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Human papillomavirus (HPV) vaccine coverage achievements in low and middle-income countries 2007–2016

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ABSTRACT

Introduction: Since 2007, HPV vaccine has been available to low and middle income countries (LAMIC) for small-scale 'demonstration projects', or national programmes. We analysed coverage achieved in HPV vaccine demonstration projects and national programmes that had completed at least 6 months of implementation between January 2007–2016.

Methods: A mapping exercise identified 45 LAMICs with HPV vaccine delivery experience. Estimates of coverage and factors influencing coverage were obtained from 56 key informant interviews, a systematic published literature search of 5 databases that identified 61 relevant full texts and 188 solicited unpublished documents, including coverage surveys. Coverage achievements were analysed descriptively against country or project/programme characteristics. Heterogeneity in data, funder requirements, and project/programme design precluded multivariate analysis.

Results: Estimates of uptake, schedule completion rates and/or final dose coverage were available from 41 of 45 LAMICs included in the study. Only 17 estimates from 13 countries were from coverage surveys, most were administrative data. Final dose coverage estimates were all over 50% with most between 70% and 90%, and showed no trend over time. The majority of delivery strategies included schools as a vaccination venue. In countries with school enrolment rates below 90%, inclusion of strategies to reach out-of-school girls contributed to obtaining high coverage compared to school-only strategies. There was no correlation between final dose coverage and estimated recurrent financial costs of delivery from cost analyses. Coverage achieved during joint delivery of HPV vaccine combined with another intervention was variable with little/no evaluation of the correlates of success.

Conclusions: This is the most comprehensive descriptive analysis of HPV vaccine coverage in LAMICs to date. It is possible to deliver HPV vaccine with excellent coverage in LAMICs. Further good quality data are needed from health facility based delivery strategies and national programmes to aid policymakers to effectively and sustainably scale-up HPV vaccination.

1. Introduction

Persistent infection with high-risk human papillomavirus (HPV) genotypes is the cause of almost all cases of cervical cancer and is also associated with multiple other anogenital and oropharyngeal cancers [1]. Cervical cancer is the third most common cause of cancer-related deaths in women in low- and middle-income countries (LAMIC) [2]. In settings with effective screening programmes, most cervical abnormalities are identified and treated before they progress to cervical cancer. In many LAMIC the coverage of screening services is low [3] leading to women developing advanced stage disease and high cervical cancer mortality rates. Additionally, HIV, a major problem in many LAMIC, increases an individual's risk of HPV infection, persistence [4] and progression to cervical cancer [5–8].

There are currently three prophylactic HPV vaccines. A bivalent vaccine targets HPV 16 and 18 (Cervarix®), and a quadrivalent vaccine (Gardasil®) additionally targets HPV 6 and 11 that cause genital warts. A nonavalent vaccine (Gardasil 9®) has recently been licensed in the US,

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Europe, and other high income countries and targets additional oncogenic HPV serotypes: 31, 33, 45, 52 and 58. All three vaccines have proven to be highly efficacious against persistent infection of their vaccine genotypes and associated cervical intraepithelial neoplasia [9–11]. The World Health Organisation (WHO) currently recommends vaccination of 9–13 year olds as vaccination is most effective prior to sexual debut and first exposure to HPV [12]. In 2014, the Strategic Advisory Group of Experts on Immunisation (SAGE) revised recommendations from a schedule of 3 doses [13], to 2 doses given at a 6–12 month interval [14] for girls aged 9–14 years [15,16].

HPV vaccine first became available for use in LAMIC in 2007 with vaccine donations through the GARDASIL® Access Program (GAP) [17], manufacturer donations, the Bill & Melinda Gates Foundation through PATH, or other means. Demonstration projects were designed as pilot projects in small areas of a country to enable experience to be gained in delivering an expensive, gender-specific vaccine to, what was in many countries, a novel target age group [18]. In 2012, Gavi, the Vaccine Alliance, commenced support for HPV vaccination demonstration projects or national programmes in 53 Gavi-eligible countries [19]. Gavi support included some funds for formal evaluation of HPV vaccine delivery and required a coverage survey, post-introduction evaluation and costing analysis after the first year of implementation.

This paper presents the HPV vaccine coverage achieved in demonstration projects and national programmes in LAMIC that had completed at least six months of implementation between January 2007 and May 2016. Related publications summarising lessons learnt from HPV vaccination in 45 LAMICs have not had space to interrogate the substantial coverage data available [20–22].

2. Methods

2.1. Study design

This is a descriptive synthesis of data collected as part of a large study collating lessons learnt from HPV vaccine projects/programmes in LAMIC [20].

2.2. Country selection

A mapping exercise identified all low (LIC) and lower-middle income countries (LMIC) that were known to international organisations to have completed at least six months of a HPV vaccine demonstration or pilot project or an HPV vaccination national programme by May 2016, all were included in data collection. Data from upper-middle income countries (UMIC) that had completed demonstration project(s) in the same time period were also included. In total data were examined from 45 LAMIC for this study (Table 1; 18 LIC, 22 LMIC, 5 UMIC).

2.3. Definitions

A '*demonstration project*' refers to a small-scale project, often limited to one or two districts or smaller administrative units in a country, and were defined by the funder and/or implementer and grant award details, e.g. GAP or Gavi or other funder. A '*programme*' is a national vaccination programme. '*Delivery strategies*' were defined by the vaccination sites used (schools, health facilities, outreach sites) and the target population (age or school grade). Within each demonstration project or national programme, if multiple different delivery strategies were piloted or the delivery strategy changed over time, these were defined as distinct *delivery experiences* (Supplementary Fig. 1). Countries often implemented multiple different projects/programmes over time and tested different delivery strategies so a country could have a number of different delivery experiences. More information on the different experiences is published elsewhere [20].

Uptake was defined as first dose coverage among the target population and was analysed alongside final dose coverage. Completion was defined as the proportion of girls who received the final dose of the vaccine schedule among those who had received the first dose. Coverage surveys were defined as surveys that used the WHO coverage survey guidelines [23] or similar, to assess the vaccination status of the general population.

2.4. Data collection

Methods are fully described elsewhere [20]. After obtaining informed consent, we conducted interviews over the phone or in person with key informants (KIs) e.g. EPI managers, HPV coordinators or equivalent, a systematic search of five databases for published literature and solicited unpublished documents including coverage surveys and country reports. Estimates of coverage results from projects/programmes were collated from written published and unpublished reports only. KIs and contacts supplying unpublished data were assured that the data would be anonymised to garner detailed reports on challenges as well as successes in implementing HPV vaccine delivery. Data were extracted onto a template informed by the WHO New Vaccine Introduction Guidelines [24]. National primary school enrolment data from the most recent year available were sourced from the UNESCO Institute of Statistics data centre [25].

2.5. Analysis

Coverage achievements were analysed descriptively by delivery experience. Due to the heterogeneity of funder requirements, project/programme organisation, design, and overall experience, multivariate analyses of the correlates of coverage were not appropriate. Where coverage and costing data were available, correlations were described. Reported coverage is for the selected target group of each distinct delivery experience. Where more than one estimate of coverage was available for the same delivery experience, the data considered to be of best quality were selected for descriptive analyses, e.g. estimates from coverage surveys were used wherever possible.

3. Results

A total of 56 KI interviews with representatives from 40 countries were completed, 188 unpublished documents were received, and 61 published articles and 11 conference abstracts identified. Lessons learnt on other topics have been published elsewhere [20–22,26].

3.1. Data availability

As of May 2016, only 17 delivery experiences in 13 countries had completed and finalised their coverage survey results (Fig. 1; Supplementary Fig. 2) [23]. All other coverage data came from administrative statistics that divided the reported number of doses administered by the estimated target population. Of the 91 distinct delivery experiences in 45 countries identified, 76 experiences (84%) across 40 LAMICs (89%) provided at least one estimate of uptake, completion, or final dose coverage. Over half (55%) of data were sourced from unpublished reports obtained from KI interviews for as there were no published coverage results available. Estimates for the remaining experiences were obtained from the published literature.

Estimates of uptake were available from 54 experiences in 35 countries and estimates of completion from 54 experiences in 30 countries. HPV vaccine final dose coverage estimates were available from 59 delivery experiences in 33 of the 45 countries [20].

3.2. Data accuracy

Across the 59 delivery experiences contributing final dose coverage data, the 42 administrative coverage estimates were, on average, higher than the 17 results from actual coverage surveys (Table 3). Only 8