Systematic Review Article
http://mjiri.iums.ac.ir
Medical Journal of the Islamic Republic of Iran (MJIRI)

Med J Islam Repub Iran. 2022 (1 Sep);36.100. https://doi.org/10.47176/mjiri.36.100

A Systematic Review on the Economic Evaluations Evidence of Enhanced External Counter-Pulsation (EECP) for Managing Chronic Stable Angina

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Received: 15 Nov 2021 Published: 1 Sep 2022

Abstract

Background: Chronic Stable Angina (CSA) does not respond to clinical interventions always. Therefore, enhanced external counter pulsation (EECP) has been approved by the Food and Administration Drug (FDA) as an effective technology. This study aimed to synthesize evidence on the economic evaluation of EECP in managing CSA through a systematic approach.

Methods: In this systematic review study, PubMed/Medline, Cochrane Library, Web of Sciences, Scopus, National Institute for Health Research Journals Library, and the University of York Centre for Review and Dissemination (CRD) were searched. The targeted population was people who suffered from CSA, and the main therapeutic intervention was EECP. The comparators were not limited to any particular ones. Outcomes were changes in the Canadian Cardiovascular Society grading of angina pectoris, quality of life, and any other investigated relevant outcomes in the retrieved studies. The quality of studies was assessed through Philips et al and Joanna Briggs Institute Critical Appraisal tools. We synthesized data through a narrative approach.

Results: We retrieved 7821 studies; among which 3 studies were included in the final phase. Two studies were systematic reviews and the Markov model economic evaluation. Another study was a partial economic evaluation.

Conclusion: All studies only considered direct costs. EECP is a cost-effective technology in managing CSA, however, the sensitivity analysis of the studies showed the cost-effectiveness ratio is varied considerably and further studies are needed to extrapolate its economic value.

Keywords: Cost Benefit Analysis, Heart Failure, Stable Angina, Systematic Review

Conflicts of Interest: None declared
Funding: This study was a part of a research project funded by the Health Management and Economics Research Center affiliated to Iran University of Medical Sciences. The grant number was 97-02-163-33657.

Cite this article as: Rezapour A, Naghdi S, Ghiasvand H, Moradi T, Kabir MJ, Yousefzadeh N. A Systematic Review on the Economic Evaluations Evidence of Enhanced External Counter-Pulsation (EECP) for Managing Chronic Stable Angina. *Med J Islam Repub Iran.* 2022 (1 Sep);36:100. https://doi.org/10.47176/mjiri.36.100

Introduction

Chronic stable angina (CSA) is an initial symptom of coronary artery disease (CAD) that causes pain and discomfort in the chest. It usually occurs in predictable and manageable episodes (1). Stable angina is a prevalent type of cardiovascular diseases (CVDs) arou nd the world. The Global Burden of Disease (GBD) study in 2017 has reported that ~70,969,300 (95% CI: 66,224,100 –75,830,100) people suffered from this problem (2).

Stable angina can lead to a high-cost impact on health systems. Evidence from the United States showed that the

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↑What is "already known" in this topic:
EECP is an effective technology in managing chronic stable angina. However, there is enormous uncertainty around its cost-effectiveness.

→What this article adds:
Through a systematic review; we tried to find any relevant evidence about the economic consideration of EECP. We found a lack of rigorous evidence in this regard, and policymakers need further evidence to consider EECP as a cost-effective technology.

mean total cost for managing stable angina was ~$28,590 per patient (3). Estimations in the United Kingdom showed that stable angina imposes more than £700,000,000 on the National Health Service (NHS) per year (4). In Canada, the total cost for treating CSA was $19,209 per patient per year by the end of 2008 (5).

CSA causes limited physical activities, depression, and subsequently lower quality of life (QoL) (6). Patients in the advanced stages of CSA are experiencing even much lower QoL. Even after treatment, many patients rate their QoL lower than what they have expected (7). Although the aim of the medical therapies for CSA is relieving the symptoms and subsequently improving the QoL, in some cases those interventions are not effective (8-10).

The Canadian Cardiovascular Society has developed a grading indicator to measure how the treatment progression in angina. Enhanced External Counter Pulsation (EECP) is a nonpharmacological intervention in managing stable angina (Class IIb), approved by the Food and Drug Administration (FDA) (11). Also, the European Society of Cardiology guidelines has provided some evidence on the effectiveness of EECP in reliving the symptoms and QoL. However, the guideline highlights that EECP should be considered in symptomatic treatment in those patients with invalidating refractory angina. In addition, in the guideline, any expected treatment effectiveness and QoL improvements have been subjected to further randomized controlled trials (RCTs) (12). This improvement is more evident among those patients in higher classes (e.g. IV) (13).

EECP is provided in an outpatient set-up, and treatment encompasses cyclical inflation and deflation of wrapped cuffs around the calf, lower and higher thigh (14). CSA treatment by using EECP includes 35 sessions per hour for 5 weeks (15). However, according to the physician's diagnosis and depending on the patient's recovery, more treatment sessions may be prescribed by considering patients' safety and effectiveness to achieve the desired result. Even under certain circumstances, the duration of the sessions can be increased to 2 hours for the patient's convenience (16).

CSA can cause adverse effects on the patient's QoL and the health system's financial resources. Therefore, finding rigorous evidence in terms of economic considerations can help policymakers allocate financial resources more reasonably. Economic evaluation implies directives to spend money on the best possible effective health and medical alternatives. Therefore, we aimed to synthesize the current economic evaluation evidence about the cost-effectiveness of EECP in comparison with other comparators in managing CSA.

Methods

Databases and Search Strategies

We searched PubMed/Medline, Cochrane Library, Web of Sciences, Scopus, National Institute for Health Research Journals Library, and the University of York Centre for Review and Dissemination (CRD). We also used the Google Scholar search engine alongside the mentioned databases. We used Medical Sub Heading (Mesh) to find relevant and appropriate terms and expressions for stable angina. The general search strategy for MedLine via PubMed was as follows:

(((((stable angina[Title/Abstract]) OR (chronic angina[Title/Abstract]) OR refractory angina[Title/Abstract])) OR (heart failure diseases[Title/Abstract])) OR (coronary heart disease[Title/Abstract])) AND (Enhanced external counterpulsation [Title/Abstract])) OR (EECP[Title/Abstract]).

Table 1 provides search strategy in the Web of Sciences database and Appendix 1 presents the general employed search strategies for Cochrane Library and Scopus.

Primary Assessment: We used the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) (17) for performing the primary and critical assessments process.

Inclusion Criteria

- *Population:* Patients who have chronic stable angina.
- *Intervention:* EECP, through the standard recommended procedure, including 35 continuous sessions (each session takes 1 hour).
- *Comparator:* A variety of current standard procedures from prescribed medicines, rehabilitation services for cardiac problems, placebo, no-intervention, and cardiac revascularization.
- *Outcomes:* Remission rate, treatment-refractory rate, changes in the severity of angina based on the Canadian Cardiovascular Society grading of angina pectoris, quality of life, hospitalization, and other health care services costs, direct and indirect costs of treatment, incremental cost-effectiveness ratios (ICERs), and any other available reported outcomes.
- *Study Design:* All types of full or partial economic evaluation alongside RCTs, decision-making model-based economic evaluation, and health technology assessment studies, which encompass a systematic review, observational, longitudinal, and cross-sectional studies.
- *Language:* No limitation.
- *Time:* No restriction.

Table 1. Search strategy in the Web of Sciences

Set	Run Search
	Web of Science Search History - " XXXX"
#10	#9 AND #8 DocType=All document types; Language=All languages;
#9	#5 OR #4 OR #3 OR #2 OR #1 DocType=All document types; Language=All languages;
#8	#7 OR #6 DocType=All document types; Language=All languages;
#7	TITLE: ("EECP") DocType=All document types; Language=All languages;
#6	TITLE: ("Enhanced external counterpulsation") DocType=All document types; Language=All languages;
#5	TITLE: ("heart failure diseases") DocType=All document types; Language=All languages;
#4	TITLE: ("coronary heart diseases") DocType=All document types; Language=All languages;
#3	TITLE: ("refractory angina") DocType=All document types; Language=All languages;
#2	TITLE: ("chronic angina") DocType=All document types; Language=All languages;
#1	TITLE: ("stable angina") DocType=All document types; Language=All languages;

[DOI: 10.47176/mjiri.36.100]

Exclusion Criteria

- *Population:* Patients not suffering from CSA.
- *Intervention:* Not using EECP as the main or alternative therapeutic intervention.
- *Comparators:* Not restricted.
- *Outcomes:* Not limited.
- *Study Design:* Case reports, notes, letters to editors, studies on non-human samples.

Critical appraisal

We used Philips et al study for the quality assessment of the model-based economic evaluation (18). We also assessed the quality of other retrieved economic evaluations through the Joanna Briggs Institute Critical Appraisal; Checklist for Economic Evaluations (19). Two team members (S.N. and T.M.) were responsible for the quality appraisal process in compliance with the assessment tools. Any discrepancies were referred to the third reviewer (H.G.H.) to reach a consensus. Appendix 2 (Tables 1 to 4) presents the results of the quality appraisal.

Data Collection

We used the suggested data extraction form by Wijnen et al. (20). We developed the template in an MS Excel spreadsheet and included data on the following topics:

The author's name, year of publication, name of the country, study title, type of economic evaluation (full/partial economic evaluation, decision model/non-decision model, and RCT), population, sampling methods, sample size, cost ratio per unit of effectiveness in the study, cost ratio per unit of quality of life, cost ratio per symptom relief, saved costs, uncertainty/sensitivity analysis (type), discounting rate (general, costs, outcomes), the base case scenario data for both EECP and other comparators (alternatives), policymaking implications, and conclusions on the dominancy of EECP on other comparators/alternatives.

Two team members (N.Y. and A.R.) conducted the data extraction.

Data Synthesis: We synthesized data through a narrative approach**.**

Ethical considerations: This study has been approved by the Research Ethics Committee of Iran University of Medical Sciences (IUMS). (Ethics Code: IR.IUMS.1397.609).

Results

We retrieved a total of 7821 documents from the search of databases and the Google Scholar. After removing the duplicate documents and primary screening, 5 documents remained. Three studies remained in the final phase. Figure 1 shows the study stream by the PRISMA stages.

Table 2 presents the characteristics of studies in the final phase.

Three studies were included in the final phase. Of them, the study by McKenna et al (2010) is a paper in a peer-review journal as a part of a health technology assessment study in 2009. All studies were from the United Kingdom and the United States. Both McKenna et al studies are full model-based economic evaluations. Another study (Lawson) is a partial economic evaluation with a cross-sectional design.

McKenna has adopted the UK NHS as his economic evaluations perspective, with a lifetime horizon. Lawson's study perspective has not been identified; however, due to the study timelines (6 and 12 months), those mentioned timelines are considered as the time horizon. Lawson's study conflict of interest statement has mentioned that one of the authors is a shareholder of an EECP brand machine marketing company in the USA. McKenna's studies have performed a full decision-making cost-utility analysis with a probabilistic sensitivity analysis. It also includes a value of information (VOI) extrapolation because of the lack of robust synthesized evidence in RCTs, longitudinal, or observational studies designs. Lawson's study has used a cost-effectiveness analysis. It considered the change in hospitalization costs due to EECP in treating stable angina as the main outcome.

McKenna's study has obtained the primary data originally from an earlier RCT whose data were collected from experts' elicitation exercises. Lawson's study data are from International EECP Patient Registry (IEPR-II).

Table 3 presents the results of cost-utility and cost-effectiveness analysis, sensitivity analysis, and VOI analysis for McKenna's study.

Table 3 shows that McKenna's studies imply an Incremental Cost-Effectiveness Ratio (ICER) equates to £18,643 for EECP against no treatment as a comparator. Also, these studies have concluded that the EECP can be a cost-effective treatment for stable angina, although there is considerable uncertainty around the calculated ICER. In Lawson's study, the mean annual cost saving per patient was $17,074. The quality appraisal results were very good for studies by McKenna and acceptable for the study by Lawson.

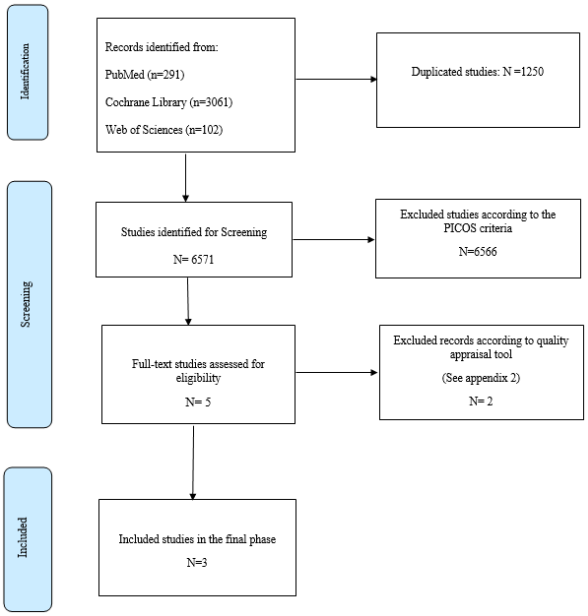

Fig. 1. The screening process of the studies

[DOI: 10.47176/mjiri.36.100]

Table 2. Study characteristics

Author(s)	Year	Funder	Competing Interests	Publication Type	Setting	Patient characteristics	Type of intervention	Control treatment	Eligibility criteria	Study perspective
McKenna C., et al McKenna C., et al	2009 2010	HTA program from NIHR	None	HTA report Article	UK	Adult Patients who have chronic stable angina	EECP through 35 hours treatment over a continues period	No treatment with EECP (Inactive EECP, however patients are receiving their current standard treatment)	Patients with CCS Class I through III, Coronary artery diseases documented, positive test of exercise treadmill	NHS and Personal Social Services (PSS)
Lawson WE., et al.	2015	Not reported	None, however one of the authors is a shareholder in a company where marketing the EECP machine	Article	USA	Not reported	All patients completed at least the recommended 35 hours of EECP treatment over a period of ≥7 weeks.	Hospitalization services	Treated patients with complete 6-month pre-EECP treatment and 12-month follow-up data. All patients completed at least the recommended 35 hours of EECP treatment over a period of ≥7 weeks. All-cause hospitalization data were collected in the 6-month period before	Not reported

Table 2. Continued

Author(s)	Type of EE	Analytic approach	Discount rate (Reference year)	Type and category of costs	Data source of resource use	Data source of effects	Methods of measurement of effects	Methods of valuation of effects	Analyses of uncertainty	Analysis Value of Future Study
McKenna C., et al McKenna C., et al	Cost–Utility Analysis	Probabilistic, Markov decision analytic model	4% (2008)	All direct costs related to capital (buying the machine, depreciation, instalments), Equipment replacement costs, Consumables (for all 35 sessions), Staffing costs	for machine and staffing through a personal communication, for equipment replacement through Vasogenics' current price list	MUST-RCT as the basis of the study and then expert elicitation exercise	Quality Adjusted Life Years Change	At the end of 12 months after EECP intervention the reported QALYs of the study's baseline earlier trial (MUST-trial), and for time over that, the Expert Elicitation Exercise	Monte Carlo simulation	Bayesian Expected Value of Information (the expected net benefit of sampling (ENBS))
Lawson WE., et al.	Cost-Effectiveness Analysis	Calculation the average of cots and effectiveness variables for 6 months and 12 months, and analysing the results by using a Logistic regression	Not reported	Direct costs attributed to hospitalization and EECP	phase II of the International EECP Patient Registry (IEPR-II)	Data from phase II of the International EECP Patient Registry (IEPR-II)	Canadian Cardiovascular Society functional class, Duke Activity Status Index, and number of hospitalizations in the 6 months prior to EECP and in the 6- and 12-month intervals following EECP	Estimates of the changes in annual cost of all-cause hospitalization before and after EECP therapy were calculated by the product of the differences in hospitalization rates in the 6-month interval before and after EECP treatment and estimated hospitalization and physician charges after subtracting the average cost of EECP	Not reported	Not reported

Discussion

EECP as a treatment option for chronic stable angina has been approved by the United States Food and Drug Administration since 1995 (21,22). However, from 1995 to now, to the best of our knowledge, there is only 1 RCT-based evidence on EECP efficacy in the treatment of CSA (23). Subsequently, we have not observed rigorous economic evaluation studies. Due to the paucity in the robust evidence about the long-term effectiveness of EECP on the patients' QoL and total improvement, McKenna et al have tried to use the shorter term effectiveness data (at 2 follow-ups: 6 and 12 months) of an earlier conducted RCT by Arora (23). They have used an expert elicitation exercise to extract the prediction about the probability of change in those short terms QoL for a long-term horizon.

EECP is a recognized technology for managing CSA, but it seems there is not enough evidence on its economic considerations. Therefore, here, we face a cautionary situation on concluding about the impact of EECP on the QoL and its associated cost-effectiveness. However, studies by McKenna are well-designed to address most of the challenges on the lack of evidence in this regard. This study

[DOI: 10.47176/mjiri.36.100]

Table 3. Results of the studies

Author(s)	Year	Costs (CI)	Effects (CI/Range)	Base Case Incremental cost–effectiveness ratios (Range)	Outcome(s) of analyses of sensitivity analyses	Value of Future Study Result	Outcome(s) of analyses of sensitivity analyses	Authors' conclusions	Quality Assessment Results
McKenna C., et al McKenna C., et al	2009 2010	£4,347	£4,347(4,464-5,117)	£18,643 (Best-case scenario £5831 to Worst-case scenario £63,072	The cost-effectiveness of EECP is highly sensitive to the probability of sustaining QoL benefits over time. In addition, reducing the costs of EECP by £1000, can improve the ICER to £14,354, and increasing the cost of EECP by £500, increased the ICER by £2145 per QALY.	Individual patient EVPI for the cost-effectiveness threshold were £971.29, and £440.16 for Scenarios ICERS equate to £20,000 and £30,000. Also, the population EVPI for mentioned cost-effectiveness thresholds were: £107,556,668, and £48,741,220. Further research in this area is likely to be of significant value	The cost-effectiveness of EECP is highly sensitive to the probability of sustaining QoL benefits over time. In addition, reducing the costs of EECP by £1000, can improve the ICER to £14,354, and increasing the cost of EECP by £500, increased the ICER by £2145 per QALY	The results from a single randomised controlled trial (MUST-EECP) do not provide firm evidence of the clinical effectiveness of EECP in refractory stable angina or in heart failure. High-quality studies are required to investigate the benefits of EECP, whether these outweigh the common adverse effects and its long-term cost-effectiveness in terms of quality of life benefits.	Good Good
Lawson WE., et al.	2015	$4880	annual cost savings/patient of $17 074	Not reported	Not reported	Not reported	Not reported	hospitalization and physician charge in the United States was equal to $ 17 995 , and the average EECP treatment cost was $4880	Acceptable

contains significant aspects of the decision-making model for EECP impact on managing stable angina, including length of time horizon, suitable perspective, and rigorous data management, and using probabilistic sensitivity analysis. However, transferability of its results to other contexts, particularly developing countries, does not seem like a straightforward and clear process (20). It is more important to make sure that evidence is not very sensitive to the input parameters changes. In McKenna's studies, we can observe a meaningful change in the ICER attributed to the change in the main inputs parameters to the model. Furthermore, their VOI analysis showed that we might still need further studies to investigate the economic considerations of EECP in managing CSA (16). Lawson's study had a low quality, and because of its cross-sectional design, it does not cover the main economic evaluation targeted parameters (QoL and ICER). Therefore, it is hard to attain robust conclusions about the economic considerations of EECP in managing CSA.

Allocating financial resources to make a health or medical technology, intervention, medicine, or procedure affordable and accessible for the general population through public financing or social/national health insurance requires economic evaluation based on evidence. However, about the EECP and its benefits for patients diagnosed with CSA, the current evidence is probably not convincing enough to expand the benefit package to cover it.

Limitations

Several limitations of our study are worth mentioning. First, the included studies were limited to a few studies. Another limitation of this review was that unpublished studies were not identified by our literature search.

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Conclusion

From an economic evaluation perspective, EECP is one of those technologies that have not been studied enough, despite its importance. The results from the included studies in this review are limited in terms of the generalizability of the results. In addition, there are differences in terms of the cost level in different countries. Therefore, we need to conduct further studies to understand the cost-effectiveness of EECP in the treatment of CSA.

Acknowledgment

The authors would like to thank the manager and staff of Health Management and Economics Research Center for their great supports during the study conduction.

Ethical Approval

This study has been approved by the Research Ethics Committee of Iran University of Medical Sciences (IUMS). The Ethics Code: IR. IUMS.1397.609.

List of abbrevations

Chronic Stable Angina (CSA)
Enhanced External Counter pulsation (EECP)
Food and Administration Drug (FDA)
Coronary Artery Diseases (CAD)
Cardio-Vascular Diseases (CVDs)
United States (US)
United Kingdom (UK)
National Health Service (NHS)
Quality of Life (QoL)
Canadian Cardiovascular Society (CCS)
Centre for Review and Dissemination (CRD)
Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA)
Incremental Cost-Effectiveness Ratios (ICERs)
Randomized Control Trials (RCTs)
Health Technology Assessment (HTA)

Conflict of Interests

The authors declare that they have no competing interests.

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[DOI: 10.47176/mjiri.36.100]

Appendix 1. Search Strategy by Databases

- Scopus:

(TITLE-ABS-KEY ("stable angina") OR TITLE-ABS-KEY ("chronic angina") OR TITLE-ABS-KEY ("refractory angina") OR TITLE-ABS-KEY ("coronary heart diseases") AND TITLE-ABS-KEY ("enhanced external counterpulsation") OR TITLE-ABS-KEY ("EECP"))

- Cochrane Library:
  Results: 3061
- #1 stable angina
- #2 chronic angina
- #3 refractory angina
- #4 enhanced counterpulsation therapy
- #5 EECP
- #1 OR #2 OR #3 AND #4 OR #5

Appendix 2. Result of Quality Assessment

Table 1. Results of Quality Assessment for McKenna et al. Study by Using Philips et al. for model based Economic Evaluation

Row	Item	Reviewer No.1	Reviewer No.2
		Philips et. Al Checklist	
		McKenna C., et al	McKenna C., et al
1	Is there a clear statement of the decision problem?	Yes	Y
2	Is the objective of the model specified and consistent with the stated decision problem?	Yes	Y
3	Is the primary decision maker specified?	Yes	Y
4	Is the perspective of the model stated clearly?	Yes	Y
5	Are the model inputs consistent with the stated perspective?	Yes	Y
6	Has the scope of the model been stated and justified?	Yes	Y
7	Are the outcomes of the model consistent with the perspective, scope and overall objective of the model?	Yes	Y
8	Is the structure of the model consistent with a coherent theory of the health condition under evaluation?	Yes	N
9	Are the sources of the data used to develop the structure of the model specified?	Yes	Y
10	Are the causal relationships described by the model structure justified appropriately?	No	N
11	Are the structural assumptions transparent and justified?	Yes	Uncertain
12	Are the structural assumptions reasonable given the overall objective, perspective and scope of the model?	Yes	Uncertain
13	Is there a clear definition of the options under evaluation?	Yes	Y
14	Have all feasible and practical options been evaluated?	No	Y
15	Is there justification for the exclusion of feasible options?	Yes	Y
16	Is the chosen model type appropriate given the decision problem and specified casual relationships within the model?	Yes	Y
17	Is the time horizon of the model sufficient to reflect all important differences between the options?	Yes	Y
18	Are the time horizon of the model and the duration of treatment described and justified?	No	Uncertain
19	Do the disease states (state transition model) or the pathways (decision tree model) reflect the underlying biological process of the disease in question and the impact of interventions?	Yes	Y
20	Is the cycle length defined and justified in terms of the natural history of disease?	Yes	Y
21	Are the data identification methods transparent and appropriate given the objectives of the model?	Yes	Y
22	Where choices have been made between data sources are these justified appropriately?	UNC	Y
23	Has particular attention been paid to identifying data for the important parameters of the model?	Yes	Y
24	Has the quality of the data been assessed appropriately?	UNC	Uncertain
25	Where expert opinion has been used are the methods described and justified?	Yes	Y
26	Is the data modelling methodology based on justifiable statistical and epidemiological techniques?	Yes	Y
27	Is the choice of baseline data described and justified?	Yes	Y
28	Are transition probabilities calculated appropriately?	Yes	Y
29	Has a half-cycle correction been applied to both costs and outcomes?	NA	NA
30	If not, has the omission been justified?	NA	NA
31	If relative treatment effects have been derived from trial data, have they been synthesised using appropriate techniques?	Yes	Y
32	Have the methods and assumptions used to extrapolate short-term results to final outcomes been documented and justified?	Yes	Y
33	Have alternative extrapolation assumptions been explored through sensitivity analysis?	Yes	Y
34	Have assumptions regarding the continuing effect of treatment once treatment is complete been documented and justified?	UNC	Y
35	Have alternative assumptions regarding the continuing effect of treatment been explored through sensitivity analysis	Yes	Y

[DOI: 10.47176/mjiri.36.100]

Table 1. Continued

Row	Item	Reviewer No.1	Reviewer No.2
		Philips et. Al Checklist	
		McKenna C., et al	McKenna C., et al
36	Are the costs incorporated into the model justified?	Yes	Y
37	Has the source for all costs been described?	Yes	Y
38	Have discount rates been described and justified given the target decision maker?	Yes	Y
39	Are the utilities incorporated into the model appropriate?	Yes	Y
40	Is the source of utility weights referenced?	Yes	Y
41	Are the methods of derivation for the utility weights justified?	Yes	Y
42	Have all data incorporated into the model been described and referenced in sufficient detail?	Yes	Y
43	Has the use of mutually inconsistent data been justified (i.e. are assumptions and choices appropriate)?	Yes	Y
44	Is the process of data incorporation transparent?	Yes	Y
45	If data have been incorporated as distributions, has the choice of distributions for each parameter been described and justified?	UNC	N
46	If data have been incorporated as distributions, is it clear that second order uncertainty is reflected?	UNC	Y
47	Have the four principal types of uncertainty been addressed?	No	Y
48	If not, has the omission of particular forms of uncertainty been justified?	No	Y
49	Have methodological uncertainties been addressed by running alternative versions of the model with different methodological assumptions?	No	Y
50	Is there evidence that structural uncertainties have been addressed via sensitivity analysis?	No	Y
51	Has heterogeneity been dealt with by running the model separately for different subgroups?	No	Y
52	Are the methods of assessment of parameter uncertainty appropriate?	Yes	Y
53	If data are incorporated as point estimates, are the ranges used for sensitivity analysis stated clearly and justified?	NA	NA
54	Is there evidence that the mathematical logic of the model has been tested thoroughly before use?	Yes	Y
55	Are any counterintuitive results from the model explained and justified?	Yes	Y
56	If the model has been calibrated against independent data, have any differences been explained and justified?	UNC	Y
57	Have the results been compared with those of previous models and any differences in results explained?	NA	NA
	Inclusion/Exclusion	Included	Included
	Comments (Inclusion/Exclusion reason(s))	This study contains significant aspects of decision making model for EECP impact on the managing Stable Angina. Length of time horizon, suitable perspective, and rigorous data management, complimentary experts' views to making the partial previous data more valid, using probabilistic sensitivity analysis and value of information technique, alongside good interpretation of results make it convincing enough to be included as a robust economic evidence.	

Table 2. Results of Quality Assessment for Bondesson et al. Study by Using Joanna Briggs Institute Critical Appraisal for Economic Evaluation

Row	Item	Reviewer No. 1	Reviewer No.2
		Bondesson SM., et al.	Bondesson SM., et al.
1	Is there a well-defined question?	Yes	Y
2	Is there comprehensive description of alternatives?	No	N
3	Are all important and relevant costs and outcomes for each alternative identified?	No	N
4	Has clinical effectiveness been established?	No	Y
5	Are costs and outcomes measured accurately?	No	N
6	Are costs and outcomes valued credibly?	No	N
7	Are costs and outcomes adjusted for differential timing?	No	N
8	Is there an incremental analysis of costs and consequences?	No	N
9	Were sensitivity analyses conducted to investigate uncertainty in estimates of cost or consequences?	No	N
10	Do study results include all issues of concern to users?	Yes	N
11	Are the results generalizable to the setting of interest in the review?	No	N
Overall appraisal		Excluded	Excluded
Comments (Inclusion/Exclusion reason(s))		Study doesn't use a conventional economic evaluation design and the results have not been interpreted in valuable perspective. Measuring the cots and valuing the outcomes is partial and not completely address the main concerns of an economic view	Study has some substantial weakness in terms of a full economic evaluation, however it implies on some worthwhile economic implications about EECP

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Table 3. Results of Quality Assessment for Lawnson et al. Study by Using Joanna Briggs Institute Critical Appraisal for Economic Evaluation

Row	Item	Reviewer No. 1	Reviewer No. 2
		Lawson WE. , et al.	Lawson WE. , et al.
1	Is there a well-defined question?	Yes	Y
2	Is there comprehensive description of alternatives?	No	Y
3	Are all important and relevant costs and outcomes for each alternative identified?	No	N
4	Has clinical effectiveness been established?	Yes	Y
5	Are costs and outcomes measured accurately?	Yes	Y
6	Are costs and outcomes valued credibly?	Yes	N
7	Are costs and outcomes adjusted for differential timing?	No	Y
8	Is there an incremental analysis of costs and consequences?	Yes	Y
9	Were sensitivity analyses conducted to investigate uncertainty in estimates of cost or consequences?	No	Y
10	Do study results include all issues of concern to users?	Yes	Y
11	Are the results generalizable to the setting of interest in the review?	No	N
Overall appraisal		Included	Included
Comments (Inclusion/Exclusion reason(s))		Although the study could be categorized as a partial economic evaluation with some limitations in terms of methods and results, however it implies on meaningful results with a good addressing notes on the study limitations.	

Table 4. Results of Quality Assessment for Canadian Medical Advisory Secretariat Study by Using Joanna Briggs Institute Critical Appraisal for Economic Evaluation

Row	Item	Medical Advisory Secretariat	Medical Advisory Secretariat
		Reviewer No.1	Reviewer No.2
1	Is there a well-defined question?	Yes	Y
2	Is there comprehensive description of alternatives?	No	N
3	Are all important and relevant costs and outcomes for each alternative identified?	No	N
4	Has clinical effectiveness been established?	No	N
5	Are costs and outcomes measured accurately?	No	N
6	Are costs and outcomes valued credibly?	No	N
7	Are costs and outcomes adjusted for differential timing?	No	N
8	Is there an incremental analysis of costs and consequences?	No	N
9	Were sensitivity analyses conducted to investigate uncertainty in estimates of cost or consequences?	No	No
10	Do study results include all issues of concern to users?	Yes	No
11	Are the results generalizable to the setting of interest in the review?	No	No
Overall appraisal		Excluded	Excluded
Comments (Inclusion/Exclusion reason(s))		At the first instance, the researchers have developed very good reasoning for conducting an economic evaluation. They have designed a systematic review to retrieve the economic evidence of EECP and management of stable angina, then they could not find any evidence and so developed very initial and partial economic evaluation. In fact, their analysis is more a financial one rather than being an economic one.	

[DOI: 10.47176/mjiri.36.100]