

Patient-level costs of major cardiovascular conditions: a review of the international literature

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Objective: Robust cost estimates of cardiovascular (CV) events are required for assessing health care interventions aimed at reducing the economic burden of major adverse CV events. This review synthesizes international cost estimates of CV events.

Methods: MEDLINE database was searched electronically for English language studies published during 2007-2012, with cost estimates for CV events of interest – unstable angina, myocardial infarction, heart failure, stroke, and CV revascularization. Included studies provided at least one estimate of patient-level direct costs in adults for any identified country. Information on study characteristics and cost estimates were collected. All costs were adjusted for inflation to 2013 values.

Results: Across the 114 studies included, the average cost was US \$6,466 for unstable angina, \$11,664 for acute myocardial infarction, \$11,686 for acute heart failure, \$11,635 for acute ischemic stroke, \$37,611 for coronary artery bypass graft, and \$13,501 for percutaneous coronary intervention. The ranges for cost estimates varied widely across countries with US cost estimate being at least twice as high as European Union costs for some conditions. Few studies were found on populations outside the US and European Union.

Conclusion: This review showed wide variation in the cost of CV events within and across countries, while showcasing the continuing economic burden of CV disease. The variability in costs was primarily attributable to differences in study population, costing methodologies, and reporting differences. Reliable cost estimates for assessing economic value of interventions in CV disease are needed.

Keywords: cardiovascular diseases, health care costs, hospitalization economics, follow-up studies

Introduction

For decades, the broad class of cardiovascular diseases (CVD) has been the leading cause of mortality worldwide, responsible for 30% of all deaths (~17 million annually).¹ CVD is responsible for >7.5 million inpatient cardiovascular (CV) procedures in the US² and just >2,500 inpatient discharges per 100,000 persons in Europe.³ CVD places a significant economic burden on patients and health care systems. In 2010, the direct medical costs of CVD totaled US \$272 billion in the US alone (2008 USD).² In the European Union (EU), direct medical costs of CVD are estimated to reach €106 billion annually.⁴ The health care burden of CVD continues to grow with an aging population as well as the contribution of clinical risk factors, such as obesity, high-lipid levels, and consequent atherosclerosis and hypertension.

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The clinical complexity and extensive economic burden of CVD has led to a number of studies examining the costs of major CV conditions. As the standard of care for the treatment of CV conditions evolves, the cost of care also increases. A considerable literature focused on reviews of economic evaluations in CVD exists but few reviews on cost-of-illness (COI) studies in CVD have been published recently. The COI study reviews that have been published in the past 5 years have focused solely on costs of stroke.^{5,6} No review to date has synthesized international COI studies on all the major components of CVD. Reliable and recent cost estimates are necessary components of economic evaluations and decision making on reimbursement for CV interventions.

This review aims to summarize patient-level estimates from CVD COI studies published in English, between 2007 and 2012. CV events are expensive worldwide both in terms of direct medical costs at the time of event and through subsequent follow-up health care costs after the event. Therefore, the objectives of this review are to identify short-term (initial hospitalization) and follow-up (through 1 year after initial hospitalization) costs of each condition and identify gaps in the COI literature.

Methods

Search strategy

An electronic search of the published scientific literature was conducted to identify relevant cost studies for CV events of interest using PubMed to query the MEDLINE electronic bibliographic database. The review focused on English language studies published between January 1, 2007, and December 31, 2012. Each CV event MeSH term, such as “angina”, “myocardial infarction (MI)”, “stroke”, “heart failure”, “coronary revascularization”, “peripheral arterial disease”, and “cerebral revascularization”, was paired with MeSH term “health care costs”. Searches were otherwise limited to human studies published in English language only.

Selection criteria

Original studies providing patient-level cost estimates for any condition identified in the search strategy were included. Review articles were excluded, but reference lists of review articles were hand searched for relevant original studies. No restriction was made on the country of origin. Cost-effectiveness studies of specific interventions and treatments were excluded due to specificity of the patient population and treatment arms, which are unlikely to be generalizable to overall cost estimates. Additional exclusion criteria were as follows: 1) population size <100 patients, 2) studies on child or adolescent populations, and 3) studies providing

only indirect medical costs or population-level costs. Table 1 presents the selection criteria for this review.

This article focuses on the subset of studies evaluating the following CV events: unstable or unspecified angina, MI, ischemic or unspecified stroke, heart failure, and coronary revascularization procedures. Studies without cost estimates in one of these categories were excluded from this review.

Study selection

Four reviewers reviewed all abstracts against eligibility criteria. Abstracts selected for full-text review by the reviewers were retrieved. One reviewer reassessed the full list of abstracts recommended for inclusion. Full-text review was conducted by four reviewers to assess eligibility for abstractions. Any disagreements were adjudicated by discussion. Abstract and full-text review was conducted using Microsoft Excel software.

Table 1 Selection criteria for studies of cardiovascular event costs

Domain	Inclusion criteria
Population	Adults (18+ years)
Intervention	Primary prevention interventions aimed at lowering cholesterol Secondary prevention of cardiovascular events Burden of disease analyses
Outcomes	Direct medical costs of cardiovascular events listed in review question Must report cost (modeled or primary) for requested cardiovascular event
Timing	No restriction on time horizon
Setting	All countries
Study design	Randomized controlled trials Prospective or retrospective observational studies Systematic reviews with or without meta-analyses (for hand searching primary articles)
Publication dates	January 2007–December 2012
Language	English
Domain	Exclusion criteria
Population	Children (<18 years) Sample size (N<100) Adults with congenital heart conditions Adults with traumatic brain injuries Brain aneurysms
Intervention	Primary prevention interventions not aimed at lowering cholesterol (eg, smoking cessation) Disease management studies Cost-effectiveness studies* HTA submissions* Trials of diagnostic therapies Screening or monitoring trials
Outcomes	Indirect medical costs (eg, absenteeism and caregiver burden)

Note: *Cost-effectiveness studies and health technology assessment submissions were excluded in the original search strategy protocol for this project. However, results from a separate literature review examining statin cost-effectiveness trials have been incorporated in this report.

Abbreviation: HTA, health technology assessment.

Data extraction and synthesis

Titles and abstracts were screened to assess relevance of the study to review. Relevant full-text articles were obtained for study, and cost estimates and methodology as reported by authors were abstracted. Though no formal assessment of quality was undertaken, study design, sample sizes, and presence of precision estimates (eg, standard deviation) were abstracted to give context to cost estimates. Cost estimates derived from hospital charges unconverted to costs were collected but not abstracted. Thus, articles where only hospital charge data were reported are not included in this article. Cost estimates may be calculated based on a number of methods: reimbursement-based methods, eg, Medicare Diagnosis-Related Groups, top-down methods, and bottom-up methods. We have included the inclusion population and study design in [Supplementary material](#). Costs for patients with comorbidities or other subpopulations were collected and abstracted. Where possible, only inpatient cost estimates provided by authors were abstracted for comparison between studies. If inpatient costs were not available, costs as reported by study authors and the type of cost recorded were included. Studies were stratified by the type of cost as follows:

- Acute cost: inclusive of a procedure or initial hospitalization,
- Follow-up cost: inclusive of rehospitalization episodes, second procedures, continuing care after initial procedure, hospitalization, or routine care, occurring from the day after discharge until 1 year after an event.
- End-of-life cost: specific to the period immediately preceding death (for heart failure studies only).

All costs were inflated to 2013 values in each country's currency utilizing the medical component of the Consumer Price Index.⁷ Costs were then adjusted to international dollars using the 2013 purchasing power parity index.⁸ Currency year as reported by author was utilized for inflation to 2013 values; if authors did not specify the currency year, the latest source data year was used for inflation. If source data year was not specified, the study publication year was used for inflation.

Results

The search identified 1,178 abstracts. Of these abstracts, 252 (21%) abstracts were retrieved for full-text review. The bibliographies of systematic reviews were searched, yielding an additional seven studies, for a total of 259 studies reviewed. Of the 259 studies retrieved, 83 studies were discarded for having an excluded study design (eight studies), indirect costs or population costs only (22 studies), no event cost estimate

(33 studies), review articles (twelve studies), and a sample size of <100 patients (eight studies). A total of 176 studies were abstracted after full-text review (Figure 1).

Due to the breadth of the results, this article focuses on studies evaluating the following CV events: unstable or unspecified angina, MI, ischemic or unspecified stroke, heart failure, and coronary revascularization procedures, for which 114 studies (65% of abstracted studies) were abstracted.

Study characteristics

Included studies provided estimates from 26 countries, with more than half of studies based on US population samples (n=60; 53%), followed by UK (n=10; 9%), Germany (n=7; 6%), and Sweden (n=6; 6%), (Table 2). Mean costs for coronary revascularization procedures were found in 48 studies, with ischemic stroke estimates found in 32 studies. Two US studies^{9,10} and one EU study¹¹ provided cost estimates for all events of interest. Cost estimates were aggregated by region, based on the presence of two or more studies in a geographical area. A list of the full population and study design characteristics of each included study is provided in [Supplementary material](#).

Cost reporting

Costs were categorized based on the authors' reported cost components. Only direct medical costs were abstracted from the studies and classified into either acute (inpatient hospitalization for event) or follow-up (after discharge for initial event). All inpatient costs were abstracted based on authors' definition of a hospitalization for treatment of a defined CV event, regardless of the length of stay. Length of hospitalization stay was not assessed in this article. For comparison, only follow-up costs through the first year after initial event were abstracted.

Costs were categorized for each CV event, as defined by the authors. We have separately identified costs for procedures (coronary bypass graft surgery [CABG] and percutaneous coronary intervention [PCI]) and hospitalizations due to causal events (unstable angina and MI), based on how the authors identified the costs in the article. Therefore, cost estimates for unstable angina or MI events may potentially include embedded revascularization components that were not identified as a separate cost component.

Source data

Source data were identified through methods indicated by study authors in the following five study designs: claims database analyses, disease registry studies, population-based

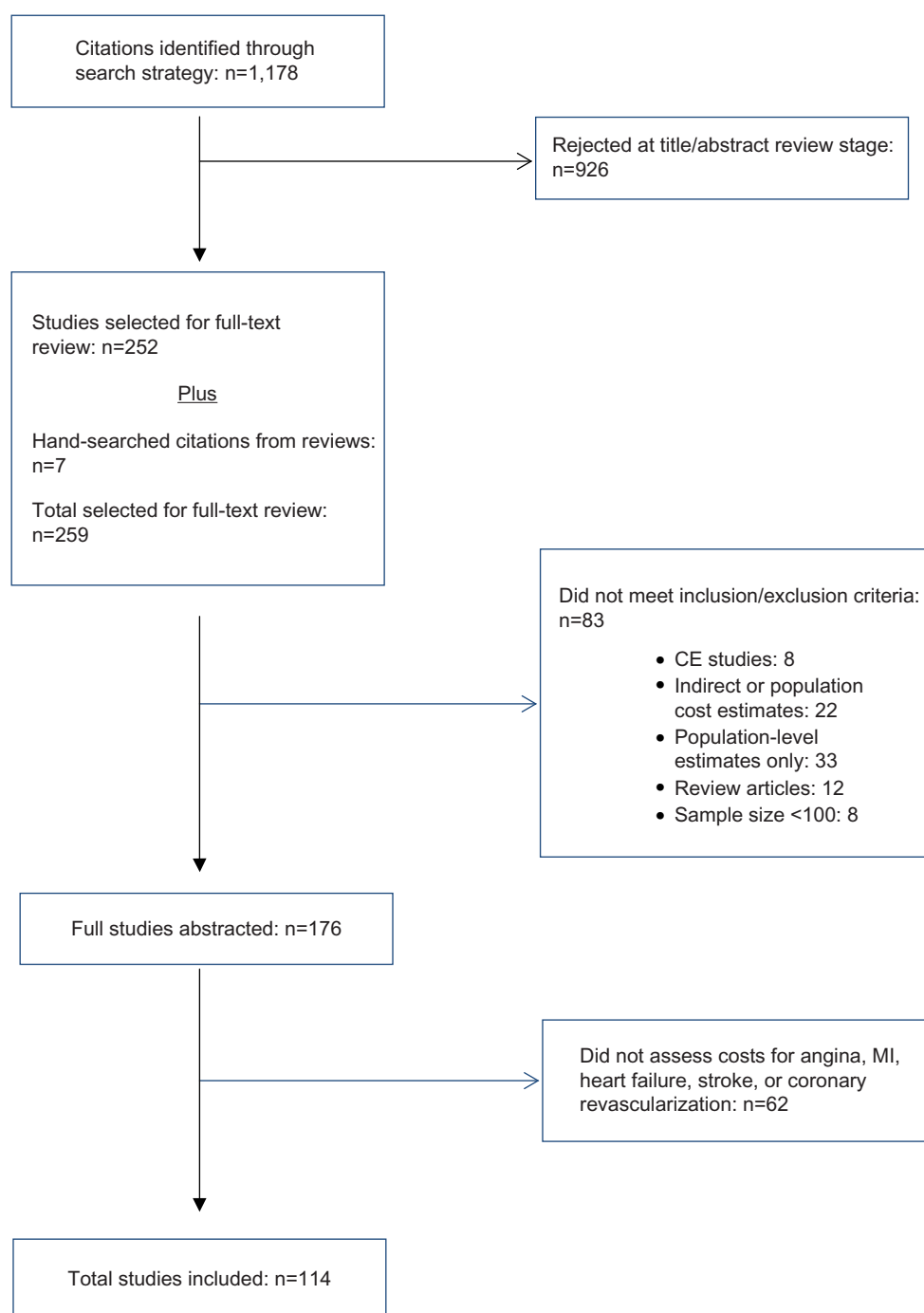


Figure 1 Workflow of included studies.

Abbreviations: MI, myocardial infarction; CE, cost-effectiveness.

registry studies, retrospective cohorts from a single hospital, and a randomized control trial (RCT). Claims data analyses were utilized in US-based 46 studies (39%); retrospective and prospective hospital cohorts were utilized in 35 studies (30%), and disease-specific registries were utilized in 16 studies (14%). RCT economic substudies were the basis of 16 studies (14%) (Table 2). Studies predominantly used source data collected within the past 10 years (2003 or later). Only

14 studies (12%) reported cost estimates where all data were collected before 2003.

Comorbidity and history of event subgroups

Though several studies (n=37; 32%) used multivariate models to assess cost predictors, only 21 (18%) studies provided cost estimates among high-risk patients (such as patients with

Table 2 Summary of characteristics of cost-of-illness study

Study characteristics	Number of studies
CV event cost ^a	
Coronary revascularization	48
Unstable angina	8
Heart failure	29
Ischemic stroke	32
Myocardial infarction	18
Source data type ^a	
Claims database	46
Disease registry	16
Hospital cohort	35
Population registry	9
Randomized controlled trial	16
Region	
Asia	
People's Republic of China	5
Japan	3
Singapore	1
Taiwan	1
Thailand	2
Australia	1
Global	3
Latin America	
Argentina	4
Brazil	4
Europe	
Belgium	3
Denmark	1
Estonia	1
Finland	4
France	5
Germany	7
Greece	2
Hungary	1
The Netherlands	2
Poland	1
Spain	6
Sweden	6
Switzerland	3
Turkey	1
UK	10
Middle East	
Iran	1
North America	
Canada	6
US	60

Note: ^aA study may be counted more than once if it provides estimates in more than one country for more than CV event or if it uses multiple data sources.

Abbreviation: CV, cardiovascular.

comorbidities and a history of the event). Diabetics were the most prominent subgroup, with cost estimates found in five studies. Costs among patients with a history of the CV event were provided in four studies (Figure 2).

Costs of unstable angina hospitalization

In the US, two studies reported acute hospitalization costs, with an average of \$7,916 (median: \$7,841),^{9,10} with a

slightly higher estimate for diabetics (\$8,032).¹⁰ Outside the US, acute costs for angina were only found in a Thai hospital cohort of acute coronary syndrome patients (\$2,893) (Table 3).¹²

Of the three studies reporting follow-up costs, two studies were US claims analyses^{10,13,14} and one study was a Swiss population registry.¹⁵ Costs ranged from \$9,282 for rehospitalization among diabetics¹⁰ to \$28,509 in attributable costs at 1 year.¹³ One-year follow-up costs in the only European study, a Swiss population registry, averaged \$18,224.¹⁵

Costs of MI

Of 18 studies on MI, eight (44%) studies were conducted in the US.^{9,10,13,16,17–20} Nine studies assessed data from one or more European countries (50%).^{11,15,21–27} Outside the US and Europe, two cost estimates were found in a Thai cohort of acute coronary syndrome patients¹² and an Australian CVD registry.²⁸

Over all studies, the mean cost of an acute MI was \$11,664 (median: \$7,324). Cost of acute hospitalization for MI ranged from \$547 in Hungary²¹ to \$30,021 for US diabetics.¹⁰ In the US, the mean cost of acute MI was \$24,695 (median: \$26,749). Cost estimates of acute MI averaged \$5,966 (median: \$6,749) in Europe and \$11,682–\$12,006 among diabetics based on a Swedish registry.²⁶

An average cost of follow-up over a 1-year period was \$32,379 (median: \$27,430) based on three US claims analyses^{10,13,20} and one Swiss registry analysis (Table 4).¹⁵

Costs of heart failure

Heart failure costs were abstracted from 28 studies, mostly using US data (n=23; 79%).^{9,10,16,30–49} Three economic sub-studies of multicountry RCT populations also included US samples.^{50–52} One Argentinian hospital cohort,⁵³ a Canadian hospital cohort,⁵⁴ and a Thai hospital cohort⁵⁵ are the only studies with cost estimates outside the US.

The average cost of an acute heart failure hospitalization across all studies was \$11,686 (median: \$10,291). Costs ranged from \$529 in the Argentinian hospital cohort⁵³ to \$27,006 in a US claims analysis of patients aged 18–64 years.⁴³ Acute costs for diabetics were found in one US claims analysis (\$12,757).¹⁰ Follow-up costs through 1 year were estimated at \$12,931 (median: \$15,238), comprised solely of US studies. No follow-up costs were found in European studies. End-of-life costs (past 6 months) were estimated at an average \$23,606 based on a US Medicare claims analysis and a Canadian registry cohort (Table 5).^{38,54}

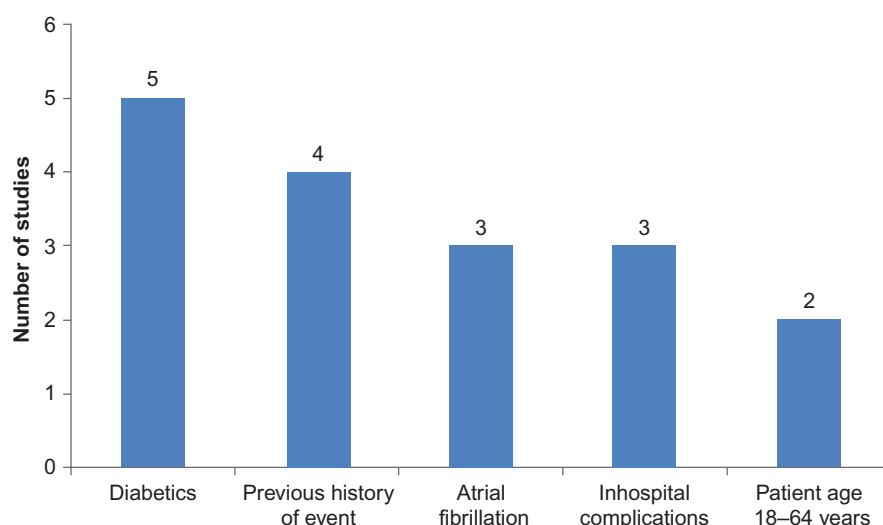


Figure 2 Number of studies with comorbid patient populations or subgroup cost estimates.

Table 3 Average cost of angina across all reported studies

Time horizon	Mean cost	Median cost	Range	Number of studies
Acute ^a	\$6,821	\$7,859	\$2,893–\$8,032	3
US only	\$7,916	\$7,841	\$7,841–\$8,032	2
Follow-up through 1 year ^b	\$17,015	\$18,224	\$9,282–\$28,509	3
US only	\$16,713	\$14,531	\$9,282–\$28,509	2

Notes: ^aUS acute estimates plus Thai estimate. ^bAll US follow-up estimates plus Swiss estimate. Costs are shown in US\$.

Table 4 Average cost of myocardial infarction across all reported studies

Time horizon	Mean cost	Median cost	Range	Number of studies
Acute ^a	\$11,664	\$7,324	\$547–\$30,021	18
US only	\$24,695	\$26,749	\$17,346–\$30,021	7
EU only	\$5,966	\$6,749	\$547–\$10,435	9
Western	\$5,025	\$6,749	\$3,957–\$7,842	2
Northern	\$6,747	\$6,852	\$3,435–\$9,849	3
Eastern	\$992	\$992	\$547–\$1,437	2
Southern	\$7,386	\$8,270	\$2,569–\$10,435	3
Follow-up through 1 year ^b	\$32,379	\$27,430	\$28,777–\$60,857	4
US only	\$34,463	\$26,082	\$22,264–\$60,857	3

Notes: European regions are based on the United Nations Statistics Division categories.²⁹ ^aAll acute estimates plus Australian and Thai estimates. ^bAll US follow-up estimates plus Swiss estimate. Costs are shown in US\$.

Abbreviation: EU, European Union.

Costs of ischemic stroke

Cost estimates for ischemic or unspecified stroke were abstracted from 32 studies. US ($n=13$; 41%),^{9,10,13,19,34,56–63} European ($n=12$; 38%),^{11,26,64–73} and Asian ($n=4$; 13%)^{74–77} cost estimates comprise the majority of studies, along with two Latin American hospital cohorts,^{78,79} a Canadian RCT,⁸⁰ and an Australian registry.²⁸ All but one of the US studies found analyzed claims data for cost estimates; the remaining US study provided cost estimates from a US CVD registry.⁶¹ Half of European estimates ($n=6$) were based on hospital cohorts with the other half from disease/population registries.

Across all studies, the average cost of an acute ischemic stroke hospitalization was \$11,635 (median: \$8,097). In the

US, the mean cost was higher at \$18,543 (median: \$18,296). Costs in the US ranged from \$8,069 in a Medicare claims analysis⁶⁰ to \$38,231 in young patients (aged 18–44 years).⁵⁶ Acute stroke cost was \$13,469 for patients with diabetes¹⁰ and \$20,303 for patients with a previous stroke or transient ischemic attack.⁵⁸ The average cost of acute ischemic stroke across Europe was \$11,900, with a low estimate of \$5,016 in a German hospital cohort⁷² and a high estimate of \$24,451 in a Scottish population registry.⁶³ Acute costs for diabetics were found in one Swedish regional registry (\$21,060).²⁶ One-year follow-up costs averaged \$13,683 (median: \$10,248), with a European average of \$3,720 and a US average of \$17,819 (Table 6).

Table 5 Average cost of heart failure across all reported studies

Time horizon	Mean cost	Median cost	Range	Number of studies
Acute ^a	\$11,686	\$10,291	\$529–\$27,006	12
US only	\$12,383	\$10,667	\$5,343–\$27,006	11
Follow-up through 1 year	\$12,931	\$15,238	\$2,258–\$24,084	7
Follow-up through 1 year (inpatient costs only)	\$11,584	\$15,238	\$2,258–\$19,844	6
End of life costs (past 6 months) ^b	\$23,606	\$23,606	\$19,637–\$27,574	2

Notes: ^aAcute estimates include all US plus Argentinian hospital cohort. ^bEstimates from Canada and US. Costs are shown in US\$.

Table 6 Average cost of ischemic stroke across all reported studies

Time horizon	Mean cost	Median cost	Range	Number of studies
Acute ^a	\$11,635	\$8,097	\$1,077–\$38,231	21
US only	\$18,543	\$18,296	\$8,069–\$38,231	6
EU only ^b	\$11,900	\$8,325	\$5,016–\$24,451	8
Western	\$10,230	\$7,520	\$5,016–\$21,060	4
Northern	\$17,776	\$20,018	\$8,858–\$24,451	3
Asia only	\$4,183	\$3,508	\$1,077–\$8,097	3
Latin America only	\$3,388	\$3,388	\$2,225–\$4,550	2
Follow-up through 1 year ^c	\$13,683	\$10,248	\$1,169–\$52,333	13
EU only	\$3,720	\$2,133	\$1,169–\$10,248	4
US only	\$17,819	\$16,547	\$2,362–\$52,333	9
Follow-up through 1 year (inpatient costs only) ^{c,d}	\$6,819	\$5,128	\$1,169–\$20,169	9

Notes: European regions are based on the United Nations Statistics Division categories.²⁹ ^aIncludes all acute estimates in table plus one Australian cohort. ^bIncludes all EU estimates plus Greek estimate. ^cIncludes all US and EU estimates plus Singapore estimate. ^dEstimates of rehabilitation care are included in inpatient costs. Costs are shown in US\$.

Abbreviation: EU, European Union.

Costs of coronary revascularization

Forty-eight studies provided estimates on a coronary revascularization procedure – CABG, PCI, and a hybrid CABG–PCI procedure. Nearly half of the study estimates on revascularization were based on US populations ($n=24$; 48%);^{9,10,13,81–102} the remainder came from eleven European (23%),^{103–113} six Asian (13%),^{114–119} three Latin American studies (6%),^{120–122} and three multicountry RCTs (6%).^{123–125} Hospital cohorts ($n=19$; 40%), claims analyses ($n=14$; 29%) and RCTs ($n=10$; 20%) were the predominant methodologies for revascularization estimates.

CABG cost in the US averaged \$57,577 (median: \$61,445) with a range of cost estimates from \$17,731 to \$124,221 in eleven studies. Average CABG cost in Europe was \$14,562 (median: \$13,732) with a range of costs from \$924 to \$27,724 in four studies. There were too few studies to allow aggregation of CABG cost in Asia or elsewhere (Table 7).

Overall cost of PCI across all studies was \$13,501 (median: \$14,025) ranging from \$520 in the multicountry RCT¹²³ to \$25,641 in a US-managed care claims analysis.⁸³ PCI cost in Europe (\$12,208; median: \$11,296) and Asia (\$11,717; median: \$11,739) were comparable but based on only three studies each. PCI cost in the US was estimated at \$20,146 (median: \$19,429) based on six studies. Mean PCI costs in the US (\$20,146) were nearly one-third of the mean CABG costs in US studies (\$57,577). Mean CABG costs in

Europe, however, were only slightly higher (\$14,562) than PCI costs (\$12,208) (Table 7).

Discussion

Previous reviews evaluating patient-level costs of care have focused on the cost burden of single components of CVD, such as stroke. These reviews have reported significant variation in cost estimates. Prior assessment of the ischemic stroke literature by Luengo-Fernandez et al⁶ found 20-fold difference in US costs of ischemic stroke (\$468–\$146,149) and a mean cost of \$19,018. A review of COI from Demaerschalk et al⁵ reported a narrower range of \$8,000–\$23,000 (2008 USD) for acute care costs in the US and 1-year follow-up costs of care from \$15,102 to \$30,000. An earlier analysis of follow-up stroke costs among Western countries (US, Australia, Western Europe, and New Zealand) reported annual follow-up costs ranging from \$7,975 to \$54,546 (1998 USD).¹²⁶ Only one study assessing chronic angina COI studies was identified, with reported annual costs of treatment in the US from \$2,569 (1995 USD) to \$7,207 (1992 USD).¹²⁷

The mean cost of stroke found in this review, \$18,543 in the US and \$11,900 in Europe, are in-line with findings in previous reviews, with a fourfold variation between studies in this review comparable to prior work. For other CV events, substantial variation in cost estimates within regions was evident. For follow-up costs, estimate differentials may

Table 7 Average cost of coronary revascularization over all reported studies

Time horizon	Mean cost	Median cost	Range	Number of studies
Acute CABG	\$37,611	\$28,512	\$249–\$124,221	24
US only	\$57,577	\$61,445	\$17,731–\$124,221	11
EU only	\$14,562	\$13,732	\$924–\$27,724	4
Latin America only	\$3,331	\$3,331	\$2,836–\$3,826	2
Acute PCI	\$13,501	\$14,025	\$520–\$25,641	14
US only	\$20,146	\$19,429	\$16,104–\$25,641	6
EU only	\$12,208	\$11,296	\$8,068–\$18,173	3
Asia only	\$11,717	\$11,739	\$9,383–\$14,029	3
Follow-up through 1 year – PCI	\$11,012	\$6,017	\$1,686–\$33,964	4
Follow-up through 1 year – CABG	\$28,903	\$36,045	\$1,170–\$49,494	3

Note: Costs are shown in US\$.

Abbreviations: CABG, coronary bypass graft surgery; EU, European Union; PCI, percutaneous coronary intervention.

likely be the result of follow-up length; a 6-month follow-up period and a 1-year follow-up period will necessarily have much different cost estimates attached. Acute cost estimates, however, had significant variation as well. In the EU, cost estimates for MI varied 19-fold, and a CABG procedure varied 30-fold. Similarly, high estimates for CABG costs were seven times higher than the lowest cost in the US and eight times higher than the lowest cost in Asia. Acute costs for CABG procedures, in particular, have outpaced other CV event costs.

Follow-up event costs, comprised largely from US studies, were found to be as high as acute costs, or in the case of MI nearly three times higher than acute costs. Care in the year following an acute episode, therefore, may be an important lever in the reduction of the economic burden of CVD. However, follow-up length varied widely from 30 days posthospitalization to 1 year posthospitalization. Different cost components may have been reported in various studies, such as inpatient, outpatient, medication, and rehabilitation care, and the cost components included in calculating the reported cost estimate were not always clearly reported by the authors. Reporting differences add to the variability in estimates.

This is the first review as far as the authors are aware that synthesizes the costs of multiple CV conditions from COI studies. The present review reports costs from COI studies evaluating all major CV events and conditions reported globally from 2007 to 2012. As evidenced by the findings in this review, the worldwide cost burden of CVD remains significant. Though comparison of results is hampered by the differences in study design, several themes emerge. The findings of the literature suggest that in the US and Europe, revascularization procedures and MI are CV events with the highest acute costs. Though fewer studies are available, costs of revascularization procedures throughout Asia are also higher than other reported event costs. Costs in the US remain higher than other countries, though significant variation

within the US and other regions was found. Methodological cost accounting, setting, and population differences may account for some of this variation. Less variation was seen among European estimates, with the exception of the cost of MI in Eastern Europe, which was reported much lower compared to the rest of Europe (\$992 versus \$5,966 across EU).

Subgroup cost estimates were not widely available in this literature. Cost estimates across all events were reported in only one US study.¹⁰ Based on this study alone, costs among diabetic population appeared to be slightly higher than the cost among the general population. More research on this and other high-risk populations, including patients with a history of a CV event or a previous CV event, is needed.

Though the broad scope of this literature review was intended, several limitations remain. This review is intended as a descriptive, narrative summary of global cost studies, and as such no quantitative methods to assess effect size are calculated. Cost-effectiveness models were excluded from the selection criteria for this review due to very specific treatments and patient population inherent in those studies. As a result, additional literature or submissions to governing bodies assessing costs of care for specific therapies or treatments published outside of MEDLINE is not provided in this review. Cost estimates for any comorbidity are included for abstraction in this review. Although comorbid conditions may increase costs, patients with multiple conditions portray “real-world” patient populations. We did not stratify costs by the severity of conditions, largely due to methodological differences in reporting by study authors. An assessment of country-specific patient-level costs by, eg, patients with ST elevation MI versus those without would add significantly to the economic burden literature. This review included English language literature only, and therefore, some cost estimates in other languages may have been missed. Finally, we did not include cost-effectiveness analyses in these results, and additional robust data may be found in that literature. Though

differences in study design were noted, the quality of each study design was not formally addressed.

Country-specific cost estimates are integral to health care decision making. Findings from this review indicate that a majority of evidence was collected in the US and Europe, and a dearth of patient-level cost estimates remains in other global regions. This review attempted to locate studies in any country available; yet a dearth of patient-level cost estimates outside the US and Europe remain unclear. Wide variation in cost estimates underscores the need for more reliable estimates of CV conditions, not only within the US but also globally. Given the importance and potential implications of these COI studies, standardized and endorsed protocols for the estimation of costs will facilitate comparison across countries and illnesses. The absence of specific guidelines for measurement in COI studies will continue to hamper efforts to compare estimates across studies.

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Disclosure

Shravanthi R Gandra is employed by Amgen, Inc., and Akshara Richarriya was previously employed by Amgen, Inc., at the time this work was completed. At the time this work was completed, Robert J Nordyke, Ronald J Halbert, and Gina Nicholson were employed by ICON plc, which was a paid consultant to Amgen, Inc., in the development of this article. The authors report no other conflicts of interest in this work.

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