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Assessment of patient-reported outcomes after a polytrauma: protocol for a systematic review

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Keywords:	Patient-reported Outcomes, Quality of Life, Polytrauma, Multiple Trauma, Activities of Daily Living, Social Participation

Assessment of patient-reported outcomes after a polytrauma: protocol for a systematic review

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Keywords: Patient-reported Outcomes, Quality of Life, Polytrauma, Multiple Trauma, Activities of Daily Living, Social Participation

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Abstract:

Introduction: Survivors of polytrauma experience long- and short-term burden that influence their quality of life. The patients' view of relevant short and long-term outcomes should be captured in instruments that measure quality of life and other patient-reported outcomes (PROs) after a polytrauma. The aim of this systematic review is to (1) collect instruments that assess patient-reported outcomes (e.g. quality of life) during the follow-up after a polytrauma, (2) describe the instrument´s application (e.g. duration period of follow-up), and (3) investigate other relevant patient-reported outcomes that are additionally assessed in the included studies (e.g. activities of daily living).

Methods and analysis: The systematic review protocol will be performed in line with the PRISMA-P statement. MEDLINE, EMBASE, CINAHL, PsycINFO, Cochrane Central Register of Controlled Trials (CENTRAL) and the trials registers ClinicalTrials.gov and WHO ICTRP will be searched. Keywords, e.g., "polytrauma", "multiple trauma", "quality of life", "activities of daily living" or "pain" will be used. Publications published from 2005 until August 2016 will be included. The data

extraction and a content analysis will be carried out systematically. A critical appraisal will be performed.

Ethics and Dissemination: Formal ethical approval is not required as primary data will not be collected. The results will be published in a peer-reviewed publication. The systematic review was registered at PROSPERO (registration number CRD42017060825).

Strengths and limitations of this study

- To the best of our knowledge, there are no systematic reviews in the literature that provide an overview about the assessed patient-reported outcomes after polytrauma and therefor applied instruments.
- The systematic review will also display the times of measurement and follow up periods for identified quality of life measures.
- We will show additional measure for further relevant patient-reported outcomes after polytrauma, e. g. social participation, activities of daily living.
- A limitation of the review might be that publications will be included which are published since 2005. It cannot be ruled out in that case that relevant literature published before 2005 is missing.

Introduction

Severe injuries represent a leading cause of death and permanent disability [1]. Especially in the central European region such severely injured patients are termed as “polytrauma patients” or “polytraumatised”. Actually, “polytrauma” is defined as having at least two severe injuries in different body regions that are potentially life-threatening. In the Anglo-American literature these patients are mostly entitled as “multiple injury”, “multiple trauma” or “severely injured patients”. All these descriptions have in common, that a certain degree of injury is mandatory. The severity of the trauma is indicated by the Injury Severity Score (ISS). In general, an ISS ≥16 indicating the severity of a trauma is included in the description of “polytrauma” or “multiple trauma” or “severely injured” patients [1, 2] In the following we refer to the term „polytrauma“.

In Germany the number of severely multiply injured patients counts up to approximately 18.400 patients per year, mostly males (72%) [2] with a mean age of 45.9 years [3].

Due to strategies for early advanced life support, high quality in health care services, progress in treatment options and more traffic safety the survival rate after polytrauma is increasing. However, survivors are faced with long- and short-term burden after polytrauma: after one year polytrauma patients are still suffering from remaining problems in mobility (34%), self-care (15%) and activities of daily living (51%) [4]. Furthermore, they experience pain and/or discomfort (58%) as well as anxiety and/or depression (37%) [3]. Relevant disabilities, like respiration limitations, para- or

tetraplegia are severe causes for 40% not returning to their former workplace [3,5, 6] and have impact on socio-economical and quality of life aspects [5-8]. For the necessary acute and rehabilitative care the social economic impact is estimated to be 106.000 € per patient. In Germany additional costs of 935.000 € accrue if patients are not returning to their former workplace [6].

Consequently, the aim to reduce short- and long-term burden after polytrauma is essentially important [6, 8]. Thereby clinical parameters are necessary to support treatment processes and services in acute care facilities and to display short-term outcomes. Additionally, measures capturing the patients´ view of short and long-term outcomes regarding e.g. psychological and physical factors, functioning status and social interaction are becoming more and more important for doctors and nurses as well as for patients and their relatives [8, 9]. The measurement of these patient-reported outcomes (PROs), which can also be reported e.g. by relatives in case of mental disability, are important for completing the assessment of relevant clinical outcomes after injury. To assess the impact of a polytrauma on quality of life and other relevant PROs it is necessary to question the patients [9, 10]. As preferred gold standard follow up questioning as repeated snapshots of outcomes would track trends and focus on long-term conditions and outcomes after polytrauma [10]. Therefore, it is necessary to know which instruments for assessing PROs are applied and how. Thus, this systematic review will provide an overview of instruments used to measure PROs, like quality of life, and other currently reported outcome measures for patients with polytrauma and describe their application in detail.

Currently the TraumaRegister (DGU®) collects data on emergency care, treatment in the shock rooms, intensive care unit (ICU) and discharge [2, 9]. In respect of the comprehensive evaluation of the short and long-term burden the register plans to expand their measurement battery by assessing patient-reported outcomes, e.g. quality of life.

Aim of the study

The aim of this systematic review is to

1. collect instruments that assess patient-reported outcomes (e.g. quality of life, participation, activities of daily living) during the follow-up after a polytrauma and
2. describe the instrument´s application (e.g. duration period of follow-up, frequency of application, time of measurements during follow-up)
3. investigate other relevant patient-reported outcomes that are additionally assessed in the included studies (e.g. activities of daily living, social participation, pain, depression, anxiety, cognitive function)

Method

The systematic review protocol was performed in line with the quality requirements of the PRISMA-P statement [11] and PRISMA Statement will be considered during the review procedure [12]. It was registered on 8 April 2017 at PROSPERO (registration number CRD42017060825).

Databases

The literature search will be conducted in the following databases: MEDLINE, EMBASE, CINAHL, PsycINFO, Cochrane Central Register of Controlled Trials (CENTRAL) and the trials registers ClinicalTrials.gov and WHO ICTRP. To ensure literature saturation reference lists of eligible studies will be examined for further relevant publications.

Search strategy

The search strategy will be developed in cooperation with an information specialist using database-specific controlled vocabulary and additional free text terms. Appendix A provides the Medline search strategy which will be adapted to the other databases accordingly.

Inclusion and exclusion criteria

Studies will be included if they match following inclusion criteria: i) the study assesses patient-reported outcomes, like quality of life (QoL)/health-related quality of life (HRQoL), participation, activities of daily living (ADL), pain, depression, anxiety or cognitive function in people aged 18-75 years during a temporally clear defined follow-up period after a polytrauma (at least two injuries, ISS >15, AIS≥3); ii) original qualitative, quantitative, mixed methods studies and randomized controlled trial studies (RCT) which are published between 2005 and 2016; iii) publications are in English or German language will be considered, iv) the full text of the study is available (e. g. contacting the authors).

Studies will be excluded from this review if they mention one of the following criteria: i) an injury-severity-score (ISS) ≤ 15 or an abbreviated injury scale (AIS) <3 or no reporting of ISS or AIS; ii) low-energy injuries, single or mono injuries or geriatric injuries, burn injuries, war injuries (group of veterans or military staff are excluded), cancer and other chronic diseases as secondary diagnosis; iii) publications were the primary aim does not focus on patient-reported outcomes iv) grey literature, books, letters/short reports, abstracts, editorials, comments or discussion papers as well as case studies, systematic reviews and meta-analysis. However, the two latter will be screened to identify further appropriate studies.

Study selection process

On the basis of predefined in- and exclusion criteria suitable publications will be selected by title and abstract, independently screened by two reviewers. A third reviewer will solve differences concerning

the in- or exclusion of studies. In order to foster the process of suitability decisions, in- and exclusion of the first fifty publications by title and abstract screening will be discussed between the two reviewers. Subsequently, two reviewers assessing eligibility for final inclusion in this review will screen the full texts of the remaining publications again independently. A third reviewer will solve conflicts in the final in- or exclusion of studies. Inter-rater reliability will be determined after the title-abstract as well as after the full text screening.

Data extraction and synthesis

The data extraction will be performed according to the requirements of Cochrane reviews [13]. For data extraction two experienced researchers will use a piloted data extraction sheet independently. Extracted data from the included studies will give an overview of: first author and publication year, study design, country, study population (number of subjects, proportion of men, mean age with standard deviation and range, kind of injury, ISS, AIS, other characteristics), treatment, aim of the study, findings, and furthermore the reported PROs, applied instruments to assess these PROs, description of the instrument, data collection (method of assessment, time of measurements, length of follow-up period, quality criteria of instruments (e.g. validity, reliability) and modifications of the instruments. Furthermore, the result of the critical appraisal of the study quality will be added.

Critical appraisal

In the final selection of eligible studies two reviewers will independently perform a quality appraisal to assess the methodological quality and the risk of bias in each study type using standardised checklists of the National Institute for Health and Care Excellence (NICE) [14], Checklist of the Scottish Intercollegiate Guidelines Network (SIGN) [15] or the Mixed Method Appraisal Tool (MMAT) [16]. Reviewers will resolve disagreements by discussion.

Discussion

We will perform the proposed systematic review to generate an overview of the instruments used to assess PROs in the field of polytrauma. The results of this systematic review serve as a basis to expand the TraumaRegister DGU® with focus on quality of life measures. Likewise, might the additional knowledge on further patient-reported outcomes, e. g. social participation and activities of daily living expand the view from the patients' perspectives on relevant outcomes after polytrauma and lead its adaptation on health services. Subsequently, health care providers and policymakers may draw their attention on this topic and will implement the assessment of PROs in decision-making regarding the treatment process.

Contributorship statement

AI is the guarantor. IG, MR, SA, SK and AI drafted the manuscript. IG, MR, AHF, MIM, SA and SK developed the search strategy. All authors contributed to the development of the selection criteria, the risk of bias assessment strategy and data extraction criteria. All authors read, provided feedback and approved the final manuscript.

Competing interests

Johannes Sturm is executive secretary of the AUC. The authors declare that they have no competing interests.

Funding

This systematic review is funded by the Academy for Trauma Surgery (AUC). The funding will support the conduct of this systematic review.

Data sharing statement

There will be no additional unpublished data.

Consent for publication

All authors have approved the manuscript for submission. The content of the manuscript has not been published, or submitted for publication elsewhere.

Ethics committee approval information

Since this is a protocol for a systematic review, which will be based on published data and, as such, ethical approval is not required.

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Appendix A

Medline (PubMed, 03.08.2016)

#1

"Multiple Trauma"[mh] OR multiple trauma*[tw] OR polytrauma*[tw]

#2

"Quality of Life"[mh] or "quality of life"[tw] or "life quality"[tw] OR QoL[tw] OR HRQoL[tw] OR satisf*[tw] OR "self reported health"[tw] OR "Activities of Daily Living"[mh] OR "activities of daily living"[tw] OR "daily living activity"[tw] OR "daily living activities"[tw] OR "activity of daily living"[tw] OR "limitation of activity"[tw] OR "self care"[tw] OR "physical functioning"[tw] OR functional abilit*[tw] OR "functional assessment"[tw] OR "Social Participation"[mh] OR "social participation"[tw] OR social activit*[tw] OR "social functioning"[tw] OR "social interaction"[tw] OR "social isolation"[tw] OR "social integration"[tw] OR "Pain"[mh] OR pain[tw] OR "Depression"[mh] OR "Depressive Disorder"[mh] OR depress*[tw] OR "emotional distress"[tw] OR "Stress, Psychological"[mh] OR stress[tw] OR "Anxiety"[mh] OR anxiet*[tw] OR "Independent Living"[mh] OR "independent living"[tw] OR "community dwelling"[tw] OR "wellbeing"[tw] OR "well being"[tw] OR "Cognition Disorders"[mh] OR cognitive function*[tw] OR "mental health"[tw] OR "cognitive impairment"[tw] OR "Patient Outcome Assessment"[mh] OR "patient reported outcome"[tw] OR "patient reported outcomes"[tw] OR "patient related outcome"[tw] OR "patient related outcomes"[tw] OR "patient centered outcomes"[tw] OR "patient centered outcome"[tw] OR rehabilitation outcome*[tw] OR "Work Capacity Evaluation"[mh] OR "work capacity"[tw] OR "occupational function"[tw] OR "Stress Disorders, Post-Traumatic"[mh] OR PTSD[tw] OR "traumatic stress disorder"[tw] OR "posttraumatic stress disorder"[tw]

#3

#1 AND #2

#4

#3 AND Filters: Publication date from 2005/01/01 to 2016/12/31; English; German

= 836

PRISMA-P (Preferred Reporting Items for Systematic review and Meta-Analysis Protocols) 2015 checklist: recommended items to address in a systematic review protocol*

Section and topic	Item No	Checklist item	
ADMINISTRATIVE INFORMATION			**Check**
Title:			
Identification	1a	Identify the report as a protocol of a systematic review	Yes
Update	1b	If the protocol is for an update of a previous systematic review, identify as such	NA
Registration	2	If registered, provide the name of the registry (such as PROSPERO) and registration number	Yes
Authors:			
Contact	3a	Provide name, institutional affiliation, e-mail address of all protocol authors; provide physical mailing address of corresponding author	Yes
Contributions	3b	Describe contributions of protocol authors and identify the guarantor of the review	Yes
Amendments	4	If the protocol represents an amendment of a previously completed or published protocol, identify as such and list changes; otherwise, state plan for documenting important protocol amendments	NA
Support:			
Sources	5a	Indicate sources of financial or other support for the review	Yes
Sponsor	5b	Provide name for the review funder and/or sponsor	Yes
Role of sponsor or funder	5c	Describe roles of funder(s), sponsor(s), and/or institution(s), if any, in developing the protocol	Yes
INTRODUCTION			
Rationale	6	Describe the rationale for the review in the context of what is already known	Yes
Objectives	7	Provide an explicit statement of the question(s) the review will address with reference to participants, interventions, comparators, and outcomes (PICO)	Yes
METHODS			
Eligibility criteria	8	Specify the study characteristics (such as PICO, study design, setting, time frame) and report characteristics (such as years considered, language, publication status) to be used as criteria for eligibility for the review	Yes
Information sources	9	Describe all intended information sources (such as electronic databases, contact with study authors, trial registers or other grey literature sources) with planned dates of coverage	Yes
Search strategy	10	Present draft of search strategy to be used for at least one electronic database, including planned limits, such that it could be repeated	Yes

Study records:			
Data management	11a	Describe the mechanism(s) that will be used to manage records and data throughout the review	Yes
Selection process	11b	State the process that will be used for selecting studies (such as two independent reviewers) through each phase of the review (that is, screening, eligibility and inclusion in meta-analysis)	Yes
Data collection process	11c	Describe planned method of extracting data from reports (such as piloting forms, done independently, in duplicate), any processes for obtaining and confirming data from investigators	Yes
Data items	12	List and define all variables for which data will be sought (such as PICO items, funding sources), any pre-planned data assumptions and simplifications	Yes
Outcomes and prioritization	13	List and define all outcomes for which data will be sought, including prioritization of main and additional outcomes, with rationale	Yes
Risk of bias in individual studies	14	Describe anticipated methods for assessing risk of bias of individual studies, including whether this will be done at the outcome or study level, or both; state how this information will be used in data synthesis	Yes
Data synthesis	15a	Describe criteria under which study data will be quantitatively synthesised	NA
	15b	If data are appropriate for quantitative synthesis, describe planned summary measures, methods of handling data and methods of combining data from studies, including any planned exploration of consistency (such as I^2, Kendall's τ)	NA
	15c	Describe any proposed additional analyses (such as sensitivity or subgroup analyses, meta-regression)	NA
	15d	If quantitative synthesis is not appropriate, describe the type of summary planned	NA
Meta-bias(es)	16	Specify any planned assessment of meta-bias(es) (such as publication bias across studies, selective reporting within studies)	NA
Confidence in cumulative evidence	17	Describe how the strength of the body of evidence will be assessed (such as GRADE)	NA

*** It is strongly recommended that this checklist be read in conjunction with the PRISMA-P Explanation and Elaboration (cite when available) for important clarification on the items. Amendments to a review protocol should be tracked and dated. The copyright for PRISMA-P (including checklist) is held by the PRISMA-P Group and is distributed under a Creative Commons Attribution Licence 4.0.**

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Primary Subject Heading:	Health services research
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Keywords: patient-reported outcomes, quality of life, polytrauma, multiple trauma, activities of daily living, social participation

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Abstract:

Introduction: Survivors of polytrauma experience long- and short-term burden that influences their lives. The patients' view of relevant short- and long-term outcomes should be captured in instruments that measure quality of live and other patient-reported outcomes (PROs) after a polytrauma. The aim of this systematic review is to i) collect instruments that assess patient-reported outcomes (quality of life, social participation, activities of daily living) during follow-up after polytrauma, ii) describe the instruments' application (e.g. duration of period of follow-up), and iii) investigate other relevant patient-reported outcomes that are also assessed in the included studies (pain, depression, anxiety, cognitive function).

Methods and analysis: The systematic review protocol is developed in line with the PRISMA-P statement. MEDLINE, EMBASE, CINAHL, PsycINFO, Cochrane Central Register of Controlled Trials (CENTRAL) and the trials registers ClinicalTrials.gov and WHO ICTRP will be searched. Keywords, e.g. 'polytrauma', 'multiple trauma', 'quality of life', 'activities of daily living' or 'pain' will be used. Publications published between January 2005 and August 2016 will be included. The

data extraction and a content analysis will be carried out systematically. A critical appraisal will be performed.

Ethics and Dissemination: Formal ethical approval is not required as primary data will not be collected. The results will be published in a peer-reviewed publication. The systematic review is registered at PROSPERO (registration number CRD42017060825).

Strengths and limitations of this study

- To the best of our knowledge, there are no published systematic reviews providing an overview of assessed patient-reported outcomes after polytrauma, different instruments used to measure these as well as the application of these instruments.
- This systematic review will report the identified instruments used to assess quality of life, social participation and activities of daily living, and describe their application.
- We will show to a lesser extent additional measures for further relevant patient-reported outcomes following polytrauma, e.g. pain, depression, anxiety, cognitive function.
- A limitation of the review might be that publications will be included which were published since 2005. It cannot be ruled out in that case that relevant literature published before 2005 is missing.

Introduction

Severe injuries represent a leading cause of death and permanent disability [1]. Especially in the central European region, such severely injured patients are termed as 'polytrauma patients' or as being 'polytraumatised'. 'Polytrauma' is defined as having at least two severe injuries in different body regions that are potentially life-threatening. In the Anglo-American literature these patients are mostly referred to as 'multiple-injury', 'multiple-trauma' or 'severely injured'. All these descriptions have in common that a certain degree of injury is required. The severity of trauma is usually indicated by the Injury Severity Score (ISS) [2]. In general, an ISS ≥16 falls within the definition of polytrauma, multiple-trauma or severely injured patients [1, 3]. In the following we use the term polytrauma. Comparing the incidence of trauma is challenging, considering the different definitions or conditions of trauma, and due to inconsistencies in the available data [4]. In 2015, according to the TraumaRegister DGU®, the number of severely multiply injured patients was 17,630 (ISS ≥16) [5]. In 2012 the number of severely multiply injured patients (ISS ≥16) reached approximately 18,400 per year. This corresponds to a cumulative incidence of 0.02% per year for Germany [6]. Persons affected are mostly male (72%) with a mean age of 46.5 years [7].

Due to strategies for early advanced life support, high quality in healthcare services, progress in treatment options and more traffic safety, survival rates after polytrauma are increasing. However, survivors are faced with long- and short-term burden after polytrauma: one year after polytrauma,

patients continue to suffer from persisting problems with mobility (34%), self-care (15%) and activities of daily living (51%). Furthermore, they experience pain and/or discomfort (58%) as well as anxiety and/or depression (37%) [8]. Relevant disabilities, such as respiration limitations, para- or tetraplegia, are major causes for 40% of those affected not returning to their former workplace [6, 9, 10] and impact on socio-economic and quality of life aspects [9-12]. For the necessary acute and rehabilitative care, the social economic impact is estimated to be 106,000 EUR per patient. In Germany additional costs of 935,000 EUR accrue if patients do not return to their former workplace [10].

Consequently, the aim to reduce short- and long-term burden after polytrauma is critically important [10, 12]. Thus, clinical parameters are necessary to support treatment processes and services in acute care facilities and to display short-term outcomes. Additionally, evaluations capturing a patient's views of short- and long-term outcomes in terms of e.g. psychological and physical factors, functional status and social interaction, are becoming increasingly important for doctors and nurses as well as for patients and their family members [12, 13]. The measurement of these patient-reported outcomes (PROs), which can also be reported e.g. by relatives in case of mental disability, is important for completing the assessment of relevant clinical outcomes after injury. To assess the impact of a polytrauma on quality of life and other relevant PROs it is necessary to question the patients [13, 14]. The preferred gold-standard is a measurement at multiple times during the follow-up period to track trends and focus on long-term conditions and outcomes associated with polytrauma [14]. Therefore, it is necessary to know which instruments for assessing PROs are applied and how. So far, no systematic review has been identified providing an overview of assessed PROs after polytrauma, different instruments used to measure these as well as the application of these instruments. Thus, this systematic review will provide an overview of instruments used to measure PROs, including quality of life and other currently reported outcome measures for patients with polytrauma, and describe their application in detail.

Currently the TraumaRegister DGU® collects data on emergency care, treatment in shock rooms, intensive care unit (ICU) and discharge [3, 13]. Regarding the comprehensive evaluation of the short and long-term burden, the register plans to expand their measurement battery by assessing patient-reported outcomes, e.g. quality of life.

Aim of the study

The aim of this systematic review is to:

i. collect instruments that assess patient-reported outcomes (quality of life, social participation, activities of daily living) during the follow-up after polytrauma
ii. describe the application of these instruments in detail (e.g. duration of period of follow-up, frequency of application, time of measurements during follow-up)

iii. investigate other relevant patient-reported outcomes that are additionally assessed in the included studies (e.g. pain, depression, anxiety, cognitive function) without reporting the application of instruments in detail.

Method

The systematic review protocol is developed in line with the quality requirements of the PRISMA-P statement [15], and the PRISMA statement will be considered during the review procedure [16]. The protocol was registered on 8 April 2017 at PROSPERO (registration number CRD42017060825).

Databases

The literature search will be conducted in the following databases: MEDLINE, EMBASE, CINAHL, PsycINFO, Cochrane Central Register of Controlled Trials (CENTRAL) and the trials registers ClinicalTrials.gov and WHO ICTRP. To ensure literature saturation, reference lists of eligible studies will be examined for further relevant publications.

Search strategy

The search strategy will be developed in cooperation with a specialist for systematic reviews using database-specific controlled vocabulary and additional free-text terms. Appendix A provides the Medline search strategy that will be adapted to the other databases accordingly.

Inclusion and exclusion criteria

Studies will be included if they match the following inclusion criteria: i) the study assesses patient-reported outcomes, such as quality of life (QoL)/health-related quality of life (HRQoL), social participation, activities of daily living (ADL), pain, depression, anxiety or cognitive function in people aged 18–75 years during a temporally clearly defined follow-up period after polytrauma (injuries involving at least two different areas of the body or organ systems, ISS >15, AIS ≥3); ii) original qualitative, quantitative, mixed-methods studies and all kinds of original empirical research that were published between 1 January 2005 and 3 August 2016; iii) English or German language publications will be considered; iv) the full text of the study is available (i.e. for contacting the authors). The interest in quality of life in research and its implication in practice has been growing since 2005 [17]. As one of our main aims is to collect instruments measuring quality of life, we decided to include publications as of 2005. Our procedure is supported by the burgeoning perspective in clinical research on PROs and its relevance for the future in addition to clinical data [18]. A further reason was to capture the most recent developments in research on PROs. Therefore, we looked specifically for publications from the last 11 years.

Studies will be excluded from this review if they mention one of the following criteria: i) an injury-severity-score (ISS) ≤15 or an abbreviated injury scale (AIS) <3 or no reporting of ISS or AIS; ii) low-

energy injuries, single or mono injuries or geriatric injuries, burn injuries, war injuries (group of veterans or military staff are excluded), cancer and other chronic diseases as secondary diagnosis; iii) publications in which the primary aim does not focus on patient-reported outcomes; iv) grey literature, books, letters/short reports, abstracts, editorials, comments or discussion papers as well as case studies, systematic reviews and meta-analysis. However, the two latter will be screened to identify further appropriate studies.

Study selection process

On the basis of predefined inclusion and exclusion criteria, suitable publications will be selected by title and abstract, and independently screened by two reviewers. A third reviewer will solve differences concerning the inclusion or exclusion of studies. In order to foster the process of suitability decisions, inclusion and exclusion of the first 50 publications by title and abstract screening will be discussed between the two reviewers. Subsequently, two reviewers assessing eligibility for final inclusion in this review will screen the full texts of the remaining publications again independently. A third reviewer will solve conflicts in the final inclusion or exclusion of studies. Inter-rater reliability will be determined after the title abstract as well as after the full-text screening.

Data extraction and synthesis

The data extraction will be performed according to the requirements of Cochrane reviews [19]. For data extraction two experienced researchers will use a piloted data extraction sheet independently. Extracted data from the included studies will provide an overview of: first author and publication year, study design, country, study population (number of subjects, proportion of men, mean age with standard deviation and range, kind of injury, ISS, AIS, other characteristics), treatment, aim of the study, findings, and, furthermore, for the reported PROs according to aim 1, applied instruments to assess these PROs, description of the instrument, data collection (method of assessment, time of measurements, length of follow-up period, quality criteria of instruments (e.g. validity, reliability) and modifications of the instruments. Furthermore, the result of the critical appraisal of the study quality will be added.

Critical appraisal

In the final selection of eligible studies two reviewers will independently perform a quality appraisal to assess the methodological quality and the risk of bias in each study type using standardised checklists of the UK National Institute for Health and Care Excellence (NICE) [20] or Scottish Intercollegiate Guidelines Network (SIGN) [21] or the Mixed Method Appraisal Tool (MMAT) [22]. Reviewers will resolve disagreements through discussion.

Discussion

We will perform the proposed systematic review to generate an overview of the instruments used to assess PROs in the field of polytrauma. The results of this systematic review will serve as a basis to expand the TraumaRegister DGU® with a focus on quality of life measures. Likewise, the additional knowledge on further PROs, e.g. pain, depression, anxiety, cognitive function, might emphasise the patients' perspectives on relevant outcomes after polytrauma and lead to its consideration in the provision of health services. Subsequently, health care providers and policymakers may draw their attention on this topic and will implement the assessment of PROs in decision-making regarding the treatment process.

Contributorship statement

A.I. is the guarantor. I.G., M.R., S.A., S.K. and A.I. drafted the manuscript. I.G., M.R., A.H.F., M.I.M., S.A. and S.K. developed the search strategy. A.I., I.G., M.R., S.A., S.K., K.M., A.H.F., M.I.M., S.F., J.S. and J.W. contributed to the development of the selection criteria, the risk of bias assessment strategy and data extraction criteria. A.I., I.G., M.R., S.A., S.K., K.M., A.H.F., M.I.M., S.F., J.S. and J.W. read, provided feedback and approved the final manuscript.

Competing interests

Johannes Sturm is executive secretary of the Academy for Trauma Surgery (AUC). The authors declare that they have no competing interests.

Funding

This systematic review is funded by the AUC. The funding will support the conduct of this systematic review.

Data sharing statement

There will be no additional unpublished data.

Consent for publication

All authors have approved the manuscript for submission. The content of the manuscript has not been published or submitted for publication elsewhere.

Ethics committee approval information

Since this is a protocol for a systematic review that will be based on published data, ethical approval is not required.

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Appendix A

Medline (PubMed, 03.08.2016)

#1

"Multiple Trauma"[mh] OR multiple trauma*[tw] OR polytrauma*[tw]

#2

"Quality of Life"[mh] or "quality of life"[tw] or "life quality"[tw] OR QoL[tw] OR HRQoL[tw] OR satisf*[tw] OR "self reported health"[tw] OR "Activities of Daily Living"[mh] OR "activities of daily living"[tw] OR "daily living activity"[tw] OR "daily living activities"[tw] OR "activity of daily living"[tw] OR "limitation of activity"[tw] OR "self care"[tw] OR "physical functioning"[tw] OR functional abilit*[tw] OR "functional assessment"[tw] OR "Social Participation"[mh] OR "social participation"[tw] OR social activit*[tw] OR "social functioning"[tw] OR "social interaction"[tw] OR "social isolation"[tw] OR "social integration"[tw] OR "Pain"[mh] OR pain[tw] OR "Depression"[mh] OR "Depressive Disorder"[mh] OR depress*[tw] OR "emotional distress"[tw] OR "Stress, Psychological"[mh] OR stress[tw] OR "Anxiety"[mh] OR anxiet*[tw] OR "Independent Living"[mh] OR "independent living"[tw] OR "community dwelling"[tw] OR "wellbeing"[tw] OR "well being"[tw] OR "Cognition Disorders"[mh] OR cognitive function*[tw] OR "mental health"[tw] OR "cognitive impairment"[tw] OR "Patient Outcome Assessment"[mh] OR "patient reported outcome"[tw] OR "patient reported outcomes"[tw] OR "patient related outcome"[tw] OR "patient related outcomes"[tw] OR "patient centered outcomes"[tw] OR "patient centered outcome"[tw] OR rehabilitation outcome*[tw] OR "Work Capacity Evaluation"[mh] OR "work capacity"[tw] OR "occupational function"[tw] OR "Stress Disorders, Post-Traumatic"[mh] OR PTSD[tw] OR "traumatic stress disorder"[tw] OR "posttraumatic stress disorder"[tw]

#3

#1 AND #2

#4

#3 AND Filters: Publication date from 2005/01/01 to 2016/12/31; English; German

= 836

PRISMA-P (Preferred Reporting Items for Systematic review and Meta-Analysis Protocols) 2015 checklist: recommended items to address in a systematic review protocol*

Section and topic	Item No	Checklist item	
ADMINISTRATIVE INFORMATION			**Check**
Title:			
Identification	1a	Identify the report as a protocol of a systematic review	Yes, p. 1
Update	1b	If the protocol is for an update of a previous systematic review, identify as such	NA
Registration	2	If registered, provide the name of the registry (such as PROSPERO) and registration number	Yes p. 4
Authors:			
Contact	3a	Provide name, institutional affiliation, e-mail address of all protocol authors; provide physical mailing address of corresponding author	Yes, p. 1-3
Contributions	3b	Describe contributions of protocol authors and identify the guarantor of the review	Yes, p. 8
Amendments	4	If the protocol represents an amendment of a previously completed or published protocol, identify as such and list changes; otherwise, state plan for documenting important protocol amendments	NA
Support:			
Sources	5a	Indicate sources of financial or other support for the review	Yes, p. 8
Sponsor	5b	Provide name for the review funder and/or sponsor	Yes, p. 8
Role of sponsor or funder	5c	Describe roles of funder(s), sponsor(s), and/or institution(s), if any, in developing the protocol	Yes, p.8
INTRODUCTION			
Rationale	6	Describe the rationale for the review in the context of what is already known	Yes, p. 4-5
Objectives	7	Provide an explicit statement of the question(s) the review will address with reference to participants, interventions, comparators, and outcomes (PICO)	Yes, p. 5
METHODS			
Eligibility criteria	8	Specify the study characteristics (such as PICO, study design, setting, time frame) and report characteristics (such as years considered, language, publication status) to be used as criteria for eligibility for the review	Yes, p. 6
Information sources	9	Describe all intended information sources (such as electronic databases, contact with study authors, trial registers or other grey literature sources) with planned dates of coverage	Yes, p. 6
Search strategy	10	Present draft of search strategy to be used for at least one electronic database, including planned limits, such that it could be repeated	Yes, p. 11

Study records:			
Data management	11a	Describe the mechanism(s) that will be used to manage records and data throughout the review	NA
Selection process	11b	State the process that will be used for selecting studies (such as two independent reviewers) through each phase of the review (that is, screening, eligibility and inclusion in meta-analysis)	Yes, p. 7
Data collection process	11c	Describe planned method of extracting data from reports (such as piloting forms, done independently, in duplicate), any processes for obtaining and confirming data from investigators	Yes, p. 7
Data items	12	List and define all variables for which data will be sought (such as PICO items, funding sources), any pre-planned data assumptions and simplifications	Yes, p. 7
Outcomes and prioritization	13	List and define all outcomes for which data will be sought, including prioritization of main and additional outcomes, with rationale	Yes, p. 5
Risk of bias in individual studies	14	Describe anticipated methods for assessing risk of bias of individual studies, including whether this will be done at the outcome or study level, or both; state how this information will be used in data synthesis	Yes, p. 7
Data synthesis	15a	Describe criteria under which study data will be quantitatively synthesised	NA
	15b	If data are appropriate for quantitative synthesis, describe planned summary measures, methods of handling data and methods of combining data from studies, including any planned exploration of consistency (such as I^2, Kendall's τ)	NA
	15c	Describe any proposed additional analyses (such as sensitivity or subgroup analyses, meta-regression)	NA
	15d	If quantitative synthesis is not appropriate, describe the type of summary planned	NA
Meta-bias(es)	16	Specify any planned assessment of meta-bias(es) (such as publication bias across studies, selective reporting within studies)	NA
Confidence in cumulative evidence	17	Describe how the strength of the body of evidence will be assessed (such as GRADE)	NA

*** It is strongly recommended that this checklist be read in conjunction with the PRISMA-P Explanation and Elaboration (cite when available) for important clarification on the items. Amendments to a review protocol should be tracked and dated. The copyright for PRISMA-P (including checklist) is held by the PRISMA-P Group and is distributed under a Creative Commons Attribution Licence 4.0.**

From: Shamseer L, Moher D, Clarke M, Ghersi D, Liberati A, Petticrew M, Shekelle P, Stewart L, PRISMA-P Group. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015: elaboration and explanation. BMJ. 2015 Jan 2;349(jan02 1):g7647.

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Assessment of patient-reported outcomes after polytrauma: protocol for a systematic review

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Primary Subject Heading:	Health services research
Secondary Subject Heading:	Patient-centred medicine
Keywords:	Patient-reported Outcomes, Quality of Life, Polytrauma, Multiple Trauma, Activities of Daily Living, Social Participation

Assessment of patient-reported outcomes after polytrauma: protocol for a systematic review

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Introduction: Survivors of polytrauma experience long- and short-term burden that influences their lives. The patients' view of relevant short- and long-term outcomes should be captured in instruments that measure quality of live and other patient-reported outcomes (PROs) after a polytrauma. The aim of this systematic review is to i) collect instruments that assess patient-reported outcomes (quality of life, social participation, activities of daily living) during follow-up after polytrauma, ii) describe the instruments' application (e.g. duration of period of follow-up), and iii) investigate other relevant patient-reported outcomes that are also assessed in the included studies (pain, depression, anxiety, cognitive function).

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2016) will be included. In order to present the latest possible results, an update of the search is conducted before publication. The data extraction and a content analysis will be carried out systematically. A critical appraisal will be performed.

Ethics and Dissemination: Formal ethical approval is not required as primary data will not be collected. The results will be published in a peer-reviewed publication. The systematic review is registered at PROSPERO (registration number CRD42017060825).

Strengths and limitations of this study

- To the best of our knowledge, there are no published systematic reviews providing an overview of assessed patient-reported outcomes after polytrauma, different instruments used to measure these as well as the application of these instruments.
- This systematic review will report the identified instruments used to assess quality of life, social participation and activities of daily living, and describe their application.
- We will show additional measures for further relevant patient-reported outcomes following polytrauma, e.g. pain, depression, anxiety, cognitive function.
- A limitation of the review might be that publications will be included which were published since 2005. It cannot be ruled out in that case that relevant literature published before 2005 is missing.

Introduction

Severe injuries represent a leading cause of death and permanent disability [1]. Especially in the central European region, such severely injured patients are termed as 'polytrauma patients' or as being 'polytraumatised'. 'Polytrauma' is defined as having at least two severe injuries in different body regions that are potentially life-threatening. In the Anglo-American literature these patients are mostly referred to as 'multiple-injury', 'multiple-trauma' or 'severely injured'. All these descriptions have in common that a certain degree of injury is required. The severity of trauma is usually indicated by the Injury Severity Score (ISS) [2]. In general, an ISS ≥16 falls within the definition of polytrauma, multiple-trauma or severely injured patients [1, 3]. In the following we use the term polytrauma. Comparing the incidence of trauma is challenging, considering the different definitions or conditions of trauma, and due to inconsistencies in the available data [4]. In 2015, according to the TraumaRegister DGU®, a German registry that cover patients with severe injuries, the number of severely multiply injured patients was 17,630 (ISS ≥16) [5]. In 2012 the number of severely multiply injured patients (ISS ≥16) reached approximately 18,400 per year. This corresponds to a cumulative incidence of 0.02% per year for Germany [6]. Persons affected are mostly male (72%) with a mean age of 46.5 years [7].

Due to strategies for early advanced life support, high quality in healthcare services, progress in treatment options and more traffic safety, survival rates after polytrauma are increasing. However, survivors are faced with long- and short-term burden after polytrauma: one year after polytrauma, patients continue to suffer from persisting problems with mobility (34%), self-care (15%) and activities of daily living (51%). Furthermore, they experience pain and/or discomfort (58%) as well as anxiety and/or depression (37%) [8]. Relevant disabilities, such as respiration limitations, para- or tetraplegia, are major causes for 40% of those affected not returning to their former workplace [6, 9, 10] and impact on socio-economic and quality of life aspects [9-12]. For the necessary acute and rehabilitative care, the social economic impact is estimated to be 106,000 EUR per patient. In Germany additional costs of 935,000 EUR accrue if patients do not return to their former workplace [10].

Consequently, the aim to reduce short- and long-term burden after polytrauma is critically important [10, 12]. Thus, clinical parameters are necessary to support treatment processes and services in acute care facilities and to display short-term outcomes. Additionally, evaluations capturing a patient's view of short- and long-term outcomes in terms of e.g. psychological and physical factors, functional status and social interaction, are becoming increasingly important for doctors and nurses as well as for patients and their family members [12, 13]. The measurement of these patient-reported outcomes (PROs), which can also be reported e.g. by relatives in case of mental disability, is important for completing the assessment of relevant clinical outcomes after injury. To assess the impact of a polytrauma on quality of life and other relevant PROs it is necessary to question the patients [13, 14]. The preferred gold-standard is a measurement at multiple times during the follow-up period to track trends and focus on long-term conditions and outcomes associated with polytrauma [14]. Therefore, it is necessary to know which instruments for assessing PROs are applied and how. So far, no systematic review has been identified providing an overview of assessed PROs after polytrauma, different instruments used to measure these as well as the application of these instruments. Thus, this systematic review will provide an overview of instruments used to measure PROs, including quality of life and other currently reported outcome measures for patients with polytrauma, and describe their application in detail.

Currently the TraumaRegister DGU® collects data on emergency care, treatment in shock rooms, intensive care unit (ICU) and discharge [3, 13]. Regarding the comprehensive evaluation of the short and long-term burden, the register plans to expand their measurement battery by assessing patient-reported outcomes, e.g. quality of life.

Aim of the study

The aim of this systematic review is to:

i. collect instruments that assess patient-reported outcomes (quality of life, social participation, activities of daily living) during the follow-up after polytrauma
ii. describe the application of these instruments in detail (e.g. duration of period of follow-up, frequency of application, time of measurements during follow-up)
iii. investigate other relevant patient-reported outcomes that are additionally assessed in the included studies (e.g. pain, depression, anxiety, cognitive function) without reporting the application of instruments in detail.

Method

The systematic review protocol is developed in line with the quality requirements of the PRISMA-P statement [15], and the PRISMA statement will be considered during the review procedure [16]. The protocol was registered on 8 April 2017 at PROSPERO (registration number CRD42017060825). Prior to publication an update of the search will be performed to be able to present the latest results.

Databases

The literature search will be conducted in the following databases: MEDLINE, EMBASE, CINAHL, PsycINFO, Cochrane Central Register of Controlled Trials (CENTRAL) and the trials registers ClinicalTrials.gov and WHO ICTRP. To ensure literature saturation, reference lists of eligible studies will be examined for further relevant publications.

Search strategy

The search strategy will be developed in cooperation with a specialist for systematic reviews using database-specific controlled vocabulary and additional free-text terms. Appendix A provides the Medline search strategy that will be adapted to the other databases accordingly.

Inclusion and exclusion criteria

Studies will be included if they match the following inclusion criteria: i) the study assesses patient-reported outcomes, such as quality of life (QoL)/health-related quality of life (HRQoL), social participation, activities of daily living (ADL), pain, depression, anxiety or cognitive function in people aged 18–75 years during a temporally clearly defined follow-up period after polytrauma (injuries involving at least two different areas of the body or organ systems, ISS >15, AIS ≥3); ii) all kinds of original empirical research that were published between 1 January 2005 and currently 3 August 2016; iii) English or German language publications will be considered; iv) the full text of the study is available (i.e. for contacting the authors). The interest in quality of life in research and its implication

in practice has been growing since 2005 [17]. As one of our main aims is to collect instruments measuring quality of life, we decided to include publications as of 2005. Our procedure is supported by the burgeoning perspective in clinical research on PROs and its relevance for the future in addition to clinical data [18]. A further reason was to capture the most recent developments in research on PROs. Therefore, we looked specifically for publications from the last 11 years.

Studies will be excluded from this review if they mention one of the following criteria: i) an injury-severity-score (ISS) ≤15 or an abbreviated injury scale (AIS) <3 or no reporting of ISS or AIS; ii) low-energy injuries, single or mono injuries or geriatric injuries, burn injuries, war injuries (group of veterans or military staff are excluded), cancer and other chronic diseases as secondary diagnosis; iii) publications in which the primary aim does not focus on patient-reported outcomes; iv) grey literature, books, letters/short reports, abstracts, editorials, comments or discussion papers as well as case studies, systematic reviews and meta-analysis. However, systematic reviews and meta-analysis will be screened to identify further appropriate studies.

Study selection process

On the basis of predefined inclusion and exclusion criteria, suitable publications will be selected by title and abstract, and independently screened by two reviewers. A third reviewer will solve differences concerning the inclusion or exclusion of studies. In order to foster the process of suitability decisions, inclusion and exclusion of the first 50 publications by title and abstract screening will be discussed between the two reviewers. Subsequently, two reviewers assessing eligibility for final inclusion in this review will screen the full texts of the remaining publications again independently. A third reviewer will solve conflicts in the final inclusion or exclusion of studies. Inter-rater reliability will be determined after the title abstract as well as after the full-text screening.

Data extraction and synthesis

The data extraction will be performed according to the requirements of Cochrane reviews [19]. For data extraction two experienced researchers will use a piloted data extraction sheet independently. Extracted data from the included studies will provide an overview of: first author and publication year, study design, country, study population (number of subjects, proportion of men, mean age with standard deviation and range, kind of injury, ISS, AIS, other characteristics), treatment, aim of the study, findings, and, furthermore, for the reported PROs according to aim 1, applied instruments to assess these PROs, description of the instrument, data collection (method of assessment, time of measurements, length of follow-up period, quality criteria of instruments (e.g. validity, reliability) and modifications of the instruments. Furthermore, the result of the critical appraisal of the study quality will be added.

Critical appraisal

In the final selection of eligible studies two reviewers will independently perform a quality appraisal to assess the methodological quality and the risk of bias in each study type using standardised checklists of the UK National Institute for Health and Care Excellence (NICE) [20] or Scottish Intercollegiate Guidelines Network (SIGN) [21] or the Mixed Method Appraisal Tool (MMAT) [22]. Reviewers will resolve disagreements through discussion.

Discussion

We will perform the proposed systematic review to generate an overview of the instruments used to assess PROs in the field of polytrauma. The results of this systematic review will serve as a basis to expand the TraumaRegister DGU® with a focus on quality of life measures. Likewise, the additional knowledge on further PROs, e.g. pain, depression, anxiety, cognitive function, might emphasise the patients' perspectives on relevant outcomes after polytrauma and lead to its consideration in the provision of health services. Subsequently, health care providers and policymakers may draw their attention on this topic and will implement the assessment of PROs in decision-making regarding the treatment process.

Contributorship statement

A.I. is the guarantor. I.G., M.R., S.A., S.K. and A.I. drafted the manuscript. I.G., M.R., A.H.F., M.I.M., S.A. and S.K. developed the search strategy. A.I., I.G., M.R., S.A., S.K., K.M., A.H.F., M.I.M., S.F., J.S. and J.W. contributed to the development of the selection criteria, the risk of bias assessment strategy and data extraction criteria. A.I., I.G., M.R., S.A., S.K., K.M., A.H.F., M.I.M., S.F., J.S. and J.W. read, provided feedback and approved the final manuscript.

Competing interests

Johannes Sturm is executive secretary of the Academy for Trauma Surgery GmbH (AUC). The authors declare that they have no competing interests.

Funding

This systematic review is funded by the Academy for Trauma Surgery GmbH (AUC). The funding will support the conduct of this systematic review.

Data sharing statement

There will be no additional unpublished data.

Consent for publication

All authors have approved the manuscript for submission. The content of the manuscript has not been published or submitted for publication elsewhere.

Ethics committee approval information

Since this is a protocol for a systematic review that will be based on published data, ethical approval is not required.

Ethics and Dissemination

Formal ethical approval is not required. The results will be published in a peer-reviewed publication.

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Appendix A

Medline (PubMed, 03.08.2016)

#1

"Multiple Trauma"[mh] OR multiple trauma*[tw] OR polytrauma*[tw]

#2

"Quality of Life"[mh] or "quality of life"[tw] or "life quality"[tw] OR QoL[tw] OR HRQoL[tw] OR satisf*[tw] OR "self reported health"[tw] OR "Activities of Daily Living"[mh] OR "activities of daily living"[tw] OR "daily living activity"[tw] OR "daily living activities"[tw] OR "activity of daily living"[tw] OR "limitation of activity"[tw] OR "self care"[tw] OR "physical functioning"[tw] OR functional abilit*[tw] OR "functional assessment"[tw] OR "Social Participation"[mh] OR "social participation"[tw] OR social activit*[tw] OR "social functioning"[tw] OR "social interaction"[tw] OR "social isolation"[tw] OR "social integration"[tw] OR "Pain"[mh] OR pain[tw] OR "Depression"[mh] OR "Depressive Disorder"[mh] OR depress*[tw] OR "emotional distress"[tw] OR "Stress, Psychological"[mh] OR stress[tw] OR "Anxiety"[mh] OR anxiet*[tw] OR "Independent Living"[mh] OR "independent living"[tw] OR "community dwelling"[tw] OR "wellbeing"[tw] OR "well being"[tw] OR "Cognition Disorders"[mh] OR cognitive function*[tw] OR "mental health"[tw] OR "cognitive impairment"[tw] OR "Patient Outcome Assessment"[mh] OR "patient reported outcome"[tw] OR "patient reported outcomes"[tw] OR "patient related outcome"[tw] OR "patient related outcomes"[tw] OR "patient centered outcomes"[tw] OR "patient centered outcome"[tw] OR rehabilitation outcome*[tw] OR "Work Capacity Evaluation"[mh] OR "work capacity"[tw] OR "occupational function"[tw] OR "Stress Disorders, Post-Traumatic"[mh] OR PTSD[tw] OR "traumatic stress disorder"[tw] OR "posttraumatic stress disorder"[tw]

#3

#1 AND #2

#4

#3 AND Filters: Publication date from 2005/01/01 to 2016/12/31; English; German

= 836

PRISMA-P (Preferred Reporting Items for Systematic review and Meta-Analysis Protocols) 2015 checklist: recommended items to address in a systematic review protocol*

Section and topic	Item No	Checklist item	
ADMINISTRATIVE INFORMATION			**Check**
Title:			
Identification	1a	Identify the report as a protocol of a systematic review	Yes, p. 1
Update	1b	If the protocol is for an update of a previous systematic review, identify as such	NA
Registration	2	If registered, provide the name of the registry (such as PROSPERO) and registration number	Yes p. 4
Authors:			
Contact	3a	Provide name, institutional affiliation, e-mail address of all protocol authors; provide physical mailing address of corresponding author	Yes, p. 1-3
Contributions	3b	Describe contributions of protocol authors and identify the guarantor of the review	Yes, p. 8
Amendments	4	If the protocol represents an amendment of a previously completed or published protocol, identify as such and list changes; otherwise, state plan for documenting important protocol amendments	NA
Support:			
Sources	5a	Indicate sources of financial or other support for the review	Yes, p. 8
Sponsor	5b	Provide name for the review funder and/or sponsor	Yes, p. 8
Role of sponsor or funder	5c	Describe roles of funder(s), sponsor(s), and/or institution(s), if any, in developing the protocol	Yes, p.8
INTRODUCTION			
Rationale	6	Describe the rationale for the review in the context of what is already known	Yes, p. 4-5
Objectives	7	Provide an explicit statement of the question(s) the review will address with reference to participants, interventions, comparators, and outcomes (PICO)	Yes, p. 6
METHODS			
Eligibility criteria	8	Specify the study characteristics (such as PICO, study design, setting, time frame) and report characteristics (such as years considered, language, publication status) to be used as criteria for eligibility for the review	Yes, p. 6-7
Information sources	9	Describe all intended information sources (such as electronic databases, contact with study authors, trial registers or other grey literature sources) with planned dates of coverage	Yes, p. 6
Search strategy	10	Present draft of search strategy to be used for at least one electronic database, including planned limits, such that it could be repeated	Yes, see Appendix

Study records:			
Data management	11a	Describe the mechanism(s) that will be used to manage records and data throughout the review	NA
Selection process	11b	State the process that will be used for selecting studies (such as two independent reviewers) through each phase of the review (that is, screening, eligibility and inclusion in meta-analysis)	Yes, p. 7
Data collection process	11c	Describe planned method of extracting data from reports (such as piloting forms, done independently, in duplicate), any processes for obtaining and confirming data from investigators	Yes, p. 7
Data items	12	List and define all variables for which data will be sought (such as PICO items, funding sources), any pre-planned data assumptions and simplifications	Yes, p. 7
Outcomes and prioritization	13	List and define all outcomes for which data will be sought, including prioritization of main and additional outcomes, with rationale	Yes, p. 6
Risk of bias in individual studies	14	Describe anticipated methods for assessing risk of bias of individual studies, including whether this will be done at the outcome or study level, or both; state how this information will be used in data synthesis	Yes, p. 8
Data synthesis	15a	Describe criteria under which study data will be quantitatively synthesised	NA
	15b	If data are appropriate for quantitative synthesis, describe planned summary measures, methods of handling data and methods of combining data from studies, including any planned exploration of consistency (such as I^2, Kendall's τ)	NA
	15c	Describe any proposed additional analyses (such as sensitivity or subgroup analyses, meta-regression)	NA
	15d	If quantitative synthesis is not appropriate, describe the type of summary planned	NA
Meta-bias(es)	16	Specify any planned assessment of meta-bias(es) (such as publication bias across studies, selective reporting within studies)	NA
Confidence in cumulative evidence	17	Describe how the strength of the body of evidence will be assessed (such as GRADE)	NA

*** It is strongly recommended that this checklist be read in conjunction with the PRISMA-P Explanation and Elaboration (cite when available) for important clarification on the items. Amendments to a review protocol should be tracked and dated. The copyright for PRISMA-P (including checklist) is held by the PRISMA-P Group and is distributed under a Creative Commons Attribution Licence 4.0.**

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