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Cost-effectiveness of human papillomavirus vaccination in low and middle income countries: A systematic review

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ABSTRACT

The World Health Organization recommends establishing that human papillomavirus vaccination is cost-effective before vaccine introduction. We searched Pubmed, Embase and the Cochrane Library to 1 April 2012 for economic evaluations of human papillomavirus vaccination in low and middle income countries. We found 25 articles, but almost all low income countries and many middle income countries lacked country-specific studies. Methods, assumptions and consequently results varied widely, even for studies conducted for the same country. Despite the heterogeneity, most studies conclude that vaccination is likely to be cost-effective and possibly even cost saving, particularly in settings without organized cervical screening programmes. However, study uncertainty could be reduced by clarity about vaccine prices and vaccine delivery costs. The review supports extending vaccination to low income settings where vaccine prices are competitive, donor funding is available, cervical cancer burden is high and screening options are limited.

1. Introduction

Cervical cancer is the second most common cancer in women. About 250,000 deaths due to cervical cancer occur annually, with over 80% of them in low and middle income countries (LMICs) [1]. This is partly because many high income countries have well-organized screening programmes which can detect and treat precursors to cervical cancer before they develop into invasive cancer [2,3]. Most LMICs lack such screening programmes; those that have screening programmes in place often struggle with issues around coverage, quality assurance of the screening test and treatment availability for detected precancerous lesions [4,5].

Infection with an oncogenic type of human papillomavirus (HPV) is a necessary cause of cervical cancer [6]. Hence prophylactic vaccines that protect against persistent infection with oncogenic HPV types offer a complementary preventive option to screening. Two HPV vaccines have been pre-qualified by the World Health Organization (WHO): Cervarix(R), a bivalent vaccine that protects against infection with two HPV types (16 and 18) causing 70% of cervical cancer cases worldwide, and Gardasil(R), a quadrivalent vaccine that protects against HPV types 16 and 18, but also against two HPV types (6 and 11) which cause almost all cases of anogenital warts [7–9]. In addition, both vaccines may be cross-protective against other oncogenic HPV types [10].

The WHO recommends that the cost-effectiveness of HPV vaccination is established before it is offered as part of national vaccination programmes [11]. Numerous country-specific cost-effectiveness evaluations of HPV vaccination in high income countries have been conducted and extensively reviewed [12,13]. This has driven widespread HPV vaccine introduction in those countries. In contrast, HPV vaccine introduction in LMICs is more limited [14]. LMICs face different issues with regards to HPV vaccine introduction compared to high income countries but there are fewer cost-effectiveness studies to inform decisions in LMICs, and those that exist are unequally distributed among the different world regions [15]. To complicate matters, in some countries several evaluations have been conducted with seemingly conflicting results [16–18]. Hence decision makers in LMICs as well as donors supporting vaccination programmes face difficulties in understanding how to use the economic literature to guide decision making.

To date, no systematic review focusing on economic evaluations of HPV vaccination in LMICs has ever been conducted. The aim of this study is to review published cost-effectiveness studies of HPV vaccination in LMICs to provide guidance for decision making. We discuss study results and investigate how they are affected by

Abbreviations: CVG, cost per vaccinated girl; GDP, gross domestic product; HPV, human papillomavirus; ICER, incremental cost-effectiveness ratio; LMIC, low or middle income country; QALY, quality adjusted life year; WHO, World Health Organization.

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model characteristics and underlying assumptions. These characteristics are discussed in relation to issues specific to LMICs such as vaccine affordability, delivery costs, uncertainty about vaccine price and the relationship between primary and secondary prevention strategies. Our discussion is illustrated by a comparison of results from two countries (Mexico and Thailand) for which three separate single country studies have been published.

2. Methods

2.1. Search strategy

PubMed, Embase and the Cochrane Library were searched for economic evaluations of HPV vaccination published before 1 April 2012. The search terms used are given in Appendix A. Selected articles were limited to original research papers (not reviews) published in English, French, German, Italian or Spanish in peer-reviewed journals, describing full economic evaluations including cervical cancer outcomes of HPV vaccination in at least one LMIC, based on World Bank classification of income groups [19].

2.2. Data extraction

Study assumptions, methodology, parameters and results were extracted from full text articles. Supplementary appendices were consulted if any information was not available in the main text. Data were independently extracted by two reviewers (M.F. and M.J.); differences were resolved by consensus. Gross domestic product (GDP) per capita in 2011 US$ was obtained from the World Bank [20]. When several screening strategies were compared, the scenario with the lowest incremental cost effectiveness ratio (ICER) was extracted. The most comprehensive cost-effectiveness league table was used when there were several giving different lists of screening options. To facilitate inter-study comparability, ICERs for two scenarios were extracted: (i) vaccination compared to no intervention, and (ii) vaccination with screening compared to screening alone (rather than vaccination compared to the next most effective non-dominated option). The ICER corresponding to the lowest vaccine price or cost per vaccinated girl (CVG) was extracted when none was indicated as the base case. Affiliation was determined by the first listed institutional affiliation of the first author. The funding source of a study was determined by any support directly received for the study stated in the acknowledgments or declarations. If any co-authors were employees of a vaccine manufacturer, this was included as a funding source regardless of whether it was declared as a conflict of interest.

2.3. Currency conversions

Unit costs were converted into 2011 international dollars (I$) to facilitate inter-country comparisons. Purchasing power parity conversions provided by the United Nations Statistics Division [21] were used. Local currencies were first converted into I$ using the stated year of currency conversion, or (if not available) base year for prices, or (if neither available) article publication year. For the case of the New Taiwan Dollar (where United Nations data are not available), historic US$ currency conversion rates were used. Costs given in US$ were converted back into national currencies before converting to I$. Costs in I$ were then inflated to 2011 values using the US$ Consumer Price Index for all urban consumers (CPI-U) [22], since the US$ by definition has the same inflation rate as the I$ [23]. Vaccine purchase costs (but not CVGs) and GDP per capita thresholds are set internationally, so these were converted into United States dollars (US$) using historic US Federal Reserve exchange rates [24] on 1 July of the base year and not inflated.

3. Study characteristics

Titles and abstracts of 537 published articles were searched (see Fig. 1). The search yielded 25 economic evaluations of HPV vaccines in low and middle income settings. Key characteristics of the articles are shown in Fig. 2 and discussed below (see Appendix B for full details).

3.1. Single or multi-country

There were nine multi-country studies. The most extensive were two studies covering 72 GAVI-eligible countries [25] and every LMIC in the world on a regional basis [26], respectively. Such multi-country studies facilitate access to economic analyses in settings which may lack resources for such analyses. However there may be trade-offs, such as the use of data from large multi-country databases rather than in-country primary data, as well as reduced opportunities to engage in-country investigators, stakeholders and policy makers in model development and application [27]. Indeed, all multi-country studies were commissioned by transnational organizations (such as the WHO, Bill and Melinda Gates Foundation and vaccine manufacturers) rather than national decision makers.

3.2. Country, funding and authorship

Single-country studies largely focused on upper middle income countries in Latin America and South-East Asia (see Fig. 3). In contrast, there were only two single-country studies for lower middle income countries (Vietnam [28] and India [29]), none for low income countries, and only one for an African country (South Africa [30]). Furthermore, unlike studies in high income countries, the studies reviewed were mainly funded and conducted by private sector actors. The Bill and Melinda Gates Foundation was the sole or joint funder of almost half (11) the reviewed studies, while a further 9 studies were funded by either of the two HPV vaccine manufacturers (MSD or GSK). Only 11 studies were first authored by investigators based in the countries being studied; most studies were first authored by investigators in high income countries. These features of the literature may stem from lack of technical capacity and funding in low and lower middle income countries to conduct their own economic evaluations [27]. Furthermore, low income countries are reliant on donor funding for HPV vaccination programmes, so they may have less impetus for cost-effectiveness studies to inform local decision making since priorities are driven by external considerations.

3.3. Comparators and study question

Almost all (22) studies investigated the cost-effectiveness of introducing HPV vaccination to girls aged 12 or younger. Two studies looked at vaccinating 15 year old girls while one remaining study [16] explored the impact of varying the age range from 15 to 60 years. All studies investigated vaccination either as an addition to existing screening programmes or (more commonly) to opportunistic preventive programmes or none at all. Most studies (14) also considered a range of vaccination and screening options to find the most cost-effective combination. Different screening methods were examined, including conventional cytology alone (mainly in Latin American countries), and various combinations of visual inspection, HPV DNA testing and conventional cytology. Two studies looked at the cost-effectiveness of expanding vaccination to boys as well as girls [31,32].

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