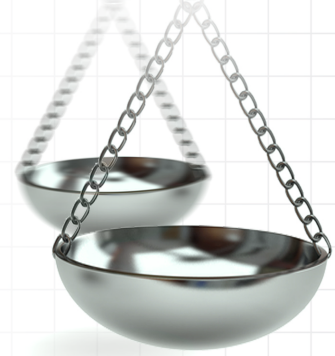
Research Article



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Adoption of the HPV vaccine: a case study of three emerging countries

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Background: The human papillomavirus (HPV) vaccine has recently attracted considerable attention in emerging countries, due to its potential to reduce the impact of HPV-related diseases. This case study sheds new light about the variety of HTA arrangements, methods and processes involved in the adoption and use of HPV vaccines in a selected sample of central, eastern and southern Europe and Latin America and the Caribbean, all of them emerging in the use of HTA. **Materials & Methods:** A multi-country case study was designed. Mixed methods, document review, semi-structured surveys and personal communication with experts, were used for data collection and triangulation. **Results:** This study shows that common elements of good practice exist in the processes and methods used, with all countries arriving at the same appraisal recommendations. However, the influence of socio-politico-economic factors appears to be determinant on the final decisions and restrictions to access made. **Conclusion:** This case study intends to draw useful lessons for policymakers in emerging settings interested in the adoption of the HPV vaccine supported by evidence-informed processes, such as those offered by institutionalized HTA. Future studies are also recommended to elucidate the specific roles that social values and uncertainties play in vaccine decision-making across different societies.

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Each year, there are 530,232 new cases and 275,008 deaths from cervical cancer worldwide, with 85.5% of these cases in developing countries (15% of all cancer cases in women) [1–4]. Temporal projections indicate that there will be 0.7 million new cases of cervical cancer by 2020 and 90% of these will occur in low- and middle-income settings [5]. Over 100 human papillomavirus (HPV) genotypes are known, and about a dozen high-risk types have been identified. However, just HPV 16 and 18 are responsible for about 70% of all cervical cancers, with genotype 16 having the greatest oncogenic potential [6,7]. Up to date, three HPV vaccines have been approved by the US FDA and the EMA: Cervarix® (GlaxoSmithKline, Brentford, UK) in 2007 (bivalent, against HPV -16 and -18), Gardasil® or Silgard® (Merck Sharpe & Dohme, NJ, USA), in 2006 (quadrivalent, against HPV-6, -11, -16 and -18), and Gardasil 9® in 2015 (against HPV-6, -11, -16, -18, -31, -33, -45, -52 and -58). As a consequence, the possibility of preventing new cases of cervical cancer triggered by high-risk HPV genotypes has become a reality in many countries [8].

In order to make decisions on vaccine adoption, where innovation, restricted budgets and fragmented evidence come into play, policymakers in many countries have become interested in health technology assessment

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(HTA) as a support tool [9]. HTA is an interdisciplinary approach that aims to support the process of decision-making by providing relevant evidence and reliable information. An HTA should be systematic, participatory, transparent, timely, relevant and patient-focused procedure. Notwithstanding that, different models of organization of health systems, along with other elements such as political traditions, national income differences or expenditure capacities resulting in different HTA systems and often different types of decisions, such as adoption, approved with restrictions or denied [10,11].

In recent years, considerable attention has been drawn to understand the international variability in the adoption of HPV vaccines from an HTA perspective. In particular, the EU-funded VENICE 2 project found a variety of coverage strategies in the 29 European countries studied, including differences in age for vaccination and for catch-up rounds [12]. A limited budget was the most cited reason for nonadoption [9]. However, a few countries from central, eastern and southeastern Europe (CESEE) were included in the study, and – due to that – a few data are currently known. Some studies have also focused on similar issues in Latin America and the Caribbean (LAC) [13,14], but both the selection of covered countries and the data collected are limited. Overall, previous papers fail to provide in-depth insights into the HTA of HPV vaccines.

This case study provides descriptive information on the adoption and use of HPV vaccines in a selected sample of CESEE and LAC country settings from where scarce information exists on this issue. This study is part of ADVANCE_HTA, a multipartner research project funded by the European Commission's Research Framework Program (FP7). It comprises several complementary streams of research which aim to advance and strengthen the methodological tools and practices related to the application and implementation of HTA [15]. In particular, HPV vaccines were chosen as a technology being studied by the ADVANCE_HTA working group with the following criteria: high public interest, epidemiological and health system relevance; an HTA had to be already performed (or be in process) in the selected countries for the same therapeutic indication; and country of interest had to be gauged in both regions.

Accordingly, this case study aims to describe the variety of HTA arrangements, methods and processes involved in the adoption and use of a contentious preventive intervention in a selection of countries from the CESEE and LAC regions, in order to clarify the current state of vaccine implementation in low–middle-income countries and to provide recommendations to those countries.

Materials & methods

A multi-country collective case study was designed, and a review of relevant HTA literature was conducted to identify good HTA practices, concepts to be used and previous HTA surveys.

A questionnaire was developed according to Drummond *et al.*'s key principles for HTA [16], and key trends and issues in HTA methodology, application and process from several studies/international experiences [17,18]. The instrument – consisting of 38 questions – grouped according to the three dimensions: first, the HTA process – introduction, institutions, unbiased and transparent, stakeholders; second, methods and criteria for conducting HTA – structure and methods, evidence, methods for assessing cost and benefits, social perspective, uncertainty; third, link between HTA and decision-making – implementation, decision-making, timely and communicated. The questionnaire was revised and pilot-tested with HTA experts from different countries and organizations (e.g., for format, structure, formulation of questions and answer options). It included both dichotomous and multiple choice questions, as well as a number of open-ended questions to allow for clarification and explanation of responses (full questionnaire available upon request).

Key informants were purposively selected from HTA organizations that were members of Health Technology Assessment Network of the Americas (RedETSA; Colombia and Brazil, among 14 countries 27 institutions that comprise it) and of the European Network for Health Technology Assessment (EUnetHTA; Poland). The contacts were mainly identified through personal contact and internet searches. By email, they were asked whether they had evaluated the HPV vaccine and invited to complete the survey (among EUnetHTA members, seven countries were invited to participate and Poland was the only country that accepted to participate). E-mails were sent from July to October 2014, and respondents were followed up by e-mail and telephone until survey completion (December 2014). The data gathered from survey responses (n = 3) were examined following a content analysis approach. Results were contrasted with the information available on the vaccine health technology assessment/appraisal reports that were carried out by these countries [19–21]. In addition, to ensure the quality of information, those results were contrasted with a previous mapping survey from the ADVANCE_HTA project [22], highlight that this study had a clarification and validation step provided by country experts. The ADVANCE_HTA project had the necessary authorizations; furthermore, at the local level, the project was authorized by the research committee of the Andalusian School of Public Health.

Results

Overall, the HPV vaccine was evaluated as an established technology, and recommended by the respective appraisal committees for inclusion in the national immunization programs (NIP) in all three countries. Findings are presented according to the following three domains: HTA process from topic selection to appraisal, methods and criteria for conducting HTA and the link between HTA and decision-making.

HTA process

In both Colombia and Poland, the vaccine assessments were conducted independently of the bodies making recommendations for NIP inclusion. In particular, the Colombian Health Regulation Commission (CRES) commissioned the assessments to the National Cancer Institute (NCI) and the National University of Colombia. In Poland, a submission from the manufacturer was the basis for the vaccine assessment, which was followed by a review/validation by the Agency for Health Technology Assessment and Tariff System (AOTMiT) and an appraisal by the Transparency Council. By contrast, it appears that the National Committee for Technology Incorporation (CONITEC) conducted both the assessment and the appraisal in Brazil. Decisions of Ministry of Health (MoH) on vaccine adoption were clearly informed by appraisal recommendations in all three countries. Table 1 shows the main bodies that constitute the HTA systems described.

The selection of the HPV vaccine as a technology to be assessed was always made at the ministerial level. In Colombia, CRES was in charge of topic selection, while the Health Surveillance Agency (ANVISA) and the MoH managed this procedure in Brazil and Poland, respectively. In the latter countries, pharmaceutical manufacturers were the stakeholders requesting the assessments with the intent of gaining reimbursement for their products.

The Polish appraisal committee was composed of independent experts from several clinical areas, health service researchers and public health specialists. In Colombia, gynecologists and public health experts were involved in the NCI assessment, while policymakers were the members of CRES. The stakeholders involved in the CONITEC (Brazil) process were the members of its plenary board – composed of policymakers and civil society representatives.

In Poland, manufacturers, patients groups, public payers and clinical specialists provided comments at the final stage of the assessment, and these were taken into account at the appraisal stage. In Brazil, patients groups, clinical specialists, manufacturers and civil society were able to provide comments on the appraisal recommendations. In the case of Colombia, no external stakeholders were involved at other stage of the process.

In terms of transparency, assessment reports, appraisal recommendations and final decisions were made available online in all three countries. Brazil also published the comments from external stakeholders in response to the appraisal recommendation. Only Poland reported having an established procedure to manage conflicts of interest of stakeholders and confidential data from manufacturers. In Brazil and Colombia, it was possible for the manufacturer to appeal formally against the decisions, while in Poland this possibility is not contemplated.

Although HTA reports were disseminated in all countries, no separate versions of reports were produced for different audiences. Moreover, only Brazil reported to have a known communication plan for HPV vaccine recommendations and decisions.

Methods & criteria for the conduct of HTA

The HPV vaccine was prioritized as a technology for assessment according to clinical and socio-economic criteria in the cases of Colombia and Brazil as reported in the survey. Meanwhile, a minimum set of technical standards were used by the Polish MoH to decide whether to forward the vaccine to AOTMiT or not. Across countries, information used for scoping included the epidemiology and natural history of cervical cancer, as well as the description of the two types of vaccines available on the market.

Clinical evidence and end points considered by each of the HTA bodies in their assessments are shown in Tables 2 and 3. Across countries, the evaluation of

Table 1. Main bodies conforming the health technology assessment system by setting.

Setting	Assessment body	Appraisal body	Decision-making body
Poland	AOTMiT†	TC	MoH
Colombia	NCI + NUC	CRES	CRES/MoH
Brazil	CONITEC†	CONITEC	Secretary of SCTIE

†AOTMiT and CONITEC based their reports on manufacturers' dossiers and/or externally commissioned assessments.
AOTMiT: Agency for Health Technology Assessment and Tariff System; CONITEC: National Committee for Health Technology Incorporation; CRES: The Health Regulatory Commission; MoH: Ministry of Health; NCI: National Cancer Institute; NUC: National University of Colombia; SCTIE: Science and Technology Secretariat; TC: Transparency Council.

Table 2. Clinical evidence considered by the countries in the human papillomavirus vaccine assessment.

Clinical evidence and limitation in the review of evidence	Poland	Brazil	Colombia
Clinical evidence:			
– Phase I–II trials	–	✓	–
– Phase III trials (RCTs)	✓	✓	–
– Postmarketing registry	✓	✓	–
– Observational studies	–	✓	–
– HTA reports	✓ DAHTA, SBU, DACEHTA, NOCK, CADTH	No	✓ DACEHTA, HIQA, UCSC, KCE, DAHTA
Limitations in the review of evidence:			
– Duration of protection between the different vaccines available	–	✓	✓
– Follow-up periods to estimate the level of antibodies and the duration of immunity	–	✓	✓
– Related to cross-protection against nonvaccine HPV types	–	✓	–
– Related to trial methodology	✓	–	–
– Related to the age of the patient	✓	–	–
Comparator	The actual screening without vaccine and between vaccines	The actual screening without vaccine	The actual screening without vaccine

CADTH: Canadian Agency for Drugs and Technologies in Health; CUSH: Catholic University of the Sacred Heart (Institute of Hygiene); DACEHTA: Danish Centre for Health Technology Assessment; DAHTA: The German Agency of Health Technology Assessment; HIQA: Health Information and Quality Authority; HPV: Human papillomavirus; HTA: Health technology assessment; KCE: Belgian Health Care Knowledge Centre; NOCK: Norwegian National Knowledge Center for the Health Services; SBU: The Swedish Council on Health Technology Assessment; RCT: Randomized controlled trial; UCSC: Health Technology Assessment Public Health Unit.

efficacy/effectiveness was based on systematic reviews and randomized controlled trials, while postmarketing data were considered for assessing safety (Colombia re-evaluated safety in a later assessment). All agencies considered HTA reports and/or economic evaluations from other settings to help in their decisions. Of particular note, Poland took into account foreign reimbursement decisions. In terms of end points, both Poland and Brazil also considered vaccine protection.

Costing was conducted locally from the payer (patient; Poland) and health system perspectives (Brazil and Colombia), with only some direct costs being considered in Poland. Although economic evaluations were conducted in all countries, utilities were only considered in Poland and Brazil. To aid decision-making, all reports included budget impact analyses. As for modeling, Markov models were employed in the Polish and Colombian assessments, while a decision tree (CERVIVAC) was employed in Brazil (Table 4).

Uncertainties were explored in all assessments: in Poland, they were relative to the natural history and sexual transmission, specifically those related to clinical parameters; CONITEC in Brazil also identified study design, comparator and HPV vaccination program. And, in the Colombian report, the variables that affected the results were mostly operational features and costs of screening, diagnosis and treatment. In particular, uncertainties on duration of protection after 5 years of vaccination were highlighted in all countries.

Link between HTA & decision-making

HTA recommendations for vaccine adoption were taken into account for decision-making in all three countries. Despite this, Polish decision-makers decided not to include the vaccine in the NIP. Key features in the assessment, appraisal and decision-making for HPV vaccines are described in Table 5.

After AOTMiT assessment and appraisal, the MoH entered into pricing and reimbursement negotiations with industry. In this case, budget impact (and ultimately price) appears to have been a key factor to reject the vaccines. By contrast, both value for money and

budget impact analysis seem to have been the main factors considered for reaching a favorable decision in Colombia and Brazil. Additionally, factors such as priorities in public policy, organizational structure and social, ethical and equity aspects seem to have been weighed to decide in favor of vaccine adoption in Brazil.

In terms of implementation, Brazil adopted the quadrivalent vaccine to cover girls aged 10–13 years in 2014, with a different dosing schedule to the one assessed due to equity reasons. The MoH also planned additional investments for vaccine vigilance and educational campaigns, while reinforcing the established cervical cancer screening program. A specific system for monitoring was established including follow-up of vaccinated girls and active search for absent population. Moreover, further studies were planned to determine HPV prevalences in adolescents or factors influencing adherence.

In Colombia, the quadrivalent vaccine with the same schedule as Brazil was implemented in 2012 covering girls aged 9 years and above. The MoH, in collaboration with the NCI, initiated a monitoring program in two demonstration areas, reaching 92% coverage of schoolgirls in the first 2 years of implementation.

Discussion

This case study provides a description and comparison of the HTA of the HPV vaccine – including relevant stakeholders, criteria considered and final decisions – across three emerging settings in the use of HTA. This study shows that there are common elements of good practice in the processes and methods used, as reported by some authors [11,18], with all countries arriving at the same appraisal recommendations. However, the influence of socio-politico-economic factors appears to be determinant on the final decisions and restrictions to access made, as the case of Poland (in the other two countries no signs of being pressure). This case study intends to draw useful lessons for other emerging countries interested in the adoption of the HPV vaccine supported by evidence-informed processes, such as those offered by institutionalized HTA.

The value of our contribution lies in offering an overview of the HTA processes that the HPV vaccine underwent, from the institution charged of the selection as a topic for assessment to its implementation as part of the NIP in the countries adopting it. Although earlier case studies of decision-making related to the HPV vaccine have been published [23–25], our paper provides first-hand information on HTA processes themselves, rather than an examination of external influences on the policy debate arising from the launch of the vaccine.

We are aware that our research may have some limitations. The first is related to the comparability of results. Although all settings compared are emergent in the use of HTA, they are part of different geographic regions with specific socio-political environments. Nonetheless, there is evidence indicating that countries may reach the same conclusions due to similar political pressures [24]. The second one is related to the difficulty of collecting data in this field. The authors could not ensure that the survey was always filled out by the most informed person on the subject. In addition, full HTA products could only be retrieved from Brazil and Colombia, because part of this information was confidential in Poland. Another factor that affects the reliability of the results is that the HPV vaccine was evaluated in Colombia by CRES and an HTA unit that does not currently exist. Thus, the country survey was completed by a professional from Institute for Health Technology Assessment (IETS), who was unaware of certain information asked. Despite these issues, the authors have paid special attention to the analysis and triangulation of data, confirming data with country experts and available HTA reports.

Table 3. Clinical end points included by the countries in the human papillomavirus vaccine assessment.

Clinical end points	Primary end points			Secondary end points		
	Poland	Brazil	Colombia	Poland	Brazil	Colombia
Vaccine efficacy/effectiveness:						
– Cervical cancer	✓	✓	✓	–	–	–
– Genital warts	✓	–	✓	–	–	–
– Cervical abnormalities	✓	–	✓	–	–	–
– Antibody levels	✓	–	–	–	✓	–
– Duration of vaccine-induced protection	–	–	–	✓	✓	–
Vaccine safety	✓	–	✓	–	✓	–
Quality of life	✓	–	–	–	–	–

Table 4. Economic methods and considerations to assess human papillomavirus vaccine.

Methods and considerations	Poland	Brazil	Colombia
Types of costs considered in the HTA report for HPV vaccine:			
– Some direct cost (like drugs, diagnostic/therapeutic tests)	✓	✓	–
– Healthcare cost from the health service perspective	–	✓	✓
– Indirect cost (e.g., productivity gains and losses and cost for informal care)	No	No	No
Type of economic evaluation:			
– Cost–effectiveness analysis	–	✓	✓
– Cost–utility analysis	✓	✓	–
– Cost–consequence analysis	✓	–	–
– Budget impact analysis	✓	✓	✓
End points included in the HPV vaccine cost–effectiveness model:			
– Cost per life year	–	–	✓
– Cost per event avoided	–	✓	–
– Cost per quality adjusted life year saved	✓	–	–
– Consideration of sexual transmission	✓	✓	✓
The HPV vaccine model uncertainties:			
– Clinical parameters (e.g., HPV prevalence rates, progression, cervical cancer screening and HPV epidemiology)	✓	✓	✓
– Efficacy evidence (for HPV types)	✓	✓	–
– Safety evidence	✓	✓	–
– The expected health benefits of introducing an HPV vaccinations program	✓	✓	✓
– Study design (e.g., sample size and time horizon)	–	✓	✓
Comparator	–	✓	–
Target population and generalizability	✓	✓	✓
Disease characteristics (and burden of disease)	✓	✓	✓
HPV vaccination program (catch-up campaign)	–	✓	✓
The discount rate and the cost of the technology	–	–	✓

HPV: Human papillomavirus; HTA: Health technology assessment.

In general, most countries evaluated the HPV vaccine within well-structured HTA processes, with an acceptable degree of transparency supported by publicity of rules/criteria and outcomes of the process. An area that was not as well developed across all settings was the provision of rationales supporting the recommendations and decisions made. Although some countries provided a discussion around these items, it is not possible to ascertain the weight that each scientific/social value carried compared with others. There is also scope for improving the level of participation of stakeholders at the appraisal phase of HTA, and for creating channels for the appeal against the decisions made. In particular, there was no broad and genuine participation of relevant actors in the case of Colombia, and stakeholders were only present at the final stages of the assessment and appraisal in Poland and Brazil, respectively [16,26]. As others have highlighted [27], a multitiered and wider involvement of stakeholders throughout HTA promotes local relevance, accountability and transparency, thereby creating legitimacy and reducing contestability.

As recommended by some authors [28–30], the assessment of the vaccine evidence took account of long-term

effectiveness, postmarketing safety and cost–effectiveness in all settings. Given the fact that vaccines are administered to healthy populations and long-term benefits of the HPV vaccine are still uncertain, the societal acceptance of risks is generally lower than for drugs. In line with this, it is important to highlight that a re-assessment of safety and effectiveness was needed in Colombia a few years after the initial evaluation. Moreover, the duration of vaccine protection – an end point not yet well known – was taken into consideration across all countries.

According to our analysis of the different HTA bodies, only one of them took account of quality-of-life dimensions by using quality adjusted life years (QALYs) as an outcome, 'the best measure currently available for valuing health states' [29]. A rigorous assessment should allow determining how the costs of vaccination to gain a quality adjusted life year compared with those of other health interventions, such as cervical cancer screening or sexual and reproductive health promotion programs [31].

In terms of models used, all were static in nature. Although it has been argued that dynamic models are more suitable for responding complex policy questions (e.g., coverage levels), static models are equipped to answer simpler questions and give more conservative results, such as whether to introduce a vaccine or not, and are easier to develop and interpret, thus these appraisal could be an acceptable choice [29]. In line with the latter, the CERVIVAC decision-tree software – developed by the ProVac Initiative for Latin America – was used by CONITEC to build their model. In addition, direct health costs from the payer's perspective were used across all evaluations, when indirect costs are typically high in infectious diseases.

Although all three countries concluded that the HPV vaccine was cost effective and recommended it for NIP inclusion, Polish decision-makers decided against it. All countries considered value for money and budget impact, given the high government investment required [24], but none included the social perspective in estimating costs. The role that other criteria, such as burden of disease, uncertainties (e.g., effectiveness and safety), industrial policy and ethical issues, played in the final decisions is less clear. In some countries, industrial policies can be indirect implicit criteria in order to set the medicines or vaccines prices, producing as effect higher prices of the national companies or companies with higher number of employees in the country.

Similarly to the case of Poland, about 21% of EU and Economic Area and 60% of LAC countries had not yet adopted the HPV vaccine due to financial restrictions and uncertain evidence (data 2014) [30,32–33]. Both Brazil and Colombia decided to administer the third vaccine dose at 60 months instead of the manufacturer's recommendation at 6 months. Equity

Table 5. Key features in the assessment, appraisal and decision-making for human papillomavirus vaccines.

Feature	Poland	Brazil	Colombia
Vaccines (commercial name and valence)	Cervarix® (bivalent) and Silgard® (quadrivalent)	Cevarix (bivalent) and Gardasil® (quadrivalent)	Cevarix (bivalent) and Gardasil (quadrivalent)
Assessment results	ICUR: confidential Value for money (threshold in line with WHO guideline)	ICUR: US$9000/DALY Value for money (threshold in line with WHO guideline)	CER: US$4.207/LYG Value for money (threshold in line with WHO guideline: US$12.018, 2010)
Recommendation (year)	Favorable (2013)	Favorable (2013)	Favorable (2011)
Factors considered in the recommendation	Value for money Budget impact Ethical and social values	Value for money Priorities in public policy Organizational structure Ethical and social values (including equity)	Value for money Budget impact
Final decision	Nonfavorable	Favorable	Favorable
Target population (years old)	NA	Girls: 9–13	Girls: ≥9
Implementation	NA	2014: 11–13 years old 2015: 9–11 years old 2016: 9 years old	2012: 9 years old
Dosing schedule (months)	NA	(1, 6, 60)	(1, 6, 60)

DALY: Disability-adjusted life year; ICER: Incremental cost–effectiveness ratio; ICUR: Incremental cost–utility ratio; LYG: Life years gained; NA: Not available.

principles (increasing coverage) were declared in Brazil, although other reasons may have influenced the implementation program, such as feasibility and deferment of expenditures [30].

According with our experience, there are some common future trends in the use of HTA as a criteria for setting price and reimbursement of vaccines and medicines:

- HTA will be used as an instrument to increase transparency in the decision-making process;
- Different countries will be used different elements in the HTA process, but some common elements will be found: efficacy, efficiency and budget impact; some other elements that will be used in several countries will be equity, innovation, R&D investment, among others;
- No need to have a single explicit threshold, but probably countries will have implicit threshold adjusted by several criteria (e.g., severity of the disease and priority for rare diseases);
- Confidential agreements will be part of the HTA process, but mainly in the last part of the process and only for some specific cases.

Conclusion

The findings of this study suggest that decisions should be based on a wide range of criteria, such as burden of disease, available evidence, value for money, affordability, the value of other alternative interventions and health system sustainability, but it is difficult to know the weight assigned to each. Therefore, it is important for policymakers in emerging settings to support the establishment and development of HTA systems, which provide a framework that at least the main determinants of decision were transparent, thanks to a clear HTA process supporting decisions [34]. There is a challenge of avoiding duplication of work and obtaining a more effective use of national HTA. There is a need to find more standardized approaches in order to provide tools that help HTA actors to reuse the work of others. Future studies are also recommended to elucidate the specific roles that social values and uncertainties play in vaccine decision-making across different societies [35].

Author contributions

J Espín Balbino and A Lemgruber conceived the study. J Espín Balbino, A Lemgruber and A Caro Martínez designed the study. A Caro Martínez and F Lessa collected data. A Caro Martínez drafted the first version of the manuscript. All authors contributed with ideas for discussion, reviewed the manuscript, and approved the final version.

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Summary points

- This case study provides a description and comparison of the health technology assessment (HTA) of the human papillomavirus (HPV) vaccine – including relevant stakeholders, criteria considered and final decisions – across three emerging settings in the use of HTA.
- Most countries evaluated the HPV vaccine within well-structured HTA processes, with an acceptable degree of transparency supported by publicity of rules/criteria and outcomes of the process.
- There is scope for improving the level of participation of stakeholders at the appraisal phase of HTA, and for creating channels for the appeal against the decisions made. There was no broad and genuine participation of relevant actors in the case of Colombia, and stakeholders were only present at the final stages of the assessment and appraisal in Poland and Brazil, respectively.
- The duration of vaccine protection was taken into consideration across all countries and static models were used, specifically the CERVIVAC decision-tree software – developed by the ProVac Initiative for Latin America – was used by National Committee for Technology Incorporation to build their model.
- All countries considered value for money and budget impact, given the high government investment required, but none included the social perspective in estimating costs.
- The HPV vaccine was evaluated as an established technology and recommended by the respective appraisal committees for inclusion in the national immunization programs in all three countries. However, the influence of socio-politico-economic factors appears to be determinant on the final decisions and restrictions to access made, as the case of Poland.
- Future studies are also recommended to elucidate the specific roles that social values and uncertainties play in vaccine decision-making across different societies.

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• of interest; •• of considerable interest

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