Vaccine 37 (2019) 7–10

Contents lists available at ScienceDirect

Vaccine

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

Review of the economic evidence presented to the United States Advisory Committee on Immunization Practices, 2012–2016 ☆

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ARTICLE INFO

Article history:
Received 3 August 2018
Received in revised form 16 November 2018
Accepted 19 November 2018
Available online 23 November 2018

Keywords:
Advisory Committee on Immunization Practices
Economics
Cost-effectiveness
Immunization

ABSTRACT

We identified 16 Advisory Committee on Immunization Practices (ACIP) presentations from 2012 to 2016 that indicated 'cost' or 'economic' content. Characteristics were reviewed, abstracted, and tabulated to quantify and assess the transparency and consistency of economic evidence presented to ACIP. To assess transparency, we documented if each study identified author affiliation, conflicts of interest, study limitations, a clearly described model structure and other model attributes. To assess consistency, we identified the frequency of specific modeling choices, including the perspective, types of health outcomes considered, inclusion of specific types of costs, discount rate, and use of sensitivity analyses. Our results indicate that the content in these presentations appear to be transparent overall and consistent in several important areas, such as study perspective and health outcomes. However, we find the inclusion of particular types of direct costs, indirect costs, program costs, and sensitivity analyses are areas that could improve consistency.

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1. Introduction

The United States (US) immunization program has been one of the most effective preventive health care activities in recent history [1,2]. Deaths due to common vaccine-preventable diseases (VPDs), such as diphtheria, mumps, pertussis and tetanus, have decreased by more than 99% compared to estimated pre-vaccine levels [3]. Economic models have estimated that routine childhood vaccinations have prevented millions of cases of disease and over 40,000 premature deaths with net economic savings to society of more than $68.8 billion [2]. In 1964, the Surgeon General of the US Public Health Service established the Advisory Committee on Immunization Practices (ACIP) to advise the US government on the use of vaccines and related agents for effective control of VPDs in the civilian population [4].

The ACIP Charter states that, when considering recommendations for use of a vaccine, ACIP members' deliberations should include consideration of epidemiology, disease burden, vaccine efficacy, vaccine safety, economic analyses, implementation issues, and the quality of evidence reviewed [5]. In addition to making new recommendations, the committee may revise or withdraw their recommendation(s) as new information becomes available [5]. Economic analyses of vaccinations that are considered by ACIP are often conducted by various teams of experts, including scientists from CDC, academic research institutions, and vaccine manufacturers.

In 2007, CDC published the *Guidance for Health Economics Studies Presented to the Advisory Committee on Immunization Practices* (Guidance) [6]. The Guidance was developed to standardize the presentation of economic evidence to ACIP. According to the Guidance, all researchers (internal or external to CDC) wishing to present a health economics study to ACIP must submit at least two documents, (1) a report providing methods and results, and (2) a slide set or other presentation materials. The Guidance asks that the documents clearly describe the methods and results of health economics studies. Similar guidelines have been established for other national advisory committees on immunization (NITAGs) in developed countries, such as Australia, Germany, the Netherlands, and Spain; while other countries have developed economic evaluation guidelines for health technologies in general, such as Canada [7–11].

☆ All authors have read and approved the manuscript, and there are no financial disclosures, conflicts of interests and/ or acknowledgements necessary. The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

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https://doi.org/10.1016/j.vaccine.2018.11.055
0264-410X/Published by Elsevier Ltd.

All economic analyses to be presented to ACIP are reviewed by a CDC health economist or other qualified economist before presentation to ACIP to ensure that key methods are followed and to review underlying assumptions. The purpose of this study is to review recent economic-related presentations to ACIP and summarize the extent to which these presentations were transparent and consistent in their description of their methods and findings.

2. Materials and methods

We reviewed ACIP agendas from the last five years (2012 through 2016) and identified 16 ACIP presentations that indicated 'cost' or 'economic' content, which included cost-effectiveness analyses (CEA), CEA reviews, and Cost-of-Outbreak analyses. Characteristics of these presentations were reviewed, abstracted, and tabulated. We then focused on presentations that represented stand-alone CEA and assessed their transparency and consistency.

To assess the transparency of these studies, we documented if each study identified the author's affiliation, any conflicts of interest, study limitations, a clearly described model structure and other model attributes. To assess consistency, we identified the frequency of specific modeling choices, including the perspective used, the types of health outcomes considered, the inclusion of specific types of costs (direct, indirect, program[1]), the discount rate, and the use of sensitivity analyses. As an example, in the assessment of consistency related to study perspective, we identified the percentage of studies that presented results from the societal perspective or health care perspective. A complete list of all the information collected from the stand-alone CEA presentations is found in Appendix A, Table A1. We also evaluated which economic analyses were associated with an ACIP recommendation by reviewing ACIP agendas and recommendation documents.

3. Results

Table 1 presents an overview of findings from the 16 presentations reviewed. These characteristics include the year of the ACIP presentation, the VPD and/or vaccine(s) studied, the title, the type of study, the ACIP decision, and any associated publications. Of the 16 presentations, four were presented by academic affiliated researchers, two were conducted by pharmaceutical companies, one was conducted by a consulting firm, and ten were conducted by CDC affiliated researchers. One study described the cost of a vaccine-preventable-disease outbreak. The remaining 15 studies presented CEAs related to potential ACIP decisions. Of those CEA studies associated with an ACIP decision (8/15 or 53%), all of the presentations occurred within one year prior to the related ACIP vote. Three of the 15 CEAs were either updates or reviews of previously presented or published material. The remaining 12 presentations constituted stand-alone CEAs and these 12 presentations are the focus of the transparency and consistency assessment. The economic models in the 12 stand-alone CEAs pertained to the following diseases: pertussis (3), human papillomavirus-related diseases (2), influenza (1), meningococcal (1), hepatitis B infection (1), pneumococcal (3), and shingles or herpes zoster (1). Vaccines analyzed in these presentations included Tdap (3), HPV vaccine (2), inactivated influenza vaccine, trivalent (IIV3), high-dose influenza (1), MenACWY (1), HepB vaccine (1), PCV13 (3), PPSV23 (1), and herpes zoster vaccine (zoster vaccine live) (1). Details of all information collected from each presentation are listed in Appendix A, Table 1.

3.1. Transparency

Of the 12 stand-alone CEA presentations, we found the majority included author affiliations (92%) and clearly stated whether or not conflicts of interest existed (75%). All 12 presentations included either a text description or a diagram of the model, with 75% using a diagram to describe the model. All 12 presentations also clearly stated several other important attributes of an economic study, including: target population, study perspective, time horizon, discount rate, and conducted some type of sensitivity analysis. Limitations of the analysis, such as uncertainty related to waning of vaccine effectiveness or disease, were identified in 83% of the presentations.

3.2. Consistency

We examined the frequency that the CEAs had a particular model characteristic (Table 2). All 12 presentations clearly stated a result from the societal perspective, while 17% also presented a result from the healthcare perspective. Quality-adjusted life-years (QALYs) were utilized to measure health outcomes in all of the presentations. Other health outcomes were also utilized, in particular: cases averted (33%), deaths averted (8%), life years saved (17%), hospitalizations averted (8%), and number needed to vaccinate (17%). Looking at the types of direct costs that were included, general medical costs were the most common, included in all 12 studies. Smaller percentages of studies also included direct costs associated with adverse events from the vaccine (33%), general non-medical (such as transportation) (25%), caregiver time (17%), and patient time (33%). Indirect mortality costs were included in 33% of the presentations, while 42% included indirect morbidity costs. The studies that included indirect costs focused on Tdap, herpes zoster vaccine (zoster vaccine live), MenACWY, and inactivated influenza, trivalent (high-dose versus standard-dose) vaccines. All of the studies included vaccine material costs and 83% included vaccine administration costs. All of the studies assumed a 3% discount rate and presented results from sensitivity analyses (univariate or multivariate). All studies had at least one type of sensitivity analysis that focused on the effectiveness of the vaccine. Most studies (83%) presented at least one multivariate sensitivity analysis with the scenario-based analyses being the most common (83%). Probabilistic sensitivity analyses (17%) appeared less frequently and threshold analyses (0%) were not presented.

4. Discussion and conclusion

This study reviewed presentations of health economics studies to ACIP from 2012 through 2016. Our study found economic presentations to ACIP appear to be transparent overall and consistent across the majority of modeling characteristics we examined. While a certain amount of variability across different studies may be reasonable, the inclusion of particular types of direct costs, indirect costs, program costs, and sensitivity analyses are areas that could have higher levels of consistency. Our findings are based solely on the content of the presentation slides used at ACIP meetings and the published text of ACIP recommendations, not transcripts or minutes of ACIP meetings or associated peer-reviewed publications or reports. Therefore, the information related to the content economic evidence that we assessed likely under-states the entirety of the information presented to ACIP in their sessions. Furthermore, the ACIP process is supported by numerous Work

[1] Direct costs refer to medical costs, such as cost of treatment, and non-medical costs, such as caregiver time. Indirect costs refer to lost production (in the form of foregone gross earnings or household production) resulting from morbidity and mortality. Program costs are the costs of implementing the health intervention, such as vaccine administration.

Table 1
Overview of recent economic-related presentations to the Advisory Committee for Immunization Practices (2012–2016).

Year	VPD or vaccine	Short title	Study Type	ACIP Decision	Associated peer-reviewed publication (if any)
2012	Mumps, MMR	Third dose in Guam outbreak	COO	No change to recommendations	[14]
	Pertussis, Tdap	Tdap substitution for Td for 65 years and older	CEA	Recommend 1 dose of Tdap for adults aged ≥65 years	[15]
	Pertussis, Tdap	Boostrix in adults 65 years of age and older	CEA		
	Hepatitis B	Hepatitis B protection among HCP	CEA	No change to recommendations	[16]
	PCV	PCV13 for adults with immunocompromising conditions	CEA	Recommend PCV13 for adults aged ≥19 years with immunocompromising conditions	[17]
	Hepatitis B	Hepatitis B: Long-term vaccine-induced protection	Update	No change to recommendations	
2013	Tdap	Decision and cost effectiveness analysis for a second Tdap for adolescents and adults	CEA	No change to recommendations	[18]
	Herpes zoster	Herpes zoster vaccination in adults 50 years of age and older	CEA	No change to recommendations	
	PCV	Primary doses in the 13-valent pneumococcal conjugate vaccination schedule	CEA	No change to recommendations	[19]
2014	PPSV and PCV	Modifying PPSV and PCV recommendations for adults age 50 and over	CEA	Recommend PCV13 and PPSV23 for adults aged ≥65 years	[20]
	HPV	9-valent vs. the 4-valent HPV vaccine	CEA	Recommend 9vHPV as one of three HPV vaccines for routine vaccination of adolescents	[21]
2015	HPV	Overview of cost-effectiveness of 9-valent HPV vaccination	Review		
	HPV	HPV vaccination for persons who have completed an HPV vaccination series	Review	No change to recommendations	[22]
	Influenza	High-dose versus standard-dose inactivated influenza vaccine in adults aged 65 years and older	CEA	No change to recommendations	[23]
2016	HPV	Comparing 2- and 3-dose 9-valent HPV vaccine schedules	CEA	Recommended 2-dose series of 9vHPV for persons initiating vaccination before age 15 years	[24]
	Meningococcal	Meningococcal vaccination in HIV infected people	CEA	Recommend MenACWY for HIV-infected people aged ≥2 months	

Note(s): VPD = vaccine preventable disease; COO = cost of outbreak; CEA = cost-effectiveness analysis; MMR = measles, mumps, and rubella; Tdap = tetanus, diphtheria, and acellular pertussis; HCP = healthcare provider; PCV = pneumococcal conjugate vaccine; PPSV = pneumococcal polysaccharide vaccine; HPV = human papillomavirus; 9vHPV = 9-Valent Human Papillomavirus; MenACWY = Meningococcal ACWY.

Table 2
Percentages of selected characteristics among cost-effectiveness models (N = 12) presented at ACIP.

Model characteristics		Percentages of studies
What perspectives were considered?	Societal	100%
	Healthcare	17%
What types of health outcomes were considered?	QALYs	100%
	Cases Averted	33%
	Deaths Averted	8%
	Life Years Saved	17%
	Hospitalizations Averted	8%
	Number Needed to Vaccinate	17%
What kinds of direct costs were included?	General Medical	100%
	Adverse Events	33%
	General Non-Medical	25%
	Caregiver Time	17%
	Patient Time	33%
What kinds of indirect costs were included?	Mortality	33%
	Morbidity	42%
What program costs were included?	Vaccine Materials	100%
	Vaccine Administration	83%
	Other	17%
What discount rate was used?	0.03 (or 3%)	100%
What kind of sensitivity analyses were presented?	Any kind (univariate or multivariate)	100%
	Any univariate	100%
	Effectiveness	75%
	Costs	83%
	Discount Rates	17%
	Any multivariate	83%
	Scenario-based	83%
	Threshold	0%
	Probabilistic	17%

Groups, each of which has periodic meetings, receives information, and hears presentations that we were unable to incorporate into our study for reasons of scope and logistics.

While there is no threshold for cost-effectiveness that vaccines must exhibit in order to be implemented in the US, ACIP is charged with being good stewards for the immunization program and therefore having an understanding of the importance of the economic impact of new immunization recommendations is a priority [12]. Additionally, economic analyses can help inform deliberations by comparing the impact of different immunization strategies. ACIP provides advice and guidance to the Director of the CDC regarding use of vaccines and related agents for effective control of VPDs in the civilian population of the US [5]. As suggested by the ACIP Charter, consideration of economic and implementation issues is necessary to achieve the most thoughtful and effective ACIP deliberations and recommendations. The 2007 Guidance was developed to standardize the presentation of this evidence and to improve the communication of economic data to ACIP decision-makers.

While some areas may be improved, we find that our results indicate the content and assumptions used in economic-related evidence presented to ACIP appear to be transparent, according to our measures, as well as consistent in important areas, such as perspective and health outcomes. In addition, these economic studies appear to contribute beneficially to the ACIP policy-making process. In February 2018, ACIP adopted the use of an Evidence to Recommendations (EtR) framework to support the process of moving from evidence to decisions and provide transparency around the impact of additional factors on deliberations when considering a recommendation [13]. This review presents an opportunity to not only assess and improve transparency and

consistency of economic presentations at ACIP, but to also ensure that economic analyses are systematically integrated into the EtR frameworks moving forward.

Appendix A. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.vaccine.2018.11.055.

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