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Impact of image-guided surgery on perioperative outcomes and quality of life in patients with chronic rhinosinusitis who underwent endoscopic sinus surgery: a systematic review and meta-analysis protocol

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ABSTRACT

Introduction: Endoscopic sinus surgery (ESS) is a standard procedure, mainly performed in patients with chronic rhinosinusitis. Image-guided surgery (IGS) is a valuable tool used primarily in cases considered complex or challenging. Therefore, we aim to compare the quality of life and perioperative outcomes of patients with chronic rhinosinusitis who underwent ESS with and without IGS.

Methods and analysis: PubMed, Embase, Scopus, Web of Science, Scielo, Cochrane Central Register of Controlled Trials, CINAHL, LILACS, and Clinicaltrials.gov will be searched for reported clinical trials comparing outcomes of endoscopic endonasal surgery with and without navigation. Two independent authors will select eligible articles and extract their data. The risk of bias will be assessed using the Cochrane Handbook for Systematic Reviews of Interventions. The Grading of Recommendation Assessment, Development, and Evaluation method will evaluate the strength of the evidence. Data synthesis will be performed using the Review Manager software V.5.4.1. To assess heterogeneity, we will compute I2 statistics. Additionally, quantitative synthesis will be performed if the included studies are sufficiently homogenous.

Ethics and dissemination: This study will be a review of published data, and thus it is not necessary to obtain ethical approval. The findings of this systematic review will be published in a peer-reviewed journal.

PROSPERO registration number: CRD42020214791

Keywords: Sinusitis, Nasal Surgical Procedures, Computer-Assisted Surgery, systematic review.

STRENGTHS AND LIMITATIONS OF THIS STUDY

- This systematic review aims to improve decision making in patients with chronic rhinosinusitis and define the indications for the use of image-guided surgery through evidence-based medicine.

- Three independent reviewers will select the studies to be included in this review, extract data and assess the risk of bias using the Cochrane Risk of Bias Tool.
- Randomized clinical trials with a high risk of bias may compromise the reliability of the systematic review results.
- Potential limitations could be the inclusion of a small sample size and a limited number of studies, which may influence the validity and reliability of the findings.

INTRODUCTION

Chronic rhinosinusitis (CRS) is a clinical syndrome characterized by persistent symptomatic inflammation of the nasal and paranasal mucosa, such as nasal obstruction or nasal discharge, for more than 12 weeks, according to the European Position Paper on Rhinosinusitis and Nasal Polyps (EPOS 2020).[1,2]

CRS affects 5%–28% of the general population, with a higher prevalence in women (60%–67%) and a progressive increase in its occurrence with age until its decline after 60 years.[2,3] This disorder has a tremendous impact on the socioeconomic condition and quality of life of the patient. A previous study demonstrated a greater effect of CRS on social performance of patients than of angina and chronic heart failure.[4]

Chronic rhinosinusitis has a multifactorial etiology. It involves bacterial superantigens, epithelial cell defects, biofilm, T helper 1 and 2 inflammation responses, and tissue remodeling.[5] CRS is classified into three main phenotypes: eosinophilic, non-eosinophilic, and atopic disease of the central compartment. [6, 7] This classification has helped us manage patients, including the decision to perform surgery.[5, 6, 8]

The advent of endoscopic sinus surgery (ESS) in the late ’80s and the early ’90s brought revolutionary advances, resulting in a shift from open paranasal surgery to a minimally invasive approach.[9] However, this approach has the potential for major complications due to the close anatomical relationship of the paranasal sinus with delicate and essential structures such as the skull base, orbit, internal carotid artery, and optic nerve.[10] The risk of one or more injuries is even higher in revision surgeries, which are common in pathologies such as chronic rhinosinusitis with or without nasal polyps due to removal of critical anatomical landmarks in previous surgeries.[11-13]

Intraoperative image-guided surgery (IGS) is firmly established as a valuable technology in managing nasal and paranasal diseases, with the power to increase surgeons' confidence by confirming locations in anatomically challenging fields.[9] The evidence regarding the cost of IGS is controversial. Studies have shown an increase in the procedure's value, while others suggest decreased overall expenses for patients treated surgically.[14-16]

There is a lack of robust scientific evidence to determine indications and recommend using IGS in CRS. Improvements in surgical efficacy and safety are believed to be relevant.[17]

OBJECTIVES

This systematic review and meta-analysis aims to compare perioperative complications and quality of life in patients with CRS who underwent ESS with and without IGS.

METHODS AND ANALYSIS

This systematic review and meta-analysis protocol conforms to the Preferred Reporting Items for Systematic Reviews and Meta-Analysis Protocols (PRISMA-P) guidelines.[18] It is registered with the International Prospective Register of Systematic Reviews (PROSPERO CRD42020214791).

Inclusion criteria

This study will include randomized control trials (RCTs) that compared outcomes in patients with CRS who underwent ESS with and without IGS. There were no language restrictions when selecting the studies.

The PICOT strategy

- Population/Participants: adults diagnosed with chronic rhinosinusitis.
- Intervention: Endoscopic sinus surgery with image guidance.
- Comparator/control: Endoscopic sinus surgery without image guidance.

- Outcomes: Complications, quality of life, length of hospital stay, operative time, revision surgery, recurrence, and attitude of the health personnel.
- Type of Study: Randomized control trials.

Types of patients

Participants will be adult patients diagnosed with chronic rhinosinusitis according to the EPOS 2020 criteria.[19]

Types of intervention

This review will include studies that evaluate the use of IGS in the endoscopic treatment of patients with CRS.

Types of outcome measures

Primary outcome:

Quality of life (evaluated using validated tools such as SNOT-22) [20]

Secondary outcomes:

Perioperative complications (bleeding, intracranial injuries, intraorbital injuries) [21]
Length of stay [22]
Operative time [23]
Need for revision surgery [24]
Disease recurrence [25]
Attitude of health personnel [26]

Patient and public involvement

This study consists of a systematic review protocol; therefore, individual patient data will not be presented. An extensive literature search will be conducted using defined databases. For this reason, no patient will be involved in the study planning or application process, neither during the analysis nor dissemination of results.

Search strategy

PubMed, Embase, Scopus, Web of Science, Scielo, Cochrane Central Register of Controlled Trials (CENTRAL), CINAHL, LILACS, and Clinicaltrials.gov will be searched with no limitations to date or language.

Medical Subject Headings (MeSH) terms used for searching PubMed are presented in Table 1 and will be adapted to each database.

Table 1	Search strategy for PubMed
1	Sinusitis
2	Skull Base
3	Chronic Rhinosinusitis
4	Nasal Polyps
5	Nasal surgical procedures
6	Endoscopic sinus surgery
7	Nasal surgery
8	OR/1-8
9	Image Guided Surgery
10	Neuronavigation
11	Computer Assisted Surgery
12	OR/ 9-12
13	Quality of life
14	Life quality
15	Health Related Quality of Life

16	Morbidity
17	Complication
18	Intraoperative Complication
19	Postoperative Complication
20	Patient Reported Outcome Measures
21	Bleeding
22	Death
23	Cerebrospinal Fluid Leak
24	Operative Time
25	Length of Stay
26	Orbital Diseases
27	Brain Diseases
28	Revision Surgery
29	Recurrence
30	OR/13-29
31	8 AND 12 AND 30

Other sources

Eligible studies may also be selected from the reference lists of the retrieved articles. The scope of the computerized literature search may be widened based on the reference lists of the retrieved articles.

Data collection and analysis

Selection of studies

The articles retrieved by the search will be imported to EndNote Web, and duplicates will be removed. Three authors, MLN, MGN, and KSM, will independently screen the results by title, abstracts, and full text to determine whether they meet the inclusion criteria. A fourth reviewer, AKG, will resolve any discrepancies. The study selection process is summarized in a PRISMA flow diagram (Figure 1).[27]

Data extraction and management

Three independent authors (MLN, MGN and HPB) will extract data from the eligible and included studies. The latter will be inserted into a database following this designed form: publication year, first author, number of patients per group, number of follow-up losses per group, mean age, intervention description, control group description, follow-up time, randomization, allocation, blinding, complication, mean SNOT-22 score, recurrence rate, revision surgery rate, mean operative time, and mean length of stay. A meta-analysis will be conducted if a pool of included articles with sufficiently similar characteristics is obtained.

Addressing missing data

If any of the selected articles have insufficient information, we will contact the corresponding author via email or phone to obtain the missing data. If unsuccessful, the data will be deleted or imputed and will be discussed in the Discussion section.

Risk of bias assessment

The Cochrane Risk of Bias tool will be applied to evaluate random sequence generation, allocation concealment, blinding, and evaluation of clinical results.[28] We will also assess missing data, incomplete reports, financial aids, and potential conflicts of interest of each study.

Assessment of heterogeneity

Heterogeneity will be assessed by I2 statistics, in which a percentage < 25% will be considered no heterogeneity, between 25% and 50% moderate heterogeneity, and > 50% high heterogeneity.

Measures of treatment effect

Scores in validated tools will assess the primary outcome (quality of life). Since this will be continuous data, the mean and standard deviation will be calculated and presented. The risk ratio will be calculated for dichotomous data (complication). This will be performed using Review Manager (RevMan, version 5.4) software.

Analysis

RevMan 5.4 will be used to perform the statistical analysis. In the heterogeneity assessment, if I2> 50%, a random-effects model will be used, while if I2<50%, a fixed-effect model will be applied.

Subgroup analyses

Subgroup analyses will be based on the type of intervention, participant age, and study settings. Meta-regressions will be conducted to compare the risk ratio to investigate whether any observed differences between the subgroups were statistically significant.

Grading quality of evidence

We will use the Grading of Recommendations Assessment Development and Evaluation (GRADE) approach to evaluate the strength of evidence of the systematic review results. The GRADE tool classifies studies as low, moderate, and high quality.[29]

DISCUSSION

The paranasal sinuses are in close anatomical proximity to vital and delicate structures such as the skull base, orbit, internal carotid artery, and optic nerve. Broad and detailed anatomic knowledge is essential for surgeons to perform safe and effective procedures.[9]

The complication rate of ESS is approximately 0.5%, with 0.11% for intracranial complications and 0.04% for orbital complications, which can be considered low risk, even when surgical revisions are considered.[30,31] However, complications can result in serious repercussions.[30,32]

In this context, surgeons acquired a greater operative domain with the advent of intraoperative imaging. However, its exact correlation with the patient's clinical outcome is still subject to further studies, evaluating, for example, the postoperative quality of life or the complications.[12] In addition, we found literature already seeking to understand the future of robotic surgery for ESS and what its benefits would be.[33, 34]

The most recent systematic review on the subject was undertaken by Vreudenburg et al.,[32] who found a reduction in the likelihood of total, major, and orbital complications in complex ESS procedures with the use of IGS. This study was not limited to patients diagnosed with CRS nor did it evaluate quality of life outcomes.

This review proposes to provide evidence-based decision-making information that may help reduce complications, prevent recurrence, and improve patients' quality of life.

ETHICS AND DISSEMINATION

This study is a systematic review with a possible meta-analysis, which will use data from previously conducted studies; therefore, it does not require ethical approval. The outcome of this research will be submitted for publication in a peer-reviewed journal.

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Authors' contributions

MLN, MGN, ACAS, and AKG were responsible for the design of this review. MLN and MGN wrote a draft of the protocol's manuscript, and RNC and AKG revised it. MLN, ACAS, and HPB developed search strategies. MLN and KSM completed formatting the manuscript. All the authors approved the final version for publication.

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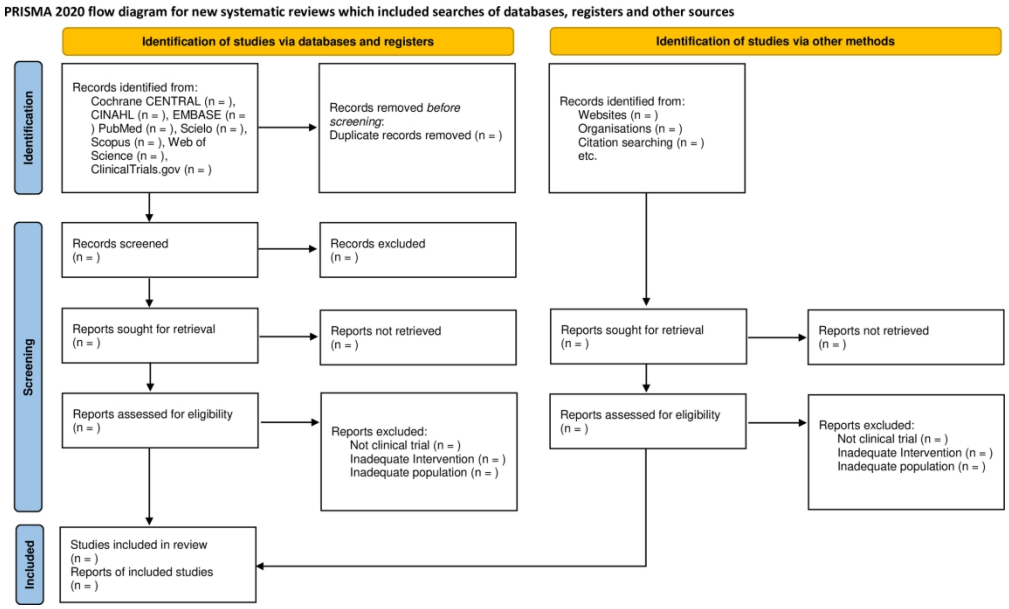
Competing interests

None declared.



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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			
Title:			
Identification	1a	Identify the report as a protocol of a systematic review	x
Update	1b	If the protocol is for an update of a previous systematic review, identify as such	-
Registration	2	If registered, provide the name of the registry (such as PROSPERO) and registration number	x
Authors:			
Contact	3a	Provide name, institutional affiliation, e-mail address of all protocol authors; provide physical mailing address of corresponding author	x
Contributions	3b	Describe contributions of protocol authors and identify the guarantor of the review	x
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	-
Support:			
Sources	5a	Indicate sources of financial or other support for the review	x
Sponsor	5b	Provide name for the review funder and/or sponsor	x
Role of sponsor or funder	5c	Describe roles of funder(s), sponsor(s), and/or institution(s), if any, in developing the protocol	-
INTRODUCTION			
Rationale	6	Describe the rationale for the review in the context of what is already known	x
Objectives	7	Provide an explicit statement of the question(s) the review will address with reference to participants, interventions, comparators, and outcomes (PICO)	x
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	x
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	x

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	x
Study records:			
Data management	11a	Describe the mechanism(s) that will be used to manage records and data throughout the review	x
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)	x
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	x
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	x
Outcomes and prioritization	13	List and define all outcomes for which data will be sought, including prioritization of main and additional outcomes, with rationale	x
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	x
Data synthesis	15a	Describe criteria under which study data will be quantitatively synthesised	
	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)	x
	15c	Describe any proposed additional analyses (such as sensitivity or subgroup analyses, meta-regression)	x
	15d	If quantitative synthesis is not appropriate, describe the type of summary planned	x
Meta-bias(es)	16	Specify any planned assessment of meta-bias(es) (such as publication bias across studies, selective reporting within studies)	x
Confidence in cumulative evidence	17	Describe how the strength of the body of evidence will be assessed (such as GRADE)	x

*** 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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ABSTRACT

Introduction: Endoscopic sinus surgery (ESS) is a standard procedure, mainly performed in patients with chronic rhinosinusitis. Image-guided surgery (IGS) is a valuable tool used primarily in cases considered complex or challenging. Therefore, we aim to analyse trials that compare ESS with and without IGS.

Methods and analysis: PubMed, Embase, Scopus, Web of Science, Scielo, Cochrane Central Register of Controlled Trials, CINAHL, LILACS, and Clinicaltrials.gov will be searched for reported clinical trials comparing the quality of life and perioperative outcomes of ESS with and without navigation. The search is planned for November 30, 2021. Three independent authors will select eligible articles and extract their data. The risk of bias will be assessed using the Cochrane Handbook for Systematic Reviews of Interventions. The Grading of Recommendation Assessment, Development, and Evaluation method will evaluate the strength of the evidence. Data synthesis will be performed using the Review Manager software V.5.4.1. To assess heterogeneity, we will compute I2 statistics. Additionally, meta-analysis will be performed if the included studies are sufficiently homogenous.

Ethics and dissemination: This study will be a review of published data, and thus it is not necessary to obtain ethical approval. The findings of this systematic review will be published in a peer-reviewed journal.

PROSPERO registration number: CRD42020214791

Keywords: Sinusitis, Nasal Surgical Procedures, Computer-Assisted Surgery, systematic review.

STRENGTHS AND LIMITATIONS OF THIS STUDY

- This systematic review aims to improve decision making in patients with chronic rhinosinusitis and define the indications for the use of image-guided surgery through evidence-based medicine.
- Three independent reviewers will select the studies to be included in this review, extract data and assess the risk of bias using the Cochrane Risk of Bias Tool.

- Randomized clinical trials with a high risk of bias may compromise the reliability of the systematic review results.
- Potential limitations could be the inclusion of a small sample size and a limited number of studies, which may influence the validity and reliability of the findings.

INTRODUCTION

Chronic rhinosinusitis (CRS) is a clinical syndrome characterized by persistent symptomatic inflammation of the nasal and paranasal mucosa, such as nasal obstruction or nasal discharge, for more than 12 weeks, according to the European Position Paper on Rhinosinusitis and Nasal Polyps (EPOS 2020).[1,2] It affects 5%–28% of the general population, with a slight female preponderance and a progressive increase in its occurrence with age until its decline after 60 years.[2,3]

The persistence of rhinosinusitis has a multifactorial etiology. It involves bacterial superantigens, epithelial cell defects, biofilm, T helper 1 and 2 inflammation responses, and tissue remodeling.[4] CRS is originally classified into with and without nasal polyps (CRSwNP and CRSsNP).[5, 6] This classification has helped us manage patients, including the decision to perform surgery.[4, 6]

This disorder has a tremendous impact on the socioeconomic condition and quality of life of patients. A previous study demonstrated a greater effect of CRS on social performance of patients than of angina and chronic heart failure.[7] The direct enconomic costs are high, especially in patients with CRSwNP; but the indirect costs are even greater since it affects working age leading to absenteeism and decreased productivity.[2, 8]

The advent of endoscopic sinus surgery (ESS) in the late ’80s and the early ’90s brought revolutionary advances, resulting in a shift from open paranasal surgery to a minimally invasive approach.[9] However, this approach has the potential for major complications due to the close anatomical relationship of the paranasal sinus with delicate and essential structures such as the skull base, orbit, internal carotid artery, and optic nerve.[10] The risk of one or more injuries is even higher in revision surgeries, which are common in pathologies such as chronic rhinosinusitis with or without nasal polyps due to removal of critical anatomical landmarks in previous surgeries.[11-13]

Intraoperative image-guided surgery (IGS) is firmly established as a valuable technology in managing nasal and paranasal diseases, with the power to increase surgeons' confidence by confirming locations in anatomically challenging fields.[9] The evidence regarding the cost of IGS is controversial. Studies have shown an increase in the procedure's value, while others suggest decreased overall expenses for patients treated surgically.[14-16]

There is a lack of robust scientific evidence to determine indications and recommend using IGS in CRS. Improvements in surgical efficacy and safety are believed to be relevant.[17] Within this context, this review seeks to answer if IGS reduces perioperative complications and improves the quality of life in patients with CRS submitted to ESS.

OBJECTIVES

This systematic review and meta-analysis aims to compare perioperative complications and quality of life in patients with CRS who underwent ESS with and without IGS.

METHODS AND ANALYSIS

This systematic review and meta-analysis protocol conforms to the Preferred Reporting Items for Systematic Reviews and Meta-Analysis Protocols (PRISMA-P) guidelines.[18] It is registered with the International Prospective Register of Systematic Reviews (PROSPERO CRD42020214791).

Inclusion criteria

This study will include randomized control trials (RCTs) that compared outcomes in patients with CRS who underwent ESS with and without IGS. There were no language restrictions when selecting the studies.

The PICOT strategy

- Population/Participants: adults diagnosed with chronic rhinosinusitis.
- Intervention: Endoscopic sinus surgery with image guidance.

- Comparator/control: Endoscopic sinus surgery without image guidance.
- Outcomes: Complications, quality of life, length of hospital stay, operative time, revision surgery and recurrence.
- Type of Study: Randomized control trials.

Types of patients

Participants will be adult patients diagnosed with chronic rhinosinusitis according to the EPOS 2020 and EPOS 2012 criteria.[2, 19]

Types of intervention

This review will include studies that evaluate the use of IGS in the endoscopic treatment of patients with CRS.

Types of outcome measures

Primary outcome:

Quality of life (evaluated using validated tools such as SNOT-22) [20]

Secondary outcomes:

Perioperative complications (bleeding, intracranial injuries, intraorbital injuries) [21]
Length of stay [22]
Operative time [23]
Need for revision surgery [24]
Disease recurrence [25]

Patient and public involvement

This study consists of a systematic review protocol; therefore, individual patient data will not be presented. An extensive literature search will be conducted using defined databases. For this reason, no patient will be involved in the study planning or application process, neither during the analysis nor dissemination of results.

Search strategy

PubMed, Embase, Scopus, Web of Science, Scielo, Cochrane Central Register of Controlled Trials (CENTRAL), CINAHL, LILACS, and Clinicaltrials.gov will be searched with no limitations to date or language. This search is planned for November 30, 2021.

Medical Subject Headings (MeSH) terms used for searching PubMed are presented in Table 1 and will be adapted to each database.

Table 1	Search strategy for PubMed
1	Sinusitis
2	Skull Base
3	Chronic Rhinosinusitis
4	Nasal Polyps
5	Nasal surgical procedures
6	Endoscopic sinus surgery
7	Nasal surgery
8	OR/1-8
9	Image Guided Surgery
10	Neuronavigation
11	Computer Assisted Surgery
12	OR/ 9-12
13	Quality of life
14	Life quality
15	Health Related Quality of Life

16	Morbidity
17	Complication
18	Intraoperative Complication
19	Postoperative Complication
20	Patient Reported Outcome Measures
21	Bleeding
22	Death
23	Cerebrospinal Fluid Leak
24	Operative Time
25	Length of Stay
26	Orbital Diseases
27	Brain Diseases
28	Revision Surgery
29	Recurrence
30	OR/13-29
31	8 AND 12 AND 30

Other sources

Eligible studies may also be selected from the reference lists of the retrieved articles. The scope of the computerized literature search may be widened based on the reference lists of the retrieved articles.

Data collection and analysis

Selection of studies

The articles retrieved by the search will be imported to EndNote Web, and duplicates will be removed. Three authors, MLN, MGN, and KSM, will independently screen the results by title, abstracts, and full text to determine whether they meet the inclusion criteria. A fourth reviewer, AKG, will resolve any discrepancies. The study selection process is summarized in a PRISMA flow diagram (Figure 1).[26]

Data extraction and management

Three independent authors (MLN, MGN and HPB) will extract data from the eligible and included studies. The latter will be inserted into a database following this designed form: publication year, first author, number of patients per group, number of follow-up losses per group, mean age, intervention description, control group description, follow-up time, randomization, allocation, blinding, complication, mean SNOT-22 score, recurrence rate, revision surgery rate, mean operative time, and mean length of stay. A meta-analysis will be conducted if a pool of included articles with sufficiently similar characteristics is obtained.

Addressing missing data

If any of the selected articles have insufficient information, we will contact the corresponding author via email or phone to obtain the missing data. If unsuccessful, the data will be deleted or imputed and will be discussed in the Discussion section.

Risk of bias assessment

The Cochrane Risk of Bias tool will be applied to evaluate random sequence generation, allocation concealment, blinding, and evaluation of clinical results.[27] We will also assess missing data, incomplete reports, financial aids, and potential conflicts of interest of each study.

Assessment of heterogeneity

Heterogeneity will be assessed by I2 statistics, in which a percentage < 25% will be considered no heterogeneity, between 25% and 50% moderate heterogeneity, and > 50% high heterogeneity.

Measures of treatment effect

Scores in validated tools will assess the primary outcome (quality of life). Since this will be continuous data, the mean and standard deviation will be calculated and presented. The risk ratio will be calculated for dichotomous data (complication). This will be performed using Review Manager (RevMan, version 5.4) software.

Analysis

RevMan 5.4 will be used to perform the statistical analysis. In the heterogeneity assessment, if I2> 50%, a random-effects model will be used, while if I2<50%, a fixed-effect model will be applied. Moreover, to assess the possible reporting bias, a funnel plot will be constructed to observe and test the symmetry of distribution of the results from the included studies.

Subgroup analyses

Subgroup analyses will be based on the type of intervention, participant age, and study settings. Meta-regressions will be conducted to compare the risk ratio to investigate whether any observed differences between the subgroups were statistically significant.

Grading quality of evidence

We will use the Grading of Recommendations Assessment Development and Evaluation (GRADE) approach to evaluate the strength of evidence of the systematic review results. The GRADE tool classifies studies as low, moderate, and high quality.[28]

Amendments

If any important aspect of the methods of the review need to be modified for improvement, an amendment will be made. In case any alteration occurs from the original protocol it will be added to the registration record and reported on the final review.

DISCUSSION

The paranasal sinuses are in close anatomical proximity to vital and delicate structures such as the skull base, orbit, internal carotid artery, and optic nerve. Broad and detailed anatomic knowledge is essential for surgeons to perform safe and effective procedures.[9]

The complication rate of ESS is approximately 0.5%, with 0.11% for intracranial complications and 0.04% for orbital complications, which can be considered low risk, even when surgical revisions are considered.[29,30] However, complications can result in serious repercussions.[29,31]

In this context, surgeons acquired a greater operative domain with the advent of intraoperative imaging. However, its exact correlation with the patient's clinical outcome is still subject to further studies, evaluating, for example, the postoperative quality of life or the complications.[12]

The most recent systematic review on the subject was undertaken by Vreudenburg et al.,[31] who found a reduction in the likelihood of total, major, and orbital complications in complex ESS procedures with the use of IGS. This study was not limited to patients diagnosed with CRS nor did it evaluate quality of life outcomes.

This review proposes to provide evidence-based decision-making information that may help reduce complications, prevent recurrence, and improve patients' quality of life.

ETHICS AND DISSEMINATION

This study is a systematic review with a possible meta-analysis, which will use data from previously conducted studies; therefore, it does not require ethical approval. The outcome of this research will be submitted for publication in a peer-reviewed journal.

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Authors' contributions

MLN, MGN, ACAS, and AKG were responsible for the design of this review. MLN and MGN wrote a draft of the protocol's manuscript, and RNC and AKG revised it. MLN,

ACAS, and HPB developed search strategies. MLN and KSM completed formatting the manuscript. All the authors approved the final version for publication.

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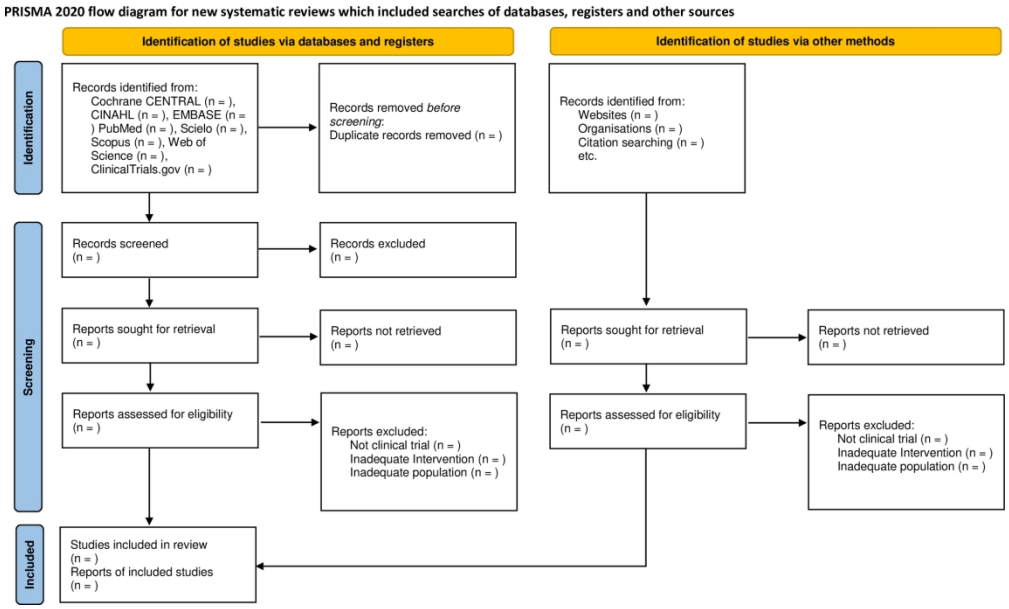
Competing interests

None declared.



190x114mm (300 x 300 DPI)

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			
Title:			
Identification	1a	Identify the report as a protocol of a systematic review	01
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	02
Authors:			
Contact	3a	Provide name, institutional affiliation, e-mail address of all protocol authors; provide physical mailing address of corresponding author	01
Contributions	3b	Describe contributions of protocol authors and identify the guarantor of the review	12
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	09
Support:			
Sources	5a	Indicate sources of financial or other support for the review	12
Sponsor	5b	Provide name for the review funder and/or sponsor	NA
Role of sponsor or funder	5c	Describe roles of funder(s), sponsor(s), and/or institution(s), if any, in developing the protocol	NA
INTRODUCTION			
Rationale	6	Describe the rationale for the review in the context of what is already known	04
Objectives	7	Provide an explicit statement of the question(s) the review will address with reference to participants, interventions, comparators, and outcomes (PICO)	04
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	04
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	05-06

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	06
Study records:			
Data management	11a	Describe the mechanism(s) that will be used to manage records and data throughout the review	07
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)	07
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	08
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	08
Outcomes and prioritization	13	List and define all outcomes for which data will be sought, including prioritization of main and additional outcomes, with rationale	08
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	08
Data synthesis	15a	Describe criteria under which study data will be quantitatively synthesised	08
	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)	08
	15c	Describe any proposed additional analyses (such as sensitivity or subgroup analyses, meta-regression)	08
	15d	If quantitative synthesis is not appropriate, describe the type of summary planned	09
Meta-bias(es)	16	Specify any planned assessment of meta-bias(es) (such as publication bias across studies, selective reporting within studies)	09
Confidence in cumulative evidence	17	Describe how the strength of the body of evidence will be assessed (such as GRADE)	09

*** 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.

BMJ Open

Image guidance for endoscopic sinus surgery in patients with chronic rhinosinusitis: a systematic review and meta-analysis protocol

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Primary Subject Heading:	Ear, nose and throat/otolaryngology
Secondary Subject Heading:	Ear, nose and throat/otolaryngology, Evidence based practice
Keywords:	Adult otolaryngology < OTOLARYNGOLOGY, Endoscopic surgery < OTOLARYNGOLOGY, Protocols & guidelines < HEALTH SERVICES ADMINISTRATION & MANAGEMENT

Image guidance for endoscopic sinus surgery in patients with chronic rhinosinusitis: a systematic review and meta-analysis protocol

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Word Count: 1.592

ABSTRACT

Introduction: Endoscopic sinus surgery (ESS) is a current procedure for treating chronic rhinosinusitis (CRS) patients. Image-guided surgery (IGS) for ESS may help reduce complications and improve precision. However, it is uncertain in which cases IGS is beneficial. This work aims to compare ESS with and without IGS in patients with CRS.

Methods and analysis: PubMed, Embase, Scopus, Web of Science, Scielo, Cochrane Central Register of Controlled Trials, CINAHL, LILACS, and Clinicaltrials.gov will be searched for reported clinical trials comparing quality of life and perioperative outcomes of ESS with and without navigation. The search is planned for February 20, 2022. Three independent authors will select eligible articles and extract their data. The risk of bias will be assessed using the Cochrane Handbook for Systematic Reviews of Interventions. The Grading of Recommendation Assessment, Development, and Evaluation method will evaluate the strength of the evidence. Data synthesis will be performed using the Review Manager software V.5.4.1. To assess heterogeneity, I2 statistics will be computed. Additionally, meta-analysis will be performed if the included studies are sufficiently homogenous.

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Keywords: Sinusitis, Nasal Surgical Procedures, Computer-Assisted Surgery, systematic review.

STRENGTHS AND LIMITATIONS OF THIS STUDY

- This systematic review aims to improve decision-making in patients with chronic rhinosinusitis and define indications for the use of image-guided surgery through evidence-based medicine.

- Three independent reviewers with experience in conducting systematic reviews and meta-analysis will select the studies to be included in this review, extract data and assess the risk of bias using the Cochrane Risk of Bias Tool.

- The low incidence of complication even in challenging surgical cases of ESS may reduce the possibility of demonstrating statistical benefits in the use of IGS.

- Potential limitations could be the inclusion of small sample size and a limited number of studies, which may influence the validity and reliability of the findings.

INTRODUCTION

Description of the condition

Chronic rhinosinusitis (CRS) is a clinical syndrome defined by persistent symptomatic inflammation of the nasal and paranasal mucosa, characterized by two or more symptoms, one of which should either be nasal blockage/obstruction/congestion or nasal discharge. [1-3].

The latter affects 5%–28% of the general population and tremendously impacts patients' socio-economic conditions and quality of life. The health care costs are higher in rhinosinusitis than in other diseases such as peptic ulcer, asthma, and hay fever. Indirect costs are also significant, since it affects working age, leading to absenteeism and decreased productivity. [2-7] A health state utility research found that patients with CRS had worse utility value than those with chronic obstructive pulmonary disease, coronary artery disease, chronic heart failure and Parkinson's disease. [8]

CRS's etiology involves bacterial superantigens, epithelial cell defects, biofilm, T helper 1 and 2 inflammation responses, and tissue remodeling. [9,12] It is classified into CRS with nasal polyps and CRS without nasal polyps (CRSwNP and CRSsNP). [10, 11]

The advent of endoscopic sinus surgery (ESS) in the late '80s and the early '90s brought revolutionary advances to CRS's treatment.[12] Reduction in type 2 inflammation and prevention of irreversible remodeling of the mucosa by facilitating improved access to topical therapies are potentially disease-modifying benefits of surgery.[2]

However, this approach has the potential for significant complications due to the close anatomical relationship of the paranasal sinus with delicate and essential structures such as the skull base, orbit, internal carotid artery, and optic nerve.[13] The risk of one or more injuries is even higher in revision surgeries due to removal of critical anatomical landmarks in previous procedures.[14-16] The complication rate of ESS is approximately 0.5%, with 0.11% for intracranial complications and 0.04% for orbital complications, which

can be considered low risk.[17,18] Nevertheless, complications can result in serious repercussions.[17,19]

Description of the intervention

Intraoperative image-guided surgery (IGS) is firmly established as a valuable technology in managing nasal and paranasal diseases, with the power to increase surgeons' confidence by confirming locations in anatomically challenging fields.[12]

The systems used for IGS have the following components: a computer workstation, video monitor, tracking system, surgical instrumentation, and data transfer hardware. The tracking system allows real-time determination of instrument location relative to anatomical landmarks. These can use an electromagnetic (EM) or optical tracking (OT) technology to perform this position determination in the operating field against pre-operative imaging data sets. [3,20]

How the intervention might work

Considering the complex anatomy and proximity with vital structures, the possibility of confirming anatomical position of the instruments during surgery may allow the surgeon to remove more of the patient's disease. One can speculate that if a more complete surgery is performed, in which all diseased sinus compartments are addressed, than quality of life of patients may be improved and revision rates may be reduced. [3,20]

Why it is important to conduct this review

There is a lack of robust scientific evidence to determine indications and recommend the use of IGS in CRS. Improvements in surgical efficacy and safety are believed to be relevant. [21] This review seeks to analyse trials that compare ESS with and without IGS.

OBJECTIVES

The aim of this systematic review and meta-analysis is to analyse clinical trials that compare ESS with and without IGS.

METHODS AND ANALYSIS

This systematic review and meta-analysis protocol follow the Preferred Reporting Items for Systematic Reviews and Meta-Analysis Protocols (PRISMA-P) guidelines. [22]

It is registered with the International Prospective Register of Systematic Reviews (PROSPERO CRD42020214791).

Inclusion criteria

This study will include clinical trials that compared outcomes in patients with CRS who underwent ESS with and without IGS. There will be no language restrictions when selecting the studies.

The PICOT strategy

- Population/Participants: adults diagnosed with chronic rhinosinusitis.
- Intervention: Endoscopic sinus surgery with image guidance.
- Comparator/control: Endoscopic sinus surgery without image guidance.
- Outcomes: Complications, quality of life, length of hospital stay, operative time, revision surgery and recurrence.
- Type of Study: clinical trials.

Types of patients

Participants will be adult patients diagnosed with chronic rhinosinusitis according to the EPOS 2020 and EPOS 2012 criteria. [2, 23]

Types of intervention

This review will include studies that evaluate the use of IGS in the endoscopic surgical treatment of patients with CRS.

Types of outcome measures

Primary outcome:

Health Related Quality of Life (HRQOL) measured by any of the following instruments:

Sinonasal Outcome Test (SNOT-16, SNOT-20 or SNOT-22) [24-26]

Rhinosinusitis Quality of Life Survey Instrument (RhinoQoL) [27]

Rhinosinusitis Outcome Measurement (RSOM-31) [28]

Rhinosinusitis Disability Index (RSDI) [29]

Visual Analogue Scale (VAS) [30]

Secondary outcomes:

Perioperative complications (bleeding, intracranial injuries, intraorbital injuries) [31]

Length of stay [32]

Operative time [33]

Need for revision surgery [34]

Disease recurrence [35]

Patient and public involvement

This study consists of a systematic review protocol; therefore, individual patient data will not be presented. An extensive literature search will be conducted using defined databases. For this reason, no patient will be involved in the study planning or application process, neither during the analysis nor dissemination of results.

Search strategy

PubMed, Embase, Scopus, Web of Science, Scielo, Cochrane Central Register of Controlled Trials (CENTRAL), CINAHL, LILACS, and Clinicaltrials.gov will be searched with no limitations to date or language. This search is planned for february 20, 2022.

Medical Subject Headings (MeSH) terms used for searching PubMed are presented in Table 1 and will be adapted to each database.

Table 1	Search strategy for PubMed
1	Sinusitis
2	Skull Base
3	Chronic Rhinosinusitis
4	Nasal Polyps

5	Nasal surgical procedures
6	Endoscopic sinus surgery
7	Nasal surgery
8	OR/1-8
9	Image Guided Surgery
10	Neuronavigation
11	Computer Assisted Surgery
12	OR/ 9-12
13	Quality of life
14	Life quality
15	Health Related Quality of Life
16	Morbidity
17	Complication
18	Intraoperative Complication
19	Postoperative Complication
20	Patient Reported Outcome Measures
21	Bleeding
22	Death
23	Cerebrospinal Fluid Leak
24	Operative Time
25	Length of Stay

26	Orbital Diseases
27	Brain Diseases
28	Revision Surgery
29	Recurrence
30	OR/13-29
31	8 AND 12 AND 30

Other sources

Eligible studies may also be selected from the reference lists of the retrieved articles. The scope of the computerized literature search may be widened based on the reference lists of the retrieved articles.

Data collection and analysis

Selection of studies

The articles retrieved by the search will be imported to EndNote Web, and duplicates will be removed. Three authors, MLN, MGN, and KSM, will independently screen the results first by title, abstracts, and then full text to determine whether they meet the inclusion criteria. A fourth reviewer, AKG, will resolve any discrepancies. The study selection process is summarized in a PRISMA flow diagram (Figure 1).[36]

Data extraction and management

Three independent authors (MLN, MGN and HPB) will extract data from the eligible and included studies. The latter will be inserted into a database following this designed form: publication year, first author, number of patients per group, number of follow-up losses per group, mean age, intervention description, control group description, follow-up time, randomization, allocation, blinding, complication, mean HRQOL score, recurrence rate, revision surgery rate, mean operative time, and mean length of stay. A meta-analysis

will be conducted if a pool of included articles with sufficiently similar characteristics is obtained.

Addressing missing data

If any of the selected articles have insufficient information, we will contact the corresponding author via email or phone to obtain the missing data. If unsuccessful, the data will be deleted or imputed and will be discussed in the Discussion section.

Risk of bias assessment

The Cochrane Risk of Bias tool will be applied to evaluate random sequence generation, allocation concealment, blinding, and evaluation of clinical results.[37] We will also assess missing data, incomplete reports, financial aids, and potential conflicts of interest of each study.

Assessment of heterogeneity

Heterogeneity will be assessed by I2 statistics, in which a percentage < 25% will be considered no heterogeneity, between 25% and 50% moderate heterogeneity, and > 50% high heterogeneity.

Measures of treatment effect

Scores in validated tools will assess the primary outcome (quality of life). Since this will be continuous data, the mean and standard deviation will be calculated and presented. The risk ratio will be calculated for dichotomous data (complication). This will be performed using Review Manager (RevMan, version 5.4) software.

Analysis

RevMan 5.4 will be used to perform the statistical analysis. In the heterogeneity assessment, if I2> 50%, a random-effects model will be used, while if I2<50%, a fixed-effect model will be applied. Moreover, to assess the possible reporting bias, a funnel plot will be constructed to observe and test the symmetry of distribution of the results from the included studies.

Subgroup analyses

Subgroup analyses will be based on the type of intervention, participant age, and study settings. Meta-regressions will be conducted to compare the risk ratio and investigate whether any observed differences between the subgroups were statistically significant.

Grading quality of evidence

We will use the Grading of Recommendations Assessment Development and Evaluation (GRADE) approach to evaluate the strength of evidence of the systematic review results. The GRADE tool classifies studies as low, moderate, and high quality.[38]

Amendments

If any important aspect of the methods of the review needs to be modified for improvement, an amendment will be made. In case any alteration occurs from the original protocol it will be added to the registration record and reported on the final review.

DISCUSSION

The paranasal sinuses are in close anatomical proximity to vital and delicate structures such as the skull base, orbit, internal carotid artery, and optic nerve. Broad and detailed anatomic knowledge is essential for surgeons to perform safe and effective procedures.[12]

Surgeons have acquired a greater operative domain with the advent of intraoperative imaging. However, its exact correlation with the patient's clinical outcome is still subject to further studies, evaluating, for example, the postoperative quality of life or the complications.[15]

Vreudenburg et al.,[19] found a reduction in the likelihood of total, major, and orbital complications in complex ESS procedures with the use of IGS. However, this study was not limited to patients diagnosed with CRS nor did it evaluate quality of life outcomes.

This review proposes to provide evidence-based decision-making information that may help reduce complications, prevent recurrence, and improve patients' quality of life.

ETHICS AND DISSEMINATION

This study is a systematic review with a possible meta-analysis, which will use data from previously conducted studies; therefore, it does not require ethical approval. The outcome of this research will be submitted for publication in a peer-reviewed journal.

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Authors' contributions

MLN, MGN, ACAS, and AKG were responsible for the design of this review. MLN and MGN wrote a draft of the protocol's manuscript, and RNC and AKG revised it. MLN, ACAS, and HPB developed search strategies. MLN and KSM completed formatting the manuscript. All the authors approved the final version for publication.

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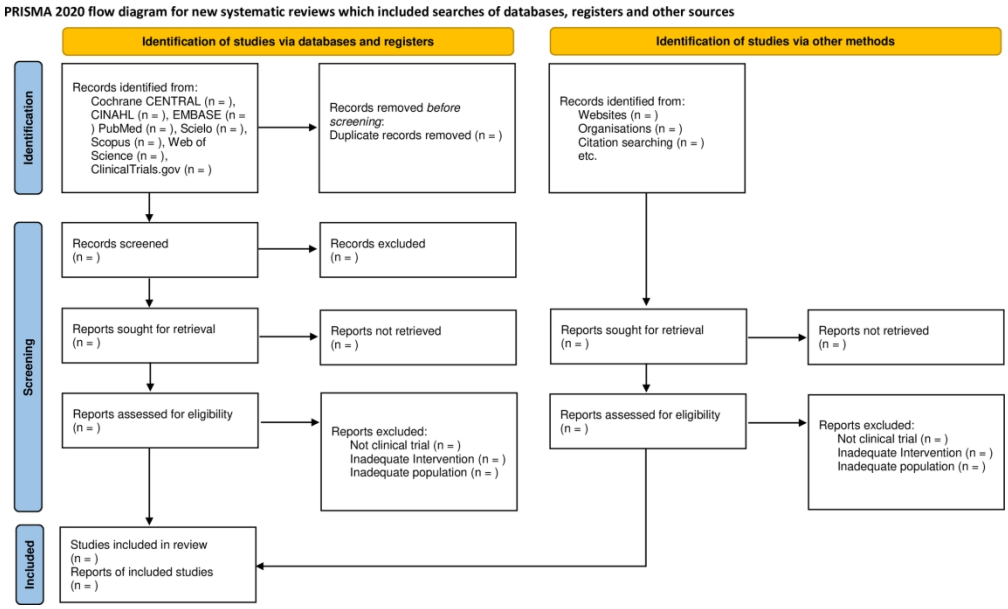
Competing interests

None declared.

Figure 1- PRISMA flow diagram.



190x114mm (300 x 300 DPI)

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			
Title:			
Identification	1a	Identify the report as a protocol of a systematic review	01
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	02
Authors:			
Contact	3a	Provide name, institutional affiliation, e-mail address of all protocol authors; provide physical mailing address of corresponding author	01
Contributions	3b	Describe contributions of protocol authors and identify the guarantor of the review	12
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	09
Support:			
Sources	5a	Indicate sources of financial or other support for the review	12
Sponsor	5b	Provide name for the review funder and/or sponsor	NA
Role of sponsor or funder	5c	Describe roles of funder(s), sponsor(s), and/or institution(s), if any, in developing the protocol	NA
INTRODUCTION			
Rationale	6	Describe the rationale for the review in the context of what is already known	04
Objectives	7	Provide an explicit statement of the question(s) the review will address with reference to participants, interventions, comparators, and outcomes (PICO)	04
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	04
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	05-06

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	06
Study records:			
Data management	11a	Describe the mechanism(s) that will be used to manage records and data throughout the review	07
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)	07
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	08
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	08
Outcomes and prioritization	13	List and define all outcomes for which data will be sought, including prioritization of main and additional outcomes, with rationale	08
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	08
Data synthesis	15a	Describe criteria under which study data will be quantitatively synthesised	08
	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)	08
	15c	Describe any proposed additional analyses (such as sensitivity or subgroup analyses, meta-regression)	08
	15d	If quantitative synthesis is not appropriate, describe the type of summary planned	09
Meta-bias(es)	16	Specify any planned assessment of meta-bias(es) (such as publication bias across studies, selective reporting within studies)	09
Confidence in cumulative evidence	17	Describe how the strength of the body of evidence will be assessed (such as GRADE)	09

*** 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.

BMJ Open

Image guidance for endoscopic sinus surgery in patients with chronic rhinosinusitis: a systematic review and meta-analysis protocol

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Primary Subject Heading:	Ear, nose and throat/otolaryngology
Secondary Subject Heading:	Ear, nose and throat/otolaryngology, Evidence based practice
Keywords:	Adult otolaryngology < OTOLARYNGOLOGY, Endoscopic surgery < OTOLARYNGOLOGY, Protocols & guidelines < HEALTH SERVICES ADMINISTRATION & MANAGEMENT

Image guidance for endoscopic sinus surgery in patients with chronic rhinosinusitis: a systematic review and meta-analysis protocol

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Word Count: 1.592

ABSTRACT

Introduction: Endoscopic sinus surgery (ESS) is a current procedure for treating chronic rhinosinusitis (CRS) patients. Image-guided surgery (IGS) for ESS may help reduce complications and improve precision. However, it is uncertain in which cases IGS is beneficial. This work aims to compare ESS with and without IGS in patients with CRS.

Methods and analysis: PubMed, Embase, Scopus, Web of Science, Scielo, Cochrane Central Register of Controlled Trials, CINAHL, LILACS, and Clinicaltrials.gov will be searched for reported clinical trials comparing the quality of life and perioperative outcomes of ESS with and without navigation. The search is planned for April 20, 2022. Three independent authors will select eligible articles and extract their data. The risk of bias will be assessed using the Cochrane Handbook for Systematic Reviews of Interventions. The Grading of Recommendation Assessment, Development, and Evaluation method will evaluate the strength of the evidence. Data synthesis will be performed using the Review Manager software V.5.4.1. To assess heterogeneity, I2 statistics will be computed. Additionally, meta-analysis will be performed if the included studies are sufficiently homogenous.

Ethics and dissemination: This study reviews published data, and thus it is not necessary to obtain ethical approval. The findings of this systematic review will be published in a peer-reviewed journal.

PROSPERO registration number: CRD42020214791

Keywords: Sinusitis, Nasal Surgical Procedures, Computer-Assisted Surgery, Systematic Review.

STRENGTHS AND LIMITATIONS OF THIS STUDY

- This systematic review aims to improve decision-making in patients with chronic rhinosinusitis and define indications for the use of image-guided surgery through evidence-based medicine.

- Three independent reviewers with experience in conducting systematic reviews and meta-analysis will select the studies to be included in this review, extract data and assess the risk of bias using the Cochrane Risk of Bias Tool.

- The low incidence of complication even in challenging surgical cases of ESS may reduce the possibility of demonstrating statistical benefits in the use of IGS.

- Potential limitations could be the inclusion of a small sample size and a limited number of studies, which may influence the validity and reliability of the findings.

INTRODUCTION

Description of the condition

Chronic rhinosinusitis (CRS) is a clinical syndrome defined by persistent symptomatic inflammation of the nasal and paranasal mucosa, characterized by two or more symptoms, one of which should either be nasal blockage/obstruction/congestion or nasal discharge. [1-3].

The latter affects 5%–28% of the general population and tremendously impacts patients' socio-economic conditions and quality of life. The health care costs are higher in rhinosinusitis than in other diseases such as peptic ulcers, asthma, and hay fever. Indirect costs are also significant, since it affects working age, leading to absenteeism and decreased productivity. [2-7] A health state utility research found that patients with CRS had worse utility value than those with chronic obstructive pulmonary disease, coronary artery disease, chronic heart failure, and Parkinson's disease. [8]

The etiology of CRS involves bacterial superantigens, epithelial cell defects, biofilm, T helper 1 and 2 inflammation responses, and tissue remodeling. [9,12] It is classified into CRS with nasal polyps and CRS without nasal polyps (CRSwNP and CRSsNP). [10, 11]

The advent of endoscopic sinus surgery (ESS) in the late '80s and the early '90s brought revolutionary advances to the treatment of CRS.[12] Reducing type 2 inflammation and preventing irreversible remodeling of the mucosa by facilitating improved access to topical therapies are potentially disease-modifying benefits of surgery.[2]

However, this approach has the potential for significant complications due to the close anatomical relationship of the paranasal sinus with delicate and essential structures such as the skull base, orbit, internal carotid artery, and optic nerve.[13] The risk of one or more injuries is even higher in revision surgeries due to the removal of critical

anatomical landmarks in previous procedures.[14-16] The complication rate of ESS is approximately 0.5%, with 0.11% for intracranial complications and 0.04% for orbital complications, which can be considered low risk.[17,18] Nevertheless, complications can result in serious repercussions.[17,19]

Description of the intervention

Intraoperative image-guided surgery (IGS) is firmly established as a valuable technology in managing nasal and paranasal diseases, with the power to increase surgeons' confidence by confirming locations in anatomically challenging fields.[12]

The systems used for IGS have the following components: a computer workstation, video monitor, tracking system, surgical instrumentation, and data transfer hardware. The tracking system allows real-time determination of instrument location relative to anatomical landmarks. These can use an electromagnetic (EM) or optical tracking (OT) technology to perform this position determination in the operating field against pre-operative imaging data sets. [3,20]

How the intervention might work

Considering the complex anatomy and proximity with vital structures, the possibility of confirming the anatomical position of the instruments during surgery may allow the surgeon to remove more of the patient's disease. One can speculate that if a more complete surgery is performed, in which all diseased sinus compartments are addressed, then the quality of life of patients may be improved and revision rates may be reduced. [3,20]

Why it is important to conduct this review

There is a lack of robust scientific evidence to determine indications and recommend the use of IGS in CRS. Improvements in surgical efficacy and safety are believed to be relevant. [21] This review seeks to analyse trials that compare ESS with and without IGS.

OBJECTIVES

This systematic review and meta-analysis aim to analyse clinical trials that compare ESS with and without IGS.

METHODS AND ANALYSIS

This systematic review and meta-analysis protocol follows the Preferred Reporting Items for Systematic Reviews and Meta-Analysis Protocols (PRISMA-P) guidelines. [22] It is registered with the International Prospective Register of Systematic Reviews (PROSPERO CRD42020214791).

Inclusion criteria

This study will include clinical trials that compared outcomes in patients with CRS who underwent ESS with and without IGS. There will be no language restrictions when selecting the studies.

The PICOT strategy

- Population/Participants: adults diagnosed with chronic rhinosinusitis.
- Intervention: Endoscopic sinus surgery with image guidance.
- Comparator/control: Endoscopic sinus surgery without image guidance.
- Outcomes: Complications, quality of life, length of hospital stay, operative time, revision surgery, and recurrence.
- Type of Study: clinical trials.

Types of patients

Participants will be adult patients diagnosed with chronic rhinosinusitis according to the EPOS 2020 and EPOS 2012 criteria. [2, 23]

Types of intervention

This review will include studies that evaluate the use of IGS in the endoscopic surgical treatment of patients with CRS.

Types of outcome measures

Primary outcome:

Health-Related Quality of Life (HRQOL) measured by any of the following instruments:

Sinonasal Outcome Test (SNOT-16, SNOT-20 or SNOT-22) [24-26]

Rhinosinusitis Quality of Life Survey Instrument (RhinoQoL) [27]

Rhinosinusitis Outcome Measurement (RSOM-31) [28]

Rhinosinusitis Disability Index (RSDI) [29]

Visual Analogue Scale (VAS) [30]

Secondary outcomes:

Perioperative complications (bleeding, intracranial injuries, intraorbital injuries) [31]

Length of stay [32]

Operative time [33]

Need for revision surgery [34]

Disease recurrence [35]

Patient and public involvement

This study consists of a systematic review protocol; therefore, individual patient data will not be presented. An extensive literature search will be conducted using defined databases. Furthermore, there will be no patient or public involvement in the study planning or application process, neither during the analysis nor dissemination of results.

Search strategy

PubMed, Embase, Scopus, Web of Science, Scielo, Cochrane Central Register of Controlled Trials (CENTRAL), CINAHL, LILACS, and Clinicaltrials.gov will be searched with no limitations to date or language. This search is planned for April 20, 2022.

Medical Subject Headings (MeSH) terms used for searching PubMed are presented in Table 1 and will be adapted to each database.

Table 1	Search strategy for PubMed

1	Sinusitis
2	Skull Base
3	Chronic Rhinosinusitis
4	Nasal Polyps
5	Nasal surgical procedures
6	Endoscopic sinus surgery
7	Nasal surgery
8	OR/1-8
9	Image Guided Surgery
10	Neuronavigation
11	Computer Assisted Surgery
12	OR/ 9-12
13	Quality of life
14	Life quality
15	Health Related Quality of Life
16	Morbidity
17	Complication
18	Intraoperative Complication
19	Postoperative Complication
20	Patient Reported Outcome Measures
21	Bleeding

22	Death
23	Cerebrospinal Fluid Leak
24	Operative Time
25	Length of Stay
26	Orbital Diseases
27	Brain Diseases
28	Revision Surgery
29	Recurrence
30	OR/13-29
31	8 AND 12 AND 30

Other sources

Eligible studies may also be selected from the reference lists of the retrieved articles. The scope of the computerized literature search may be widened based on the reference lists of the retrieved articles.

Data collection and analysis

Selection of studies

The articles retrieved by the search will be imported to EndNote Web, and duplicates will be removed. Three authors, MLN, MGN, and KSM, will independently screen the results first by title, abstracts, and then full text to determine whether they meet the inclusion criteria. A fourth reviewer, AKG, will resolve any discrepancies. A PRISMA flow diagram summarizes the study selection process (Figure 1).[36]

Data extraction and management

Three independent authors (MLN, MGN, and HPB) will extract data from the eligible and included studies. The latter will be inserted into a database following this

designed form: publication year, first author, number of patients per group, number of follow-up losses per group, mean age, intervention description, control group description, follow-up time, randomization, allocation, blinding, complication, mean HRQOL score, recurrence rate, revision surgery rate, mean operative time, and mean length of stay. A meta-analysis will be conducted if a pool of included articles with sufficiently similar characteristics is obtained.

Addressing missing data

If any of the selected articles have insufficient information, we will contact the corresponding author via email or phone to obtain the missing data. If unsuccessful, the data will be deleted or imputed and will be discussed in the Discussion section.

Risk of bias assessment

The Cochrane Risk of Bias tool will be applied to evaluate random sequence generation, allocation concealment, blinding, and evaluation of clinical results.[37] We will also assess missing data, incomplete reports, financial aids, and potential conflicts of interest of each study.

Assessment of heterogeneity

Heterogeneity will be assessed by I2 statistics, in which a percentage < 25% will be considered no heterogeneity, between 25% and 50% moderate heterogeneity, and > 50% high heterogeneity.

Measures of treatment effect

Scores of validated tools will assess the primary outcome (quality of life). Since this will be continuous data, the mean and standard deviation will be calculated and presented. The risk ratio will be calculated for dichotomous data (complication). This will be performed using Review Manager (RevMan, version 5.4) software.

Analysis

RevMan 5.4 will be used to perform the statistical analysis. In the heterogeneity assessment, if I2> 50%, a random-effects model will be used, while if I2<50%, a fixed-effect model will be applied. Moreover, to assess the possible reporting bias, a funnel plot will be constructed to observe and test the symmetry of distribution of the results from the included studies.

Subgroup analyses

Subgroup analyses will be based on the type of intervention, participant age, and study settings. Meta-regressions will be conducted to compare the risk ratio and investigate whether any observed differences between the subgroups were statistically significant.

Grading quality of evidence

We will use the Grading of Recommendations Assessment Development and Evaluation (GRADE) approach to evaluate the strength of evidence of the systematic review results. The GRADE tool classifies studies as low, moderate, and high quality.[38]

Amendments

If any important aspect of the methods of the review needs to be modified for improvement, an amendment will be made. In case any alteration occurs from the original protocol it will be added to the registration record and reported on the final review**.**

DISCUSSION

The paranasal sinuses are in close anatomical proximity to vital and delicate structures such as the skull base, orbit, internal carotid artery, and optic nerve. Broad and detailed anatomic knowledge is essential for surgeons to perform safe and effective procedures.[12]

Surgeons have acquired a greater operative domain with the advent of intraoperative imaging. However, its exact correlation with the patient's clinical outcome is still subject to further studies, evaluating, for example, the postoperative quality of life or the complications.[15]

Vreudenburg et al.,[19] found a reduction in the likelihood of total, major, and orbital complications in complex ESS procedures with the use of IGS. However, this study was not limited to patients diagnosed with CRS nor did it evaluate the quality of life outcomes.

This review proposes to provide evidence-based decision-making information that may help reduce complications, prevent disease recurrence, and improve patients' quality of life.

ETHICS AND DISSEMINATION

This study is a systematic review with a possible meta-analysis, which will use data from previously conducted studies; therefore, it does not require ethical approval. The outcome of this research will be submitted for publication in a peer-reviewed journal.

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Authors' contributions

MLN, MGN, ACAS, and AKG were responsible for the design of this review. MLN and MGN wrote a draft of the protocol's manuscript, and RNC and AKG revised it. MLN, ACAS, and HPB developed search strategies. MLN and KSM completed formatting the manuscript. All the authors approved the final version for publication.

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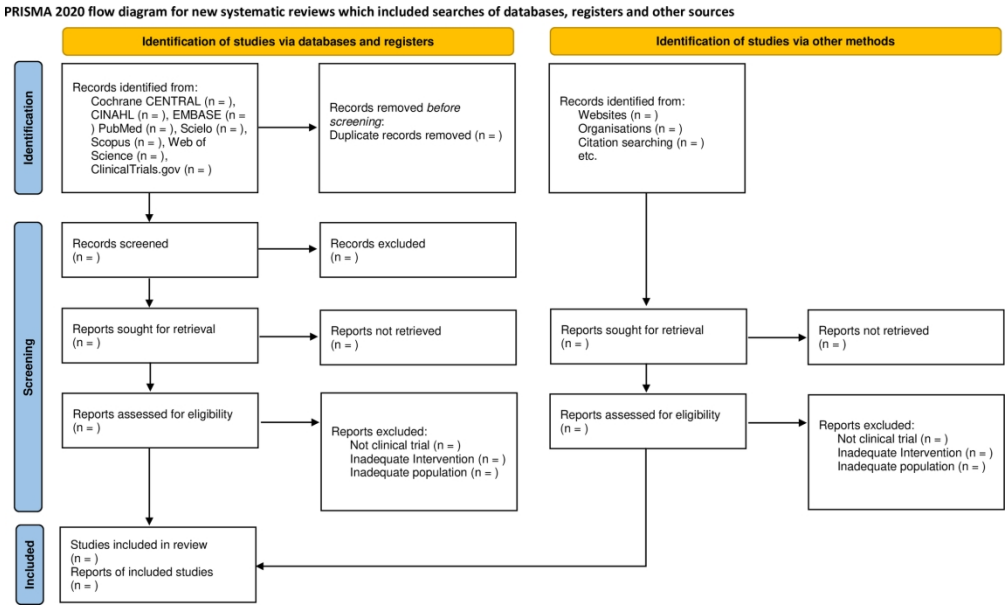
Competing interests

None declared.

Figure 1- PRISMA flow diagram.



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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			
Title:			
Identification	1a	Identify the report as a protocol of a systematic review	01
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	02
Authors:			
Contact	3a	Provide name, institutional affiliation, e-mail address of all protocol authors; provide physical mailing address of corresponding author	01
Contributions	3b	Describe contributions of protocol authors and identify the guarantor of the review	12
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	09
Support:			
Sources	5a	Indicate sources of financial or other support for the review	12
Sponsor	5b	Provide name for the review funder and/or sponsor	NA
Role of sponsor or funder	5c	Describe roles of funder(s), sponsor(s), and/or institution(s), if any, in developing the protocol	NA
INTRODUCTION			
Rationale	6	Describe the rationale for the review in the context of what is already known	04
Objectives	7	Provide an explicit statement of the question(s) the review will address with reference to participants, interventions, comparators, and outcomes (PICO)	04
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	04
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	05-06

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	06
Study records:			
Data management	11a	Describe the mechanism(s) that will be used to manage records and data throughout the review	07
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)	07
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	08
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	08
Outcomes and prioritization	13	List and define all outcomes for which data will be sought, including prioritization of main and additional outcomes, with rationale	08
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	08
Data synthesis	15a	Describe criteria under which study data will be quantitatively synthesised	08
	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)	08
	15c	Describe any proposed additional analyses (such as sensitivity or subgroup analyses, meta-regression)	08
	15d	If quantitative synthesis is not appropriate, describe the type of summary planned	09
Meta-bias(es)	16	Specify any planned assessment of meta-bias(es) (such as publication bias across studies, selective reporting within studies)	09
Confidence in cumulative evidence	17	Describe how the strength of the body of evidence will be assessed (such as GRADE)	09

*** 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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