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Original Publication:

Nathalie Eckard, Magnus Janzon and Lars-Åke Levin, Compilation of cost-effectiveness evidence for different heart conditions and treatment strategies, 2011, Scandinavian Cardiovascular Journal, (45), 2, 72-76.
http://dx.doi.org/10.3109/14017431.2011.557438

Compilation of cost-effectiveness evidence for different heart conditions and treatment strategies

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ABSTRACT

Objectives: Despite the continuing interest in health economic research, we could find no accessible data set on cost-effectiveness, useful as practical information to decision makers who must allocate scarce resources within the cardiovascular field. The aim of this paper was to present cost-effectiveness ratios, based on a systematic literature search for the treatment of heart diseases.

Design: A comprehensive literature search on cost-effectiveness analyses of intervention strategies for the treatment of heart diseases was conducted. We compiled available cost-effectiveness ratios for different heart conditions and treatment strategies, in a cost-effectiveness ranking table. The cost effectiveness ratios were expressed as a cost per quality adjusted life year (QALY) or life year gained.

Results: Cost-effectiveness ratios, ranging from dominant to those costing more than 1,000,000 Euros per QALY gained, and bibliographic references are provided for. The table was categorized according to disease group, making the ranking table readily available.

Conclusions: Cost-effectiveness ranking tables provide a means of presenting cost-effectiveness evidence. They provide valid information within a limited space aiding decision makers on the allocation of health care resources. This paper represents an extensive compilation of health economic evidence for the treatment of heart diseases.

KEY WORDS

Cost, cost-effectiveness, rankings, heart disease, priority setting, evidence-based medicine

INTRODUCTION

Economic evaluations are used to inform decision makers about the efficient allocation of scarce health care resources, i.e. comparing value for money of alternative treatment strategies for a particular patient group. Moreover, economic evaluations provide a means of translating the relevant evidence into estimates of both costs and effects of the alternative treatment strategies being compared, drawing on evidence from a number of sources, rather than just the use of randomized controlled clinical trials. Economic evaluations may also be used to extrapolate end-points over an appropriate time horizon, often beyond the scope of a clinical trial.

Cost-effectiveness rankings or league tables provide a means of presenting results from economic evaluations and have been published both in North America and the UK [1,2]. An extensive list of over five hundred cost-effectiveness ratios for life-saving interventions, including interventions for heart diseases, has also been presented by Tengs (1995) [3].

Despite the continuing interest in cost-effectiveness, it is difficult to find both accessible and comprehensive data sets on costs and effects, useful as practical information for decision makers who must allocate scarce resources within the cardiovascular field. To this end, we compiled information from a systematic literature search in a cost-effectiveness ranking table for different heart conditions and treatment strategies expressed as a cost per quality adjusted life year (QALY) or life year (LY) gained. Presenting cost-effectiveness information in for example a cost-effectiveness ranking table constitutes a first step in making evidence accessible to decision makers. The aim of this paper was to present the results, based on a

systematic literature search for the treatment of heart diseases with regard to cost-effectiveness.

Cost-effectiveness ratios

Cost-effectiveness results are often calculated in terms of cost per QALY or LY gained for one treatment strategy compared to another. The results are known as the incremental cost-effectiveness ratios (ICERs), i.e. the ratio of the difference in health outcome (QALYs) between two alternatives; treatment A and treatment B. Thus, the ICER shows the mean incremental cost of gaining an extra QALY by employing the treatment A strategy compared to the treatment B strategy. A low ICER indicates greater cost-effectiveness compared to a higher ICER value.

$$ICER = (Cost\ A - Cost\ B) / (Effect\ A - Effect\ B)$$

MATERIAL AND METHODS

Systematic literature search

We conducted a comprehensive and extensive literature search on available economic analyses of intervention strategies within the cardiovascular field. The systematic literature search was conducted for the 2008 and updated version of the Swedish national guidelines for heart diseases [4]. The following databases were used to identify health economic analyses for the literature search; Cumulative Index to Nursing & Allied Health Literature (CINAHL), Health Technology Assessment (HTA) Database, MEDLINE/PubMed and NHS Economic Evaluation Database (NHS EED). The database Embase was used in the literature search conducted for the 2004 version of the national guidelines. However, as the search did not give additional hits, we did not include this database in the update.

The search term ´Heart Diseases´ was classified according to six disease groups; Coronary Artery Disease, Heart Failure, Arrhythmias, Heart Valve Disease, Inflammatory Heart Disease and Congenital Heart Disease and secondary prevention. Search terms referring to primary prevention were not covered in the literature search. Using a public health definition, primary prevention refers to intervention strategies aimed at preventing or postponing healthy individuals from getting ill, including lifestyle issues aimed at reducing risk factors due to for example smoking, obesity. Within each disease group, search terms were chosen in collaboration with a librarian. These search terms consist of diagnosis and standard medical treatment procedures reflecting the contents of each group respectively (Table I). Medical Subject Headings (MeSH) were used as search terms in MEDLINE/PubMed when available and the search terms were extended with a free text search term when necessary.

Inclusion and exclusion criteria

After the initial database search, all abstracts were read and judged by two examiners. Obvious irrelevant references were disregarded. Thereafter, the full references were acquired. Each article was once again judged by two examiners working independently. A template was used to judge the quality of the cost-effectiveness analyses for data extraction. This was based on criteria generally accepted by the health economic community including; a description of a well-defined intervention strategy and a clearly defined comparator for a specific patient population. Information on study design, costs and effects (outcome) and discount rates were noted. Studies reporting the outcome measures as a cost per QALY or LY gained were included. Articles which met our inclusion criteria but could not be adapted to a Swedish setting and not included in the national guidelines were excluded. Articles were also excluded when they did not constitute an economic evaluation or did not have the right outcome measure (QALYs or LY gained). In a few cases, the treatment strategy was considered dominant though the outcome measures; QALY or LY, were not used. The health outcomes were considered the same or better than the alternative treatment strategy at a lower cost and were reported as dominant (<0) per event avoided in the Appendix tables. An intervention strategy is considered dominant, i.e. is said to dominate another, when its effectiveness is higher and its costs lower.

Compilation of results

The information compiled from the literature search was presented as a cost-effectiveness ranking table for different heart conditions and treatment strategies. The cost-effectiveness evidence compiled for the tables was adapted to a Swedish setting and complies with the 2008 version of the Swedish national guidelines. All included cost-effectiveness ratios prior to

2002 were used in the previous edition of the guidelines using the same methods for the literature search. The results were integrated in the current cost-effectiveness ranking table.

Using implantable cardioverter defibrillators (ICDs) for primary prevention as an example, we illustrate how cost-effectiveness evidence should be interpreted when there is a range of cost-effectiveness estimates for one single medical technology. The primary preventive use of implantable cardioverter defibrillators (ICDs) is aimed at patients with an already manifested cardiac disease for example heart failure with a risk of sudden cardiac death, i.e. for patients not yet experiencing arrhythmia. ICDs may also be considered for patients with cardiac conditions such as long QT syndrome, hypertrophic cardiomyopathy and congenital heart disease.

The ICERs for the different treatment strategies were expressed as cost per QALY or LY gained by replacing one treatment strategy with another. All costs were adjusted to SEK using purchasing power parities (PPPs). The costs are in 2009 prices and have been converted to Euros using the average exchange rate of 1 Euro = 10.63 SEK.

RESULTS

More than a thousand abstracts were identified and read and over a hundred full bibliographical references were acquired and judged. Cost-effectiveness analyses which met our selection criteria gave sufficient information for more than two hundred cost-effectiveness ratio estimates. A hundred and thirty nine of these could be referred to Swedish treatment

strategies used in the guidelines, ranging from dominant to those costing more than 1 000 000 Euros per QALY or LY gained.

The cost-effectiveness ranking table (Appendix) is separated into five sections according to the following; the first column contains the intervention strategy and the compared intervention and disease group, the second column contains patient population and possible sub- or risk group, the third column; ICERs presented as cost per QALY or LY gained. The fourth column includes information of the society from which the data originates, and the fifth column contains study references from which ICERs were drawn.

The table was categorized according to the disease group areas. The majority of ICERs refer to treatment strategies for coronary artery disease (acute coronary artery disease 63 (14) and stable angina 23 (10)), followed by arrhythmias 32 (10), heart failure 19 (7) and congenital heart disease 2 (1). Within each category there were several cost-effectiveness studies found referring to the same intervention strategy (referred to in parenthesis). For example, stable angina; twenty three cost-effectiveness ratios were found corresponding to ten different categories of interventions. Thus, instead of presenting one long list of cost-effectiveness ratios, each disease group constitutes its own cost-effectiveness ranking table and may be broken down even further if categorized for specific interventions.

When interpreting variations in ICERs for the same medical technology, different patient groups greatly affect the ICERs. Of the thirty two cost-effectiveness estimates provided for patients suffering from arrhythmias, there were several cost-effectiveness analyses relating to primary preventive use of ICDs in the cost-effectiveness ranking table.

[Table IIa and IIb]

Table IIa presents ICERs for patients with high and low risk of sudden cardiac death. A high risk subgroup of patients results in an ICER of 33,890 Euro per QALY gained [5]. A low risk subgroup results in 109,350 Euro per QALY gained [5]. Using different risks for sudden cardiac death thus gives important information in the guidance to decision makers and identifying high risk individuals would imply that the ICD treatment strategy would be cost-effective compared to medical management. Table IIb presents how age and gender influence the ICERs of the ICD treatment strategy used for the prevention of sudden death in young people with inherited cardiac arrhythmias [6]. The ICER for any specific medical technology, may be categorized according to age, gender and other risk factors thus affecting the ICERs.

DISCUSSION

We have presented ICERs for the treatment of heart diseases based on an extensive systematic literature search. Available cost-effectiveness data represents an effort to amass cost-effectiveness information presented in a cost-effectiveness ranking table for different heart conditions and treatment strategies. Though, most of the studies found were categorized within coronary artery disease, cost-effectiveness analyses covering a wide range of interventions strategies for the treatment of heart diseases were included.

The cost-effectiveness ranking table was not only compiled but also categorized according to disease group areas, summarized and broken down in order to convey as much information as possible to the reader in a simplified manner. Focusing on a single treatment strategy for patients with arrhythmias; implantable cardioverter defibrillators (ICDs), we have illustrated how cost-effectiveness information may be conveyed from cost-effectiveness ranking tables. Presenting the ICERs for different risk groups (patient groups) may provide critical information to decision makers. Differentiating between patient groups, depending on low or high risk, gives important information, for example decision makers trying to optimize both the number of patients and which patients might benefit from a treatment.

Cost-effectiveness ranking tables provide a means of presenting cost-effectiveness evidence in terms of cost per QALY or LY gained. Using a generic outcome measure such as QALYs enables comparisons across different cost-effectiveness analyses. Both QALY and LY gained were included as outcome measures. The implication of this may be that the ICERs are overestimated as the outcome measure LY had not been adjusted. The cost-effectiveness analyses using LY as outcome measure were included in the rankling table when the analyses were judged to be of high quality and no other analyses using QALYs as outcome measure was found.

There are a number of methodological issues of importance when interpreting cost-effectiveness rankings and comparing ICERs. The accuracy of the results presented in a cost-effectiveness ranking table is always limited by the accuracy of data and assumptions upon which the original analysis were based, including the range of cost and consequences considered, the method for estimating utility values for health states, the discount rate used and the choice of comparator [7]. If a programme is to be considered cost-effective, depends

on what we compare it to. The choice of comparison programme is probably the most important for the interpretation of ICERs [7-9]. They are to a large extent context specific [10]. Transferring results from one setting to the other (demography, availability of health care resources, relative prices etc.) may also constitute a problem, as different countries have different health systems, different perspectives for example use different discount rates [11].

Another aspect of cost-effectiveness ranking tables is that they often use point-estimates giving a false sense of precision and rarely include measures of uncertainty for these estimates [12]. An alternative methodological approach would be to provide information on mean values as well as variance. Another way would be to use graphical framework such as the cost-effectiveness plane to present results [13]. A scatterplot diagram is a simple solution to illustrate the uncertainty in the results of cost-effectiveness analyses. Stochastic rankings have also been proposed to be used in a budgetary context [14-18].

However, in the absence of systematic comparisons such as cost-effectiveness rankings, comparisons between health care programmes are likely to take place informally [19]. Assembling data on a range of interventions gives greater prominence to cost-effectiveness data than does the reporting of cost-effectiveness studies individually [7,8]. The type of evidence included in a cost-effectiveness ranking table is a condensed form of information. It constitutes a quality assessment and structured summary on economic evaluations and may be used as guide to navigate within the field of heart diseases and economic evaluations. This compilation of ICERs may also be used to identify areas which lack cost-effectiveness analyses.

Swedish national guidelines are produced using evidence-based knowledge for health care priority setting decisions. The decisions are based on the severity of the disease and clinical effectiveness as well as economic evidence, i.e. weighing different sources of evidence. Cost-effectiveness evidence may therefore be viewed as part of the evidence-based knowledge used for decision-making. When the cost-effectiveness ratios are considered high or in controversial policy decision making cases the original studies have to be consulted and discussed further. In order to play a role in the decision-making process, cost-effectiveness evidence needs to be both accessed and accepted by the decision maker. Decision makers need evidence, both in a condensed and extensive form. However crude, cost-effectiveness ranking tables may provide valid information within a limited space, aiding decision makers on the allocation of health care resources [12].

CONCLUSIONS

This paper represents a comprehensive and accessible compilation of health economic evidence for the treatment of heart diseases, useful in aiding health care decision-making when combined with supplementary information on the severity of the disease and clinical evidence.

ACKNOWLEDGEMENTS

The project on which this paper is based was funded by The National Board of Health and Welfare. We would like to thank Thomas Davidson for participation in compiling the cost-effectiveness ranking table.

CONFLICT OF INTEREST

None declared.

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Table I: *Example of search strategy in MEDLINE/PubMed for Echocardiography.*

Database	
MEDLINE/PubMed	
Limits	
2002-01-01 – 2006-12-30 /English	
Search terms	
Heart Diseases [MeSH]	#1
"cost analysis" OR "cost effectiveness" OR "cost utility" OR "life years saved" OR "life years gained" OR "quality adjusted life years" OR QALY"	#2
Echocardiography [MeSH]	#1 AND #2

Search terms: Adrenergic beta-Antagonists; Aggregation; Aneurysm, Dissecting; Angioplasty, Transluminal, Percutaneous Coronary; Angiotensin-Converting Enzyme Inhibitor; Aortic Aneurysm, Thoracic; Antagonists and inhibitors; Antilipemic agents; Aortic arch replacement; Aortic valve; Aspirin; Blood platelets; Cardiac rehabilitation; Cardiac stimulation; Catheter ablation; Cholesterol; Coronary Angiography; Coronary Artery Bypass; Creatinin; CRP; CT; Defibrillation; Digoxin; Diuretics; Echocardiography; Electrocardiogram; Electrocardiography; Endocarditis; Exercise Test; Glycoprotein inhibitor; Glycoproteins; Heart Catheterization; Heart murmurs; Heart valve; Heart Valve Disease; Heart valve surgery; Hemoglobins; Heparin, Low-Molecular-Weight; Imaging; Implantable cardioverter defibrillator; Ischaemia monitoring; Lipids; Mitral valve; MR; Myocardial diseases /Cardiomyopathies; Myocarditis; Nitroglycerin; Pacemaker; Peak Expiratory Flow Rate; Pericarditis; Perimyocarditis; Permanent pacing; Platelet Aggregation Inhibitors; Potassium; Pulmonary valve; Radiofrequency ablation; Secondary prevention; Sodium; Statins; T4; Thrombolytic Therapy, TSH; Ultrasonography; X-rays.

Table IIa: *Cost-effectiveness ratios for primary prevention with implantable cardioverter defibrillators in Euro (2009).*

Intervention and compared intervention strategy	Patient group	ICER, Euro per QALY or LY gained	References
ICD vs. antiarrhythmic drug treatment (amiodarone) for patients with arrhythmias	High risk patients	33 890 /QALY	Owens et al. [5] (2002)
ICD vs. antiarrhythmic drug treatment (amiodarone) for patients with arrhythmias	Moderate risk patients	51 590 /QALY	Owens et al. [5] (2002)
ICD vs. antiarrhythmic drug treatment (amiodarone) for patients with arrhythmias	Low risk patients	109 350 /QALY	Owens et al. [5] (2002)

ICD, implantable cardioverter defibrillator; ICER, incremental cost-effectiveness ratio; LQTS, long QT syndrome; LY, life year; QALY, quality adjusted life year.

Table IIb: *Cost-effectiveness ratios for primary prevention with implantable cardioverter defibrillators in Euro (2009).*

Intervention and compared intervention strategy	Patient group	ICER, Euro per QALY or LY gained	References
ICD vs. no ICD for prevention of sudden death in young people with inherited cardiac arrhythmias	Men with LQTS	3 140 QALY	Goldenberg et al. [6] (2005)
ICD vs. no ICD for prevention of sudden death in young people with inherited cardiac arrhythmias	Women with LQTS	6 680 /QALY	Goldenberg et al.[6] (2005)
ICD vs. no ICD for prevention of sudden death in young people with inherited cardiac arrhythmias	Women with hypertrophic cardiomyopathy	16 490 /QALY	Goldenberg et al.[6] (2005)
ICD vs. no ICD for prevention of sudden death in young people with inherited cardiac arrhythmias	Men med hypertrophic cardiomyopathy	16 890 /QALY	Goldenberg et al. [6] (2005)

ICD, implantable cardioverter defibrillator; ICER, incremental cost-effectiveness ratio; LQTS, long QT syndrome; LY, life year; QALY, quality adjusted life year.

APPENDIX: *Cost-effectiveness rankings for acute coronary artery disease, stable angina, arrhythmias, heart failure and congenital heart disease in Euro (2009).*

Acute Coronary Artery Disease

Intervention and compared intervention strategy	Patient group	ICER (Euro) per QALY or LY gained	Country	References
PCI and glycoprotein IIb/IIIa receptor antagonist (abciximab) vs. no abciximab for the treatment of coronary heart disease	All patients	< 0 /QALY	UK	Vella [1] (2003)
Primary PCI vs. thrombolysis for acute myocardial infarction	All patients	< 0 /QALY	US	Lieu et al. [2] (1997)
SPECT imaging and coronary angiography vs. exercise electrocardiography and coronary angiography for the diagnosis of coronary artery disease	Women, age 60	< 0 /QALY	UK	Mowatt et al. [3] (2004)
Primary PCI vs. thrombolytic therapy for acute myocardial infarction (STEMI)	All patients	< 0 /LY	Norway	Selmer et al. [4] (2005)
Statin (fluvastatin) vs. no statin treatment after PCI	LIPS, patients with diabetes	100 /QALY	UK	Scuffham et al. [5] (2005)
Clopidogrel and ASA vs. standard treatment (ASA) in patients with acute coronary syndromes	CURE	910 /LY	Sweden	Lindgren et al. [6] (2004)
ACE inhibitor (trandolapril) vs. placebo after myocardial infarction	All patients (TRACE)	1 420 /LY	France	LePen et al. [7] (1998)
ACE inhibitor (ramipril) vs. placebo for heart failure after acute myocardial infarction, 3.8 year treatment	AIRE	1 620 /LY	Sweden	Erhardt et al. [8] (1997)

Statin (simvastatin) vs. placebo for the treatment of coronary heart disease	Men, direct and indirect costs	1 720 /LY	Sweden	Johannesson et al. [9] (1997)
ACE inhibitor (ramipril) vs. placebo for heart failure after acute myocardial infarction, 2 year treatment	AIRE	2 020 /LY	Sweden	Erhardt et al. [8] (1997)
Early invasive strategy vs. medical treatment in patients with unstable coronary artery disease	FRISC II	2 330 /QALY	Sweden	Janzon et al. [10] (2003)
PCI and glycoprotein IIb/IIIa receptor antagonist (abciximab) vs. no abciximab for the treatment of coronary heart disease	All patients	2 930 /LY	US	Kereiakes et al. [11] (2000)
Thrombolysis (streptokinase) vs. ASA for acute myocardial infarction < 4 hours after symptom onset	Age 65	3 030 /QALY	Ireland	Kellett [12] (1996)
ACE inhibitor (ramipril) vs. placebo for heart failure after acute myocardial infarction, 1 year treatment	AIRE	3 740 /LY	Sweden	Erhardt et al. [8] (1997)
ACE inhibitor (captopril) vs. placebo after myocardial infarction	Age 80, no survival benefit beyond 4 years	4 350 /QALY	US	Tsevat et al. [13](1995)
Glycoprotein IIb/IIIa receptor antagonist (abciximab) vs. placebo after PCI	EPIC, high risk patients	4 450 /LY	Australia	Aristides et al. [14] (1998)
ACE inhibitor (captopril) vs. placebo after myocardial infarction	Age 80, difference in survival benefit beyond 4 years	4 450 /QALY	US	Tsevat et al. [13] (1995)
ACE inhibitor (ramipril) vs. placebo for patients with coronary artery disease	HOPE	4 550 /LY	UK	Malik et al. [15] (2001)
Statin (fluvastatin) vs. no statin following successful first PCI	LIPS	4 960 /QALY	UK	Scuffham et al. [16] (2004)

ACE inhibitor (captopril) vs. placebo after myocardial infarction	Age 70, difference in survival benefit beyond 4 years	5 160 /QALY	US	Tsevat et al. [13] (1995)
Statin (simvastatin) vs. placebo for the treatment of coronary artery disease	Women, direct and indirect costs	5 360 /LY	Sweden	Johannesson et al. [9] (1997)
Statin (simvastatin) vs. placebo for the treatment of coronary artery disease	Men, direct costs	5 560 /LY	Sweden	Johannesson et al. [9] (1997)
ACE inhibitor (captopril) vs. placebo after myocardial infarction	Age 70, no survival benefit beyond 4 years	5 870 /QALY	US	Tsevat et al. [13] (1995)
Thrombolysis (streptokinase) vs. ASA for acute myocardial infarction < 4 hours after symptom onset	Age 80	6 270 /QALY	Ireland	Kellett [12] (1996)
ACE inhibitor (captopril) vs. placebo after myocardial infarction	Age 60, difference in survival benefit beyond 4 years	6 780 /QALY	US	Tsevat et al. [13] (1995)
Thrombolysis (t-PA) vs. ASA for acute myocardial infarction < 4 hours after symptom onset	Age 65	6 880 /QALY	Ireland	Kellett [12] (1996)
Clopidogrel vs. placebo in patients with acute coronary syndromes	CURE	7 280 /LY	US	Weintraub et al. [17] (2005)
Statin (pravastatin) vs. placebo in patients with established ischeamic heart disease	LIPID	7 890 /LY	Australia	Glasziou et al. [18] (2002)
Clopidogrel during 12 months vs. 6 months for acute coronary syndromes	CURE	7 990 /QALY	UK	Main et al. [19] (2004)
Thrombolysis (streptokinase) vs. ASA for acute myocardial infarction < 4 hours after symptom onset	Age 50	8 090 /QALY	Ireland	Kellett [12] (1996)

Glycoprotein IIb/IIIa receptor antagonist (GPA) vs. no GPA for patients with non ST elevation acute coronary syndromes	All patients	8 290 /QALY	UK	Palmer et al. [20] (2005)
Clopidogrel during 12 months vs. standard treatment for acute coronary syndromes	CURE	9 410 /QALY	UK	Main et al. [19] (2004)
Thrombolysis (t-PA) vs. ASA for acute myocardial infarction < 4 hours after symptom onset	Age 80	9 410 /QALY	Ireland	Kellett [12] (1996)
Statin (pravastatin) vs. placebo after myocardial infarction	CARE, ≥ age 60	9 510 /QALY	US	Tsevat et al. [21] (2001)
ASA vs. no treatment for the secondary prevention of coronary heart disease	All patients	10 420 /QALY	US	Gaspoz et al. [22] (2002)
ACE inhibitor (captopril) vs. placebo after myocardial infarction	Age 60, no survival benefit beyond 4 years	10 820 /QALY	US	Tsevat et al. [13] (1995)
Clopidogrel during 6 months vs. 3 months for acute coronary syndromes	CURE	11 430 /QALY	UK	Main et al. [19] (2004)
Glycoprotein IIb/IIIa receptor antagonist (eptifibatide) vs. placebo for the treatment of acute coronary syndromes	PURSUIT	11 430 /LY	Germany	Brown et al. [23] (2002)
Early invasive vs. conservative strategy for the treatment of unstable angina and non-ST elevation myocardial infarction	TACTICS-TIMI	12 040 /LY	US	Mahoney et al. [24] (2002)
Thrombolysis (alteplase) vs. streptokinase for the treatment of acute myocardial infarction	All patients	12 140 /QALY	UK	Boland et al. [25] (2003)
Thrombolysis vs. non-thrombolysis for acute myocardial infarction	Time to treatment, 0-6h	12 440 /LY	US	Castillo et al. [26] (1997)

ACE inhibitor (captopril) vs. placebo after myocardial infarction	Age 50, difference in survival benefit beyond 4 years	12 540 /QALY	US	Tsevat et al. [13] (1995)
Thrombolysis (t-PA) vs. thrombolysis (streptokinase) for acute myocardial infarction < 4 hours after symptom onset	Age 65	12 950 /QALY	Ireland	Kellett [12] (1996)
Primary PCI vs. non-thrombolysis for acute myocardial infarction	All patients	13 350 /QALY	US	Lieu et al. [2] (1997)
SPECT imaging and coronary angiography vs. exercise electrocardiography and coronary angiography for the diagnosis of coronary artery disease	Age 60	13 450 /QALY	UK	Mowatt et al. [3] (2004)
Glycoprotein IIb/IIIa receptor antagonist (abciximab) in patients undergoing PCI vs. no abciximab	Patients with acute myocardial infarction	13 660 /LY	US	McCollam et al. [27] (2003)
Clopidogrel plus ASA vs. ASA alone for the treatment of coronary artery disease	CURE, high risk patients	14 570 /QALY	US	Schleinitz et al. [28] (2005)
Thrombolysis (reteplase) vs. streptokinase for the treatment of acute myocardial infarction	All patients	14 670 /QALY	UK	Boland et al. [25] (2003)
Thrombolysis (t-PA) vs. thrombolysis (streptokinase) for acute myocardial infarction < 4 hours after symptom onset	Age 80	15 070 /QALY	Ireland	Kellett [12] (1996)
Thrombolysis vs. non-thrombolysis for acute myocardial infarction	All patients	15 170 /LY	US	Castillo et al. [26] (1997)
Thrombolysis (tenecteplase) vs. streptokinase for the treatment of acute myocardial infarction	All patients	15 880 /QALY	UK	Boland et al. [25] (2003)

Thrombolysis vs. non-thrombolysis for acute myocardial infarction	Time to treatment, 7-12h	18 310 /LY	US	Castillo et al. [26] (1997)
Glycoprotein IIb/IIIa receptor antagonist (eptifibatide) vs. placebo in patients with non ST-elevation acute coronary syndromes	PURSUIT	20 530 /QALY	US	Mark et al. [29] (2000)
Thrombolysis (t-PA) vs. ASA for acute myocardial infarction < 4 hours after symptom onset	Age 50	20 740 /QALY	Ireland	Kellett [12] (1996)
Glycoprotein IIb/IIIa receptor antagonist (abciximab) vs. no abciximab for the treatment of acute myocardial infarction with PCI	CADILLAC	23 770 /QALY	US	Bakhai et al. [30] (2003)
Clopidogrel for patients not eligible for ASA (ASA intolerance) vs. no treatment for secondary prevention of coronary heart disease	Patients with ASA intolerance	29 230 /QALY	US	Gaspoz et al. [22] (2002)
Physical exercise-based rehabilitation vs. conventional treatment for secondary prevention after an acute coronary event	All patients	30 650 /QALY	Australia	Briffa et al. [31] (2005)
Statin (pravastatin) vs. placebo after myocardial infarction	CARE	32 270 /QALY	US	Tsevat et al. [21] (2001)
Thrombolysis (t-PA) vs. thrombolysis (streptokinase) for acute myocardial infarction	GUSTO	40 360 /LY	US	Mark et al. [32] (1995)
Thrombolysis (t-PA) vs. thrombolysis (streptokinase) for acute myocardial infarction < 4 hours after symptom onset	Age 50	40 970 /QALY	Ireland	Kellett [12] (1996)
Thrombolysis (t-PA) vs. thrombolysis (streptokinase) for acute myocardial infarction	GUSTO, inferior myocardial infarction, ≤ age 40	226 180 /LY	US	Mark et al. [32] (1995)

Stable Angina

Intervention and compared intervention strategy	Patient group	ICER (Euro) per QALY or LY gained	Country	References
CABG vs. PCI for patients with multivessel coronary disease	BARI, patients with diabetes	< 0 /LY	US	Hlatky et al. [33] (1997)
Exercise echocardiography vs. exercise electrocardiography for the diagnosis of suspected or known coronary artery disease	All patients	2 430 /LY	US	Marwick et al. [34] (2003)
Clopidogrel and ASA (12 months) vs. clopidogrel and ASA (28 days) following PCI	CREDO	3 030 /QALY	Sweden	Ringborg et al. [35] (2005)
Stent plus glycoprotein IIb/IIIa receptor antagonist (abciximab) vs. PCI plus abciximab	EPISTENT	5 360 /LY	US	Topol et al. [36] (1999)
Clopidogrel vs. placebo for patients after PCI	CREDO	6 580 /LY	US	Beinart et al. [37] (2005)
Clopidogrel plus ASA vs. ASA alone in patients with unstable coronary artery disease undergoing PCI	PCI-CURE	7 490 /LY	Sweden	Lindgren et al. [38] (2005)
Stent vs. no stent for the treatment of coronary artery heart disease with PCI	New patients	9 310 /QALY	UK	Vella [1] (2003)
CABG vs. PCI for the treatment of multivessel coronary artery disease	BARI	12 640 /LY	US	Hlatky et al. [39] (2004)
Prolonged treatment (1 month-12 months) with clopidogrel vs. no treatment after PCI	CREDO	14 770 /LY	US	Cowper et al. [40] (2005)

Exercise echocardiography vs. SPECT imaging in patients with stable chest	Patients with annual risk of cardiac death or myocardial infarction (MI) < 0.02	19 420 /LY	US	Shaw et al. [41] (2006)
CABG vs. PCI among coronary disease patients appropriate for CABG only	All patients	27 010 /QALY	UK	Griffin et al. [42] (2007)
CABG vs. PCI for patients with ≥ 2 vessel coronary disease or > 50 percent stenosis	BARI	27 510 /LY	US	Hlatky et al. [33] (1997)
SPECT imaging vs. exercise echocardiography in patients with stable chest pain	Patients with established coronary disease	30 550 /LY	US	Shaw et al. [41] (2006)
Exercise echocardiography vs. SPECT imaging in patients with stable chest pain	Patients with intermediate risk Duke Treadmill score (>-11 and <4)	37 230 /LY	US	Shaw et al. [41] (2006)
Exercise echocardiography vs. exercise electrocardiography for the diagnosis of chest pain	Men, age 55, typical angina	43 600 /QALY	US	Kuntz et al. [43] (1999)
Exercise echocardiography vs. SPECT imaging in patients with stable chest pain	All patients	68 080 /LY	US	Shaw et al. [41] (2006)
Screening with computor tomography vs. Framingham risk index alone to identify patients at risk for coronary artery disease	Age 39-45	81 830 /QALY	US	O'Malley et al. [44] (2004)
Whole-body computor tomography screening vs. no screening for asymptomatic 50-year old men	All patients	142 330 /LY	US	Beinfeld et al. [45] (2005)
Exercise echocardiography vs. SPECT imaging in patients with stable chest pain	Patients with annual risk of cardiac death or myocardial	324 610 /LY	US	Shaw et al. [41] (2006)

	infarction (MI) > 0.02			
Drug eluting stents (DES) vs. conventional stents for patients with coronary artery disease undergoing PCI	Patients with diabetes	517 820 /QALY	UK	NICE [46] (2007)
Drug eluting stents (DES) vs. conventional stents for patients with coronary artery disease undergoing PCI	All patients	619 880 /QALY	UK	NICE [46] (2007)
PCI vs. CABG among coronary disease patients appropriate for CABG only	All patients	∞ /QALY	UK	Griffin et al. [42] (2007)

Arrhythmias

Intervention and compared intervention strategy	**Patient group**	**ICER, Euro per QALY or LY gained**	**Country**	**References**
Rate control (medical treatment) vs. rhythm control for the treatment of persistent atrial fibrillation	RACE	< 0 /event avoided	Netherlands	Hagens et al. [47] (2004)
Initial radiofrequency ablation vs. episodic medical management for supraventricular tachycardia	All patients	< 0 /QALY	US	Cheng et al. [48] (2000)
Initial radiofrequency ablation vs. long-term medical management supraventricular tachycardia	All patients	< 0 /QALY	US	Cheng et al. [48] (2000)
Warfarin vs. ASA for patients with atrial fibrillation	Patients with high stroke risk	< 0 /QALY	US	Gage et al. [49] (1995)
Warfarin vs. no prophylaxis for patients with atrial fibrillation	Patients with high stroke risk	< 0 /QALY	US	Sullivan et al. [50] (2006)

ICD vs. no ICD for prevention of sudden death in young people with inherited cardiac arrhythmias	Men with LQTS	3 140 /QALY	US	Goldenberg et al. [51] (2005)
Dual chamber pacing vs. ventricular pacing for patients with sick sinus syndrome	MOST	6 370 /QALY	US	Rinfret et al. [52] (2005)
ICD vs. no ICD for prevention of sudden death in young people with inherited cardiac arrhythmias	Women with LQTS	6 680 /QALY	US	Goldenberg et al. [51] (2005)
Warfarin vs. ASA for patients with atrial fibrillation	Patients with moderate stroke risk	9 100 /QALY	US	Gage et al. [49] (1995)
Dual chamber pacing vs. single chamber ventricular pacing for patients with bradycardia due to AV-block	All patients	12 950 /QALY	UK	Castelnuovo et al. [53] (2005)
Dual chamber pacing vs. single chamber ventricular pacing for patients with bradycardia due to sick sinus syndrome	All patients	14 570 /QALY	UK	Castelnuovo et al. [53] (2005)
ICD vs. no ICD for prevention of sudden death in young people with inherited cardiac arrhythmias	Women with hypertrophic cardiomyopathy	16 490 /QALY	US	Goldenberg et al. [51] (2005)
ICD vs. no ICD for prevention of sudden death in young people with inherited cardiac arrhythmias	Men med hypertrophic cardiomyopathy	16 890 /QALY	US	Goldenberg et al. [51] (2005)
ICD vs. antiarrhythmic drug treatment (amiodarone) for patients with arrhythmias	High risk patients	33 890 /QALY	US	Owens et al. [54] (2002)
ICD vs. antiarrhythmic drug treatment used as secondary prevention for arrhythmias	Patients having survived a cardiac arrest, LVEF<0.35	38 440 /QALY	UK	NICE [55] (2006)
CRT-ICD vs. medical treatment alone for	COMPANION	40 560 /QALY	US	Feldman et al.

patients with heart failure				[56] (2005)
ICD vs. conventional medical treatment for patients with a history of myocardial infarction (MI)	MADIT II, EF<0.3	47 640 /LY	US	Al-Khatib et al. [57] (2005)
ICD vs. conventional treatment for patients after myocardial infarction (MI)	MADIT II, EF<0.3	47 950 /QALY	US	Sanders et al. [58] (2004)
ICD vs. control treatment for patients after myocardial infarction (MI)	MADIT II, EF<0.3	50 980 /QALY	US	Sanders et al. [59] (2005)
ICD vs. antiarrhythmic drug treatment (amiodarone) for patients with arrhthymias	Moderate risk patients	51 590 /QALY	US	Owens et al. [54] (2002)
ICD vs. medical treatment for patients with chronic heart failure	SCD-HeFT, patients with NYHA II or III	55 230 /LY	US	Mark et al. [60] (2006)
CRT with ICD vs. CRT alone for patients with heart failure	CARE-HF, battery life 5 years	59 990 /QALY	UK	Yao et al. [61] (2007)
ICD vs. antiarrhythmic drug treatment for the treatment of ventricular tachyarrhythmias	Patients with severe ventricular tachycardia	62 820 /LY	US	Larsen et al. [62] (2002)
ICD vs. conventional medical treatment for patients after myocardial infarction (MI)	MADIT II, EF<0.3	86 290 /LY	US	Zwanziger et al. [63] (2006)
ICD vs. conventional medical treatment for congestive heart failure (sudden death prevention)	Patients with NYHA II or III	92 250 /QALY	US	Chen et al. [64] (2004)
ICD vs. antiarrhythmic drug treatment (amiodarone) for patients with arrhthymias	Low risk patients	109 350 /QALY	US	Owens et al. [54] (2002)
CRT-ICD vs. CRT alone for patients with heart failure	COMPANION	169 030 /QALY	US	Feldman et al. [56] (2005)

Dual chamber pacing vs. single chamber atrial pacing for patients with bradycardia due to sick sinus syndrome	All patients	∞ /QALY	UK	Castelnuovo et al. [53] (2005)
Screening of young active athletes vs. no screening for sudden death prevention	Age 12	∞ /QALY	Sweden	Brodtkorb [65] (2006)

Heart Failure

Intervention and compared intervention strategy	**Patient group**	**ICER (Euro) per QALY or LY gained**	**Country**	**References**
Aldactone (spironolactone) vs. placebo for the treatment of severe heart failure	RALES, high risk patients	< 0 /QALY	US	Glick et al. [66] (2002)
BNP vs. echocardiography as a screening test for heart failure	Breathless patients	< 0 /event avoided	UK	Sim et al. [67] (2003)
ARB (candesartan) vs. placebo for patients with heart failure	CHARM-Added, NYHA II-IV, LVEF <0.40	< 0 /LY	UK	McMurray et al. [68] (2006)
Beta blockade (metoprolol) vs. placebo for the treatment of heart failure	All patients	2 630 /LY	US	Gregory et al. [69] (2001)
Beta blockade (bisoprolol) vs. placebo for the treatment of heart failure	All patients	3 540 /LY	US	Gregory et al. [69] (2001)
Beta blockade (carvedilol) vs. placebo for the treatment of heart failure	All patients	7 080 /LY	US	Gregory et al. [69] (2001)
CRT in combination with optimal medical treatment vs. medical treatment alone for patients with heart failure	COMPANION	18 410 /QALY	US	Feldman et al. [56] (2005)
CRT plus medical treatment vs. medical treatment alone for patients with severe	CARE-HF, NYHA III-IV, LVEF<0.35	19 420 /QALY	UK	Calvert et al. [70] (2005)

heart failure				
Screening with BNP plus echocardiography vs. no screening to identify asymptomatic patients with heart failure	Men, age 60	21 040 /QALY	US	Heidenreich et al. [71] (2004)
Beta blockade (carvedilol) vs. placebo for the treatment of heart failure	The US Carvedilol Heart Failure Trials Program	29 840 /LY	US	Delea et al. [72] (1999)
CRT plus medical treatment vs. medical treatment alone for patients with heart failure	Patients with NYHA III or IV	34 490 /QALY	Germany	Banz [73] (2005)
Screening with echocardiography vs. no screening to identify asymptomatic patients with heart failure	Men, age 60	53 210 /QALY	US	Heidenreich et al. [71](2004)
Screening med BNP plus echocardiography vs. no screening to identify asymptomatic patients with heart failure	Women, age 60	72 830 /QALY	US	Heidenreich et al. [71] (2004)
Screening BNP vs. no screening to identify asymptomatic patients with heart failure	Men, age 60	85 170 /QALY	US	Heidenreich et al. [71] (2004)
CRT vs. medical treatment for patients with symptomatic heart failure	Patients with reduced ventricular function	99 130 /QALY	US	Nichol et al. [74] (2004)
Left ventricular assist device (LVAD) used as bridge for heart transplantation vs. medical treatment for end-stage heart failure	Patients on the heart transplantation waiting list	99 330 /QALY	UK	Clegg et al. [75] (2005)
Left ventricular assist device (LVAD) used as long-term chronic support vs. medical treatment for end-stage heart failure	Patients excluded from the heart transplantation waiting list	259 870 /QALY	UK	Clegg et al. [75] (2005)

Screening with echocardiography vs. no screening to identify asymptomatic patients with heart failure	Women, age 60	447 710 /QALY	US	Heidenreich et al. [71] (2004)
Screening with BNP vs. no screening to identify asymptomatic patients with heart failure	Women, age 60	958 040 /QALY	US	Heidenreich et al. [71] (2004)

Congenital Heart Disease

Intervention and compared intervention strategy	**Patient group**	**ICER (Euro) per QALY or LY gained**	**Country**	**References**
Antibiotic prophylaxis (clarithromycin) vs. no treatment for patients undergoing dental procedures	Patients with increased risk for endocarditis	82 950 /QALY	US	Agha et al. [76] (2005)
Antibiotic prophylaxis (cephalexin) vs. no treatment for patients undergoing dental procedures	Patients with increased risk for endocarditis	93 130 /QALY	US	Agha et al. [76] (2005)

ACE, angiotensin-converting enzyme; ARB, angiotensin receptor blocker; ASA, Acetylsalicylic Acid (aspirin); BNP, B-type natriuretic peptide; CABG, coronary artery bypass grafting; CRT, cardiac resynchronization therapy; Dominant (<0), a treatment strategy associated with incremental gain in effects with reduced costs; EF, ejection fraction; ICD, implantable cardioverter defibrillator; ICER, incremental cost-effectiveness ratio; LQTS, long QT syndrome; LVEF, left ventricular ejection fraction; LY, life year; NYHA, New York Heart Association; PCI, percutaneous coronary intervention; QALY, quality adjusted life year; SPECT, single-photon emission computed tomography.

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