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26 **PREDICTORS OF HEALTH-RELATED QUALITY OF LIFE AFTER CARDIAC SURGERY: A SYSTEMATIC**

27 **REVIEW**

28 **ABSTRACT**

29

30 **BACKGROUND**

31 Health-related quality of life (HRQoL) is important in determining surgical success, particularly from
32 the patients' perspective.

33

34 **AIMS**

35 To identify predictors for HRQoL outcome after cardiac surgery in order to identify potentially
36 modifiable risk factors where interventions to improve patient outcomes could be targeted.

37

38 **METHODS**

39 Electronic databases (including MEDLINE, CINAHL, Embase) were searched between January 2001
40 and December 2020 for studies determining risk predictors of HRQoL (using a recognised and
41 validated tool) in adult patients undergoing cardiac surgery. Data extraction and quality assessments
42 were undertaken and data was summarised using descriptive statistics and narrative synthesis, as
43 appropriate.

44

45 **RESULTS**

46 Overall, 3924 papers were screened with 41 papers included in the review. Considerable
47 methodological heterogeneity between studies was observed. Most were single-centre (75.6%)
48 prospective observational studies (73.2%) conducted in patients undergoing coronary artery bypass
49 graft (CABG) (n=51.2%) using a version of the SF-36 (n=63.4%). Overall, 103 independent predictors
50 (62 pre-operative, five intra-operative and 36 post-operative) were identified, where 34 (33.0%)
51 were reported in more than one study. Potential pre-operative modifiable risk factors include

52 alcohol use, BMI/weight, depression, pre-operative quality of life and smoking while in the post-
53 operative period pain and strategies to reduce post-operative complications and intensive care and
54 hospital length of stay are potential therapeutic targets.

55

56 **CONCLUSION**

57 Despite a lack of consistency across studies, several potentially modifiable risk factors were
58 identified that could be targeted in interventions to improve patient or treatment outcomes. This
59 may contribute to delivering more person-centred care involving shared decision-making to improve
60 patient HRQoL after cardiac surgery.

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62 **KEYWORDS:** Health-related quality of life; predictors; cardiac surgery; quality of life; patient
63 reported outcome

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77 **PREDICTORS OF HEALTH-RELATED QUALITY OF LIFE AFTER CARDIAC SURGERY: A SYSTEMATIC**

78 **REVIEW**

79

80 **INTRODUCTION**

81 High quality surgical care should include mortality, morbidity and patient-centred outcome
82 measurement¹. However, patient reported outcomes (PRO) are rarely recorded. Even in research
83 contexts, PROs have only been reported in 29% of cardiac surgery trials², despite the fact that those
84 experiencing post-operative complications have worse quality of life³, which can last three years
85 after surgery⁴.

86

87 Despite clinicians previously considering health-related quality of life (HRQoL) less important than
88 clinical measures⁵, globally health ministers have stated the need to invest in measures that matter
89 most to people⁶. HRQoL measurement allows a holistic, patient-centred perspective of recovery and
90 it is becoming increasingly recognised that HRQoL is important in determining surgical success both
91 from the patients⁷ and health-care commissioners⁸ perspective.

92

93 Factors that predict cardiac surgery mortality do not predict post-operative HRQoL outcome⁹. Thus,
94 an understanding of the factors that do predict HRQoL would be useful to inform patients of the
95 implications of surgery and interventions to improve potentially modifiable risk factors could be
96 implemented. Certainly in the UK, HRQoL, and factors associated with it, was identified as the top
97 ten research priority for adult cardiac surgery research¹⁰. We therefore undertook a literature
98 review to ascertain the predictors of HRQoL after cardiac surgery, to identify potentially modifiable
99 risk factors that could be targeted for intervention.

100

101 **METHODS**

102

103 **Protocol and registration**

104 This review was registered on PROSPERO, an international prospective register of systematic review
105 (February 2019, reference CRD42019120080) and conducted in accordance with the Preferred
106 Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) guidelines.

107

108 **Eligibility criteria**

109 All studies that undertook multivariable analysis to identify independent predictors of HRQoL after
110 cardiac surgery were eligible for inclusion. The detailed inclusion and exclusion criteria are detailed
111 in Table 1.

112 **Table 1. Inclusion and exclusion criteria.**

Inclusion criteria	Exclusion criteria
Adult patients (≥ 18 years of age)	Surgical ablation procedures in isolation
Primary research	Ventricular Assist Device (VAD) procedures
English language	Studies that did not include multivariable analysis of
Published 2001 – 2020	predictors of HRQoL only
Patients undergoing cardiac surgical	Congenital heart disease
procedures	Heart transplantation
	Transcatheter aortic valve implantation
	Descriptive exploration of interventions such as cardiac
	rehabilitation
	Studies that did not use a recognised quality of life instrument
	Comparison of quality of life in patients who underwent
	cardiac surgery with those who received percutaneous
	coronary intervention

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114

115 **Information sources, search strategy and study selection**

116 A search of MEDLINE, Cumulated Index of Nursing and Allied Health Literature (CINAHL), Embase,
117 Cochrane Library and clinicaltrials.gov (www.clinicaltrials.gov) was undertaken for relevant papers in
118 English between January 2001 and December 2020. Search terms included cardiac surgery OR
119 Cardiac Surgical Procedures AND quality of life OR outcome assessment and were adapted for each
120 database (Supplementary material 1). Two authors screened the title and abstracts of all citations
121 for suitability against the inclusion and exclusion criteria (Table 1). The reference lists of any
122 identified systematic reviews were also screened for eligible papers.

123

124 **Data collection and syntheses (data items and data collection process)**

125 Data were extracted by two authors into a standardised proforma with disagreements resolved
126 through discussion until consensus was achieved. Data extraction included author, country, year,
127 study design, type of surgery, sample size, HRQoL tool used including the time-points where HRQoL
128 was measured, and the independent predictors of HRQoL.

129

130 **Risk of bias and quality assessment**

131 All included papers were quality reviewed using an adapted Critical Appraisal Skills Programme
132 (CASP) template for cohort studies ([https://casp-uk.net/wp-content/uploads/2018/01/CASP-Clinical-
133 Prediction-Rule-Checklist_2018.pdf](https://casp-uk.net/wp-content/uploads/2018/01/CASP-Clinical-Prediction-Rule-Checklist_2018.pdf)). Initial papers were reviewed independently by two authors to
134 ensure consistency and subsequent papers were reviewed by two of four authors with additional
135 random checks undertaken at the end to be assured of continued assurance. A risk of bias graph was
136 generated. Studies were not excluded on the basis of the quality assessment.

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141 **Analysis**

142 Following data extraction, results were summarised using descriptive statistics, tables and narrative
143 synthesis, as appropriate. Interpretation of the analysis was discussed and agreed by all members of
144 the authorship team. Meta-analysis was not possible due to the heterogeneity of studies.

145

146 **RESULTS**

147 **Study selection**

148 A total of 3924 papers were identified for possible inclusion (Figure 1) with 100 papers undergoing
149 independent full-text assessment. This resulted in 41 papers being included for data synthesis.

150

151 **Study characteristics**

152 Thirty-two studies were conducted in Europe (two of which were in the UK), four each in Australia
153 the USA, and one in Canada (Table 2). The vast majority were single centre (n=31) with seven studies
154 conducted in two centres and three studies conducted in multiple centres. Most were prospective
155 observational studies (n=30) on patients undergoing coronary artery bypass graft (CABG) (n=21),
156 CABG and/or valve surgery (n=10), valve only (n=1) or all types of cardiac surgery (n=9), with sample
157 sizes in the HRQoL analysis ranging from 34 to 8676. A version of the SF-36 was used in the majority
158 of studies (n=26).

159

160 In most studies HRQoL was measured pre-operatively (n=35) in addition to at least one post-
161 operative assessment (Table 2), usually within six months of surgery (n=20) with twenty-four studies
162 assessing outcome at one year or beyond (some studies assessed at more than one time-point).

163 HRQoL was not the primary outcome in all studies.

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166

167 **Risk of Bias**

168 Figures 2 and 3 demonstrate the variable risk of bias across studies and also in considering studies
169 individually.

170

171 **Independent predictors of HRQoL**

172 The independent predictors associated with HRQoL by operative and follow-up time-frame are
173 detailed in Table 3 (and by study are included in are detailed in Supplementary Table 1). Overall,
174 variables that were examined were predominantly focused on the clinical condition and experience
175 of patients across the pre-, intra- and post-operative course. Of note, few demographic, social or
176 psychological factors were incorporated into the analysis. Despite 26 studies (63.4%) using a version
177 of the SF-36, how it was implemented and categorised to determine predictors varied across studies.
178 For example, four studies explored predictors in relation to the overall score^{4,11,12,13}. 13 explored the
179 physical component (PCS) and mental component score (MCS) separately^{14,15,16,17,18,19,20,21,22,23,24,25,26},
180 four studies explored one domain^{27,28,29,30} two studies explored predictors in all SF-36 domains^{31,32}
181 while only Falcoz and colleagues explored both PCS and MCS and all domains³³. Furthermore, Kube
182 and colleagues used the SF-12 which measures physical and psychological quality of life³⁴.

183

184 Due to the variation in analysis and reporting across the studies, the independent predictors
185 identified were grouped by operative and follow-up time-frame (Table 3). In total, 103 independent
186 predictors (62 pre-operative, 5 intra-operative and 36 post-operative) were identified. Of those 103
187 variables 34 (33.0%) were identified as significant in more than one study and almost all of those
188 (n=33 (97.1%)) were also found to be non-significant in other studies (non-significant variable data
189 detailed in Supplementary Table 2). Variables found to be predictive at all three time-points were
190 age, angina, chronic obstructive pulmonary disease (COPD), diabetes, gender, hypertension and
191 NYHA class and peripheral vascular disease.

192

193 **Potentially modifiable risk factors**

194 Of the 62 pre-operative variables identified as independent risk factors for HRQoL outcome those
195 that are potentially modifiable pre-surgery include alcohol use, body mass index (BMI)/weight,
196 depression, pre-operative quality of life and smoking (Table 3).

197 Similarly, in the post-operative period independent predictors with the potential to be modified to
198 improve HRQoL outcome were pain, traumatic memories and restlessness in the intensive care unit
199 (ICU). Furthermore, general strategies to reduce post-operative complications (including infection,
200 myocardial infarction, arrhythmias and readmission) and shorten ICU and hospital length of stay are
201 also identified as potential targets to improve post-surgical HRQoL (Table 3).

202

203 **DISCUSSION**

204 The inclusion, measurement and use of HRQoL and PRO in cardiac surgery is lacking. Healthcare
205 organisations need to work with patients to deliver more person-centred care, sharing decision-
206 making, to meaningfully improve care outcomes³⁵. The ‘holy grail’ of prognostic factor research is to
207 improve patient outcomes by providing a personalised approach to healthcare and risk prediction
208 and how such factors could be used to improve patient or treatment outcomes³⁶. Thus, we sought to
209 identify known risk predictors for HRQoL outcome after cardiac surgery, specifically to focus on
210 modifiable risk factors where interventions to improve patient or treatment outcomes could be
211 targeted. We identified 41 studies, which were predominantly European-based single-centre
212 prospective observational studies conducted in CABG patients. Certainly, recognition of the non-
213 modifiable risk factors found to be particularly impactful both on short and longer-term HRQoL (age,
214 angina, COPD, diabetes, gender, hypertension and NYHA class and peripheral vascular disease) may
215 assist in identifying high risk patients and the identification of interventions and associated
216 resources that might then be directed to assisting these patients to recover. In terms of potential
217 modifiable risk factors, pre-operative factors include alcohol use, smoking, BMI/weight depression,
218 and pre-operative quality of life, while ongoing pain management, prevention of post-operative

219 complications and general strategies to reduce ICU and hospital length of stay could also be
220 beneficial.
221
222 Individually focused lifestyle and therapeutic interventions have shown effectiveness in weight and
223 BMI reduction³⁷, decreasing alcohol consumption³⁸, psychological preparation (including depression
224 and anxiety)³⁹ and smoking cessation⁴⁰. Given that BMI⁴¹, alcohol use⁴², depression and anxiety⁴³ and
225 smoking⁴⁴ have also been identified to be associated with many in-hospital post-operative
226 complications, strategies to encourage their reduction are likely to have beneficial impacts on
227 improving overall morbidity and general recovery. As yet, interventions specifically targeting pre-
228 operative HRQoL do not exist. While most tools combine physical, mental and social wellbeing
229 traditionally greater emphasis clinically has placed on physical health. Nonetheless, the importance
230 of psychological readiness and inclusion of social support and anxiety reduction in prehabilitation
231 programmes is now recognised as part of cardiac surgery enhanced recovery⁴⁵. Furthermore, we
232 found that severe pain during the ICU stay was an independent predictor of HRQoL at six months⁴⁶,
233 while high pain scores at 15 months were predictive of HRQoL eight years after surgery in elderly
234 patients⁴⁷. Since up to 10% of cardiac surgery patients develop severe chronic post-surgical pain⁴⁸,
235 with predictors of chronic pain including early severe pain⁴⁹ personalised effective pain management
236 is vital. Current recommendations suggest the use of multimodal opioid-sparing pain management
237 alongside the use of a pain assessment tool to ensure the lowest opioid dose⁴⁵.
238
239 Certainly, future work requires more methodologically robust studies, including large multi-site
240 studies with appropriate control of confounding factors. However, generally a greater emphasis on
241 HRQoL as an outcome measure after cardiac surgery, both clinically and in research, is needed.
242 Although HRQoL has been previously undervalued by clinicians⁵, the landscape is changing with the
243 importance of HRQoL now recognised in cardiac surgery clinical guidelines⁵⁰, the enhanced recovery
244 recommendations⁴⁵, the cardiac surgery core outcome dataset⁵¹ and that PROs are included in the

245 Swedish national registers⁵² and emerging in the USA STS National Database⁵³. Similarly, HRQoL is
246 reported as a top research priority in cardiac surgery, both in the UK¹⁰ and in the USA⁵⁴. Therefore,
247 our review is timely, in that it collates the available evidence on predictors of HRQoL, highlights
248 potential modifiable factors on which interventions could be based in improve patient outcome and
249 emphasises where greater research quality in prognosis factor research should reside in this area.

250

251 **Strengths and limitations**

252 Despite the methodological robustness of this review, there are three main limitations. Firstly, the
253 methodological heterogeneity of the included studies restricts the ability to make strong conclusions
254 or undertake a meta-analysis. Our review reflects that despite the considerable growth in prognosis
255 research, the quality is often sub-standard⁵⁵. Secondly, although only English language publications
256 were included, studies from around the World have been included, providing a relatively wide base
257 of evidence. Finally, included studies were limited to those published from 2001. A balance was
258 struck between including all evidence and ensuring the results of this review were clinically
259 appropriate outcome risk factors for the current time. A period of 20-years was deemed sufficient to
260 address the balance needed.

261

262 In conclusion, despite a lack of consistency across studies, several potentially modifiable risk factors
263 on which interventions to improve patient HRQoL outcomes could be targeted were identified.

264 While this review has robustly collated the current best prognosis factor evidence relating to risk
265 predictors of HRQoL after cardiac surgery, there is still a need for large multi-site studies, with
266 appropriate control of confounding factors, to examine the role of these factors in affecting HRQoL
267 outcome. Now that considerably more emphasis is placed on the importance of HRQoL and PROs
268 after cardiac surgery, the hope is that this will contribute to delivering more person-centred care
269 involving shared decision-making to improve patient short- and longer-term recovery.

270

271 **IMPLICATIONS FOR PRACTICE**

- 272 • Cardiac surgery and enhanced recovery guidelines highlight the importance of HRQoL
- 273 • Pre-operative lifestyle and therapeutic interventions relating to weight, alcohol use,
- 274 psychological preparation and smoking cessation may improve HRQoL
- 275 • Reducing chronic post-operative pain, in-hospital complications and length of hospital stay
- 276 could also improve HRQoL.
- 277 • More person-centred care, including HRQoL and shared decision-making, is needed to
- 278 improve patient short- and longer-term recovery

279

280 **ABBREVIATIONS**

281	BMI	body mass index
282	CABG	coronary artery bypass graft
283	CASP	Critical Appraisal Skills Programme
284	COPD	chronic obstructive pulmonary disease
285	HRQoL	health-related quality of life
286	ICU	intensive care unit
287	MCS	mental component score
288	NYHA	New York Heart Association
289	PCS	physical component score
290	PRISMA	Preferred Reporting Items for Systematic reviews and Meta-Analyses
291	PRO	patient reported outcomes
292	PROSPERO	International Prospective Register of Systematic Reviews
293	SF-36	Short-Form 36

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295

296

297 **DECLARATIONS**

298 **Ethics approval and consent to participate**

299 Not applicable

300

301 **Consent for publication**

302 Not applicable

303

304 **Availability of data and materials**

305 Not applicable

306

307 **Competing interests**

308 The authors declare that they have no competing interests

309

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313

314 **Authors' contributions**

315 **JS:**Conceptualisation, data curation, formal analysis, investigation, methodology, project
316 administration, supervision, validation, visualisation, writing-original draft; **TB:**data curation, formal
317 analysis, investigation, validation, writing-review and editing; **NW:**data curation, investigation,
318 writing-review and editing; **MS:**data curation, formal analysis, investigation, writing-review and
319 editing; **LA:**Conceptualisation, data curation, formal analysis, funding acquisition, investigation,
320 methodology, validation, writing-review and editing.

321

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505 **Table 2: Study characteristics (n=41).**

Study (Author, year, country)	Study design (including (number of sites))	Patients (population (type of surgery) and sample size)			HRQoL tool used and time-point of predictive model (months unless otherwise stated)
		Type of surgery	Sample size		
			Participation rate of eligible persons	Completed follow-up: total cohort	
Myles 2001 ¹¹ Australia	Pre-op post-op (1)	CABG, valve, combined, other	120/125 (96%)	108/120 (90%)	SF-36(3)
Baldassarre 2002 ¹⁴ Canada	Prospective cohort (1)	Isolated CABG (primary)	34/64 (53%)	30/34 (88%)	SF-36(3)

Falcoz 2003 ³³ France	Prospective cohort (1)	CABG, valve, combined, other (elective)	293/452 (65%)	264/293 (90%)	SF-36(12)
Herlitz 2003 ⁵⁶ Sweden	Prospective cohort (2)	Isolated CABG (primary)	1225/2000 (61%)	976/2000 (49%)	NHP(10years)
Schelling 2003 ⁵⁷ Germany	Prospective cohort (1)	CABG, valve, combined	223/387 (58%)	148/223 (66%)	SF-36(6)
Baberg 2004 ¹⁶ Germany	Prospective and retrospective cohort (1)	AVR +/- MVR	201/414 (47%)	201/414 (49%)	SF-36(3years) ^a
Jarvinen 2004 ²⁷ Finland	Prospective cohort (1)	Isolated CABG	501/1128 (44%)	458/501 (91%)	SF-36(12)

Rumsfeld 2004 ¹⁷ America	Prospective cohort (14)	Isolated CABG (primary)	2480/3956 (63%)	1973/2480 (80%)	SF-36(6)
Al-Ruzzeh 2005 ¹⁸ UK	Cross-sectional (1)	Isolated CABG (primary)	437/463 (94%)	NA	SF-36(12) ^a
Herlitz 2005 ⁵⁸ Sweden	Prospective cohort (1)	Isolated CABG (primary)	1225/2000 (61%)	637/1225 (52%)	NHP(10years) ^b
Peric 2005 ⁵⁹ Serbia and Montenegro	Prospective cohort (1)	Elective CABG	243 (no mention of consent/refusal rate)	226/243 (93%)	NHP(6)
Le Grande 2006 ¹⁹	Pre-op post-op (1)	Elective CABG	182/407 (45%)	117/182 (64%)	SF-36(2, 6)

Australia					
Myles 2006 ⁴ Australia	Pre-op post-op (1)	CABG, valve, combined, other	108/120 (90%)	93/108 (86%)	SF-36(3, 3years)
Noyez 2006 ⁶⁰ Netherlands	Retrospective cohort (1)	Isolated CABG	428/428 (100%)	428/428 (100%)	EQ-5D(12)
Panagopoulou2 006 ⁶¹ Greece	Prospective cohort (1)	Elective CABG	157/256 (61%)	1mo:117/157 (75%) 6mo:104/157 (66%)	MNHD-Q(1,6)
Dunning 2008 ⁶² England	Prospective cohort (1)	Isolated CABG	911/1180 (77%)	621/911 (68%)	EQ-5D(10) ^a
El Baz 2008 ³¹ Netherlands	Prospective observational (2)	CABG	198/256 (73%)	168/198 (85%)	SF-36(6)

Jokinen 2008 ⁴⁷ Finland	Prospective observational cohort (1)	CABG, valve, combined, other	91/98 (93%)	46/91 (51%)	NHP(15, 8.2years) ^b
Peric 2008 ⁶³ Serbia	Pre-op post-op (1)	Isolated CABG	Not reported	192/208 (92%)	NHP(6)
Deaton 2009 ³⁰ USA	Prospective cohort (2)	Isolated CABG	317/442 (72%)	270/317 (85%)	SF-36(3) ^a
Herlitz 2009 ⁶⁴ Sweden	Prospective cohort (2)	Isolated CABG (primary)	Not reported. 2000 screened	639/2000 (32%)	NHP(15 years)
Maisano 2009 ⁶⁵ Italy (implied by authorship, not stated)	Retrospective cohort with prospective assessment of HRQoL (1) (implied)	Mitral valve surgery (± AVR,± TV surgery,± CABG)	225/225 (100%)	220/225 (98%)	MLHF(3 years) ^a
Rantanen 2009 ⁶⁶	Prospective cohort (1)	Elective CABG	1mo:274/367 (75%) 6mo:244/271 (90%)	1mo:270/274 (99%) 6mo:240/244 (98%)	15D(1,6,12)

Finland			12mo:236/266 (89%)	12mo:235/236 (100%)	
Juergens 2010 ²⁹ Germany	Prospective cohort (1)	Elective CABG, valve, combined	56/85(65%)	42/65(75%)	SF-12(3)
Peric 2010 ⁶⁷ Serbia	Prospective pre-op post-op (1)	Elective CABG	243/243 (100%)	226/243 (93%)	NHP(6)
Grady 2011 ²⁰ America	Prospective cohort (1)	CABG, valve, maze, combined	840/2524 (33%)	0mo:173/840 (21%) 6mo:177/840 (21%) 12mo:174/840 (21%) 24mo:129/840 (15%) 36mo:69/840 (8%) Total:816/840 (97%)	SF-36(3, 6, 12, 2years, 3years)
Vainiola 2013 ⁴⁶ Finland	Prospective cohort (1)	CABG, valve, combined, aortic, other	785/980 (80%)	571/785 (73%)	15-D(6)

Kurfirist 2014 ¹³ Czech republic	Prospective cohort (1)	CABG, valve, combined (elective)	310 eligible.	260/310 (84%)	SF-36(12)
Humphreys 2016 ³² Australia	Prospective cohort (1)	Elective CABG	180 agreed to participate. No further details	173/180 (96%)	SF-36(6)
Patron 2016 ²¹ Italy	Pre-op post-op (1)	CABG, valve, combined (primary, elective)	92/92 (100%)	75/92 (82%)	SF-12(12)
Bjornnes 2017 ⁶⁸ Norway	Secondary analysis of RCT (2)	CABG, valve, combined	416/525 (79%)	349/416 (84%)	15D(2 weeks, 3,6,12)

Norkiene 2018 ¹² Lithuania	Prospective cohort (1)	CABG, valve, combined	210 / 210 (100%) No further details	105/210(50%)	SF-36(12)
Bishawi 2018 ⁶⁹ America	Secondary analysis of RCT (18)	Isolated CABG (urgent or elective)	2203/3670 (60%)	1770 / 2203 (80%)	SAQVR-36(12)
Grand 2018 ²² France	Prospective cohort (1)	CABG, valve, combined (elective)	495/548 (90%)	326/495 (66%)	SF-36(6)
Coelho 2019 ²³ Portugal	Prospective cohort (1) (implied)	CABG, valve, combined (elective)	Not stated	384/430 (89%)	SF-36(12)
Blokzijl 2019 ²⁴ Netherlands	Retrospective cohort multicentre (3)	Elective CABG	2606/8643 (30%)	2606/8643 (30%)	SF-36 or SF12(10- 14)
Joskowiak 2019 ²⁵ Germany	Prospective cohort (1)	CABG, valve, combined, aortic, other, redo (elective)	164 consented but does not state number	164/164 (100%)	SF-36(12)

			who were eligible and screened		
Perrotti 2019 ²⁶ France	Prospective cohort (1)	Isolated CABG (elective)	272/272 (100%)	118/272 (43%)	SF-36(10years)
Kube 2020 ³⁴ Germany	Prospective cohort (2)	CABG, valve, combined (elective)	70/110 (64%)	53/70 (76%)	SF-12(6)
Rijnhart-de Jong 2020 ²⁸	Prospective cohort (1)	Non-salvage cardiac surgery	1544/1773 (87%)	874/1544 (57%)	SF-36(12)
Schaal 2020 ⁷⁰ Germany	Prospective cohort (1)	CABG, valve, combined, aortic,	8676/14043 (62%)	8676/14043 (62%)	NHP(6)

506 ^a no preoperative HRQoL assessment performed; ^b preoperative HRQoL assessment carried out in some, but not all patients; **Abbreviations:** AVR:aortic
507 valve replacement; CABG:Coronary Artery Bypass Surgery; EQ-5D:EuroQoL- 5 Dimension; HRQoL:Health-related Quality of Life; MLHF:Minnesota Living with
508 Heart Failure questionnaire; MNHD-Q:MacNew Heart Disease Quality of Life Questionnaire; MVR:mitral valve replacement; NHP:Nottingham Health Profile;

509 PF:physical function; SAQ:Seattle Angina Questionnaire; SF-12:12 item short form health survey; SF-36:36 item short form health survey; TV:tricuspid valve;

510 VR-36:Veteran’s Rand(version of SF36)

511 **Table 3: Independent variables by operative and follow-up time period**

	Independent predictors of HRQoL between 1 and 6 months follow-up	Independent predictors of HRQoL between 1year and 3.5years follow-up	Independent predictors of HRQoL at 8.2 years and beyond
Pre-operative variables	Age ^{14,17,32, 34,70} Alcohol use ³² ASA score ^{15,22} Angina ^{22, 31,70} BMI ³⁰ Cerebrovascular disease ^{32, 33,69} Charlton Comorbidity Index ³⁰ Chronic Heart Failure ³² Chronic neurological disease ¹⁷	Atrial fibrillation ⁶⁵ Age ^{20, 23,25,65,66, 68} Angina class ³³ Back/neck problems ⁶⁸ BMI ²⁰ Chronic Heart Failure ^{18,20} COPD ^{20, 33,69} Cerebrovascular accident ⁶⁹ Depression ^{21,68,69}	Age ^{56,58,64} Angina ²⁶ COPD ⁵⁸ COPD/asthma ⁶² CCSC ⁶² Diabetes ^{26,47,58,62,64} Duration of cardiac symptoms pre-op >120 days ⁴⁷ Dyspnea ²⁶

<p>COPD¹⁷</p> <p>Delirium³²</p> <p>Depression³²</p> <p>Diabetes mellitus^{46,63,67,}</p> <p>Ejection fraction^{17,63}</p> <p>Ethnicity (aboriginal)³²</p> <p>Everyday functioning questionnaire¹⁹</p> <p>EuroSCORE^{31,59}</p> <p>FEV1¹⁷</p> <p>Gender^{63,67}</p> <p>Gender:Male^{46,70}</p> <p>Gender:Female³⁰</p> <p>Geriatric depression scale³⁰</p> <p>Health behaviours³²</p> <p>History of renal insufficiency³¹</p>	<p>Diabetes Mellitus^{16, 28,65,69}</p> <p>Education^{21,33,68}</p> <p>Ejection Fraction^{24,33}</p> <p>Ethnicity (non-white)²⁰</p> <p>EuroSCORE^{21,65}</p> <p>Gastrointestinal tract problems¹⁸</p> <p>Gender²³</p> <p>Gender:Female^{20,28}</p> <p>Gender/marital status interaction⁶⁸</p> <p>Hypertension²⁰</p> <p>Infection²⁸</p> <p>MI²⁰</p> <p>Mobility⁶⁰</p> <p>Neurological disease²⁵</p> <p>NYHA class^{16,20, 33,65}</p>	<p>Gender:Female^{62,64}</p> <p>Height⁵⁸</p> <p>Hypertension^{56,58}</p> <p>NYHA class^{56,64}</p> <p>Obesity^{58,64}</p> <p>Pre-op Nottingham Health Profile⁵⁶</p> <p>Pre-op inferior QoL⁶⁴</p> <p>Protective use of statin⁴⁷</p> <p>Peripheral Vascular Disease⁶²</p> <p>Redo surgery⁶²</p> <p>Smoking⁶²</p>
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	<p>Hypertension^{17,32}</p> <p>Illness perception questionnaire²⁹</p> <p>Living alone^{30,70}</p> <p>NYHA class^{17,19,31,70}</p> <p>Peripheral vascular disease¹⁷</p> <p>Previous cardiac surgery¹⁹</p> <p>Pre-op 15-D⁴⁶</p> <p>Pre-op expectations (IPQ-E)³⁴</p> <p>Pre-op MacNew score⁶¹</p> <p>Pre-op MCS¹⁷</p> <p>Pre-op PCS¹⁷</p> <p>Pre-op SF-12 physical QoL³⁴</p> <p>Pre-op SF-12 psychological Qo³⁴</p> <p>Profile of mood state vigor-activity¹⁹</p> <p>Profile of mood state fatigue-inertia¹⁹</p>	<p>Other diseases⁶⁶</p> <p>Pain intensity⁶⁸</p> <p>Parsonnet score³³</p> <p>PCI<1yr²⁸</p> <p>Peripheral or cerebral vascular Disease³³</p> <p>Peripheral Vascular Disease^{18,20}</p> <p>Pre-op MCS^{13,12,23 24,25}</p> <p>Pre-op PCS^{13,12,21, 23 24,25,28}</p> <p>Pre-op SAQ⁶⁹</p> <p>Pre-op SF-36⁴</p> <p>Pre-op VAS⁶⁰</p> <p>Pre-op VR36⁶⁹</p> <p>Presence coronary artery disease²⁰</p> <p>Pulmonary disease²⁴</p> <p>QoR-40⁴</p>	
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	Psychiatric disease ¹⁷ Psychological distress ⁶¹ QoR-40 ¹¹ Serum creatinine ¹⁷ Smoking ^{17, 31,67} Stress symptom score ¹⁵ Work:Not in workforce ^{19,70} Work manual occupation ¹⁹	Redo surgery ²⁰ Renal disease ²⁴ Segment wall motion (abnormal) ³³ Serum creatinine ⁶⁵ Type D personality ¹⁸ Type valvular heart disease ¹⁶	
Intra-operative variables	Cardiopulmonary bypass duration ²² Higher mean pulmonary pressure ¹⁹ CABG procedure ⁷⁰	On cardiopulmonary bypass ³³ Prosthetic valve type ¹⁶ CABG procedure ²⁵	Inotropic drugs at time of surgery ⁶⁴
Post-operative variables	Aid from network members ⁶⁶ Complications ^{63,67} Dobutamine ²² Length of hospital stay ³¹	Infective complications ¹⁸ Ejection fraction at follow-up ⁶⁵ Hospital LOS ^{4,23} ICU LOS ²³	High pain score at 15 months ⁴⁷ ICU time ⁶⁴ ICU 2 days ⁶² ICU >3 days ⁴⁷

	<p>MI⁶⁶</p> <p>Prolonged LOS³⁰</p> <p>New cardiac arrhythmia¹⁹</p> <p>No of categories of traumatic memory¹⁵</p> <p>Other diseases⁶⁶</p> <p>Pain:severe and unbearable⁴⁶</p> <p>Physical exertion causing symptoms⁶⁶</p> <p>Post-op expectations (IPQ-E)³⁴</p> <p>Post-op SF-12 physical QoL³⁴</p> <p>Post-op SF-12 psychological QoL³⁴</p> <p>QoL at 1month (15D)^{61,66}</p> <p>Readmission to hospital within 6weeks³¹</p> <p>Reexploration³¹</p> <p>Renal replacement for acute renal failure²²</p> <p>Restlessness during ICU treatment⁴⁶</p>	<p>Mitral regurgitation at follow-up echo⁶⁵</p> <p>Perioperative MI²⁷</p> <p>QoL at 1month (15D)⁶⁶</p> <p>Quality of life at 3months⁴</p> <p>Poor QOR-40 at 1month⁴</p> <p>Physical exertion causing symptoms⁶⁶</p> <p>Post-operative rhythm¹⁶</p> <p>Sternal complications¹⁶</p> <p>Symptoms on mild exertion or at rest⁶⁶</p> <p>Systolic pulmonary artery pressure at follow-up⁶⁵</p>	<p>Length ventilator time⁵⁸</p> <p>Low energy score at 15months⁴⁷</p>
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	Sternal resuturing ³¹ Symptoms on mild exertion or at rest ⁶⁶ Ventilation >48hrs ²²		
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512 BMI:Body Mass Index; CABG:Coronary Artery Bypass Graft; CCSC: Canadian Cardiovascular Society; COPD:Chronic obstructive pulmonary disease;

513 FEV1:Forced Expiratory Volume; ICU:Intensive Care Unit; LOS:Length of Stay; MCS:mental component score; MI:Myocardial Infarction; NYHA:New York

514 Heart Association classification; PCI:Percutaneous Coronary Intervention; PCS:Physical Component Score; QoL:Quality of Life; SAQ:Seattle Angina

515 Questionnaire; VAS:Visual Analogue Scale; VR36:Veteran's Ran

