

ORIGINAL RESEARCH

# Conversion of the Seattle Angina Questionnaire into EQ-5D utilities for ischemic heart disease: a systematic review and catalog of the literature

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Background: There is a paucity of preference-based (utility) measures of health-related quality of life for patients with ischemic heart disease (IHD); in contrast, the Seattle Angina Questionnaire (SAQ) is a widely used descriptive measure. Our objective was to perform a systematic review of the literature to identify IHD studies reporting SAQ scores in order to apply a mapping algorithm to convert these to preference-based scores for secondary use in economic evaluations.

Methods: Relevant articles were identified in MEDLINE (Ovid), EMBASE (Ovid), Cochrane Library (Wiley), HealthStar (Ovid), and PubMed from inception to 2012. We previously developed and validated a mapping algorithm that converts SAQ descriptive scores to European Quality of Life-5 Dimensions (EQ-5D) utility scores. In the current study, this mapping algorithm was used to estimate EQ-5D utility scores from SAQ scores.

Results: Thirty-six studies met the inclusion criteria. The studies were categorized into three groups, ie, general IHD (n=13), acute coronary syndromes (n=4), and revascularization (n=19). EQ-5D scores for patients with general IHD were in the range of 0.605-0.843 at baseline, and increased to 0.649-0.877 post follow-up. EQ-5D scores for studies of patients with recent acute coronary syndromes increased from 0.706-0.796 at baseline to 0.795-0.942 post follow-up. The revascularization studies had EQ-5D scores in the range of 0.616-0.790 at baseline, and increased to 0.653-0.928 after treatment; studies that focused only on coronary artery bypass grafting increased from 0.643-0.788 at baseline to 0.653-0.928 after grafting, and studies that focused only on percutaneous coronary intervention increased in score from 0.616-0.790 at baseline to 0.668-0.897 after treatment.

**Conclusion:** In this review, we provide a catalog of estimated health utility scores across a wide range of disease severity and following various interventions in patients with IHD. Our catalog of EQ-5D scores can be used in IHD-related economic evaluations.

Keywords: health-related quality of life, Seattle Angina Questionnaire, utilities, European Quality of Life-5 Dimensions, mapping algorithm, ischemic heart disease

#### Introduction

Economic evaluations with cost-effectiveness analyses are important in the decisionmaking process for health resource allocation. Cost-effectiveness analysis involves estimation of the incremental cost of a new intervention as well as its incremental net health benefit, in comparison with a reference. To facilitate the comparison of different interventions, it is important that the health effects be reported in standardized units. Current guidelines recommend that the metric of choice for reporting health benefits in cost-effectiveness analysis is the quality-adjusted life-year. 1-5

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A variety of techniques have been developed to assess patient quality of life. Available instruments can be generally classified into two major categories, ie, descriptive measurement instruments or preference-based methods. Descriptive measurement instruments are designed to measure quality of life across important aspects of a patient's health state, such as physical, psychosocial, or functional well-being.6 Such instruments provide a score for each health domain and a quantitative measure that represents a patient's current health state. In contrast, preference-based or utility instruments, such as the European Quality of Life-5 Dimensions (EQ-5D), add a valuation component to a patient's reported health state. These instruments are designed to reflect both a quantitative description of a patient's health state and society's preference for that particular health state. This preference component is the primary distinction between a utility instrument and a descriptive measurement instrument. Preference-based instruments allow for the calculation of quality-adjusted life-years.

In ischemic heart disease (IHD) research, there is an abundance of published literature on the Seattle Angina Questionnaire (SAQ), a descriptive quality of life instrument. The SAQ is a validated descriptive instrument that evaluates quality of life in patients with IHD across five domains, specifically physical limitation, treatment satisfaction, angina frequency, angina stability, and disease perception. In contrast, there is a paucity of studies that report utility weights for patients with IHD. The absence of available and up-to-date utility weights is a substantial limitation when performing economic analyses in IHD. To address this lack of utility information, we have previously published a mapping algorithm to convert SAQ descriptive scores to utility weights, based on the EQ-5D preference-based utility instrument.

In this study, we extended our previous work by performing a systematic review of the literature to identify all previous studies that used the SAQ to measure health state, and then applied our validated mapping algorithm to create a comprehensive catalog of utility weights across the spectrum of IHD, with the intention that our catalog be used for future economic evaluations in IHD.

# Materials and methods

# Search strategy

First, we conducted a systematic review of the published literature, conforming to the standards recommended by the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines.<sup>11</sup> We used the search terms "Seattle Angina Questionnaire", "SAQ", or slight modifica-

tions of these terms (see Supplementary material for full search strategy) to identify potentially relevant citations from inception to November 7, 2012 using the following medical literature databases: MEDLINE (Ovid), EMBASE (Ovid), Cochrane Library (Wiley), HealthStar (Ovid), and PubMed. We subsequently performed a citation search in Google Scholar (Google), Web of Science (Thomson Reuters), and Scopus (Elsevier) to identify articles citing the original paper by Spertus et al<sup>8</sup> that first examined the validity and reliability of the SAQ. Finally, we searched major clinical trial registries (clinicaltrials.gov and clinicaltrialsregister.eu) from inception to November 7, 2012 for studies that used the SAQ as an outcome measure, using the search terms "Seattle Angina Questionnaire" or "SAQ".

Upon removal of duplications, two independent reviewers (SF and HCW) screened each reference. We utilized a hierarchal approach, screening citations by title, then abstract, and finally by full text to determine relevance. Reviewers assessed the eligibility of these selected articles according to two prespecified inclusion criteria, ie, that publication was in English and that mean scores and standard errors (or the ability to calculate standard errors from the available data) were reported for all five domains of the SAQ. Although the SAQ has been translated into multiple languages, the original SAQ validation studies were based on the English version; as such, we restricted our algorithm to English articles. All five domains were needed to utilize our mapping algorithm. Exclusion criteria were articles that reported on experimental interventions (eg, transmyocardial laser revascularization, herbal medicine) that are not part of standard therapy. The following information was extracted from eligible studies: baseline characteristics of study participants (age, gender); inclusion and exclusion criteria for each study, interventions (eg, myocardial infarction, revascularization) and follow-up duration; and reported SAQ scores and standard errors.

# Data synthesis

We have previously created and published a prediction algorithm using multivariable linear regression modeling, with the utility weight from the EQ-5D being our response variable of interest. Details of the derivation and validation of the mapping algorithm are available elsewhere. In brief, all model fitting was done using Bayesian methods. The posterior probability distribution for each of the model parameters was estimated using Markov Chain Monte Carlo simulation methods, with noninformative prior distributions for all model parameters. The data for model development

were from 1,992 consecutive patients who underwent coronary angiography in 2004 as part of the Alberta Provincial Project for Outcome Assessment in Coronary Heart Disease database. The final mapping algorithm was a linear regression model, with the dependent variable being the EQ-5D, and a conditional distribution of  $Y_i \sim N(\mu_i, \sigma_i)$ . The specification of the mean was given by:

$$\mu_{i} = \beta_{0} + \beta_{1}AF_{i} + \beta_{2}AS_{i} + \beta_{3}DP_{i} + \beta_{4}PL_{i} + \beta_{5}TS_{i}$$

with the following parameter estimates: intercept 0.4388 (0.4015–0.4763),  $\beta$  AF 0.0010 (0.0007–0.0013),  $\beta$  AS –0.0002 (–0.0005 to 0.0000),  $\beta$  DP 0.0023 (0.0020–0.0027),  $\beta$  PL 0.0019 (0.0017–0.0022),  $\beta$  TS 0.0004 (–0.0001 to 0.0008).

Using the posterior distribution for the coefficients of the final linear regression mapping algorithm, we calculated the EQ-5D based on the scores for the five SAQ domains for each included study. To fully incorporate uncertainty in the estimated EQ-5D utilities, we assumed that the inputted SAQ values from each paper had a normal distribution, based on the mean and standard error. We sampled from this distribution to calculate the mean and 95% credible interval of the estimated EQ-5D.

The mapping algorithm and EQ-5D estimates were calculated using WinBUGS version 1.4 (Medical Research Council, London, UK).

### **Results**

## Study selection

We identified 2,776 citations from various sources using our search criteria. After removing duplications, 1,092 articles were screened to identify articles in English that were potentially relevant and that reported scores and standard errors (or standard deviation and sample size, or confidence intervals, in order to calculate the standard error) for all five domains of the SAQ. Full review was done on 60 articles. We excluded 24 of these articles because they provided SAQ scores following experimental interventions, ie, neurostimulation (six articles), autologous bone marrow transplant (three articles), transmyocardial laser revascularization (six articles), herbal medicine (two articles), fibroblast growth factor (one article), granulocyte colony-stimulating factor (one article), cognitive behavioral therapy (one article), and other (four articles). A total of 36 articles met our eligibility criteria and were included in the final analysis. Figure 1 presents the flow diagram of our review process.

## Study characteristics

The 36 studies in our systematic review represent a wide spectrum of patients with IHD. Eight of these studies focused exclusively on patients with stable angina, 12-19 and four included patients with a previous myocardial infarction. 12,20-22 Four studies specifically assessed SAQ in patients with advanced IHD unsuitable for revascularization. 18,23-25 These studies reported SAQ scores in patients with general angina, or specifically with severe or refractory angina. Five studies were restricted to an elderly population, 23,26-29 one study was restricted to women with IHD,30 and one study reported SAO data in diabetic patients with IHD.17 SAQ data were compared among South Asians versus Europeans with IHD in one study,31 while another study reported the SAQs of Caucasians and African Americans with IHD.<sup>20</sup> The studies ranged from cross-sectional evaluations with no follow-up to longitudinal studies with follow-up ranging from 7 days to a mean of 6 years and 11 months.

Given our intent to form a catalog such that estimated utility scores can be easily referenced, we categorized the 36 included articles in three groups, as shown in Tables 1–3. Thirteen studies focused on general IHD patients (Table 1), four focused on patients with recent acute coronary syndrome (Table 2), and 19 assessed revascularized patients (Table 3), of which eight included only patients who underwent coronary artery bypass grafting (CABG)<sup>23,28,29,32–36</sup> and six included only patients who had percutaneous coronary intervention. <sup>19,21,27,37–39</sup>

# Predicted EQ-5D

The SAQ scores from the original publications and the calculated EQ-5D scores are shown in Tables 1–3. The estimated baseline EQ-5D scores for the general IHD patients were in the range of 0.605–0.843, increasing to 0.649–0.877 post follow-up (Table 1). The baseline range was 0.706–0.796 for the studies focused on patients with a recent acute coronary syndrome, increasing to 0.795–0.942 post follow-up (Table 2). The revascularization studies had EQ-5D scores in the range of 0.616–0.790 at baseline, increasing to 0.653–0.928 after treatment (Table 3). Studies that included only CABG as the revascularization modality had an EQ-5D score range that increased from 0.643–0.788 at baseline to 0.653–0.928 after CABG; the studies that focused only on percutaneous coronary intervention had scores that increased from 0.616–0.790 at baseline to 0.668–0.897 after treatment.

#### **Discussion**

In this report, we have provided a comprehensive catalog of predicted EQ-5D utility scores for patients with IHD. We first

- Ovid MEDLINE searched on November 7, 2012 (432 citations)
- Ovid EMBASE searched on November 7, 2012 (574 citations)
- PubMed searched on November 7, 2012 (366 citations)
- Cochrane Library searched on November 7, 2012 (63 citations)
- Ovid HealthStar searched on November 7, 2012 (388 citations)
- SCOPUS searched on November 7, 2012 (131 citations)
- Web of Science searched on November 7, 2012 (322 citations)
- Google Scholar searched on November 7, 2012 (476 citations)
- ClinicalTrials.gov searched on November 7, 2012 (23 citations)
- EU Clinical Trials Register searched on November 7, 2012 (one citation)

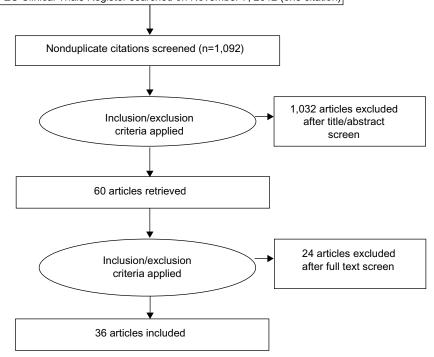


Figure I Process of study selection.

performed a systematic review of the literature to identify studies that reported SAQ scores and then applied our previously validated mapping algorithm to convert SAQ scores to EQ-5D scores. The studies included in our systematic review represent a broad spectrum of IHD patients and assessed quality of life at baseline and/or following a broad range of nonpharmacologic, medical, or surgical interventions.

Patient-reported health status has gained an increasingly important role in the decision-making process for health resource allocation. 40 Patient health status independently predicts mortality, cardiovascular events, hospitalizations, and costs of care in cardiovascular illnesses. 41-43 Current methodologic guidelines emphasize the importance of preference-based measures in comparative effectiveness studies of health technologies. For example, the National Institute for Health and Clinical Excellence suggests that EQ-5D is the preferred method in quantifying the health outcome of various interventions. 44 However, in many

circumstances, preference-based instruments have not been included in cardiovascular studies. In the absence of such information, mapping techniques such as that applied in the current study can be used to estimate utility weights from available descriptive quality of life data.<sup>45</sup>

Dyer et al recently published a summary of available EQ-5D scores from the entire spectrum of cardiovascular diseases, 46 and were able to identify 18 studies in IHD. They observed significant heterogeneity in the reported EQ-5D scores across these studies, in the range of 0.45–0.88. We believe our study is an important addition to this early work, by providing utility scores on additional studies in IHD, covering a wide spectrum of revascularization modalities and patient populations. Similar to the previous work by Dyer et al, we found heterogeneity between studies. This heterogeneity in utility weights between studies underscores the importance of a catalog such as ours. When researchers are developing economic models, it is essential that the

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Table I

Reference	Inclusion/exclusion	Intervention/Subgroup	2	Mean age,	Gender	Time	PL	SAO				
				years	(% male)	point		AS	AF	TS	DP	EQ-5D
Bainey et al <sup>31</sup>	(I) Diagnosed with IHD.	I. South Asians	635	62.1	6.77	l year	75.0	77.0	86.0	86.0	71.0	0.852
		7	10 027	3 6 7	0 77	300	(0.91)	(E)	(0.91)	(0.75)	(0.95)	(0.84–0.86)
			6,0	r: 00	2	ا کوما	80.0	0. 5	88.0	0.68	0.9 6	0.877
Broddadottir	(I) Women with IHD who consented to	I. All ages	437	66.4	0:0	Baseline	(0.44) 56.4	(0.52) 75.8	(0.38) 76.7	(0.30) 85.9	(0.40)	(0.8/-0.88) 0.781
et al <sup>30</sup>	participate in the study.	)					(1.12)	(1.45)	(1.23)	(0.78)	(1.13)	(0.77–0.79)
		<ol><li>Age 32–59 years</li></ol>	133	52.3	0.0	Baseline	57.4	72.9	72.1	82.0	52.5	0.760
							(2.02)	(2.66)	(2.18)	(1.66)	(2.06)	(0.75-0.78)
		3. Age 60–74 years	190	68.7	0.0	Baseline	0.09	77.7	79.0	87.7	62.8	0.797
		7 A 7 OO	=	707	C	0000	(I.70)	(2.26)	(1.93)	(I.10)	(1.71)	(0.78–0.81)
			<u>+</u>	0.27	9	Daseille	(2.06)	(2.70)	(2.28)	(1.24)	(2.06)	(0.76–0.79)
Leung et al <sup>47</sup>	(I) IHD and eligible for cardiac rehabilitation.	I. All patients	1,056	66.3	71.8	9 months	61.7	75.1	86.9	78.7	67.3	0.816
							(0.64)	(16.0)	(0.67)	(0.78)	(0.84)	(0.81-0.83)
		2. No rehabilitation	725	6.99	70.1	9 months	59.0	71.4	84.8	76.5	9.59	0.805
							(0.81)	(1.14)	(0.87)	(0.99)	(1.01)	(0.79-0.82)
		3. Rehabilitation	148	63.3	71.9	9 months	689	83.1	6.06	85.5	72.4	0.847
							(1.19)	(2.09)	(1.42)	(1.56)	(2.09)	(0.83-0.86)
		4. Rehabilitation	183	65.7	72.0	9 months	66.7	83.3	91.7	82.0	2.69	0.836
		>6 months					(1.29)	(1.81)	(1.02)	(1.73)	(2.06)	(0.82-0.85)
Ohldin et al <sup>20</sup>	(I) Veterans, IHD: self-reported angina,	I. Caucasians	6,704	66.3	98.3	Baseline	50.8	56.2	76.5	83.0	63.0	0.781
	history of myocardial infarction, coronary						(0.32)	(0.33)	(0.29)	(0.25)	(0.31)	(0.77–0.79)
	artery disease, or a coronary artery	2. African Americans	1,281	64.0	9.86	Baseline	51.9	57.6	76.0	9'.//	58.5	0.769
	revascularization procedure on the						(0.72)	(0.85)	(0.69)	(0.70)	(0.77)	(0.76–0.78)
Fathi et al <sup>24</sup>	(I) Angina, symptomatic IHD, unsuitable for	1. Usual therapy of lipids	30	63.4	80.0	Baseline	59.0	57.0	64.0	85.0	29.0	0.775
	revascularization. (E) LVEF $<$ 30%, could not	(target LDL < 116)					(4.74)	(6.20)	(5.47)	(2.73)	(4.38)	(0.74-0.81)
	comply with follow-up, had a condition that					12 weeks	58.0	64.0	65.0	82.0	57.0	0.767
	precluded the performance of stress testing,						(4.92)	(4.74)	(5.84)	(3.28)	(4.56)	(0.74-0.80)
	and had compromised life expectancy.	<ol><li>Aggressive lipid</li></ol>	30	63.9	77.0	Baseline	67.0	64.0	72.0	92.0	0.09	0.802
		reduction/target					(4.56)	(4.92)	(5.84)	(2.55)	(4.92)	(0.77-0.83)
		LDL <77				12 weeks	73.0	78.0	80.0	91.0	70.0	0.842
							(4.19)	(5.29)	(4.56)	(1.82)	(4.01)	(0.81-0.87)
Moore et al <sup>25</sup>	(I) Refractory angina (rejected for	Refractory angina	69	62.3	81.0	Baseline	25.2	32.8	26.9	62.8	31.3	0.605
	revascularization) and referred to refractory	program					(1.49)	(2.85)	(2.32)	(2.80)	(2.38)	(0.58-0.63)
	angina clinic.					l year	27.7	43.5	37.7	72.0	42.9	0.649
							(1.73)	(3.32)	(2.78)	(2.78)	(3.17)	(0.63-0.67)
												(Continued)

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Reference	Inclusion/exclusion	Intervention/Subaroun	2	Mean age	Gender	Lime	ā	0 40				
		500000000000000000000000000000000000000	:	years	(% male)	point		AS	AF	TS	DP	EQ-5D
Spertus et al <sup>12</sup>	(I) Chronic, stable, symptomatic IHD,	I. Usual antianginal	49	64.6	₹ Z	Baseline	54.2	57.1	6.99	83.6	55.3	092'0
	documented history of coronary disease	medications					(3.61)	(3.41)	(3.52)	(2.07)	(3.14)	(0.74–0.78)
	(prior MI, coronary revascularization, or	2. Long-acting diltiazem $\pm$	21	65.3	Ϋ́	Baseline	48.9	50.5	26.7	9.08	48.7	0.724
	history of typical angina pectoris), taking at	nitroglycerin patches $\pm$					(3.05)	(3.01)	(3.87)	(2.31)	(2.99)	(0.70-0.75)
	least 2 regular antiangina medications for	atenolol										
	control of symptoms.											
	(E) Hospitalizations within 4 months, aortic											
	stenosis, EF $<$ 40%, sick sinus syndrome,											
	advanced heart block, or other significant											
	comorbidity limiting life expectancy.											
Beltrame et al <sup>13</sup>	(I) Stable angina. Not required to have		2,031	71.0	64.0	Baseline	70.0	63.0	84.0	0.06	70.0	0.843
	ongoing angina symptoms.						(0.62)	(0.59)	(0.51)	(0.31)	(0.54)	(0.84-0.85)
Makolkin and	(I) Stable angina with average of $>$ 3 angina	Trimetazidine and	846	58.7	0.19	Baseline	50.7	57.6	33.3	62.3	36.7	0.667
Osadchiy <sup>14</sup>	attacks/week, 1–2 antianginal agents with	conventional therapy					(0.70)	(0.90)	(0.70)	(0.70)	(09:0)	(0.65-0.68)
	hemodynamic action at stable doses at the					8 weeks	0.19	92.5	55.6	77.4	55.5	0.751
	time of inclusion for $\geq 3$ months.						(09:0)	(0.70)	(0.80)	(0.50)	(0.70)	(0.74-0.76)
	(E) NYHA class ≥II, unstable angina, recent											
	MI or stroke within 6 months, severe											
	arrhythmia or conduction impairment.											
Stone et al <sup>15</sup>	(I) Age ≥ 18 years, chronic stable angina and	1. Placebo + amlodipine	283	61.3	73.0	Baseline	48.9	57.2	40.0	75.4	41.5	0.687
	≥3 episodes of angina/week despite treatment						(1.02)	(1.05)	(0.88)	(0.83)	(1.05)	(0.67-0.70)
	with 10 mg of amlodinine.	2. Ranolazine +	281	62.0	72.0	Baseline	49.2	54.7	40.6	74.6	41.6	0.688
	(E) NYHA class IV CHE prior MI unstable						(1.03)	(1.07)	(0.78)	(0.85)	(1.02)	(0.68-0.70)
	angina within 2 months, active acute							•	•	•		
	myocarditis, pericarditis, hypertrophic											
	cardiomyopathy, uncontrolled hypertension,											
	history of torsades de pointes, agents to											
	prolong QTc interval, QTc interval											
	≥500 msec, receiving inhibitors of											
	cytochrome P450-3A4, hepatic disease,											
	creatinine clearance $<\!\!30$ mL/min, chronic											
	illness likely to interfere with protocol											
	compliance, taking any digitalis preparation,											
	perhexiline, trimetazidine, beta-blockers, or											
	calcium channel blockers other than											
	amlodipine, proscribed antianginal medications											
	within 4 weeks before initiation of the study											
	drug, participation in another investigative trial											
	within 30 days before study start.											

.78)	.79)	.76)	(7.7.1) (7.7.1)
	0.766 (0.74–0.79)	0.750 (0.74–0.76) 0.767	0.746 0.726 0.727 (0.70–0.75)
53.0 (3.33) 61.0 (2.66)	(3.83)	(1.45) (1.45) 49.0	(3.36) 47.7 (3.63) 42.3 (3.36)
70.0 (3.16) 77.0 (2.50)	(3.83)	(1.17) 85.0	(2.55) 83.1 (2.55) 79.4 (2.75)
(3.50) (7.0) (3.16)	(4.00)	(1.56) (1.56) (1.02)	57.5 (4.67) 54.3 (4.58)
54.0 (2.66) 67.0 (3.66)	(3.66)	(1.84) 51.0	46.3 (3.95) 48.8 (3.99)
60.0 (2.33) 64.0 (2.50)	(3.50)	(1.48) (5.0	(4.29) (4.29) 57.7 (4.29)
Baseline  1. 2 weeks of dietary management	2. z weeks of placebo	Baseline Baseline	Baseline I week pre- angiography
77.8		84.0	67.5
65.9		62.0	64.6
38		320	4
Dietary management (2 L-arginine-enriched nutrient bars/day)		Diabetic     Nondiabetic	Coronary angiogram
(l) CCS II and III stable angina and ≥1 mm ST Dietary management depression during treadmill exercise testing (2 L-arginine-enriche before achieving 14.5 Mets. (E) Unstable angina, MI, major surgery or angioplasty within the past 3 months,	symptomatic H1; impaired renal or hepatic function, or any other systemic illness, congenital heart disease, valvular heart disease, atrial fibrillation, uncontrolled hypertension, type I diabetes, diseases other than IHD that would interfere with treadmill testing.	(l) Stable, symptomatic IHD and coronary anatomy suitable for PCI.	(l) Elective, first time coronary angiogram, planned angiography date 3–8 weeks from the time of referral, understand written or spoken English.  (E) Previous coronary angiography, CABG surgery, PCI, or other cardiac procedures such as valve surgery, awaiting coronary
Maxwell et al <sup>16</sup>		Deaton et al <sup>17</sup>	de Jong-Watt et al⁴

**Note:** SAQ values include standard error; EQ-5D values include 95% confidence intervals.

Abbreviations: I, inclusion criteria; E, exclusion criteria; EF, ejection fraction; IHD, ischemic heart disease; LVEF, left ventricular ejection fraction; LDL, low-density lipoprotein; MI, myocardial infarction; NYHA class, New York Heart Association classification; CHF, congestive heart failure; Mets, metabolic equivalents; HF, heart failure; PCI, percutaneous coronary intervention; CABG, coronary artery bypass graft; CCS, Canadian Cardiovascular Society; NA, not available; SAQ, Seattle Angina Questionnaire; PL, physical limitation; TS, treatment satisfaction; AF, angina frequency; AS, angina stability; DP, disease perception; EQ-5D, European Quality of Life-5 Dimensions; QTc, corrected QT.

Table 2 Acute coronary syndrome, MI, and acute chest pain

Reference	Inclusion/exclusion	Intervention/	-	Mean age.	Gender	Time	1	AS	AF	TS	DP	EO-5D
		Subgroup		years	(% male)	point						,
Arnold et al <sup>51</sup>	(I) Myocardial ischemia at rest for	I. Prior history of	3,565	66.0 (median)	62.6							
	$\geq$ 10 minutes presenting within the	angina										
	previous 48 hours, and elevated	A. Ranolazine				Baseline	54.5	30.8	52.1	77.5	37.7	0.708
	biomarkers of myocardial necrosis,						(0.57)	(0.70)	(0.63)	(0.43)	(0.45)	(0.70-0.72)
	ST depression of at least 0.1 mV,	B. Placebo				Baseline	<b>54</b> .	30.6	51.2	77.5	37.5	0.706
	diabetes mellitus or a TIMI risk						(0.57)	(0.72)	(0.65)	(0.44)	(0.47)	(0.69-0.72)
	score of $\geq 3$ .	2. No prior history	2,995	62.0 (median)	0.89							
	(E) Persistent ST segment elevation,	of angina										
	successful revascularization	A. Ranolazine				Baseline	73.0	39.2	76.4	85.9	47.6	0.793
	before randomization, and ECG						(0.65)	(0.70)	(0.64)	(0.40)	(0.54)	(0.78-0.80)
	abnormalities that interfere with	B. Placebo				Baseline	73.5	40.2	7.97	86.5	48.4	0.796
	interpretation of ischemia.						(0.65)	(0.74)	(0.62)	(0.41)	(0.54)	(0.79–0.81)
Arnold et al <sup>52</sup>	(I) ≥ 18 years, symptoms of	Rose Dyspnea Scale: 0	972	59.5	75.3	I month	9.76	54.7	95.4	92.5	83.0	0.942
	myocardial ischemia at rest lasting						(0.31)	(0.50)	(0.40)	(0.37)	(0.54)	(0.93-0.95)
	at least 10 minutes and present	Rose Dyspnea Scale: I	318	59.7	67.3	I month	93.1	56.9	92.7	0.06	76.8	0.914
	within the previous 48 hours,						(0.84)	(1.03)	(0.82)	(0.71)	(I.I.)	(0.90-0.93)
	and had at least one of: elevated	Rose Dyspnea Scale: 2	205	6.09	61.5	I month	1.68	55.6	88.0	8.06	71.0	0.889
	biomarkers of myocardial necrosis,						(1.36)	(1.45)	(1.32)	(0.87)	(1.57)	(0.88-0.90)
	ST depression of $\geq 0.1$ mV, diabetes	Rose Dyspnea Scale: 3	170	2.09	57.6	I month	80.0	57.9	86.0	86.9	65.8	0.855
	mellitus or a TIMI risk score of $\geq 3$ .						(1.85)	(1.77)	(1.53)	(1.18)	(2.06)	(0.84-0.87)
	(E) Persistent ST segment	Rose Dyspnea Scale: 4	170	9.09	64.1	I month	60.5	1.95	81.1	85.7	58.4	0.795
	elevation, revascularization						(2.35)	(1.83)	(1.90)	(1.18)	(2.23)	(0.78–0.81)
	before randomization, and ECG											
	abnormalities that would interfere											
	with interpretation of Holter											
	monitoring for ischemia.											
Pettersen et al <sup>22</sup>	(I) Discharge diagnosis of acute MI.		408	65.5	71.0	2–3 years	73.0	0.89	86.0	81.0	72.0	0.851
							(1.23)	(1.29)	(1.10)	(1.09)	(1.15)	(0.84-0.86)
Asadi-Lari et al <sup>53</sup>	<ul> <li>(I) Admitted to acute cardiac unit with chest pain.</li> </ul>		242	69.7	59.0							
		I. Women				Baseline	49.3	48.1	73.9	84.2	57.7	0.765
							(2.79)	(1.92)	(3.00)	(2.11)	(2.70)	(0.75-0.79)
		2. Men				Baseline	55.1	53.2	75.6	97.8	63.1	0.791
							(2.45)	(1.61)	(2.34)	(1.46)	(2.13)	(0.77–0.81)

Notes: SAQ values include standard error; EQ-5D values include 95% confidence intervals.

Abbreviations: I, inclusion criteria; E, exclusion criteria; TIMI, Thrombolysis in Myocardial Infarction; ECG, electrocardiogram; SAQ, Seattle Angina Questionnaire; PL, physical limitation; TS, treatment satisfaction; AF, angina frequency; AS, angina stability; DP, disease perception; EQ-5D, European Quality of Life-5 Dimensions.

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Reference	Inclusion/Exclusion	Intervention/Subgroup	u	Mean	Gender	Time	PL	AS	AF	TS	DP	EQ-5D
				age	(% male)	point						
Zhang	(I) Multivessel IHD, revascularization	I. PCI	488	0.19	80.0	Baseline	56.6	47.4	55.8	86.7	39.5	0.720
et al <sup>48</sup>	was clinically indicated and appropriate.						(1.02)	(1.45)	(1.26)	(0.65)	(0.90)	(0.71-0.73)
	(E) Previous revascularization,	2. CABG	200	62.0	78.0	Baseline	54.3	45.0	53.8	86.2	37.0	0.708
	thoracotomy, intervention for pathology						(0.98)	(1.41)	(1.25)	(0.67)	(0.91)	(0.70–0.72)
	of the valves, great vessels, or aorta.											
Andréll	(I) Refractory and severe stable angina	I. Refractory angina	139	70.0	73.0	Baseline	51.9	50.3	48.4	6.99	46	0.710
et al <sup>18</sup>	(CCS class III-IV) despite optimal						(2.16)	(2.83)	(3.09)	(2.65)	(2.63)	(0.69-0.73)
	conventional pharmacological therapy.					l year	55.8	59.4	60.7	72.7	53.4	0.747
							(2.39)	(3.77)	(4.45)	(2.76)	(3.09)	(0.73-0.77)
		2. Stable angina and	139	72.0	73.0	l year	99	71.7	80.9	78.5	64.4	0.813
		revascularization					(3.43)	(4.60)	(4.11)	(3.51)	(4.21)	(0.79-0.84)
Kim et al <sup>49</sup>	(I) Chest pain at rest, documented	1. Early interventional	895	63.0	0.19	4 months	75.4	70.3	80.2	1.06	72.1	0.853
	electrocardiographic or arteriographic	strategy – maximal					(0.90)	(1.00)	(0.90)	(0.50)	(0.60)	(0.84-0.86)
	evidence of IHD.	medical therapy and early				l year	76.9	67.7	82.4	91.2	75.9	0.868
		coronary arteriography					(1.00)	(1.00)	(0.90)	(0.50)	(0.60)	(0.86-0.88)
		with possible myocardial										
		<ol><li>Conservative strategy –</li></ol>	915	62.0	64.0	4 months	8.69	63.9	72.6	86.3	64.4	918.0
		maximal medical therapy					(0.90)	(I.00)	(0.90)	(0.50)	(0.80)	(0.81 - 0.82)
		and ischemia – or				l year	73.3	63.7	78.0	9.88	71.2	0.845
		symptom-provoked					(1.00)	(1.00)	(0.90)	(0.50)	(0.90)	(0.84 - 0.85)
		angiography and										
		revascularization.										
Hofer	(I) Patients with angina symptoms	I. All patients	158	64.5	2'.29	Baseline	9.19	53.9	45.0	84.7	48.9	0.738
et al <sup>50</sup>	referred for angiographic screening						(2.99)	(2.68)	(1.92)	(1.35)	(2.08)	(0.72-0.76)
	of IHD. Following angiogram treatment					l year	63.7	68.4	72.7	82.5	64.7	0.803
	decision (CABG, PCI, or medical						(2.13)	(2.44)	(2.18)	(0.46)	(2.16)	(0.79-0.82)
	management) was made as per clinical	2. CCS class I	22	Ϋ́	Υ Z	Baseline	64.9	57.1	40.0	9.68	51.9	0.747
	indication.						(9.45)	(11.19)	(10.41)	(3.85)	(98.6)	(0.68–0.81)
		3. CCS class II	70	<b>∀</b> Z	Υ V	Baseline	67.9	46.4	54.2	89.5	53.2	0.774
							(6.48)	(10.15)	(8.51)	(3.48)	(7.44)	(0.73-0.82)
		4. CCS class III	62	<b>∀</b> Z	Υ Z	Baseline	61.5	1.19	44.9	82.0	55.3	0.751
							(3.90)	(4.71)	(4.27)	(2.34)	(3.77)	(0.72-0.78)
		5. CCS class IV	54	Ϋ́	Υ V	Baseline	60.5	54.7	45.1	84.8	41.7	0.719
							(4.47)	(4.66)	(3.72)	(2.52)	(3.61)	(0.69-0.75)
Graham	(I) IHD.		,	0	0		9	,	-	3	-	,
et al~	(E) Undergoing investigation for	A. Medical therapy	3,488	7.69	68.9	l year	8.7/	75.3	84.1	4.4		0.846
	valvular heart disease, without IHD on angiography, no consent for follow-up.			(median)			(0.18)	(0.07)	(0.10)	(0.05)	(0.07)	(0.84–0.85)
	.d											(Continued)
												(Containacu)

Reference	Inclusion/exclusion	Intervention/Subgroup	<b>-</b>	Mean	Gender (% male)	Time point	П	AS	ΑF	TS	DP	EQ-5D
						3 vears	73.5	749	84.6	848	716	0.849
						5 100/ 6	ξ (c)	(200	5.5	9.05	5 6	(0.84.0.84)
		()	107	` ;	000	-	(0.10)	(0.0)	(2.5)	(6.6)	(0.0/)	(0.84-0.96)
		p. CABG	1,07/	0.10	63.7	ı year	74.7	0.0	7.00	00.7	73.3	0.000
				(median)			(0.26)	(0.10)	(0.13)	(0.05)	(0.10)	(0.85–0.86)
						3 years	74.7	78.1	9.98	87.1	74.0	0.859
							(0.28)	(0.10)	(0.13)	(0.07)	(0.10)	(0.85 - 0.87)
		C. PCI	2,698	59.1	78.4	l year	74.9	7.97	85.4	85.5	72.5	0.855
				(median)			(0.20)	(0.07)	(0.10)	(0.02)	(0.07)	(0.85-0.86)
						3 years	75.5	76.2	82.8	85.9	73.0	0.858
							(0.18)	(0.70)	(0.07)	(0.05)	(0.07)	(0.85-0.86)
		<ol> <li>Age /0-/9 years:</li> <li>A. Medical therapy</li> </ol>	1,302	73.9	62.7	l year	62.1	77.0	83.0	86.3	74.9	0.833
		:		(median)			(0.36)	(0.15)	(0.15)	(0.07)	(0.15)	(0.82-0.84)
						3 years	62.2	7.97	83.6	9.98	75.1	0.835
				í	i I		(0.41)	(0.13)	(0.15)	(0.07)	(0.15)	(0.83–0.84)
		B. CABG	818	73.6	77.2	l year	63.3	80.5	85.5	9.88	77.3	0.844
				(median)			(0.46)	(0.18)	(0.52)	(0.10)	(0.18)	(0.84–0.85)
						3 years	67.9	80.0	85.9	88.7	4.//	0.844
							(0.49)	(0.18)	(0.20)	(0.10)	(0.18)	(0.84 - 0.85)
		C. PCI	819	73.9	1.89	l year	63.2	78.2	84.0	87.1	75.8	0.839
				(median)			(0.44)	(0.18)	(0.20)	(0.10)	(0.15)	(0.83 - 0.85)
						3 years	63.1	77.8	84.5	87.4	76.0	0.840
							(0.46)	(0.15)	(0.20)	(0.10)	(0.18)	(0.83-0.85)
		<ol><li>Age ≥80 years:</li></ol>										
		A. Medical therapy	220	82.4	65.5	l year	51.9	75.0	79.9	87.9	73.5	0.808
				(median)			(1.01)	(0.33)	(0.41)	(0.20)	(0.36)	(0.80–0.82)
						3 years	53.8	8.9/	7.18	88.3	74.2	0.815
		R CARG	6	α α	744	reav	(1.27)	(0.39) 78 I	(0.4g)	(0.23) 89 6	(0.3%) 75.3	0.80-0.83)
		) ) i	5	(median)	:	- / cm	(1.56)	(0.54)	(0.62)	0.31)	(0.54)	(0.81–0.83)
						3 years	54.2	80.3	83.8	90.1	76.2	0.823
						•	(1.69)	(0.52)	(0.62)	(0.33)	(0.59)	(0.81 - 0.83)
		C. PCI	137	82.1	56.2	l year	51.9	7.4.7	79.3	88.0	72.9	908.0
				(median)			(1.06)	(0.41)	(0.46)	(0.23)	(0.44)	(0.80-0.82)
						3 years	53.3	6.9/	81.0	88.7	73.9	0.813
							(1.25)	(0.41)	(0.46)	(0.23)	(0.44)	(0.80-0.82)
Neil et al <sup>21</sup>	(I) Age 21–81 years, with stable or	I. Primary stent	230	0.19	75.0	6 months	84.0	82.0	0.06	88.0	77.0	0.887
	unstable angina and a positive functional			(median)	i		(1.51)	(1.84)	(1.18)	(1.18)	(1.45)	(0.88-0.90)
	study for ischemia or undergoing	2. Optimal PTCA/	249	0.09	72.0	6 months	86.0	83.0	90.0	0.16	77.0	0.892
	angioplasty after a recent MI with target	provisional stent		(median)			(1.33)	(1.58)	(1.07)	(0.82)	(1.33)	(0.88-0.90)
	lesions that were potentially treatable by											
	balloon angioplasty or a stent											

0.704 (0.69–0.72) 0.845 (0.83–0.86) 0.897 (0.88–0.91)	0.790 (0.77–0.81) 0.873 (0.85–0.89)	0.776 (0.77-0.79) 0.839 (0.86-0.87) 0.869 (0.86-0.88) 0.868 (0.86-0.88) 0.871 (0.86-0.88) 0.871 (0.87-0.88) 0.871 (0.77-0.79) 0.874 (0.81-0.82) 0.813 (0.81-0.82) 0.814 (0.81-0.82) 0.836 (0.84-0.85) 0.836 (0.84-0.85) 0.836 (0.84-0.85) 0.836 (0.85-0.86) 0.854 (0.85-0.86) 0.856 (0.85-0.88)
30.0 (2.09) 64.0 (2.38) 83.0 (2.21)	55.8 (2.93) 77.1 (2.75)	51.0 (0.80) (6.81) 7.3 (0.75) 75.0 (0.73) 75.0 (0.73) 77.0 (0.80) 62.0 (0.80) 62.0 (0.80) 62.0 (0.78) 70.0 (0.78) 70.0 (0.78) 70.0 (0.78) 70.0 (0.78) 70.0 (0.78) 70.0 (0.78) 70.0 (0.78) 70.0
80.0 (2.09) 91.0 (1.33) 94.0 (0.90)	75.5 (1.51) 85.6 (1.91)	88.0 (0.48) 92.0 (0.40) 92.0 (0.41) 92.0 (0.43) 92.0 (0.47) 92.0 (0.50) 90.0 (0.48) 90.0 (0.48) 90.0 (0.48) 92.0 (0.48) 92.0 (0.48) 92.0 (0.48) 92.0 (0.48) 92.0 (0.48) 92.0
56.0 (2.38) 86.0 (2.09) 93.0 (1.30)	74.2 (3.34) 91.5 (0.76)	68.0 (0.83) 82.0 (0.77) 85 87.0 (0.66) 87.0 (0.64) 89.0 (0.65) 89.0 (0.74) 69.0 (0.78) 80.0 (0.78) 80.0 (0.78) 84.0 (0.77) 86.0 (0.77) 86.0
30.0 (2.47) 81.0 (2.66) 90.0 (2.61)	62.5 (3.62) 65.5 (2.80)	54.0 (1.06) 81.0 (0.88) 77 76.0 (0.94) 73.0 (1.16) 73.0 (0.97) 70.0 70 70 70 70 70 70 70 70 70 70 70 70 70
59.0 (1.71) 79.0 (1.04) 80.0 (1.00)	67.6 (2.30) 74.2 (3.24)	66.0 (0.81) 73.0 (0.82) 76 (0.82) 77.0 (0.77) 75.0 (0.88) 74.0 (1.00) 66.0 (0.81) 70.0 (0.82) 72.0 (0.79) 72.0 (0.79) 72.0 (0.79) 74.0 (0.82) 74.0 (0.82) 74.0 (0.82) 74.0 (0.83) 74.0 (0.83) 74.0 (0.83) 74.0 (0.84) 74.0 (0.84) 74.0 (0.84) 74.0
Baseline 6 months 1 year	Baseline I month	Baseline I month months year years years Baseline month month months year years years years years
0.89	75.4	85.0
62.8	66.0	2.
9	65	1,138
Ü	PCI	1. PCI + OMT
(i) IHD.  (E) Unsuccessful procedures (a residual stenosis >30% or TIMI flow 0/1 after stenting, or in-hospital major adverse cardiovascular events (death, MI, or urgent revascularization), severe cardiac disease other than IHD, ejection fraction <40%, severe neurologic disease, neoplasia, pregnancy, periprocedural hemodynamic instability, parient refusal	(l) Chinese, $\geq$ 21 years old, no mental disorder, no prior PCI, understand and speak Cantonese, no severe medical illness.	(I) >70% stenosis in at least one major epicardial coronary artery with objective evidence of myocardial ischemia or >80% stenosis in at least one coronary artery and classic angina without provocative testing.
de Quadros et al <sup>37</sup>	Wong and Chair <sup>38</sup>	Weintraub et al <sup>39</sup>

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Table 3 (Continued)	ontinued)											
Reference	Inclusion/exclusion	Intervention/Subgroup	ء	Mean	Gender	Time	PL	AS	AF	TS	DP	EQ-5D
				age	(% male)	point						
Agarwal	(I) Age ≥80 years, undergoing 1 or	PCI	74	82.5	0.89	Baseline	24.4	50.0	45.8	74.3	38.8	0.640
et al <sup>27</sup>	2 vessel PCI.						(3.82)	(19.9)	(6.51)	(3.85)	(4.97)	(0.61–0.67)
						6 months	42.3	72.4	76.5	83.7	2.99	0.769
							(2.55)	(3.54)	(3.67)	(1.77)	(3.04)	(0.75-0.79)
						l year	4.4	66.3	73.5	83.7	62.3	0.756
							(5.68)	(4.01)	(4.11)	(2.08)	(3.30)	(0.73-0.78)
Lowe et al <sup>19</sup>	(I) Severe stable angina (CCS class III or	PCI	=	29.0	82.0	Baseline	38.0	45.0	40.0	63.0	21.0	919.0
	IV) despite maximum tolerated doses			(median)			(3.01)	(6.03)	(6.93)	(6.33)	(3.91)	(0.59-0.65)
	of at least two antianginal drugs, a left-					Pre-PCI	37.0	43.0	49.0	76.0	38.0	899.0
	ventricular ejection fraction of $\geq$ 30%,						(4.52)	(8.74)	(6.33)	(6.33)	(8.14)	(0.62-0.71)
	and reversible perfusion defects on the					Post PCI	36.0	0.09	0.19	80.0	45.0	0.692
	thallium stress test.						(4.82)	(9.64)	(8.74)	(6.33)	(8.44)	(0.64-0.74)
Ascione	(I) Conventional or off-pump CABG.	1. Conventional CABG	159	4.19	1.18	2-4 years	75.2	9.69	8.98	- R88.	74.8	0.865
et al <sup>32</sup>	(E) LVEF <30%, recent MI within						(2.03)	(5.66)	(1.83)	(1.72)	(2.01)	(0.85-0.88)
	I month (trial I of 2 only), history	2. Off-pump CABG	691	63.1	83.4	2-4 years	74.7	66.3	85.1	9.88	74.4	0.862
	of supraventricular arrhythmia,						(1.88)	(2.81)	(1.79)	(1.28)	(1.79)	(0.85-0.88)
	previous CABG, renal or											
	respiratory impairment, previous											
	stroke, transient ischemic attack,											
	coagulopathy, coronary disease in											
	the branches of the circumflex											
	artery distal to the first obtuse											
	marginal branch (trial 1 of 2 only).											
Angelini	(I) Conventional or off-pump CABG.	I. Conventional CABG	149	6.09	9.98	6 years,	72.4	45.6	88.8	89.2	74.0	0.866
et al <sup>33</sup>	(E) LVEF <30%, recent MI within					months	(2.21)	(3.77)	(1.90)	(1.96)	(2.37)	(0.85-0.88)
	I month (trial I of 2 only), history					(mean)						
	of supraventricular arrhythmia,	2. Off-pump CABG	150	62.1	84.7	6 years,	75.0	46.5	9.68	91.5	77.0	0.879
	previous CABG, renal or					11 months	(2.18)	(3.67)	(1.67)	(1.55)	(2.15)	(0.86–0.90)
	respiratory impairment, previous					(mean)						
	stroke, transient ischemic attack,											
	coagulopathy, coronary disease											
	in the branches of the circumflex											
	artery distal to the first obtuse											
	marginal branch (trial I of 2 only).											
Karolak	(I) Conventional or off-pump CABG.	1. Conventional CABG	120	63.7	80.0	l year	80.0	86.0	91.0	79.0	81.0	0.886
et al	(E) Reoperation, emergency CABG,	()	-	0		-	(1.06)	(67.1)	(cc.1)	(1.46)	(1.67)	(0.67-0.90)
	concomitant major cardiac	2. Off-pump CABG	74	7.79	7:18	l year	/8.0	86.0	92.0	0.67	81.0	0.883
	טו טרפטעו כט, מווט בו יטליט.						(00:1)	(20:1)	· - : .	(20:1)	(-, '-,	(0.0)

		(0.783 (0.77–0.80) (0.912 (0.90–0.92)			0.655 (0.62–0.69) 0.918 (0.87–0.96)	0.928
22.6 (0.89) 36.1 (0.94)	50.4 (1.02) 83.3 (0.84)	(1.07) 83.6 (0.86)	40.3 (1.81) 82.3 (2.05)	29.0 (3.12) 76.0 (3.64)	34.0 (3.12) 93.0 (4.68)	91.9 (1.84)
37.8 (1.11) 59.4 (0.76)	91.2 (0.54) 94.1 (0.54)	92.0 (0.51) 93.8 (0.57)	92.5 (1.49) 93.3 (1.39)	52.0 (4.16) 76.0 (5.20)	51.0 (4.16) 88.0 (5.98)	89.3 (1.92)
9.9 (1.62) 5.8 (1.77)	(1.15) 92.5 (0.65)	(1.16) 91.7 (0.70)	53.8 (2.97) 93.4 (1.45)	42.0 (8.59) 79.0 (6.25)	39.0 (7.03) 92.0 (5.46)	92.3 (2.14)
9.8 (2.31) 8.3 (2.20)	37.9 (1.12) 51.8 (0.64)	37.0 (1.08) 52.7 (0.67)	51.8 (3.41) 92.7 (1.69)	32.0 (7.03) 67.0 (6.51)	35.0 (7.03) 94.0 (4.42)	94.4 (1.86)
71.6 (1.44) 53.1 (2.66)	(0.99) (0.82) (0.82)	(1.05) 83.3 (0.95)	40.2 (2.12) 63.8	42.0 (4.42) 77.0 (7.55)	44.0 (5.72) 83.0 (9.63)	86.8 (2.84)
Baseline I week	Baseline I year	Baseline I year	Baseline 3 months	Baseline 5 years, 9 months (median)	Baseline 5 years, 9 months (median)	l year, 4 months (mean)
0.09	0.66	0.66	0.99	49.0	68.9	49.6
0.09	62.0	0. 19	78.8	83.0	72.0	83.0
30	367	366	00	1,142	1,213	127
CABG	I. Saphenous vein CABG	2. Radial artery CABG	CABG	I. Age ≥80 years	<ol> <li>Age 70–79 years</li> </ol>	CABG
(I) Admitted to hospital for CABG, consented to participate in the study.	<ul><li>(I) Veterans: non-emergent first time CABG surgery.</li><li>(E) Single-vessel bypass with the internal mammary artery, concerns</li></ul>	about arm functioning, creatinine level requiring hemodialysis or a level higher than 2.0 mg/dL, cardiogenic shock, allergic reactions to contrast material, robotic surgery, concomitant valve surgery,* concomitant Dor or Maze procedure,** no suitable radial target, participation in other research studies involving an	(i) Age $\geq$ 75 years, candidates for CABG.	(I) Age ≥70 years, undergoing cardiac surgical procedures.		<ul> <li>(l) Age ≥80 years, accepted for cardiac surgical procedures at a peer review conference.</li> <li>(E) Preoperative neurological diseases.</li> </ul>
Chaudhury et al³⁵	Wagner et al³		MacDonald et al <sup>28</sup>	Gelsomino et al <sup>23</sup>		Fruitman et al <sup>29</sup>

Notes: SAQ values include standard error, EQ-5D values include 95% confidence intervals. \* Valve surgery is aortic or mitral valve replacement/repair. \*\* Dor or Maze is for treatment of atrial fibrillation.

Abbreviations: I, inclusion criteria; E, exclusion criteria; IHD, ischemic heart disease; LVEF, left ventricular ejection fraction; MI, myocardial infarction; PCI, percutaneous coronary intervention; coronary artery bypass graft; CCS, Canadian Cardiovascular Society; PTCA, percutaneous translumninal coronary angioplasty; TIMI, Thrombolysis in Myocardial Infarction; OMT, optimal medical therapy; SAQ, Seattle Angina Questionnaire; PL, physical limitation; TS, treatment satisfaction; AF, angina frequency; AS, angina stability; DP, disease perception; EQ-5D, European Quality of Life-5 Dimensions.

utility weights inputted are reflective of the population being studied. Our catalog provides detailed information on the population being evaluated, as well as interventions, which will provide researchers with the information needed such that they can utilize the most appropriate utility weights when developing economic models.

Our mapping algorithm was designed to estimate EQ-5D scores using the scores and standard errors in all five domains of the SAQ. An important limitation is that we had to exclude studies that did not publish scores on all five domains of the SAQ. However, our final catalog included estimated EQ-5D scores across a wide range of baseline patient demographics, disease severity, and various treatment interventions. A weakness of our systematic review is that we failed to capture studies that did not use the name of the SAQ scale in the text of the paper and failed to cite the source of the questionnaire.

In conclusion, in the current era of budgetary constraints, cost-effectiveness analysis has become increasingly important in decision-making for health resource allocation. In the absence of directly measured individual patient preference-based data, our catalog of estimated EQ-5D scores can be useful in IHD-related economic evaluations.

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#### **Author contributions**

HCW was involved in the conception, design, acquisition, analysis and interpretation of the data, and critically revised the manuscript. SFZ was involved in the conception and design, acquisition of data, and interpretation of the data, and drafted the manuscript. WW was involved in conception of the study, performed the systematic search, and revised the manuscript critically. MCB was involved in the acquisition of data, analysis and interpretation of data, and revised the manuscript critically. All authors approved the final manuscript for publication and agree to be accountable for all aspects of the work.

#### **Disclosure**

The authors report no competing interests in this work.

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# Supplementary material

The following method describes the search strategy used to collect the references analyzed in this study. This strategy had three primary facets, outlined below.

- Identification of materials in the primary databases of medical literature that referenced the Seattle Angina Questionnaire. These databases were MEDLINE (Ovid), EMBASE (Elsevier), OVID HealthStar, MEDLINE (PubMed), and the Cochrane Library (Wiley).
- Use of the citation mapping tools Google Scholar (Google), Scopus (Elsevier), and Web of Science (Thomson Reuters), to find all available references to the paper in which Seattle Angina Questionnaire was first described by John Spertus et al in the *Journal of the American College of Cardiology* in 1995. The search strategy was to locate the original article by Spertus et al and export the references that the tool identified as having cited that article.
- Use of the major clinical trial registries to determine the studies that used the SAQ as an outcome measure. These registries have simple search functions, and so our search terms were "Seattle Angina Questionnaire" or "SAQ". The strategy then underwent peer review by a librarian experienced in the creation and review of systematic search strategies.

## Search strategy

The following search strategy was applied to MEDLINE (Ovid), HealthStar (Ovid), and EMBASE (Ovid). It was adapted for use in PubMed by updating the syntax to match that offered in the PubMed search tool. When searching the Cochrane Library, only the words "Seattle Angina Questionnaire" were used. Databases were searched from inception until 2013.

- (Development and evaluation of the Seattle Angina Questionnaire: a new functional status measure for coronary artery disease).m\_titl.
- 2. seattle angina questionnaire.mp.
- 3. seattle angina questionnaire.tw.
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- 6. saq.mp.
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