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Cost-effectiveness of adult vaccinations: A systematic review

Andrew J. Leidner[a,*], **Neil Murthy**[b,c], **Harrell W. Chesson**[d], **Matthew Biggerstaff**[b], **Charles Stoecker**[e], **Aaron M. Harris**[d], **Anna Acosta**[b], **Kathleen Dooling**[b], and **Carolyn B. Bridges**[a]

[a]Berry Technology Solutions, USA

[b]National Center for Immunization and Respiratory Diseases, CDC, USA

[c]Epidemic Intelligence Service, CDC, USA

[d]National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention, CDC, USA

[e]School of Public Health and Tropical Medicine, Tulane University, USA

Abstract

Background: Coverage levels for many recommended adult vaccinations are low. The cost-effectiveness research literature on adult vaccinations has not been synthesized in recent years, which may contribute to low awareness of the value of adult vaccinations and to their under-utilization. We assessed research literature since 1980 to summarize economic evidence for adult vaccinations included on the adult immunization schedule.

Methods: We searched PubMed, EMBASE, EconLit, and Cochrane Library from 1980 to 2016 and identified economic evaluation or cost-effectiveness analysis for vaccinations targeting persons aged ≥18 years in the U.S. or Canada. After excluding records based on title and abstract reviews, the remaining publications had a full-text review from two independent reviewers, who extracted economic values that compared vaccination to "no vaccination" scenarios.

Results: The systematic searches yielded 1688 publications. After removing duplicates, off-topic publications, and publications without a "no vaccination" comparison, 78 publications were included in the final analysis (influenza = 25, pneumococcal = 18, human papillomavirus = 9, herpes zoster = 7, tetanus-diphtheria-pertussis = 9, hepatitis B = 9, and multiple vaccines = 1). Among outcomes assessing age-based vaccinations, the percent indicating cost-savings was 56% for influenza, 31% for pneumococcal, and 23% for tetanus-diphtheria-pertussis vaccinations. Among age-based vaccination outcomes reporting $/QALY, the percent of outcomes indicating a cost per QALY of ≤$100,000 was 100% for influenza, 100% for pneumococcal, 69% for human papillomavirus, 71% for herpes zoster, and 50% for tetanus-diphtheria-pertussis vaccinations.

Conclusions: The majority of published studies report favorable cost-effectiveness profiles for adult vaccinations, which supports efforts to improve the implementation of adult vaccination recommendations.

[*]Corresponding author: Berry Technology Solutions, Contractor for Immunization Services Division, National Center for Immunization and Respiratory Disease, Centers for Disease Control and Prevention, 1600 Clifton Road, NE, MS A-19, Atlanta, GA 30333, USA. aleidner@cdc.gov (A.J. Leidner).

Keywords

Vaccines; Adults; Cost-effectiveness

1. Introduction

The Advisory Committee on Immunization Practices (ACIP) recommends vaccinations for adults in the U.S. based on their age, medical conditions, and prior vaccinations as part of the U.S. immunization schedule for routine vaccination of adults [1]. Vaccines commonly administered to adults include influenza, pneumococcal, herpes zoster (HZ), tetanus-diphtheria/tetanus-dip htheria-acellular pertussis (Td/Tdap), and hepatitis B vaccines. The burden of disease among adults, including illness, hospitalization, death and disability, from vaccine preventable diseases (VPDs) is substantial [2]. However, vaccination coverage rates for many routinely-recommended adult vaccines are low [3]. Missed opportunities for adult vaccinations contribute to an overall disease burden that was estimated at $26.5 billion among persons aged 50 years and older for four common VPDs: influenza, pneumococcal disease, HZ, and pertussis [4].

Among the many challenges that exist for implementation of the adult vaccinations [5–8], potential reasons for lower than expected adult vaccination coverage rates could be perceptions about risks, clinical value, and economic value held by providers [9] or patients [10]. Value perceptions may be especially important among providers since provider recommendations substantially contribute to patients' decisions regarding vaccination [11]. To date, reviews of cost-effectiveness analyses of adult immunization services have focused onjust one vaccine at a time [12–16], such as vaccines for HZ [12,14], influenza [13,16], or human papillomavirus (HPV) [15], or specific target populations, such as healthcare personnel [16]. Reviews that focus on specific vaccines can be useful to investigate modeling choices that contribute to variations in results across models. A review that is broader in scope is needed to address other types of questions that may be of interest to clinicians and policy makers. These kinds of questions are related to how the cost-effectiveness of a given vaccine compares to other vaccines that also are recommended for a similar age group or a similar target population and, taken a step further, how the cost-effectiveness of vaccines in general relates to other clinical services. Prior cost-effectiveness analyses of the multiple vaccines on the pediatric immunization schedule have been conducted, but to our knowledge no analyses of the cost-effectiveness of vaccinations included in the adult vaccination schedule has been done. The adult immunization standards of practice emphasize the need for providers to assess adult patients for all vaccines recommended by ACIP. This review provides information for providers regarding the adult vaccination schedule and the cost-effectiveness of recommended vaccines, with the objective of addressing potential limitations in awareness of the cost-effectiveness of vaccines recommended for adults. To meet this objective, we conducted a systematic review of the research literature since 1980, collecting and summarizing the cost-effectiveness findings related to vaccinations included in the U.S. adult vaccine schedule.

2. Methods

We identified publications that estimated cost-effectiveness or economic value by directly comparing a vaccination strategy to a non-vaccination strategy among adult populations in the U.S. or Canada. This study searched online research literature databases, identified relevant publications, and analyzed the cost-effectiveness findings related to adult vaccinations.

This review focused on six vaccine groups: influenza, pneumococcal, HPV, HZ, Td/Tdap, and hepatitis B. We included HPV vaccinations even though that vaccine provides the greatest benefit when administered at age 11 or 12 years, as recommended by ACIP [17]. However, as of 2016 only 43% of adolescents were up to date on HPV vaccination [18], leaving many young adults unvaccinated or under-vaccinated and at risk of HPV-related cancers that occur predominantly during adulthood, such as cervical, penile, vaginal, and head and neck cancers [19]. We focused on these vaccines because they are routinely recommended for adults.

2.1. Search criteria

We conducted a systematic search of medical and economic research literature contained in four electronic databases: PubMed, Embase, Cochrane Libraries (Economic Evaluations), and EconLit. Our search included records from 1980 to 2016. We included studies as early as 1980 to capture some of the earliest economic research on vaccines in the U.S. [20,21]. To identify relevant economic evaluations, we included “cost-effectiveness” or “cost-utility” in our search terms. To identify vaccine-related publications, we included “vaccine,” “vaccination,” or “immunization” in our search terms. The economic and vaccine-related search terms were combined with additional terms designed to identify each vaccine or VPD. The terms to identify each vaccine group included “tetanus,” “diphtheria,” “pertussis,” “Td,” or “Tdap” for tetanus-diphtheria-pertussis vaccinations; “HPV” or “human papillomavirus” for e HPV vaccinations; “herpes zoster,” “zoster,” or “shingles” for herpes zoster vaccinations; “hepatitis B” for hepatitis B vaccinations; “influenza” or “flu” for influenza vaccinations; and “pneumococcal” for pneumococcal vaccinations. The complete set of electronic database search results and search terms is summarized in the appendix. During the review process, we consulted with subject matter experts in the area of each vaccine group and VPD to identify additional publications to include. We also investigated citations found in literature reviews that focused on adult vaccine cost-effectiveness [12,22–33] to identify any additional publications.

2.2. Exclusion criteria and full text review process

Following the electronic database search results, we identified and excluded duplicate publications. The remaining publications and those identified through subject matter experts or referenced in other publications were subjected to a title and abstract review. During the title and abstract reviews, publications were excluded if the publication (1) did not

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Appendix. Supplementary material
Supplementary data to this article can be found online at https://doi.org/10.1016/j.vaccine.2018.11.056.

investigate a U.S. or Canadian population; (2) conducted an economic evaluation that was not a cost-effectiveness or cost-utility analysis, such as a cost-of-illness study; (3) focused exclusively on vaccinating children, defined as 17 years old or younger; (4) was written in a non-English language; and/or (5) was a review article, a letter to the editor, a commentary, or a conference presentation only.

Two independent reviewers conducted the full text review and data abstraction for all remaining publications using a standardized data abstraction form. Any initial differences in the two reviews were documented, discussed, and resolved. During the full text review, additional publications were excluded if the publications did not provide an adult-only, "no vaccination" comparator scenario that allowed for estimation of a cost-effectiveness ratio comparing adult vaccination to a scenario of no adult vaccination. If a publication reported the cost-effectiveness of an age group that included children (such as the cost effectiveness of HPV vaccination for ages 13–26 years), but did not report the cost-effectiveness specifically for an adult-only age group (such as ages 18–26 years), the publication would be excluded. Among the publications that were fully abstracted, several reported more than one cost-effectiveness ratio that were relevant to the adult vaccinations. In these cases, multiple cost-effectiveness ratios, or outcomes, were abstracted.

We did not conduct quality assessments of the studies we reviewed, owing to challenges such as the substantial diversity of diseases prevented by adult vaccination. However, all studies included in the full text review of this study did meet minimum standards of technical quality, including the presentation of sufficient detail to calculate a cost-effectiveness ratio for an adult vaccination strategy. In addition, we used the number of citations in the literature as a proxy measure for study quality and importance. The quality of a study has been found to be a predictor for number of citations [34]. According to the Scopus database on research literature citations, the studies included in our final sample have been cited by the literature a total of 5961 times, with an average per study of 77 (median = 36, interquartile range = 17–93). Citation counts for each study are included in the appendix.

2.3. Analysis

Outcomes were categorized according to vaccine group and type of vaccinations. The two types of vaccinations that were considered included age-based vaccinations and medical indication-based vaccinations. Age-based vaccinations are those given on the basis of age level, including the elderly. Medical indication-based vaccinations are given based on other indications, such as comorbidity or status as a health care worker. Health economic analyses can utilize a number of different outcome metrics [35,36]. The types of outcome metrics included cost-benefit measures, such as net benefit or total social cost, cost-savings, cost per case prevented, cost per life saved, cost per life-year saved, and cost per quality-adjusted life-year (QALY) saved. To assess cost-savings and cost-effectiveness, we focused our analyses on the outcomes that were either completely monetized, such as cost-benefit measures, or measured as cost per life-year gained or cost per QALY saved. In some publications, the total costs and total outcomes were presented for the vaccination and "no vaccination" scenario but the cost-effectiveness ratio(s) of interest to this review were not explicitly presented. In these cases, the abstractors computed the cost-effectiveness ratio(s) from reported total costs and total outcomes.

For outcomes that utilized cost-benefit measures, cost per life-year saved, or cost per QALY saved, we calculated the percent of outcomes that indicated vaccinations were cost-saving. Specifically, a cost-saving outcome was one in which the benefits exceeded the cost (i.e., savings) in a cost-benefit measure, the cost per life-year saved was less than $0, or the cost per QALY gained was less than $0.

Among outcomes that utilized cost per QALY saved, we presented each outcome graphically, stratified by vaccine group and by type of vaccination. In the text we also reported the percentage of outcomes that fell within three different $/QALY thresholds of $50,000/QALY, $100,000/QALY, and $300,000/QALY. Because no single $/QALY threshold is utilized for health-related decision-making, we present results utilizing three different thresholds to provide a range for assessing overall trends in cost-effectiveness. The presentation of results across multiple cost-effectiveness thresholds is supported by recent recommendations by the Second Panel on Cost-Effectiveness in Health and Medicine [35,37]. In cases where the abstracted outcome was a range of values, we utilized the lower end of the range to assess the percentage of outcomes that fall below a given threshold. Both the cost-saving and the $/QALY analyses were stratified by vaccine group and by study population. All costs were adjusted to 2016 U.S. dollars using the consumer price index [38] and, for publications reporting values in Canadian dollars, the US-Canadian exchange rate [39].

3. Results

Our search strategy identified 1688 publications (Fig. 1). After removing duplicates and excluding for relevance, 78 publications, including 25 influenza, 9 Td/Tdap, 7 HZ, 18 pneumococcal, 9 hepatitis B, 9 HPV, and 1 publication including both influenza and pneumococcal vaccines, were fully abstracted and incorporated into the final analysis.

3.1. Number and type of outcomes identified

The 78 abstracted publications yielded 161 outcomes (Table 1). All the identified outcomes from the publications in the final set of records are summarized in the appendix [66–133]. The percent of outcomes associated with age-based vaccination recommendations by vaccine group was 75 for influenza, 62 for pneumococcal, 74 for HPV, 100 for HZ, and 72 for Td/Tdap. All outcomes for hepatitis B focused on populations that have indication-based recommendations (e.g. diabetes, healthcare workers, injection drug users, etc.). Across all vaccine groups we investigated, the most common outcome measure was cost per QALY saved. Other outcomes identified were cost per case prevented, found in 10% of influenza outcomes and 42% of hepatitis B outcomes; and cost per life-year saved, found in 22% of Td/Tdap outcomes and 11% of hepatitis B outcomes (Table 1).

3.2. Outcomes that evaluate the cost savings of adult vaccinations

For the outcomes assessing age-based vaccinations, the percent of outcomes that reported cost-savings were 56 for influenza, 31 for pneumococcal, and 23 for Td/Tdap vaccinations

(Table 2). For the outcomes assessing indication-based vaccinations, the percent of outcomes that reported cost-saving values were 46 for influenza, 44 for pneumococcal, 40 for Td/Tdap, and 37 for hepatitis B vaccinations. No cost-saving outcomes were identified in publications assessing HPV or HZ vaccinations for either age-based or indication-vaccinations (Table 2).

3.3. Outcomes that evaluate the cost per QALY saved of adult vaccinations

Among outcomes reported as cost per QALY saved, many publications across all adult vaccinations estimated costs per QALY saved that might be considered cost-effective [40,41]. Every cost per QALY saved outcome that was identified is presented graphically, with a panel for outcomes that assessed age-based vaccinations (Fig. 2a) and another panel for outcomes that assessed indication-based vaccinations (Fig. 2b). For outcomes assessing age-based vaccinations, the percent indicating any cost-effectiveness estimate equal to or below $50,000/QALY were 100 for influenza, 78 for pneumococcal, 54 for HPV, 36 for HZ, and 30 for Td/Tdap vaccinations. For outcomes assessing indication-based vaccinations, the percent indicating any cost-effectiveness estimate equal to or below $50,000/QALY were 73 for influenza, 77 for pneumococcal, 40 for HPV, 25 for Td/Tdap, and 38 for hepatitis B vaccinations. Among age-based vaccination outcomes reporting $/QALY, the percent of outcomes indicating a cost per QALY of ≤$100,000 was 82 for influenza, 100 for pneumococcal, 69 for HPV, 71 for HZ, and 50 for Td/Tdap vaccinations. Across all vaccinations, substantial percentages of outcomes assessing age-based or indication-based vaccinations indicated cost-effectiveness that were equal to or below $300,000/QALY (Fig. 2). As a summary measure, when looking across all vaccine groups and including both the age-based and the indication- based outcomes that we collected in our review, we found 32% of all outcomes indicated that adult vaccination was cost-saving. Looking at costs per QALY saved, 80% of outcomes indicated a cost per QALY of ≤$100,000 and 60% of outcomes indicated a cost per QALY of ≤$50,000.

4. Discussion

This systematic review provides an updated synthesis of the cost-effectiveness research literature on adult vaccinations, with a focus on estimates of cost-effectiveness that compare adult vaccination to “no vaccination”. Consistent with previous reviews, we found that adult vaccinations have a favorable cost-effectiveness profile in the majority of the outcomes we reviewed. Indeed, a substantial portion of influenza, pneumococcal, and Td/Tdap related outcomes estimated appear to be cost-saving. For influenza and pneumococcal vaccinations, the majority of outcomes reported either cost savings or cost-effectiveness ratios ≤$50,000/QALY. For HPV and HZ vaccinations, the majority of outcomes reported cost-effectiveness ratios ≤$100,000/QALY. While our findings reflect favorable cost-effectiveness among outcomes for most vaccine groups, we do find a small number of exceptions to this overall trend. These exceptions can be understood based on particular underlying assumptions and modeling choices that contribute to a cost-effectiveness estimate that may be higher than expected. In one case, particular scenarios investigating Tdap vaccination utilized an incidence assumption for pertussis that is low relative to the incidence used in other scenarios of the same study [42–44]. In another case, scenarios were designed to investigate patient groups that are not currently recommended for vaccinations. Examples include hepatitis B vaccinations of diabetics who are 60 years and older [45], HPV vaccination of persons older than 26 years [46], and HZ vaccination with the zoster live vaccine of persons aged 50–59 [47]. These outcomes tend to report higher cost-effectiveness ratios because the assumptions inherent in these scenarios represent populations or conditions that have lower risks for VPD or VPD-associated costly outcomes. Our overall findings would demonstrate even more favorable overall cost-effectiveness if we restricted our sample to outcomes that more exclusively investigate ACIP vaccination recommendations. The broad finding of our study that adult vaccinations exhibit favorable cost-effectiveness appears to be consistent, across age-based and indication-based vaccinations.

The percentage of outcomes using a cost per QALY saved is highest among vaccines that were more recently approved and recommended (Table 1). Greater than 90% of outcomes assessed cost per QALY among both HZ and HPV vaccination outcomes. In particular, influenza and hepatitis B vaccination outcomes contained a more diverse set of outcome types, and the influenza and hepatitis B vaccines have been in use for much longer than HZ and HPV vaccines. Older publications in our sample tended to include more outcomes that were measured in strictly monetary terms (e.g., net benefit) or as cost per cases prevented. This trend seems to reflect the growing influence and prevalence of the QALY as a health measure in CEAs. Variation in cost per QALY within a particular vaccine group and recommendation type can be observed in Fig. 2. This variation can be due to a wide range of potential modeling choices. Some of those modeling choices may include the severity of an influenza season, the effect of herd immunity on HPV or pneumococcal transmission, as well as changes in vaccine technology.

While cost-effectiveness estimates appear to be generally favorable, vaccination coverage among adults for whom vaccination is recommended remains low for influenza (45% among adults ≥19 - years old), pneumococcal (23% among adults 19–64 at increased risk), Td/Tdap (23% among adults ≥19 years old), HZ (31% among adults >60 years old), and hepatitis B (25% among adults ≥19 years old) [3]. Lower vaccination coverage rates have been found among minority racial and ethnic groups compared to non-Hispanic white populations [48,49]. In addition, differences in vaccination coverage rates across states suggest that local factors may be an important source of vaccination coverage rates disparities [50]. A number of additional obstacles to high vaccination coverage among adults have been documented. Patient perceptions about infection risks and vaccine efficacy can influence vaccine uptake [51]. Concerns regarding vaccination payments have been reported as major barriers to adult vaccination implementation by healthcare providers, including family physicians, internists and obstetricians and gynecologists [52,53]. Vaccination billing and coding errors may be responsible for perceptions of inadequate payment [54]. Medicaid payments for adult vaccinations vary substantially by state and may be a barrier to vaccinating adults on Medicaid in some states [54,55], especially pregnant women where substantially lower Tdap coverage has been documented for those on Medicaid compared to private insurance [56,57]. Coverage of some vaccines as part of Medicare Part B (influenza, pneumococcal, Td for wound treatment and hepatitis B vaccine for persons with high risk conditions) and Medicare Part D (e.g., Td, Tdap, and hepatitis B for prevention, and zoster vaccination) and payment complexities are also provider-level barriers that must be considered during implementation and planning [52,58].

Other preventive services, such as hypertension screening and breast/colorectal cancer screening, appear to have similar cost-effectiveness profiles as adult vaccinations [59–61], however these services appear to be given greater priority during clinical practice. A survey of internal medicine and family medicine physicians suggested that physicians had a lower priority for HZ and Td/Tdap vaccinations than other age-relevant preventive services [9]. For vaccinations, provider awareness of the economic value may be particularly important because the influence of a provider recommendation has been found to be important for patients' decision to receive a vaccine [11]. These challenges are particularly unfortunate in light of the main finding of this study, which is that the majority of outcomes we investigated found attractive cost-effectiveness estimates for adult vaccinations. Efforts to improve healthcare providers and health systems' awareness of the cost-effectiveness of adult vaccines may prompt efforts to improve the implementation of vaccination recommendations and reduce missed opportunities for adult vaccinations.

4.1. Limitations

Our analysis is subject to limitations. While we made every reasonable effort to identify and utilize all cost-effectiveness and economic evaluation publications related to adult vaccinations, publications may have been missed. In particular, research that was not indexed by the electronic research literature databases that we used in our searches may also have been missed. Given that our searches primarily identified studies in the published research literature, publication-bias may have influenced our results. Because all the outcomes from any particular study may be correlated, the abstraction of more than one outcome from a study could lead to a bias. Our abstraction of cost-effectiveness outcomes from each publication intended to best represent the majority of currently available vaccines for adults. However, additional adult vaccines have become available since our electronic database searches were conducted, such as for the new adjuvant vaccine for HZ [62]. While we did not identify a published, peer-reviewed cost-effectiveness on this new HZ vaccine at the time of our literature search, analyses provided to the Advisory Committee on Immunization Practices suggests a favorable cost effectiveness profile for the new HZ vaccine when compared to "no vaccination" [63]. Our review specifically targeted publications that assessed vaccination versus "no vaccination", so we did not review the numerous publications and outcomes that only assessed cost-effectiveness comparing two or more vaccination strategies, or comparing two or more vaccines. Due to the relatively broad scope of this review, we were also unable to assess the overall quality of the publications or to assess the quality and influence of any specific inputs. Finally, the cost components of the outcomes investigated by our study captured a mixture of medical and non-medical costs. The inflation adjustment we applied to these outcomes did not account for differing rates of price increases among medical and non-medical costs.

4.2. Conclusions

Adult vaccinations prevent substantial morbidity, disability and death among adults and have cost-effectiveness profiles that are considered favorable across multiple age- and medical-indication-based recommendations. Efforts to increase the implementation of adult vaccination recommendations, including communication of the economic value of adult vaccines to providers and patients and addressing barriers to implementation, are needed.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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The findings and conclusions in this report are those of the authors and do not necessarily represent the views of the Centers for Disease Control and Prevention.

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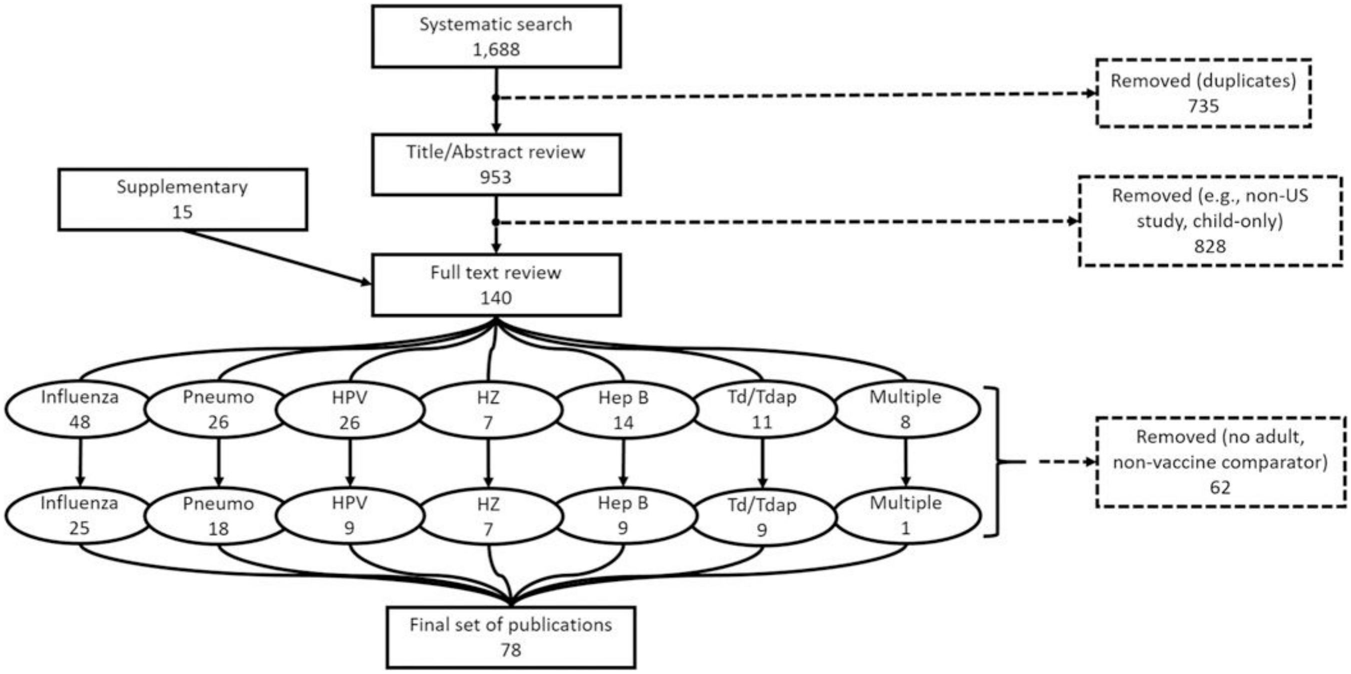

Fig. 1.

Cascade diagram of search results and exclusion criteria from a systematic review of adult vaccination cost-effectiveness and economic evaluation publications. *Note (s):* Td/Tdap = tetanus-diphtheria-pertussis; Pneumo = pneumococcal; Hep B = hepatitis B; HPV = human papillomavirus; HZ = herpes zoster.

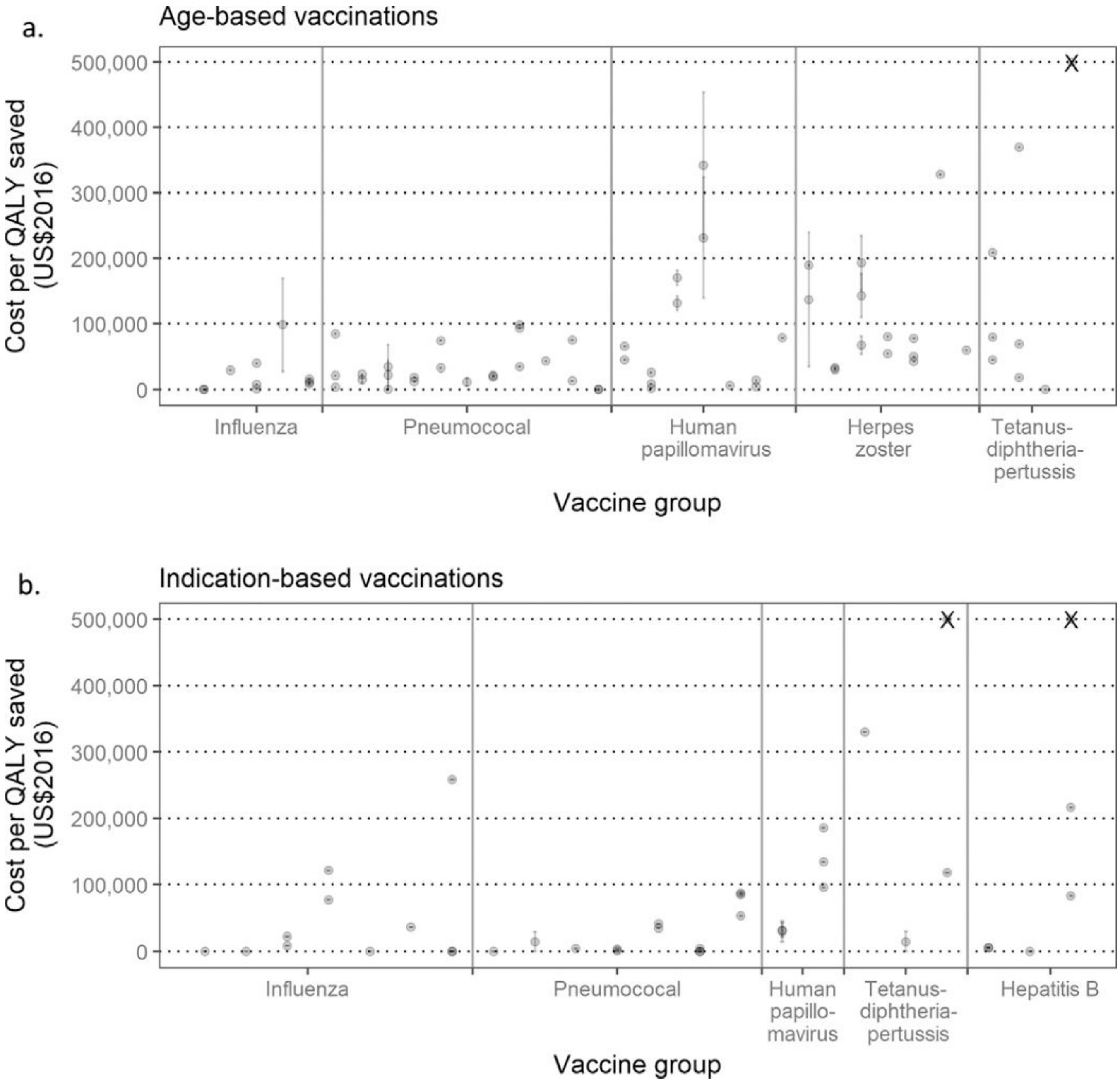

Fig. 2.

Summary of cost-effectiveness results on (a) age-based vaccinations and (b) indication-based vaccinations, stratified by vaccine group, from a systematic review of adult vaccination cost-effectiveness and economic evaluation publications. *Note(s):* Each data point or range represents one outcome that assessed cost-effectiveness in terms of cost per QALY saved. The data points are partially transparent such that darker points represent two or more observations. Each column represents a single study, e.g., multiple data points in a single column are different cost-effectiveness ratios or ranges taken from the same study. The data points with error bars or lines indicate outcomes where a range of cost-effectiveness was abstracted and in these cases the midpoints of the ranges are illustrated with the data point. In the age-based vaccinations, there were no hepatitis B studies, and in the indication-based studies there were no herpes zoster studies. To simplify presentation, cost-effectiveness ratios that were cost-saving (where costs were less and outcomes were greater than the "no vaccination" comparator) are located on the x-axis where $/QALY equals zero. Also to simply presentation, cost-effectiveness ratios that were greater than $500,000 per QALY saved are indicated with an "X" on the figure.

Table 1

Summary of publications and characteristics of outcomes identified in a systematic review of adult vaccination cost-effectiveness and economic evaluation publications, stratified by vaccine group.

	Vaccine group					
	Influenza	**Pneumococcal**	**Human papillomavirus**	**Herpes zoster**	**Tetanus-diphtheria-pertussis**	**Hepatitis B**
Number of publications	26[a]	19[a]	9	7	9	9
Number of outcomes[b]	48	42	19	15	18	19
Outcomes identified for age-based vaccinations (%)	75	62	74	100	72	0
Outcomes identified for indication-based vaccinations (%)	25	38	26	0	28	100
Percentages of outcome types						
$ (net benefit, or other CBA metrics) (%)	27	14	0	0	0	5
Cost-savings at hospitals (%)	6	0	0	0	0	0
$/person vaccinated, excluding vaccination costs[c] (%)	2	0	0	0	0	0
$/case-prevented (or $/averted infection) (%)	10	0	0	7	0	42
$/life (%)	4	0	0	0	0	0
$/life-year (%)	6	0	5	0	22	11
$/quality-adjusted life-year (%)	44	86	95	93	78	42

Note(s): CBA = cost-benefit analysis.

[a]One publication reported outcomes for both influenza and pneumococcal vaccines, therefore the number of publications row sums to 79 instead of 78.

[b]The number of outcomes is greater than the number of publications because each publication could contain multiple outcomes, or economic value estimates, that were relevant to adult vaccinations.

[c]This outcome type only includes outcomes from one publication [64] that reported as costs per person vaccinated while excluding the costs of vaccines. The majority of publications reporting outcomes as costs (or savings) per person vaccinated *did include* the costs of vaccine materials and administration, which we considered to be a cost- benefit metric, or a $ (net benefit or other CBA metric).

Table 2

Summary of cost-savings and cost-effectiveness results from a systematic review of adult vaccination cost-effectiveness and economic evaluation publications, stratified by vaccine group.

Type of vaccination	Cost-savings results	Vaccine group					
		Influenza	**Pneumococcal**	**Human papillomavirus**	**Herpes zoster**	**Tetanus-diphtheria-pertussis**	**Hepatitis B**
Age-based vaccinations	Outcomes using monetary units, \$/LY, or \$/QALY	32[a]	26[a]	14	15	13	0
	Percentage of outcomes indicating cost-savings	56	31	0	0	23	
	Percentage of studies indicating cost-savings[b]	56	15	0	0	29	
Indication-based vaccinations	Outcomes using monetary units, \$/LY, or \$/QALY	13	16	5	0	5	19
	Percentage of outcomes indicating cost-savings	46	44	0		40	37
	Percentage of studies indicating cost-savings[b]	39	57	0		50	46

Note(s): QALY = quality-adjusted life-year; LY = life-year.

[a] Cost-savings could not be ascertained for one outcome related to influenza age-based vaccinations [64].

[b] For these results, we combined all abstracted outcomes into a single outcome for each study. As an example, Prosser et al. 2011 [65] had two abstracted outcomes, one that was not cost-saving: \$27,000 to \$170,000 per QALY saved among low-risk adults aged 18 years and older, and one that was cost-saving (less than \$0 per QALY saved) among high-risk adults aged 18–64. These two abstracted outcomes were combined into a proportional value of 0.5 for this study. The proportional values for each study were then combined across vaccine groups and type of vaccinations.