Review Article

A Literature Review of Health Economic Evaluation:
A Case of Vaccination on Systematic Review Analysis

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ABSTRACT

This study tries to provide a comparative analysis of the systematic review of economic evaluation literature available about vaccines. PubMed database were searched by using the following keywords: "vaccination/economics [MeSH]". All articles were included if: 1) A literature or systematic review of vaccination studies; 2) primary or secondary data; 3) published in English; 4) related to human. Exclusion criteria were as followings: 1) editorial, review or methodological articles; 2) not in health sector; 3) not applied from 2009 to 2013. From 22 records found, eleven articles met selection criteria. Only 27.3 percent (3 of 11 studies) was recorded about the methodology of conducting systematic review studies based on the PRISMA, and AMSTAR guideline. Two of eleven studies (18.1 percent) in this review, the authors evaluated the quality of vaccination systematic review studies with different levels including "Moderate" to "Moderate to good" and "Moderate to good". According to this study, it helps to understand the current situation for conducting and reporting the economic evaluation of vaccination systematic review studies. Currently, the large number of studies and systematic reviews on the effects of vaccination, high quality evidence to inform policy decisions on how best to use vaccination in health care is still lacking.

Keywords: Economic analysis, economic evaluation, vaccination, systematic review, literature review.

INTRODUCTION

Evidence-based policy making can rarely rely on single studies, so policy makers and the researchers that support them try to make best use of the various partially relevant studies already available[1]. Nowadays, economic evaluation studies is very important to ameliorate decisions about apportion of human resources in health care. Economic evaluation of drugs, medical devices, services and interventions is a useful tool for assessing important decisions regarding the optimal utilization of scarce resources[2]. Nevertheless, systematic reviews of economic studies have become a key feature of many policy making and technology assessment processes, and also a common form of published study in certain health economics journals[1]. The healthcare literature contains hundreds of thousands of studies of healthcare interventions, growing at tens of thousands per year[3]. More recently, calls have been made for 'rapid reviews' to provide decision-makers with the evidence they need in a shorter time frame, but the possible limitations of such 'rapid reviews', compared to full systematic reviews, require further research[4].

In the last two decades, several vaccines have been developed that target a range of infectious diseases of global public health importance.

Vaccines may bring economic benefits beyond just health gains and there may be various pathways for these benefits to accrue. Unlike other health interventions, studies find that vaccines avert illness both directly through immunization and indirectly through herd immunity[5]. While all such changes can have an immense impact on a country's economy, it is difficult to get a full picture of the economic impact resulting from immunization. Understanding the full economic benefits of vaccines is vital to policy makers whose decisions to introduce new vaccines not only impact the health of a society, but also its economy. Evidence on such economic benefits is therefore critical in assessing the full return on investment in vaccines[6].

Current systematic reviews, within economic evaluation types (including cost minimization analysis (CMA), cost effectiveness analysis (CEA), cost utility analysis (CUA), cost benefit analysis (CBA). However, in some economic evaluation types, no systematic review currently exists and there may be few or even no trials. A systematic review of systematic reviews is a means of summarizing current evidence across specialties of the same or very similar intervention, to provide a synthesis of treatment effects[7,8].

In the last two decades, several vaccines have been developed that target a range of infectious diseases of global public health importance[7]. However, the list price of these vaccines in high income countries is substantially greater than for traditional vaccines. Recently, several frameworks have been proposed by which these wider benefits of vaccination can be categorized[4,9]. Nevertheless, the extent to which these broader benefits are considered in current economic evaluations of vaccines is unclear.

This study tries to provide a comparative analysis of the literature review including: general information, the methods and the quality of systematic reviews on the economic evaluation of vaccination studies with the purpose of synthesizing evidence to date on the effectiveness of vaccination in various countries between 2000 and 2013. This study also analyses the vaccination systematic review studies including: The design, the method or guidelines (e.g. PRISMA, York and so on), keywords and searching, databases, the quality checklist of papers reviewed, presentation format (quality checklist of the review).

MATERIALS AND METHODS

Literature Search

This study was designed as a systematic review that was carried out in December 2013 to identify vaccination systematic review studies conducted in many countries with a combination of key words and MeSH term. PubMed databases were used for searching with the following keywords were used in different combinations: "vaccination/economics [MeSH]" with filter criteria: Systematic review, five years ago and human.

All publications were included if: Systematic review set out to identify and include all articles that included a literature review of vaccination studies. Published articles were considered studies that used primary or secondary data. Economic evaluation studies were published in English language and were related to humans. All publications were excluded if: They were editorial, review or methodological articles and did not present both the costs and outcomes of a study. Studies were also rejected if they were not in health sector, were not implemented in humans and were not applied from 2009 to present. Figure 1 illustrates the progress of selection of articles.
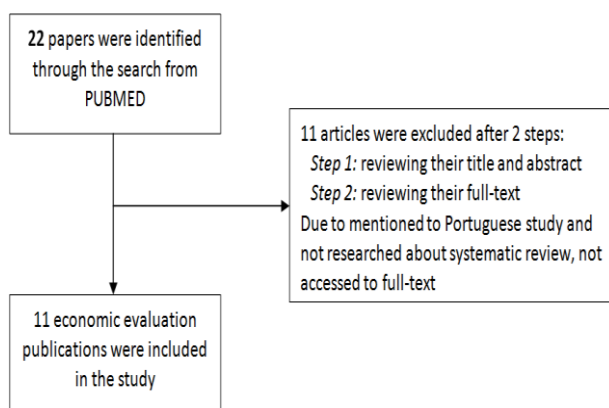
Figure 1: Flow chart for selection of articles included in this study

Evaluation of Studies

This study was analysis two parts, such as: general information section including the number of vaccination economic evaluations published per year, number of paper reviewed in economic evaluations of vaccines review studies, type of the design or the method or guidelines, number of databases, and the quality of economic evaluation.

About the quality and strength of evidence presented in the individual, included reviews should influence the conclusions drawn in the systematic review of these. Although the researchers will usually have to do this via an assessment of the quality of report, with the hope that initiatives such as design or method or guideline (e.g. PRISMA, York), keywords and techniques, databases, quality checklist of papers reviewed, presentation format (quality checklist of the review). Two reviewers were separately reviewed for all of articles. After comparison of the results, two reviewers had discussed.

RESULTS

The search yielded 22 articles about vaccination/economic from PubMed database between January 2009 to December 2013. Based on inclusion and exclusion criteria, 11 remain publications related this study. Reviewers applied the inclusion and the exclusion criteria to remain 11 papers after two steps: reviewing their title and abstract, reviewing their full-text due to mentioned to Portuguese study and not researched about systematic review, not accessed to full-text.

General Information Section

Table 1 illustrates the amount of publication year by year from 2009 to 2013. According the table, we can see that the number of papers were stable from two to three studies. However, in 2010, there is no study to review in this field. Of the 11 systematic review studies selected, 4 studies (3 studies had conducted in 2012 and one study were conducted in 2013) reviewed many different vaccination studies. Furthermore, seven of 11 studies evaluated the economic evaluation of one vaccination studies including: rubella vaccination, Herpes Zoster vaccination, Pneumococcal Conjugate vaccination, auto-immune inflammatory rheumatic diseases, influenza vaccination, pneumococcal polysaccharide vaccination and human papillomavirus (HPV) vaccine.

Table 1 also shows the number of articles in economic evaluations of vaccines review studies. In above table, we can see in 11 papers, number of paper studies less than or equal to 20 is five articles (45.2 %). The number of paper studies from 21 to 100 and over 100 studies are four (36.4 percent) and two (18.2 percent) papers, respectively.

Of two literature reviews with over 100 studies, first study examined the cost effectiveness and economic benefits of vaccines in low- and middle-income countries and authors in this review defined 108 relevant articles from 51 countries spanning 23 vaccines from three major electronic databases (PubMed, EmBase[TM], and Econlit) (Ozawa, 2012) The remain study show the impact of new vaccine introduction on immunization and health systems with 130 studies from December 31, 1911 to September 29, 2010. These articles represented vaccines introduced

to protect against ten different diseases (Hepatitis A, Hepatitis B, *Haemophilus influenza* type b disease, human papilloma virus infection, influenza, Japanese encephalitis, meningococcal meningitis, Streptococcus Pneumonia disease, rotavirus diarrhea and typhoid), in various formulations and combinations from seven publication databases.

The Methods of the Vaccination Systematic Review Studies

According Table 1, we can see that the percentage of systematic review studies, which were not conducted base on guidelines, is 72.7 percent (8 studies).

While only 27.3 percent (3 of 11 studies) was mentioned about the method of conducting systematic review studies. The methodology of literature review was carried out by the PRISMA guideline.

Of 11 systematic review studies, the authors performed a systematic search of online different databases. In Table 2, we present findings of the number of databases clearly, such as two databases (3 studies), three databases (4 studies), four databases (1 study), five databases (2 studies), and seven databases (4 study). The highest amount of databases for vaccination systematic review studies used for searching papers is seven databases, including Medline®, EmBase™, Nursing Update, West African Journal of Nursing, CINAHL®, Web of Science®, and

Global Health.All of studies in this systematic review (11/11 studies) were selected from PubMed (Medline®) database. The number of using times to use EmBase™, Center for Reviews and Dissemination (CRD), NHSEED and HTA databases for conducting systematic review are recorded four, four and three databases, respectively. For Scopus, Cochrane and EconLit databases, there are two times for using search to find the publications from reviewers.

On the other hand, Databases of the CRD, they used databases in the Spanish Medical Index, University of York, and Database of Abstracts of Reviews of Effects [DARE] in the vaccination systematic review studies. Moreover, the authors had used other databases, including ISI Web of Knowledge, the Spanish Bibliographic Index of Health Sciences (IBECS), Nursing Update, West African Journal of Nursing, CINAHL®, Web of Science®, Global Health, The abstracts from the meetings of EULAR 2008 and 2009, The American College of Rheumatology (ACR) 2007 and 2008, AHRQ Evidence, and Google Scholar.

For developing search strategy and locate studies, searching is the stage where a reference librarian can be extremely helpful in terms of helping to develop and run electronic searches.

Table 1: Characteristic of Included Studies

Characteristics of Included Studies	N (%)		Characteristics of Included Studies	N (%)
Year			**Number of Paper Reviewed**	
2009	3 (27.3)		1-20	5 (45.5)
2010	- (0)		21-100	4 (36.4)
2011	2 (18.2)		>100	2 (18.2)
2012	3 (27.3)			
2013	3 (27.3)			
Type of the Design or the Method or Guidelines			**Number of Database used in each Study**	
Mentioned (PRISMA)	3 (27.3)		Joseph	2
Not mentioned	8 (72.7)		Anna García-Altés	5
Amount of times Databases Searching			Thomas D. Szucs	2
PubMed (Medline®)	11		Sachiko Ozawa	3
EmBase™	4		Rohan Deogao-nkar	3
NHSEED and HTA (*)	3		Terri B. Hyde	7
Scopus (Science Direct)	2		Chantal W.B. Boonacker	4
Cochrane	2		S. Van Assen	3
EconLit	2		Anthony T. Newall	3
CRD	4		Isla Ogilvie	5
Others	11		Jaume Puig-Junoy	2

Notes: NHSEED=The National Health Service Economic Evaluation Database

HTA=Health Technology Assessment Database; **CRD**=Databases of the Center for Reviews and Dissemination

Table 2: The Number of Databases

No.	Studies (Review year)	Database								Total	Notes Other Databases
		PubMed (Medline®)	EmBase ™	NHSEED And HTA (*)	Scopus (Science Direct)	Co-chrane	Econ-Lit	CRD	Others		
1	Joseph	✓		✓						2	
2	Anna García-Altés	✓			✓			✓	✓ (2)	5	- ISI Web of Knowledge - IBECS
3	Thomas D. Szucs	✓	✓							2	
4	Sachiko Ozawa	✓	✓				✓			3	
5	Rohan Deogaonkar	✓		✓			✓			3	
6	Terri B. Hyde	✓	✓						✓ (5)	7	- Nursing Update - West African Journal of Nursing - CINAHL® - Web of Science®, - Global Health

NHSEED = The National Health Service Economic Evaluation Database; **HTA =** Health Technology Assessment Database

CRD = Databases of the Center for Reviews and Dissemination; **IBECS =** The Spanish Bibliographic Index of Health Sciences; **ACR =** The American College of Rheumatology

Table 2: The Number of Databases (cont.)

No.	Studies (Review year)	Database								Total	Notes Other Databases
		PubMed (Medline®)	EmBase ™	NHSEED And HTA (*)	Scopus (Science Direct)	Co-chrane	Econ-Lit	CRD	Others		
7	Chantal W.B. Boonacker	✓		✓		✓		✓		4	
8	S. Van Assen	✓							✓ (2)	3	- The abstracts from EULAR 2008 and 2009 - ACR 2007 and 2008
9	Anthony T. Newall	✓			✓				✓ (1)	3	- Google Scholar
10	Isla Ogilvie	✓	✓			✓		✓	✓ (1)	5	- AHRQ Evidence
11	Jaume Puig-Junoy	✓		✓						2	
Total		**11**	**4**	**3**	**2**	**2**	**2**	**4**	**11**	**39**	

NHSEED = The National Health Service Economic Evaluation Database; **HTA =** Health Technology Assessment Database

CRD = Databases of the Center for Reviews and Dissemination; **IBECS =** The Spanish Bibliographic Index of Health Sciences; **ACR =** The American College of Rheumatology

Generally, it is important to come up with a comprehensive list of key terms (i.e., Medical Subject Headings ("MeSH") terms) related to each component of participants, interventions, comparators, outcomes, and study design (PICOS) to be able to identify all relevant trials in an area. Ten studies (90.9%). Of these vaccination systematic review studies were mentioned about searching including keywords and techniques. By contrast, only one study (9.1 percent) was not mentioned that how the authors used keywords and the process of searching. Of ten studies, four studies (36.4 percent) showed the process of searching and six studies (54.5 percent) show keywords. Only one study of six studies show the keywords used MeSH term (Table 3).

Table 6 provides information that articles evaluated in this review (N=11).

At present, there are many instruments to evaluate quickly and accurately measure aspects of the quality health economics studies and has been used to identify evidence to enhance decision-making of quality of studies.

A high score on the quality of checklist of papers reviewed guidelines indicates a study better quality. When using the results to identify potential gaps in the evidence on the economics of vaccination as it relates to helped reduce the burden of disease and mortality from infection disease.

According to Table 4, there are five (45.5 percent) the economic evaluation of vaccination systematic review studies to evaluate the quality of checklist of papers reviewed.

Many the quality of checklist of papers reviewed guidelines were evaluated by different authors. For instances, the guidelines embrace the Quality of Health Economics Studies questionnaire (QHES), British Medical Journal guidelines (BMJ), Grades of Recommendation Assessment, Development and Evaluation (GRADE), The Consensus on Health Economic Criteria list (CHEC) and Drummond. guideline. Six studies which were not mentioned the quality of checklist guidelines are account for 54.5 percent.

We were recorded two studies of 11 (18.2 percent) which were mentioned the quality of each studies (Table 5).

The authors in these studies evaluated the vaccination systematic review studies two results, including "Moderate" to "Moderate to good" and "Moderate to good". Nine studies (81.8 percent) were not evaluated the quality of articles reviewed. Three of nine studies had gave the quality checklist of papers reviewed, however the authors were not mentioned the results because of differences in study design and specific data elements collected, we were unable to compare studies or evaluate data quality.

Table 3: Searching (keywords and techniques) for the Vaccination Systematic Review Studies

Type of Searching (Keywords and Techniques)		Number (n)	Proportion (%)	Total
Mentioned	The process of searching (keywords and techniques)	4	36.4	90.9
	Show keywords	6	54.5	
Not mentioned		1	9.1	9.1
Total		11	100	100

Table 4: The Quality of Checklist of Papers Reviewed

Quality of Checklist of Papers Reviewed		Number (n)	Proportion (%)	Total
Mentioned	16 items-QHES	1	9.1	45.5
	QHES and BMJ guideline	1	9.1	
	GRADE method	1	9.1	
	Drummond checklist	1	9.1	
	Evers S, Chiou CF, Gerkens S. (QHES, CHEC or BMJ)	1	9.1	
Not mentioned		6	9.1	54.5
Total		11	100	100

QHES = Quality of Health Economics Studies questionnaire; **BMJ =** British Medical Journal guidelines
GRADE = Grades of Recommendation Assessment, Development and Evaluation
CHEC = The Consensus on Health Economic Criteria list

Table 5: Evaluate the papers reviewed in each systematic review studies from 2009 to 2013

	Mentioned		Not mentioned	Total
	"Moderate" to "Moderate to good"	*"Moderate to good"*		
Number of studies	1	1	9	11
Proportion	9.1	9.1	81.8	100

Table 6: Articles Evaluated in this Review (N=11)

No.	Study (Review year)	Design / Method / Guideline	Databases	Search strategy (Keywords + Techniques)	Quality Checklist of Papers Reviewed	Presentation Format (Quality Checklist of the Review)
1	Joseph	PRISMA	-MEDLINE (PubMed) -The National Health Services Economic Evaluation	'rubella and economics', 'rubella and costs', 'rubella and cost-effectiveness', 'rubella and cost -utility', 'rubella and cost-benefit', 'CRS and economics', and 'CRS and costs'	The 16-item Quality of Health Economics Studies (QHES) questionnaire	n/a
2	Anna García-Altés	n/a	- PubMed/MEDLINE; - SCOPUS - ISI Web of Knowledge - Databases of the Center for Reviews and Dissemination, as well as in the Spanish Medical Index (IME) - The Spanish Bibliographic Index of Health Sciences (IBECS).	Appendix 1.	n/a	n/a
3	Thomas D. Szucs	n/a	- PubMed - EmBase	- 'Herpes zoster vaccine' or 'herpes zoster vaccination' or 'varicella zoster vaccine' or 'varicella zoster vaccination' • and 'cost(-)effectiveness' or and 'economic evaluation'	- The British Medical Journal guidelines of Drummond and Jefferson - The Quality of Health Economic Studies (QHES)	"Moderate" To "Moderate to good"
4	Sachiko Ozawa	PRISMA	- Pubmed (MEDLINE) - EmBase - Econlit (EBSCO host)	"economic benefit" and "vaccine" and "low- and middle-income country" [MeSH]	n/a	n/a
5	Rohan Deogaonkar	PRISMA	- MEDLINE; - EconLit - The National Health Service Economic Evaluation Database (NHSEED)	n/a	n/a	n/a
6	Terri B. Hyde	n/a	- Medline®; - Embase™; - Nursing Update; - West African Journal of Nursing; - CINAHL®; - Web of Science®, - Global Health	n/a	GRADE method	Because of differences in study design and specific data elements collected, we were unable to compare studies or to evaluate data quality.
7	Chantal W.B. Boonacker	n/a	- PubMed; - Cochrane - The Centre for Reviews and	'otitis media', children',	The Drummond checklist	Moderate to good

			Dissemination databases (Database of Abstracts of Reviews of Effects [DARE] - NHS Economic Evaluation Database [NHS EED] and Health Technology Assessment database [HTA])	'cost effectiveness', 'cost' and 'vaccine'			
8	Anthony T. Newall	n/a	- PubMed; - Scopus - Google Scholar	'influenza', 'adult', 'vaccination', 'cost', 'cost-benefit analysis'	n/a		n/a
9	Isla Ogilvie	n/a	- PubMed; - Embase; - Cochrane reviews - AHRQ Evidence - the Center for Reviews and Dissemination databases.	cost; economic; cost effectiveness; cost utility; cost benefit; and pneumococcal polysaccharide vaccine	Evers S, Chiou CF, Gerkens S (QHES, CHEC or BMJ)		n/a
10	Jaume Puig-Junoy	n/a	- Pubmed; - NHS EED and HTA, from the Centre for Reviews and Dissemination (University of York)	n/a	n/a		n/a

Table 7: Recommendations based on AMSTAR guideline for good reporting of systematic review studies (n=11)

S. No.	Studies	1= Yes		2= No		3= Can't answer		4= Not applicable		Total	
		n	%	n	%	n	%	n	%	n	%
1.	Was a priori design provided?	2	18.2	-	-	9	81.8	-	-	11	100
2.	Was there duplicate study selection and data extraction?	8	72.7	2	18.2	1	9.1	-	-	11	100
3.	Was a comprehensive literature search performed?	11	100	-	-	-	-	-	-	11	100
4.	Was the status of publication (i.e. grey literature) used as an inclusion criterion?	3	27.3	2	18.2	6	54.5	-	-	11	100
5.	Was a list of studies (included and excluded) provided?	4	36.4	2	18.2	5	45.4	-	-	11	100
6.	Were the characteristics of the included studies provided?	9	81.8	1	9.1	1	9.1	-	-	11	100
7.	Was the scientific quality of the included studies assessed and documented?	2	18.2	5	45.4	2	18.2	2	18.2	11	100
8.	Was the scientific quality of the included studies used appropriately in formulating conclusions?	2	18.2	5	45.4	-	-	4	36.4	11	100
9.	Were the methods used to combine the findings of studies appropriate?	-	-	4	36.4	-	-	7	63.6	11	100
10.	Was the likelihood of publication bias assessed?	-	-	5	45.5	3	27.3	3	27.3	11	100
11.	Was the conflict of interest included?	-	-	2	18.2	8	72.7	1	9.1	11	100

Notes: 1=Yes; 2= No; 3= Can't answer; 4= Not applicable; **_"Can't answer"_** is chosen when the item is relevant but not described by the authors; **_"not applicable"_** is used when the item is not relevant, such as when a meta-analysis has not been possible or was not attempted by the authors.

The Quality of the Vaccination Systematic Review Reporting Practice

There are presently two known validated tools available for assessing the quality of systematic review [i.e. AMSTAR (an acronym for: 'a measurement tool to assess systematic reviews'), and an overview quality assessment questionnaire (OQAQ)[10]; a number of authors have also devised their own measures (Table 7).

DISCUSSION AND CONCLUSION

Systematic reviews (or overviews) of reviews are a logical and appropriate next step, allowing the findings of separate reviews to be compared and contrasted, providing clinical decision makers with the evidence they need.

Currently, the large number of studies and systematic reviews on the effects of vaccination, high quality evidence to inform policy decisions on how best to use vaccination in health care is still lacking.

AMSTAR, if used widely after external validation, could also enable methodological research (i.e. meta-regression of item of AMSTAR and effect size of reviews).

Our instrument is an attempt to achieve consensus amongst current mainstream opinions.

Inevitably, new evidence will modify current thinking in some areas and at that point, the AMSTAR will be updated.

This is indeed likely to be the case with techniques to identify and quantify publication bias. Although a number of alternative tests for publication bias exist, none has yet been validated[11,12].

Publication bias remains an area of contention amongst those who assess the quality of systematic reviews.

It remains a research priority because it is unclear what the impact of publication bias is on making decisions in health care.

We are aware of the 20 years of work that has gone in this area of research. This has given us some clear answers as to the effect publication bias may have on the overall results of estimating the impact of interventions.

AMSTAR will remain a living document and advances in empirical methodological research will be reflected in further improvements to the instrument.

A measurement tool for assessment of multiple systematic reviews (AMSTAR) was developed.

The tool consists of 11 items and has good face and content validity for measuring the methodological quality of systematic reviews.

Additional studies are needed with a focus on the reproducibility and construct validity of AMSTAR, before strong recommendations can be made on its use.

Limitation of this study: As the current article is the first to review reviews of reviews, there was no existing measure of quality to assess reviews of reviews.

Accordingly, this review devised the following eleven-item measure of methodological quality of reviews of reviews based on recently published guidelines for conducting systematic review of systematic review.

As the field is rapidly, evolving, different kinds of knowledge are also in demand, e.g. a stronger focus on economic analyses of vaccination, the methodology of conducting the vaccination systematic review studies including technique (databases, the keywords), and the process of searching, and so on. Information needs of stakeholders from different sectors (including health, finance and external donors) should be obtained to guide incorporation of broader benefits into economic evaluation, as well as their effective national immunization program.

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