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Cost-effectiveness of coronary artery bypass graft and percutaneous coronary intervention compared to medical therapy in patients with coronary artery disease: a systematic review

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Abstract
Coronary artery disease (CAD) has significant social and economic implications. It is necessary to create tools to identify the most cost-effectiveness treatments, which can assist clinicians in their therapeutic decisions so that the maximum possible benefit is reached with the lowest possible cost. Effectiveness must be measured by final treatment goals in which the most effective interventions are those with the lowest costs. This study is aimed to systematically review and compare the studies conducted on the cost-effectiveness of the three coronary artery disease treatment strategies (medical treatment, percutaneous coronary intervention, and coronary artery bypass graft). In this systematic review, the databases NHS Economic Evaluation Database, Embase, MEDLINE, Science Direct, and Scopus were searched for studies on the cost-effectiveness of coronary artery bypass graft (CABG) and percutaneous coronary intervention (PCI) compared to medical therapy (MT) in patients with coronary artery disease between 1 January 2004 to 30 September 2018. The quality appraisal of the included studies was examined using the Consolidated Health Economics Evaluation Reporting Standards (CHEERS) statement. Out of 186 unique retrievals, 8 studies were included. The results showed that the all studies clearly stated the time horizon of the study and included direct medical costs in their analysis. In addition, in most of the studies, quality-adjusted life years (QALY) were the main outcome used for measuring the effectiveness. The studies reported various ranges of the incremental cost-effectiveness ratio (ICER); accordingly, the highest ratio was observed in the USA ($212,800) for PCI v MT and the lowest ratio was observed in Brazil ($4403) for CABG v MT. Although the results of the studies were different in terms of a number of aspects, such as the viewpoint of the study, the study horizons, and the costs of expenditure items, they reached similar results. Based on the result of the present study, it seems that each three treatment strategies for CAD yielded improvements in QALY.

Keywords Cost-effectiveness · Coronary artery disease · Coronary artery bypass graft · Percutaneous coronary intervention · Medical therapy · Economic evaluation

Introduction

The prevalence of cardiovascular disease is high and increases each year. In the USA, it is estimated that 15.4 million adults have coronary artery disease (CAD), which is responsible for about one in every six deaths. Moreover, in the EU, CAD causes over1.8 million deaths annually. The economic implications of treatments for CAD are increasingly important, as the direct and indirect costs are enormous. CAD is estimated to cost the EU economy almost £60 billion a year, of which 29% is due to losses in productivity, 38% is toward the informal care of people, and around 33% is due to direct healthcare costs. In 2009, production losses due to mortality and morbidity associated with CAD cost the EU £18 billion. In the USA, the total direct and indirect cost estimated for CAD was US$204.4 billion in 2010, of which US $97.2 billion was due to indirect costs related to the loss of productivity or mortality. Furthermore, by 2030, medical costs of CAD are projected to increase by about 100% [1, 2].

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Therapeutic strategies for multivessel coronary artery disease (CAD) with stable angina and preserved ventricular function are medical treatment (MT), percutaneous coronary intervention (PCI), and coronary artery bypass graft (CABG). All three treatment regimens have similar efficacy regarding prevention of myocardial infarction (MI) and death [3, 4]. The difference is that surgical patients have a lower necessity of further revascularization procedures. In this scenario of therapeutic equivalence, the economic consequences of therapeutic strategies are an important outcome. An initial cost of PCI is usually lower than that of CABG; however, additional procedures, even with the use of stents, increase the cost [5–7]. Medical treatment is less costly, although it is usually less effective for alleviating symptoms [8]. This apparent economic advantage can hide the costs applied to the long-term follow-up with repeated examinations, minor clinical interventions, clinical events involving hospitalization, or even percutaneous interventions or a surgical emergency. Thus, the costs of conservative treatment may hide higher costs that interventional treatments do not. Currently, there is a lack of clinical trials comparing economic outcomes of these three therapeutic strategies for CAD. Trials mainly analyze the comparative costs between the surgical and percutaneous intervention or between PCI and MT [6, 9, 10].

The initial cost of medical treatment is usually lower than costs for percutaneous coronary intervention (PCI) and coronary artery bypass graft (CABG), but it is less effective for symptom relief [11]. In addition, in the medium and long terms, patients may require interventions that increase their costs. Therefore, further need for percutaneous interventions in patients who initially underwent angioplasty may impact changes in cost-effectiveness in the long-term follow-up. Considerations regarding the occurrence of major adverse cardiovascular events (MACE) associated with the costs and effectiveness of these strategies may contribute to better decision-making [12]. Due to lack of resources and increased demand especially in the health system, developing solutions and implementing cost-effective interventions can improve allocative efficiency and reduce equality [13–15].

The result of this review can help assist physicians and health managers in the process of decision-making to finance cost-effective interventions for patients with coronary artery disease.

Methods

Literature search

Using a systematic review method, this study was conducted to review published studies on the cost-effectiveness of coronary artery bypass graft and percutaneous coronary intervention compared to medical therapy in patients with coronary artery disease between 1 January 2004 to 30 September 2018. The studies were extracted from the following databases: NHS Economic Evaluation Database, Embase, MEDLINE, Science Direct, and Scopus. The following keywords were used to search the relevant studies: Cost-effectiveness OR cost-utility OR cost-benefit OR cost-minimization OR economic evaluation AND Coronary artery disease AND Coronary Artery Bypass Graft AND Percutaneous coronary intervention AND Medical therapy AND CABG AND PCI AND MT.

Inclusion and exclusion criteria

The following inclusion criteria were used in this study: full publication or available manuscript, assessed percutaneous intervention, coronary artery bypass graft surgery and medical therapy together, conducted a full economic evaluation which valued both costs and benefits of different original treatments; studies which had measured quality-adjusted life years (QALYs), life years gained, or rehospitalization and mortality as their outcomes of the study; studies that assessed coronary artery bypass graft and percutaneous coronary intervention compared to medical therapy in patients with coronary artery disease; and studies published in English during the years from 2004 to 2018.

In this research, studies that do not meet the following criteria were excluded: studies with a partial economic evaluation (such as those evaluating effectiveness, evaluating costs, and assessing the quality of life), not actual cost-effectiveness analysis (e.g., methods or protocol papers), conference paper abstracts where full analysis not available, case reports, and studies with a low quality in methodology based on the CHEERS checklist.

Quality assessment of methodology of the studies

The quality of the methodology of the studies was evaluated using the CHEERS checklist. This checklist contains 24 items that assess the design of economic evaluation studies in terms of the following items: Title and abstract, background and objectives, target population and subgroups, setting and location, study perspective, comparators, time horizon, discount rate, choice of health outcomes, measurement of effectiveness, measurement and valuation of preference-based outcomes estimating resources and costs, currency, price date and conversion, choice of model, assumptions, analytical methods, study parameters, incremental costs and outcomes, characterizing uncertainty, characterizing heterogeneity, discussion, source of funding, and conflicts of interest [16]. After searching the studies, using the CHEERS checklist, the selected studies which were evaluated by two researchers independently screened all citations and abstracts for relevance. The reviewers also solved any disagreement for study inclusion by arbitration and/or by a third reviewer. Full-text retrieval was performed for studies that met all pre-specified inclusion criteria. Studies that were poor in methodology were excluded (Table 1).

Table 1 Results of analysis against CHEERS statement

Author	CHEERS items satisfied	Relevant CHEERS items	Percent satisfied
Brando et al.	22	24	92%
Caruba et al.	24	24	100%
Vieira et al.	12	24	50%
Hlatky et al.	21	24	88%
Weintrab et al.	23	24	96%
Griffin et al.	23	24	96%
Fidan et al.	22	24	92%
Claude et al.	22	24	92%

Due to their nature, not all CHEERS items were relevant to all studies

Data analysis

The selected studies were fully reviewed, and the required data were extracted and summarized using designed tables. The Endnote X7 software was used to organize the studies, read the titles and abstracts, and identify duplicates.

Results

Search result

In the initial search, 186 studies were identified. After screening the studies using the exclusion criteria, 45 studies were selected. Then, through thorough reviews of the full text of studies, 35 studies were excluded from the study and two studies were omitted due to the low quality of methodology checked using the CHEERS checklist [16]. Finally, we selected and assessed the results of eight studies that carried out a full economic evaluation of three intervention care in patients with coronary artery disease [9, 10, 16–21]. Figure 1 presents the results of the systematic review.

Study characteristics

In this study, the characteristics of the studies are summarized as follows: country setting and year of study, disease severity/patient group, comparators, effectiveness measure, model, time period, included cost, sensitivity analysis, discount rate for cost and effectiveness, and the incremental cost-effectiveness ratio (Table 2).

The reviewed studies have been conducted in the USA, Brazil, Switzerland, Mexico, the Czech Republic, Austria, Argentina, Netherlands, England, and Wales. The findings of this review study also indicated that all the studies included direct medical costs in their analysis. They did not include direct non-medical costs and indirect costs. The findings of this review study also show that four studies did not use discount rate and in four studies discount rate was used [10, 17–19]. The quality-adjusted life year (QALY) is the most common outcome used for measuring the effectiveness of interventions. One study used QALY only [18], three studies applied life years gained in addition to QALY [10, 17, 20], one study applied death and MI [21], one study applied QALY and event-free survival [11], one study applied LY [19], and one study applied QOL [20]. Sensitivity analysis is used when dealing with the effect of uncertainty in results and in the generalize ability of results [22–25]. In order to compare different ICER, all of them were inflated by 2017 at an annual rate of 3%. Figure 2 shows that the highest cost and the lowest cost per QALY were observed in the USA ($212,800) for PCI v MT [10] and in Brazil ($4403) for CABG v MT, respectively [20]. The findings of this review study also indicated that all the studies included direct medical costs in their analysis. And they did not include direct non-medical costs and indirect costs.

Discussion

The present study, which systematically reviewed the results of eight valid studies, found which interventions (coronary artery bypass graft, percutaneous coronary intervention, and medical therapy) were cost-effectiveness in patient with coronary artery disease.

The analysis of cost-effectiveness is directly related to the ability to identify the consumption of resources and expenditures related to a health intervention. Evaluation of a particular health intervention should take in to account effectiveness, availability of an intervention, costs, and how a particular intervention is compared with available alternatives. Furthermore, costs of a new medical intervention should contemplate direct costs such as hospital infrastructure, medical equipment, and managerial and human resources involved and indirect costs related to mortality and morbidity. Moreover, in most studies, the utility value was obtained on the basis of literature review, which could lead to an overestimation or underestimation of QALY. The direct comparison of ICERs from different economic evaluations is not recommended. While clinical practice across different healthcare systems may be similar, leading to similar clinical outcomes, a multitude of factors may contribute to varying ICERs across different studies. These factors may include differences in geographic context, perspective, healthcare system costs, policies governing stent use, and methodological aspects, such as the time horizon, health-related utility weights, and modeling methods considered in economic evaluations. In addition, the amount of health expenditure and the opportunity cost vary from country to country; it can prevent us from generalizing the results to other settings.

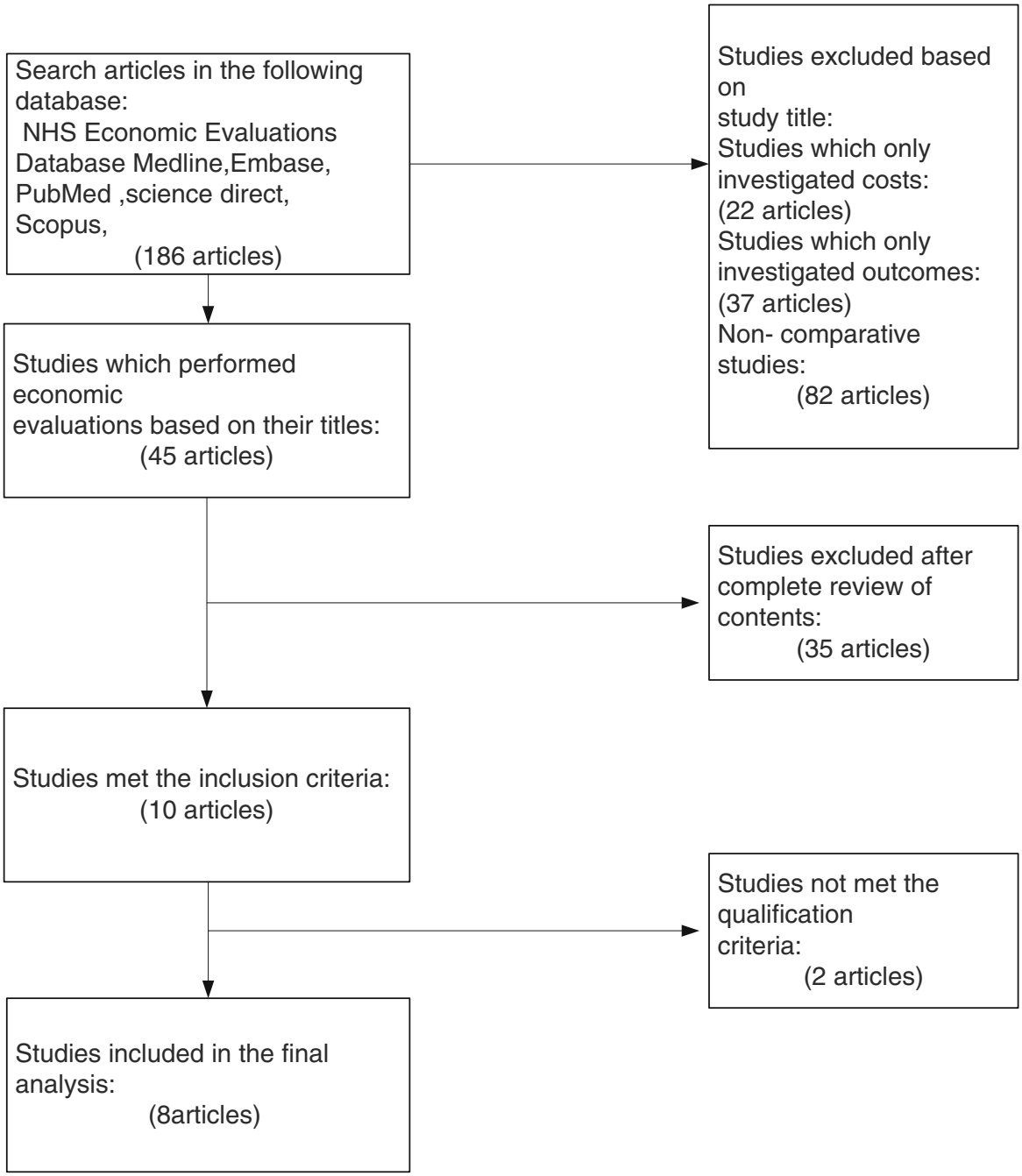

Fig. 1 Result of systematic literature search

Various factors can affect the ICER, such as age and sex, threshold values in different countries, incidence and prevalence of heart diseases, methods of measuring costs and outcomes, and the amount of prices in different countries [26]. However, different countries reported different ICER values, varying from $212,800 for PCI v MT in the USA [10] and $4403 in brazil for CABG v MT [20].

The results of this review study also showed that the target population in the majority of studies was symptomatic patients with coronary artery disease.

The resource analyzed included (1) for patients in the surgical or PCI group and MT, the costs were applied for each patient based on the standard cost of these interventions; (2) in-hospital complications of revascularization procedures; (3) outpatients visits; (4) medications; (5) subsequent hospitalization for cardiovascular disease (MI, unstable angina, stroke, and death); and (6) subsequent revascularization procedures and in-hospital complication. In most reviewed studies, MT was compared with the invasive treatment (PCI and CABG). And in a study, MT was compared with PCI.

Table 2 Description of cost-effectiveness study characteristics

Author	Year	Country	Disease severity/patient group	Comparators	Effectiveness measure	Model	Time period	Included cost	Sensitivity analysis	Discount rate for cost and effectiveness	ICER
Brando et al.	2018	Brazil	Multivessel coronary stenosis greater than 70%	Invasive treatment (PCI or CABG) versus MT	QALY,LY	Trial-based (RCT) survival analyses	5 years	Direct medical cost	Yes	No	ICER PCI v MT 4854 ($/QALYs) CABG v MT 4403 ($/QALYs)
Caruba et al.	2014	Data from studies in: Argentina, Australia, Netherlands, UK, USA	Stable or stabilized unstable angina Excl. studies on acute conditions, and in-stent restenosis patients	MT, PTCA, BMS, DES, CABG	Death, MI	Meta-analysis	1 year, 3 years	Direct medical cost	No	No	No
Vieira et al.	2012	Brazil	Stable multivessel disease with normal systolic ventricular function	MT, PCI, CABG	QALY, event-free survival	Trial-based (RCT) survival analyses	5 years	Direct medical cost	No	No	ICER PCI v MT 37305 ($/event-free QALYs) CABG v MT 15075 ($/event-free QALYs)
Hlatky et al.	2009	USA, Canada, Brazil, Mexico, the Czech Republic, and Austria	Stable coronary artery disease, diabetes	MT, PCI, CABG	LY, QALY (sensitivity analysis only)	Trial-based (RCT) regression and survival analyses	4 years, lifetime	Direct medical cost	Yes	3%	ICER MT versus PCI US$600/life year added for MT ICER CABG versus MT: $47,000/life year added for CABG
Weintrab et al.	2008	USA, Canada	Evidence of myocardial ischemia and coronary artery disease	PCI (most with BMS) versus MT	LY, QALY	Courage trial and survival analyses	3 years	Direct medical cost	Yes	3%	ICER US$168,019/quality-adjusted lifetime for PCI
Griffin et al.	2007	England	ACRE cohort. No exclusion criteria. Both stable and acute presentations. Patients rated as clinically appropriate for CABG, PCI or both	PCI, CABG, MT	QALY	Trial-based (prospective observational) regression analyses	6 years	Direct medical cost	Yes	3/5%	ICER CABG v MT:11000 (£/QALY) (from adjusted values) PCI v MT:47000 (£/QALY) (from adjusted values)
Fidan et al.	2007	England and Wales	AMI, secondary prevention after AMI, stable angina, unstable angina	36 condition treatment scenarios	LY	Cohort-based model (IMPACT)	10 years	Direct medical cost	Yes	3/5%	No
Claude et al.	2004	Switzerland	Elderly patient with chronic angina	Invasive treatment (PCI or CABG) versus MT	QOL	Trial-based (RCT) regression and survival analyses	1 year	Direct medical cost	Yes	No	Incremental costs £6965 to prevent one major event by invasive treatment

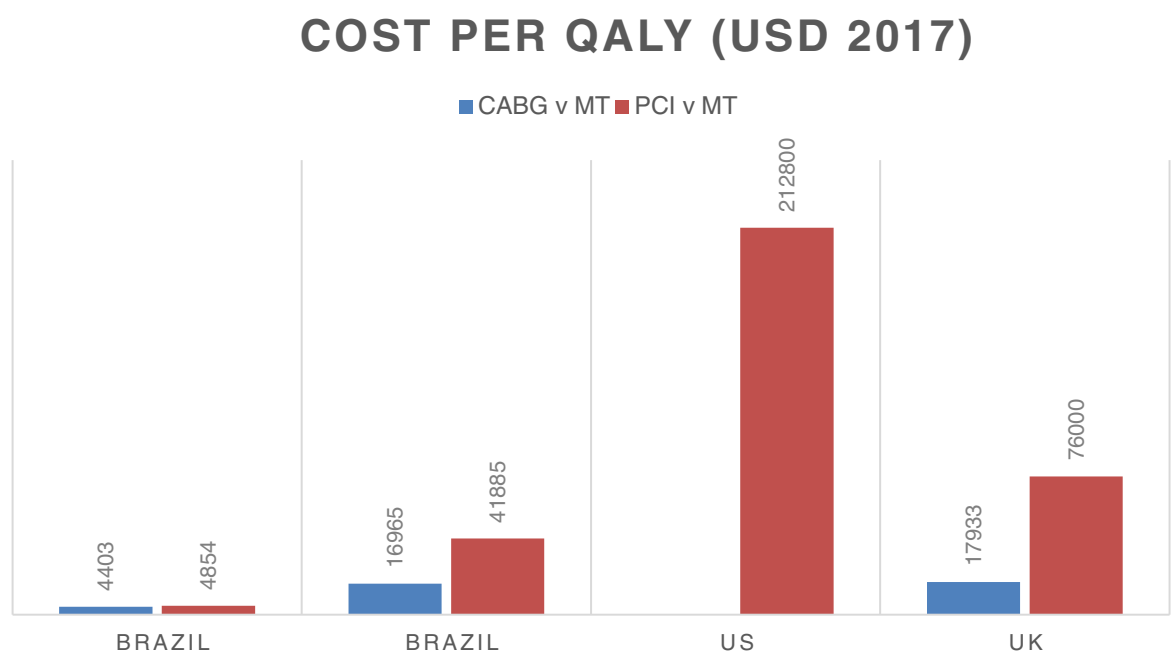

Fig. 2 The cost QALY (cost inflated to 2017 at an annual rate 3%)

The result of this review revealed that each three interventions were cost-effectiveness (Table 3). For example, Claude et al. showed that the invasive strategy was cost-effective (a difference of £3730 higher for invasive treatment, $p = 0.08$, and an incremental cost to prevent one additional major event of £6900), although this analysis reported a follow-up of only 1 year [27]. Weintrab et al. showed that the strategy of PCI versus MT alone was evaluated in the COURAGE trial, which found that PCI (most with BMS) reduced angina symptoms and improved the quality of life at 3 years, but did not reduce the rate of death or myocardial infarction [28]. Besides that, PCI was not cost-effective compared with MT and resulted in an ICER of > US$168,000/QALY [10].

Vieira et al. also conducted a trial-based analysis using data from the MASS II Trial (Medical, Angioplasty or Surgery Study). This was the only trial revealed in searches which randomized patients to each of the three treatment options. Its major conclusions were that medical therapy which was cost-effectiveness compared to CABG, and CABG was cost-effectiveness compared to PCI [11].

Hlatky et al. in economic evaluation of the BARI 2D study showed that outcomes concluded that medical therapy was cost-effective compared with revascularization (PCI or CABG), in the short term (4 years) [17].

Caruba et al. carried out a meta-analysis of cost-effectiveness studies. After concluding that there was no statistically significant difference between treatment strategies on clinical end points of myocardial infarction or death, the analysis was conducted on costs only, over 1 and 3 years [21].

Griffin et al. found that coronary artery bypass grafting was cost-effective compared with percutaneous coronary intervention in patients classified as appropriate for bypass grafting only or for both bypass grafting and percutaneous intervention and percutaneous coronary intervention was not cost-effective when compared with medical therapy for patients classified as appropriate for percutaneous coronary intervention only [18].

Fidan et al. showed that all treatments were examined against the baseline mortality rates, and they found that medical and surgical treatments prevented or postponed over 25,000 deaths in patients with coronary artery disease [19].

Brando et al., at 5-year follow-up, found that the three treatment options yielded improvements in quality of life, with comparable and acceptable costs. However, despite higher initial costs, the comparison of cost-effectiveness after 5 years of follow-up among the three treatments showed both interventions (CABG and PCI) to be cost-effective strategies compared with MT [20].

Very few studies have been conducted on the economic evaluation of the CABG and PCI in comparison with MT intervention in patients with coronary artery disease in developing countries, while most people with heart diseases are living in countries with middle and low income [29].

Study limitation

This study had some limitations. It is important to realize that many clinical studies have important limitations in the cost-effectiveness analysis which are short follow-up

Table 3 Summary of cost-effectiveness results reported. Most papers reported more than one timeframe

Author	Year	Effectiveness measure	Timeframe of analysis	Cost-effective treatment		
				MT	PCI	CABG
Brando et al.	2018	QALY,LY	5 years		■	■
Caruba et al.	2014	Death, MI	1 year, costs only	■		
			3 years, costs only	■		
Vieira et al.	2012	QALY, event-free survival	5 years, event-free costs	■		
			5 years, event-free plus angina-free costs	■		
Hlatky et al.	2009	LY, QALY (sensitivity analysis)	Lifetime			■
			4 years	■		
Weintrab et al.	2008	LY, QALY	3 years	■		
Griffin et al.	2007	QALY	6 years, clinically appropriate for PCI	■		
			6 years, clinically appropriate for CABG			■
			6 years, clinically appropriate for both PCI & CABG			■
Fidan et al.	2007	LY	10 years			
Claude et al.	2004	QOl	1 year		■	■

Shading indicates treatment reported as cost-effective. Fidan et al.'s paper did not make direct comparisons of the relevant treatments. Brando et al. and Claude et al. compared the invasive treatment (CABG and PCI) v medical therapy

CABG coronary artery bypass grafting, *LY* life years, *MI* myocardial infarction, *MT* medical therapy, *PCI* percutaneous coronary intervention, *QALY* quality-adjusted life year, *QOL* quality of life

time, heterogeneity among the clinical trials to evaluate cost-effectiveness (studies using direct analysis of cost and clinical effectiveness and studies using ICER), lack of standardization in the analysis of health outcomes, funding of sources (studies funded by industry are more likely to report favorable cost-effectiveness ratios), and the quality of the study (prospective and retrospective studies, number of patients, correct methodology).

These observations are very important for a critical analysis of such different studies and consequently, for the correct interpretation of the results presented basically; however, costs are from a payer or provider perspective. It is also not generally possible to account for all costs. Evaluation of utility, used to make quality adjustments for survival, is also problematic. Utility could only be measured in a minority of subjects, with data for the rest derived from statistical modeling. In addition, the amount of health expenditure and the opportunity cost vary from country to country; it can prevent us from generalizing the results to other settings.

Conclusion

Based on the result of the reviewed studies in this systematic review, it seems that the three treatment strategies for CAD yielded improvements in QALY. Whereas CABG had the highest initial costs, it was associated with fewer clinical events and further revascularizations, fewer medications, and consequently fewer subsequent long-term costs. PCI had intermediate initial costs and higher need for further revascularizations, but good results in terms of quality of life measures. Finally, MT had lower initial costs, but was associated with higher clinical events and need of medications and slightly lower quality of life measures after 5 years.

In this regard, most of the studies were designed and conducted in high-income countries; thus, the application of these results in low- and middle-income countries will be limited. Therefore, if policymakers and clinicians decide to use CABG or PCI or MT in their own health care system, they should design and conduct specialized studies according to income level and own local setting with the help of specialists and experts in health economics.

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Compliance with ethical standards

The manuscript does not contain clinical studies or patient data.

Conflict of interest The authors declare that they have no conflict of interest.

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