

Quality Assessment in Systematic Reviews: A Literature Review of Health Economic Evaluation of Hepatitis Studies

Quang Vinh Tran^{1,2}, Phuong Hong Le^{1,2}, Trung Quang Vo^{1,2*}

¹Department of Pharmacy Administration, Faculty of Pharmacy, University of Medicine and Pharmacy, Ho Chi Minh City 700000, VIETNAM.

²Professional Healthcare Management, Education and Research center (ProHES), Ho Chi Minh City 700000, VIETNAM.

ABSTRACT

The trend of carrying out a systematic review of systematic reviews has just been concentrated in clinical-effectiveness. In aspect of cost-effectiveness, there has not been any review of reviews implemented in economic evaluation of hepatitis. The aim of this study is to appraise qualitatively a range of systematic reviews of economic evaluation in case of hepatitis based on PRISMA guidelines. A systematic search was made on Medline, Science Direct, and Cochrane Library databases till August 2016. Search terms used were "review" OR ("literature"; "systematic") AND "economic evaluation" OR ("cost effectiveness"; "cost benefit"; "cost utility"; "cost minimization") AND "hepatitis" OR ("hep*"; "H?V"). A total of 25 articles researching economic evaluations of hepatitis were identified. Approximately three-fourth of articles (n=18; 72%) are classified in "Intermediate"; following by "Bad" with five papers (20%). The categories "Very Bad" and "Good" share the last two papers. None of papers achieves the "Excellent". Seventeen is the most popular point gained by seven papers (28%). In short, PRISMA was proved to be an effective instrument due to its im-

portant role in assessing included reviews. Even though there are various systematic reviews of economic evaluation published, their qualities are not synchronous and the number of studies which was really carried out based on PRISMA is modest.

Key words: Economic evaluation, Hepatitis, Literature review, Review, Systematic review, Vaccination.

Correspondence:

Trung Quang Vo,

Department of Pharmacy Administration, Faculty of Pharmacy, University of Medicine and Pharmacy, Ho Chi Minh City, VIETNAM. Address: 41 Dinh Tien Hoang Street, Ben Nghe District, District 1, Ho Chi Minh City 700000, VIETNAM.

Phone no: (84.8)38295641

E-mail: voquangtrungdk@gmail.com

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INTRODUCTION

According to the definition of systematic review of systematic reviews, it is a means of summarizing current evidence across specialties of the same or very similar intervention, to provide a synthesis of treatment effects.^{1,2} A systematic review of systematic reviews is also known as an assessment on quality of those reviews in order to build a methodical orientation for future studies. Quality of systematic review methods was assessed using the following criteria that were adapted from different guidelines³⁻⁵ (a) Is it unlikely that important relevant studies were missed? (b) Were the inclusion criteria used to select articles appropriate? (c) Was the assessment of studies reproducible? (d) Were the design and/or methods and/or topic of included studies broadly comparable? (e) How reproducible are the overall results? (f) Will the results help resource allocation in health care? Each question was answered with "impossible to judge", "no", "partly", or "yes".⁶

To assess the qualitative or quantitative synthesis of a systematic review, a number of checklists were published, such as CONSORT,⁷ STARD,⁸ PRISMA⁹ and so on, which is appropriate to various research methods of only one topic. Therein, PRISMA is widely known to be a functional instrument to qualitatively appraise a systematic review of economic evaluation. PRISMA is an evidence-based minimum set of items for reporting in systematic reviews and meta-analyses. PRISMA not only focuses on the reporting of reviews which evaluates randomized trials, but can also be used as a basis for reporting systematic reviews of other types of research, particularly evaluations of interventions. This aims to help authors improve the reporting of systematic reviews and meta-analyses and also be useful for critical appraisal of published systematic reviews.^{1,10} Economic evaluations have increased as an advantageous tool for decision making in health care for the last two decades.^{11,12} Reviews performed almost ten years ago, however, presented noticeable gaps in the

quality of methods applied to economic evaluations of health care interventions.⁶ Nevertheless, quality of these reviews might vary and not follow any principle of assessment. On the other hand, the trend of building a systematic review of systematic reviews has just been concentrated in clinical-effectiveness.¹³⁻¹⁵ In aspect of cost-effectiveness, it is rare to find a review of reviews, in addition, there is not any study proceed in economic evaluation of hepatitis.

Therefore, the aim of this study is to qualitatively appraise the range of systematic reviews of economic evaluation in case of hepatitis. We analyze quality of these reviews based on PRISMA guidelines including design, methods, results and discussion.

MATERIALS AND METHODS

Study design

This study was designed as a systematic review following the PRISMA guidelines to access the quality of systematic reviews studies on health economic evaluation of hepatitis. It was scoped in publications up to 2016 in international journals.

Search strategy

A literature search was conducted with the support of three databases including MEDLINE, SCIENCE DIRECT and COCHRANE LIBRARY. The search string used was: "review" OR ("literature"; "systematic") AND "economic evaluation" OR ("cost effectiveness"; "cost benefit"; "cost utility"; "cost minimization") AND "hepatitis" OR ("hep*"; "H?V"). During the search, we applied following limits; search fields: Title, Abstract, Keywords; article type: review; species: humans. In order to get an adequate number of papers as necessity, the publication year was not considered. After the last search in August 2016, 851 published papers and accepted

manuscripts were identified.

Inclusion and exclusion criteria

The studies were selected by following a three-stage procedure. At the first stage, some papers were eliminated due to duplications and unavailable titles. At the next stage, we read the title initially, then continued with abstract if the title did not provide sufficient information to allow neither selection nor exclusion. All publications were included if they were recommended in their title and/or abstract as systematic reviews of hepatitis in economic evaluations. Nonetheless, exclusion was also applied in case of publications published in non-English languages and/or not related to humans. After all, the last stage was proceeded to procure eligible papers' full-text. Rejection was once again made since we were not able to accessed full-text and some of them were not presented as articles but book sections or conference posters.

Data extraction and data analysis

The study data were retrieved by reading the entire article. The information obtained was summarized using an Endnote (Thomson Reuters') library. Papers were reported in a table with the following fields: record number, name of author(s), publication year, article title and journal. We divided qualified articles into two groups, vaccination and non-vaccination.

Before handing in data, PRISMA checklist was edited by splitting each

item into specific particles. Seven parts that should be included (Title, Abstract, Introduction, Methods, Results, Discussion and Funding) are divided into twenty-seven items using as appraisal criteria. Item is ticked as one point if it is mentioned in the publication directly or indirectly through relevant factors. Eligibility criteria for each item were set out by reviewers based on quantity and importance of particles. Two reviewers were independently reviewed full-text for all of articles. After comparison of the results, two reviewers had discussed. Data extracted from checklists was assembled and figured out into primary results. Two branches of analyzed data which were quality of each article and quality of each PRISMA checklist's item were carried on to accentuate.

RESULTS

Figure 1 shows the flow chart of the selection process with the potentially relevant studies identified, studies retrieved for more detail evaluation, studies included and those excluded. As can be seen, the combined searches found 851 potential publications (448 through Medline, 310 through Science Direct and 93 through The Cochrane Library). Among the 851 references, 30 were duplicates (3.5%). Additionally, after reviewing titles and/or abstracts, 796 publications were eliminated for several reasons. Finally, there are 25 papers included in this study.

Fig. 1: Search flow diagram for systematic review

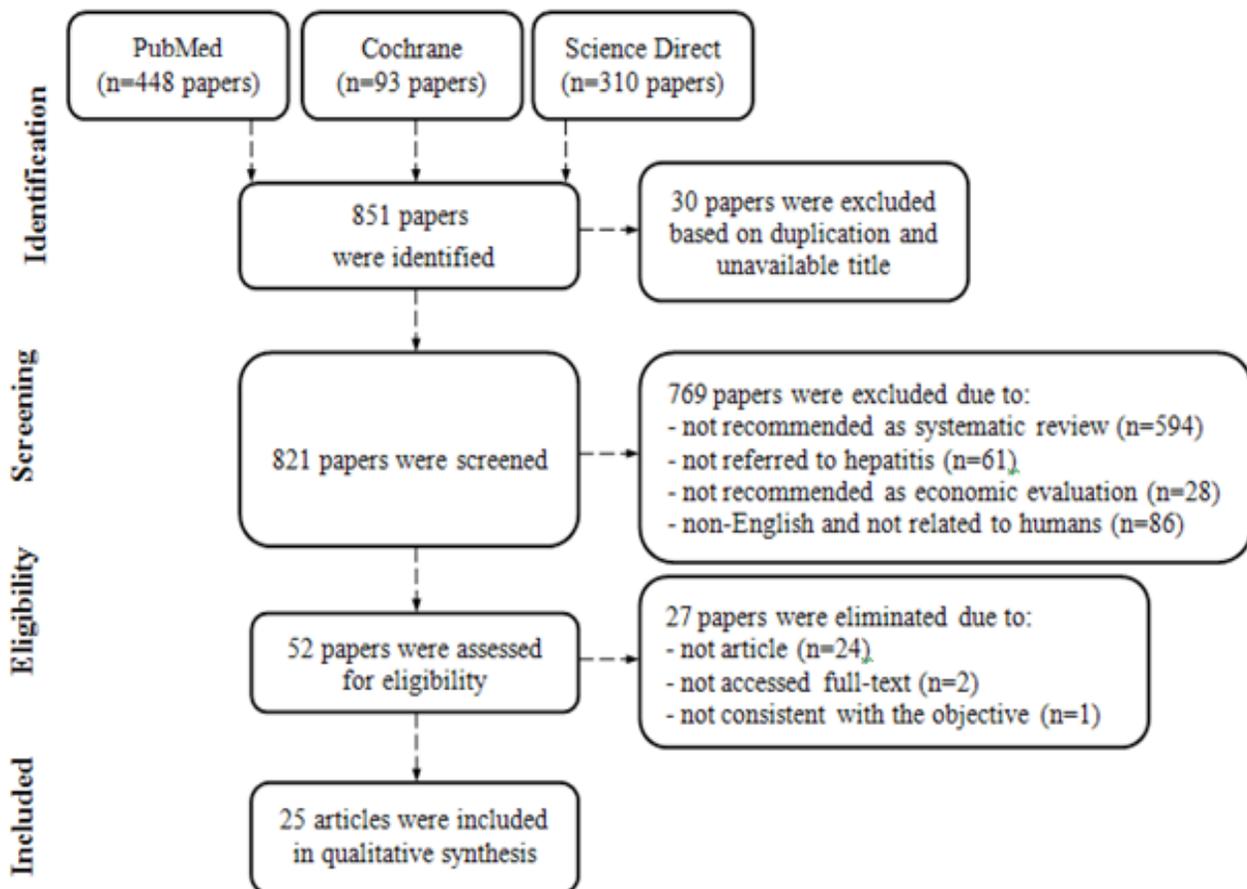


Figure 1: Search flow diagram for systematic review

Table 1: General characteristics of included studies (n=25)

Record No.	Authors	Continent	Assessment field	Types of disease	Objectives	Results
1	De Soarez PC <i>et al.</i> (2012) (19)	South America	CEA	HAV	To present the contributions of a SR of EE to the development of a national study on childhood hepatitis A vaccination.	The most important parameters for the results were cost of the vaccine, hepatitis A incidence, and medical costs of the disease.
2	Luyten J <i>et al.</i> (2009) (35)	Europe	CEA	HAV	To understand and estimate the economic impact of out-breaks of community-acquired infections.	In countries with low hepatitis A incidence rates, cases arise in out-break situations rather than sporadically. The cost of out-break management are relevant to include when estimating the direct cost of hepatitis A cases.
3	Anonychuk AM <i>et al.</i> (2008) (20)	North America	CEA	HAV	To review the literature on cost-effectiveness of hepatitis A vaccination to collate what is known, and to explore effects of methodological quality and key modeling issue on the economic attractiveness.	Analyses evaluating vaccination in children produced the most attractive ICERs. Cost-effectiveness was dependent on the risk of infection. Incidence, vaccine cost and discount rate were the most influential parameters.
4	Crossan C <i>et al.</i> (2015) (36)	Europe	CEA	LFC	To determine the diagnostic accuracy of different NITs in the diagnosis and monitoring of LFC, and to estimate the ICERs of the NITs.	The most cost-effective NITs to select patients for intensive HC surveillance and monitoring was Forns index.
5	Hahne SJ <i>et al.</i> (2013)(23)	Europe	CEA	HBCV	To inform screening polices	HCV screening of people who inject drugs and HBsAg screening of pregnant women and migrants is cost-effective.
6	Buti M <i>et al.</i> (2012) (27)	Europe	CEA	HBV	To review the quality of cost-effectiveness evidence on first-line treatment with ETV or TDF for patients with CHB.	ETV and TDF are both cost-effective interventions.
7	Jones J <i>et al.</i> (2009) (28)	Europe	CCEA	HBV	To update and extend a technology assessment report published in 2006.	PEG- β -2b had a probability of being cost-effective (compared with IFN- β -2b).
8	Sun X <i>et al.</i> (2007) (24)	Asia	CEA	HBV	To overview economic evidence of antiviral therapies for CHB.	Quality was various among studies. The major problems of quality are costing methods and analysis and the presentation of result.
9	Takeda A <i>et al.</i> (2006) (25)	Europe	CCEA	HBV	To assess the clinical- and cost-effectiveness of ADV and PEG- α -2a for the treatment of adults with CHB.	ICERs per QALY for a range of comparisons were between £5,994 and £16,569, and within the range considered by NHS decision-makers to represent good value for money.
10	Shepherd J <i>et al.</i> (2006) (29)	Europe	CCEA	HBV	To assess the clinical- and cost-effectiveness of ADV and PEG for the treatment of adults with CHB.	ICERs per QALY for a range of comparisons were between £5,994 and £16,569, and within the range considered by NHS decision-makers to represent good value for money.

General characteristics of publications

In 25 articles we found, Beutels P (2001)¹⁶ is the first study published and the most up-to-date studies are Luhn M *et al* (2016) and La Torre G *et al* (2016).^{17,18} Articles published for the last five years take up half of the total number. Each year from 2004 to 2011, only one or two papers were released focusing on economic evaluations of hepatitis. 2012 and 2015 appeared to be the most remarkable years as having the most papers published – 4 papers per year. In addition, 80% (n=20) were conducted in Europe while the other articles were from North America, South America and Asia, which had three papers, one paper and one paper respectively. Especially, almost all articles published for the last four years belong to Europe.

The additional concerned factor is whether the article is relevant to immunization or not. Only 20% (n=5) focus on vaccination strategy,^{16,18-21} and La Torre G *et al* (2016) is the most up-to-date. There is a notice-

able number of publications (n=9; 36%) analyzing not only cost- but also clinical-effectiveness.

Quality assessment of publications

Each article is examined carefully using PRISMA checklist. Based on the number of items ticked, those articles could be divided into various quality categories. Up to now, however, there is no standard for classification that has been set out. Therefore, a frame of points is recommended to set them into categories. An article acquires the “Excellent” if it has at least 25 points and the “Very bad” if it is under 10 points. The last three categories which are “Bad”, “Intermediate” and “Good” could be gained when holding 10 to 14, 15 to 19 and 20 to 24 ticked items respectively.

As presented in Table 2, approximately three-fourth of articles (n=18; 72%) are classified in “Intermediate”, following by “Bad” with 5 papers (20%). The categories “Very Bad” and “Good” share the last two papers.

Table 1: General characteristics of included studies (n=25) (continued)

Record No.	Authors	Continent	Assessment field	Types of disease	Objectives	Results
11	Beutels P (2001) (16)	Europe	CEA	HCV	To review the economic evaluations of hepatitis B immunization published between 1994 and 2000.	In areas of low, intermediate and high endemicity, universal vaccination seems justifiable on the basis of economic evaluation. In countries of very low endemicity economic evaluations have yielded contradictory results.
12	Smith-Palmer J <i>et al.</i> (2015) (30)	Europe	CEA	HCV	To examine the clinical, economic and quality of life benefits associated with achieving SVR.	Medical costs for patients achieving SVR are 13-fold lower than patients not achieving SVR.
13	San Miguel R <i>et al.</i> (2014) (31)	Europe	CCEA	HCV	To analyze the published economic evaluation studies that included the new protease inhibitors associated with PEG plus RBV in patients with CHC.	Most of the options evaluated on a naïve population presented ICERs below the acceptability threshold. The same occurred in the pre-treated population.
14	John-Baptiste A <i>et al.</i> (2012) (26)	North America	CEA	HCV	To determine the cost effectiveness of hepatitis C interventions targeting substance users and other groups with a high proportion of substance users.	ICERs ranged from dominant to \$US603,352 per QALY. Screening and treatment interventions were cost-effective.
15	Tandon P <i>et al.</i> (2010) (22)	North America	CCEA	HCV	To evaluate the effectiveness, safety and cost-effectiveness of G-CSF versus PEG dose reduction for HCV treatment of naïve adults.	G-CSF is not cost-effective.
16	Hartwell D <i>et al.</i> (2011) (32)	Europe	CCEA	HCV	To assess the clinical- and cost-effectiveness of PEG plus RBV for treatment of chronic HCV in three subgroups.	Treatment with PEG-α in the subgroups of patients will yield QALY gains, without excessive increase in cost, and may be cost saving in some situations.
17	Shepherd J <i>et al.</i> (2007) (37)	Europe	CCEA	HCV	To assess the clinical- and cost-effectiveness of PEG and IFN and RBV for the treatment of CHC.	Early treatment and watchful waiting strategies are associated with acceptable cost per QALY estimate.
18	Shepherd J <i>et al.</i> (2004) (38)	Europe	CCEA	HCV	To assess the clinical- and cost-effectiveness of PEG combined with RBV for the treatment of CHC.	PEG is cost-effective in both monotherapy and dual therapy, with cost per QALY remaining under £30,000.
19	Luhnen M <i>et al.</i> (2016) (17)	Europe	CEA	HCV	To compare health EE of sofosbuvir for the treatment of CHC.	The treatment combination of sofosbuvir with PEG and RBV with the comparison with the old standard of care is cost-effective.

It is dissatisfied that none of papers achieve the “Excellent”. Seventeen is the most popular point gained by seven papers (28%). Noticeably, the only one²² article attained the “Good” grips 22 points.

On the other hand, among 27 marked items, there are four items perfectly obtained by all 25 articles, which are “Title”, “Abstract”, “Results of individual studies” and “Summary the evidence”. On the contrary, when being obtained by only one or even no paper, four items “Data items”, “Summary measures”, “Risk of bias across studies” and “Risk of bias within studies” are assessed to be unqualified. The number of articles get point in each item seems to be diffused but mainly oscillating in the range of 15 to 24.

DISCUSSION

When using PRISMA guidelines for assessing included systematic reviews, another concern about quality of individual seven sections is raised over the quality of items. Similar to item assessment, this research gives a recommendation for section assessment. A section is appraised to be good if it has over half of good items involved. According to this type of assessing, there should be an awareness that quality of sections in individual article is diverse.

In consequence, “Titles” and “Discussion” are the two sections that are accomplished excellently (n=25; 100%). “Abstract”, however, gains 60% (n=15) of articles. This section is divided into twelve particles which should be included in, most of publications, however, achieve only six to nine per twelve. In particular, five articles do not contain “Abstract”, others focus mainly on objectives, participants and results. Only one article includes limitations in “Abstract”, and approximate half of them focus on other particles.

“Introduction” is appraised to be good in 92% (n=23) of studies. Participants, Interventions, Comparisons, Outcomes and Study design (PICOS) is the most essential part that should be included in this section. Nonetheless, only four of twenty-five articles (16%) present a consummate PICOS (23-26). Jones J *et al* (2009) is the only one that does not contain objectives, and La Torre G *et al* (2016) mentions inadequate PICOS. The section Methods, which has ten (40%) papers, are unqualified. In Methods, included studies concentrate chiefly on databases sought, years published, and partly on PICOS and key words. However, “Risk of bias” “Summary measures” as well as “Additional analysis” seems to be ignored. “Results” is the lowest-point section with only six papers (24%). While some particles are greatly presented such as “Results of individual

Table 1: General characteristics of included studies (n=25) (continued)

Record No.	Authors	Continent	Assessment field	Types of disease	Objectives	Results
20	Geue C <i>et al.</i> (2015) (39)	Europe	CEA	HBCV	To assess existing economic models for HBCV to identify the main methodological differences in modeling approaches.	The overall approach to analyzing the cost-effectiveness of screening strategies was found to be broadly consistent for HBV and HCV.
21	La Torre G <i>et al.</i> (2016) (18)	Europe	CEA	HBV	To conduct a SR of the EE of HBV vaccination, taking into account the studies published in the new millennium.	Studies were concerning EE of UV, regards to low and low-medium income countries. For high income countries, EE focus on the possible implementation of HBV vaccination in particular settings.
22	Crossan C <i>et al.</i> (2015) (40)	Europe	CEA	HCV	To assess the diagnostic accuracy and cost-effectiveness of NITs in patients with CHB.	For HBeAg-positive patients, using Fibroscan was the most cost-effective. For HBeAg-negative patients, strategies excluding NITs were the most-effective
23	Ruggeri M (2012) (33)	Europe	CEA	HCC	To review the available evidence with respect to the cost-effectiveness of key technologies in the prevention HCC.	Incidence is the key parameter which determining the type of technology to be used. Ultrasound alone or in association with AFP technology is the most cost-effective and the use of computed tomography gives controversial results.
24	Tu HA <i>et al.</i> (2009) (21)	Europe	CEA	HBV	To give a SR on HBV vaccination, with a focus on developing countries and EE.	It is cost-effective to implement universal immunization against HBV.
25	Shepherd J <i>et al.</i> (2005) (34)	Europe	CCEA	HCV	To assess the clinical- and cost-effectiveness of PEG- α (2a and 2b) combine with RBV in previously untreated patients with moderate to severe CHC.	The ICER per QALY for PEG dual therapy compares with non-PEG dual therapy was £12,123, representing good value for the money.

ADV: adefovir dipivoxil

EFV: entecavir

AFP: alpha fetoprotein

G-CSF: granulocyte colony-stimulating factor

CCEA: clinical- and cost-effectiveness analysis

HAV: hepatitis A virus

CEA: cost-effectiveness analysis

HBV: hepatitis B virus

CHB: chronic hepatitis B

UV: universal vaccinat

EE: economic evaluations

HCC: hepatocellular carcinoma

HBsAg: hepatitis B surface antigen

PEG: peginterferon

HBeAg: hepatitis B envelope antigen

QALY: quality-adjusted-life-year

CHC: chronic hepatitis C

HCV: hepatitis C virus

HBCV: hepatitis B virus and hepatitis

C virus

ICER: incremental cost-effectiveness ratio

RBV: ribavirin

IFN: interferon

SR: systematic review

LFC: liver fibrosis and cirrhosis

SVR: sustained virologic response

NHS: national health service

TDF: tenofovir difumarate

NIT: noninvasive test

Table 2: Results of quality analysis (n=25)

Item	n	%	Item	n	%	Classification	N	%
0						Excellent	-	-
1	3	12	15	2	8	Good	1	4
2	-	-	16	-	-	Intermediate	18	72
3	-	-	17	3	12	Bad	5	20
4	1	4	18	1	4	Vary bad	1	4
6	1	4	20	1	4	Section	N	%
7	-	-	21	2	8	Title	25	100
8	-	-	22	-	-	Abstract	15	60
9	-	-	23	1	4	Introduction	21	84
10	-	-	24	1	4	Methods	10	40
11	1	4	25	4	16	Results	6	24
12	-	-	26	-	-	Discussion	25	100
13	-	-	27	-	-	Finding	20	80

studies” and “Numbers of included studies”, others are not paid attention to. It is sorrowful that many articles omit to illustrate selection process by a flow diagram as well as add citations to the text. “Risk of bias” and “Additional analysis” are once again overlooked. Despite being a good section, some particles in Discussion should be recovered. The number of publications presenting the consideration to crucial groups and implications for future research is rather low, which are 56% (n=14)^{16-19,21,26-34} and 72% (n=18)^{16-19,21-24,28,29,31,33-39} respectively. Limitations should also be considered due to its lack of good publications. In addition, 80% (n=20) of articles list their source of funding as well as conflict of interests, however, only 16 of them mention the role of funders.

The current study has several limitations that should be acknowledged with the regard to interpretation of the findings. Our review was impeded by a number of assumptions and uncertainties. We restricted our assessment of cost-effectiveness to published evidence. Gray or unpublished literature is unlikely to have undergone peer review and its methodological quality cannot be guaranteed. The number of database sought out was more modest than other reviews, and language constraint was also applied, so that there might be a series of publications that was ignored. As criteria in selection and assessment were set up based on subjective authors’ points of view, quality of included studies may not be appraised appropriately. Moreover, during statistical analyzing as well as text presenting, errors could be made clumsily.

CONCLUSION

This study was designed to be a systematic review of systematic reviews using PRISMA guidelines to bring out an overview of quality of systematic reviews of economic evaluation in hepatitis. During the period of research, PRISMA was proved to be an effective instrument due to its important role in assessing included reviews. As a consequence, even though there are various systematic reviews of economic evaluation published, their qualities are not synchronous and there is a modesty in quantity of studies which was really carried out based on PRISMA. This study makes a suggestion to future researches that rather focus on PRISMA guidelines in study design and report appearance.

After searching times and times, we propose that our study is the first systematic review using PRISMA for assessment, leading to face to many difficulties in article classification. A future research is in need to map out a frame for section assessment as well as classify articles into certain categories according to individuals’ quality.

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CONFLICT OF INTEREST

There is no conflict of interest regarding to the publication of this article to declare.

ABBREVIATION USED

PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analyses; CONSORT: Consolidated Standards of Reporting Trials; STARD: Standards for Reporting Diagnostic accuracy studies; ADV: adefovir dipivoxil; AFP: alpha fetoprotein; CCEA: clinical- and cost-effectiveness analysis; CEA: cost-effectiveness analysis; CHB: chronic hepatitis B; CHC: chronic hepatitis C; EE: economic evaluations; EFV: entecavir; G-CSF: granulocyte colony-stimulating factor; HAV: hepatitis A virus; HBV: hepatitis B virus; HBCV: hepatitis B virus and hepatitis C virus; HBeAg: hepatitis B evolope antigen; HBsAg: hepatitis B surface

antigen; HCC: hepatocellular carcinoma; HCV: hepatitis C virus; ICER: incremental cost-effectiveness ratio; IFN: interferon; NHS: national health service; LFC: liver fibrosis and cirrhosis; NIT: noninvasive test; PEG: peg-interferon; SR: systematic review; QALY: quality-adjusted-life-year; RBV: ribavirin; SVR: sustained virologic response; TDF: tenofovir difumarate; UV: universal vaccination.

REFERENCES

1. Bowater RJ, Abdelmalik SM, Lilford RJ. Efficacy of adjuvant chemotherapy after surgery when considered over all cancer types: a synthesis of meta-analyses. *Annals of surgical oncology*. 2012. <https://doi.org/10.1245/s10434-012-2388-1> PMID:22644506.
2. Bowater RJ, Stirling SA, Lilford RJ. Is antibiotic prophylaxis in surgery a generally effective intervention?: testing a generic hypothesis over a set of meta-analyses. *Annals of surgery*. 2009. <https://doi.org/10.1097/SLA.0b013e318199f202> PMID:19300236.
3. Clark M, Hutton J. Economic evaluation of magnetic resonance imaging: results of a systematic review of the published literature. *Annual Meeting of International Society of Technology Assessment In Health Care*. 1997.
4. Deery C. The economic evaluation of pit and fissure sealants. *Int J Paediatr Dent*. 1999. <https://doi.org/10.1111/j.1365-263X.1999.00141.x> PMID:10815581.
5. Delaney B, Moayyedi P, Wilson S, Hobbs R. The Dyspepsia Trials Collaborators’ Group. Abstract Workshops Science Session International Cochrane Collaboration.
6. Jefferson T, Demicheli V, Falck-Ytter Y, Vailant-Bejot L, Davenport D, Altman D, et al. Quality of systematic reviews of economic evaluations in health care. *JAMA*. 2002;287(16):2147-2154 (Print).
7. Kenneth F Schulz, Douglas G Altman, David Moher, The CONSORT Group. CONSORT 2010 Statement: updated guidelines for reporting parallel group randomised trials. 2010.
8. Bossuyt PM, Reitsma JB, Bruns DE, Gatsonis CA, Glasziou PP, Irwig LM, et al. The STARD statement for reporting studies of diagnostic accuracy: explanation and elaboration. 2003.
9. David Moher, Alessandro Liberati, Jennifer Tetzlaff, Douglas G. Altman, The PRISMA Group. Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. 2009.
10. Prisma-statement.org [Web site]. Ottawa Hospital Research Institute, University of Oxford. c2015-01 [cited 2015]. Available from: <http://www.prisma-statement.org/>.
11. Blades CA, Culyer AJ, Walker AM. Health service efficiency: appraising the appraisers: a critical review of economic appraisal in practice. *Soc Sci Med*. 1987. [https://doi.org/10.1016/0277-9536\(87\)90169-9](https://doi.org/10.1016/0277-9536(87)90169-9).
12. Brown ML, Fintor L. Cost-effectiveness of breast cancer screening: preliminary results of a systematic review of the literature. *Res Policy*. 1993. <https://doi.org/10.1007/bf00662136>.
13. Hemming K, Pinkney T, Futaba K, Pennant M, Morton DG, Lilford RJ. A systematic review of systematic reviews and panoramic meta-analysis: staples versus sutures for surgical procedures. *PloS one*. 2013;8(10):e75132. <https://doi.org/10.1371/journal.pone.0075132> PMID:24116028 PMCID:PMC3792070.
14. Ernst E, P H Canter. A systematic review of systematic reviews of spinal manipulation. *JR Soc Med*. 2006. <https://doi.org/10.1258/jrsm.99.6.279> <https://doi.org/10.1258/jrsm.99.4.192> PMID:16574972.
15. Ernst E. A systematic review of systematic reviews of homeopathy. *Br J Clin Pharmacol*. 2002. <https://doi.org/10.1046/j.1365-2125.2002.01699.x> PMID:12492603 PMCID:PMC1874503.
16. Beutels P. Economic evaluations of hepatitis B immunization: a global review of recent studies (1994-2000). *Health economics*. 2001;10(8):751-74. <https://doi.org/10.1002/hec.625> PMID:11747055.
17. Luhn M, Waffenschmidt S, Gerber-Grote A, Hanke G. Health Economic Evaluations of Sofosbuvir for Treatment of Chronic Hepatitis C: a Systematic Review. *Applied health economics and health policy*. 2016. <https://doi.org/10.1007/s40258-016-0253-2> PMID:27329481.
18. La Torre G, Mannocci A, Saule R, Colamesta V, Meggiolaro A, Mipatrini D, et al. Economic evaluation of HBV vaccination: A systematic review of recent pub-

- lications (2000-2013). Human vaccines and immunotherapeutics. 2016;1:1-13. <https://doi.org/10.1080/21645515.2016.1166328>.
19. De Soarez PC, Sartori AM, Santos A, Itria A, Novaes HM, Martelli CM. Contributions from the systematic review of economic evaluations: the case of childhood hepatitis A vaccination in Brazil. *Cadernos de Saude Publica*. 2012;28(2):211-28. <https://doi.org/10.1590/S0102-311X2012000200002> PMID:22334390.
 20. Anonychuk AM, Tricco AC, Bauch CT, Pham B, Gilca V, Duval B, et al. Cost-effectiveness analyses of hepatitis A vaccine: a systematic review to explore the effect of methodological quality on the economic attractiveness of vaccination strategies. *Pharmaco Economics*. 2008;26(1):17-32. <https://doi.org/10.2165/00019053-200826010-00003>.
 21. Tu HA, Woerdenbag HJ, Kane S, Riewpaiboon A, van Hulst M, Postma MJ. Economic evaluations of hepatitis B vaccination for developing countries. *Expert Review of Vaccines*. 2009;8(7):907-20. <https://doi.org/10.1586/erv.09.53> PMID:19538116.
 22. Tandon P, Doucette K, Fassbender K, Vandermeer B, Durec T, Dryden DM. Granulocyte colony-stimulating factor for hepatitis C therapy-associated neutropenia: systematic review and economic evaluation. *Journal of Viral Hepatitis*. 2011;18(7):e381-93. <https://doi.org/10.1111/j.1365-2893.2011.01445.x> PMID:21692951.
 23. Hahne SJ, Veldhuijzen IK, Wiessing L, Lim TA, Salminen M, Laar M. Infection with hepatitis B and C virus in Europe: a systematic review of prevalence and cost-effectiveness of screening. *BMC Infectious Diseases*. 2013;13:181. <https://doi.org/10.1186/1471-2334-13-181> PMID:23597411 PMCid:PMC3716892.
 24. Sun X, Qin WX, Li YP, Jiang XH. Comparative cost-effectiveness of antiviral therapies in patients with chronic hepatitis B: a systematic review of economic evidence. *Journal of Gastroenterology and Hepatology*. 2007;22(9):1369-77. <https://doi.org/10.1111/j.1440-1746.2007.05068.x> PMID:17716343.
 25. Takeda A, Jones J, Shepherd J, Davidson P, Price A. A systematic review and economic evaluation of adefovir dipivoxil and pegylated interferon-alpha-2a for the treatment of chronic hepatitis B. *Journal of Viral Hepatitis*. 2007;14(2):75-88. <https://doi.org/10.1111/j.1365-2893.2006.00808.x> PMID:17244247.
 26. John-Baptiste A, Yeung MW, Leung V, van der Velde G, Krahn M. Cost effectiveness of hepatitis C-related interventions targeting substance users and other high-risk groups: a systematic review. *Pharmaco Economics*. 2012;30(11):1015-34. <https://doi.org/10.2165/11597660-000000000-00000> PMID:23050771.
 27. Buti M, Oyaguez I, Lozano V, Casado MA. Cost effectiveness of first-line oral antiviral therapies for chronic hepatitis B : a systematic review. *Pharmaco Economics*. 2013;31(1):63-75. <https://doi.org/10.1007/s40273-012-0009-2> PMID:23329593.
 28. Jones J, Shepherd J, Baxter L, Gospodarevskaya E, Hartwell D, Harris P, et al. Adefovir dipivoxil and pegylated interferon alpha for the treatment of chronic hepatitis B: an updated systematic review and economic evaluation. *Health technology assessment (Winchester, England)*. 2009;13(35):1-172, iii. <https://doi.org/10.3310/hta13350>.
 29. Shepherd J, Jones J, Takeda A, Davidson P, Price A. Adefovir dipivoxil and pegylated interferon alfa-2a for the treatment of chronic hepatitis B: a systematic review and economic evaluation. *Health technology assessment (Winchester, England)*. 2006;10(28):iii-iv, xi-xiv, 1-183.
 30. Smith-Palmer J, Cerri K, Valentine W. Achieving sustained virologic response in hepatitis C: a systematic review of the clinical, economic and quality of life benefits. *BMC Infectious Diseases*. 2015;15:19. <https://doi.org/10.1186/s12879-015-0748-8> PMID:25596623 PMCid:PMC4299677.
 31. San Miguel R, Gimeno-Ballester V, Mar J. Cost-effectiveness of protease inhibitor based regimens for chronic hepatitis C: a systematic review of published literature. *Expert Review of Pharmacoeconomics and Outcomes Research*. 2014;14(3):387-402. <https://doi.org/10.1586/14737167.2014.906307> PMID:24758525.
 32. Hartwell D, Jones J, Baxter L, Shepherd J. Peginterferon alfa and ribavirin for chronic hepatitis C in patients eligible for shortened treatment, re-treatment or in HCV/HIV co-infection: a systematic review and economic evaluation. *Health technology assessment (Winchester, England)*. 2011;15(17):i-xii, 1-210. <https://doi.org/10.3310/hta15170> PMID:21473834 PMCid:PMC4780942.
 33. Ruggeri M. Hepatocellular carcinoma: cost-effectiveness of screening. A systematic review. *Risk management and healthcare policy*. 2012;5:49-54. <https://doi.org/10.2147/RMHP.S18677> PMID:22826645 PMCid:PMC3401970.
 34. Shepherd J, Brodin HF, Cave CB, Waugh NR, Price A, Gabbay J. Clinical- and cost-effectiveness of pegylated interferon alfa in the treatment of chronic hepatitis C: a systematic review and economic evaluation. *International Journal of Technology Assessment in Health Care*. 2005;21(1):47-54. <https://doi.org/10.1017/S0266462305050063> PMID:15736514.
 35. Luyten J, Beutels P. Costing infectious disease outbreaks for economic evaluation: a review for hepatitis A. *Pharmaco Economics*. 2009;27(5):379-89. <https://doi.org/10.2165/00019053-200927050-00003> PMID:19586076.
 36. Crossan C, Tsochatzis EA, Longworth L, Gurusamy K, Davidson B, Rodriguez-r Alvarez M, et al. Cost-effectiveness of non-invasive methods for assessment and monitoring of liver fibrosis and cirrhosis in patients with chronic liver disease: systematic review and economic evaluation. *Health technology assessment (Winchester, England)*. 2015;19(9):1-409, v-vi. <https://doi.org/10.3310/hta19090> PMID:25633908 PMCid:PMC4781028.
 37. Shepherd J, Jones J, Hartwell D, Davidson P, Price A, Waugh N. Interferon alpha (pegylated and non-pegylated) and ribavirin for the treatment of mild chronic hepatitis C: a systematic review and economic evaluation. *Health technology assessment (Winchester, England)*. 2007;11(11):1-205, iii. <https://doi.org/10.3310/hta11110> PMID:17346498.
 38. Shepherd J, Brodin H, Cave C, Waugh N, Price A, Gabbay J. Pegylated interferon alpha-2a and -2b in combination with ribavirin in the treatment of chronic hepatitis C: a systematic review and economic evaluation. *Health technology assessment (Winchester, England)*. 2004;8(39):iii-iv, 1-125. <https://doi.org/10.3310/hta8390> PMID:15461877.
 39. Geue C, Wu O, Xin Y, Heggie R, Hutchinson S, Martin NK, et al. Cost-Effectiveness of HBV and HCV Screening Strategies—A Systematic Review of Existing Modelling Techniques. *PloS One*. 2015;10(12):e0145022. <https://doi.org/10.1371/journal.pone.0145022> PMID:26689908 PMCid:PMC4686364.
 40. Crossan C, Tsochatzis EA, Longworth L, Gurusamy K, Papastergiou V, Thalassinou E, et al. Cost-effectiveness of noninvasive liver fibrosis tests for treatment decisions in patients with chronic hepatitis B in the UK: systematic review and economic evaluation. *Journal of Viral Hepatitis*. 2016;23(2):139-49. <https://doi.org/10.1111/jvh.12469> PMID:26444996 PMCid:PMC5132027.

Appendix: Quality assessment for individual studies (n=25)																											
Section	Items No.	(19)	(35)	(20)	(36)	(23)	(27)	(28)	(24)	(25)	(29)	(16)	(30)	(31)	(26)	(22)	(32)	(37)	(38)	(17)	(39)	(18)	(40)	(33)	(21)	Points	
TITLE																											
• Title	1	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	25
ABSTRACT																											
• Structured summary	2		✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	15
INTRODUCTION																											
• Rationale	3	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	25
• Objectives	4	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	21
METHODS																											
• Protocol and registration	5	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	17
• Eligibility criteria	6	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	18
• Information source	7	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	24
• Search	8	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	15
• Study selection	9	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	19
• Data collection process	10	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	17
• Data items	11						✓																			1	
• Risk of bias in individual studies	12					✓		✓									✓								✓	5	
• Summary measures	13																									-	
• Synthesis of results	14	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	17
• Risk of bias across studies	15															✓										1	
• Additional analysis	16	✓			✓						✓						✓							✓		6	

Section		Ref.																		Points			
Items No.		(19)	(20)	(23)	(27)	(28)	(24)	(25)	(29)	(16)	(30)	(31)	(26)	(22)	(32)	(37)	(38)	(17)	(39)	(18)	(40)		
Appendix: Quality assessment for individual studies (n=25) (continued)																							
RESULTS																							
• Study selection	17	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	23
• Study characteristic	18	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	14
• Risk of bias within studies	19													✓									1
• Results of individuals studies	20	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	25
• Synthesis of results	21						✓							✓	✓							✓	4
• Risk of bias across studies	22																						-
• Additional analysis	23	✓		✓		✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	11
DISCUSSION																							
• Summary of evidence	24	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	25
• Limitations	25	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	19
• Conclusions	26	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	21
FUNDING																							
• Funding	27	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	20
Points		17	15	15	17	17	18	18	13	11	15	22	17	11	7	19	15	14	17	18			
	17	17																					

SUMMARY

- The aim of this study is to appraise qualitatively a range of systematic reviews of economic evaluation in case of hepatitis based on PRISMA guidelines.
- A total of 25 articles researching economic evaluations of hepatitis were identified. Approximately three-fourth of articles (n=18; 72%) are classified in “Intermediate”, following by “Bad” with five papers (20%).
- The categories “Very Bad” and “Good” share the last two papers. None of papers achieves the “Excellent”.

ABOUT AUTHORS

“Quang Vinh Tran, Phuong Hong Le are under-graduated students at Department of Pharmacy Administration, Faculty of Pharmacy, University of Medicine and Pharmacy, Ho Chi Minh, Vietnam. We also work as part-time researcher at Professional Healthcare Management, Education and Research center (ProHES), Ho Chi Minh city, Vietnam

Trung Quang Vo had graduated Doctor of Philosophy Program of Social, Economic and Administrative Pharmacy, Faculty of Pharmacy, Mahidol University, Thailand. I am work as a lecturer at Department of Pharmacy Administration, Faculty of Pharmacy, University of Medicine and Pharmacy, Ho Chi Minh, Vietnam. My areas of interest are Health economics/ Pharmacoeconomics and Outcomes Research; hospital cost analysis, unit cost of medical services, cost of illness, and economic evaluation.”