies, and risk of confounding in observational implementation studies. Where evidence is derived from RCTs, a higher starting certainty will apply. For observational or programme studies, lower starting certainty will be applied, with potential upgrading for consistency and magnitude.

For Research Question 3, certainty of evidence will reflect integration across cost and performance domains and will involve assessing certainty separately for cost evidence and performance outcomes. Subsequently, overall certainty for value-for-money will be judged based on i) alignment between cost and outcome evidence, ii) strength and consistency of linkages between resource use and delivery performance and iii) plausibility and coherence of inferred relationships. Given the integrative nature of this analysis, certainty for value for money findings will often be moderate to low and will be explicitly justified. Summary of findings (SoF) tables will be developed for each review question and key outcome domain. These will include:

- Number of included studies
- Study designs and populations
- Delivery strategies or comparisons assessed
- Key findings:
    - Cost estimates (LSR 3)
    - Performance outcomes (LSR 4)
    - Integrated cost - outcome interpretations (RQ3)
- Measures of variability (ranges, medians where appropriate)
- Risk of bias assessment
- Overall certainty rating (GRADE)
- Key explanatory notes (including context and assumptions)

Given the nature of the evidence, effect estimates will not always be pooled, as such findings will often be presented as ranges, structured summaries and narrative interpretations. Certainty assessments will be used to inform interpretation of findings, guide strength of conclusions and recommendations and to identify priority evidence gaps. In addition, attention will be given to aspects with high policy relevance but low certainty and domains where evidence is consistent but context-specific.

Within the LSR framework, certainty assessments will be updated iteratively as new evidence emerges and changes in certainty (e.g. upgrading due to new consistent evidence) will be explicitly documented and transparently reported in updated outputs.

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Appendices

Appendix 1. Search Strategy

Draft search string : Medline (Ovid)

1	exp Human Papillomavirus Viruses/	10041
2	papilloma*.ti,ab,kf.	81242
3	HPV.ti,ab,kf.	63588
4	((wart* or verruca*) adj virus*).ti,ab,kf.	149
5	cervical cancer.ti,ab,kf.	73557
6	or/1-5	145750
7	exp Vaccination/	125560
8	vaccines/	31634
9	exp Immunization/	233276
10	vaccin*.ti,ab,kf.	501170
11	immuni#ation*.ti,ab,kf.	138561
12	immuni#e.ti,ab,kf.	4774
13	EPI.ti,ab,kf.	30898
14	or/7-13	666747
15	6 and 14	23025
16	exp papillomavirus vaccines/	12278
17	gardasil*.ti,ab,kf.	748
18	cervarix.ti,ab,kf.	389
19	walrinvax.ti,ab,kf.	6
20	HPVMAX.ti,ab,kf.	0
21	cervavac.ti,ab,kf.	8
22	Cecolin.ti,ab,kf.	30
23	2vHPV.ti,ab,kf.	57
24	4vHPV.ti,ab,kf.	151
25	9vHPV.ti,ab,kf.	224
26	cervical cancer prevention.ti,ab,kf.	2538
27	or/16-26	14455
28	15 or 27	25260
29	exp "Costs and Cost Analysis"/	289290
30	Cost-Effectiveness Analysis/	2096
31	exp Health Care Costs/	77131
32	cost*.ti,ab,kf.	988812
33	econom*.ti,ab,kf.	547247
34	money.ti,ab,kf.	27670

35	value.ti,ab,kf.	1499311
36	price*.ti,ab,kf.	59658
37	budget*.ti,ab,kf.	43297
38	monetary*.ti,ab,kf.	14172
39	or/29-38	2972496
40	Vaccination Coverage/	3863
41	exp Health Services Accessibility/	151864
42	reach.ti,ab,kf.	238522
43	uptake.ti,ab,kf.	492786
44	coverage*.ti,ab,kf.	201692
45	equit*.ti,ab,kf.	91713
46	impact*.ti,ab,kf.	2216644
47	distribut*.ti,ab,kf.	1537820
48	public health.ti,ab,kf.	498797
49	access*.ti,ab,kf.	913221
50	outreach*.ti,ab,kf.	24388
51	acceptability.ti,ab,kf.	73116
52	utili#ation*.ti,ab,kf.	360483
53	rate*.ti,ab,kf.	4166717
54	population health.ti,ab,kf.	22107
55	("quality-adjusted life year" or "quality-adjusted life years" or QALY).ti,ab,kf.	23827
56	("disability-adjusted life year" or "disability-adjusted life years" or DALY).ti,ab,kf.	11237
57	performance*.ti,ab,kf.	1818135
58	or/40-57	10248620
59	39 or 58	11866062
60	28 and 59	15252
61	limit 60 to ez=20000101-20260603	15070
62	limit 60 to ed=20000101-20260603	12883
63	61 or 62	15075

Appendix 2. Eligibility Criteria: LSR 3 & 4: Costs, performance and value for money of HPV vaccine delivery

Domain	Inclusion Criteria	Exclusion Criteria
Study types	**LSR 3:** - Primary costing studies (ingredient-based, top-down, bottom-up); - Cost analyses embedded in programme evaluations; - Empirical data from retrospective costing studies, - prospective studies and budget impact analyses. **LSR 4:** - Programme evaluations and implementation studies, - Observational studies (cross-sectional, cohort), modeling studies (that include empirical data inputs) and trials of delivery strategies. Where available, economic evaluations (CEA, CUA, CBA) will be included.	For both LSR 3 & 4: - Editorials, commentaries; - Studies reporting only HPV vaccine effectiveness outcomes; - Studies without extractable HPV vaccine delivery-specific cost/ performance data.
Publication status	Peer-reviewed journal articles; preprints (with sufficient methodological detail); grey literature (e.g. government reports, programme evaluations, WHO/UNICEF/GAVI reports).	Conference abstracts without sufficient data; documents lacking transparency or extractable methodological detail.

Concept	**LSR 3 & 4**: Must involve HPV vaccine delivery strategy/platform **LSR 3:** Must report at least one financial/economic cost (e.g., cost per dose, cost per fully vaccinated individual, incremental delivery cost), budget impact analyses, cost components, delivery phases (introduction, pilot, routine), or cost drivers. **LSR 4:** Studies must report at least one HPV vaccine delivery performance outcome such as reach, uptake, coverage, completion rates, equity indicators, health impact or programme effectiveness (non-clinical) Where available, studies reporting cost-effectiveness outcomes (ICERs, DALYs/QALYs averted, cases prevented), value-for-money assessments of HPV vaccine delivery strategy or platforms. **NB:** Studies do NOT need to report cost data to be included in LSR 4.	**LSR 3 & 4:** HPV Vaccine relevant studies without delivery costing/ focus E.g., vaccine efficacy, or immunogenicity; Vaccine pricing/ manufacturing without delivery relevance; and non-HPV vaccination programmes. **LSR 3:** Studies reporting only health outcomes without cost data; Studies comparing vaccination vs no vaccination only (no HPV delivery comparison); **LSR 4**: Studies reporting only cost data without any outcome measure Studies comparing vaccination vs no vaccination (no HPV delivery comparison)
Participants	Adolescents eligible for HPV vaccination (girls, or girls and boys); populations targeted through HPV vaccination programmes across introduction, pilot, or routine implementation phases.	Populations not relevant to HPV vaccination programmes; studies unrelated to vaccine delivery contexts.

Geographical context	Low- and middle-income countries (LMICs) as defined by the World Bank for the year the study was conducted; multi-country studies including LMIC data (where disaggregated or attributable).	Studies conducted exclusively in high-income countries; studies where LMIC-specific data cannot be isolated.
Language	No language restrictions; inclusion of non-English studies where translation is feasible (via team, collaboration networks or AI translation).	Studies where translation is not feasible or where data cannot be reliably interpreted.
Year	Search from 2000	No upper limit restriction as LSR

Appendix 3. Triage Checklist

Triage Checklist LSR 3 (Cost) | LSR 4 (programme performance)

Use this checklist to guide classification of studies at the full-text triage stage into:
☐ LSR 3 ☐ LSR 4 ☐ Both ☐ Exclude

Key triage principles:

- Apply consistently across all studies
- Focus on what is reported (not implied)
- When in doubt, flag rather than guess
- Maintain a clear audit trail for all decisions

Step 1: Core Eligibility Check *(to be completed before LSR 3 & 4 triage classification)*

☐ Study relates to HPV vaccine delivery
☐ Conducted in LMIC setting (or extractable LMIC data)
☐ Includes relevant population (HPV vaccination programmes)

If NO to any → ☐ EXCLUDE ; If YES to all → proceed

Step 2: Cost Evidence (LSR 3) *study reports*:

☐Cost per dose / per vaccinated individual ☐Programme costs (total/incremental)

☐Cost components

☐Resource use with costing

☐Cost drivers

☐Prospective/retrospective costing

If YES to any, mark to include in for LSR 3 portfolio

Step 3: HPV delivery performance (LSR 4) *Check all that apply*:

☐ Reach

☐ Uptake

☐ Completion

☐ Coverage

☐ Equity differences

☐ Acceptability

☐ Feasibility

☐ Barriers

☐ Sustainability

If YES to any, mark to include in LSR 4 portfolio

Step 4: Dual eligibility (LSR 3 + LSR 4) - *check all that apply*:

☐Cost + outcome evidence

☐ Cost per outcome

☐ HPV vaccine delivery strategy comparison (cost + performance)

Step 5: Economic evaluation (context only) check:

☐ Economic evaluation methods (e.g. CEA, CUA, CBA)

☐ Reports of ICER (incremental cost-effectiveness ratio)

Step 6: Documentation. For every included study:

☐ Record final classification (LSR 3 / LSR 4 / Both / Exclude)
☐ Add brief justification (1/2 lines)
☐ Flag dual-eligible studies for coordinated extraction

If unclear at any stage:
☐ Flag for third reviewer/ team discussion
☐ Add note in screening log

Appendix 4. Data Extraction Pro-forma (https://wafersktc-my.sharepoint.com/:x:/g/personal/e_ayinmode_wafers_org/IQCPtXGOL1RnSZGP3nNYTT5yAYm_dEvcInUgURQv3d0FY7M?e=gsZYla)