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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

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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

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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 Cochranes 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 [1 2]. It is characterised by a number of clinical symptoms including unstable angina, non-ST-segment elevation myocardial infarction, and ST-segment elevation myocardial infarction[2]. 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 [2 3]. 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 [3-5].

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 [6-8]. These methods thereafter inform the treatment choice based on strategies that include percutaneous coronary intervention (PCI) and coronary angiography [9 10]. Despite the existence of these risk assessment techniques, however, physicians still use their clinical intuition to prescribe therapies and estimate potential benefit and harm [11 12]. 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 [11 13 14].

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-

making [11 15 16]. Unfortunately, these group of patients are also at high risk of increased adverse outcomes of ACS management [17 18]. However, evidence of the impact of HRQoL on decision-making and risk assessment is lacking. 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, ii) the impact of HRQoL on physician's therapy in ACS patients, and iii) the impact of patient's HRQoL on mortality and bleeding risk estimation by physicians.

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 conducted in developed and developing countries.

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, 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 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[19]. 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[19]. In addition, we will assess the risk of bias via the Agency for Healthcare Research and Quality (AHRQ) criteria[20].

Data extraction

Quantitative and qualitative data will be extracted from papers based on the Cochrane's extracting tool and scoring criteria[19]. 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 [11]. 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)[21-23], Seattle angina questionnaire (SAQ) [24 25], duke activity status index (DASI) [26], Nottingham health profile (NHP)[27 28] 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[29]. We will consider meta-analysis if I^2 will be below 85%[30]. 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)[31] estimates and their 95% confidence intervals (CI) using random or fixed effect meta-analysis[30]. 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[32 33]. 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 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.

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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

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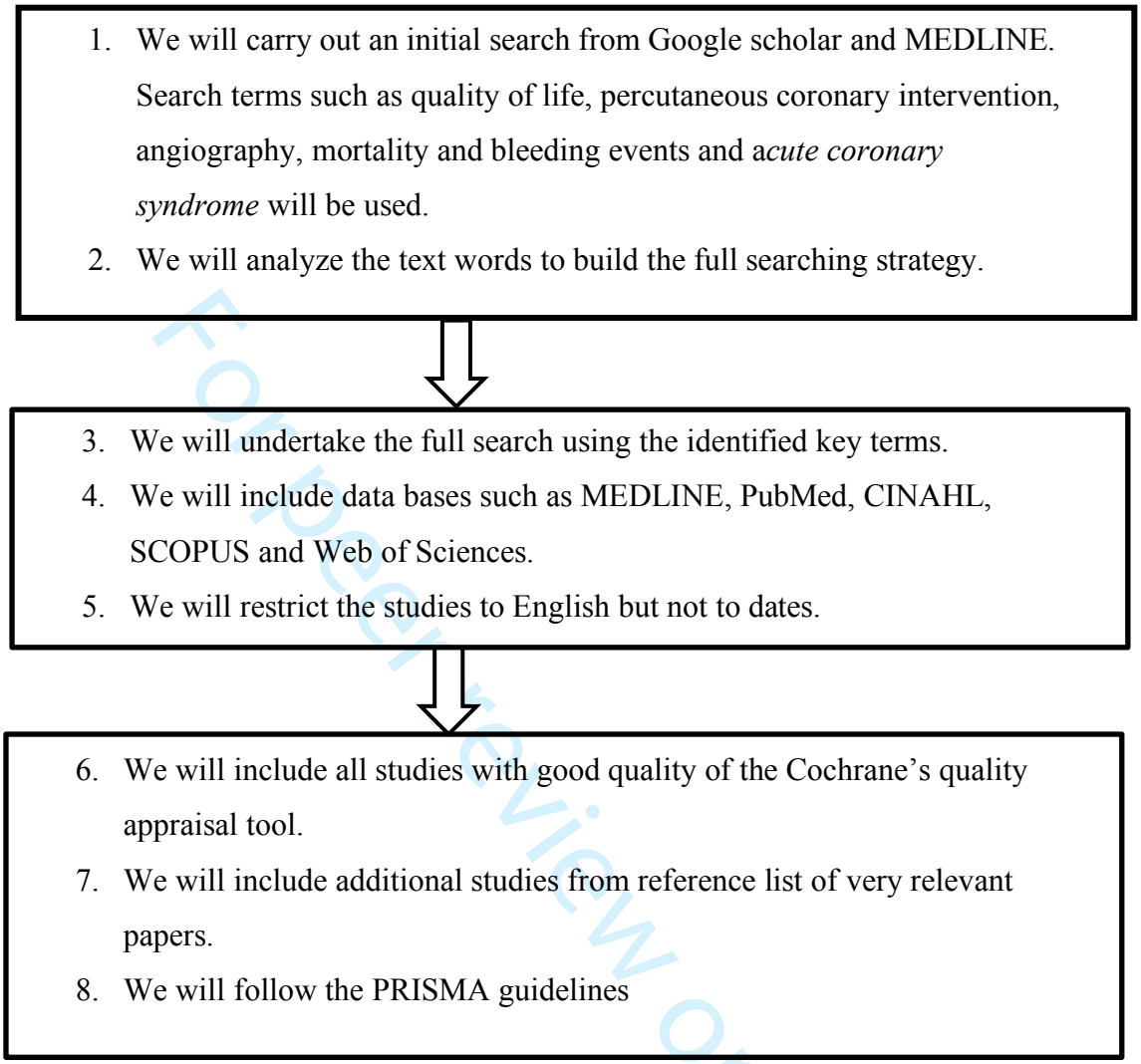

Figure 1 A schematic of the process of the systemic review using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA).

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

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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.

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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.

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 [1]. It is characterised by a number of clinical symptoms including unstable angina, non-ST-segment elevation myocardial infarction, and ST-segment elevation myocardial infarction[1]. 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 [1]. 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 [2-4]. 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 [5]. These methods thereafter inform the treatment choice based on strategies that include percutaneous coronary intervention (PCI) and coronary angiography [6 7]. Despite the existence of these risk assessment techniques, however, physicians still use their clinical intuition to prescribe therapies and estimate potential benefit and harm [8 9]. 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 interpterion. For example, Short Form 6, 12 and 36 dimension (SF-6D, SF-12 and SF-36)[10-12], Seattle angina questionnaire (SAQ) [13 14], duke activity status index (DASI) [15], Nottingham health profile (NHP)[16 17] 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-

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-making [8 18 19]. Unfortunately, these group of patients are also at high risk of increased adverse outcomes of ACS management [20]. However, evidence of the impact of HRQoL on decision-making and risk assessment is lacking. 'Impact' in this review is referred to a situation where treatment risk estimation was modified or altered as a result of HRQoL.

A review in United States America[21] found that that several ACS patients consider HRQoL while deciding to choose a treatment strategy although the survival benefit is similar among the available therapies. In particular, the review noticed that there were variations in preferences over the duration of HRQoL. Some patients chose easy treatment strategy that brings favourable HRQoL for short duration—for instance, patients chose PCI instead of CABG. To the contrary, other patients chose a complex treatment strategy to have a favourable QoL for longer period of time—for instance, patients chose CABG instead of PCI. Most patients understood less these existing trade-offs. It is against this impact that the review recommended that physicians should have to consider advising their patients about the HRQoL benefit before deciding to choose a treatment strategy. Thus, there will be a need to consider provide objective information on HRQoL by physicians. Furthermore, the literature review revealed that clinical trials, treatment guidelines and polices should have to consider HRQoL while deciding to prescribe among treatment strategies.

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[22 23]. For example, Amin et al found a 24% prevalence of bleeding among ACS patients undergoing PCI, and the six-month QoL was worse[22]. Furthermore, evidence show the association between change in QoL and mortality[24 25]. Nevertheless, the degree to which this HRQoL affects the estimation of the risk of mortality or bleeding events in ACS patients is uncertain [8 26 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 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.

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 a standardized Joanna Briggs Institute (JBI) appraisal instruments[28] (Annex 2). 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 the JBI (Annex 2). In addition, we will assess the risk of bias via the Agency for Healthcare Research and Quality (AHRQ) criteria[29].

Data extraction

Quantitative and qualitative data will be extracted from papers based on the JBI data extraction tool (Annex 3). 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 [8]. 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)[10-12], Seattle angina questionnaire (SAQ) [13 14], duke activity status index (DASI) [15], Nottingham health profile (NHP)[16 17] 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[30]. We will consider meta-analysis if I^2 will be below 85%[31]. 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)[32] estimates and their 95% confidence intervals (CI) using random or fixed effect meta-analysis[31]. 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[33 34]. 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.

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.

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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

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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.

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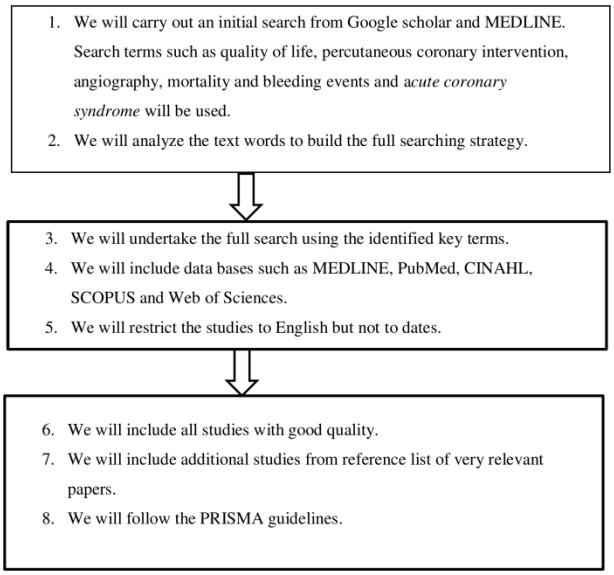

Figure 1 A schematic of the process of the systemic search and a use of Preferred Reporting Items for Systematic Reviews and Meta-Analyses for protocol (PRISMA-P) for reporting findings.

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)

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 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	ALL ("acute coronary syndrome" OR "ACS" OR "coronary heart disease" OR "myocardial infarction" OR "MI" OR heart infarction) " LIMITED to English
4	1 AND 2 AND 3; Limited Subject area medicine/sociology/psychology AND English

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?	☐	☐	☐	☐
2. Were the criteria for inclusion in the sample clearly defined?	☐	☐	☐	☐
3. Were confounding factors identified and strategies to deal with them stated?	☐	☐	☐	☐
4. Were outcomes assessed using objective criteria?	☐	☐	☐	☐
5. If comparisons are being made, was there sufficient descriptions of the groups?	☐	☐	☐	☐
6. Was follow up carried out over a sufficient time period?	☐	☐	☐	☐
7. Were the outcomes of people who withdrew described and included in the analysis?	☐	☐	☐	☐
8. Were outcomes measured in a reliable way?	☐	☐	☐	☐
9. Was appropriate statistical analysis used?	☐	☐	☐	☐

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?	☐	☐	☐	☐
2. Are the patients at a similar point in the course of their condition/illness?	☐	☐	☐	☐
3. Has bias been minimised in relation to selection of cases and of controls?	☐	☐	☐	☐
4. Are confounding factors identified and strategies to deal with them stated?	☐	☐	☐	☐
5. Are outcomes assessed using objective criteria?	☐	☐	☐	☐
6. Was follow up carried out over a sufficient time period?	☐	☐	☐	☐
7. Were the outcomes of people who withdrew described and included in the analysis?	☐	☐	☐	☐
8. Were outcomes measured in a reliable way?	☐	☐	☐	☐
9. Was appropriate statistical analysis used?	☐	☐	☐	☐

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?	☐	☐	☐	☐
2. Were participants blinded to treatment allocation?	☐	☐	☐	☐
3. Was allocation to treatment groups concealed from the allocator?	☐	☐	☐	☐
4. Were the outcomes of people who withdrew described and included in the analysis?	☐	☐	☐	☐
5. Were those assessing outcomes blind to the treatment allocation?	☐	☐	☐	☐
6. Were the control and treatment groups comparable at entry?	☐	☐	☐	☐
7. Were groups treated identically other than for the named interventions	☐	☐	☐	☐
8. Were outcomes measured in the same way for all groups?	☐	☐	☐	☐
9. Were outcomes measured in a reliable way?	☐	☐	☐	☐
10. Was appropriate statistical analysis used?	☐	☐	☐	☐
	☐	☐	☐	☐

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?	☐	☐	☐	☐
2.	Were the inclusion criteria appropriate for the review question?	☐	☐	☐	☐
3.	Was the search strategy appropriate?	☐	☐	☐	☐
4.	Were the sources and resources used to search for studies adequate?	☐	☐	☐	☐
5.	Were the criteria for appraising studies appropriate?	☐	☐	☐	☐
6.	Was critical appraisal conducted by two or more reviewers independently?	☐	☐	☐	☐
7.	Were there methods to minimize errors in data extraction?	☐	☐	☐	☐
8.	Were the methods used to combine studies appropriate?	☐	☐	☐	☐
9.	Was the likelihood of publication bias assessed?	☐	☐	☐	☐
10.	Were recommendations for policy and/or practice supported by the reported data?	☐	☐	☐	☐
11.	Were the specific directives for new research appropriate?	☐	☐	☐	☐

Overall appraisal: Include ☐ Exclude ☐ Seek further info ☐

_____

_____

Annex 3: JBI-data extraction instruments

JBI Data Extraction Form for Experimental / Observational Studies

Reviewer _____ Date _____

Author _____ Year _____

Journal _____ Record Number _____

Study Method

RCT ☐ Quasi-RCT ☐ Longitudinal ☐

Retrospective ☐ Observational ☐ Other ☐

Participants

Setting _____

Population _____

Sample size

Group A _____ Group B _____

Interventions

Intervention A _____

_____

Intervention B _____

_____

Authors Conclusions:

_____

_____

_____

Reviewers Conclusions:

_____

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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:	*BMJ Open*
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 Gesesew, Hailay; Jimma University, Epidemiology Horsfall, Matthew; South Australian Health & Medical Research Institute, SAHMRI, Adelaide, Australia Chew, Derek; Flinders Medical Centre, Department of Cardiovascular Medicine
Primary Subject Heading:	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

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.

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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.

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 [1]. It is characterised by a number of clinical symptoms including unstable angina, non-ST-segment elevation myocardial infarction, and ST-segment elevation myocardial infarction[1]. 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 [1]. 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 [2-4]. 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[5]. These methods thereafter inform the treatment choice based on strategies that include percutaneous coronary intervention (PCI) and coronary angiography [6 7]. Despite the existence of these risk assessment techniques, however, physicians still use their clinical intuition to prescribe therapies and estimate potential benefit and harm [8 9]. 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)[10-12], Seattle Angina Questionnaire (SAQ) [13 14], Duke Activity Status Index (DASI) [15], Nottingham Health Profile (NHP)[16 17] 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-

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-making [8 18 19]. Unfortunately, these group of patients are also at high risk of increased adverse outcomes of ACS management [20]. However, evidence of the impact of HRQoL on decision-making and risk assessment is lacking. 'Impact' in this review is referred to a situation where treatment risk estimation was modified or altered as a result of HRQoL.

A review in United States America[21] found that that several patients with ACS consider HRQoL while deciding to choose a treatment strategy although the survival benefit is similar among the available therapies. In particular, the review noticed that there were variations in preferences over the duration of HRQoL. Some patients chose easy treatment strategy that brings favourable HRQoL for short duration—for instance, patients chose PCI instead of CABG. To the contrary, other patients chose a complex treatment strategy to have a favourable QoL for longer period of time—for instance, patients chose CABG instead of PCI. Most patients understood less these existing trade-offs. It is against this impact that the review recommended that physicians should have to consider advising their patients about the HRQoL benefit before deciding to choose a treatment strategy. Thus, there will be a need to consider provide objective information on HRQoL by physicians. Furthermore, the literature review revealed that clinical trials, treatment guidelines and polices should have to consider HRQoL while deciding to prescribe among treatment strategies.

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 event and QoL is scarce, the existing evidence demonstrated worse QoL following a bleeding event[22 23]. For example, Amin et al found a 24% prevalence of bleeding among patients with ACS undergoing PCI, and the six-month QoL was worse[22]. Furthermore, evidence show the association between change in QoL and mortality[24 25]. Nevertheless, the degree to which this HRQoL affects the estimation of the risk of mortality or bleeding events in patients with ACS is uncertain [8 26 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

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

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 a standardized Joanna Briggs Institute (JBI) appraisal instruments[28] (Annex 2). 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 the JBI (Annex 2). In addition, we will assess the risk of bias via the Agency for Healthcare Research and Quality (AHRQ) criteria[29].

Data extraction

Quantitative and qualitative data will be extracted from papers based on the JBI data extraction tool (Annex 3). 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 Patients with ACS
- 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 [8]. 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)[10-12], Seattle angina questionnaire (SAQ) [13 14], duke activity status index (DASI) [15], Nottingham health profile (NHP)[16 17] 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[30]. We will consider meta-analysis if I^2 will be below 85%[31]. 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)[32] estimates and their 95% confidence intervals (CI) using random or fixed effect meta-analysis[31]. 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[33 34]. 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.

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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

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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.

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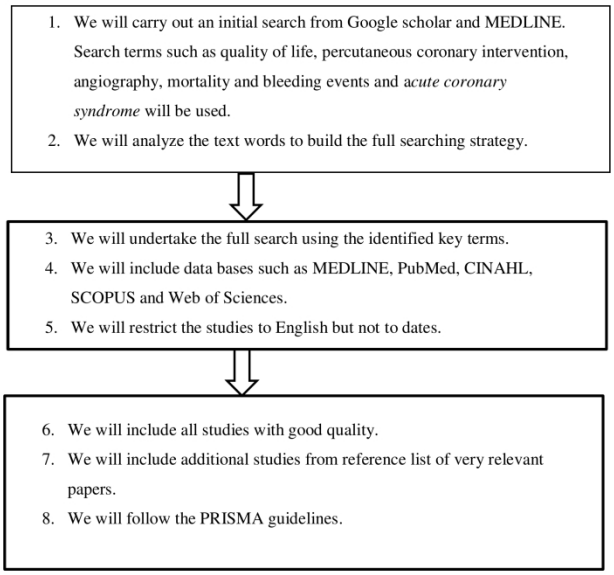

Figure 1 A schematic of the process of the systemic search and a use of Preferred Reporting Items for Systematic Reviews and Meta-Analyses for protocol (PRISMA-P) for reporting findings.

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)

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 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	ALL ("acute coronary syndrome" OR "ACS" OR "coronary heart disease" OR "myocardial infarction" OR "MI" OR heart infarction) " LIMITED to English
4	1 AND 2 AND 3; Limited Subject area medicine/sociology/psychology AND English

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?	☐	☐	☐	☐
2. Were the criteria for inclusion in the sample clearly defined?	☐	☐	☐	☐
3. Were confounding factors identified and strategies to deal with them stated?	☐	☐	☐	☐
4. Were outcomes assessed using objective criteria?	☐	☐	☐	☐
5. If comparisons are being made, was there sufficient descriptions of the groups?	☐	☐	☐	☐
6. Was follow up carried out over a sufficient time period?	☐	☐	☐	☐
7. Were the outcomes of people who withdrew described and included in the analysis?	☐	☐	☐	☐
8. Were outcomes measured in a reliable way?	☐	☐	☐	☐
9. Was appropriate statistical analysis used?	☐	☐	☐	☐

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?	☐	☐	☐	☐
2. Are the patients at a similar point in the course of their condition/illness?	☐	☐	☐	☐
3. Has bias been minimised in relation to selection of cases and of controls?	☐	☐	☐	☐
4. Are confounding factors identified and strategies to deal with them stated?	☐	☐	☐	☐
5. Are outcomes assessed using objective criteria?	☐	☐	☐	☐
6. Was follow up carried out over a sufficient time period?	☐	☐	☐	☐
7. Were the outcomes of people who withdrew described and included in the analysis?	☐	☐	☐	☐
8. Were outcomes measured in a reliable way?	☐	☐	☐	☐
9. Was appropriate statistical analysis used?	☐	☐	☐	☐

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?	☐	☐	☐	☐
2. Were participants blinded to treatment allocation?	☐	☐	☐	☐
3. Was allocation to treatment groups concealed from the allocator?	☐	☐	☐	☐
4. Were the outcomes of people who withdrew described and included in the analysis?	☐	☐	☐	☐
5. Were those assessing outcomes blind to the treatment allocation?	☐	☐	☐	☐
6. Were the control and treatment groups comparable at entry?	☐	☐	☐	☐
7. Were groups treated identically other than for the named interventions	☐	☐	☐	☐
8. Were outcomes measured in the same way for all groups?	☐	☐	☐	☐
9. Were outcomes measured in a reliable way?	☐	☐	☐	☐
10. Was appropriate statistical analysis used?	☐	☐	☐	☐
	☐	☐	☐	☐

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?	☐	☐	☐	☐
2.	Were the inclusion criteria appropriate for the review question?	☐	☐	☐	☐
3.	Was the search strategy appropriate?	☐	☐	☐	☐
4.	Were the sources and resources used to search for studies adequate?	☐	☐	☐	☐
5.	Were the criteria for appraising studies appropriate?	☐	☐	☐	☐
6.	Was critical appraisal conducted by two or more reviewers independently?	☐	☐	☐	☐
7.	Were there methods to minimize errors in data extraction?	☐	☐	☐	☐
8.	Were the methods used to combine studies appropriate?	☐	☐	☐	☐
9.	Was the likelihood of publication bias assessed?	☐	☐	☐	☐
10.	Were recommendations for policy and/or practice supported by the reported data?	☐	☐	☐	☐
11.	Were the specific directives for new research appropriate?	☐	☐	☐	☐

Overall appraisal: Include ☐ Exclude ☐ Seek further info ☐

_____

_____

Annex 3: JBI-data extraction instruments

JBI Data Extraction Form for Experimental / Observational Studies

Reviewer _____ Date _____

Author _____ Year _____

Journal _____ Record Number _____

Study Method

RCT ☐ Quasi-RCT ☐ Longitudinal ☐

Retrospective ☐ Observational ☐ Other ☐

Participants

Setting _____

Population _____

Sample size

Group A _____ Group B _____

Interventions

Intervention A _____

_____

Intervention B _____

_____

Authors Conclusions:

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Reviewers Conclusions:

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