



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

Maria Luisa Nobre <sup>1,2</sup>, Ayane Cristine Alves Sarmiento,<sup>1</sup> Maria Gabriela Nobre,<sup>3</sup> Henrique de Paula Bedaque,<sup>3</sup> Kleyton Santos Medeiros,<sup>1,4</sup> Ricardo Ney Cobucci,<sup>5</sup> Ana Katherine Gonçalves <sup>1</sup>

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<sup>1</sup>Health Sciences Postgraduate Program, Federal University of Rio Grande do Norte, Natal, Brazil

<sup>2</sup>Department of Surgery, Federal University of Rio Grande do Norte, Natal, Brazil

<sup>3</sup>Federal University of Rio Grande do Norte, Natal, Brazil

<sup>4</sup>Instituto de Ensino, Pesquisa e Inovação, Liga Contra o Câncer, Natal, Brazil

<sup>5</sup>Postgraduate Program in Biotechnology, Potiguar University, Natal, Brazil

## Correspondence to

Dr Ana Katherine Gonçalves; [anakatherine\\_ufrnet@yahoo.com.br](mailto:anakatherine_ufrnet@yahoo.com.br)

## ABSTRACT

**Introduction** Endoscopic sinus surgery (ESS) is a current procedure for treating patients with chronic rhinosinusitis (CRS). 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 20 April 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,  $I^2$  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.

## INTRODUCTION

### Description of the condition

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

The latter affects 5%–28% of the general population and tremendously impacts patients' socioeconomic conditions and quality of life. The healthcare costs are higher in rhinosinusitis than in other diseases such

## 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 (IGS) 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.

as peptic ulcers, asthma and hay fever. Indirect costs are also significant, since it affects working age, leading to absenteeism and decreased productivity.<sup>2–7</sup> 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.<sup>8</sup>

The aetiology of CRS involves bacterial superantigens, epithelial cell defects, biofilm, T helper 1 and 2 inflammation responses and tissue remodelling.<sup>9 10</sup> It is classified into CRS with nasal polyps and CRS without nasal polyps.<sup>11 12</sup>

The advent of endoscopic sinus surgery (ESS) in the late 1980s and the early 1990s brought revolutionary advances to the treatment of CRS.<sup>10</sup> Reducing type 2 inflammation and preventing irreversible remodelling of the mucosa by facilitating improved access



to topical therapies are potentially disease-modifying benefits of surgery.<sup>2</sup>

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.<sup>13</sup> The risk of one or more injuries is even higher in revision surgeries due to the removal of critical anatomical landmarks in previous procedures.<sup>14–16</sup> 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.<sup>17 18</sup> Nevertheless, complications can result in serious repercussions.<sup>17 19</sup>

### 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.<sup>10</sup>

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 or optical tracking technology to perform this position determination in the operating field against preoperative imaging datasets.<sup>3 20</sup>

### 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.<sup>3 20</sup>

### 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.<sup>21</sup> 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.<sup>22</sup> 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 CRS.
- ▶ Intervention: ESS with image guidance.
- ▶ Comparator/control: ESS 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 CRS according to the European Position Paper on Rhinosinusitis and Nasal Polyps (EPOS) 2020 and EPOS 2012 criteria.<sup>2 23</sup>

### 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:

1. Sinonasal Outcome Test (SNOT-16, SNOT-20 or SNOT-22).<sup>24–26</sup>
2. Rhinosinusitis Quality of Life Survey Instrument (RhinoQoL).<sup>27</sup>
3. Rhinosinusitis Outcome Measurement (RSOM-31).<sup>28</sup>
4. Rhinosinusitis Disability Index (RSDI).<sup>29</sup>
5. Visual Analogue Scale (VAS).<sup>30</sup>

#### Secondary outcomes

1. Perioperative complications (bleeding, intracranial injuries, intraorbital injuries).<sup>31</sup>
2. Length of stay.<sup>32</sup>
3. Operative time.<sup>33</sup>
4. Need for revision surgery.<sup>34</sup>
5. Disease recurrence.<sup>35</sup>

### 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

**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

will be searched with no limitations to date or language. This search is planned for 20 April 2022.

Medical Subject Headings terms used for searching PubMed are presented in [table 1](#) and will be adapted to each database.

### Other sources

Eligible studies may also be selected from the reference lists of the retrieved articles. The scope of the computerised 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 summarises the study selection process ([figure 1](#)).<sup>36</sup>

### Data extraction and management

Three independent authors (MLN, MGN and HdPB) 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, randomisation, 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.<sup>37</sup> 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  $I^2$  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 SD will be calculated and presented. The risk ratio will be calculated for dichotomous data (complication). This will be performed using Review Manager (RevMan, V.5.4) software.

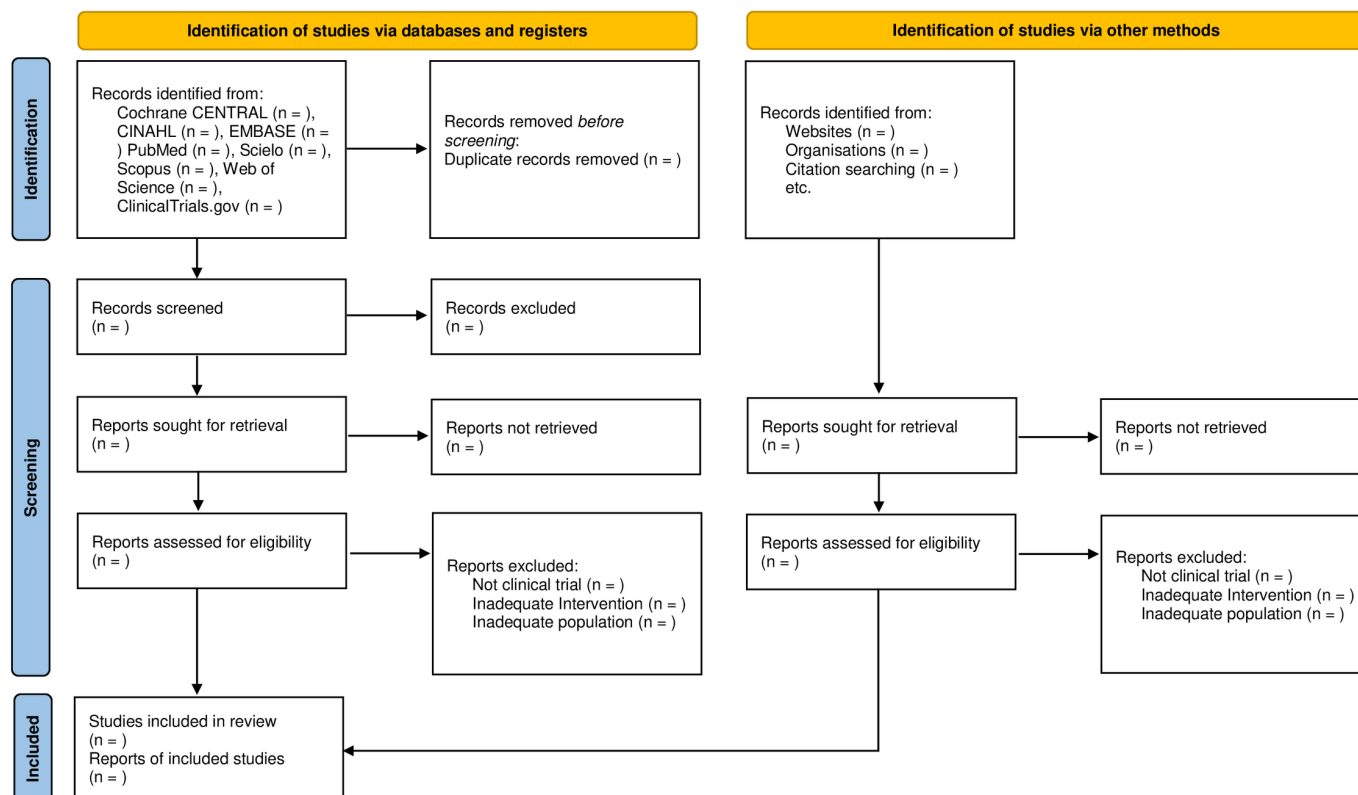
### Analysis

RevMan V.5.4 will be used to perform the statistical analysis. In the heterogeneity assessment, if  $I^2 > 50%$ , a random-effects model will be used, while if  $I^2 < 50%$ , 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

## PRISMA 2020 flow diagram for new systematic reviews which included searches of databases, registers and other sources



**Figure 1** Preferred Reporting Items for Systematic Reviews and Meta-Analyses flow diagram.

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.<sup>38</sup>

### 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.<sup>10</sup>

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.<sup>15</sup>

Vreugdenburg *et al*,<sup>19</sup> 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.

**Contributors** 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 HdPB 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.

**Patient and public involvement** Patients and/or the public were not involved in the design, or conduct, or reporting or dissemination plans of this research.

**Patient consent for publication** Not applicable.

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#### ORCID iDs

Maria Luisa Nobre <http://orcid.org/0000-0003-0969-4806>

Ana Katherine Gonçalves <http://orcid.org/0000-0002-8351-5119>

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