Vaccine xxx (2018) xxx–xxx

Contents lists available at ScienceDirect

Vaccine

journal homepage: www.elsevier.com/locate/vaccine

Review

Systematic review of cost-effectiveness studies of human papillomavirus (HPV) vaccination: 9-Valent vaccine, gender-neutral and multiple age cohort vaccination

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ARTICLE INFO

Article history:
Received 17 October 2017
Received in revised form 25 January 2018
Accepted 7 March 2018
Available online xxxx

Keywords:
Human papillomavirus
Cost-effectiveness
Vaccination
Immunization
Systematic review
Vaccine

ABSTRACT

Background: The success of human papillomavirus (HPV) national immunization program depends on effective strategies in optimizing the uptake of HPV vaccine. Given the increasing number of economic evaluations, this review was conducted to update the economic evidence on HPV vaccination, by focusing on: (i) 9-valent vaccine compared to bi- or quadrivalent vaccine; (ii) gender-neutral vaccination compared to female only vaccination; and (iii) multiple age cohort immunization compared to single age cohort immunization.

Methods: Searches were performed until June 2016 using 4 databases: PubMed; Embase; Cochrane Library; and LILACS. The combined WHO, Drummond and CHEERS checklist were used to evaluate the quality of included studies.

Results: Thirty-four studies were included in the review and most of them were conducted in high-income countries. The inclusion of adolescent boys in vaccination program was found to be cost-effective if vaccine price and coverage was low. When coverage for female was above 75%, gender-neutral vaccination was less cost-effective than when targeting only girls aged 9–18 years. Current evidence does not show conclusive proof of greater cost-effectiveness of 9-valent vaccine compared to the older HPV vaccines as the price for 9-valent vaccine was still uncertain. Multicohort immunization strategy was cost-effective in the age range 9–14 years but the upper age limit at which vaccination was no longer cost-effective needs to be further investigated. Key influential parameters identified were duration of vaccine protection, vaccine price, coverage, and discounting rates.

Conclusions: These findings are expected to support policy-makers in making recommendations for HPV immunization programs on either switching to the 9-valent vaccine or inclusion of adolescent boys' vaccination or extending the age of vaccination.

Contents

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https://doi.org/10.1016/j.vaccine.2018.03.024
0264-410X/

1. Introduction

Human papillomavirus (HPV) is the most common sexually-transmitted viral infection, which causes a range of conditions including cervical cancer and non-cervical HPV-attributable diseases such as genital warts, oropharyngeal, penile, vaginal and anogenital cancers [1]. Three HPV vaccines; a bivalent (Cervarix), a quadrivalent (Gardasil) and the new 9-valent vaccine (Gardasil-9) are currently licensed in the market for the prevention of HPV-related diseases. However, as of March 2017, only 71 countries (37% of all countries) have introduced HPV vaccines in their national immunization programs for girls and 11 countries (6%) for additional boys [2].

The first global recommendation on HPV vaccination was proposed by the WHO's SAGE (Strategic Advisory Group of Experts) on Immunization in October 2008 [3], whereby HPV vaccination was recommended in all girls aged 9–13 years old. This recommendation was then updated in April 2014 [4], with the emphasis to include extended 2-dose HPV immunization for girls aged 9–14 years, who were not immunocompromised. With the recent licensing of the 9-valent vaccine and the introduction of various HPV vaccination strategies, an update in the current recommendations of HPV vaccination is inevitable. Hence, this review was conducted to assist the WHO SAGE 2016 meeting in updating the economic evidence on HPV vaccination, with the focus on: (i) 9-valent vaccine compared to bi- or quadrivalent vaccine, (ii) gender-neutral immunization compared to female only immunization and (iii) multiple age cohort immunization compared to single age cohort immunization.

2. Materials and methods

2.1. Search strategy

Searches were performed till June 2016 using 4 databases: PubMed; EMBASE; Cochrane Library; and LILACS (Index of scientific and technical literature of Latin American and the Caribbean). Reference lists of relevant published studies and grey literature were also searched. This review was an extension of the previous work by Fesenfeld et al. [5] and thus, similar search strategy was adopted but modified to include all countries regardless of income levels. (See Appendix A for full search strategy).

2.2. Study selection

All identified studies were considered based on title and abstract, and included for further review if they evaluated either a 9-valent HPV vaccine or gender-neutral or multicohort immunization strategy. The included study must be a full economic evaluation considering both costs and outcomes. Reviews, editorials, and conference abstract were excluded. Studies which evaluated on a specific population (e.g. HIV positive patients, renal transplant patients and neonatal) were also excluded. No language restrictions were applied.

2.3. Data extraction & synthesis

Two reviewers (SSN and NC) independently reviewed the titles and abstract. Data from all eligible studies were extracted by the same two authors using a standardized data collection form. Supplementary appendices were referred to if insufficient information was obtained from the main text. Studies were categorized based on three themes: (i) 9-valent HPV vaccine compared to bi- or quadrivalent vaccine, (ii) gender-neutral vaccination compared to female only vaccination and (iii) multiple age cohort immunization compared to single age cohort immunization. The income levels for each country were determined based on the World Bank classification [6]. Gross domestic product (GDP) per capita in United States Dollars (US$) of 2016 was obtained from the World Bank [7]. To compare results across studies, we presented raw study-reported incremental cost-effectiveness ratios (ICERs) and standardized cost-effectiveness. Standardized cost-effectiveness was based on

Please cite this article in press as: Ng SS et al. Systematic review of cost-effectiveness studies of human papillomavirus (HPV) vaccination: 9-Valent vaccine, gender-neutral and multiple age cohort vaccination. Vaccine (2018), https://doi.org/10.1016/j.vaccine.2018.03.024