



BMJ Open is committed to open peer review. As part of this commitment we make the peer review history of every article we publish publicly available.

When an article is published we post the peer reviewers' comments and the authors' responses online. We also post the versions of the paper that were used during peer review. These are the versions that the peer review comments apply to.

The versions of the paper that follow are the versions that were submitted during the peer review process. They are not the versions of record or the final published versions. They should not be cited or distributed as the published version of this manuscript.

BMJ Open is an open access journal and the full, final, typeset and author-corrected version of record of the manuscript is available on our site with no access controls, subscription charges or pay-per-view fees (<http://bmjopen.bmj.com>).

If you have any questions on BMJ Open's open peer review process please email [info.bmjopen@bmj.com](mailto:info.bmjopen@bmj.com)

# BMJ Open

## The impact of patient's health related quality of life on physicians' therapy and perceived benefit in acute coronary syndromes: protocol for a systemic review of quantitative and qualitative studies

Journal:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2018-026595
Article Type:	Protocol
Date Submitted by the Author:	10-Sep-2018
Complete List of Authors:	Kaambwa, Billingsley; Flinders University Faculty of Medicine Nursing and Health Sciences, Health Economics Gesese, Hailay; Jimma University, Epidemiology Horsfall, Matthew; South Australian Health & Medical Research Institute, SAHMRI, Adelaide, Australia Chew, Derek; Flinders Medical Centre, Department of Cardiovascular Medicine
Keywords:	Quality of life, percutaneous coronary intervention, angiography, physician therapy, mortality, bleeding events

SCHOLARONE™  
Manuscripts

**The impact of patient’s health related quality of life on physicians’ therapy and perceived benefit in acute coronary syndromes: protocol for a systemic review of quantitative and qualitative studies**

**Authors:** B Kaambwa<sup>1#\*</sup>, HA Gesesew<sup>2#</sup>, M Horsfall<sup>3</sup>, D Chew<sup>3</sup>

# Joint first authors

**Affiliations:** <sup>1</sup>Health Economics, College of Medicine and Public Health, Flinders University, Adelaide, Australia

<sup>2</sup>Public Health, College of Medicine and Public Health, Flinders University  
Adelaide, Australia

<sup>3</sup> Cardiology, Flinders Medical Centre, Southern Adelaide Local Health Network, Adelaide, Australia

**Corresponding Author\***

Billingsley Kaambwa, Health Economics Unit, College of Medicine & Public Health, Flinders University, Health Sciences Building, Bedford Park Campus, Sturt Road, Bedford Park, SA 5042, Australia

P: +61 8 8201 5377 F: +61 8 8201 5378 Email: [billingsley.kaambwa@flinders.edu.au](mailto:billingsley.kaambwa@flinders.edu.au)

**Running Title:** Impact of patients’ quality of life on physicians’ treatment decisions

**Word count:** Abstract— 258; Main text— 1416; Figure—1; Box—1; Table—0.

**Keywords:** Quality of life; percutaneous coronary intervention; angiography; physician therapy; mortality; bleeding events; acute coronary syndrome; systematic review

## ABSTRACT

**Introduction:** Percutaneous coronary interventions (PCIs) and coronary angiography are two of the treatments administered to acute coronary syndrome (ACS) patients. However, whether and how patients' health-related quality of life (HRQoL) influences treatment decisions and subsequent risk benefit analyses is unclear. In this study, we will review the available evidence on the impact of patients' HRQoL on physicians' prescribing or treatment decisions and on the estimation of mortality and bleeding risk in ACS patients.

**Methods and analysis:** We will undertake a systematic review of all quantitative and qualitative studies. The search will include studies that describe the impact of HRQoL on prescribing PCIs or angiography, and impact of HRQoL on perceived risks in terms of mortality and bleeding events. We will conduct an initial search on Google scholar and MEDLINE to build the searching terms followed by a full search strategy using all identified keywords and index terms across the five databases namely MEDLINE, PubMed, CINAHL, SCOPUS and Web of Sciences. We will use the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines to select the studies, and appraise their quality before inclusion to review. Only English language articles will be included for the review. We will use a standardized Cochrane data extraction tool to synthesize the information extracted from the selected studies into themes with summary findings presented in a table.

**Ethics and dissemination:** We will not require a formal ethical approval as we will not be collecting primary data. Review findings will be disseminated through a peer-reviewed publication, workshops, conference presentations and a media release.

**Trial registration number:** International Prospective Register for Systematic Reviews (PROSPERO) number is CRD42018108438.

### Strengths and limitations of this study

- This is a systematic review of all quantitative and qualitative studies on physicians' treatment decisions and estimation of risk in acute coronary syndrome patients.
- This will offer comprehensive and high level of evidence of the impact of patients' health-related quality of life on treatment decisions.
- This study will also clarify if physician's estimation of risk is also influenced by patients' health-related quality of life.
- The measurement of quality of life may be based on dissimilar tools and may have its own limitations on estimating outcomes.

## Key words

Quality of life; percutaneous coronary intervention; angiography; physician therapy; mortality; bleeding events; acute coronary syndrome; systematic review.

## INTRODUCTION

Acute coronary syndrome (ACS) is one of the most common set of conditions that patients in emergency departments present with and which often leads to hospitalization<sup>1 2</sup>. It is characterised by a number of clinical symptoms including unstable angina, non-ST-segment elevation myocardial infarction, and ST-segment elevation myocardial infarction<sup>2</sup>. The accurate diagnosis, management and outcomes of ACS depend on multiple range of activities including history taking, physical examination and reviews of electrocardiography, chest radiograph and cardiac biomarker test results<sup>2 3</sup>. Evidence from the literature shows that risk stratification is an essential prerequisite to decision-making, particularly when determining whether (i) patients will be treated in a coronary care unit or monitored step-down unit (ii) treatment will be invasive or non-invasive or (iii) prognosis will be good or bad<sup>3-5</sup>.

Physicians have developed a number of multivariable risk assessment methods to help them provide a comprehensive assessment of risk and an accurate method of prognosis for ACS patients<sup>6-8</sup>. These methods thereafter inform the treatment choice based on strategies that include percutaneous coronary intervention (PCI) and coronary angiography<sup>9 10</sup>. Despite the existence of these risk assessment techniques, however, physicians still use their clinical intuition to prescribe therapies and estimate potential benefit and harm<sup>11 12</sup>. Whether, and the extent to which, patients' health-related quality of life (HRQoL) influences this treatment choice is unclear in the literature. The degree to which this HRQoL affects the estimation of the risk of mortality or bleeding events in ACS patients is also uncertain<sup>11 13 14</sup>.

Few studies report on what factors influence physicians' decision-making in terms of treatment and risk assessment for ACS patients. For example, some studies report that being in high-risk clinical subgroups such as old age, male gender as well as having diabetes, renal failure, other cardiac comorbidities or a previous history of ACS are significant factors that influence this decision-

1 making<sup>11 15 16</sup>. Unfortunately, these group of patients are also at high risk of increased adverse  
2 outcomes of ACS management<sup>17 18</sup>. However, evidence of the impact of HRQoL on decision-  
3 making and risk assessment is lacking. Therefore, this study will review the available evidence on  
4 HRQoL and other factors affecting physicians' therapy decisions and their assessment of risk for  
5 ACS patients. In particular we will review, i) the status of HRQoL in ACS patients, ii) the impact of  
6 HRQoL on physician's therapy in ACS patients, and iii) the impact of patient's HRQoL on  
7 mortality and bleeding risk estimation by physicians.

9 **METHODS AND DESIGN**

11 **Population**

12 The systematic review will include studies on physicians who screen and diagnose patients with  
13 ACS and prescribe PCI or angiography therapy.

15 **Study design**

16 The systematic review will consider quantitative and qualitative studies of good quality conducted  
17 in developed and developing countries.

19 **Search strategy**

20 We will perform the following steps to undertake the searching strategy. First, we will carry out a  
21 limited search through Google scholar and MEDLINE in order to develop key terms for the three  
22 pre-defined concepts relating to the research question. : concept 1 (predictors, factors, quality of  
23 life, or life quality), concept 2 (physician's therapy, percutaneous coronary intervention, PCI,  
24 angiography, revascularization, bleeding events, mortality, death, clinical intuition, perceived  
25 benefit, perceived risk, risk stratification, estimated benefit, or estimated risk) and concept 3 (acute  
26 coronary syndrome, ACS, coronary heart disease, myocardial infarction (MI) or heart infarction).  
27 Second, we will carry out a full search using all identified keywords and index terms across the

following databases: MEDLINE, PubMed, CINAHL, SCOPUS and Web of Sciences. Concepts 1, 2 and 3 will be connected by 'AND' to run the full searching strategy in the aforementioned databases. Next, titles and abstracts from each database will be screened and relevant titles/abstracts selected for a full text appraisal. Finally, we will undertake backward and forward citation chaining of relevant documents. Figure 1 describes the schematic presentation of the search strategy using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.

### Study selection

Prior to inclusion in the review, two primary but independent reviewers, HAG and BK, will assess the selected papers for methodological validity using standardized critical appraisal instruments from Cochrane's systematic reviews critical appraisal guide<sup>19</sup>. Any disagreement will be resolved by consensus among the research team.

### Quality assessment

The two primary reviewers will independently assess the methodological quality of the included studies using an appraisal form developed by Cochrane<sup>19</sup>. In addition, we will assess the risk of bias via the Agency for Healthcare Research and Quality (AHRQ) criteria<sup>20</sup>.

### Data extraction

Quantitative and qualitative data will be extracted from papers based on the Cochrane's extracting tool and scoring criteria<sup>19</sup>. We will extract relevant information from all articles included in the review into a spreadsheet. Whenever, there is missing or unclear data, we will contact authors of primary studies. Both primary reviewers will independently check the data extraction.

### Outcomes

The review will consider the following physician outcomes:

- Prescription of PCI for ACS patients



- Prescription of angiography for ACS patients
- Estimation of mortality risk to ACS patients
- Estimation of bleeding events for ACS patients.

Definitions and measurements of estimated (perceived) mortality and bleeding events benefit are described elsewhere<sup>11</sup>. Briefly, bleeding events were measured using Thrombolysis in Myocardial Infarction (TIMI), Global Use of Strategies to Open Occluded Coronary Arteries (GUSTO) and the AUCITY bleeding criteria

## Exposures

The primary exposure in this review will be HRQoL as defined by a number of HRQoL instruments. These will include the Short Form 6, 12 and 36 dimension (SF-6D, SF-12 and SF-36, respectively)<sup>21-23</sup>, Seattle angina questionnaire (SAQ)<sup>24 25</sup>, duke activity status index (DASI)<sup>26</sup>, Nottingham health profile (NHP)<sup>27 28</sup> and the Euro-Qol 5 dimensions 3 or 5 level measure (EQ-5D-3L or EQ-5D-5L). The secondary exposures or confounders will include age, sex, diabetes mellitus, renal failure, smoking, family history of cardiac illnesses, presenting with cardiac shock or cardiac arrest, other cardiac comorbidities and previous history of ACS.

## ANALYSIS

A narrative synthesis of outcomes along with the exposure variable of selected studies will be demonstrated in the final review. We will include the following information to summarize the main data from the included studies: author (year), setting, study design, population, sample size, outcome, and main findings. The factors for both outcomes, physicians' treatment decision and assessment of perceived risk, will be summarized into themes, and summary findings of each study included in the review will be presented in tables.

If data will be available, meta-regression and meta-analyses will be conducted to see the association of the factors with the aforementioned outcomes. We will assess the clinical and statistical

heterogeneity before conducting the meta-analyses. The research team will check the clinical heterogeneity to decide which variable and outcome will be added in the meta-analysis. We will use standard Chi-square and  $I^2$  tests to diagnose the statistical heterogeneity, with significant heterogeneity detected at the P value < 0.05. In addition, meta-analyses will be carried out separately for each outcome and each exposure of interest using RevMan-5 Software<sup>29</sup>. We will consider meta-analysis if  $I^2$  will be below 85%<sup>30</sup>. In order to calculate effect sizes, we will use a Mantel Haenszel statistical method with forest plots used to graphically depict the relationship between exposures of interest and outcomes or events.

Based on the degree of statistical heterogeneity, we will calculate a pooled unadjusted odds ratio (OR)<sup>31</sup> estimates and their 95% confidence intervals (CI) using random or fixed effect meta-analysis<sup>30</sup>. If the number of studies that reported the exposure and outcome of interest will be small ( $n < 5$ ), we will only consider fixed effect model irrespective of the level of heterogeneity<sup>32 33</sup>. We will consider pooling if at least two studies assess the outcomes and the exposures of interest. To assess the publication bias, we will use a funnel plot. We will also consider a sensitivity test via omitting and entering small studies and deviant results from the rest of the studies (outliers).

## CONCLUSION

This systematic review will provide evidence in support of, or against, the hypothesis that patients' HRQoL has a role in physicians' treatment decisions and in estimating the mortality and bleeding event risk for ACS patients. Particularly, this review will assess the impact that HRQoL, measured using validated instruments, has on prescribing PCI and angiography. Furthermore, the role of HRQoL on estimating mortality and bleeding events benefit will also be enumerated. We will apply descriptive and inferential statistical analysis to summarise the quantitative data from the review and synthesise the qualitative component of the findings into themes. In general, the review will contribute to the clinical evidence base on what drives clinical intuition during the treatment decision-making for ACS patients.

1  
2  
3  
4  
5  
6  
7  
8  
9  
10  
11  
12  
13  
14  
15  
16  
17  
18  
19  
20  
21  
22  
23  
24  
25  
26  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

1  
2     **Acknowledgements:** We thank Flinders University for enabling us to access not freely available  
3 articles. We also acknowledge authors of primary studies.

4  
5     **Contributors:** BK & HAG contributed equally to this paper. DC, BK & HAG conceived the idea.  
6 BK & HAG drafted the protocol. All authors contributed to the development of the selection  
7 criteria, the risk of bias assessment strategy and data extraction criteria. BK & HAG developed the  
8 search strategy. DC & MH provided expertise on acute coronary syndrome. All authors read,  
9 provided feedback and approved the final manuscript

10  
11     **Funding** None

12  
13     **Competing interests** None declared

14  
15     **Provenance and peer review** Not commissioned; externally peer reviewed

## REFERENCES

1. GRACE. Rationale and design of the GRACE (Global Registry of Acute Coronary Events) Project: a multinational registry of patients hospitalized with acute coronary syndromes. *American heart journal* 2001;141(2):190-9. [published Online First: 2001/02/15]
2. Kumar A, Cannon CP. Acute Coronary Syndromes: Diagnosis and Management, Part I. *Mayo Clinic Proceedings* 2009;84(10):917-38.
3. Anderson JL, Adams CD, Antman EM, et al. ACC/AHA 2007 guidelines for the management of patients with unstable angina/non ST-elevation myocardial infarction: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to Revise the 2002 Guidelines for the Management of Patients With Unstable Angina/Non ST-Elevation Myocardial Infarction): developed in collaboration with the American College of Emergency Physicians, the Society for Cardiovascular Angiography and Interventions, and the Society of Thoracic Surgeons: endorsed by the American Association of Cardiovascular and Pulmonary Rehabilitation and the Society for Academic Emergency Medicine. *Circulation* 2007;116(7):e148-304. doi: 10.1161/circulationaha.107.181940 [published Online First: 2007/08/08]
4. Falk V, Baumgartner H, Bax JJ, et al. 2017 ESC/EACTS Guidelines for the management of valvular heart disease. *European Journal of Cardio-Thoracic Surgery* 2017;52(4):616-64. doi: 10.1093/ejcts/ezx324
5. Marechaux S, Hachicha Z, Bellouin A, et al. Usefulness of exercise-stress echocardiography for risk stratification of true asymptomatic patients with aortic valve stenosis. *European heart journal* 2010;31(11):1390-7. doi: 10.1093/eurheartj/ehq076 [published Online First: 2010/03/24]
6. Antman EM, Cohen M, Bernink PJ, et al. The TIMI risk score for unstable angina/non-ST elevation MI: A method for prognostication and therapeutic decision making. *Jama* 2000;284(7):835-42. [published Online First: 2000/08/11]
7. Eagle KA, Lim MJ, Dabbous OH, et al. A validated prediction model for all forms of acute coronary syndrome: estimating the risk of 6-month postdischarge death in an international registry. *Jama* 2004;291(22):2727-33. doi: 10.1001/jama.291.22.2727 [published Online First: 2004/06/10]
8. Boersma E, Pieper KS, Steyerberg EW, et al. Predictors of outcome in patients with acute coronary syndromes without persistent ST-segment elevation. Results from an international trial of 9461 patients. The PURSUIT Investigators. *Circulation* 2000;101(22):2557-67. [published Online First: 2000/06/07]
9. Henriques JP, Claessen BE, Dangas GD, et al. Performance of currently available risk models in a cohort of mechanically supported high-risk percutaneous coronary intervention--From the PROTECT II randomized trial. *International journal of cardiology* 2015;189:272-8. doi: 10.1016/j.ijcard.2015.04.084 [published Online First: 2015/04/25]
10. Kirtane AJ, Doshi D, Leon MB, et al. Treatment of Higher-Risk Patients With an Indication for Revascularization: Evolution Within the Field of Contemporary Percutaneous Coronary Intervention. *Circulation* 2016;134(5):422-31. doi: 10.1161/circulationaha.116.022061 [published Online First: 2016/08/03]
11. Chew DP, Juergens C, French J, et al. An examination of clinical intuition in risk assessment among acute coronary syndromes patients: observations from a prospective multi-center international observational registry. *International journal of cardiology* 2014;171(2):209-16. doi: 10.1016/j.ijcard.2013.12.010 [published Online First: 2014/01/02]
12. Yan AT, Yan RT, Huynh T, et al. Understanding physicians' risk stratification of acute coronary syndromes: insights from the Canadian ACS 2 Registry. *Archives of internal medicine* 2009;169(4):372-8. doi: 10.1001/archinternmed.2008.563 [published Online First: 2009/02/25]
13. Fox KAA, Anderson FA, Dabbous OH, et al. Intervention in acute coronary syndromes: do patients undergo intervention on the basis of their risk characteristics? The Global Registry of Acute Coronary Events (GRACE). *Heart* 2007;93(2):177-82. doi: 10.1136/hrt.2005.084830
14. Scott IA, Derhy PH, O'Kane D, et al. Discordance between level of risk and intensity of evidence-based treatment in patients with acute coronary syndromes. *The Medical journal of Australia* 2007;187(3):153-9. [published Online First: 2007/08/08]
15. Hung J, Brieger DB, Amerena JV, et al. Treatment disparities and effect on late mortality in patients with diabetes presenting with acute myocardial infarction: observations from the ACACIA registry. *The Medical journal of Australia* 2009;191(10):539-43. [published Online First: 2009/11/17]
16. Jneid H, Fonarow GC, Cannon CP, et al. Sex differences in medical care and early death after acute myocardial infarction. *Circulation* 2008;118(25):2803-10. doi: 10.1161/circulationaha.108.789800 [published Online First: 2008/12/10]
17. Dai X, Busby-Whitehead J, Alexander KP. Acute coronary syndrome in the older adults. *Journal of Geriatric Cardiology : JGC* 2016;13(2):101-08. doi: 10.11909/j.issn.1671-5411.2016.02.012
18. Franklin K, Goldberg RJ, Spencer F, et al. Implications of diabetes in patients with acute coronary syndromes. The Global Registry of Acute Coronary Events. *Archives of internal medicine* 2004;164(13):1457-63. doi: 10.1001/archinte.164.13.1457 [published Online First: 2004/07/14]
19. Julian H, Sally G. Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0 [updated March 2011], 2011.

20. Viswanathan M, Ansari MT, Berkman ND, et al. AHRQ Methods for Effective Health Care: Assessing the Risk of Bias of Individual Studies in Systematic Reviews of Health Care Interventions. Methods Guide for Effectiveness and Comparative Effectiveness Reviews. Rockville (MD): Agency for Healthcare Research and Quality (US) 2008:14.

21. van Domburg RT, Daemen J, Morice MC, et al. Short- and long-term health related quality-of-life and anginal status of the Arterial Revascularisation Therapies Study part II, ARTS-II; sirolimus-eluting stents for the treatment of patients with multivessel coronary artery disease. *EuroIntervention : journal of EuroPCR in collaboration with the Working Group on Interventional Cardiology of the European Society of Cardiology* 2010;5(8):962-7. doi: 10.4244/ [published Online First: 2010/06/15]

22. Favarato ME, Hueb W, Boden WE, et al. Quality of life in patients with symptomatic multivessel coronary artery disease: a comparative post hoc analyses of medical, angioplasty or surgical strategies-MASS II trial. *International journal of cardiology* 2007;116(3):364-70. doi: 10.1016/j.ijcard.2006.06.001 [published Online First: 2006/08/01]

23. Thiele H, Neumann-Schneiderwind P, Jacobs S, et al. Randomized comparison of minimally invasive direct coronary artery bypass surgery versus sirolimus-eluting stenting in isolated proximal left anterior descending coronary artery stenosis. *Journal of the American College of Cardiology* 2009;53(25):2324-31. doi: 10.1016/j.jacc.2009.03.032 [published Online First: 2009/06/23]

24. Borkon AM, Muehlebach GF, House J, et al. A comparison of the recovery of health status after percutaneous coronary intervention and coronary artery bypass. *The Annals of thoracic surgery* 2002;74(5):1526-30; discussion 30. [published Online First: 2002/11/21]

25. Zhang Z, Mahoney EM, Stables RH, et al. Disease-specific health status after stent-assisted percutaneous coronary intervention and coronary artery bypass surgery: one-year results from the Stent or Surgery trial. *Circulation* 2003;108(14):1694-700. doi: 10.1161/01.cir.0000087600.83707.f0 [published Online First: 2003/09/17]

26. Hlatky MA, Boothroyd DB, Melsop KA, et al. Medical costs and quality of life 10 to 12 years after randomization to angioplasty or bypass surgery for multivessel coronary artery disease. *Circulation* 2004;110(14):1960-6. doi: 10.1161/01.cir.0000143379.26342.5c [published Online First: 2004/09/29]

27. Pocock SJ, Henderson RA, Seed P, et al. Quality of life, employment status, and anginal symptoms after coronary angioplasty or bypass surgery. 3-year follow-up in the Randomized Intervention Treatment of Angina (RITA) Trial. *Circulation* 1996;94(2):135-42. [published Online First: 1996/07/15]

28. Wahrborg P. Quality of life after coronary angioplasty or bypass surgery. 1-year follow-up in the Coronary Angioplasty versus Bypass Revascularization investigation (CABRI) trial. *European heart journal* 1999;20(9):653-8. [published Online First: 1999/04/20]

29. Review Manager (RevMan) [Computer program] [program]. 5.3 version. Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2014.

30. Jo L-B, Viv R. Presenting and interpreting meta-analyses: Heterogeneity School of Nursing and Academic Division of Midwifery, University of Nottingham; 2007 [cited 2016 May 02]. Available from: <http://www.nottingham.ac.uk/nmp/sonet/rlos/ebp/meta-analysis2/4.html> accessed May 02 2016.

31. Sen S. Odds ratios revisited. *Evidence-Based Med* 1998;3(71)

32. Borenstein M, Hedges L, Rothstein H. Meta-Analysis: Fixed effect vs. random effects 2007 [cited 2016 17 May]. Available from: <https://www.meta-analysis.com/downloads/Meta-analysis%20fixed%20effect%20vs%20random%20effects.pdf> accessed 17 May 2016.

33. Tufanaru C, Munn Z, Stephenson M, et al. Fixed or random effects meta-analysis? Common methodological issues in systematic reviews of effectiveness. *International Journal of Evidence-Based Healthcare* 2015;13(3):196-207.

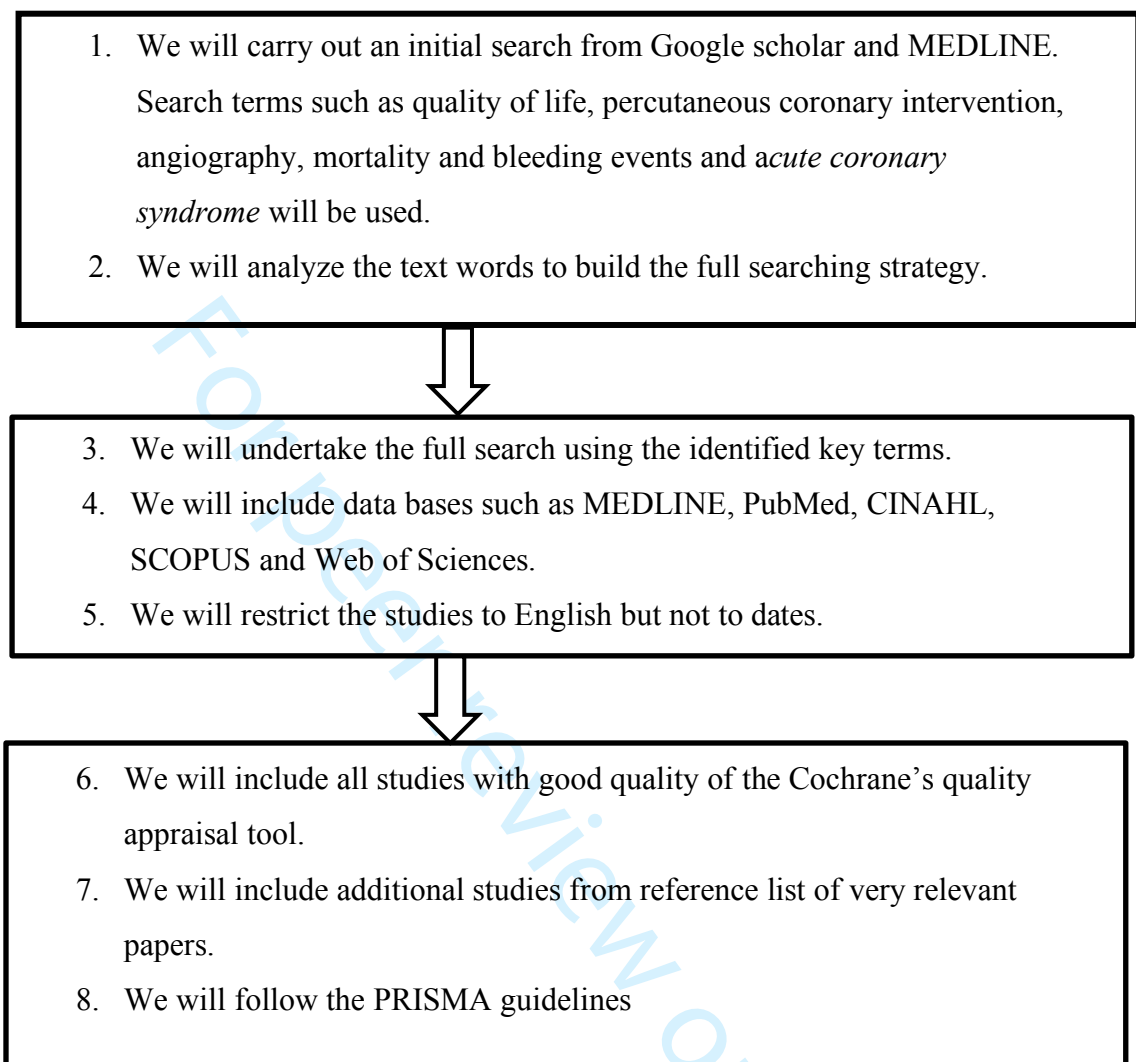


Figure 1 A schematic of the process of the systemic review using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA).

# BMJ Open

## The impact of patient's health related quality of life on physicians' therapy and perceived benefit in acute coronary syndromes: protocol for a systemic review of quantitative and qualitative studies

Journal:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2018-026595.R1
Article Type:	Protocol
Date Submitted by the Author:	13-Nov-2018
Complete List of Authors:	Kaambwa, Billingsley; Flinders University Faculty of Medicine Nursing and Health Sciences, Health Economics Gesese, Hailay; Jimma University, Epidemiology Horsfall, Matthew; South Australian Health & Medical Research Institute, SAHMRI, Adelaide, Australia Chew, Derek; Flinders Medical Centre, Department of Cardiovascular Medicine
<b>Primary Subject Heading</b>:	Cardiovascular medicine
Secondary Subject Heading:	Cardiovascular medicine, Evidence based practice, Patient-centred medicine
Keywords:	Quality of life, percutaneous coronary intervention, angiography, physician therapy, mortality, bleeding events

SCHOLARONE™  
Manuscripts



1  
2  
3  
4  
5  
6  
7  
8  
9  
10  
11  
12  
13  
14  
15  
16  
17  
18  
19  
20  
21  
22  
23  
24  
25  
26  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

**The impact of patient’s health related quality of life on physicians’ therapy and perceived benefit in acute coronary syndromes: protocol for a systemic review of quantitative and qualitative studies**

**Running Title: Impact of patients’ quality of life on physicians’ treatment decisions.**

**Authors:** B Kaambwa<sup>1#</sup>, HA Gesesew<sup>2#</sup>, M Horsfall<sup>3</sup>, D Chew<sup>3</sup>

<sup>1</sup>Health Economics Unit, College of Medicine and Public Health, Flinders University, Health Sciences Building, Bedford Park Campus, Sturt Road, Bedford Park, SA 5042, Australia

<sup>1</sup>Public Health Department, College of Medicine and Public Health, Flinders University, Health Sciences Building, Bedford Park Campus, Sturt Road, Bedford Park, SA 5042, Australia

<sup>3</sup> Cardiology Department, Flinders Medical Centre, Southern Adelaide Local Health Network, Sturt Road, Bedford Park, SA 5042, Australia

# BK and HAG contributed equally

**Corresponding Author\***

Billingsley Kaambwa, Health Economics Unit, College of Medicine & Public Health, Flinders University, Health Sciences Building, Bedford Park Campus, Sturt Road, Bedford Park, SA 5042, Australia

P: +61 8 8201 5377                      F: +61 8 8201 5378

Email: [billingsley.kaambwa@flinders.edu.au](mailto:billingsley.kaambwa@flinders.edu.au)



## ABSTRACT

**Introduction:** Percutaneous coronary interventions (PCIs) and coronary angiography are two of the treatments administered to acute coronary syndrome (ACS) patients. However, whether and how patients' health-related quality of life (HRQoL) influences treatment decisions and subsequent risk benefit analyses is unclear. In this study, we will review the available evidence on the impact of patients' HRQoL on physicians' prescribing or treatment decisions and on the estimation of mortality and bleeding risk in ACS patients.

**Methods and analysis:** We will undertake a systematic review of all quantitative and qualitative studies. The search will include studies that describe the impact of HRQoL on prescribing PCIs or angiography, and impact of HRQoL on perceived risks in terms of mortality and bleeding events. We will conduct an initial search on Google scholar and MEDLINE to build the searching terms followed by a full search strategy using all identified keywords and index terms across the five databases namely MEDLINE, PubMed, CINAHL, SCOPUS and Web of Sciences. We will use the Preferred Reporting Items for Systematic Reviews and Meta-Analyses for protocol (PRISMA-P) guidelines to present the protocol. Only English language articles will be included for the review. We will use a standardized Joanna Briggs Institute (JBI) data extraction tool to synthesize the information extracted from the selected studies into themes with summary findings presented in a table.

**Ethics and dissemination:** We will not require a formal ethical approval as we will not be collecting primary data. Review findings will be disseminated through a peer-reviewed publication, workshops, conference presentations and a media release.

**Trial registration number:** International Prospective Register for Systematic Reviews (PROSPERO) number is 108438.

1  
2  
3  
4  
5  
6  
7  
8  
9  
10  
11  
12  
13  
14  
15  
16  
17  
18  
19  
20  
21  
22  
23  
24  
25  
26  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

**Article summary**

***Strengths and limitations of this study***

- This is a systematic review of all quantitative and qualitative studies on physicians’ treatment decisions and estimation of risk in acute coronary syndrome patients.
- This will offer comprehensive and high level of evidence of the impact of patients’ health-related quality of life on treatment decisions.
- The measurement of quality of life may be based on dissimilar tools and may have its own limitations on estimating outcomes.
- The limited included studies to English may be one of the sources of information bias.

**Key words**

Quality of life; percutaneous coronary intervention; angiography; physician therapy; mortality; bleeding events; acute coronary syndrome; systematic review.

## INTRODUCTION

Acute coronary syndrome (ACS) is one of the most common set of conditions that patients in emergency departments present with and which often leads to hospitalization<sup>1</sup>. It is characterised by a number of clinical symptoms including unstable angina, non-ST-segment elevation myocardial infarction, and ST-segment elevation myocardial infarction<sup>1</sup>. The definitions of ACS depend on multiple range of activities including history taking, physical examination and reviews of electrocardiography, chest radiograph and cardiac biomarker test results<sup>1</sup>. Evidence from the literature shows that risk stratification is an essential prerequisite to decision-making, particularly when determining whether (i) patients will be treated in a coronary care unit or monitored step-down unit (ii) treatment will be invasive or non-invasive or (iii) prognosis will be good or bad<sup>2-4</sup>. For the interest of this review, we will use either of the ACS diagnosis described by the authors in the primary study in order to include as many studies as possible.

Physicians have developed a number of multivariable risk assessment methods to help them provide a comprehensive assessment of risk and an accurate method of prognosis for ACS patients<sup>5</sup>. These methods thereafter inform the treatment choice based on strategies that include percutaneous coronary intervention (PCI) and coronary angiography<sup>6 7</sup>. Despite the existence of these risk assessment techniques, however, physicians still use their clinical intuition to prescribe therapies and estimate potential benefit and harm<sup>8 9</sup>. Whether, and the extent to which, patients' health-related quality of life (HRQoL) influences this treatment choice is unclear in the literature. To date, HRQoL has several measurements with different scales, number of items, scoring calculation and interpretation. For example, Short Form 6, 12 and 36 dimension (SF-6D, SF-12 and SF-36)<sup>10-12</sup>, Seattle angina questionnaire (SAQ)<sup>13 14</sup>, duke activity status index (DASI)<sup>15</sup>, Nottingham health profile (NHP)<sup>16 17</sup> and the Euro-Qol 5 dimensions 3 or 5 level measure were some of the validated tools used to measure HRQoL. In this review, no *a priori* definition is specified in order to be more inclusive of a broad range of literature.

Few studies report on what factors influence physicians' decision-making in terms of treatment and risk assessment for ACS patients. For example, some studies report that being in high-

1 risk clinical subgroups such as old age, male gender as well as having diabetes, renal failure, other  
2 cardiac comorbidities or a previous history of ACS are significant factors that influence this decision-  
3 making <sup>8 18 19</sup>. Unfortunately, these group of patients are also at high risk of increased adverse  
4 outcomes of ACS management <sup>20</sup>. However, evidence of the impact of HRQoL on decision-making  
5 and risk assessment is lacking. 'Impact' in this review is referred to a situation where treatment risk  
6 estimation was modified or altered as a result of HRQoL.

7  
8  
9  
10  
11  
12  
13  
14  
15  
16 A review in United States America<sup>21</sup> found that that several ACS patients consider HRQoL  
17 while deciding to choose a treatment strategy although the survival benefit is similar among the  
18 available therapies. In particular, the review noticed that there were variations in preferences over the  
19 duration of HRQoL. Some patients chose easy treatment strategy that brings favourable HRQoL for  
20 short duration—for instance, patients chose PCI instead of CABG. To the contrary, other patients  
21 chose a complex treatment strategy to have a favourable QoL for longer period of time—for instance,  
22 patients chose CABG instead of PCI. Most patients understood less these existing trade-offs. It is  
23 against this impact that the review recommended that physicians should have to consider advising  
24 their patients about the HRQoL benefit before deciding to choose a treatment strategy. Thus, there  
25 will be a need to consider provide objective information on HRQoL by physicians. Furthermore, the  
26 literature review revealed that clinical trials, treatment guidelines and polices should have to consider  
27 HRQoL while deciding to prescribe among treatment strategies.

28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60  
Several definitions have been used to measure bleeding in hospital and post-discharge periods,  
including Bleeding Academic Research Consortium (BARC). Although evidence on the relationship  
between bleeding and QoL is scarce, the existing evidence demonstrated worse QoL following a  
bleeding<sup>22 23</sup>. For example, Amin et al found a 24% prevalence of bleeding among ACS patients  
undergoing PCI, and the six-month QoL was worse<sup>22</sup>. Furthermore, evidence show the association  
between change in QoL and mortality<sup>24 25</sup>. Nevertheless, the degree to which this HRQoL affects the  
estimation of the risk of mortality or bleeding events in ACS patients is uncertain <sup>8 26 27</sup>.

Therefore, this study will review the available evidence on HRQoL and other factors affecting  
physicians' therapy decisions and their assessment of risk for ACS patients. In particular we will

review, i) the status of HRQoL in ACS patients before and after treatment, ii) the impact of HRQoL on physician's treatment decision in ACS patients, and iii) the impact of patient's HRQoL on physician's estimation of the potential outcomes such as mortality and bleeding risk.

## METHODS AND DESIGN

### Population

The systematic review will include studies on physicians who screen and diagnose patients with ACS and prescribe PCI or angiography therapy.

### Study design

The systematic review will consider quantitative and qualitative studies of good quality published before June 2018.

### Search strategy

We will perform the following steps to undertake the searching strategy. First, we will carry out a limited search through Google scholar and MEDLINE in order to develop key terms for the three pre-defined concepts relating to the research question. : concept 1 (predictors, factors, quality of life, or life quality), concept 2 (physician's therapy, percutaneous coronary intervention, percutaneous transluminal angioplasty, PTA, PTCA, PCI, angiography, revascularization, bleeding events, mortality, death, clinical intuition, perceived benefit, perceived risk, risk stratification, estimated benefit, or estimated risk) and concept 3 (acute coronary syndrome, ACS, coronary heart disease, myocardial infarction (MI) or heart infarction). Second, we will carry out a full search (Annex 1) using all identified keywords and index terms across the following databases: MEDLINE, PubMed, CINAHL, SCOPUS and Web of Sciences. Concepts 1, 2 and 3 will be connected by 'AND' to run the full searching strategy in the aforementioned databases. Next, titles and abstracts from each database will be screened and relevant titles/abstracts selected for a full text appraisal. Finally, we will undertake backward and forward citation chaining of relevant documents. The search will also include unpublished studies or grey literature from ProQuest Dissertations and Theses (PQDT), WHO, Health department Data and other health data repositories.

1  
2 Figure 1 describes the schematic presentation of the search strategy using the Preferred Reporting  
3  
4 Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.  
5

6  
7 **Study selection**

8  
9 Prior to inclusion in the review, two primary but independent reviewers, HAG and BK, will assess  
10  
11 the selected papers for methodological validity using a standardized Joanna Briggs Institute (JBI)  
12  
13 appraisal instruments<sup>28</sup> (Annex 2). Any disagreement will be resolved by consensus among the  
14  
15 research team.  
16

17  
18 **Quality assessment**

19  
20 The two primary reviewers will independently assess the methodological quality of the included  
21  
22 studies using an appraisal form developed by the JBI (Annex 2). In addition, we will assess the risk  
23  
24 of bias via the Agency for Healthcare Research and Quality (AHRQ) criteria<sup>29</sup>.  
25

26  
27 **Data extraction**

28  
29 Quantitative and qualitative data will be extracted from papers based on the JBI data extraction tool  
30  
31 (Annex 3). We will extract relevant information from all articles included in the review into a  
32  
33 spreadsheet. Whenever, there is missing or unclear data, we will contact authors of primary studies.  
34  
35 Both primary reviewers will independently check the data extraction.  
36  
37

38  
39 **Outcomes**

40  
41 The review will consider the following physician outcomes:  
42

- 43  
44
  - Prescription of PCI for ACS patients
  - Prescription of angiography for ACS patients
  - Estimation of mortality risk to ACS patients
  - Estimation of bleeding events for ACS patients.

45  
46  
47  
48  
49  
50  
51

52  
53 Definitions and measurements of estimated (perceived) mortality and bleeding events benefit are  
54  
55 described elsewhere <sup>8</sup>. Briefly, bleeding events were measured using Thrombolysis in Myocardial  
56  
57 Infarction (TIMI), Global Use of Strategies to Open Occluded Coronary Arteries (GUSTO) and the  
58  
59 ACUITY bleeding criteria  
60

**Exposures**

The primary exposure in this review will be HRQoL as defined by a number of HRQoL instruments. These will include the Short Form 6, 12 and 36 dimension (SF-6D, SF-12 and SF-36, respectively)<sup>10-12</sup>, Seattle angina questionnaire (SAQ)<sup>13 14</sup>, duke activity status index (DASI)<sup>15</sup>, Nottingham health profile (NHP)<sup>16 17</sup> and the Euro-Qol 5 dimensions 3 or 5 level measure (EQ-5D-3L or EQ-5D-5L). The secondary exposures or confounders will include age, sex, diabetes mellitus, renal failure, smoking, family history of cardiac illnesses, presenting with cardiac shock or cardiac arrest, other cardiac comorbidities and previous history of ACS.

## ANALYSIS

A narrative synthesis of outcomes along with the exposure variable of selected studies will be demonstrated in the final review. We will include the following information to summarize the main data from the included studies: author (year), setting, study design, population, sample size, outcome, and main findings. The factors for both outcomes, physicians' treatment decision and assessment of perceived risk, will be summarized into themes, and summary findings of each study included in the review will be presented in tables.

If data will be available, meta-regression and meta-analyses will be conducted to see the association of the factors with the aforementioned outcomes. We will assess the clinical and statistical heterogeneity before conducting the meta-analyses. The research team will check the clinical heterogeneity to decide which variable and outcome will be added in the meta-analysis. We will use standard Chi-square and  $I^2$  tests to diagnose the statistical heterogeneity, with significant heterogeneity detected at the P value < 0.05. In addition, meta-analyses will be carried out separately for each outcome and each exposure of interest using RevMan-5 Software<sup>30</sup>. We will consider meta-analysis if  $I^2$  will be below 85%<sup>31</sup>. In order to calculate effect sizes, we will use a Mantel Haenszel statistical method with forest plots used to graphically depict the relationship between exposures of interest and outcomes or events.

Based on the degree of statistical heterogeneity, we will calculate a pooled unadjusted odds ratio (OR)<sup>32</sup> estimates and their 95% confidence intervals (CI) using random or fixed effect meta-analysis<sup>31</sup>. If the outcome is reported using continuous data, we will use a mean difference (MD) or



1  
2 standardized mean difference (SMD). MD will be used if all included studies use the same scale  
3  
4 whereas SMD will be used if the included studies applied variety scales. If the number of studies  
5  
6 that reported the exposure and outcome of interest will be small ( $n < 5$ ), we will only consider fixed  
7  
8 effect model irrespective of the level of heterogeneity<sup>33 34</sup>. We will consider pooling if at least two  
9  
10 studies assess the outcomes and the exposures of interest. To assess the publication bias, we will use  
11  
12 a funnel plot. We will also consider a sensitivity test via omitting and entering small studies and  
13  
14 deviant results from the rest of the studies (outliers). The strength of the body of evidence will be  
15  
16 assessed using GRADE.  
17  
18

19  
20 **Patient and Public Involvement** No patient or public is involved as this is a review of studies.  
21

22  
23 **CONCLUSION**

24  
25 This systematic review will provide evidence in support of, or against, the hypothesis that patients'  
26  
27 HRQoL has a role in physicians' treatment decisions and in estimating the mortality and bleeding  
28  
29 event risk for ACS patients. Particularly, this review will assess the impact that HRQoL, measured  
30  
31 using validated instruments, has on prescribing PCI and angiography. Furthermore, the role of  
32  
33 HRQoL on estimating mortality and bleeding events benefit will also enumerated. We will apply  
34  
35 descriptive and inferential statistical analysis to summarise the quantitative data from the review and  
36  
37 synthesise the qualitative component of the findings into themes. In general, the review will  
38  
39 contribute to the clinical evidence base on what drives clinical intuition during the treatment decision-  
40  
41 making for ACS patients.  
42  
43  
44  
45  
46  
47

48 **Acknowledgements:** We thank Flinders University for enabling us to access not freely available  
49  
50 articles. We also acknowledge authors of primary studies.  
51

52 **Contributors:** BK & HAG contributed equally to this paper. DC, BK & HAG conceived the idea.  
53  
54 BK & HAG drafted the protocol. All authors contributed to the development of the selection  
55  
56 criteria, the risk of bias assessment strategy and data extraction criteria. BK & HAG developed the  
57  
58 search strategy. DC & MH provided expertise on acute coronary syndrome. All authors read,  
59  
60 provided feedback and approved the final manuscript



**Funding** None

**Competing interests** None declared

**Provenance and peer review** Not commissioned; externally peer reviewed

**Figure legend:** Figure 1 showed a schematic presentation of the systemic search and use of Preferred Reporting Items for Systematic Reviews and Meta-Analyses for protocol (PRISMA-P) for reporting the findings.

## REFERENCES

1. Kumar A, Cannon CP. Acute Coronary Syndromes: Diagnosis and Management, Part I. *Mayo Clinic Proceedings* 2009;84(10):917-38.
2. Anderson JL, Adams CD, Antman EM, et al. ACC/AHA 2007 guidelines for the management of patients with unstable angina/non ST-elevation myocardial infarction: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to Revise the 2002 Guidelines for the Management of Patients With Unstable Angina/Non ST-Elevation Myocardial Infarction): developed in collaboration with the American College of Emergency Physicians, the Society for Cardiovascular Angiography and Interventions, and the Society of Thoracic Surgeons: endorsed by the American Association of Cardiovascular and Pulmonary Rehabilitation and the Society for Academic Emergency Medicine. *Circulation* 2007;116(7):e148-304. doi: 10.1161/circulationaha.107.181940 [published Online First: 2007/08/08]
3. Falk V, Baumgartner H, Bax JJ, et al. 2017 ESC/EACTS Guidelines for the management of valvular heart disease. *European Journal of Cardio-Thoracic Surgery* 2017;52(4):616-64. doi: 10.1093/ejcts/ezx324
4. Marechaux S, Hachicha Z, Bellouin A, et al. Usefulness of exercise-stress echocardiography for risk stratification of true asymptomatic patients with aortic valve stenosis. *European heart journal* 2010;31(11):1390-7. doi: 10.1093/eurheartj/ehq076 [published Online First: 2010/03/24]

5. Eagle KA, Lim MJ, Dabbous OH, et al. A validated prediction model for all forms of acute coronary syndrome: estimating the risk of 6-month postdischarge death in an international registry. *Jama* 2004;291(22):2727-33. doi: 10.1001/jama.291.22.2727 [published Online First: 2004/06/10]
6. Henriques JP, Claessen BE, Dangas GD, et al. Performance of currently available risk models in a cohort of mechanically supported high-risk percutaneous coronary intervention--From the PROTECT II randomized trial. *International journal of cardiology* 2015;189:272-8. doi: 10.1016/j.ijcard.2015.04.084 [published Online First: 2015/04/25]
7. Kirtane AJ, Doshi D, Leon MB, et al. Treatment of Higher-Risk Patients With an Indication for Revascularization: Evolution Within the Field of Contemporary Percutaneous Coronary Intervention. *Circulation* 2016;134(5):422-31. doi: 10.1161/circulationaha.116.022061 [published Online First: 2016/08/03]
8. Chew DP, Juergens C, French J, et al. An examination of clinical intuition in risk assessment among acute coronary syndromes patients: observations from a prospective multi-center international observational registry. *International journal of cardiology* 2014;171(2):209-16. doi: 10.1016/j.ijcard.2013.12.010 [published Online First: 2014/01/02]
9. Yan AT, Yan RT, Huynh T, et al. Understanding physicians' risk stratification of acute coronary syndromes: insights from the Canadian ACS 2 Registry. *Archives of internal medicine* 2009;169(4):372-8. doi: 10.1001/archinternmed.2008.563 [published Online First: 2009/02/25]
10. van Domburg RT, Daemen J, Morice MC, et al. Short- and long-term health related quality-of-life and anginal status of the Arterial Revascularisation Therapies Study part II, ARTS-II; sirolimus-eluting stents for the treatment of patients with multivessel coronary artery disease. *EuroIntervention : journal of EuroPCR in collaboration with the Working Group on Interventional Cardiology of the European Society of Cardiology* 2010;5(8):962-7. doi: 10.4244/ [published Online First: 2010/06/15]

11. Favarato ME, Hueb W, Boden WE, et al. Quality of life in patients with symptomatic multivessel coronary artery disease: a comparative post hoc analyses of medical, angioplasty or surgical strategies-MASS II trial. *International journal of cardiology* 2007;116(3):364-70. doi: 10.1016/j.ijcard.2006.06.001 [published Online First: 2006/08/01]
12. Thiele H, Neumann-Schriedewind P, Jacobs S, et al. Randomized comparison of minimally invasive direct coronary artery bypass surgery versus sirolimus-eluting stenting in isolated proximal left anterior descending coronary artery stenosis. *Journal of the American College of Cardiology* 2009;53(25):2324-31. doi: 10.1016/j.jacc.2009.03.032 [published Online First: 2009/06/23]
13. Borkon AM, Muehlebach GF, House J, et al. A comparison of the recovery of health status after percutaneous coronary intervention and coronary artery bypass. *The Annals of thoracic surgery* 2002;74(5):1526-30; discussion 30. [published Online First: 2002/11/21]
14. Zhang Z, Mahoney EM, Stables RH, et al. Disease-specific health status after stent-assisted percutaneous coronary intervention and coronary artery bypass surgery: one-year results from the Stent or Surgery trial. *Circulation* 2003;108(14):1694-700. doi: 10.1161/01.cir.0000087600.83707.fd [published Online First: 2003/09/17]
15. Hlatky MA, Boothroyd DB, Melsop KA, et al. Medical costs and quality of life 10 to 12 years after randomization to angioplasty or bypass surgery for multivessel coronary artery disease. *Circulation* 2004;110(14):1960-6. doi: 10.1161/01.cir.0000143379.26342.5c [published Online First: 2004/09/29]
16. Pocock SJ, Henderson RA, Seed P, et al. Quality of life, employment status, and anginal symptoms after coronary angioplasty or bypass surgery. 3-year follow-up in the Randomized Intervention Treatment of Angina (RITA) Trial. *Circulation* 1996;94(2):135-42. [published Online First: 1996/07/15]
17. Wahrborg P. Quality of life after coronary angioplasty or bypass surgery. 1-year follow-up in the Coronary Angioplasty versus Bypass Revascularization investigation (CABRI) trial. *European heart journal* 1999;20(9):653-8. [published Online First: 1999/04/20]

18. Hung J, Brieger DB, Amerena JV, et al. Treatment disparities and effect on late mortality in patients with diabetes presenting with acute myocardial infarction: observations from the ACACIA registry. *The Medical journal of Australia* 2009;191(10):539-43. [published Online First: 2009/11/17]
19. Jneid H, Fonarow GC, Cannon CP, et al. Sex differences in medical care and early death after acute myocardial infarction. *Circulation* 2008;118(25):2803-10. doi: 10.1161/circulationaha.108.789800 [published Online First: 2008/12/10]
20. Dai X, Busby-Whitehead J, Alexander KP. Acute coronary syndrome in the older adults. *Journal of Geriatric Cardiology : JGC* 2016;13(2):101-08. doi: 10.11909/j.issn.1671-5411.2016.02.012
21. Blankenship JC, Marshall JJ, Pinto DS, et al. Effect of percutaneous coronary intervention on quality of life: a consensus statement from the Society for Cardiovascular Angiography and Interventions. *Catheterization and cardiovascular interventions : official journal of the Society for Cardiac Angiography & Interventions* 2013;81(2):243-59. doi: 10.1002/ccd.24376 [published Online First: 2012/03/21]
22. Amin AP, Wang TY, McCoy L, et al. Impact of Bleeding on Quality of Life in Patients on DAPT Insights From TRANSLATE-ACS. *Journal of the American College of Cardiology* 2016;67(1):59-65. doi: 10.1016/j.jacc.2015.10.034
23. Doble B, Pufulete M, Harris JM, et al. Health-related quality of life impact of minor and major bleeding events during dual antiplatelet therapy: a systematic literature review and patient preference elicitation study. *Health and quality of life outcomes* 2018;16(1):191-91. doi: 10.1186/s12955-018-1019-3
24. Perl J, Karaboyas A, Morgenstern H, et al. Association between changes in quality of life and mortality in hemodialysis patients: results from the DOPPS. *Nephrology, dialysis, transplantation : official publication of the European Dialysis and Transplant Association - European Renal Association* 2017;32(3):521-27. doi: 10.1093/ndt/gfw233 [published Online First: 2016/06/09]

25. Liebman S, Li NC, Lacson E. Change in quality of life and one-year mortality risk in maintenance dialysis patients. *Quality of life research : an international journal of quality of life aspects of treatment, care and rehabilitation* 2016;25(9):2295-306. doi: 10.1007/s11136-016-1257-y [published Online First: 2016/03/05]
26. Fox KAA, Anderson FA, Dabbous OH, et al. Intervention in acute coronary syndromes: do patients undergo intervention on the basis of their risk characteristics? The Global Registry of Acute Coronary Events (GRACE). *Heart* 2007;93(2):177-82. doi: 10.1136/hrt.2005.084830
27. Scott IA, Derhy PH, O'Kane D, et al. Discordance between level of risk and intensity of evidence-based treatment in patients with acute coronary syndromes. *The Medical journal of Australia* 2007;187(3):153-9. [published Online First: 2007/08/08]
28. JBI. Joanna Briggs Institute. Joanna Briggs Institute reviewers' manual. Adelaide, SA, 2014.
29. Viswanathan M, Ansari MT, Berkman ND, et al. AHRQ Methods for Effective Health Care: Assessing the Risk of Bias of Individual Studies in Systematic Reviews of Health Care Interventions. Methods Guide for Effectiveness and Comparative Effectiveness Reviews. Rockville (MD): Agency for Healthcare Research and Quality (US) 2008:14.
30. Review Manager (RevMan) [Computer program] [program]. 5.3 version. Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2014.
31. Jo L-B, Viv R. Presenting and interpreting meta-analyses: Heterogeneity School of Nursing and Academic Division of Midwifery, University of Nottingham; 2007 [cited 2016 May 02]. Available from: <http://www.nottingham.ac.uk/nmp/sonet/rlos/ebp/meta-analysis2/4.html> accessed May 02 2016.
32. Sen S. Odds ratios revisited. *Evidence-Based Med* 1998;3(71)
33. Borenstein M, Hedges L, Rothstein H. Meta-Analysis: Fixed effect vs. random effects 2007 [cited 2016 17 May]. Available from: <https://www.meta-analysis.com/downloads/Meta-analysis%20fixed%20effect%20vs%20random%20effects.pdf> accessed 17 May 2016.

1  
2  
3  
4  
5  
6  
7  
8  
9  
10  
11  
12  
13  
14  
15  
16  
17  
18  
19  
20  
21  
22  
23  
24  
25  
26  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

34. Tufanaru C, Munn Z, Stephenson M, et al. Fixed or random effects meta-analysis? Common methodological issues in systematic reviews of effectiveness. *International Journal of Evidence-Based Healthcare* 2015;13(3):196-207.

For peer review only

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies. Enseignement Supérieur (ABES).

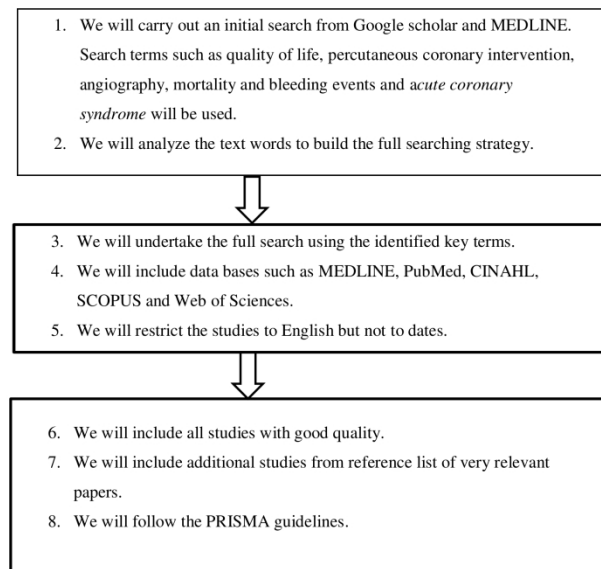


Figure 1 A schematic of the process of the systemic search and a use of Preferred Reporting Items for Systematic Reviews and Meta-Analyses for protocol (PRISMA-P) for reporting findings.

Figure 1 shows a schematic of the process of the systemic review using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses for protocol (PRISMA-P).

209x297mm (300 x 300 DPI)



1  
2  
3  
4  
5  
6  
7  
8  
9  
10  
11  
12  
13  
14  
15  
16  
17  
18  
19  
20  
21  
22  
23  
24  
25  
26  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

**Supplementary files**

**Annex 1: Full searching strategy by databases**

***Medline searching strategy\****

1	(predictors or factors or “quality of life” or “life quality”).tw.
2	(“physician therap*” or “percutaneous coronary intervention” or “PCI” or angiography or revascularization or “bleeding events” or mortality or death or “clinical intuition” or “perceived benefit” or “perceived risk” or “risk stratification” or “estimated benefit” or “estimated risk”).tw.
3	(“acute coronary syndrome” or “ACS” or “coronary heart disease” or “myocardial infarction” or “MI” or heart infarction).tw.
4	1 and 2 and 3

\*MeSH terms to be added during searching

***PubMed searching strategy\****

1	(predictors OR factors OR “quality of life” OR “life quality”)
2	(“physician therap*” OR “percutaneous coronary intervention” OR pci OR angiography OR revascularization OR “bleeding events” OR mortality OR death OR “clinical intuition” OR “perceived benefit” OR “perceived risk” OR “risk stratification” OR “estimated benefit” OR “estimated risk”)
3	(“acute coronary syndrome” OR acs OR “coronary heart disease” OR “myocardial infarction” OR mi OR heart infarction) NOT Medline[sb]) LIMITED to English
4	1 AND 2 AND 3

\* MeSH terms to be added during searching

***Web of Science searching strategy***

1	TS= (predictors or factors QOL or HRQOL or HRQL or “quality of life” or “life quality”)
2	TS= (“physician therap*” or “percutaneous coronary intervention” or “PCI” or angiography or revascularization or “bleeding events” or mortality or death or “clinical intuition” or “perceived benefit” or “perceived risk” or “risk stratification” or “estimated benefit” or “estimated risk”)
3	TS= (“acute coronary syndrome” or “ACS” or “coronary heart disease” or “myocardial infarction” or “MI” or heart infarction)
4	1 AND 2 AND 3; Limited by language (English)

***Scopus searching strategy***



1	ALL (predictors OR factors OR “quality of life” OR “life quality”)
2	ALL (“physician therap*” OR “percutaneous coronary intervention” OR “PCI” OR
3	angiography OR revascularization OR “bleeding events” OR mortality OR death OR “clinical
4	intuition” OR “perceived benefit” OR “perceived risk” OR “risk stratification” OR “estimated
5	benefit” OR “estimated risk”)
6	
7	ALL (“acute coronary syndrome” OR “ACS” OR “coronary heart disease” OR “myocardial
8	infarction” OR “MI” OR heart infarction) ” LIMITED to English
9	
10	1 AND 2 AND 3; Limited Subject area medicine/sociology/psychology AND English
11	
12	
13	
14	
15	
16	
17	
18	
19	
20	
21	
22	
23	
24	
25	
26	
27	
28	
29	
30	
31	
32	
33	
34	
35	
36	
37	
38	
39	
40	
41	
42	
43	
44	
45	
46	
47	
48	
49	
50	
51	
52	
53	
54	
55	
56	
57	
58	
59	
60	

### ***CINAHL Searching strategy\* [24.06.2018, 8:07am]***

S1	Tx predictors or factors or “quality of life” or “life quality”
S2	Tx “physician therap*” or “percutaneous coronary intervention” or “PCI” or angiography or revascularization or “bleeding events” or mortality or death or “clinical intuition” or “perceived benefit” or “perceived risk” or “risk stratification” or “estimated benefit” or “estimated risk”
S3	Tx “acute coronary syndrome” or “ACS” or “coronary heart disease” or “myocardial infarction” or “MI” or heart infarction
S4	S1 AND S2 AND S3 AND; Limited to English

\*MH words to be added during searching

### **Annex 2: JBI quality appraisal and selection tool**

**JBI Critical Appraisal Checklist for Descriptive / Case Series**

Reviewer \_\_\_\_\_ Date \_\_\_\_\_

Author \_\_\_\_\_ Year \_\_\_\_\_ Record Number \_\_\_\_\_

	Yes	No	Unclear	Not Applicable
1. Was study based on a random or pseudo-random sample?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
2. Were the criteria for inclusion in the sample clearly defined?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
3. Were confounding factors identified and strategies to deal with them stated?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
4. Were outcomes assessed using objective criteria?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
5. If comparisons are being made, was there sufficient descriptions of the groups?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
6. Was follow up carried out over a sufficient time period?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
7. Were the outcomes of people who withdrew described and included in the analysis?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
8. Were outcomes measured in a reliable way?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
9. Was appropriate statistical analysis used?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

Overall appraisal:      Include ☐                      Exclude ☐                      Seek further info ☐

Comments (Including reason for exclusion)

\_\_\_\_\_

\_\_\_\_\_

\_\_\_\_\_

## JBI Critical Appraisal Checklist for Comparable Cohort/ Case Control

Reviewer ..... Date .....

Author ..... Year ..... Record Number .....

	Yes	No	Unclear	Not Applicable
1. Is sample representative of patients in the population as a whole?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
2. Are the patients at a similar point in the course of their condition/illness?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
3. Has bias been minimised in relation to selection of cases and of controls?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
4. Are confounding factors identified and strategies to deal with them stated?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
5. Are outcomes assessed using objective criteria?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
6. Was follow up carried out over a sufficient time period?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
7. Were the outcomes of people who withdrew described and included in the analysis?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
8. Were outcomes measured in a reliable way?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
9. Was appropriate statistical analysis used?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

Overall appraisal: Include ☐ Exclude ☐ Seek further info. ☐

Comments (Including reason for exclusion)

---



---



---

**JBI Critical Appraisal Checklist for Randomised Control / Pseudo-randomised Trial**

Reviewer \_\_\_\_\_ Date \_\_\_\_\_

Author \_\_\_\_\_ Year \_\_\_\_\_ Record Number \_\_\_\_\_

	Yes	No	Unclear	Not Applicable
1. Was the assignment to treatment groups truly random?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
2. Were participants blinded to treatment allocation?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
3. Was allocation to treatment groups concealed from the allocator?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
4. Were the outcomes of people who withdrew described and included in the analysis?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
5. Were those assessing outcomes blind to the treatment allocation?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
6. Were the control and treatment groups comparable at entry?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
7. Were groups treated identically other than for the named interventions	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
8. Were outcomes measured in the same way for all groups?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
9. Were outcomes measured in a reliable way?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
10. Was appropriate statistical analysis used?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

Overall appraisal:      Include ☐                      Exclude ☐                      Seek further info. ☐

Comments (Including reason for exclusion)

\_\_\_\_\_

\_\_\_\_\_

\_\_\_\_\_

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies. Enseignement Supérieur (ABES).

## JBI Critical Appraisal Checklist for Systematic Reviews and Research Syntheses

Reviewer \_\_\_\_\_ Date \_\_\_\_\_

Author \_\_\_\_\_ Year \_\_\_\_\_ Record Number \_\_\_\_\_

	Yes	No	Unclear	Not applicable
1. Is the review question clearly and explicitly stated?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
2. Were the inclusion criteria appropriate for the review question?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
3. Was the search strategy appropriate?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
4. Were the sources and resources used to search for studies adequate?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
5. Were the criteria for appraising studies appropriate?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
6. Was critical appraisal conducted by two or more reviewers independently?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
7. Were there methods to minimize errors in data extraction?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
8. Were the methods used to combine studies appropriate?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
9. Was the likelihood of publication bias assessed?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
10. Were recommendations for policy and/or practice supported by the reported data?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
11. Were the specific directives for new research appropriate?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

Overall appraisal:      Include ☐      Exclude ☐      Seek further info ☐

\_\_\_\_\_

\_\_\_\_\_

Copyright © The Joanna Briggs Institute 2014

1  
2  
3  
4  
5  
6  
7  
8  
9  
10  
11  
12  
13  
14  
15  
16  
17  
18  
19  
20  
21  
22  
23  
24  
25  
26  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

Annex 3: JBI-data extraction instruments

**JBI Data Extraction Form for  
Experimental / Observational Studies**

Reviewer ..... Date .....

Author ..... Year .....

Journal ..... Record Number .....

**Study Method**

RCT	<input type="checkbox"/>	Quasi-RCT	<input type="checkbox"/>	Longitudinal	<input type="checkbox"/>
Retrospective	<input type="checkbox"/>	Observational	<input type="checkbox"/>	Other	<input type="checkbox"/>

**Participants**

Setting .....

Population .....

**Sample size**

Group A ..... Group B .....

**Interventions**

Intervention A .....

Intervention B .....

Authors Conclusions: .....

Reviewers Conclusions: .....

# BMJ Open

## The impact of patient's health related quality of life on physicians' therapy and perceived benefit in acute coronary syndromes: protocol for a systemic review of quantitative and qualitative studies

Journal:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2018-026595.R2
Article Type:	Protocol
Date Submitted by the Author:	19-Dec-2018
Complete List of Authors:	Kaambwa, Billingsley; Flinders University Faculty of Medicine Nursing and Health Sciences, Health Economics Gesese, Hailay; Jimma University, Epidemiology Horsfall, Matthew; South Australian Health & Medical Research Institute, SAHMRI, Adelaide, Australia Chew, Derek; Flinders Medical Centre, Department of Cardiovascular Medicine
<b>Primary Subject Heading</b>:	Cardiovascular medicine
Secondary Subject Heading:	Cardiovascular medicine, Evidence based practice, Patient-centred medicine
Keywords:	Quality of life, percutaneous coronary intervention, angiography, physician therapy, mortality, bleeding events

SCHOLARONE™  
Manuscripts

1  
2  
3  
4  
5  
6  
7  
8  
9  
10  
11  
12  
13  
14  
15  
16  
17  
18  
19  
20  
21  
22  
23  
24  
25  
26  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

**The impact of patient’s health related quality of life on physicians’ therapy and perceived benefit in acute coronary syndromes: protocol for a systemic review of quantitative and qualitative studies**

**Running Title: Impact of patients’ quality of life on physicians’ treatment decisions.**

**Authors:** B Kaambwa<sup>1#</sup>, HA Gesesew<sup>2#</sup>, M Horsfall<sup>3</sup>, D Chew<sup>3</sup>

<sup>1</sup>Health Economics Unit, College of Medicine and Public Health, Flinders University, Health Sciences Building, Bedford Park Campus, Sturt Road, Bedford Park, SA 5042, Australia

<sup>1</sup>Public Health Department, College of Medicine and Public Health, Flinders University, Health Sciences Building, Bedford Park Campus, Sturt Road, Bedford Park, SA 5042, Australia

<sup>3</sup> Cardiology Department, Flinders Medical Centre, Southern Adelaide Local Health Network, Sturt Road, Bedford Park, SA 5042, Australia

# BK and HAG contributed equally

**Corresponding Author\***

Billingsley Kaambwa, Health Economics Unit, College of Medicine & Public Health, Flinders University, Health Sciences Building, Bedford Park Campus, Sturt Road, Bedford Park, SA 5042, Australia

P: +61 8 8201 5377                      F: +61 8 8201 5378

Email: [billingsley.kaambwa@flinders.edu.au](mailto:billingsley.kaambwa@flinders.edu.au)



## ABSTRACT

**Introduction:** Percutaneous coronary interventions (PCIs) and coronary angiography are two of the treatments administered to acute coronary syndrome (ACS) patients. However, whether and how patients' health-related quality of life (HRQoL) influences treatment decisions and subsequent risk benefit analyses is unclear. In this study, we will review the available evidence on the impact of patients' HRQoL on physicians' prescribing or treatment decisions and on the estimation of mortality and bleeding risk in ACS patients.

**Methods and analysis:** We will undertake a systematic review of all quantitative and qualitative studies. The search will include studies that describe the impact of HRQoL on prescribing PCIs or angiography, and impact of HRQoL on perceived risks in terms of mortality and bleeding events. We will conduct an initial search on Google scholar and MEDLINE to build the searching terms followed by a full search strategy using all identified keywords and index terms across the five databases namely MEDLINE, PubMed, CINAHL, SCOPUS and Web of Sciences. We will use the Preferred Reporting Items for Systematic Reviews and Meta-Analyses for protocol (PRISMA-P) guidelines to present the protocol. Only English language articles will be included for the review. We will use a standardized Joanna Briggs Institute (JBI) data extraction tool to synthesize the information extracted from the selected studies into themes with summary findings presented in a table.

**Ethics and dissemination:** We will not require a formal ethical approval as we will not be collecting primary data. Review findings will be disseminated through a peer-reviewed publication, workshops, conference presentations and a media release.

**Trial registration number:** International Prospective Register for Systematic Reviews (PROSPERO) number is CRD42018108438.

1  
2  
3  
4  
5  
6  
7  
8  
9  
10  
11  
12  
13  
14  
15  
16  
17  
18  
19  
20  
21  
22  
23  
24  
25  
26  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

**Article summary**

***Strengths and limitations of this study***

- This is a systematic review of all quantitative and qualitative studies on physicians’ treatment decisions and estimation of risk in acute coronary syndrome patients.
- This will offer comprehensive and high level of evidence of the impact of patients’ health-related quality of life on treatment decisions.
- The measurement of quality of life may be based on dissimilar tools and may have its own limitations on estimating outcomes.
- Studies that will be included in the review will only be limited to English, and this could lead to information bias.

## INTRODUCTION

Acute coronary syndrome (ACS) is one of the most common set of conditions that patients in emergency departments present with and which often leads to hospitalization<sup>1</sup>. It is characterised by a number of clinical symptoms including unstable angina, non-ST-segment elevation myocardial infarction, and ST-segment elevation myocardial infarction<sup>1</sup>. The definitions of ACS depend on multiple range of activities including history taking, physical examination and reviews of electrocardiography, chest radiograph and cardiac biomarker test results<sup>1</sup>. Evidence from the literature shows that risk stratification is an essential prerequisite to decision-making, particularly when determining whether (i) patients will be treated in a coronary care unit or monitored step-down unit (ii) treatment will be invasive or non-invasive or (iii) prognosis will be good or bad<sup>2-4</sup>. For the interest of this review, we will use either of the ACS diagnosis described by the authors in the primary study in order to include as many studies as possible.

Physicians have developed a number of multivariable risk assessment methods to help them provide a comprehensive assessment of risk and an accurate method of prognosis for patients with ACS<sup>5</sup>. These methods thereafter inform the treatment choice based on strategies that include percutaneous coronary intervention (PCI) and coronary angiography<sup>6,7</sup>. Despite the existence of these risk assessment techniques, however, physicians still use their clinical intuition to prescribe therapies and estimate potential benefit and harm<sup>8,9</sup>. Whether, and the extent to which, patients' health-related quality of life (HRQoL) influences this treatment choice is unclear in the literature. To date, HRQoL has several measurements with different scales, number of items, scoring calculation and interpretation. For example, Short Form 6, 12 and 36 dimension (SF-6D, SF-12 and SF-36)<sup>10-12</sup>, Seattle Angina Questionnaire (SAQ)<sup>13,14</sup>, Duke Activity Status Index (DASI)<sup>15</sup>, Nottingham Health Profile (NHP)<sup>16,17</sup> and the Euro-Qol 5 dimensions 3 or 5 level measure were some of the validated tools used to measure HRQoL. In this review, no *a priori* definition is specified in order to be more inclusive of a broad range of literature.

Few studies report on what factors influence physicians' decision-making in terms of treatment and risk assessment for ACS patients. For example, some studies report that being in high-

1 risk clinical subgroups such as old age, male gender as well as having diabetes, renal failure, other  
2 cardiac comorbidities or a previous history of ACS are significant factors that influence this decision-  
3 making <sup>8 18 19</sup>. Unfortunately, these group of patients are also at high risk of increased adverse  
4 outcomes of ACS management <sup>20</sup>. However, evidence of the impact of HRQoL on decision-making  
5 and risk assessment is lacking. 'Impact' in this review is referred to a situation where treatment risk  
6 estimation was modified or altered as a result of HRQoL.  
7  
8  
9  
10  
11  
12  
13  
14

15 A review in United States America<sup>21</sup> found that that several patients with ACS consider  
16 HRQoL while deciding to choose a treatment strategy although the survival benefit is similar among  
17 the available therapies. In particular, the review noticed that there were variations in preferences over  
18 the duration of HRQoL. Some patients chose easy treatment strategy that brings favourable HRQoL  
19 for short duration—for instance, patients chose PCI instead of CABG. To the contrary, other patients  
20 chose a complex treatment strategy to have a favourable QoL for longer period of time—for instance,  
21 patients chose CABG instead of PCI. Most patients understood less these existing trade-offs. It is  
22 against this impact that the review recommended that physicians should have to consider advising  
23 their patients about the HRQoL benefit before deciding to choose a treatment strategy. Thus, there  
24 will be a need to consider provide objective information on HRQoL by physicians. Furthermore, the  
25 literature review revealed that clinical trials, treatment guidelines and polices should have to consider  
26 HRQoL while deciding to prescribe among treatment strategies.  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42

43 Several definitions have been used to measure bleeding in hospital and post-discharge periods,  
44 including Bleeding Academic Research Consortium (BARC). Although evidence on the relationship  
45 between bleeding event and QoL is scarce, the existing evidence demonstrated worse QoL following  
46 a bleeding event<sup>22 23</sup>. For example, Amin et al found a 24% prevalence of bleeding among patients  
47 with ACS undergoing PCI, and the six-month QoL was worse<sup>22</sup>. Furthermore, evidence show the  
48 association between change in QoL and mortality<sup>24 25</sup>. Nevertheless, the degree to which this HRQoL  
49 affects the estimation of the risk of mortality or bleeding events in patients with ACS is uncertain <sup>8 26</sup>  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

27.

Therefore, this study will review the available evidence on HRQoL and other factors affecting physicians' therapy decisions and their assessment of risk for ACS patients. In particular we will review, i) the status of HRQoL in patients with ACS before and after treatment, ii) the impact of HRQoL on physician's treatment decision in ACS patients, and iii) the impact of patient's HRQoL on physician's estimation of the potential outcomes such as mortality and bleeding risk.

## METHODS AND DESIGN

### Population

The systematic review will include studies on physicians who screen and diagnose patients with ACS and prescribe PCI or angiography therapy.

### Study design

The systematic review will consider quantitative and qualitative studies of good quality published before June 2018.

### Search strategy

We will perform the following steps to undertake the searching strategy. First, we will carry out a limited search through Google scholar and MEDLINE in order to develop key terms for the three pre-defined concepts relating to the research question. : concept 1 (predictors, factors, quality of life, or life quality), concept 2 (physician therap\*, percutaneous coronary intervention, percutaneous transluminal angioplasty, PTA, PTCA, PCI, angiography, revascularization, bleeding events, mortality, death, clinical intuition, perceived benefit, perceived risk, risk stratification, estimated benefit, or estimated risk) and concept 3 (acute coronary syndrome, ACS, coronary heart disease, myocardial infarction (MI) or heart infarction). Second, we will carry out a full search (Annex 1) using all identified keywords and index terms across the following databases: MEDLINE, PubMed, CINAHL, SCOPUS and Web of Sciences. Concepts 1, 2 and 3 will be connected by 'AND' to run the full searching strategy in the aforementioned databases. Next, titles and abstracts from each database will be screened and relevant titles/abstracts selected for a full text appraisal. Finally, we will undertake backward and forward citation chaining of relevant documents. The search will also

1  
2 include unpublished studies or grey literature from ProQuest Dissertations and Theses (PQDT),  
3  
4 WHO, Health department Data and other health data repositories.

5  
6 Figure 1 describes the schematic presentation of the search strategy using the Preferred Reporting  
7  
8 Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.

9  
10  
11 **Study selection**

12  
13 Prior to inclusion in the review, two primary but independent reviewers, HAG and BK, will assess  
14  
15 the selected papers for methodological validity using a standardized Joanna Briggs Institute (JBI)  
16  
17 appraisal instruments<sup>28</sup> (Annex 2). Any disagreement will be resolved by consensus among the  
18  
19 research team.

20  
21  
22 **Quality assessment**

23  
24 The two primary reviewers will independently assess the methodological quality of the included  
25  
26 studies using an appraisal form developed by the JBI (Annex 2). In addition, we will assess the risk  
27  
28 of bias via the Agency for Healthcare Research and Quality (AHRQ) criteria<sup>29</sup>.

29  
30  
31 **Data extraction**

32  
33 Quantitative and qualitative data will be extracted from papers based on the JBI data extraction tool  
34  
35 (Annex 3). We will extract relevant information from all articles included in the review into a  
36  
37 spreadsheet. Whenever, there is missing or unclear data, we will contact authors of primary studies.  
38  
39 Both primary reviewers will independently check the data extraction.

40  
41  
42 **Outcomes**

43  
44 The review will consider the following physician outcomes:

- 45  
46  
47  
48
  - Prescription of PCI for Patients with ACS
  - Prescription of angiography for ACS patients
  - Estimation of mortality risk to ACS patients
  - Estimation of bleeding events for ACS patients.

49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60  
Definitions and measurements of estimated (perceived) mortality and bleeding events benefit are described elsewhere <sup>8</sup>. Briefly, bleeding events were measured using Thrombolysis in Myocardial

Infarction (TIMI), Global Use of Strategies to Open Occluded Coronary Arteries (GUSTO) and the ACUITY bleeding criteria

## Exposures

The primary exposure in this review will be HRQoL as defined by a number of HRQoL instruments. These will include the Short Form 6, 12 and 36 dimension (SF-6D, SF-12 and SF-36, respectively)<sup>10-12</sup>, Seattle angina questionnaire (SAQ)<sup>13 14</sup>, duke activity status index (DASI)<sup>15</sup>, Nottingham health profile (NHP)<sup>16 17</sup> and the Euro-Qol 5 dimensions 3 or 5 level measure (EQ-5D-3L or EQ-5D-5L). The secondary exposures or confounders will include age, sex, diabetes mellitus, renal failure, smoking, family history of cardiac illnesses, presenting with cardiac shock or cardiac arrest, other cardiac comorbidities and previous history of ACS.

## ANALYSIS

A narrative synthesis of outcomes along with the exposure variable of selected studies will be demonstrated in the final review. We will include the following information to summarize the main data from the included studies: author (year), setting, study design, population, sample size, outcome, and main findings. The factors for both outcomes, physicians' treatment decision and assessment of perceived risk, will be summarized into themes, and summary findings of each study included in the review will be presented in tables.

If data will be available, meta-regression and meta-analyses will be conducted to see the association of the factors with the aforementioned outcomes. We will assess the clinical and statistical heterogeneity before conducting the meta-analyses. The research team will check the clinical heterogeneity to decide which variable and outcome will be added in the meta-analysis. We will use standard Chi-square and  $I^2$  tests to diagnose the statistical heterogeneity, with significant heterogeneity detected at the P value < 0.05. In addition, meta-analyses will be carried out separately for each outcome and each exposure of interest using RevMan-5 Software<sup>30</sup>. We will consider meta-analysis if  $I^2$  will be below 85%<sup>31</sup>. In order to calculate effect sizes, we will use a Mantel Haenszel statistical method with forest plots used to graphically depict the relationship between exposures of interest and outcomes or events.



1  
2  
3  
4  
5  
6  
7  
8  
9  
10  
11  
12  
13  
14  
15  
16  
17  
18  
19  
20  
21  
22  
23  
24  
25  
26  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

Based on the degree of statistical heterogeneity, we will calculate a pooled unadjusted odds ratio (OR)<sup>32</sup> estimates and their 95% confidence intervals (CI) using random or fixed effect meta-analysis<sup>31</sup>. If the outcome is reported using continuous data, we will use a mean difference (MD) or standardized mean difference (SMD). MD will be used if all included studies use the same scale whereas SMD will be used if the included studies applied variety scales. If the number of studies that reported the exposure and outcome of interest will be small (n<5), we will only consider fixed effect model irrespective of the level of heterogeneity<sup>33 34</sup>. We will consider pooling if at least two studies assess the outcomes and the exposures of interest. To assess the publication bias, we will use a funnel plot. We will also consider a sensitivity test via omitting and entering small studies and deviant results from the rest of the studies (outliers). The strength of the body of evidence will be assessed using GRADE.

**Ethics and dissemination:** This stud will not require a formal ethical approval because it will not involve collection of primary data. To disseminate findings of the Review, we will use the following medias: publishing in peer-reviewed journals, presenting on workshops, conference, and sharing through a media release.

**Patient and Public Involvement** No patient or public is involved as this is a review of studies.

**CONCLUSION**

This systematic review will provide evidence in support of, or against, the hypothesis that patients' HRQoL has a role in physicians' treatment decisions and in estimating the mortality and bleeding event risk for ACS patients. Particularly, this review will assess the impact that HRQoL, measured using validated instruments, has on prescribing PCI and angiography. Furthermore, the role of HRQoL on estimating mortality and bleeding events benefit will also enumerated. We will apply descriptive and inferential statistical analysis to summarise the quantitative data from the review and synthesise the qualitative component of the findings into themes. In general, the review will contribute to the clinical evidence base on what drives clinical intuition during the treatment decision-making for ACS patients.

**Acknowledgements:** We thank Flinders University for enabling us to access not freely available articles. We also acknowledge authors of primary studies.

**Contributors:** BK & HAG contributed equally to this paper. DC, BK & HAG conceived the idea. BK & HAG drafted the protocol. All authors contributed to the development of the selection criteria, the risk of bias assessment strategy and data extraction criteria. BK & HAG developed the search strategy. DC & MH provided expertise on acute coronary syndrome. All authors read, provided feedback and approved the final manuscript

**Funding** None

**Competing interests** None declared

**Provenance and peer review** Not commissioned; externally peer reviewed

**Figure legend:** Figure 1 showed a schematic presentation of the systemic search and use of Preferred Reporting Items for Systematic Reviews and Meta-Analyses for protocol (PRISMA-P) for reporting the findings.

## REFERENCES

1. Kumar A, Cannon CP. Acute Coronary Syndromes: Diagnosis and Management, Part I. *Mayo Clinic Proceedings* 2009;84(10):917-38.
2. Anderson JL, Adams CD, Antman EM, et al. ACC/AHA 2007 guidelines for the management of patients with unstable angina/non ST-elevation myocardial infarction: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to Revise the 2002 Guidelines for the Management of Patients With Unstable Angina/Non ST-Elevation Myocardial Infarction): developed in collaboration with the American College of Emergency Physicians, the Society for Cardiovascular Angiography and Interventions, and the Society of Thoracic Surgeons: endorsed by the American Association of Cardiovascular and Pulmonary Rehabilitation and the Society for

- Academic Emergency Medicine. *Circulation* 2007;116(7):e148-304. doi: 10.1161/circulationaha.107.181940 [published Online First: 2007/08/08]
3. Falk V, Baumgartner H, Bax JJ, et al. 2017 ESC/EACTS Guidelines for the management of valvular heart disease. *European Journal of Cardio-Thoracic Surgery* 2017;52(4):616-64. doi: 10.1093/ejcts/ezx324
4. Marechaux S, Hachicha Z, Bellouin A, et al. Usefulness of exercise-stress echocardiography for risk stratification of true asymptomatic patients with aortic valve stenosis. *European heart journal* 2010;31(11):1390-7. doi: 10.1093/eurheartj/ehq076 [published Online First: 2010/03/24]
5. Eagle KA, Lim MJ, Dabbous OH, et al. A validated prediction model for all forms of acute coronary syndrome: estimating the risk of 6-month postdischarge death in an international registry. *Jama* 2004;291(22):2727-33. doi: 10.1001/jama.291.22.2727 [published Online First: 2004/06/10]
6. Henriques JP, Claessen BE, Dangas GD, et al. Performance of currently available risk models in a cohort of mechanically supported high-risk percutaneous coronary intervention--From the PROTECT II randomized trial. *International journal of cardiology* 2015;189:272-8. doi: 10.1016/j.ijcard.2015.04.084 [published Online First: 2015/04/25]
7. Kirtane AJ, Doshi D, Leon MB, et al. Treatment of Higher-Risk Patients With an Indication for Revascularization: Evolution Within the Field of Contemporary Percutaneous Coronary Intervention. *Circulation* 2016;134(5):422-31. doi: 10.1161/circulationaha.116.022061 [published Online First: 2016/08/03]
8. Chew DP, Juergens C, French J, et al. An examination of clinical intuition in risk assessment among acute coronary syndromes patients: observations from a prospective multi-center international observational registry. *International journal of cardiology* 2014;171(2):209-16. doi: 10.1016/j.ijcard.2013.12.010 [published Online First: 2014/01/02]
9. Yan AT, Yan RT, Huynh T, et al. Understanding physicians' risk stratification of acute coronary syndromes: insights from the Canadian ACS 2 Registry. *Archives of internal medicine*

- 2009;169(4):372-8. doi: 10.1001/archinternmed.2008.563 [published Online First: 2009/02/25]
10. van Domburg RT, Daemen J, Morice MC, et al. Short- and long-term health related quality-of-life and anginal status of the Arterial Revascularisation Therapies Study part II, ARTS-II; sirolimus-eluting stents for the treatment of patients with multivessel coronary artery disease. *EuroIntervention : journal of EuroPCR in collaboration with the Working Group on Interventional Cardiology of the European Society of Cardiology* 2010;5(8):962-7. doi: 10.4244/ [published Online First: 2010/06/15]
11. Favarato ME, Hueb W, Boden WE, et al. Quality of life in patients with symptomatic multivessel coronary artery disease: a comparative post hoc analyses of medical, angioplasty or surgical strategies-MASS II trial. *International journal of cardiology* 2007;116(3):364-70. doi: 10.1016/j.ijcard.2006.06.001 [published Online First: 2006/08/01]
12. Thiele H, Neumann-Schriedewind P, Jacobs S, et al. Randomized comparison of minimally invasive direct coronary artery bypass surgery versus sirolimus-eluting stenting in isolated proximal left anterior descending coronary artery stenosis. *Journal of the American College of Cardiology* 2009;53(25):2324-31. doi: 10.1016/j.jacc.2009.03.032 [published Online First: 2009/06/23]
13. Borkon AM, Muehlebach GF, House J, et al. A comparison of the recovery of health status after percutaneous coronary intervention and coronary artery bypass. *The Annals of thoracic surgery* 2002;74(5):1526-30; discussion 30. [published Online First: 2002/11/21]
14. Zhang Z, Mahoney EM, Stables RH, et al. Disease-specific health status after stent-assisted percutaneous coronary intervention and coronary artery bypass surgery: one-year results from the Stent or Surgery trial. *Circulation* 2003;108(14):1694-700. doi: 10.1161/01.cir.0000087600.83707.fd [published Online First: 2003/09/17]
15. Hlatky MA, Boothroyd DB, Melsop KA, et al. Medical costs and quality of life 10 to 12 years after randomization to angioplasty or bypass surgery for multivessel coronary artery disease.

- Circulation* 2004;110(14):1960-6. doi: 10.1161/01.cir.0000143379.26342.5c [published Online First: 2004/09/29]
16. Pocock SJ, Henderson RA, Seed P, et al. Quality of life, employment status, and anginal symptoms after coronary angioplasty or bypass surgery. 3-year follow-up in the Randomized Intervention Treatment of Angina (RITA) Trial. *Circulation* 1996;94(2):135-42. [published Online First: 1996/07/15]
17. Wahrborg P. Quality of life after coronary angioplasty or bypass surgery. 1-year follow-up in the Coronary Angioplasty versus Bypass Revascularization investigation (CABRI) trial. *European heart journal* 1999;20(9):653-8. [published Online First: 1999/04/20]
18. Hung J, Brieger DB, Amerena JV, et al. Treatment disparities and effect on late mortality in patients with diabetes presenting with acute myocardial infarction: observations from the ACACIA registry. *The Medical journal of Australia* 2009;191(10):539-43. [published Online First: 2009/11/17]
19. Jneid H, Fonarow GC, Cannon CP, et al. Sex differences in medical care and early death after acute myocardial infarction. *Circulation* 2008;118(25):2803-10. doi: 10.1161/circulationaha.108.789800 [published Online First: 2008/12/10]
20. Dai X, Busby-Whitehead J, Alexander KP. Acute coronary syndrome in the older adults. *Journal of Geriatric Cardiology : JGC* 2016;13(2):101-08. doi: 10.11909/j.issn.1671-5411.2016.02.012
21. Blankenship JC, Marshall JJ, Pinto DS, et al. Effect of percutaneous coronary intervention on quality of life: a consensus statement from the Society for Cardiovascular Angiography and Interventions. *Catheterization and cardiovascular interventions : official journal of the Society for Cardiac Angiography & Interventions* 2013;81(2):243-59. doi: 10.1002/ccd.24376 [published Online First: 2012/03/21]
22. Amin AP, Wang TY, McCoy L, et al. Impact of Bleeding on Quality of Life in Patients on DAPT Insights From TRANSLATE-ACS. *Journal of the American College of Cardiology* 2016;67(1):59-65. doi: 10.1016/j.jacc.2015.10.034

23. Doble B, Pufulete M, Harris JM, et al. Health-related quality of life impact of minor and major bleeding events during dual antiplatelet therapy: a systematic literature review and patient preference elicitation study. *Health and quality of life outcomes* 2018;16(1):191-91. doi: 10.1186/s12955-018-1019-3
24. Perl J, Karaboyas A, Morgenstern H, et al. Association between changes in quality of life and mortality in hemodialysis patients: results from the DOPPS. *Nephrology, dialysis, transplantation : official publication of the European Dialysis and Transplant Association - European Renal Association* 2017;32(3):521-27. doi: 10.1093/ndt/gfw233 [published Online First: 2016/06/09]
25. Liebman S, Li NC, Lacson E. Change in quality of life and one-year mortality risk in maintenance dialysis patients. *Quality of life research : an international journal of quality of life aspects of treatment, care and rehabilitation* 2016;25(9):2295-306. doi: 10.1007/s11136-016-1257-y [published Online First: 2016/03/05]
26. Fox KAA, Anderson FA, Dabbous OH, et al. Intervention in acute coronary syndromes: do patients undergo intervention on the basis of their risk characteristics? The Global Registry of Acute Coronary Events (GRACE). *Heart* 2007;93(2):177-82. doi: 10.1136/hrt.2005.084830
27. Scott IA, Derhy PH, O'Kane D, et al. Discordance between level of risk and intensity of evidence-based treatment in patients with acute coronary syndromes. *The Medical journal of Australia* 2007;187(3):153-9. [published Online First: 2007/08/08]
28. JBI. Joanna Briggs Institute. Joanna Briggs Institute reviewers' manual. Adelaide, SA, 2014.
29. Viswanathan M, Ansari MT, Berkman ND, et al. AHRQ Methods for Effective Health Care: Assessing the Risk of Bias of Individual Studies in Systematic Reviews of Health Care Interventions. *Methods Guide for Effectiveness and Comparative Effectiveness Reviews*. Rockville (MD): Agency for Healthcare Research and Quality (US) 2008:14.
30. Review Manager (RevMan) [Computer program] [program]. 5.3 version. Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2014.

1  
2  
3  
4  
5  
6  
7  
8  
9  
10  
11  
12  
13  
14  
15  
16  
17  
18  
19  
20  
21  
22  
23  
24  
25  
26  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

31. Jo L-B, Viv R. Presenting and interpreting meta-analyses: Heterogeneity School of Nursing and Academic Division of Midwifery, University of Nottingham; 2007 [cited 2016 May 02]. Available from: <http://www.nottingham.ac.uk/nmp/sonet/rlos/ebp/meta-analysis2/4.html> accessed May 02 2016.

32. Sen S. Odds ratios revisited. *Evidence-Based Med* 1998;3(71)

33. Borenstein M, Hedges L, Rothstein H. Meta-Analysis: Fixed effect vs. random effects 2007 [cited 2016 17 May]. Available from: <https://www.meta-analysis.com/downloads/Meta-analysis%20fixed%20effect%20vs%20random%20effects.pdf> accessed 17 May 2016.

34. Tufanaru C, Munn Z, Stephenson M, et al. Fixed or random effects meta-analysis? Common methodological issues in systematic reviews of effectiveness. *International Journal of Evidence-Based Healthcare* 2015;13(3):196-207.

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies. Enseignement Supérieur (ABES).



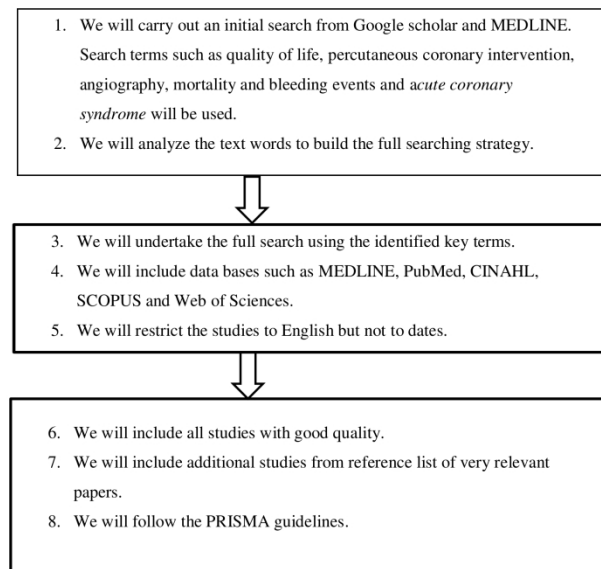


Figure 1 A schematic of the process of the systemic search and a use of Preferred Reporting Items for Systematic Reviews and Meta-Analyses for protocol (PRISMA-P) for reporting findings.

Figure 1 shows a schematic of the process of the systemic review using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses for protocol (PRISMA-P).

209x297mm (300 x 300 DPI)

1  
2  
3  
4  
5  
6  
7  
8  
9  
10  
11  
12  
13  
14  
15  
16  
17  
18  
19  
20  
21  
22  
23  
24  
25  
26  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

**Supplementary files**

**Annex 1: Full searching strategy by databases**

***Medline searching strategy\****

1	(predictors or factors or “quality of life” or “life quality”).tw.
2	(“physician therap*” or “percutaneous coronary intervention” or “PCI” or angiography or revascularization or “bleeding events” or mortality or death or “clinical intuition” or “perceived benefit” or “perceived risk” or “risk stratification” or “estimated benefit” or “estimated risk”).tw.
3	(“acute coronary syndrome” or “ACS” or “coronary heart disease” or “myocardial infarction” or “MI” or heart infarction).tw.
4	1 and 2 and 3

\*MeSH terms to be added during searching

***PubMed searching strategy\****

1	(predictors OR factors OR “quality of life” OR “life quality”)
2	(“physician therap*” OR “percutaneous coronary intervention” OR pci OR angiography OR revascularization OR “bleeding events” OR mortality OR death OR “clinical intuition” OR “perceived benefit” OR “perceived risk” OR “risk stratification” OR “estimated benefit” OR “estimated risk”)
3	(“acute coronary syndrome” OR acs OR “coronary heart disease” OR “myocardial infarction” OR mi OR heart infarction) NOT Medline[sb]) LIMITED to English
4	1 AND 2 AND 3

\* MeSH terms to be added during searching

***Web of Science searching strategy***

1	TS= (predictors or factors QOL or HRQOL or HRQL or “quality of life” or “life quality”)
2	TS= (“physician therap*” or “percutaneous coronary intervention” or “PCI” or angiography or revascularization or “bleeding events” or mortality or death or “clinical intuition” or “perceived benefit” or “perceived risk” or “risk stratification” or “estimated benefit” or “estimated risk”)
3	TS= (“acute coronary syndrome” or “ACS” or “coronary heart disease” or “myocardial infarction” or “MI” or heart infarction)
4	1 AND 2 AND 3; Limited by language (English)

***Scopus searching strategy***

1	ALL (predictors OR factors OR “quality of life” OR “life quality”)
2	ALL (“physician therap*” OR “percutaneous coronary intervention” OR “PCI” OR
3	angiography OR revascularization OR “bleeding events” OR mortality OR death OR “clinical
4	intuition” OR “perceived benefit” OR “perceived risk” OR “risk stratification” OR “estimated
5	benefit” OR “estimated risk”)
6	
7	ALL (“acute coronary syndrome” OR “ACS” OR “coronary heart disease” OR “myocardial
8	infarction” OR “MI” OR heart infarction) ” LIMITED to English
9	
10	1 AND 2 AND 3; Limited Subject area medicine/sociology/psychology AND English
11	
12	
13	
14	
15	
16	
17	
18	
19	
20	
21	
22	
23	
24	
25	
26	
27	
28	
29	
30	
31	
32	
33	
34	
35	
36	
37	
38	
39	
40	
41	
42	
43	
44	
45	
46	
47	
48	
49	
50	
51	
52	
53	
54	
55	
56	
57	
58	
59	
60	

### ***CINAHL Searching strategy\* [24.06.2018, 8:07am]***

S1	Tx predictors or factors or “quality of life” or “life quality”
S2	Tx “physician therap*” or “percutaneous coronary intervention” or “PCI” or angiography or revascularization or “bleeding events” or mortality or death or “clinical intuition” or “perceived benefit” or “perceived risk” or “risk stratification” or “estimated benefit” or “estimated risk”
S3	Tx “acute coronary syndrome” or “ACS” or “coronary heart disease” or “myocardial infarction” or “MI” or heart infarction
S4	S1 AND S2 AND S3 AND; Limited to English

\*MH words to be added during searching

### **Annex 2: JBI quality appraisal and selection tool**

**JBI Critical Appraisal Checklist for Descriptive / Case Series**

Reviewer \_\_\_\_\_ Date \_\_\_\_\_

Author \_\_\_\_\_ Year \_\_\_\_\_ Record Number \_\_\_\_\_

	Yes	No	Unclear	Not Applicable
1. Was study based on a random or pseudo-random sample?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
2. Were the criteria for inclusion in the sample clearly defined?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
3. Were confounding factors identified and strategies to deal with them stated?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
4. Were outcomes assessed using objective criteria?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
5. If comparisons are being made, was there sufficient descriptions of the groups?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
6. Was follow up carried out over a sufficient time period?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
7. Were the outcomes of people who withdrew described and included in the analysis?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
8. Were outcomes measured in a reliable way?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
9. Was appropriate statistical analysis used?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

Overall appraisal:      Include ☐                      Exclude ☐                      Seek further info ☐

Comments (Including reason for exclusion)

\_\_\_\_\_

\_\_\_\_\_

\_\_\_\_\_

## JBI Critical Appraisal Checklist for Comparable Cohort/ Case Control

Reviewer ..... Date .....

Author ..... Year ..... Record Number .....

	Yes	No	Unclear	Not Applicable
1. Is sample representative of patients in the population as a whole?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
2. Are the patients at a similar point in the course of their condition/illness?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
3. Has bias been minimised in relation to selection of cases and of controls?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
4. Are confounding factors identified and strategies to deal with them stated?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
5. Are outcomes assessed using objective criteria?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
6. Was follow up carried out over a sufficient time period?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
7. Were the outcomes of people who withdrew described and included in the analysis?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
8. Were outcomes measured in a reliable way?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
9. Was appropriate statistical analysis used?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

Overall appraisal: Include ☐ Exclude ☐ Seek further info. ☐

Comments (Including reason for exclusion)

---



---



---

**JBI Critical Appraisal Checklist for Randomised Control / Pseudo-randomised Trial**

Reviewer \_\_\_\_\_ Date \_\_\_\_\_

Author \_\_\_\_\_ Year \_\_\_\_\_ Record Number \_\_\_\_\_

	Yes	No	Unclear	Not Applicable
1. Was the assignment to treatment groups truly random?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
2. Were participants blinded to treatment allocation?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
3. Was allocation to treatment groups concealed from the allocator?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
4. Were the outcomes of people who withdrew described and included in the analysis?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
5. Were those assessing outcomes blind to the treatment allocation?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
6. Were the control and treatment groups comparable at entry?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
7. Were groups treated identically other than for the named interventions	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
8. Were outcomes measured in the same way for all groups?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
9. Were outcomes measured in a reliable way?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
10. Was appropriate statistical analysis used?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

Overall appraisal:      Include ☐                      Exclude ☐                      Seek further info. ☐

Comments (Including reason for exclusion)

\_\_\_\_\_

\_\_\_\_\_

\_\_\_\_\_

## JBI Critical Appraisal Checklist for Systematic Reviews and Research Syntheses

Reviewer \_\_\_\_\_ Date \_\_\_\_\_

Author \_\_\_\_\_ Year \_\_\_\_\_ Record Number \_\_\_\_\_

	Yes	No	Unclear	Not applicable
1. Is the review question clearly and explicitly stated?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
2. Were the inclusion criteria appropriate for the review question?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
3. Was the search strategy appropriate?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
4. Were the sources and resources used to search for studies adequate?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
5. Were the criteria for appraising studies appropriate?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
6. Was critical appraisal conducted by two or more reviewers independently?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
7. Were there methods to minimize errors in data extraction?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
8. Were the methods used to combine studies appropriate?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
9. Was the likelihood of publication bias assessed?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
10. Were recommendations for policy and/or practice supported by the reported data?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
11. Were the specific directives for new research appropriate?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

Overall appraisal:    Include ☐    Exclude ☐    Seek further info ☐

\_\_\_\_\_

\_\_\_\_\_

Copyright © The Joanna Briggs Institute 2014



1  
2  
3  
4  
5  
6  
7  
8  
9  
10  
11  
12  
13  
14  
15  
16  
17  
18  
19  
20  
21  
22  
23  
24  
25  
26  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

Annex 3: JBI-data extraction instruments

**JBI Data Extraction Form for  
Experimental / Observational Studies**

Reviewer ..... Date .....

Author ..... Year .....

Journal ..... Record Number .....

**Study Method**

RCT	<input type="checkbox"/>	Quasi-RCT	<input type="checkbox"/>	Longitudinal	<input type="checkbox"/>
Retrospective	<input type="checkbox"/>	Observational	<input type="checkbox"/>	Other	<input type="checkbox"/>

**Participants**

Setting .....

Population .....

**Sample size**

Group A ..... Group B .....

**Interventions**

Intervention A .....

Intervention B .....

Authors Conclusions: .....

Reviewers Conclusions: .....