

BMJ Open

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

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

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

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

If you have any questions on BMJ Open's open peer review process please email info.bmjopen@bmj.com

BMJ Open

Protocol for a Systematic Review on Effective Patient Positioning for Rapid Sequence Intubation

Journal:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2022-062988
Article Type:	Protocol
Date Submitted by the Author:	19-Mar-2022
Complete List of Authors:	Sivajohan, Asaanth; Schulich School of Medicine and Dentistry, Krause, Sarah; Schulich School of Medicine and Dentistry Hegazy, Ahmed; University of Western Ontario, Department of Anaesthesia and Perioperative Medicine Slessarev, Marat ; Western University, Medicine
Keywords:	Adult anaesthesia < ANAESTHETICS, Adult intensive & critical care < ANAESTHETICS, ACCIDENT & EMERGENCY MEDICINE

SCHOLARONE™
Manuscripts

Protocol for a Systematic Review on Effective Patient Positioning for Rapid Sequence

Intubation

Asaanth Sivajohan¹, Sarah Krause¹, Ahmed Hegazy², Marat Slessarev³

¹Schulich School of Medicine, Western University, London, ON, Canada

²Department of Anaesthesia and Perioperative Medicine, Western University, London, ON, Canada

³Department of Medicine, Western University, London, ON, Canada

*Correspondence: Asaanth Sivajohan, asivajohan2024@meds.uwo.ca, Tel: (647) 632 8658, 604 Winterton Way, Mississauga, ON, Canada L5R3J3

ABSTRACT

Introduction: Rapid Sequence Intubation (RSI) is an advanced airway technique to perform endotracheal intubation in patients at high risk of aspiration. Although RSI is recognized as a lifesaving technique and performed by many physicians in various settings (ER, ICUs), there is still a lack of consensus on various features of the procedure, most notably patient positioning. Previously, experts have commented on the unique drawbacks and benefits of various positions and studies have been published comparing patient positions and how it can affect endotracheal intubation in the context of RSI. The purpose of this systematic review is to compile the existing evidence to understand and compare how different patient positions can potentially affect the success of RSI.

Methods & Analysis: We will use MEDLINE, EMBASE, and the Cochrane Library to source studies that evaluate the impact of patient positioning on endotracheal intubation in the context of RSI. We will include randomized control trials, case-control studies, prospective/retrospective cohort studies and mannequin simulation studies for consideration in this systematic review. Subsequently, we will generate a PRISMA flow diagram to display how we selected our final studies for inclusion in the review. Two independent reviewers will complete the study screening, selection and extraction, with a third reviewer available to address any conflicts. The reviewers will extract this data in accordance with our outcomes of interest and display it in a table format to highlight patient-relevant outcomes and difficulty airway management outcomes. We will use the Risk of Bias tool and the Newcastle-Ottawa Scale to assess included studies for bias.

Ethics and dissemination: This systematic review does not require ethics approval as all patient-centred data will be reported from published studies.

1
2
3
4
5 **PROSPERO Registration Number: CRD42022289773**
6
7

8 **Study Strengths and Limitations:**
9

- 10
- 11 ● A comprehensive search of existing databases does not show any current
12 systematic reviews evaluating the impact of patient positioning on rapid sequence
13 intubation.
14
 - 15 ● This review will report patient-centred outcomes that are clinically relevant. In
16 addition, this review will also report outcomes associated with difficult airway
17 management which will be important for physicians who are required to intubate
18 patients.
19
 - 20 ● The limited exclusion criteria in this review will allow for a broad selection of
21 papers to be considered for the full text review stage.
22
 - 23 ● We anticipate most of the studies in the full text review will be studies involving
24 mannequin simulation scenarios.
25
- 26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

INTRODUCTION

During traditional elective surgeries requiring intubation, patients are fasted to prevent pulmonary aspiration. This is of particular importance during induction and intubation, as the administration of neuromuscular blockade prevents any protective gag reflexes, making the airways especially vulnerable to aspiration[1,2]. In an emergent patient requiring immediate intubation, the healthcare providers encounter the possibility of intubating a patient with a full stomach, which can have severe life-threatening complications. Rapid Sequence Intubation (RSI) is an advanced airway technique to achieve endotracheal intubation in patients at high risk of aspiration [3]. Despite RSI originating as an operating room procedure, its practise has extended to emergency departments, intensive care units and pre-hospital settings [4–6] and is often performed by physicians other than anaesthesiologists. Despite RSI's prevalence and recognition as a life-saving procedure there are still several features of the RSI methodology that are controversial and lack consensus [3,4].

Recently there have been systematic reviews to elucidate how various components of RSI influence safety and patient outcomes, which are crucial in refining the RSI procedure. Systematic reviews on RSI have investigated the role of specific induction agents [7], compared the efficacy of different paralytics and the ideal doses [8,9], and the effectiveness of applying cricoid pressure [10]. These are crucial aspects of RSI, however a feature of RSI that would benefit from a review of the current available evidence is patient positioning and how this contributes to safety and patient outcomes.

Patient positioning in anaesthesia can contribute to the ease or difficulty of intubation and have substantial effects on a patient's physiology such as their ventilation and hemodynamics

1
2
3 [11]. The supine position is most commonly used to anaesthetise patients because of its ease
4 of intubation, despite some compromise in ventilation abilities as the abdominal contents
5 move superiorly compressing lung volumes [3,6,11]. Despite its prevalence under standard
6 conditions there is controversy over its use in RSI as there is an increased risk of gastric
7 aspiration in this position - gastric contents do not have to work against gravity to escape the
8 upper oesophagus - potentially making this a less favourable position for RSI [11,12].
9

10
11
12
13
14
15
16
17 Considering this, healthcare practitioners have explored other patient positions with their own
18 unique drawbacks and benefits. For instance, the head-down (Trendelenburg) position may
19 be beneficial in RSI since gravity redirects gastric contents away from the trachea should
20 regurgitation occur. However, this potential benefit may come at the cost of a difficult view
21 and ventilation being further compromised (relative to the supine position) as abdominal
22 contents compress lung volume [3,11,13].
23
24
25
26
27
28
29

30
31
32
33 The controversy over patient positioning in RSI is well-recognized within the medical
34 literature [3,4]. Furthermore, the risk of aspiration during RSI (0.5%-2.8%) remains relatively
35 high when compared to standard conditions (0.01%-0.04%) [14]. A systematic review which
36 summarizes the current evidence-based understanding on the effectiveness of patient
37 positions can inform clinical practise and provide a footing for further research and
38 innovation in this field.
39
40
41
42
43
44
45
46
47
48

49 **AIMS**

50
51 The purpose of this systematic review is to evaluate the effect of different patient
52 positions in the context of Rapid Sequence Intubation on the ease of intubation, safety, and
53 patient outcome(s).
54
55
56
57
58
59
60

METHODOLOGY

The PICO strategy is outlined below in Table 1. We used the PRISMA-P guidelines to guide the development of this systematic review protocol [15].

Table 1. Inclusion and Exclusion Criteria

POPULATION	Adult (≥ 18 year-old) patients and mannequin simulation exercises
INTERVENTION	Non-conventional patient positions (Head-down position, Head-up position, etc.)
COMPARATOR	Supine patient position
OUTCOME	Patient-centred outcomes (desaturation episodes/hypoxemia events, hypoxia, lowest oxygen saturation, aspiration events, duration of mechanical ventilation, ventilator-free days, ICU-free days, overall mortality etc.) and outcomes associated with difficult airway management (laryngoscopic view, time required to intubate, successful first-pass intubation, aspiration volume etc.)

Types of Studies

Study designs will include randomized controlled trials, prospective and retrospective observational cohort studies, and case-control studies, which can each involve mannequins or human participants. To the best of our knowledge there are no systematic reviews investigating patient positioning in the context of RSI and its impact on intubation procedure, safety, and patient outcome(s). There are no restrictions with regards to the sample size or publication date of the studies. Only studies published in English will be included.

Types of Participants

Inclusion Criteria:

- (1) Adult (≥ 18 years old) patients

1
2
3 (2) RSI or emergent intubation
4

5 (3) Intubation procedures done by anaesthesiologists, anaesthetic trainees, emergency
6
7 physicians, critical care physicians and medical learners.
8
9

10 *Exclusion Criteria:*

11
12 (1) Paediatric patients

13
14 (2) Studies in languages other than English
15
16
17
18
19
20
21
22
23
24
25

26 **Types of Intervention**

27
28 Interventions of interest will include the following non-exhaustive list of patient positions:
29
30 Trendelenburg (head down) position, reverse Trendelenburg (head up) position, semi-erect
31
32 position, supine position, and ramped positions at differing angles.
33
34
35
36
37

38 **Comparator**

39
40 We expect that many studies have used the supine position as a comparator, however we do
41
42 not anticipate all studies to have done this and suspect some may have compared two non-
43
44 conventional patient positions with each other.
45
46
47
48

49 **Types of Outcome**

50
51 Outcomes of interest include desaturation episodes, aspiration events (+volumes), duration of
52
53 ventilation, mortality, time to intubation, successful first-pass intubation, and rating of
54
55 laryngoscopic view.
56
57
58
59
60

Search Strategy

We will conduct an initial search of MEDLINE with the assistance of our institute's trained clinical librarian in order to locate appropriate keywords in study titles and abstracts. We will then use these keywords to perform a comprehensive search of the following databases: MEDLINE, EMBASE, Cochrane Library. We will then upload the title and their corresponding abstracts sourced from this search into Covidence (the online systematic review system).

Study Selection

Two independent reviewers will examine the title and abstract for each study against the inclusion/exclusion criteria in Covidence. We will then consider studies with concordant approval for full text review. A third independent reviewer, not involved in the initial screening, will review studies with discordant reviews to decide whether a study will be considered for full text review. We will then appraise the full text studies to determine if they are eligible for inclusion in the review. Covidence will generate a Preferred Reporting Items for Systematic Review and Meta-Analyses (PRISMA) flow diagram, which will display the number of studies initially screened, reviewed, and excluded after full text review with their accompanying reasons(s).

Data Extraction

Two independent reviewers will conduct data extraction using Covidence's data extraction tool. We will flag missing or discordant data for review, which will be resolved by a third independent reviewer. We will extract the following information from each study:

- i. **Study Characteristics** – Study type, country, date of publication, patient/mannequin study, setting (critical care, emergency department, operating room,

1
2
3 etc.), speciality of physician performing intubation (anaesthesiologist,
4 emergency room doctor, medical learner, etc.), funding sources.
5
6

7
8 **ii. Population Characteristics**
9

- 10 **a.** For studies involving patients: age, sex, body mass index (BMI), pre-
11 existing morbidity (obstructive sleep apnea, acute respiratory distress
12 syndrome, etc.), indications for intubation, years of clinical experience of
13 participating physician(s), overall mortality.
14
15 **b.** For studies involving mannequins: mannequin model, regurgitation trigger
16 stimulated (yes/no), simulated difficult airway scenarios.
17
18

19 **iii. Intervention Characteristics** - Positioning method of the patient/mannequin
20 (Trendelenburg position, reverse Trendelenburg, etc.) including the degree of
21 incline in the ramped position and years of clinical experience of the
22 participating physician. For studies involving human participants, age, sex,
23 BMI, and pre-existing morbidity will also be extracted.
24
25

26 **iv. Comparator Characteristics** – Comparator(s) of interest include the supine
27 position and years of clinical experience of the participating physician. For
28 studies involving human participants, age, sex, BMI, and pre-existing morbidity
29 will also be extracted.
30
31

32 **v. Outcomes** – Outcomes of interest include lowest oxygenation saturation (%),
33 incidence of desaturation/hypoxemia episodes, incidence of hypoxia events,
34 incidence of aspiration events, duration of mechanical ventilation, ventilator-
35 free days, ICU-free days, and overall mortality. Secondary outcomes centred
36 around the process of intubation include rating of laryngoscopic view (ex:
37 Comrack-Lehane grade of view), time required for intubation, successful first-
38 pass intubation, and aspiration volume will also be extracted.
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

Methodological Appraisal

We will assess each study selected for data-extraction for bias using validated tools specific for the type of study. We will use the Cochrane Risk of Bias tool to assess and report the risk of bias in randomized control trials across all domains (randomization process, missing outcome data, etc.). We will use the Newcastle-Ottawa Quality Assessment Scale to assess bias in case-control and prospective/retrospective cohort studies.

Data synthesis

We will examine full-text studies for the outcomes listed above. If possible, we will stratify outcomes into patient-centred/clinical outcomes and outcomes associated with difficult airway management (laryngoscopic grade of view, time required for intubation, successful first-pass intubation, etc.). We also plan on reporting outcomes associated with difficult airway management stratified by the type of study (mannequin study versus patient study). We will report all quantitative outcomes (e.g. time to intubation) using mean/median values with an accompanying standard deviation/confidence interval in a table format. We do not anticipate sourcing enough studies to perform a meta-analysis.

Patient and Public Involvement

Patients and/or the public will not be directly involved in this systematic review as all relevant metrics will be sourced from original published studies.

FUNDING

None

CONFLICTS OF INTEREST

There are no conflicts of interest to report for any of the authors involved.

DATA SHARING STATEMENT

Data sharing is not applicable to this protocol or the systematic review as we are not creating or analysing new data. All data used in the systematic review comes from published publicly available studies.

AUTHOR CONTRIBUTIONS

AS, MS and AH all worked on designing the protocol. AS and SK worked on writing the drafts of the protocol. All authors provided feedback and edited the final version of this protocol for submission.

SUPPLEMENTARY INFORMATION

Author Contact Information

Asaanth Sivajohan: asivajohan2024@meds.uwo.ca

Sarah Krause: skrause2024@meds.uwo.ca

Ahmed Hegazy: ahmed.hegazy@lhsc.on.ca

Marat Slessarev: marat.slessarev@lhsc.on.ca

Keywords

Rapid Sequence Intubation, Rapid Sequence Induction, Emergent Intubation, Patient Positioning, Supine Position.

Wordcount: 1719 Words

REFERENCES

- 1 Takenaka I, Aoyama K. Prevention of aspiration of gastric contents during attempt in tracheal intubation in the semi-lateral and lateral positions. *World J Emerg Med* 2016;**7**:285–9. doi:10.5847/wjem.j.1920-8642.2016.04.008
- 2 Sinclair RC, Luxton MC. Rapid sequence induction. *Continuing Education in Anaesthesia Critical Care & Pain* 2005;**5**:45–8. doi:10.1093/bjaceaccp/mki016
- 3 El-Orbany M, Connolly LA. Rapid Sequence Induction and Intubation: Current Controversy. *Anesthesia & Analgesia* 2010;**110**:1318–25. doi:10.1213/ANE.0b013e3181d5ae47
- 4 Avery P, Morton S, Raitt J, *et al.* Rapid sequence induction: where did the consensus go? *Scandinavian Journal of Trauma, Resuscitation and Emergency Medicine* 2021;**29**:64. doi:10.1186/s13049-021-00883-5
- 5 Turner J, Bourn S, Raitt J, *et al.* Pre-hospital emergency anaesthesia in the United Kingdom: an observational cohort study. *Br J Anaesth* 2020;**124**:579–84. doi:10.1016/j.bja.2020.01.023
- 6 Hillman K. Critical care without walls. *Current Opinion in Critical Care* 2002;**8**:594–9.
- 7 Baekgaard JS, Eskesen TG, Sillesen M, *et al.* Ketamine as a Rapid Sequence Induction Agent in the Trauma Population: A Systematic Review. *Anesthesia & Analgesia* 2019;**128**:504–10. doi:10.1213/ANE.0000000000003568
- 8 Tran DTT, Newton EK, Mount V a. H, *et al.* Rocuronium vs. succinylcholine for rapid sequence intubation: a Cochrane systematic review. *Anaesthesia* 2017;**72**:765–77. doi:10.1111/anae.13903
- 9 Putzu A, Tramèr MR, Giffa M, *et al.* The optimal dose of succinylcholine for rapid sequence induction: a systematic review and meta-analysis of randomized trials. *BMC Anesthesiology* 2020;**20**:54. doi:10.1186/s12871-020-00968-1
- 10 Algie CM, Mahar RK, Tan HB, *et al.* Effectiveness and risks of cricoid pressure during rapid sequence induction for endotracheal intubation. *Cochrane Database Syst Rev* 2015;:CD011656. doi:10.1002/14651858.CD011656.pub2
- 11 Knight DJ, Mahajan RP. Patient positioning in anaesthesia. *Continuing Education in Anaesthesia Critical Care & Pain* 2004;**4**:160–3. doi:10.1093/bjaceaccp/mkh044
- 12 Inkster JS. THE INDUCTION OF ANAESTHESIA IN PATIENTS LIKELY TO VOMIT WITH SPECIAL REFERENCE TO INTESTINAL OBSTRUCTION. *British Journal of Anaesthesia* 1963;**35**:160–7. doi:10.1093/bja/35.3.160
- 13 Cameron JL, Zuidema GD. Aspiration Pneumonia: Magnitude and Frequency of the Problem. *JAMA* 1972;**219**:1194–6. doi:10.1001/jama.1972.03190350034009
- 14 Zdravkovic M, Berger-Estilita J, Sorbello M, *et al.* An international survey about rapid sequence intubation of 10,003 anaesthetists and 16 airway experts. *Anaesthesia* 2020;**75**:313–22. doi:10.1111/anae.14867

15 Moher D, Shamseer L, Clarke M, *et al.* Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015 statement. *Systematic Reviews* 2015;4:1. doi:10.1186/2046-4053-4-1

For peer review only

Reporting checklist for protocol of a systematic review and meta analysis.

Based on the PRISMA-P guidelines.

Instructions to authors

Complete this checklist by entering the page numbers from your manuscript where readers will find each of the items listed below.

Your article may not currently address all the items on the checklist. Please modify your text to include the missing information. If you are certain that an item does not apply, please write "n/a" and provide a short explanation.

Upload your completed checklist as an extra file when you submit to a journal.

In your methods section, say that you used the PRISMA-Reporting guidelines, and cite them as:

Moher D, Shamseer L, Clarke M, Ghersi D, Liberati A, Petticrew M, Shekelle P, Stewart LA. Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols (PRISMA-P) 2015 statement. Syst Rev. 2015;4(1):1.

	Reporting Item	Page Number
Title		
Identification	#1a Identify the report as a protocol of a systematic review	1
Update	#1b If the protocol is for an update of a previous systematic review, identify as such	n/a (the protocol is for an original systematic

review)

Registration

[#2](#) If registered, provide the name of the registry (such as PROSPERO) and registration number 3

Authors**Contact**

[#3a](#) Provide name, institutional affiliation, e-mail address of all protocol authors; provide physical mailing address of corresponding author 1,11

Contribution

[#3b](#) Describe contributions of protocol authors and identify the guarantor of the review 11

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 n/a (this protocol is for an original systematic review)

Support**Sources**

[#5a](#) Indicate sources of financial or other support for the review 10

Sponsor

[#5b](#) Provide name for the review funder and / or sponsor n/a (this review is not receiving any financial support)

Role of sponsor

[#5c](#) Describe roles of funder(s), sponsor(s), and / or n/a (this review is

1	or funder		institution(s), if any, in developing the protocol	not receiving any
2				financial support)
3				
4				
5				
6	Introduction			
7				
8				
9	Rationale	#6	Describe the rationale for the review in the context of	4-5
10			what is already known	
11				
12				
13				
14	Objectives	#7	Provide an explicit statement of the question(s) the	6
15			review will address with reference to participants,	
16			interventions, comparators, and outcomes (PICO)	
17				
18				
19				
20				
21				
22	Methods			
23				
24				
25	Eligibility criteria	#8	Specify the study characteristics (such as PICO,	6-7,12
26			study design, setting, time frame) and report	
27			characteristics (such as years considered, language,	
28			publication status) to be used as criteria for eligibility	
29			for the review	
30				
31				
32				
33				
34				
35				
36				
37	Information	#9	Describe all intended information sources (such as	7
38			electronic databases, contact with study authors, trial	
39	sources		registers or other grey literature sources) with planned	
40			dates of coverage	
41				
42				
43				
44				
45				
46				
47	Search strategy	#10	Present draft of search strategy to be used for at least	7
48			one electronic database, including planned limits,	
49			such that it could be repeated	
50				
51				
52				
53				
54	Study records -	#11a	Describe the mechanism(s) that will be used to	7-8
55			manage records and data throughout the review	
56	data			
57				
58				
59				
60				

1	management		
2			
3			
4	Study records -	#11b	8
5		State the process that will be used for selecting	
6	selection process	studies (such as two independent reviewers) through	
7		each phase of the review (that is, screening, eligibility	
8		and inclusion in meta-analysis)	
9			
10			
11			
12			
13	Study records -	#11c	8-9
14		Describe planned method of extracting data from	
15	data collection	reports (such as piloting forms, done independently,	
16		in duplicate), any processes for obtaining and	
17	process	confirming data from investigators	
18			
19			
20			
21			
22			
23	Data items	#12	8-9
24		List and define all variables for which data will be	
25		sought (such as PICO items, funding sources), any	
26		pre-planned data assumptions and simplifications	
27			
28			
29			
30			
31	Outcomes and	#13	9
32		List and define all outcomes for which data will be	
33	prioritization	sought, including prioritization of main and additional	
34		outcomes, with rationale	
35			
36			
37			
38			
39	Risk of bias in	#14	9-10
40		Describe anticipated methods for assessing risk of	
41	individual studies	bias of individual studies, including whether this will	
42		be done at the outcome or study level, or both; state	
43		how this information will be used in data synthesis	
44			
45			
46			
47			
48	Data synthesis	#15a	10
49		Describe criteria under which study data will be	
50		quantitatively synthesised	
51			
52			
53			
54	Data synthesis	#15b	10
55		If data are appropriate for quantitative synthesis,	
56		describe planned summary measures, methods of	
57			
58			
59			
60			

handling data and methods of combining data from studies, including any planned exploration of consistency (such as I², Kendall's τ)

1			
2			
3			
4			
5			
6			
7			
8	Data synthesis	#15c	n/a
9		Describe any proposed additional analyses (such as	
10		sensitivity or subgroup analyses, meta-regression)	
11			
12			
13	Data synthesis	#15d	10
14		If quantitative synthesis is not appropriate, describe	
15		the type of summary planned	
16			
17			
18	Meta-bias(es)	#16	9
19		Specify any planned assessment of meta-bias(es)	
20		(such as publication bias across studies, selective	
21		reporting within studies)	
22			
23			
24			
25			
26	Confidence in	#17	9
27	cumulative	Describe how the strength of the body of evidence will	
28	evidence	be assessed (such as GRADE)	
29			
30			
31			
32			
33			

Notes:

- 37 • 1b: n/a (the protocol is for an original systematic review)
- 38
- 39
- 40 • 4: n/a (this protocol is for an original systematic review)
- 41
- 42
- 43 • 5b: n/a (this review is not receiving any financial support)
- 44
- 45
- 46 • 5c: n/a (this review is not receiving any financial support)
- 47
- 48
- 49 • The PRISMA-P elaboration and explanation paper is distributed under the terms of the Creative
- 50 Commons Attribution License CC-BY. This checklist was completed on 14. March 2022 using
- 51 <https://www.goodreports.org/>, a tool made by the [EQUATOR Network](#) in collaboration with
- 52 [Penelope.ai](#)
- 53
- 54
- 55
- 56
- 57
- 58
- 59
- 60

BMJ Open

Protocol for a Systematic Review on Effective Patient Positioning for Rapid Sequence Intubation

Journal:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2022-062988.R1
Article Type:	Protocol
Date Submitted by the Author:	08-Aug-2022
Complete List of Authors:	Sivajohan, Asaanth; Schulich School of Medicine and Dentistry, Krause, Sarah; Schulich School of Medicine and Dentistry Hegazy, Ahmed; University of Western Ontario, Department of Anaesthesia and Perioperative Medicine Slessarev, Marat ; Western University, Medicine
Primary Subject Heading:	Anaesthesia
Secondary Subject Heading:	Emergency medicine
Keywords:	Adult anaesthesia < ANAESTHETICS, Adult intensive & critical care < ANAESTHETICS, ACCIDENT & EMERGENCY MEDICINE

SCHOLARONE™
Manuscripts

Protocol for a Systematic Review on Effective Patient Positioning for Rapid Sequence

Intubation

Asaanth Sivajohan¹, Sarah Krause¹, Ahmed Hegazy², Marat Slessarev³

¹Schulich School of Medicine, Western University, London, ON, Canada

²Department of Anaesthesia and Perioperative Medicine, Western University, London, ON, Canada

³Department of Medicine, Western University, London, ON, Canada

*Correspondence: Asaanth Sivajohan, asivajohan2024@meds.uwo.ca, Tel: (647) 632 8658, 604 Winterton Way, Mississauga, ON, Canada L5R3J3

ABSTRACT

Introduction: Rapid Sequence Intubation (RSI) is an advanced airway technique to perform endotracheal intubation in patients at high risk of aspiration. Although RSI is recognized as a lifesaving technique and performed by many physicians in various settings (Emergency Departments, Intensive Care Units), there is still a lack of consensus on various features of the procedure, most notably patient positioning. Previously, experts have commented on the unique drawbacks and benefits of various positions and studies have been published comparing patient positions and how it can affect endotracheal intubation in the context of RSI. The purpose of this systematic review is to compile the existing evidence to understand and compare how different patient positions can potentially affect the success of RSI.

Methods & Analysis: We will use MEDLINE, EMBASE, and the Cochrane Library to source studies from 1946 – 2021 that evaluate the impact of patient positioning on endotracheal intubation in the context of RSI. We will include randomized control trials, case-control studies, prospective/retrospective cohort studies and mannequin simulation studies for consideration in this systematic review. Subsequently, we will generate a PRISMA flow diagram to display how we selected our final studies for inclusion in the review. Two independent reviewers will complete the study screening, selection and extraction, with a third reviewer available to address any conflicts. The reviewers will extract this data in accordance with our outcomes of interest and display it in a table format to highlight patient-relevant outcomes and difficulty airway management outcomes. We will use the Risk of Bias tool and the Newcastle-Ottawa Scale to assess included studies for bias.

Ethics and dissemination: This systematic review does not require ethics approval as all patient-centred data will be reported from published studies.

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

PROSPERO Registration Number: CRD42022289773

Study Strengths and Limitations:

- A comprehensive search of existing databases does not show any current systematic reviews evaluating the impact of patient positioning on rapid sequence intubation.
 - This review will report patient-centred outcomes that are clinically relevant. In addition, this review will also report outcomes associated with difficult airway management which will be important for physicians who are required to intubate patients.
 - The limited exclusion criteria in this review will allow for a broad selection of papers to be considered for the full text review stage.
 - We anticipate most of the studies in the full text review will be studies involving mannequin simulation scenarios.
- peer review only

INTRODUCTION

During traditional elective surgeries requiring intubation, patients are fasted to prevent pulmonary aspiration. This is of particular importance during induction and intubation, as the administration of neuromuscular blockade prevents any protective gag reflexes, making the airways especially vulnerable to aspiration [1,2]. In an emergent patient requiring immediate intubation, the healthcare providers encounter the possibility of intubating a patient with a full stomach, which can have severe life-threatening complications. Rapid Sequence Intubation (RSI) is an advanced airway technique to achieve endotracheal intubation in patients at high risk of aspiration [3]. Despite RSI originating as an operating room procedure, its practise has extended to emergency departments (ED), intensive care units (ICU) and pre-hospital settings [4–6] and is often performed by physicians other than anaesthesiologists. Despite RSI's prevalence and recognition as a life-saving procedure there are still several features of the RSI methodology that are controversial and lack consensus [3,4].

Recently there have been systematic reviews to elucidate how various components of RSI influence safety and patient outcomes, which are crucial in refining the RSI procedure. Systematic reviews on RSI have investigated the role of specific induction agents [7], compared the efficacy of different paralytics and the ideal doses [8,9], and the effectiveness of applying cricoid pressure [10]. These are crucial aspects of RSI, however a feature of RSI that would benefit from a review of the current available evidence is patient positioning and how this contributes to safety and patient outcomes.

1
2
3 Patient positioning in anaesthesia can contribute to the ease or difficulty of intubation and
4
5 have substantial effects on a patient's physiology such as their ventilation and hemodynamics
6
7 [11]. The supine position is most commonly used to anaesthetise patients because of its ease
8
9 of intubation, despite some compromise in ventilation abilities as the abdominal contents
10
11 move superiorly compressing lung volumes [3,6,11]. Despite its prevalence under standard
12
13 conditions there is controversy over its use in RSI as there is an increased risk of gastric
14
15 aspiration in this position - gastric contents do not have to work against gravity to escape the
16
17 upper oesophagus - potentially making this a less favourable position for RSI [11,12].
18
19 Considering this, healthcare practitioners have explored other patient positions with their own
20
21 unique drawbacks and benefits. For instance, the head-down (Trendelenburg) position may
22
23 be beneficial in RSI since gravity redirects gastric contents away from the trachea should
24
25 regurgitation occur. However, this potential benefit may come at the cost of a difficult view
26
27 and ventilation being further compromised (relative to the supine position) as abdominal
28
29 contents compress lung volume [3,11,13].
30
31
32
33
34
35
36
37

38 The controversy over patient positioning in RSI is well-recognized within the medical
39
40 literature [3,4]. Furthermore, the risk of aspiration during RSI (0.5%-2.8%) remains relatively
41
42 high when compared to standard conditions (0.01%-0.04%) [14]. A systematic review which
43
44 summarizes the current evidence-based understanding on the effectiveness of patient
45
46 positions can inform clinical practise and provide a footing for further research and
47
48 innovation in this field.
49
50
51
52
53

54 AIMS

55
56
57
58
59
60

The purpose of this systematic review is to evaluate the effect of different patient positions in the context of Rapid Sequence Intubation on patient safety outcomes and procedural outcomes.

METHODOLOGY

The PICO strategy is outlined below in Table 1. We used the PRISMA-P guidelines to guide the development of this systematic review protocol [15].

Table 1. Inclusion and Exclusion Criteria

POPULATION	Adult (≥ 18 year-old) patients and mannequin simulation exercises
INTERVENTION	Non-conventional patient positions (Head-down position, Head-up position, etc.)
COMPARATOR	Supine patient position
OUTCOME	Patient-centred outcomes (desaturation episodes/hypoxemia events, hypoxia, lowest oxygen saturation, aspiration events, duration of mechanical ventilation, ventilator-free days, ICU-free days, overall mortality etc.) and outcomes associated with difficult airway management (laryngoscopic view, time required to intubate, successful first-pass intubation, aspiration volume etc.)

Types of Studies

Study designs will include randomized controlled trials, prospective and retrospective observational cohort studies, and case-control studies, which can each involve mannequins or human participants. To the best of our knowledge there are no systematic reviews investigating patient positioning in the context of RSI and its impact on intubation procedure, safety, and patient outcome(s). There are no restrictions with regards to the sample size or publication date

1
2
3 of the studies. The end date of screening will be November 24, 2021. Only studies published
4
5 in English will be included.
6
7
8
9

10 **Types of Participants**

11 *Inclusion Criteria:*

- 14 (1) Adult (≥ 18 years old) patients
- 16 (2) RSI or emergent intubation
- 17 (3) Intubation procedures done by physician anaesthesiologists, anaesthetic trainees,
18
19 emergency physicians, critical care physicians and medical learners.
20
21
22

23 *Exclusion Criteria:*

- 24 (1) Paediatric patients
- 25 (2) Studies in languages other than English
- 26 (3) The speciality of the physician performing RSI differs between intervention and
27
28 control group
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44

45 **Types of Intervention**

46 Interventions of interest will include the following non-exhaustive list of patient positions:
47
48 Trendelenburg (head down) position, reverse Trendelenburg (head up) position, semi-erect
49
50 position, supine position, and ramped positions at differing angles.
51
52
53
54
55

56 **Comparator**

1
2
3 We expect that many studies have used the supine position as a comparator, however we do
4 not anticipate all studies to have done this and suspect some may have compared two non-
5 conventional patient positions with each other. Studies comparing two non-conventional
6 positions will be reported and compared individually in relation to each other but will not be
7 included in any sensitivity analysis.
8
9
10
11
12
13
14
15
16

17 **Types of Outcome**

18
19 Our primary outcomes of interest are patient safety outcomes which include hypoxemia,
20 desaturation, aspiration, length of mechanical ventilation, ventilator-free days, ICU-free days,
21 and hospital mortality. Our secondary outcomes of interest aim to examine procedural
22 outcomes such as the glottic view, time to intubate, successful first-pass intubation, and
23 aspiration volume.
24
25
26
27
28
29

30 Given that we cannot assess our primary patient safety outcomes in mannequin studies, we will
31 only assess for secondary outcomes in these studies. In human studies both primary and
32 secondary outcomes will be evaluated.
33
34
35
36
37
38
39

40 **Search Strategy**

41
42 We will conduct an initial search of MEDLINE with the assistance of our institute's trained
43 clinical librarian in order to locate appropriate keywords in study titles and abstracts. We will
44 then use these keywords to perform a comprehensive search of the following databases:
45 MEDLINE, EMBASE, Cochrane Library. We will then upload the title and their corresponding
46 abstracts sourced from this search into Covidence (the online systematic review system).
47
48
49
50
51
52
53
54
55

56 **Study Selection**

1
2
3 Two independent reviewers will examine the title and abstract for each study against the
4 inclusion/exclusion criteria in Covidence. We will then consider studies with concordant
5 approval for full text review. A third independent reviewer, not involved in the initial screening,
6 will review studies with discordant reviews to decide whether a study will be considered for
7 full text review. We will then appraise the full text studies to determine if they are eligible for
8 inclusion in the review. Covidence will generate a Preferred Reporting Items for Systematic
9 Review and Meta-Analyses (PRISMA) flow diagram, which will display the number of studies
10 initially screened, reviewed, and excluded after full text review with their accompanying
11 reasons(s).
12
13
14
15
16
17
18
19
20
21
22
23
24
25

26 **Data Extraction**

27
28 Two independent reviewers will conduct data extraction using Covidence's data extraction
29 tool. We will flag missing or discordant data for review, which will be resolved by a third
30 independent reviewer. We will extract the following information from each study:
31
32
33

- 34
35 **i. Study Characteristics** – Study type, country, date of publication, patient/
36 mannequin study, setting (critical care, emergency department, operating room,
37 etc.), speciality of physician performing intubation (physician anaesthesiologist,
38 emergency room doctor, medical learner, etc.), materials used in intubation,
39 funding sources.
40
41
42
43
44
45
- 46
47 **ii. Population Characteristics**
 - 48
49 **a.** For studies involving patients: age, sex, body mass index (BMI), pre-
50 existing morbidity (obstructive sleep apnea, acute respiratory distress
51 syndrome, etc.), indications for intubation, years of clinical experience of
52 participating physician(s), overall mortality.
53
54
55
56
57
58
59
60

Data synthesis

We will examine full-text studies for the outcomes listed above. If possible, we will stratify outcomes into patient-centred/clinical outcomes and outcomes associated with difficult airway management (laryngoscopic grade of view, time required for intubation, successful first-pass intubation, etc.). We will stratify all the studies involving human participants by the speciality of the physician conducting intubation. We also plan on reporting outcomes associated with difficult airway management stratified by the type of study (mannequin study versus patient study). We will report all quantitative continuous variables (e.g. time to intubation) using mean/median values with an accompanying standard deviation/confidence interval and categorical variables (e.g incidence of aspiration) as a percentage in a table format. While we do not anticipate enough studies with similar methodology and outcomes, if we do encounter sufficient data, we will perform a meta-analysis using Review Manager 5.3 provided by the Cochrane Collaboration (Oxford, United Kingdom) and report heterogeneity using the I^2 statistic, where values $>50\%$ indicated moderate heterogeneity. A random-effects model will be used when combined studies demonstrated at least moderate heterogeneity.

Sensitivity Analysis

If the data is sufficient, we will perform sensitivity analyses on the speciality of the physician performing intubation and the material used during intubation to elucidate the effect of these characteristics on patient safety and procedural outcomes during RSI. In addition, with sufficient data, to ensure the consistency of results we will perform a sensitivity analysis based on the type of study design (human or mannequin)

Patient and Public Involvement

1
2
3 Patients and/or the public will not be directly involved in this systematic review as all relevant
4 metrics will be sourced from original published studies.
5
6
7
8
9

10 **Ethics and Dissemination**

11
12 Ethics approval is not required as this systematic review will use published data. The findings
13 will be disseminated through publication in a suitable peer-reviewed journal and presentation at
14 an appropriate conference.
15
16
17
18
19

20 **FUNDING**

21
22 None
23
24
25
26
27

28 **CONFLICTS OF INTEREST**

29
30 There are no conflicts of interest to report for any of the authors involved.
31
32
33
34

35 **DATA SHARING STATEMENT**

36
37 Data sharing is not applicable to this protocol or the systematic review as we are not creating
38 or analysing new data. All data used in the systematic review comes from published publicly
39 available studies.
40
41
42
43
44
45

46 **AUTHOR CONTRIBUTIONS**

47
48 AS, MS and AH all worked on designing the protocol. AS and SK worked on writing the drafts
49 of the protocol. All authors provided feedback and edited the final version of this protocol for
50 submission.
51
52
53
54
55
56
57

58 **SUPPLEMENTARY INFORMATION**

Author Contact Information

Asanth Sivajohan: asivajohan2024@meds.uwo.ca

Sarah Krause: skrause2024@meds.uwo.ca

Ahmed Hegazy: ahmed.hegazy@lhsc.on.ca

Marat Slessarev: marat.slessarev@lhsc.on.ca

Keywords

Rapid Sequence Intubation, Rapid Sequence Induction, Emergent Intubation, Patient Positioning, Supine Position.

Wordcount: 2364 Words

REFERENCES

- 1 Takenaka I, Aoyama K. Prevention of aspiration of gastric contents during attempt in tracheal intubation in the semi-lateral and lateral positions. *World J Emerg Med* 2016;**7**:285–9. doi:10.5847/wjem.j.1920-8642.2016.04.008
- 2 Sinclair RC, Luxton MC. Rapid sequence induction. *Continuing Education in Anaesthesia Critical Care & Pain* 2005;**5**:45–8. doi:10.1093/bjaceaccp/mki016
- 3 El-Orbany M, Connolly LA. Rapid Sequence Induction and Intubation: Current Controversy. *Anesthesia & Analgesia* 2010;**110**:1318–25. doi:10.1213/ANE.0b013e3181d5ae47
- 4 Avery P, Morton S, Raitt J, *et al.* Rapid sequence induction: where did the consensus go? *Scandinavian Journal of Trauma, Resuscitation and Emergency Medicine* 2021;**29**:64. doi:10.1186/s13049-021-00883-5
- 5 Turner J, Bourn S, Raitt J, *et al.* Pre-hospital emergency anaesthesia in the United Kingdom: an observational cohort study. *Br J Anaesth* 2020;**124**:579–84. doi:10.1016/j.bja.2020.01.023
- 6 Hillman K. Critical care without walls. *Current Opinion in Critical Care* 2002;**8**:594–9.
- 7 Baekgaard JS, Eskesen TG, Sillesen M, *et al.* Ketamine as a Rapid Sequence Induction Agent in the Trauma Population: A Systematic Review. *Anesthesia & Analgesia* 2019;**128**:504–10. doi:10.1213/ANE.0000000000003568
- 8 Tran DTT, Newton EK, Mount V a. H, *et al.* Rocuronium vs. succinylcholine for rapid sequence intubation: a Cochrane systematic review. *Anaesthesia* 2017;**72**:765–77. doi:10.1111/anae.13903

- 1
2
3 9 Putzu A, Tramèr MR, Giffa M, *et al.* The optimal dose of succinylcholine for rapid
4 sequence induction: a systematic review and meta-analysis of randomized trials. *BMC*
5
6 *Anesthesiology* 2020;**20**:54. doi:10.1186/s12871-020-00968-1
7
8
9
10
11 10 Algie CM, Mahar RK, Tan HB, *et al.* Effectiveness and risks of cricoid pressure during
12 rapid sequence induction for endotracheal intubation. *Cochrane Database Syst Rev*
13 2015;:CD011656. doi:10.1002/14651858.CD011656.pub2
14
15
16
17
18
19 11 Knight DJ, Mahajan RP. Patient positioning in anaesthesia. *Continuing Education in*
20 *Anaesthesia Critical Care & Pain* 2004;**4**:160–3. doi:10.1093/bjaceaccp/mkh044
21
22
23
24
25 12 Inkster JS. THE INDUCTION OF ANAESTHESIA IN PATIENTS LIKELY TO
26 VOMIT WITH SPECIAL REFERENCE TO INTESTINAL OBSTRUCTION. *British*
27 *Journal of Anaesthesia* 1963;**35**:160–7. doi:10.1093/bja/35.3.160
28
29
30
31
32
33 13 Cameron JL, Zuidema GD. Aspiration Pneumonia: Magnitude and Frequency of the
34 Problem. *JAMA* 1972;**219**:1194–6. doi:10.1001/jama.1972.03190350034009
35
36
37
38
39 14 Zdravkovic M, Berger-Estilita J, Sorbello M, *et al.* An international survey about rapid
40 sequence intubation of 10,003 anaesthetists and 16 airway experts. *Anaesthesia*
41 2020;**75**:313–22. doi:10.1111/anae.14867
42
43
44
45
46 15 Moher D, Shamseer L, Clarke M, *et al.* Preferred reporting items for systematic review
47 and meta-analysis protocols (PRISMA-P) 2015 statement. *Systematic Reviews* 2015;**4**:1.
48
49
50
51
52
53
54
55
56
57
58
59
60

Database: Ovid MEDLINE(R) ALL <1946 to November 24, 2021>

Search Strategy:

1 ((rapid\$ adj5 sequenc\$ adj5 (induct\$ or intubat\$)) or (RSII or RSI)).tw,kf. (3261)

2 exp Intubation, Intratracheal/ or ((intra?tracheal\$ or endo?tracheal\$ or oro?tracheal\$ or trachea\$) adj10 (needle\$ or tube\$ or intubat\$ or drain\$ or catheter\$)).tw,kf. (58314)

3 ((laryng\$ adj3 (tube\$1 or mask\$)) or ((crash\$ or rapid\$) adj3 (induct\$ or intubat\$)) or (emergen\$ adj2 (induct\$ or intubat\$))).tw,kf. (13332)

4 exp Respiratory Aspiration/ or ((pulmonary\$ or respirator\$) adj3 aspirat\$).tw,kf. (3733)

5 or/1-4 (69652)

6 Patient Positioning/ or head-down tilt/ or prone position/ or supine position/ (17469)

7 ((body\$ or patient\$ or supine\$ or dorsal\$ or lateral\$ or left-lateral\$ or right-lateral\$ or steep or trendelenburg\$ or head-down\$ or headdown\$ or head-up\$ or headup\$ or head\$2 or semi-erect\$ or Sellick\$ or tilt\$ or decubit\$ or ramped\$ or ramping\$ or sniffing\$ or prone\$ or chang\$ or differ\$ or side\$ or vertical\$ or degree\$ or backrest\$ or elevat\$ or semi-Fowler\$ or Fowler\$ or semi-recumbent\$ or semirecumbent\$ or upright\$ or dependent\$) adj2 position\$).tw,kf. (74920)

8 ((systematic\$ or regular\$) adj3 (turned or turning\$)).tw,kf. (69)

9 ((postur\$ adj2 chang\$) or effect\$ of position\$).tw,kf. (6486)

10 (postur\$.tw,kf. or exp posture/) and position\$.tw,kf. (32549)

11 or/6-10 (101722)

12 5 and 11 (1903)

13 limit 12 to english language (1653)

14 limit 13 to "all adult (19 plus years)" (732)

15 limit 13 to "all child (0 to 18 years)" (355)

16 13 not (15 not (14 and 15)) (1413)

17 16 not (exp Animals/ not (Human/ and exp Animals/)) (1340)

18 17 not (pediatr\$ or paediatr\$ or child\$ or adolescent\$ or infan\$ or newborn\$ or neonat\$ or animal\$1 or mice or rat or rats or cat\$1 or cattle\$1 or dog\$1 or goat\$1 or horse\$1 or rabbit\$1 or sheep\$1 or swine\$1 or pig\$1 or piglet* or canine\$1 or feline\$1 or porcine\$ or calf or primate* or rodent\$ or hamster\$ or lamb\$1 or monkey\$1 or murine or veterinar*).ti. (1297)

19 exp case-control studies/ or (case\$ and control\$).tw. or (case\$ and series).tw. [Medline case series] (1784729)

20 case reports/ or case report\$.mp. (2318607)

21 18 not (20 not (19 and 20)) (1091)

22 21 not case report.ti. (1088)

23 exp anesthesia/ or anesthesia recovery period/ or (an?esth\$ or postan?esth\$ or post-an?esth\$).mp. or (intensive care or critical\$).jw,ja,jn. or critically\$.tw. or exp Critical Care/ or intensive care units/ or *Critical Illness/ or ((critical\$ or intensive) adj care).mp. or (intensive care

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

unit\$ or ICU).mp. or ventilat\$.tw,kf. or apache/ or apache.tw. or Emergency Service, Hospital/ or emergency.af. (1459982)

24 22 and 23 (894)

For peer review only

Reporting checklist for protocol of a systematic review and meta analysis.

Based on the PRISMA-P guidelines.

Instructions to authors

Complete this checklist by entering the page numbers from your manuscript where readers will find each of the items listed below.

Your article may not currently address all the items on the checklist. Please modify your text to include the missing information. If you are certain that an item does not apply, please write "n/a" and provide a short explanation.

Upload your completed checklist as an extra file when you submit to a journal.

In your methods section, say that you used the PRISMA-Preorting guidelines, and cite them as:

Moher D, Shamseer L, Clarke M, Ghersi D, Liberati A, Petticrew M, Shekelle P, Stewart LA. Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols (PRISMA-P) 2015 statement. Syst Rev. 2015;4(1):1.

		Reporting Item	Page Number
Title			
Identification	#1a	Identify the report as a protocol of a systematic review	1
Update	#1b	If the protocol is for an update of a previous systematic review, identify as such	n/a (the protocol is for an original systematic review)
Registration			
	#2	If registered, provide the name of the registry (such as PROSPERO) and registration number	3
Authors			
Contact	#3a	Provide name, institutional affiliation, e-mail address of all protocol authors; provide physical mailing	1,11

		address of corresponding author	
1			
2	Contribution	#3b Describe contributions of protocol authors and identify the guarantor of the review	11
3			
4			
5			
6	Amendments		
7			
8			
9		#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	n/a (this protocol is for an original systematic review)
10			
11			
12			
13			
14			
15	Support		
16			
17	Sources	#5a Indicate sources of financial or other support for the review	10
18			
19			
20			
21	Sponsor	#5b Provide name for the review funder and / or sponsor	n/a (this review is not receiving any financial support)
22			
23			
24			
25			
26			
27	Role of sponsor or funder	#5c Describe roles of funder(s), sponsor(s), and / or institution(s), if any, in developing the protocol	n/a (this review is not receiving any financial support)
28			
29			
30			
31			
32	Introduction		
33			
34	Rationale	#6 Describe the rationale for the review in the context of what is already known	4-5
35			
36			
37			
38	Objectives	#7 Provide an explicit statement of the question(s) the review will address with reference to participants, interventions, comparators, and outcomes (PICO)	6
39			
40			
41			
42			
43	Methods		
44			
45			
46	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	6-7,12
47			
48			
49			
50			
51			
52			
53			
54	Information sources	#9 Describe all intended information sources (such as electronic databases, contact with study authors, trial registers or other grey literature sources) with	7
55			
56			
57			
58			
59			

		planned dates of coverage	
1			
2			
3	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	7
4			
5			
6			
7			
8	Study records -		
9	data management	#11a Describe the mechanism(s) that will be used to manage records and data throughout the review	7-8
10			
11	Study records -		
12	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)	8
13			
14			
15			
16			
17			
18	Study records -		
19	data collection	#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	8-9
20	process		
21			
22			
23			
24			
25	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	8-9
26			
27			
28			
29			
30	Outcomes and		
31	prioritization	#13 List and define all outcomes for which data will be sought, including prioritization of main and additional outcomes, with rationale	9
32			
33			
34			
35			
36	Risk of bias in		
37	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	9-10
38			
39			
40			
41			
42			
43	Data synthesis	#15a Describe criteria under which study data will be quantitatively synthesised	10
44			
45			
46	Data synthesis	#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)	10
47			
48			
49			
50			
51			
52			
53			
54	Data synthesis	#15c Describe any proposed additional analyses (such as sensitivity or subgroup analyses, meta-regression)	n/a
55			
56			
57			
58	Data synthesis	#15d If quantitative synthesis is not appropriate, describe	10
59		For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml	
60			

the type of summary planned

1 2 3 4 5 6 7	Meta-bias(es)	#16	Specify any planned assessment of meta-bias(es) (such as publication bias across studies, selective reporting within studies)	9
8 9 10 11 12	Confidence in cumulative evidence	#17	Describe how the strength of the body of evidence will be assessed (such as GRADE)	9

Notes:

- 1b: n/a (the protocol is for an original systematic review)
- 4: n/a (this protocol is for an original systematic review)
- 5b: n/a (this review is not receiving any financial support)
- 5c: n/a (this review is not receiving any financial support)
- The PRISMA-P elaboration and explanation paper is distributed under the terms of the Creative Commons Attribution License CC-BY. This checklist was completed on 14. March 2022 using <https://www.goodreports.org/>, a tool made by the [EQUATOR Network](#) in collaboration with [Penelope.ai](#)