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VACÍOS DE LA EVIDENCIA EN CIRUGÍA ORTOGNÁTICA

Josefina Bendersky Kohan

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PROGRAMA DE DOCTORADO EN METODOLOGÍA DE LA INVESTIGACIÓN BIOMÉDICA Y SALUD PÚBLICA

Departamento de Pediatría, Obstetricia y Ginecología, y Medicina Preventiva y Salud Pública

TESIS DOCTORAL

VACÍOS DE LA EVIDENCIA EN CIRUGÍA ORTOGNÁTICA

:::

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A todos los coautores de mis publicaciones, gracias por todo el esfuerzo y la ayuda para hacer esto posible.

PRESENTACIÓN

Mi nombre es Josefina Bendersky, nací en Santiago de Chile y soy cirujana dentista titulada por la Pontificia Universidad Católica de Chile (2013–2019). Posteriormente, cursé el Diplomado en Diagnóstico de Patologías de Huesos Maxilares (2020) y el Diplomado en Diagnóstico y Tratamiento de Patología de la Mucosa Oral (2021) en la misma universidad. En el año 2020 decidí mudarme a Barcelona para realizar el Máster en Investigación Clínica Aplicada a las Ciencias de la Salud en la Universitat Autònoma de Barcelona. Tras finalizar el máster, tuve el agrado de trabajar en Cochrane Iberoamérica, experiencia que fortaleció mi interés por la síntesis de evidencia y la investigación colaborativa. Esta trayectoria me llevó a participar como coordinadora del proyecto Living Evidence to Inform Health Decisions, liderado por la Dra. María Ximena Rojas-Reyes, orientado al desarrollo y aplicación de revisiones sistemáticas y evidencia viva para la toma de decisiones en salud.

Actualmente, soy residente de tercer año del programa de especialización en Cirugía y Traumatología Bucal y Maxilofacial de la Universidad de Chile, donde combino mi formación clínica con el desarrollo de proyectos de investigación en cirugía maxilofacial y metodología de la investigación biomédica. Además, colaboro en el área de docencia de la Facultad de Odontología de la Universidad de Chile, como instructora y coordinadora en cursos de práctica clínica basada en la evidencia para estudiantes de posgrado, y formo parte del equipo Cochrane de la Universidad de Chile, contribuyendo a iniciativas orientadas al fortalecimiento de la investigación basada en la evidencia en el ámbito odontológico.

DECLARACIÓN DE CONFLICTO DE INTERÉS

Declaro no tener ningún conflicto de interés relacionado con el desarrollo, los resultados ni la publicación de esta tesis doctoral.

La presente tesis doctoral titulada “Vacíos de Evidencia en Cirugía Ortognática” se ha desarrollado mediante un compendio de publicaciones para obtener el título de doctora de la Universitat Autònoma de Barcelona.

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1. RESUMEN

1.1 RESUMEN (ESPAÑOL)

INTRODUCCIÓN

Las deformidades dentofaciales constituyen alteraciones complejas del complejo craneofacial que repercuten significativamente en la estética, la función masticatoria, la respiración y la calidad de vida de los pacientes. La cirugía ortognática representa el tratamiento de elección en los casos severos, mediante técnicas quirúrgicas que permiten el reposicionamiento tridimensional de los maxilares. Sin embargo, pese al aumento sostenido de publicaciones en este ámbito durante las últimas décadas, la literatura científica presenta limitaciones sustanciales en cuanto a la pertinencia, calidad metodológica y aplicabilidad clínica de la evidencia disponible. Esto se traduce en vacíos de evidencia que dificultan la toma de decisiones clínicas fundamentadas en conocimiento sólido, poniendo de relieve la necesidad de identificar, clasificar y priorizar de manera sistemática las preguntas de investigación más relevantes.

OBJETIVOS

El objetivo general de esta tesis doctoral fue identificar, sintetizar y organizar los vacíos de evidencia clínicamente relevantes en cirugía ortognática, con el fin de orientar la investigación futura hacia áreas de mayor impacto clínico. Entre los objetivos específicos se incluyó: (i) sistematizar y representar gráficamente la distribución de la literatura científica mediante revisiones sistemáticas de mapeo; (ii) evaluar la calidad metodológica de los estudios secundarios disponibles; (iii) identificar lagunas críticas en el conocimiento científico; y (iv) determinar la relevancia clínica de dichas lagunas a través de la opinión experta, estableciendo prioridades de investigación.

MÉTODOS

La tesis se estructuró como un compendio de tres publicaciones principales. En primer lugar, se desarrolló una revisión de mapeo sobre cirugía ortognática, siguiendo los lineamientos PRISMA-ScR y la Global Evidence Mapping Initiative. Este trabajo permitió caracterizar el panorama general de la literatura, analizar el tipo de estudios, poblaciones, intervenciones quirúrgicas y co-intervenciones evaluadas, así como los desenlaces reportados. Posteriormente, se realizó una segunda revisión de mapeo focalizada en tres complicaciones críticas de la cirugía ortognática: pérdida sanguínea, infección y recidiva. En este análisis se elaboraron matrices de evidencia y mapas de burbujas para visualizar la dirección y consistencia de los hallazgos, y se evaluó la calidad metodológica mediante la herramienta AMSTAR-2. Finalmente, se llevó a cabo un estudio Delphi internacional con la participación de cirujanos maxilofaciales de 17 países, destinado a priorizar los vacíos de evidencia identificados y generar un listado consensuado de preguntas de investigación de mayor relevancia clínica. Adicionalmente, se efectuó una actualización de la literatura para verificar el estado actual de los vacíos considerados más prioritarios.

RESULTADOS

El primer mapping review incluyó 290 estudios (35 revisiones sistemáticas y 253 estudios primarios), identificando una marcada heterogeneidad en los diseños y desenlaces reportados, además de una calidad metodológica globalmente baja: más de la mitad de las revisiones fueron evaluadas como de calidad “críticamente baja”. Se detectaron 15 vacíos de evidencia iniciales, concentrados en tópicos como la eficacia de la hipotensión inducida, el número y tipo de placas de osteosíntesis, el uso de láser de baja intensidad y la aplicación de piezoeléctrico. La segunda revisión, enfocada en pérdida sanguínea, infección y recidiva, permitió constatar que, si bien algunas intervenciones como el ácido tranexámico mostraron resultados consistentemente favorables, en la mayoría de los casos los hallazgos fueron inconclusos o derivados de estudios con limitaciones metodológicas. El estudio Delphi, con una tasa de retención del 74%, permitió priorizar

15 preguntas clínicas, de las cuales el 47% se relacionaron con recidiva, el 40% con pérdida sanguínea y el 13% con infección. Entre las de mayor relevancia clínica se destacaron el impacto del número de placas de osteosíntesis en la recidiva, la eficacia del ácido tranexámico en la reducción de sangrado y la utilidad de la hipotensión controlada como estrategia anestésica. La actualización de la literatura confirmó que el vacío relativo al número de placas de osteosíntesis sigue sin resolverse, mientras que los dos últimos cuentan con evidencia robusta que respalda su eficacia.

DISCUSIÓN

El análisis integrado de los resultados puso en evidencia un claro desequilibrio temático en la literatura científica, caracterizado por sobreinvestigación en áreas de menor impacto clínico y escasa atención a cuestiones consideradas prioritarias por expertos internacionales. Asimismo, se constató que la calidad metodológica de los estudios en cirugía ortognática es en general deficiente, lo que limita la aplicabilidad de los hallazgos a la práctica clínica. Se enfatizó la importancia de desarrollar procesos formales de priorización de evidencia, así como de implementar estrategias innovadoras, entre ellas las revisiones sistemáticas vivas y la definición de conjuntos de desenlaces estandarizados (core outcome sets). Estas herramientas permitirían mejorar la pertinencia, calidad y eficiencia de la investigación en este campo.

CONCLUSIONES

La tesis demuestra que los métodos aplicados, particularmente las revisiones de mapeo y el estudio Delphi, son altamente efectivos para detectar y priorizar vacíos de evidencia en cirugía ortognática. Se concluye que la investigación futura debe concentrarse en las preguntas clínicas identificadas como prioritarias y diseñar estudios primarios de alta calidad que superen las limitaciones metodológicas actuales. Entre los vacíos de evidencia más relevantes, se identificó que:

1. El impacto del número de placas de osteosíntesis en la recidiva continúa siendo un interrogante sin resolver, que requiere estudios primarios de alta calidad;

2. La eficacia del ácido tranexámico para reducir el sangrado en cirugía ortognática ha sido confirmada con evidencia sólida y de alta certeza, constituyendo un vacío ya resuelto; y
3. La utilidad de la hipotensión controlada para disminuir la pérdida sanguínea cuenta con evidencia favorable, aunque de certeza baja, lo que sugiere que el vacío se encuentra parcialmente resuelto pero requiere estudios adicionales para consolidar la confianza en los hallazgos.

En síntesis, esta tesis aporta una base metodológica y conceptual sólida para guiar la investigación futura en cirugía ortognática, promoviendo una producción científica más eficiente, relevante y alineada con las necesidades reales de la práctica clínica.

1.2 RESUM (CATALÁ)

INTRODUCCIÓ

Les deformitats dentofacials constitueixen alteracions complexes del complex craniofacial que repercuteixen significativament en l'estètica, la funció masticatòria, la respiració i la qualitat de vida dels pacients. La cirurgia ortognàtica pretén solucionar aquestes alteracions mitjançant tècniques quirúrgiques que permeten el reposicionament tridimensional dels maxil·lars. Tanmateix, malgrat l'augment sostingut de publicacions en aquest àmbit durant les darreres dècades, la literatura científica presenta limitacions substancials pel que fa a la pertinència, la qualitat metodològica i l'aplicabilitat clínica de l'evidència disponible. Això es tradueix en buits d'evidència que dificulten la presa de decisions clíniques fonamentades en coneixement sòlid, posant de relleu la necessitat d'identificar, classificar i prioritzar de manera sistemàtica les preguntes de recerca més rellevants.

OBJECTIUS

L'objectiu general d'aquesta tesi doctoral fou identificar, sintetitzar i organitzar els buits d'evidència clínicament rellevants en cirurgia ortognàtica, amb la finalitat d'orientar la recerca futura cap a àrees d'alt impacte clínic. Entre els objectius específics s'hi inclogué: (i) sistematitzar i representar gràficament la distribució de la literatura científica mitjançant revisions sistemàtiques de mapatge; (ii) avaluar la qualitat metodològica dels estudis disponibles; (iii) identificar mancances crítiques en el coneixement científic; i (iv) determinar la rellevància clínica d'aquestes mancances a través de l'opinió experta, establint prioritats de recerca.

MÈTODES

La tesi es va estructurar com un compendi de tres publicacions principals. En primer lloc, es desenvolupà una revisió sistemàtica de mapatge sobre cirurgia ortognàtica, seguint les directrius PRISMA-ScR i la Global Evidence Mapping Initiative. Aquest treball permeté caracteritzar el panorama general de la literatura, analitzar el tipus d'estudis, poblacions, intervencions quirúrgiques i cointervencions avaluades, així com els resultats reportats. Posteriorment, es

realitzà una segona revisió de mapatge focalitzada en tres complicacions crítiques de la cirurgia ortognàtica: pèrdua sanguínia, infecció i recidiva. En aquest anàlisi es van elaborar matrius d'evidència i mapes de bombolles per visualitzar la direcció i consistència de les troballes, i es va avaluar la qualitat metodològica amb l'eina AMSTAR-2. Finalment, es dugué a terme un estudi Delphi internacional amb la participació de cirurgians maxil·lofacials de 17 països, destinat a prioritzar els buits d'evidència identificats i generar un llistat consensuat de preguntes de recerca de major rellevància clínica. Addicionalment, es realitzà una actualització de la literatura per verificar l'estat dels buits considerats més prioritaris.

RESULTATS

La primera revisió de mapatge inclogué 290 estudis (35 revisions sistemàtiques i 253 estudis primaris), identificant una marcada heterogeneïtat en els dissenys i resultats reportats, a més d'una qualitat metodològica globalment baixa: més de la meitat de les revisions foren avaluades com de qualitat "críticament baixa". Es van detectar 15 buits d'evidència inicials, concentrats en temes com l'eficàcia de la hipotensió induïda, el nombre i tipus de plaques d'osteosíntesi, l'ús de làser de baixa intensitat i l'aplicació del piezoelèctric. La segona revisió, centrada en pèrdua sanguínia, infecció i recidiva, constatà que, tot i que algunes intervencions com l'àcid tranexàmic mostraren resultats consistentment favorables, en la majoria de casos les troballes foren inconcluses o derivades d'estudis amb limitacions metodològiques. L'estudi Delphi, amb la participació de 74 cirurgians maxil·lofacials i una taxa de retenció del 74%, permeté prioritzar 15 preguntes clíniques, de les quals el 47% es relacionaven amb recidiva, el 40% amb pèrdua sanguínia i el 13% amb infecció. Entre les de major rellevància clínica destacaren l'impacte del nombre de plaques d'osteosíntesi en la recidiva, l'eficàcia de l'àcid tranexàmic en la reducció del sagnat i la utilitat de la hipotensió controlada com a estratègia anestèsica. L'actualització de la literatura confirmà que el buit relatiu al nombre de plaques d'osteosíntesi continua sense resoldre's, mentre que els dos darrers disposen d'evidència sòlida que n'avala l'eficàcia.

DISCUSSIÓ

L'anàlisi integrat dels resultats posà de manifest un clar desequilibri temàtic en la literatura científica, caracteritzat per una sobreinvestigació en àrees de menor impacte clínic i una atenció insuficient a qüestions considerades prioritàries pels experts internacionals. Així mateix, es constatà que la qualitat metodològica dels estudis en cirurgia ortognàtica és, en general, deficient, la qual cosa limita l'aplicabilitat dels resultats a la pràctica clínica. S'emfasitzà la importància de desenvolupar processos formals de priorització d'evidència, així com d'implementar estratègies innovadores, entre elles les revisions sistemàtiques vives i la definició de conjunts de resultats estandarditzats (core outcome sets). Aquestes eines permetrien millorar la pertinència, la qualitat i l'eficiència de la recerca en aquest camp.

CONCLUSIONS

La tesi demostra que els mètodes aplicats, particularment les revisions de mapatge i l'estudi Delphi, són altament efectius per detectar i prioritzar buits d'evidència en cirurgia ortognàtica. Es conclou que la recerca futura ha de concentrar-se en les preguntes clíniques identificades com a prioritàries i dissenyar estudis primaris de gran qualitat que superin les limitacions metodològiques actuals. Entre els buits d'evidència més rellevants, es va identificar que:

1. L'impacte del nombre de plaques d'osteosíntesi en la recidiva continua sent un interrogant sense resoldre, que requereix estudis primaris de gran qualitat;
2. L'eficàcia de l'àcid tranexàmic per reduir el sagnat en cirurgia ortognàtica ha estat confirmada amb evidència sòlida i d'alta certesa, constituint un buit ja resolt; i
3. La utilitat de la hipotensió controlada per disminuir la pèrdua sanguínia compta amb evidència favorable, encara que de certesa baixa, cosa que suggereix que el buit es troba parcialment resolt però requereix estudis addicionals per consolidar la confiança en els resultats.

En síntesi, aquesta tesi ofereix una base metodològica i conceptual sòlida per orientar la recerca futura en cirurgia ortognàtica, fomentant una producció científica més eficient, rellevant i alineada amb les necessitats reals de la pràctica clínica.

1.3 ABSTRACT (ENGLISH)

INTRODUCTION

Dentofacial deformities are complex craniofacial conditions that significantly affect aesthetics, masticatory function, breathing, and patients' quality of life. Orthognathic surgery aims to address these alterations through surgical techniques that allow tridimensional repositioning of the jaws. However, despite the sustained increase in publications in this field over the last decades, the scientific literature shows substantial limitations regarding relevance, methodological quality, and clinical applicability of the available evidence. This translates into evidence gaps that hinder evidence-based clinical decision-making, underscoring the need to systematically identify, classify, and prioritize the most relevant research questions.

OBJECTIVES

The overall aim of this doctoral thesis was to identify, synthesize, and systematically organize clinically relevant evidence gaps in orthognathic surgery in order to guide future research toward areas of higher clinical impact. Specific objectives included: (i) systematizing and graphically representing the distribution of the scientific literature through systematic mapping reviews; (ii) assessing the methodological quality of existing studies; (iii) identifying critical gaps in scientific knowledge; and (iv) determining the clinical relevance of such gaps through expert opinion, thus establishing research priorities.

METHODS

This thesis was structured as a compendium of three main publications. First, a systematic mapping review on orthognathic surgery was conducted, following PRISMA-ScR and Global Evidence Mapping Initiative guidelines. This study allowed characterization of the general landscape of the literature, including study designs, populations, surgical interventions, co-interventions, and reported outcomes. Subsequently, a second mapping review focused on three critical complications of orthognathic surgery: blood loss, infection, and relapse. Evidence matrices and

bubble maps were elaborated to visualize the direction and consistency of findings, and methodological quality was appraised using the AMSTAR-2 tool. Finally, an international Delphi study was conducted with maxillofacial surgeons from 17 countries, aimed at prioritizing the identified evidence gaps and generating a consensus-based list of the most clinically relevant research questions. In addition, a literature update was performed to verify the current status of the most prioritized gaps.

RESULTS

The first mapping review included 290 studies (35 systematic reviews and 253 primary studies), highlighting marked heterogeneity in designs and reported outcomes, together with an overall low methodological quality: more than half of the reviews were rated as “critically low.” Fifteen initial evidence gaps were identified, focused on topics such as the effectiveness of induced hypotension, the number and type of osteosynthesis plates, the use of low-level laser therapy, and piezoelectric devices. The second mapping review, centered on blood loss, infection, and relapse, confirmed that while some interventions such as tranexamic acid showed consistently favorable results, most findings remained inconclusive or were derived from studies with significant methodological limitations. The Delphi study, with the participation of 74 maxillofacial surgeons and a 74% retention rate, prioritized 15 clinical questions, of which 47% were related to relapse, 40% to blood loss, and 13% to infection. Among the most clinically relevant were the impact of the number of osteosynthesis plates on relapse, the effectiveness of tranexamic acid in reducing bleeding, and the usefulness of controlled hypotension as an anesthetic strategy. The updated literature search confirmed that the gap related to the number of osteosynthesis plates remains unresolved, while the other two are now supported by robust evidence demonstrating their effectiveness.

DISCUSSION

The integrated analysis of results revealed a clear thematic imbalance in the scientific literature, with over-investigation of clinically marginal topics and insufficient attention to questions considered high-

priority by international experts. Furthermore, the methodological quality of studies in orthognathic surgery was generally low, limiting the clinical applicability of findings. The importance of developing formal processes for evidence prioritization was emphasized, as well as the implementation of innovative strategies such as living systematic reviews and the establishment of standardized core outcome sets. These tools could enhance the relevance, quality, and efficiency of research in this field.

CONCLUSIONS

This thesis demonstrates that the applied methods—particularly mapping reviews and the Delphi study—are highly effective in identifying and prioritizing evidence gaps in orthognathic surgery. Future research should focus on clinically prioritized questions and design high-quality primary studies to overcome current methodological limitations. The most relevant evidence gaps were:

1. The impact of the number of osteosynthesis plates on relapse, which remains unresolved and requires high-quality primary studies;
2. The effectiveness of tranexamic acid in reducing blood loss, which has been confirmed with solid, high-certainty evidence, constituting a gap already resolved; and
3. The usefulness of controlled hypotension in reducing intraoperative bleeding, which is supported by favorable but low-certainty evidence, suggesting the gap is partially resolved but requires further studies to consolidate confidence.

In summary, this thesis provides a solid methodological and conceptual foundation to guide future research in orthognathic surgery, promoting a more efficient, relevant, and clinically aligned scientific production.

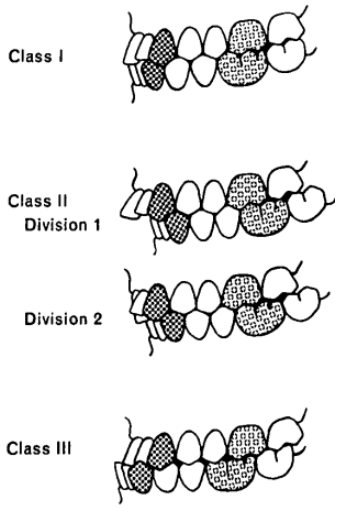
2. INTRODUCCIÓN

2.1 DEFORMIDADES DENTOFACIALES

Las deformidades dentofaciales constituyen alteraciones estructurales significativas del complejo craneofacial que afectan tanto la estética facial como funciones esenciales tales como la masticación, respiración y fonación. La etiología de estas deformidades es multifacética, involucrando factores genéticos, ambientales, traumáticos y funcionales, incluyendo hábitos parafuncionales y disfunciones musculares crónicas (1). Para un diagnóstico adecuado se requiere un enfoque integral, que comprende exámenes clínicos detallados, evaluaciones radiográficas avanzadas y análisis cefalométricos tridimensionales, complementados con modelos digitales (2).

La clasificación más ampliamente utilizada para describir estas deformidades es la propuesta por Angle, que las divide en tres clases principales: Clase I (normoclusión con pequeñas irregularidades dentarias), Clase II (retrognatismo mandibular o prognatismo maxilar) y Clase III (prognatismo mandibular o retrognatismo maxilar) (3) (Figura 1). Las repercusiones funcionales de estas alteraciones son significativas, destacando trastornos masticatorios, problemas respiratorios como apnea obstructiva del sueño y disfunciones en la articulación temporomandibular (ATM) (2).

Figura 1. Clasificación de Angle. *(Imagen tomada de Gravely JF, Johnson DB. Angle's classification of malocclusion: an assessment of reliability. Br J Orthod. 1974)* (4)



La prevalencia de las deformidades dentofaciales y de las maloclusiones varía de forma considerable según la población estudiada y los criterios diagnósticos utilizados. A nivel global, se estima que entre un 20% y 40% de la población presenta algún tipo de maloclusión que podría beneficiarse de tratamiento ortodóncico, y alrededor de un 5% a 15% requeriría tratamiento combinado con cirugía ortognática (5,6).

En un metanálisis reciente, la prevalencia de maloclusiones de Clase I se reportó entre 48–55%, de Clase II entre 15–20% y de Clase III entre 5–8%, aunque con variaciones marcadas entre regiones geográficas y grupos étnicos (7,8). En poblaciones asiáticas, por ejemplo, la Clase III presenta una prevalencia más elevada en comparación con poblaciones caucásicas, lo que refleja diferencias tanto genéticas como ambientales en el desarrollo dentofacial (9).

Además del impacto clínico, estas alteraciones representan un problema de salud pública, ya que pueden afectar la calidad de vida relacionada con la salud oral, el desempeño social y laboral de los pacientes, y generar una importante demanda asistencial en los sistemas de salud (10,11).

2.2 CIRUGÍA ORTOGNÁTICA

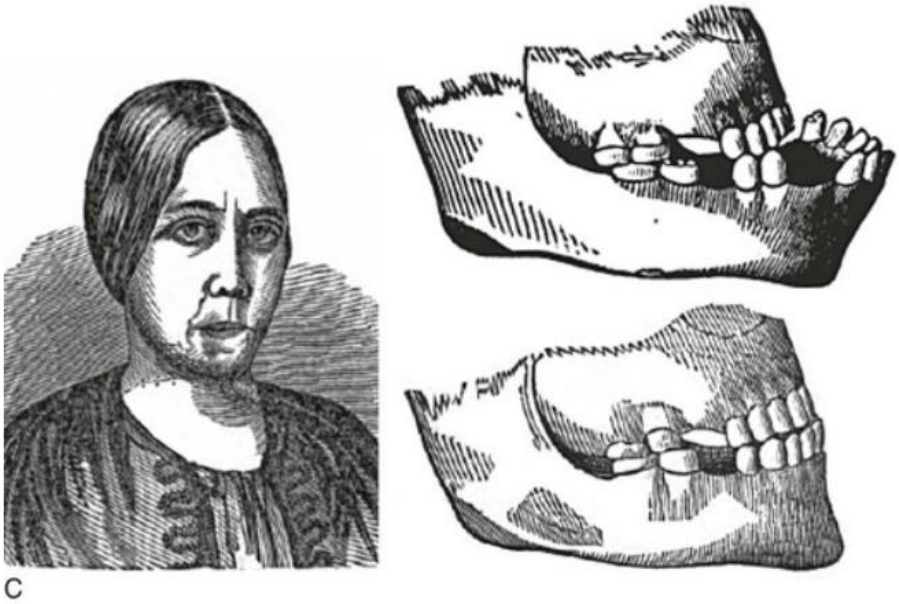
La cirugía ortognática constituye un conjunto de procedimientos quirúrgicos especializados dirigidos a corregir deformidades dentofaciales mediante el reposicionamiento quirúrgico de los maxilares y estructuras asociadas.

2.2.1 HISTORIA DE LA CIRUGÍA ORTOGNÁTICA

Se consolidó como una disciplina quirúrgica a mediados del siglo XX, aunque sus raíces se remontan al siglo XIX. Los primeros intentos de corregir deformidades dentofaciales mediante osteotomías fueron descritos por Hullihen en 1849, quien realizó una cirugía para corregir un prognatismo mandibular mediante resección segmentaria (Figura 2) (12). Posteriormente, en 1921, Blair publicó una serie de procedimientos destinados a corregir discrepancias maxilofaciales, estableciendo así las bases de la cirugía ortognática moderna (13).

Figura 2. Mandíbula preoperatoria de Huillihem. *(Imagen tomada de Hullihen SP: Case of elongation of the underjaw and distortion of the face and neck, caused by a burn, successfully treated. Am J Dent 1849)* (14)

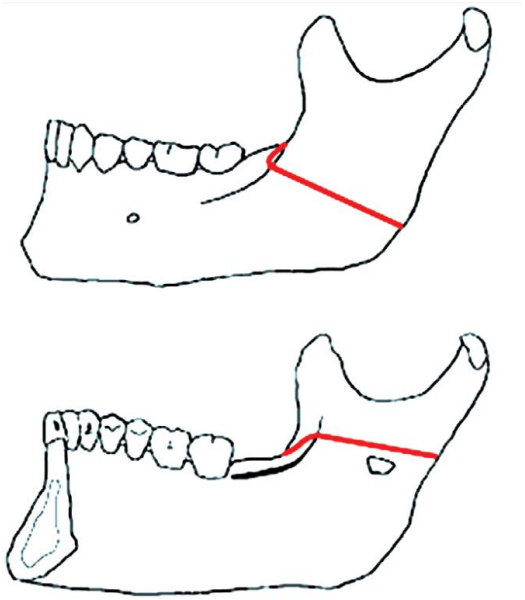




Un hito fundamental fue la descripción de la osteotomía sagital bilateral de rama mandibular (bilateral sagittal split osteotomy, BSSO) por Obwegeser en 1955, que permitió avances significativos en la corrección de las discrepancias mandibulares y se convirtió en una de las técnicas más utilizadas hasta la actualidad (Figura 3) (15,16). Del mismo modo, la osteotomía Le

Fort I, descrita y popularizada por Wassmund, Obwegeser y Bell en la década de 1960, revolucionó la posibilidad de reposicionar tridimensionalmente el maxilar (17,18). Estos desarrollos marcaron el inicio de la cirugía ortognática como una herramienta terapéutica establecida, complementada con la creciente colaboración interdisciplinaria con la ortodoncia y la anestesiología.

Figura 3. BSSO diseñada por Obwegweser. *(Imagen tomada de Böckmann R, et.al The modifications of the sagittal ramus split osteotomy: a literature review. Plast Reconstr Surg Glob Open. 2015*) (16)



En las últimas décadas, la incorporación de la planificación digital en 3D, la cirugía asistida por guías quirúrgicas y la impresión 3D han transformado la precisión y predictibilidad de los resultados quirúrgicos, consolidando a la cirugía ortognática como una disciplina en permanente evolución (19,20).

2.2.2 INDICACIONES DE LA CIRUGÍA ORTOGNÁTICA

La cirugía ortognática está indicada principalmente en pacientes con discrepancias dentoesqueléticas severas que no pueden ser corregidas únicamente con tratamiento ortodóncico. Estas alteraciones comprometen la relación adecuada entre los maxilares, los dientes y la base craneal, generando disfunciones funcionales y desarmonías estéticas que afectan de

manera significativa la calidad de vida del paciente (21). A diferencia de las maloclusiones dentarias leves o moderadas, que pueden abordarse con ortodoncia convencional, las deformidades esqueléticas requieren un enfoque combinado de ortodoncia y cirugía para lograr resultados estables y armoniosos (5).

En el plano funcional, una de las principales indicaciones corresponde a las dificultades masticatorias derivadas de discrepancias sagitales (prognatismo/retrognatismo maxilar/mandibular o combinaciones de ambos). Estas alteraciones interfieren en la eficiencia de la masticación, prolongan los tiempos de trituración de los alimentos y pueden repercutir en la digestión y nutrición del paciente. Asimismo, las maloclusiones severas se asocian con problemas de fonación, en especial en sonidos que requieren adecuada relación interincisal, y con trastornos en la respiración nasal y oral (22).

Otra indicación relevante corresponde a las alteraciones de la vía aérea superior. En este contexto, la cirugía ortognática se ha incorporado como parte del tratamiento en pacientes con síndrome de apnea obstructiva del sueño (SAOS) moderado o severo, particularmente en los casos en que existe retrusión maxilomandibular que contribuye a la obstrucción de la vía aérea (23). Procedimientos como el avance maxilomandibular han demostrado mejorar parámetros polisomnográficos, reducir episodios de apnea e incrementar la calidad de vida, consolidándose como una alternativa terapéutica eficaz y estable para determinados pacientes (23,24).

Las asimetrías faciales constituyen otra indicación frecuente, y suelen derivar de alteraciones en el crecimiento de los maxilares, ya sean de origen esquelético, articular o sindrómico. Una de las causas más frecuentes es la hiperplasia condilar, condición caracterizada por un crecimiento excesivo y unilateral del cóndilo mandibular, que provoca desviación de la línea media, inclinación del plano oclusal y asimetría progresiva del tercio inferior facial. En estos casos, el tratamiento quirúrgico debe orientarse tanto al control del crecimiento condilar (mediante condilectomía)

como a la corrección de la discrepancia esquelética residual mediante osteotomías ortognáticas (25,26).

Otra entidad relevante es la anquilosis de la articulación temporomandibular (ATM), en la que la fusión ósea o fibrosa de la articulación conduce a una restricción severa de los movimientos mandibulares, acompañada de hipoplasia y desviación mandibular progresiva en los casos unilaterales, y de micrognatia en los bilaterales (27). La cirugía ortognática en estos pacientes se combina con procedimientos reconstructivos de la ATM, con el fin de restablecer la función articular, corregir la asimetría y mejorar la estética facial (27).

De igual manera, los pacientes con síndromes craneofaciales —como microsomía hemifacial, síndrome de Treacher Collins o secuelas de craneosinostosis— presentan alteraciones complejas del desarrollo facial que incluyen asimetrías severas, deficiencias maxilares o mandibulares y compromiso de la vía aérea (28). En estos contextos, la cirugía ortognática se integra en protocolos multidisciplinarios de tratamiento, muchas veces de carácter secuencial, que buscan no solo corregir la maloclusión, sino también restablecer la simetría facial y mejorar la función masticatoria y respiratoria (29).

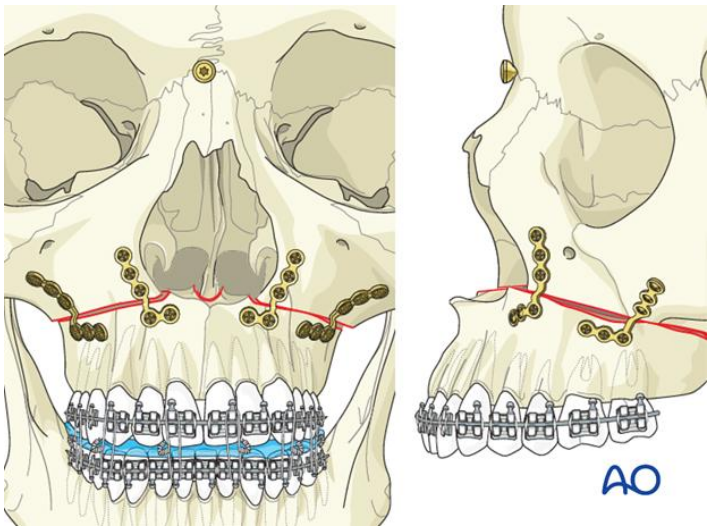
Desde el punto de vista estético, los pacientes con deformidades dentofaciales suelen presentar un deterioro en la armonía facial que impacta directamente en la autopercepción y en las interacciones sociales (30). Aunque la estética raramente constituye la única indicación quirúrgica, representa un factor determinante en la decisión terapéutica. Numerosos estudios han demostrado que la cirugía ortognática mejora de manera significativa la autoimagen, la satisfacción personal y la integración psicosocial, convirtiéndose en un objetivo esencial del tratamiento (10,30,31).

2.2.3 PLANIFICACIÓN Y TÉCNICAS QUIRÚRGICAS DE LA CIRUGÍA ORTOGNÁTICA

El abordaje interdisciplinario es fundamental en cirugía ortognática, involucrando una evaluación conjunta y detallada realizada por el cirujano maxilofacial y el ortodoncista. Esta planificación preoperatoria exhaustiva incluye la obtención y análisis riguroso de registros clínicos completos, tales como radiografías panorámicas y cefalométricas, fotografías clínicas, modelos dentales y registros oclusales. Previo al procedimiento quirúrgico, la fase ortodóncica inicial busca nivelar y alinear los dientes sobre sus bases óseas, estableciendo una correcta inclinación axial y la adecuada amplitud transversal del arco dentario (32).

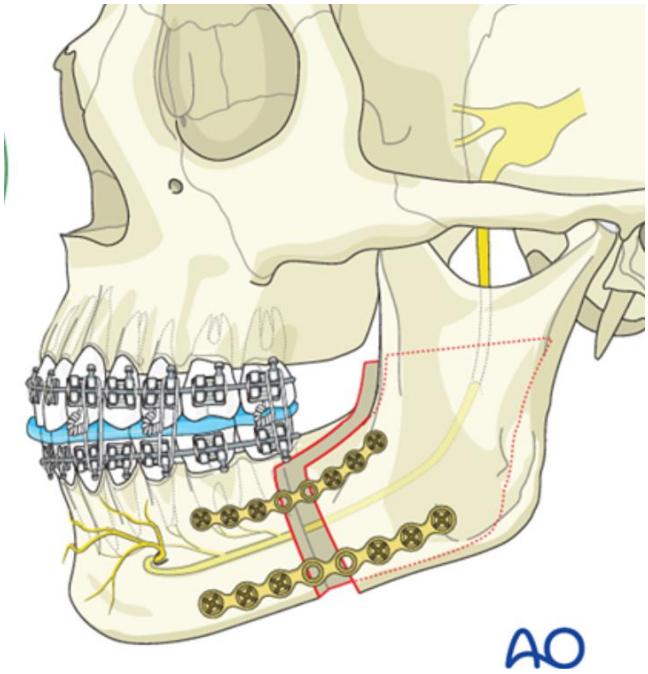
Entre las técnicas quirúrgicas empleadas destacan especialmente la osteotomía Le Fort I y la sagital bilateral de rama mandibular (OSBRM). La osteotomía Le Fort I permite el reposicionamiento tridimensional del maxilar superior mediante una osteotomía horizontal realizada por arriba de los ápices dentales, permitiendo movimientos en sentido anteroposterior, vertical y transversal (Figura 4). Esta técnica es frecuentemente combinada con procedimientos adicionales tales como expansiones palatinas o segmentaciones maxilares para optimizar tanto la función como la estética facial (32).

Figura 4. Osteotomía LeFort I fijada con placas de osteosíntesis. *(Imagen tomada de: AO Foundation. Le Fort I osteotomy. AO Surgery Reference*) (33)



Por otra parte, la osteotomía sagital bilateral de rama mandibular (OSBRM) implica la división bilateral de las ramas ascendentes mandibulares, posibilitando reposicionar el cuerpo mandibular en múltiples dimensiones (Figura 5). Este procedimiento es fundamental en la corrección de alteraciones mandibulares, particularmente retrognatismo o prognatismo, logrando una adecuada alineación oclusal y función masticatoria. La estabilización postoperatoria mediante fijación interna rígida (placas y tornillos) promueve una recuperación rápida y eficaz, facilitando el retorno precoz a la función mandibular habitual (34).

Figura 5. Osteotomía Sagital Bilateral de Rama Mandibular fijada con placas de osteosíntesis. *(Imagen tomada de: AO Foundation. Bilateral sagittal split osteotomy (BSSO). AO Surgery Reference)* (35)



Además, pueden incorporarse procedimientos complementarios como genioplastía, septoplastia y liposucción cervical para maximizar los resultados estéticos y funcionales (36). El uso de tecnologías avanzadas como la planificación virtual tridimensional mediante software especializado ha incrementado considerablemente la precisión, predictibilidad y seguridad de los procedimientos quirúrgicos, proporcionando simultáneamente una herramienta educativa valiosa para pacientes (32,37).

2.2.4 COMPLICACIONES ASOCIADAS A LA CIRUGÍA ORTOGNÁTICA

Las complicaciones asociadas a la cirugía ortognática, aunque poco frecuentes en términos absolutos, representan un aspecto de especial relevancia clínica y científica, ya que condicionan tanto la seguridad perioperatoria como la estabilidad a largo plazo de los resultados. En una serie

publicada por Olate et al., se reportó que aproximadamente un 9,76% de los pacientes presenta complicaciones posquirúrgicas, lo que refleja la necesidad de un seguimiento riguroso y de estrategias preventivas eficaces (38). Entre las complicaciones, destacan el sangrado intraoperatorio, que puede comprometer el manejo anestésico y la morbilidad posquirúrgica; la infección del sitio quirúrgico, con implicancias en la necesidad de tratamientos adicionales y potencial retiro de material de osteosíntesis; y la recidiva esquelética, que afecta la predictibilidad y estabilidad de los movimientos quirúrgicos. El análisis de estas complicaciones resulta fundamental para comprender la variabilidad reportada en la literatura y orientar estrategias de prevención, optimización de protocolos y mejora continua en los resultados de la cirugía ortognática (38–40).

El sangrado intraoperatorio es una complicación frecuente en cirugía ortognática, especialmente en procedimientos bimaxilares y en determinadas maniobras del Le Fort I. Aunque la hemorragia mayor que requiere transfusión es poco común (1%), la pérdida sanguínea puede ser sustancial: en un ensayo aleatorizado de bimaxilares, el grupo control registró pérdidas promedio en torno a 1,26 L, reducidas a 0,88 L con tranexámico (20 mg/kg) administrado preoperatoriamente (diferencia ajustada: −422 mL) (41). En una serie prospectiva de 1.000 cirugías ortognáticas con osteotomías Le Fort I, la transfusión fue necesaria en 1,1%, principalmente en cirugías bimaxilares, destacando que la mayoría de las complicaciones hemorrágicas severas se concentran cuando se combinan maxilar y mandíbula en un mismo tiempo quirúrgico (42).

Las fuentes principales de sangrado incluyen el plexo venoso pterigoideo y ramas de la arteria maxilar interna, destacando la arteria palatina descendente y la esfenopalatina (43). Factores técnicos como la impactación posterior del maxilar, los movimientos de retroceso y el mayor tiempo operatorio se asocian con incremento del sangrado (39). Estrategias farmacológicas, como el uso de ácido tranexámico, han mostrado una posible reducción significativa de la pérdida

hemática (41), mientras que otros agentes, como el magnesio intravenoso, han demostrado efectos sobre la presión arterial sin impacto consistente en el volumen de sangrado (42).

La infección del sitio quirúrgico (ISQ) es otra complicación documentada, con una incidencia variable entre 3–12% según la población y los criterios utilizados. En una cohorte de 2,268 pacientes, la prevalencia global fue 8%, observándose mayor frecuencia en cirugías bimaxilares (9,2%) en comparación con procedimientos monomaxilares (5,3%) (44). En el mismo estudio, la mayoría de las infecciones se localizó en la región mandibular (62–78% de los casos), con un 26% de recurrencia y necesidad de retiro de material en un 14% (44).

El esquema antibiótico profiláctico constituye un factor relevante: el uso de cefazolina se asoció con menor incidencia de infección en comparación con penicilina o clindamicina (44). En un análisis retrospectivo más reciente, la tasa de ISQ alcanzó el 12,4%, identificando al tabaquismo, la cirugía bimaxilar y el tipo de drenaje como factores de riesgo (45). La revisión sistemática Cochrane de Brignardello-Petersen et al., que incluyó ensayos controlados sobre profilaxis antibiótica en cirugía ortognática, concluyó que la profilaxis reduce el riesgo de infección en comparación con placebo, pero la evidencia es de calidad moderada y no permite establecer con certeza la superioridad de pautas extendidas frente a las de corta duración (46). De manera complementaria, se han descrito medidas preventivas no farmacológicas, tales como la reducción del tiempo operatorio, un manejo cuidadoso de los drenajes y la prevención de hematomas postoperatorios.

Por otro lado, la recidiva posquirúrgica constituye una complicación relacionada con factores esqueléticos, musculares y técnicos. La literatura propone una “jerarquía de estabilidad” que clasifica los movimientos quirúrgicos según su predictibilidad: entre los más estables parecieran estar la impactación maxilar superior y el avance mandibular con fijación rígida; entre los menos estables, el retroceso mandibular, la corrección de mordida abierta mediante descenso posterior del maxilar y los movimientos de gran magnitud con rotación antihoraria (47).

Una revisión sistemática de osteotomías sagitales bilaterales (BSSO) identificó que los movimientos de avance presentan escasa recidiva horizontal cuando se utiliza fijación rígida, mientras que los retrocesos mandibulares presentan mayor tendencia a la recidiva, particularmente en pacientes hiperdivergentes (48). Un metaanálisis reciente reportó tasas de recidiva muy variables, entre 2% y 50%, atribuibles a la heterogeneidad de definiciones y al tiempo de seguimiento (49). En series clínicas de seguimiento prolongado, la incidencia de recidiva clínicamente significativa se estimó en 6.4% (50).

En términos temporales, la recidiva temprana (dentro de los primeros seis meses) suele deberse al asentamiento oclusal y la adaptación de los tejidos blandos, mientras que la recidiva tardía puede estar vinculada a crecimiento residual, alteraciones condilares o cambios adaptativos musculares (47,49).

En conjunto, la evidencia disponible sugiere que la implementación de estrategias perioperatorias específicas puede contribuir a disminuir la incidencia de complicaciones en cirugía ortognática. Entre ellas destacan el uso de agentes antifibrinolíticos, como el ácido tranexámico, para la reducción de la pérdida sanguínea; la aplicación de fijación interna rígida, que ha demostrado mejorar la estabilidad esquelética y reducir la recidiva; y la administración de profilaxis antibiótica, orientada a disminuir la frecuencia de infecciones postoperatorias (41,46,51). No obstante, subsisten vacíos significativos en el conocimiento científico respecto a la eficacia comparativa y seguridad de estas estrategias, justificando la realización de investigaciones adicionales de alta calidad (52).

2.2.5 INVESTIGACIÓN CLÍNICA EN CIRUGÍA ORTOGNÁTICA

La evaluación crítica de la evidencia científica en cirugía ortognática exige comprender la importancia y las limitaciones de la investigación clínica en este campo. Los estudios primarios, tales como los ensayos clínicos aleatorizados, los cohortes prospectivos y retrospectivos y los

estudios de casos y controles, constituyen la base del conocimiento disponible y permiten generar conclusiones sobre la efectividad y seguridad de las intervenciones (53,54). Sin embargo, en el ámbito de la odontología y, en particular, de la cirugía, la generación de evidencia de alta calidad enfrenta múltiples desafíos metodológicos y éticos.

En primer lugar, la realización de ensayos clínicos controlados en cirugía presenta dificultades relacionadas con la imposibilidad de aplicar procedimientos de enmascaramiento (blinding) tanto para el cirujano como para el paciente, lo que aumenta el riesgo de sesgo. A esto se suma la heterogeneidad de los pacientes y de las técnicas quirúrgicas empleadas, que dificulta la estandarización de las intervenciones y la comparación entre estudios (55). Por otro lado, los resultados de la cirugía ortognática no se limitan a parámetros objetivos como la estabilidad esquelética, sino que también incluyen desenlaces subjetivos, como la calidad de vida, la satisfacción estética o la función masticatoria, que requieren instrumentos validados y metodológicamente sólidos para su adecuada medición (30).

Asimismo, las consideraciones éticas propias de la investigación quirúrgica limitan el uso de diseños experimentales en ciertos contextos. A diferencia de los fármacos, donde el uso de placebo puede estar justificado, resulta complejo o inaceptable ofrecer una cirugía ficticia a un grupo control. Por esta razón, gran parte de la evidencia proviene de estudios observacionales, los cuales aportan información valiosa sobre la práctica clínica real, pero presentan limitaciones en términos de control de sesgos y confusión (56).

Estas particularidades explican por qué la evidencia en cirugía ortognática, y en odontología en general, es más escasa y heterogénea que en otras áreas biomédicas, y justifican la necesidad de aplicar marcos rigurosos de evaluación metodológica para determinar la validez y la aplicabilidad de los estudios disponibles.

2.3 IDENTIFICACIÓN DE VACÍOS DE CONOCIMIENTO

La planificación de la investigación en cirugía ortognática requiere como punto de partida la identificación sistemática de vacíos de evidencia y la definición clara de prioridades de investigación, lo que permite destinar recursos a problemas de alta relevancia clínica, evitando esfuerzos fragmentados o redundantes. Sin una etapa previa de análisis y priorización, los estudios tienden a abordar problemas secundarios, con menor pertinencia para los pacientes, los clínicos y los responsables de la toma de decisiones (57). En este sentido, se hace necesario disponer de marcos conceptuales y metodológicos que permitan ordenar la evidencia disponible, detectar sus limitaciones y guiar la formulación de futuras investigaciones en función de su relevancia y factibilidad (58,59).

A partir de estos principios, se vuelve necesario disponer de herramientas metodológicas capaces de operacionalizar la identificación de vacíos de evidencia y su transformación en prioridades de investigación concretas. Dichas herramientas deben permitir organizar de manera sistemática la literatura científica, visualizar las áreas de mayor y menor densidad de conocimiento, y generar procesos participativos que integren tanto la mirada de los expertos como la de los usuarios finales de la evidencia. Este enfoque favorece la construcción de agendas de investigación coherentes, transparentes y alineadas con las necesidades clínicas, constituyendo un puente entre el diagnóstico de las carencias existentes y la planificación de estudios futuros orientados a resolverlas.

En este escenario, metodologías como los mapping reviews, orientados a la organización y visualización sistemática de la evidencia, y los estudios de consenso estructurado, como la técnica Delphi, ofrecen herramientas útiles para abordar este desafío, al facilitar tanto la identificación de vacíos de conocimiento como la priorización de las áreas de investigación más relevantes.

2.4 REVISIONES SISTEMÁTICAS DE MAPEO (MAPPING REVIEWS)

Las revisiones sistemáticas de mapeo, también denominadas mapping reviews, surgieron como una metodología clave para explorar y representar gráficamente la extensión de la evidencia científica disponible sobre temas específicos. Originadas en ciencias sociales a principios del siglo XXI, estas revisiones se utilizan para responder preguntas amplias mediante búsquedas exhaustivas, facilitando la identificación visual y sistemática de áreas investigadas y vacíos críticos (60,61). La metodología emplea un enfoque riguroso y sistemático para categorizar estudios, a menudo con la ayuda de un marco teórico predefinido o emergente, generando mapas visuales que permiten a investigadores y tomadores de decisiones localizar rápidamente evidencia existente y vacíos críticos en el conocimiento científico actual (61).

Estos métodos se han adaptado ampliamente en diversos campos, incluyendo ciencias ambientales, salud pública y ciencias biomédicas, permitiendo una visualización efectiva de la distribución y concentración temática de la investigación existente. La flexibilidad metodológica de los mapping reviews facilita su adaptación a diferentes objetivos investigativos, desde la identificación general de áreas de interés hasta la preparación para revisiones sistemáticas posteriores más específicas (62,63).

2.5 ESTUDIOS DELPHI

La técnica Delphi, creada por la Rand Corporation en los años 50, constituye un método ampliamente reconocido para lograr consenso sobre temas científicos complejos con información limitada. Este método emplea rondas sucesivas de cuestionarios estructurados, permitiendo a expertos reconsiderar sus opiniones a partir de retroalimentación grupal, hasta alcanzar un consenso o clarificar áreas de divergencia significativa (64).

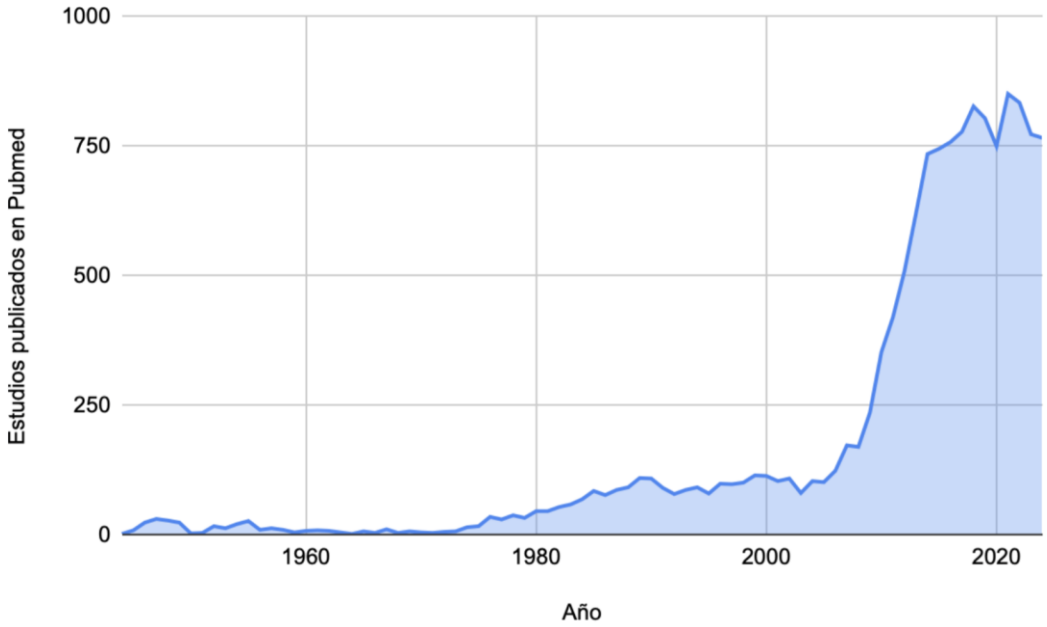
Este enfoque ha experimentado una expansión significativa en diversos campos científicos, incluyendo medicina, educación, negocios e ingeniería, principalmente por su capacidad para

estructurar discusiones complejas y minimizar sesgos personales. Además, los estudios Delphi permiten aplicaciones más profundas en contextos de incertidumbre científica y tecnológica, así como en la definición de prioridades de investigación clínica y elaboración de políticas públicas basadas en evidencia consensuada (64).

2.6 JUSTIFICACIÓN

En los últimos años, la producción científica en el campo de la cirugía ortognática y el manejo de deformidades dentofaciales ha mostrado un incremento sustancial, reflejando tanto un interés creciente por parte de la comunidad médica como los continuos avances tecnológicos y quirúrgicos en esta área (Figura 6). No obstante, este aumento en la literatura publicada no necesariamente implica una distribución adecuada y efectiva del conocimiento que resulte clínicamente relevante. Frecuentemente se observa que numerosos estudios abordan de manera repetida preguntas de investigación que ya han sido satisfactoriamente resueltas, generando redundancias científicas y un uso ineficiente de recursos investigativos.

Figura 6. Artículos sobre cirugía ortognática publicados en Pubmed a través de los años.



Simultáneamente, ciertos aspectos clínicos y preguntas críticas han sido insuficientemente investigados, resultando en importantes brechas de evidencia. Estos vacíos en el conocimiento científico pueden impactar negativamente en la calidad asistencial, la seguridad y los resultados de los procedimientos quirúrgicos realizados en pacientes con deformidades dentofaciales. Por tanto, identificar, clasificar y priorizar de forma sistemática y rigurosa estas brechas es fundamental para optimizar la utilización de recursos científicos y clínicos.

La presente tesis doctoral se justifica precisamente por la necesidad imperiosa de abordar esta problemática. A través de la realización de revisiones sistemáticas de mapeo (mapping reviews), se busca identificar exhaustivamente las brechas existentes en la literatura actual sobre cirugía ortognática. El desarrollo de un mapa visual integral que resuma y represente gráficamente el estado del conocimiento científico facilitará la identificación rápida de áreas saturadas por investigación redundante y aquellas áreas donde la investigación es escasa o inexistente.

Posteriormente, mediante un análisis crítico y consensuado sobre la relevancia clínica de estas brechas identificadas mediante un estudio Delphi, se logrará una priorización efectiva de los aspectos clínicamente más relevantes que requieren atención investigativa inmediata.

Este enfoque contribuirá significativamente a orientar los esfuerzos científicos y clínicos futuros hacia las áreas que verdaderamente necesitan investigación adicional, asegurando así un uso eficiente y eficaz de los recursos disponibles. De esta manera, la presente tesis doctoral no sólo busca prevenir la repetición innecesaria de estudios, sino también potenciar investigaciones cuyo impacto sea tangible en la práctica clínica, mejorando así los resultados quirúrgicos y la calidad de vida de los pacientes con deformidades dentofaciales.

3. OBJETIVOS

3.1 OBJETIVO GENERAL:

Esta tesis doctoral tiene como objetivo identificar, sintetizar y organizar de forma sistemática los vacíos de evidencia clínicamente relevantes en el ámbito de la cirugía ortognática utilizando revisiones sistemáticas de mapeo y técnicas Delphi.

3.2 OBJETIVOS ESPECÍFICOS:

1. Sistematizar y presentar la evidencia disponible mediante un método visual e innovador, facilitando la comprensión y análisis del estado actual del conocimiento en cirugía ortognática.
2. Evaluar la calidad metodológica de la evidencia científica secundaria existente en esta área.
3. Identificar las lagunas o vacíos en la literatura que requieren investigación adicional, con el fin de orientar eficazmente futuras líneas de estudio.
4. Describir la dirección de resultados de desenlaces de interés en la cirugía ortognática (dolor, infección, recidiva).
5. Determinar la relevancia clínica de los vacíos de evidencia detectados, estableciendo prioridades que permitan optimizar los recursos y esfuerzos en futuras investigaciones clínicas.

4. MÉTODOS

Con el fin de dar respuesta a los objetivos específicos planteados en esta tesis, se realizaron tres estudios, cuya metodología se encuentran descritos en las respectivas publicaciones resultantes. Estos estudios conforman en conjunto el fundamento que permite presentar este trabajo en la modalidad de compendio de publicaciones. En las siguientes secciones se ofrece una síntesis de los métodos aplicados en cada uno de ellos.

4.1 MÉTODOS DEL PRIMER TRABAJO

4.1.1 DISEÑO DEL ESTUDIO

Este trabajo corresponde a una revisión de mapeo de evidencia, elaborada conforme a la extensión PRISMA para revisiones de alcance (PRISMA-ScR) y siguiendo los lineamientos de la Global Evidence Mapping Initiative (GEM). Todos los procedimientos fueron establecidos a priori en un protocolo publicado en revista revisada por pares (65).

4.1.2 DEFINICIÓN DE LÍMITES Y CONTEXTO

Se consultó a cirujanos maxilofaciales expertos en cirugía ortognática para precisar el marco del estudio. Además, se realizó una búsqueda preliminar con el fin de definir los criterios de elegibilidad de los estudios incluidos.

4.1.3 CRITERIOS DE ELEGIBILIDAD

La selección se guió por la estructura PICO (población, intervención, comparador, desenlaces):

- Tipos de estudio: se incluyeron revisiones sistemáticas (RS) de ensayos clínicos aleatorizados y estudios observacionales, ensayos clínicos primarios, y estudios prospectivos o retrospectivos de cohortes y casos y controles. Se excluyeron revisiones narrativas, series o reportes de casos, estudios cualitativos y transversales.

- Población: adolescentes y adultos (>10 años) sometidos a cirugía ortognática. Se excluyeron pacientes sindrómicos.
- Intervenciones: cointervenciones y modalidades quirúrgicas en cirugía ortognática mono o bimaxilar. Se excluyeron estudios de distracción osteogénica, procedimientos ortodóncicos o de planificación quirúrgica.
- Comparadores: distintas modalidades quirúrgicas de cirugía ortognática, cointervenciones, placebo o ausencia de tratamiento.
- Desenlaces: resultados clínicos intra y postoperatorios. Se excluyeron desenlaces exclusivamente preoperatorios, económicos o de calidad de vida.

4.1.4 ESTRATEGIA DE BÚSQUEDA BIBLIOGRÁFICA

Se efectuó una búsqueda exhaustiva desde el inicio de cada base de datos hasta marzo de 2021 en MEDLINE (PubMed), EMBASE (OVID), Epistemonikos, LILACS, Web of Science y CENTRAL, sin restricciones de idioma o fecha. Se revisaron también PROSPERO y listas de referencias. Aunque estaba previsto incluir ClinicalTrials.gov, se descartó debido al elevado volumen de estudios identificados. Asimismo, se exploró literatura gris.

4.1.5 PROCESO DE SELECCIÓN Y EXTRACCIÓN DE DATOS

Dos revisores independientes evaluaron títulos y resúmenes, y posteriormente los textos completos, registrando motivos de exclusión. Las discrepancias se resolvieron por consenso o con un tercer revisor. El proceso se gestionó mediante la plataforma Covidence y se documentó en un diagrama PRISMA.

La extracción de datos fue realizada con un formulario previamente pilotado. De cada revisión sistemática se extrajo información sobre búsqueda, año, país, objetivos, número de estudios primarios, participantes, intervenciones, comparaciones y desenlaces. Para los estudios primarios

no incluidos en revisiones, se recogieron datos similares, especificada en el artículo. En caso necesario, se contactó a autores para obtener información adicional.

4.1.6 EVALUACIÓN DE CALIDAD METODOLÓGICA

La calidad de las revisiones sistemáticas incluidas fue evaluada de manera independiente por dos revisores utilizando la herramienta AMSTAR-2, que contempla 16 dominios críticos. La confianza en los resultados se categorizó en cuatro niveles: críticamente baja, baja, moderada o alta. Los estudios primarios no fueron evaluados formalmente, dado que el objetivo fue identificar vacíos de conocimiento y no servir directamente a la toma de decisiones clínicas.

4.1.7 SÍNTESIS Y ANÁLISIS DE DATOS

Se elaboraron tablas de características de los estudios y de preguntas PICO. Se diseñó un diagrama de flujo que clasificó los estudios por diseño e intervención. Con el apoyo de Epistemonikos, se construyó una matriz de evidencia vinculando los estudios primarios con sus respectivas revisiones sistemáticas. Además, se desarrollaron mapas de burbujas de evidencia, en los cuales se representaron gráficamente las intervenciones, desenlaces, número de estudios y calidad metodológica de las revisiones.

4.2 MÉTODOS DEL SEGUNDO TRABAJO

4.2.1 DISEÑO DEL ESTUDIO

Se realizó una revisión de mapeo de evidencia, enmarcada en la metodología de la Global Evidence Mapping Initiative (GEM) y reportada de acuerdo con la extensión PRISMA para revisiones de alcance. El objetivo fue identificar, describir y organizar la evidencia disponible en revisiones sistemáticas y estudios primarios acerca de modalidades quirúrgicas y cointervenciones perioperatorias en cirugía ortognática, específicamente en relación con tres desenlaces principales: pérdida sanguínea, infección y recidiva.

4.2.2 CRITERIOS DE ELEGIBILIDAD

- Tipos de estudio: revisiones sistemáticas, ensayos clínicos aleatorizados y estudios observacionales (cohortes prospectivas/retrospectivas, casos y controles).
- Población: pacientes adultos y adolescentes sometidos a cirugía ortognática bimaxilar. Se excluyeron pacientes sindrómicos.
- Intervenciones: Modalidades quirúrgicas y cointervenciones perioperatorias. Se excluyeron estudios centrados en distracción osteogénica, procedimientos ortodóncicos o planificación quirúrgica.
- Comparadores: Diferentes técnicas quirúrgicas, cointervenciones, placebo o ausencia de intervención. Se excluyeron estudios sin grupo comparador o sin cirugía ortognática.
- Desenlaces: pérdida sanguínea, infección y recidiva.

4.2.3 ESTRATEGIA DE BÚSQUEDA

Se desarrolló una búsqueda sistemática en las bases de datos MEDLINE, EMBASE, Epistemonikos, LILACS, Web of Science y CENTRAL, desde el inicio hasta marzo de 2021, sin restricciones de idioma ni fecha. Se exploró además literatura gris y protocolos en la plataforma PROSPERO.

Adicionalmente, se aplicó una estrategia de búsqueda manual (snowballing) para identificar estudios adicionales.

4.2.4 PROCESO DE SELECCIÓN DE ESTUDIOS

Dos revisores independientes realizaron la selección en dos fases:

1. Cribado de títulos y resúmenes.
2. Lectura a texto completo.

Las discrepancias fueron resueltas por consenso o mediante un tercer evaluador. Los motivos de exclusión se registraron en detalle, y el proceso se documentó siguiendo un diagrama de flujo PRISMA.

4.2.5 EXTRACCIÓN Y GESTIÓN DE DATOS

Se utilizó un formulario previamente pilotado para extraer los siguientes datos: año, país, diseño del estudio, características de la población, intervenciones, comparadores, desenlaces y conclusiones. En el caso de revisiones sistemáticas, además se registró fecha de búsqueda, número de estudios incluidos, número de participantes y preguntas PICO abordadas. Los estudios primarios no incluidos en revisiones sistemáticas se analizaron de manera independiente.

4.2.6 EVALUACIÓN DE LA CALIDAD METODOLÓGICA

La calidad de las revisiones sistemáticas incluidas fue evaluada de manera independiente por dos revisores utilizando la herramienta AMSTAR-2. La confianza global se categorizó en cuatro niveles: críticamente baja, baja, moderada o alta.

4.2.7 SÍNTESIS DE LA EVIDENCIA

La información obtenida de los estudios incluidos se organizó en tablas descriptivas que resumieron sus principales características, incluyendo diseño, población, intervenciones, comparadores y desenlaces.

Para cada uno de los desenlaces principales —pérdida sanguínea, infección y recidiva— se elaboró una matriz de evidencia utilizando la plataforma Epistemonikos. Estas matrices vincularon revisiones sistemáticas con los estudios primarios que cumplían los criterios de inclusión y permitieron identificar estudios primarios relevantes no incorporados en las revisiones sistemáticas previamente publicadas.

Adicionalmente, se desarrolló un mapa de burbujas por cada desenlace, en el que se representaron de forma gráfica las intervenciones evaluadas y los resultados reportados. El tamaño de las burbujas indicó el número de participantes o estudios, la forma correspondió al tipo de diseño (revisión sistemática, ensayo clínico aleatorizado o estudio observacional), y el color reflejó el nivel de confianza en los hallazgos de las revisiones sistemáticas según la herramienta AMSTAR-2. La dirección de los resultados de los estudios se clasificó en beneficiosos, probablemente beneficiosos, sin efecto diferencial, dañinos o inconclusos, con el fin de ofrecer una visión general de la orientación y consistencia de los hallazgos para cada intervención analizada.

4.3 MÉTODOS DEL TERCER TRABAJO

4.3.1 DISEÑO DEL ESTUDIO

Se desarrolló un estudio exploratorio utilizando la técnica Delphi, con el objetivo de evaluar las lagunas de evidencia previamente identificadas en una revisión de mapeo de la literatura sobre cirugía ortognática. Esta metodología permitió integrar la perspectiva clínica de cirujanos maxilofaciales en relación con la relevancia práctica de dichas lagunas, con el fin de orientar futuras investigaciones.

4.3.2 COMITÉ DIRECTIVO DE INVESTIGACIÓN

Se conformó un grupo coordinador integrado por especialistas en odontología, cirugía oral y maxilofacial, y metodología de la investigación. Dicho comité fue responsable de diseñar y supervisar el proceso, así como de elaborar y difundir los cuestionarios, sin participar directamente en las rondas de la encuesta.

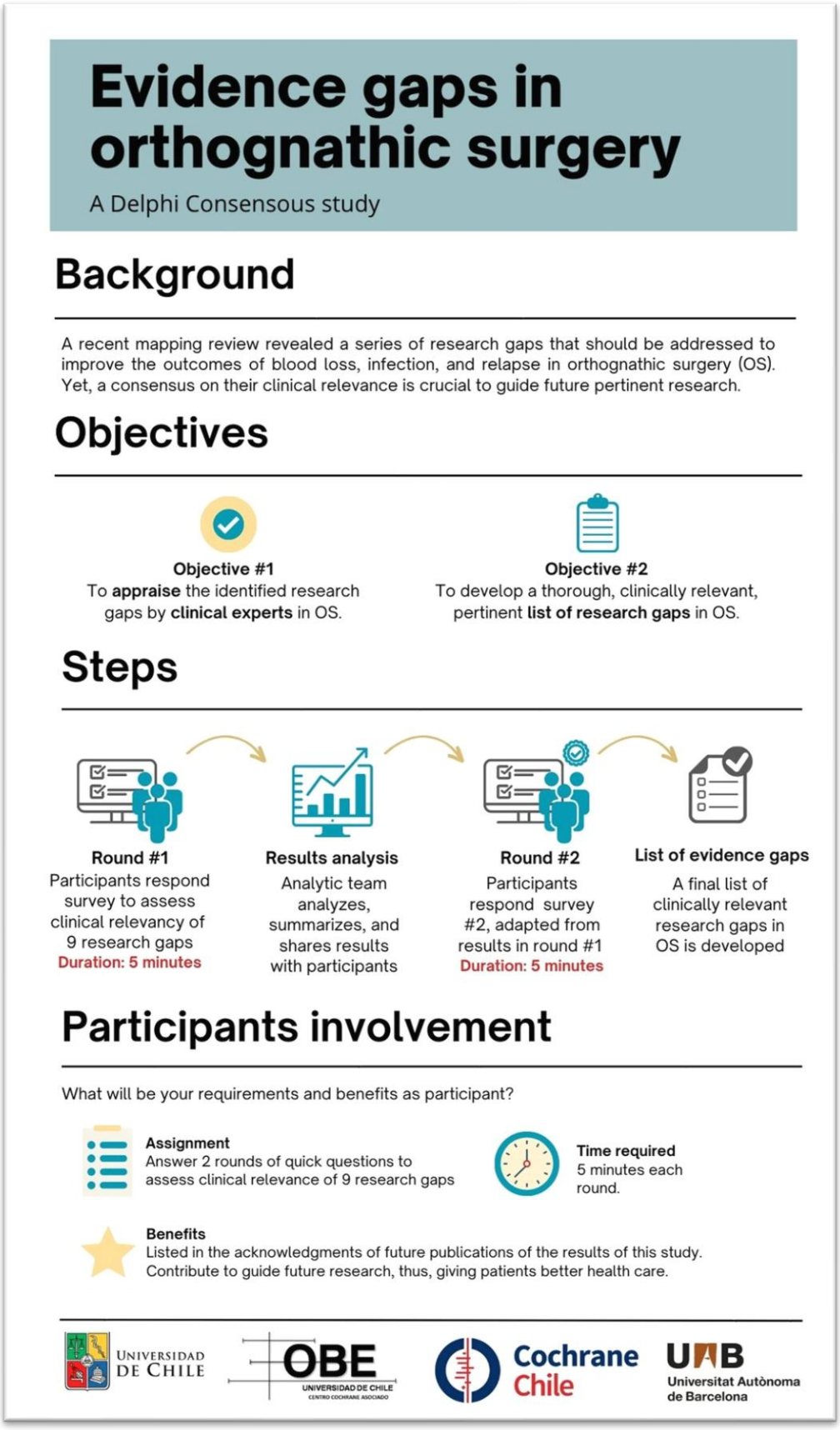
4.3.3 SELECCIÓN Y RECLUTAMIENTO DE PARTICIPANTES

Los participantes fueron cirujanos maxilofaciales en ejercicio activo de cirugía ortognática. La identificación de candidatos se realizó mediante tres estrategias:

1. Extracción de contactos de autores correspondientes de artículos incluidos en la revisión de mapeo.
2. Nominación de pares por parte de los participantes iniciales.
3. Difusión en redes sociales profesionales, principalmente LinkedIn.

Se excluyeron aquellos con menos de un año de experiencia, sin práctica clínica activa en el último año, o que no pudieran comprometerse a completar todas las rondas del Delphi. No se aplicaron restricciones de edad, género o país. Las invitaciones se enviaron por correo electrónico, incluyendo el protocolo del estudio, una infografía explicando las bases del estudio (Figura 7) y un enlace al cuestionario inicial.

Figura 7. Infografía enviada a potenciales participantes del estudio Delphi



4.3.4 DESARROLLO DEL CUESTIONARIO

Los cuestionarios se diseñaron en Google Forms, conteniendo preguntas de escala Likert de 5 puntos y preguntas abiertas. Su contenido se elaboró a partir de las lagunas de evidencia descritas en la revisión de mapeo previa y se sometió a prueba piloto por el comité directivo. Se estableció un umbral de consenso del 60%, considerado válido para definir la relevancia clínica de cada ítem.

4.3.5 PROCEDIMIENTO DE LAS RONDAS DELPHI

Se llevaron a cabo dos rondas consecutivas, de manera anónima:

- Primera ronda: Los participantes evaluaron la relevancia clínica de las lagunas de evidencia relacionadas con tres desenlaces principales (pérdida sanguínea, infección y recidiva). Se incluyó una pregunta abierta para sugerir nuevas lagunas de investigación.
- Retroalimentación: Tras la primera ronda, los participantes recibieron un informe con los resultados agregados (medias, desviaciones estándar, nivel de consenso y representación gráfica).
- Segunda ronda: Se repitieron únicamente las preguntas sin consenso en la primera ronda y se incorporaron las nuevas propuestas de lagunas que cumplían criterios de inclusión. Las preguntas con alto consenso y baja relevancia fueron eliminadas.

Las lagunas consideradas relevantes fueron aquellas clasificadas por ≥60% de los participantes como “probablemente relevantes” o “altamente relevantes”.

4.3.6 ESTRATEGIAS PARA MAXIMIZAR LA PARTICIPACIÓN

Se utilizaron invitaciones personalizadas, recordatorios periódicos (cada 7 días), entrega de certificados de participación y reconocimiento en publicaciones derivadas, con el fin de mantener un alto nivel de retención en ambas rondas.

4.3.7 ANÁLISIS ESTADÍSTICO

Se aplicó estadística descriptiva para resumir características de los participantes y resultados de cada ronda. Para cada ítem se calcularon medias, desviaciones estándar, frecuencias y rangos. Asimismo, se representaron distribuciones mediante histogramas.

El coeficiente de correlación intraclase se utilizó para evaluar la concordancia intra e intersujeto en las respuestas. Los análisis se realizaron con el software Jamovi (versión 2.5).

5. RESULTADOS

Los resultados de esta tesis, organizada bajo la modalidad de compendio de publicaciones, se sustentan en las siguientes publicaciones:

1. Bendersky, J., Uribe, M., Bravo, M., Vargas, J. P., Flores, E., Aguero, I., Villanueva, J., Urrutia, G., & Bonfill, X. (2022). Systematic mapping review of orthognathic surgery. *Journal of stomatology, oral and maxillofacial surgery*, *123*(5), e285–e305. https://doi.org/10.1016/j.jormas.2022.05.011

2. Bendersky, J., Uribe, M., Bravo, M., Vargas, J. P., Villanueva, J., Urrutia, G., & Bonfill, X. (2023). Systematic mapping review of interventions to prevent blood loss, infection and relapse in orthognathic surgery. *Medicina oral, patologia oral y cirugia bucal*, *28*(2), e116–e125. https://doi.org/10.4317/medoral.25530

3. Bendersky, J., Zapata, S., Uribe, M., Villanueva, J., Bonfill, X., & Souper, R. (2025). Evidence gaps in orthognathic surgery: an international Delphi study. *International journal of oral and maxillofacial surgery*, *54*(5), 430–437. https://doi.org/10.1016/j.ijom.2024.11.001

Se ofrece a continuación una síntesis de los hallazgos más relevantes de los tres trabajos. Para un análisis en profundidad y una comprensión completa, el lector puede remitirse a las publicaciones originales.

5.1 RESULTADOS DEL PRIMER ESTUDIO

Bendersky, J., Uribe, M., Bravo, M., Vargas, J. P., Flores, E., Aguero, I., Villanueva, J., Urrutia, G., & Bonfill, X. (2022). Systematic mapping review of orthognathic surgery. *Journal of stomatology, oral and maxillofacial surgery*, *123*(5), e285–e305. https://doi.org/10.1016/j.jormas.2022.05.011

Factor de impacto: 2.0

5.1.1 RESULTADOS DE LA BÚSQUEDA Y SELECCIÓN DE ESTUDIOS

Se identificaron inicialmente 8.531 registros. Tras eliminar duplicados y aplicar los criterios de inclusión, se evaluaron 863 artículos a texto completo. Finalmente, se incluyeron 290 estudios: 35 revisiones sistemáticas (RS) y 253 estudios primarios. De estos últimos, 103 estaban contenidos en alguna RS, mientras que 150 correspondieron a estudios adicionales no incluidos en dichas revisiones.

5.1.2 CARACTERÍSTICAS GENERALES DE LOS ESTUDIOS

Del total de estudios incluidos (n=290), el 12,1% correspondió a revisiones sistemáticas (RS) y el 87,2% a estudios primarios. Dentro de estos últimos, los diseños fueron: ensayos clínicos aleatorizados (54,7%), cohortes retrospectivos (35,3%), cohortes prospectivos (14,0%) y un estudio caso–control (0,7%). En cuanto a los participantes, la mayoría de los estudios (68,7%) incluyó exclusivamente población adulta (>16 años), mientras que un 18,0% consideró tanto adolescentes como adultos, un 0,7% solo adolescentes, un 0,7% todas las edades y un 12,0% no especificó la edad. Respecto a la deformidad esqueletal, el 22,7% de los estudios incluyó pacientes clase III, el 10,7% pacientes clase II, el 4,0% pacientes clase II y III, y el 62,7% no reportó criterios de deformidad. Finalmente, las intervenciones quirúrgicas evaluadas abarcaron procedimientos bimaxilares, mandibulares, maxilares, genioplastías y combinaciones de estas modalidades.

5.1.3 CO-INTERVENCIONES PERIOPERATORIAS

Casi la mitad de los estudios incluidos abordaron co-intervenciones perioperatorias en cirugía ortognática (18 RS (51,4%) y 68 estudios primarios (45,3%)). Las más frecuentemente evaluadas

fueron el uso de profilaxis antibiótica (5 RS (27,8%) y 2 RCTs (2,9%)), corticoides (RS (16,7%) y 1 RCT (1,5%)), ácido tranexámico (5 RS (27,8%) y 2 estudios primarios (3,0%)), hipotensión controlada (2 RS (11,1%) y 3 estudios primarios (4,4%)) y terapia láser de baja intensidad (2 RS (11,1%) y 4 RCTs (5,9%)). Otras intervenciones descritas incluyeron técnicas anestésicas, protocolos analgésicos multimodales (27,9%; ej. ibuprofeno, pregabalina, melatonina, clonidina, desmopresina, ATP IV, hierro, tramadol/diclofenaco), estrategias de control de temperatura, plasma rico en fibrina, drenajes, y métodos alternativos como fitoterapia o plásticos aplicados en acupuntos. La variedad de desenlaces dentro de estas intervenciones fue amplia, destacando pérdida sanguínea, infección, recidiva, náuseas y vómitos postoperatorios, tiempo quirúrgico, y efectos adversos.

5.1.4 MODALIDADES QUIRÚRGICAS

Diecisiete RS (48,6%) y 83 estudios primarios (55,3%) investigaron técnicas quirúrgicas intraoperatorias. Los aspectos más estudiados fueron los métodos de osteosíntesis: bicortical vs. monocortical (3 RS (17,6%) y 8 cohortes (9,6%)), titanio vs. materiales reabsorbibles (6 RS (35,3%), 2 RCTs (2,4%) y 2 cohortes (2,4%)), y fijación rígida vs. alámbrica (3 RS (17,6%) y 16 primarios (19,3%)). También se evaluaron dispositivos de corte óseo, como piezoeléctricos, frente a sierras convencionales. Otros tópicos incluyeron uso de injertos óseos, bloqueos nerviosos, técnicas de sutura (p. ej., sutura de cincha, cierre en VY), y variaciones de placas y tornillos.

5.1.5 RESULTADOS CLÍNICOS REPORTADOS

Los desenlaces fueron heterogéneos y múltiples. Los más evaluados fueron:

- Recidiva quirúrgica: reportada en la mayoría de los estudios sobre fijación (≈40% de estudios en osteosíntesis).
- Infección: evaluada principalmente en estudios con antibióticos y osteosíntesis (≈25% de RS y RCTs combinados).

- Pérdida sanguínea intraoperatoria: incluida en 6 RS (≈17%) y >30 estudios primarios, especialmente en co-intervenciones con tranexámico, hipotensión y piezoeléctrico.
- Dolor y edema: presentes en >50% de estudios de co-intervenciones y en 3 RS de corticoides y láser.
- Alteraciones neurosensoriales (NSD): analizadas en 20–25% de los estudios, particularmente en osteosíntesis, láser y piezoeléctrico.
- Duración de la cirugía: documentada en ≈15% de estudios, sobre todo en hipotensión inducida y dispositivos de corte.
- Náuseas y vómitos postoperatorios (PONV): evaluadas en ≈10% de los estudios de co-intervenciones.
- Otros: complicaciones quirúrgicas, consumo de opioides, cambios de tejidos blandos, parámetros funcionales y reacciones adversas a fármacos

5.1.6 CALIDAD METODOLÓGICA DE LAS REVISIONES SISTEMÁTICAS

Según AMSTAR-2, 57,0% de las RS (20/35) fueron de calidad críticamente baja, 14,3% baja, 20,0% moderada y solo 8,6% (3/35) de alta calidad. Los principales déficits fueron ausencia de protocolo previo, falta de justificación en la selección de diseños, omisión de financiamiento en los estudios primarios y ausencia de duplicación en selección/extracción de datos. Las tres revisiones Cochrane incluidas mostraron una calidad metodológica mayor (dos altos, uno moderado).

5.1.7 SÍNTESIS GRÁFICA Y VACÍOS DE EVIDENCIA

Se construyeron mapas de burbujas que ilustraron las áreas con mayor concentración de evidencia, destacando el uso de antibióticos, corticoides, ácido tranexámico y diferentes métodos de osteosíntesis (figuras 3 y 4 de la publicación). Además, se identificaron 15 vacíos de evidencia relevantes (tabla 3 de la publicación), como la necesidad de estudios de alta calidad sobre

hipotensión inducida, eficacia de técnicas de fijación alternativas (híbrida, slot plates), uso de láser de baja intensidad, uso de piezoeléctrico y uso de estrategias de sutura específicas. Estas áreas requieren ensayos controlados y nuevas revisiones sistemáticas para fortalecer la base de evidencia disponible.

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Review

Systematic mapping review of orthognathic surgery

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ABSTRACT

Study design: Systematic mapping review
Aim and scope: The objective of this mapping review was to identify, describe, and organize clinical research currently available from systematic reviews and primary studies regarding co-interventions and different surgical modalities used in orthognathic surgery (OS) and their outcomes.
Methods: Systematic reviews (SRs), randomized controlled trials, and observational studies that evaluated perioperative OS co-interventions and surgical modalities were identified in an exhaustive search of MEDLINE, EMBASE, Epistemonikos, Lilacs, Web of Science, and CENTRAL. Grey literature was also screened.
Results: Included were 35 SRs and 253 primary studies, 103 from SRs, and another 150 identified in our search. Overall, SR quality was rated as critically low, with only two SRs rated as of high quality. 19 questions on population, interventions, comparisons, and outcomes (PICO) extracted from the SRs focused on osteosynthesis methods, surgical cutting devices, and use of antibiotics, corticosteroids, and induced hypotension. Also identified were 15 research gaps. Evidence bubble maps were created to graphically depict the available evidence.
Conclusion: Future high-quality research, both primary and secondary, is needed to address the knowledge gaps identified in this systematic mapping review.

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1. Introduction

Orthognathic surgery (OS), a widely used procedure to correct dentofacial deformities that affects 20% of the population [1], involves surgical manipulation of facial skeletal elements [1–6]. The repositioning of maxillar and mandibular bones improves function, facial architecture [7], facial harmony, and esthetics [6,8]. Conditions that indicate the need for OS include anteroposterior, vertical, or transverse discrepancies, asymmetries, dysfunctions, temporomandibular joint disorders, speech impairments, airway dysfunctions, and psychosocial disorders [5,9]. While it is very challenging to find accurate data on the prevalence of dentofacial deformities potentially requiring OS within different populations, it is estimated that in the UK between 5–19% of children referred to an orthodontist for potential treatment, were diagnosed as having a malocclusion too severe for orthodontic treatment alone [9]. In addition, severe mandibular prognathism requiring combined orthodontic and surgical treatment is estimated to occur in 1% of the Norwegian population [10]. Although data is scant, the records of the American Dental Association (ADA) and the AAOMS [11] would indicate that the number of OS procedures performed each year is increasing. In 2007, for instance, 8,755 OS procedures were performed in the USA [11].

Abbreviations: AMSTAR, assessing the methodological quality of systematic reviews; ATP, adenosine 5'triphosphate; IV, intravenous; LLL, low-level laser; NSD, neurosensory disturbances; OS, orthognathic surgery; PICO, population, intervention, comparator, outcome; PONV, postoperative nausea and vomiting; PRF, platelet-rich fibrin; RCT, randomized controlled trial; SR, systematic review; TMJ, temporomandibular joint

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OS complications and outcomes are many, and include relapse, bleeding, infection, lack of fixation stability, neurosensory disturbances, temporomandibular joint dysfunction, etc. [1,6,12]. Great variability exists regarding not only perioperative co-interventions (e.g., antibiotics, antifibrinolytics, anesthetic techniques, etc.) but also surgical modalities (e.g., materials and types of screws and plates, surgical instruments for osteotomies, etc.) aimed at optimizing surgical results [6].

Determining recommendations for OS requires analyzing all available evidence concerning this subject. The emerging method of mapping reviews constitutes a valuable mechanism for this particular area, given the broad field covered and the vast body of literature [13,14]. To our knowledge, ours is the first evidence mapping synthesis that scopes all existing evidence regarding alternatives for OS co-interventions and surgical modalities.

Evidence mapping is an innovative and visual approach that illustrates existing evidence on the effects of specific interventions in a specific area [13,15]. As a user-friendly and didactic approach to displaying available evidence in extensive research areas, it systematically characterizes existing evidence, identifies knowledge gaps, and highlights research gaps [13–16]. It is therefore a possible first step to developing systematic reviews (SRs) or frameworks for informing policy development [13–16]. Furthermore, in identifying research gaps that have already been resolved, it avoids wasted research effort in developing primary studies or SRs.

This mapping review aimed to identify, describe, and organize clinical research currently available from SRs and primary studies regarding different OS co-interventions, surgical modalities, and their intraoperative and postoperative outcomes. It also aimed to assess the quality of the existing evidence and highlight clinical questions regarding this topic. In facilitating the identification of research gaps, this review is expected to point the way to new studies.

2. Methods

This review was drafted using the Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA)-Extension for Scoping Reviews [16]. It adheres to the Global Evidence Mapping Initiative methods (GEM) [17], incorporating the quality of supporting evidence. All methods are specified a priori in a protocol published in a peer review journal.

2.1. Mapping boundaries and context

To frame this mapping review, maxillofacial surgeons expert in OS were consulted, and a preliminary search to establish eligibility criteria for study inclusion was performed.

2.2. Eligibility criteria

The population, intervention, comparison, and outcomes (PICO) framework was used to guide the eligibility criteria.

Studies. To include a complete mapping of co-interventions and surgical modalities regarding efficacy and safety, the following study designs were considered for inclusion: SRs of randomized controlled trials (RCTs) and observational studies, as well as primary studies that corresponded to RCTs, and prospective and retrospective observational studies (case-control and cohort studies). Furthermore, only included studies published as full texts and publications ahead of print were included. Excluded were narrative reviews, case series, case reports, and qualitative and cross-sectional studies.

Population. Adult and adolescent participants (aged over 10 years) undergoing OS were included. Excluded were syndromic patients.

Interventions. Co-interventions and surgical modalities used during the OS perioperative period (mono- or bimaxillary surgery, including all types of osteotomies) were considered. Excluded were studies regarding distraction osteogenesis and those whose focus relied on orthodontic procedures or surgical planning.

Comparators. Different approaches to performing OS, different co-interventions, and use of placebo or no treatment (control group) associated with co-interventions were included. Excluded were studies with no comparison group or studies in which the comparison group did not undergo OS.

Outcomes. All outcomes arising from the intra- or postoperative OS period were considered and mapped. Studies of co-interventions with preoperative or economic outcomes were excluded. Since this mapping review only included clinical outcomes, quality of life studies were excluded.

2.3. Literature search

A literature search was performed from inception to March 2021 in the following databases; MEDLINE (via PubMed), EMBASE (via OVID), Epistemonikos, Lilacs, Web of Science, and CENTRAL. The search strategy was adapted for each database, considering differences in controlled vocabulary and syntax rules. No date or language restrictions were applied. The search strategies developed for MEDLINE, EMBASE, Web of Science and CENTRAL are summarized in Appendices A-D.

The PROSPERO protocol registration platform was also searched for unpublished SRs, and a snowball approach was used for screening reference lists to identify potentially eligible studies. Although the protocol stated that a search would be conducted in ClinicalTrials.gov to detect ongoing primary studies, due to the large quantity of studies identified, it was decided not to include articles from this platform, as the benefits would have been marginal given the extensive data already compiled.

2.4. Data collection and extraction

Two independent reviewers screened titles and abstract for results obtained from the search. The full texts of selected studies were assessed independently by two authors. Studies that did not meet the inclusion criteria were recorded with reasons for their exclusion. Any disagreements, either in the title/abstract or full-text screening phases, were resolved by consensus or, if necessary, by a third author. The Covidence platform was used for this process, and, as recommended in the Cochrane Handbook for Systematic Reviews of Intervention [18], the selection process was documented in sufficient detail to generate a PRISMA flowchart.

Data was extracted and tabulated by one author, using a previously piloted data extraction form, and was double-checked by a content expert in the subject. The following information was extracted from each SR: search date, year of publication, country, objective, number of primary studies included, number of participants, population, co-interventions, comparisons, and outcomes measured. SR research gaps were also identified based on the aim, eligibility criteria, and conclusions. The PICO format was used throughout. For primary studies not included in any identified SRs, the following data were extracted: year of publication, study design, objective, number of included patients, population, interventions, comparisons, and outcomes. The authors of the studies were contacted if additional information was required.

2.5. Methodological quality evaluation

Methodological quality was independently evaluated for all the included SRs by two authors. Any disagreements were resolved by consensus, or if necessary, by a third author. Used to evaluate the included SRs was the AMSTAR-2 instrument [19], which critically appraises SRs in 16 domains. The overall rating was based on weaknesses in critical domains, namely, items 2, 3, 7, 9, 11, 13, and 15.

Overall confidence in SR results – used for the mapping diagrams – was rated in the following four quality categories: critically low (more than one critical flaw), low (one critical flaw), moderate (more than one non-critical flaw), and high (no flaw or just one non-critical flaw). The included primary studies were not critically appraised since they were included to identify knowledge gaps rather than to inform clinical or policy decisions.

2.6. Data synthesis and analysis

Results, summarized in tabular formats, describe the included study characteristics and all the identified PICO questions. A flow diagram was created to classify the included studies, by design at the first level, and by intervention at the second level. An evidence matrix to link primary studies with their SRs was created using the Epistemonikos platform to identify primary studies not included in the SRs. Evidence bubble maps were also created.

3. Results

3.1. Search results

8,531 records were obtained through database searching, 5,373 of which were screened after removing duplicates. After screening of titles and abstracts, 4,476 records were excluded. Of 863 articles assessed by full-text reading, 262 were considered eligible for inclusion. Reasons for exclusion were wrong study design (116), wrong population (89), wrong intervention (207), wrong comparator (94), poor outcome (43), and wrong publication type (52). Manual searching retrieved a further 28 articles (1 SR and 27 primary studies) for inclusion in the mapping review. Therefore, a final total of 290 studies were included: 35 SRs [20–54] and 253 primary studies (103 included [55–158] and 150 [159–308] not included in the SRs). Two additional SRs from PROSPERO were included. Fig. 1 shows the PRISMA flowchart.

3.2. Study characteristics

A general description of the study characteristics, including design, aim, population, interventions, comparators, outcomes, number of primary studies, and number of participants is presented in Tables SM1 (SRs of co-interventions), SM2 (SRs of surgical modalities), SM3 (primary studies of co-interventions) and SM4 (primary studies of surgical modalities).

3.3. Study designs

Of the 290 included articles, 35 (35/290; 12.1%) referred to SRs and 253 (253/290; 87.2%) to primary studies. Of the latter, 103 (103/253; 40.7%) were studies included in the identified SRs. The remaining 150 (150/253; 59.3%), identified through the Covidence platform screening, were not included in the SRs. Their designs were as follows: case-control (1/150; 0.7%), prospective cohort (14/150; 14%), retrospective cohort (53/150; 35.3%), and RCT (82/150; 54.7%). Fig. 2 summarizes information on designs.

3.4. Participant characteristics

Age. Seven SRs (20%) included only adult populations, two (5.7%) included patients of all ages, and 26 (74.3%) did not mention age.

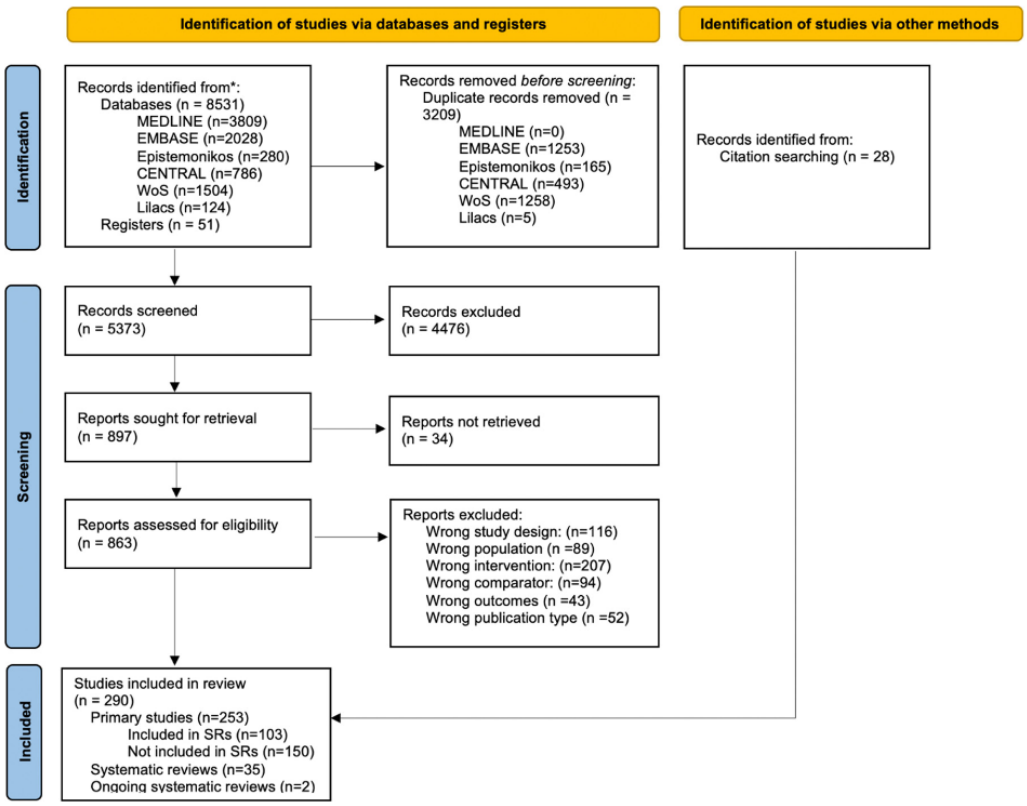


Fig. 1. PRISMA flowchart.

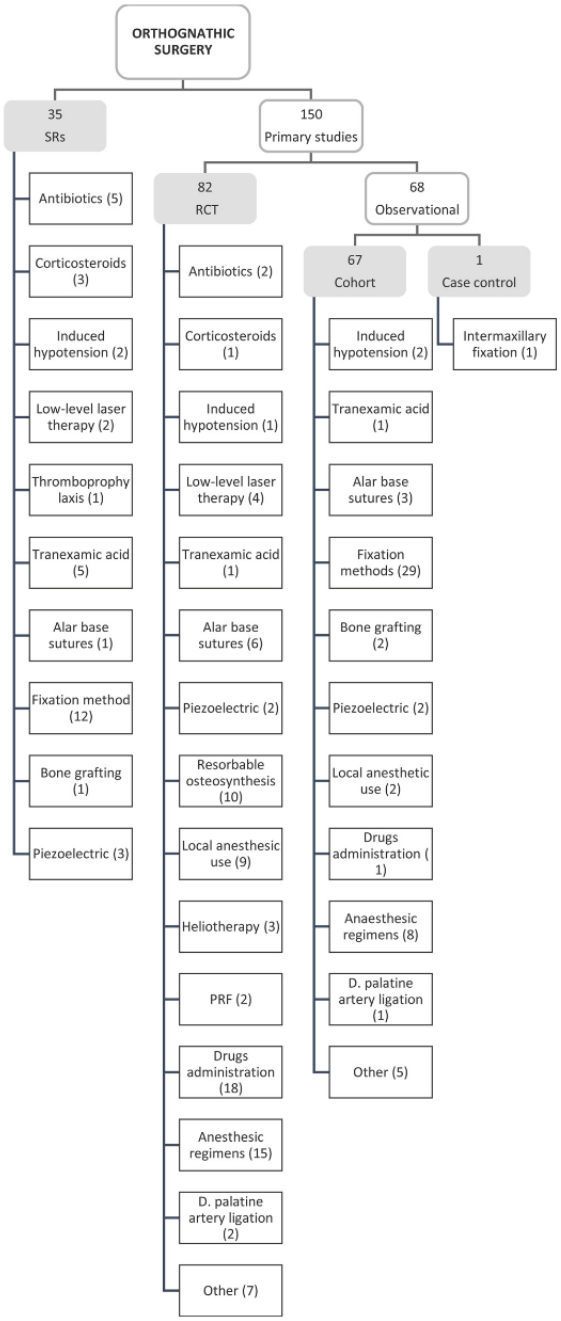


Fig. 2. Flow diagram of study designs and interventions
Abbreviations. PRF: platelet-rich fibrin; SR: systematic review.

Regarding the age of participants in the 150 primary studies not included in SRs, one study included only adolescents (0.7%), 27 studies (18%) included adolescent and adult patients, 103 studies (68.7%) included only results for adults >16 years, one study (18%) included participants of all ages, and 18 studies (12%) did not specify age.

Deformity. The type of deformity of participants was recorded in a simplified manner, grouped as either skeletal class II (mandibular retrognathism, mandibular hypoplasia, maxillary prognathism, and maxillary hyperplasia) or class III (mandibular prognathism, mandibular hyperplasia, maxillary retrognathism, and maxillary hypoplasia). Facial asymmetries in participants were also documented. Of the 35 SRs, one (2.9%) and three (8.6%) included patients with skeletal class III or class II diagnoses, respectively, while the remaining 31 (88.6%) did not specify skeletal classes as inclusion or exclusion criteria. Of the 150 primary studies, 34 (22.7%) included patients with skeletal class III diagnoses (three with facial asymmetry), six (4%) included patients with skeletal class II and class III diagnoses, 16 (10.7%) included results for patients with skeletal class II diagnoses, and 94 (62.7%) did not specify deformity inclusion criteria.

OS type. Of the 35 SRs, OS interventions were one (2.9%) bimaxillary surgery, seven (20%) mandibular surgery, two (5.7%) maxillary surgery, and one (2.9%) genioplasty. Of the 150 primary studies, OS interventions were 36 (24%) bimaxillary orthognathic surgery, seven (4.7%) bimaxillary surgery and genioplasty, two (1.3%) genioplasty alone, one (0.7%) genioplasty and another orthognathic procedure, 46 (30.7%) mandibular surgery, 18 (12%) maxillary surgery, and 25 (16.7%) a combination of the above-mentioned procedures; no procedure was specified in 15 cases (10%).

3.5. Evidence bubble maps

Evidence bubble maps were created to graphically depict the available evidence (Figs. 3 and 4). All interventions reviewed in the included studies are listed in rows, and reported outcomes are listed in columns, and symbols indicate the study design (circles for SRs, squares for RCTs, and triangles for observational studies). Bubble size represents the number of primary studies included in the SRs or the number of participants included in the primary studies. A number positioned over each bubble indicates the number of studies. Colors indicate confidence in SR findings (based on the AMSTAR-2 evaluation). The primary studies included in the maps are those not included in any of the identified SRs.

3.6. Co-interventions

Co-interventions (Fig. 3) performed in the OS perioperative period were assessed in around half of the SRs (18/35; 51.4%) and just under half of the primary studies (68/150; 45.3%). Five SRs (5/18; 27.8%) and two RCTs (2/68; 2.9%) evaluated the use of antibiotics (four SRs included any regimen or period of administration, and one focused on a postoperative extended regimen); three SRs (3/18; 16.7%) and one RCT (1/68; 1.5%) evaluated the use of corticosteroids; two SRs (2/18; 11.1%) and three primary studies (3/68; 4.4%) evaluated the use of induced hypotension, and two SRs (2/68; 2.9%) and four RCTs (4/68; 5.9%) investigated the effects of low-level laser therapy. Use of tranexamic acid was assessed for one primary study cohort and one RCT (1/68; 1.5% each), and for five SRs (5/18; 27.8%). One of those SRs corresponded to a broader topic, as it included several techniques to reduce blood loss during surgery: induced hypotension, also assessed by three primary studies (3/68; 4.4%); administration of Yunnan Baiyao capsules, evaluated also by one RCT (1/68; 1.5%); and aprotinin. Some co-interventions were only evaluated by primary studies, 23 of which focused on anesthetic technique (23/68; 33.8%), assessing different drug regimens to achieve better results (hemodynamics, blood loss, postoperative nausea and vomiting (PONV) and recovery), procedures such as gastric aspiration and throat packs, and procedures related to intubation. Identified was one ongoing SR investigating the best pharmacological protocol for induced hypotension in patients undergoing OS. As for perioperative drug use, 19 primary studies (19/68; 27.9%) included various medications to control pain, PONV, opioid consumption, etc., as follows: clonidine pre-medication, desmopressin, hemocoagulase, ibuprofen, adenosine 5'triphosphate (ATP), iron therapy, melatonin, nalbuphine hydrochloride, nefopam, paracetamol, preemptive multimodal analgesia, pregabalin

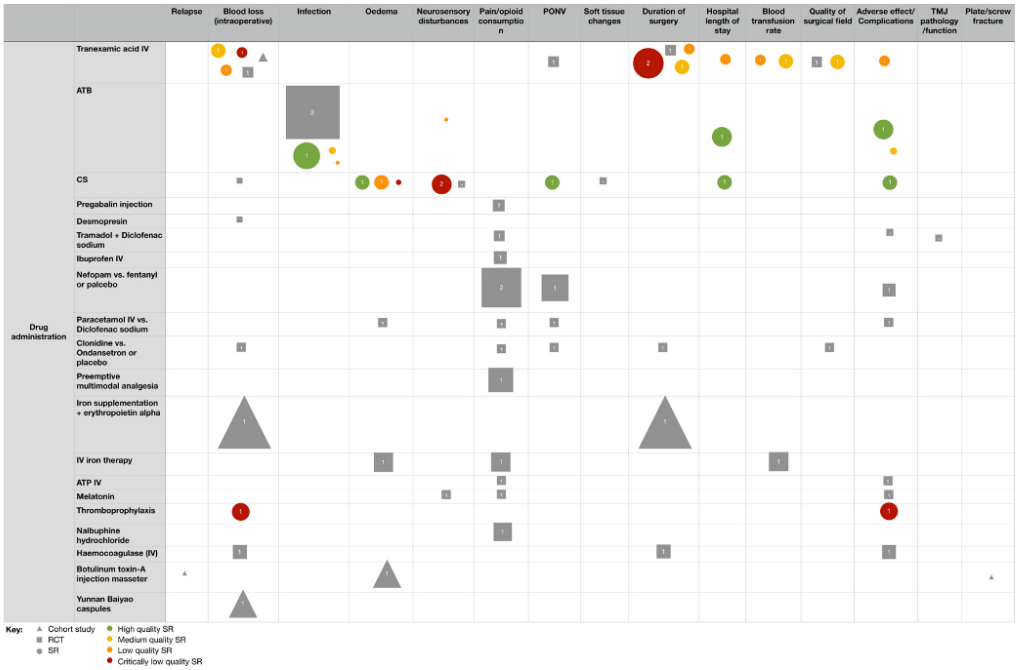


Fig. 3. Bubble map of OS co-interventions.

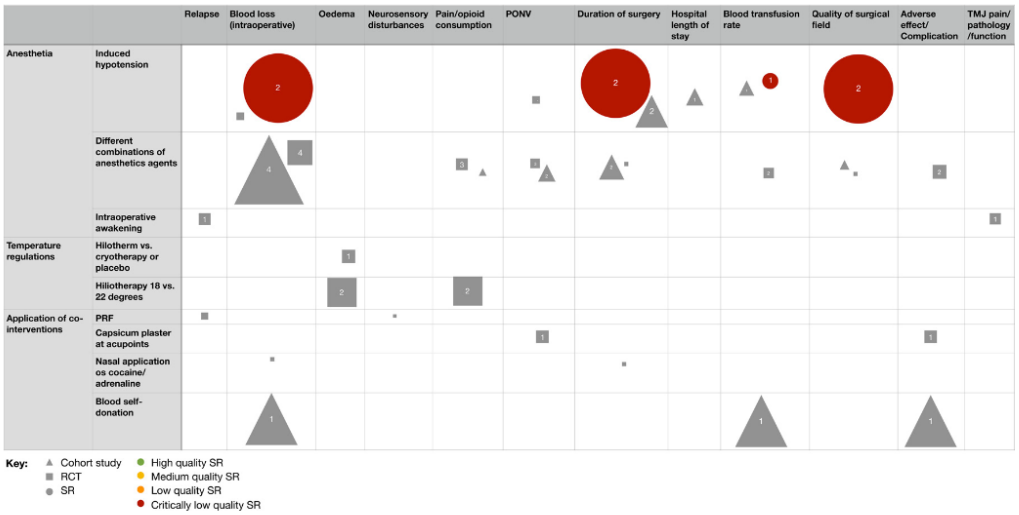


Fig. 3. Continued.

injection, systemic enzyme therapy, tramadol with diclofenac, and Yunnan Baiyao capsules. Furthermore, two primary studies (2/68; 2.9%) evaluated the efficacy of intraoperative awakening, and three primary studies (3/68; 4.4%) evaluated heliotherapy or forced-air warming blankets in managing pain and edema. Other studies assessed other co-interventions such as descending artery ligation, maxillary suction drainage, platelet-rich fibrin (PRF), pre-operative blood self-donation, nasal application of cocaine/adrenaline, and capsicum plasters at acupoints.

3.7. Surgical modalities

17 SRs (17/35; 48.6%) and 83 primary studies (83/150; 55.3%) assessed the efficacy of different approaches to intraoperative OS (Fig. 4). Osteosynthesis modalities were assessed by 12 SRs (12/17; 70.6%) and 48 primary studies (48/83; 57.8%). Three SRs (3/17; 17.6%) and eight cohort studies (8/83; 9.6%) assessed the efficacy of bicortical osteosynthesis compared to monocortical osteosynthesis, whereas six SRs (6/17; 35.3%), two RCTs (2/83; 2.4%) and two



Fig. 4. Bubble map of OS surgical modalities.

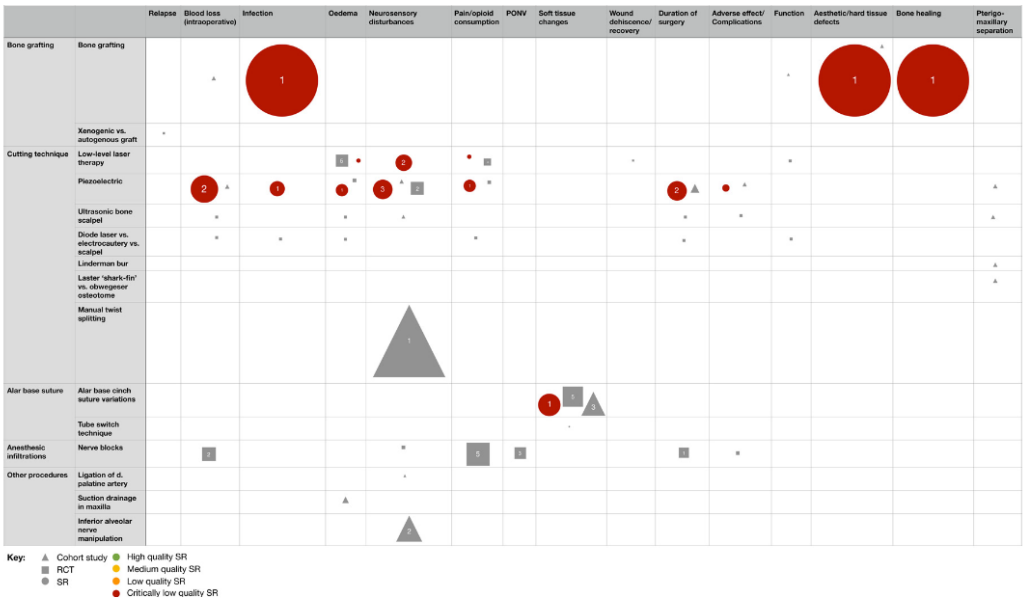


Fig. 4. Continued.

retrospective cohort studies (2/83; 2.4%) investigated the use of resorbable materials compared to titanium plates and screws. In addition, three SRs (3/17; 17.6%) and 16 primary studies (16/83; 19.3%) focused on the efficacy of rigid compared to wire fixation. Other variations in osteosynthesis methods, assessed only by primary studies (19/83; 22.9%), included the use of hybrid fixation, slot plates, three-hole vs. four-hole sliding plates, titanium plates with Biopex, modified L-type monocortical plate, miniscrews, circumferential wires, and combined fixation techniques.

Regarding surgical cutting devices, three SRs (3/17; 17.6%), two RCTs (2/83; 2.4%), and two cohort studies (2/83; 2.4%) investigated piezoelectric devices for osteotomies compared to conventional devices, such as pneumatic saws, conventional drilling, electric saws, and standard saws. The use of the ultrasonic bone scalpel compared to piezoelectric and conventional rotating devices was assessed by one RCT (1/83; 1.2%) and two retrospective cohort studies (2/83; 2.4%), but no SRs. One RCT (1/83; 1.2%) evaluated diode laser for circumventricular incision compared to the scalpel and electrocautery.

The use of bone grafting was evaluated by one SR (1/17; 5.9%) and three primary studies (3/83; 3.6%). Local anesthesia, either for nerve blocks (7/83; 8.4%) or infiltration (2/83; 2.4%), inferior nerve repositioning (1/83; 1.2%), and freedom from the proximal segment (1/83; 1.2%) were evaluated only by primary studies.

Finally, one (1/17; 5.9%) review, one RCT (1/83; 1.2%), and two retrospective cohort studies (2/83; 2.4%) focused on the use of cinch sutures and VY closures compared to a control group or placebo, whereas five RCTs (5/83; 6%) and one prospective cohort study (1/83; 1.2%) evaluated different types of cinch sutures compared to other cinch suturing techniques (extraoral base cinch suture, modified cinch suture, VY closure with muscle

reconstruction, trans-septal cinch suture, and tube switching to ensure a better field for suturing).

3.8. Outcomes

A wide variety of outcomes were measured in the included studies, with most of the primary studies and SRs evaluating more than one outcome. The principal outcomes measured were relapse, infection, blood loss, pain, edema, neurosensory disturbances, surgery duration, PONV, soft tissue changes, function, co-intervention adverse effects, and surgical complications.

3.9. Evidence matrix

To create an evidence matrix, using the Epistemonikos platform the SRs were linked with their included primary studies

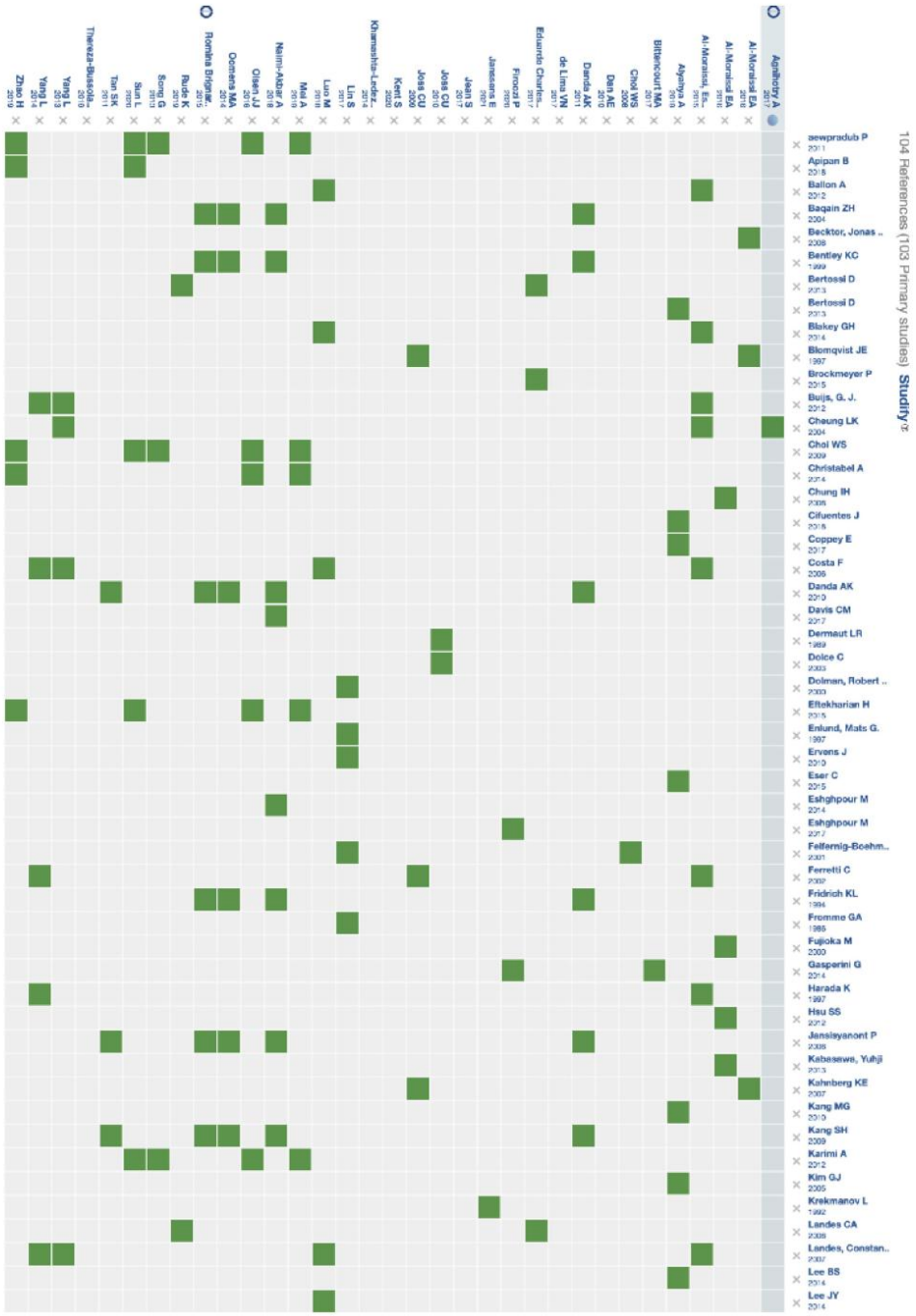


Fig. 5. Evidence matrix.

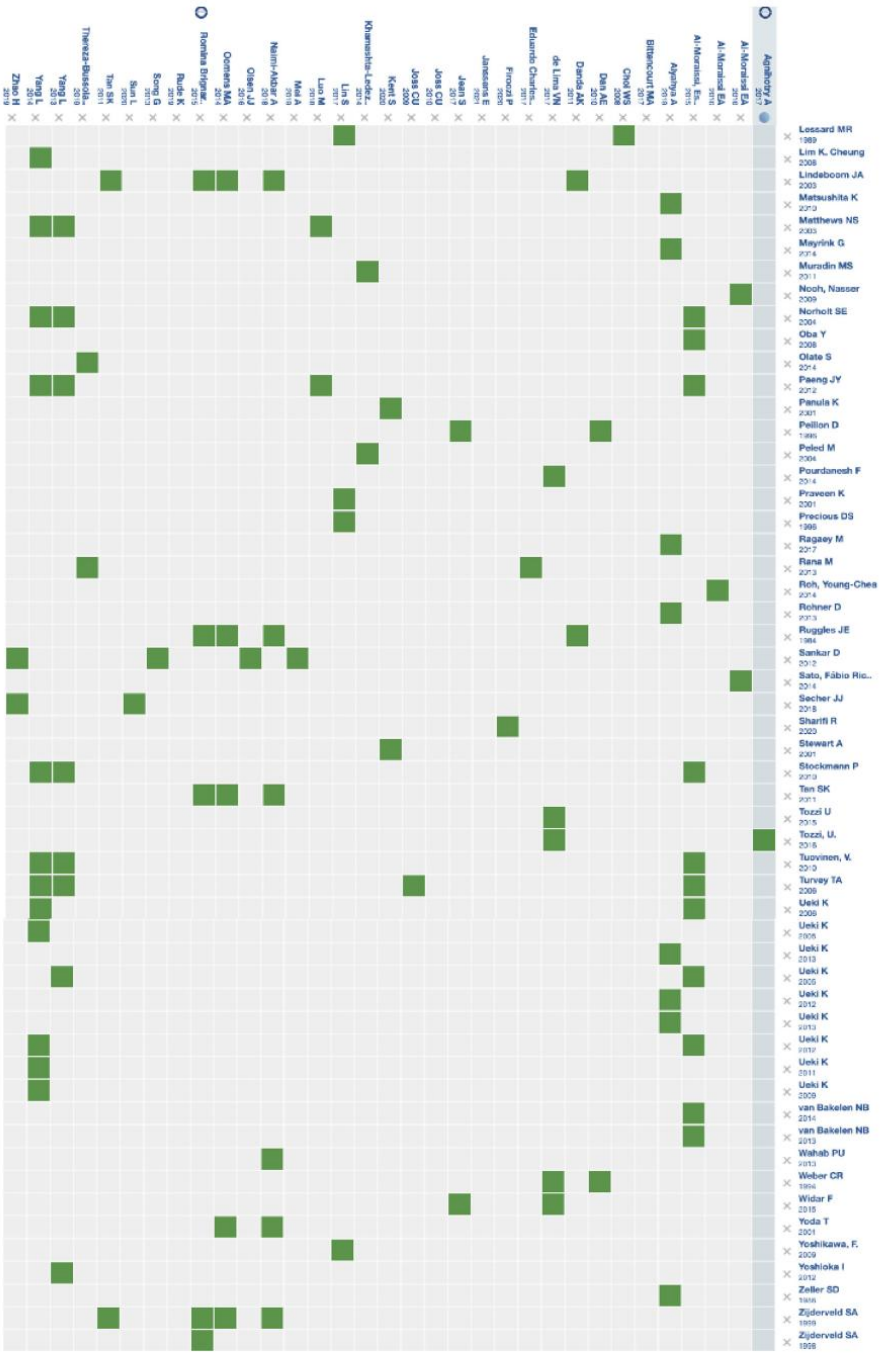


Fig. 5. Continued.

that fulfilled our selection criteria (Fig. 5). Two SRs were not included in the matrix. In one SR [36], none of its included primary studies fulfilled our inclusion criteria, and although one of the objectives was to evaluate the difference between rigid and wire fixation for soft tissue changes, none of the included primary studies addressed that topic. The other SR [32] was not included because it was an update to an already included Cochrane review [21].

Link to access complete evidence matrix: http://www.epistemonikos.org/matrixes/6122bdfe7aaac841790c8bd8.

3.10. Methodological quality

Based on AMSTAR-2 scores, methodological quality (Fig. 6) was rated as follows: 20 SRs (20/35; 57%) critically low, five SRs low (5/35; 14.3%) and three SRs high (3/35; 8.6%). SRs were mainly

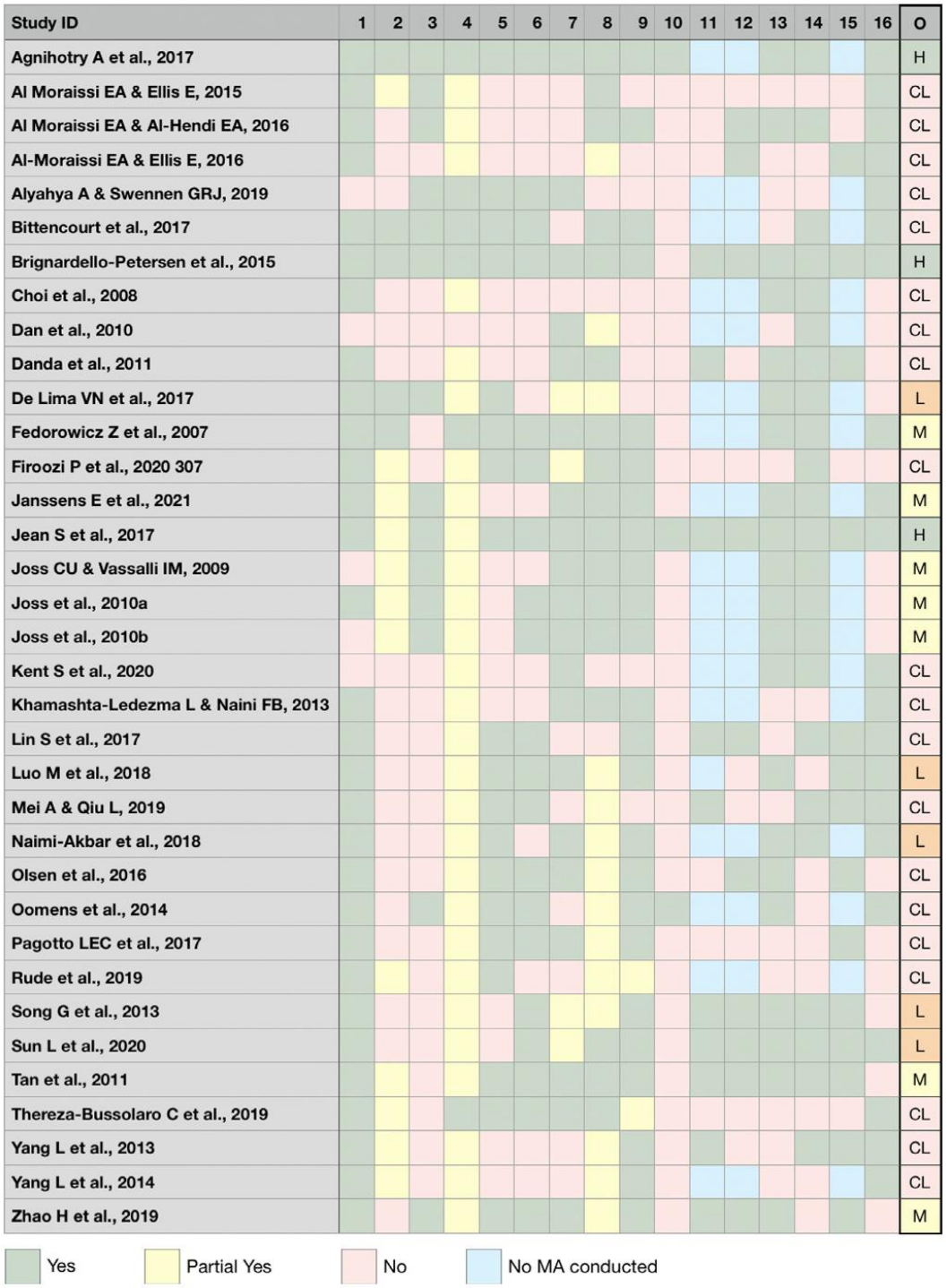


Fig. 6. Methodological quality of the included SRs.
Items
1. Did the research questions and inclusion criteria for the review include the components of PICO?
2. Did the review report contain an explicit statement that the review methods were established before the conduct of their review, and did the report justify any significant deviations from the protocol? *
3. Did the review authors explain their selection of the study designs for inclusion in the review?
4. Did the review authors use a comprehensive literature search

Table 1
PICO questions for OS co-interventions.

Population	Intervention	Comparison	Outcomes	Study
Adults undergoing orthognathic surgery	Prophylaxis antibiotics	Placebo, control group, or other regimens	Infection (systemic and surgical site) Pain Mortality Hospital length of stay Adverse effect	Brignardello-Petersen et al., 2015 [47] Danda et al., 2011 [29] Naimi Akbar et al., 2018 [44] Oomens et al., 2014 [46] Tan et al., 2011 [51]
	Induced hypotension	Placebo or control group	Intraoperative blood loss Duration of surgery Blood transfusion rate Quality of surgical field	Choi et al., 2008 [27] Lin S et al., 2017 [41] Olsen et al., 2016 [45]
	LLL therapy	Placebo or control group	Pain Edema Neurosensory disturbances	Bittencourt et al., 2017 [47]
	Corticosteroid	Placebo or control group	Edema Neurosensory disturbances Hospital length of stay PONV Adverse effects	Dan et al., 2010 [28] De Lima VN et al., 2017 [30] Jean S et al., 2017 [35]
	Thromboprophylaxis	Placebo or control group	Intraoperative blood loss Postoperative blood loss Thromboembolic events (deep vein thrombosis or pulmonary embolism)	Kent S et al., 2020 [39]
	Tranexamic acid (IV)	Placebo or control group	Intraoperative blood loss Blood parameters Duration of surgery Quality of surgical field Amounts of irrigation fluid Blood transfusion rate Hospital length of stay Adverse reactions	Mei A & Qju L, 2019 [43] Olsen et al., 2016 [45] Song G et al., 2013 [49] Sun L et al., 2020 [50] Zhao H et al., 2019 [20]
Adults undergoing mandibular orthognathic surgery	LLL therapy	Placebo	Neurosensory disturbances	Firoozi P et al., 2020 [33]

Abbreviations. LLL: low-level laser therapy; IV: intravenous; PONV: postoperative nausea and vomiting.

downgraded because authors did not refer to the development of a pre-existing protocol (18/35; 51.4%) or explain their selection or design criteria for inclusion in the SR (21/35; 60%). Moreover, for primary studies, sources of funding were often not clearly stated (32/35; 91.4%), and authors did not perform study selection (16/35; 45.7%) and data extraction (15/35; 42.9%) in duplicate. The top-rated items were search strategy, detailed scription of included studies, and investigation for publication bias.

3.11. Cochrane reviews

Of the 35 SRs identified, three [21,32,47] corresponded to Cochrane reviews. The aim of two – a review by Fedorowics et al. [32] updated by Agnihotry et al. [21] – was to compare the effects of bioresorbable fixation systems with titanium systems used during OS. The third SR assessed the effects of antibiotic prophylaxis in preventing surgical site infection in OS. According to AMSTAR-2 scores, two of the Cochrane reviews were of high quality and one was of moderate quality.

3.12. PICO questions in SRs and research gaps

We retrieved 16 PICO questions from the SRs. The PICOs, whose key characteristics are listed in Tables 1 and 2, are grouped according to OS type: all types of surgery, mandibular surgery, maxillary surgery, or genioplasty.

Table 3 lists 15 identified research gaps that remain unanswered by the evidence synthesis, either because they were identified in primary studies and not in SRs, or because of the low or critically low quality of the existing evidence.

4. Discussion

Our main aim was to identify, describe, and organize currently available clinical research in SRs and primary studies regarding OS co-interventions, surgical modalities, and their outcomes, whether intra- or postoperative. We therefore performed a systematic mapping review focused on identifying knowledge gaps, prioritizing future research needs in broad fields, and displaying results in a user-friendly format [13]. Our mapping review was based on 35 published SRs that included 103 individual studies, and an additional 150 primary studies that were not included in the identified SRs.

strategy? *
5. Did the review authors perform study selection in duplicate?
6. Did the review authors perform data extraction in duplicate?
7. Did the review authors provide a list of excluded studies and justify the exclusions? *
8. Did the review authors describe the included studies in adequate detail?
9. Did the review authors use a good technique for assessing the risk of bias (RoB) in individual studies that were included in the review? *
10. Did the review authors report on the funding sources for the studies included in the review?
11. If meta-analysis was performed, did the review authors use

Table 2
PICO questions for different OS surgical modalities.

Population	Intervention	Comparison	Outcomes	Study
Adults undergoing orthognathic surgery	Resorbable osteosynthesis	Titanium osteosynthesis	Relapse Status of occlusion Edema Infection Wound dehiscence Function Pain Analgesic medication Plate and screw fractures or removal Facial appearance Neurosensory disturbances TMJ pain or pathology Foreign body reaction Other complications	Agnihotry A et al., 2017 [21] Al-Moraissi et al., 2015 [24] Fedorowicz Z et al., 2007 [32] Luo M et al., 2018 [42] Yang L et al., 2013 [53] Yang L et al., 2014 [54]
	Bone grafting	Different types of bone grafting or control group	Infection Bone healing Aesthetic defects	Alyahya A & Swennen GRJ, 2019 [25]
	Piezoelectric	Conventional osteotomy	Intraoperative blood loss Edema Pain Neurosensory disturbances Duration of surgery	Pagotto LEC et al. 2017 [31]
Adults undergoing mandibular orthognathic surgery	Bicortical osteosynthesis	Monocortical osteosynthesis using mini plates	Relapse	Al-Moraissi EA & Al-Hendi EA, 2016 [22] Al-Moraissi EA & Ellis E, 2016 [23] Joss CU & Vassalli IM, 2009 [38]
	Rigid fixation method	Wire fixation method	Soft tissue changes	Joss CU et al., 2010a [36] Joss et al., 2010b [37]
	Piezoelectric	Conventional osteotomy	Intraoperative blood loss Duration of surgery Intraoperative complications	Rude et al., 2019 [48]
Adults undergoing maxillary orthognathic surgery	Alar base cinch suture, V–Y closure, or anterior nasal spine recontouring	Placebo or control group	Maxillary incisor exposure Soft tissue changes (upper lip) Hard tissue changes associated with changes in lip position	Khamashta-Ledezma L & Naini FB, 2013 [40]
	Piezoelectric	Conventional osteotomy	Intraoperative blood loss Neurosensory disturbances Oroantral fistula/communication/perforation Soft tissue, tooth, or permanent nerve injury Osteonecrosis	Thereza-Bussolaro C et al., 2019 [52]
Patients undergoing Genioplasty	Rigid fixation method	Wire fixation method	Relapse Soft tissue changes	Janssens E et al., 2021[34]

Abbreviations. TMJ: temporomandibular joint.

Methodological quality evaluation using AMSTAR-2 classified most of the SRs as of critically low quality (21/35; 60%), and only identified three SRs as of high quality. Domains that need to be improved in future SRs are primarily the following: (1) development of an a priori protocol that state that a method was established before conducting the SR; (2) explanation of the selection of study designs for inclusion in the SR; (3) reporting of funding sources for primary studies; and (4) study selection and data extraction performed in duplicate. Noteworthy was the higher methodological quality of the three Cochrane reviews: two rated as of high quality and the third as of moderate quality. Although quality evaluation is not a requirement of mapping reviews, we considered it beneficial in terms of drawing more accurate conclusions.

The co-interventions most frequently evaluated by SRs were antibiotic therapy, corticosteroid administration, IV tranexamic acid injection, and induced hypotension. The most frequently reported outcomes were blood loss, pain, infection, surgery duration, adverse effects, and intra- or postoperative complications. It was noteworthy that, while no SR reported the outcome of painkiller or opioid consumption, a high proportion of primary studies did. Moreover, several co-interventions concerning drug administration were the target of single RCTs and observational studies: e.g., IV ibuprofen [169], tramadol with diclofenac sodium [288], Yunnan Baiyao capsules [285], IV ATP [211], iron therapy [171,228,253], desmopressin [206], systemic enzyme therapy [271]. Reported co-intervention outcomes mainly included pain, PONV, edema, blood loss, and adverse effects; however, no firm conclusions can be drawn because of the small number of studies. Temperature regulation techniques, such as heliotherapy [167,192,239] and air-warming blankets [250] to achieve lower edema and pain levels, were studied by several RCTs. While it would undoubtedly be interesting to analyze and compare the results of those studies in an SR, comparator variability (e.g., different cryotherapy approaches, variations in heliothermic temperature, placebo) makes any comparative analysis difficult.

While several studies assessed variations in anesthetic regimens, procedures to reduce blood loss, hemodynamic parameters, surgical field quality, and decreased pain and PONV in OS [161,165,173,180,181,194,196,199,208,210,214,215,219

Table 3
Identified research gaps.

Research gap	Reason
1. To compare the use of nefopam vs fentanyl or placebo in pain, opioid consumption and PONV in patients undergoing orthognathic surgery	**RCTs available** [179,251]
2. To evaluate the efficacy of thromboprophylaxis in blood loss and adverse effects in patients undergoing orthognathic surgery	**SR of critically low quality** [39]
3. To evaluate the efficacy of induced hypotension in blood loss, duration of surgery, blood transfusion rate and quality of surgical field	**SRs of critically low quality** [27,41] and primary studies [170,197] available
4. To compare the use of heliotherapy at 18 degrees vs. 22 degrees for edema, pain and opioid consumption	**RCTs available** [167,192]
5. To compare the use of rigid vs wire fixation on relapse in patients undergoing orthognathic surgery	**Cohort studies** [162,190,191,255,259,267,276,278] **and RCTs** [187,188,201,297] **available, one SR of moderate quality** [34]
6. To compare the use of resorbable vs. titanium osteosynthesis on infection, NSD, wound recovery, TMJ pathology, (relapse, infection, NSD, wound recovery, TMJ pain or pathology) in patients undergoing orthognathic surgery	**Low quality SRs** [24,53,54] **and new RCTs** [176,305]
7. To compare the use of bicortical vs mono cortical osteosynthesis in relapse, NSD, status of occlusion and function in patients undergoing orthognathic surgery	**Two critically low quality SRs to assess relapse** [22,23] **and cohort studies that assess other outcomes** [166,202,217,223,244,283,291,302–304]
8. To assess the efficacy of hybrid fixation in patients undergoing orthognathic surgery	**RCTs and cohort studies available** [163,209,223,262,291–293]
9. To assess the efficacy of slot plates in patients undergoing orthognathic surgery	**Cohort studies available**[307,308]
10. To assess the use of bone grafting on infection, hard tissue defects and bone healing in patients undergoing orthognathic surgery	**One large SR of critically low quality** [25]
11. To assess the efficacy of LLL therapy on edema, NSD, pain, opioid consumption, wound dehiscence and function in patients undergoing orthognathic surgery	**Critically low quality SR** [26,33], **new RCTs**[182,189,265,309]
12. To assess the efficacy of piezoelectric on blood loss, infection, edema, NSD, pain, opioid consumption, duration of surgery, complications in patients undergoing orthognathic surgery	**Critically low quality SRs** [31,48,52], **new RCT**[225,263] **and cohort studies** [218,224]
13. To assess the use of alar base cinch sutures in alar base width in patients undergoing orthognathic surgery	**RCTs available**[174,212,258] **and cohort study available**[235,257]
14. To assess the use of nerve blocks in blood loss, NSD, pain, opioid consumption, PONV, duration of surgery and adverse effects in patients undergoing orthognathic surgery	**RCTs available**[172,195,273,296,298]
15. To asses inferior alveolar nerve manipulation in NSD in patients undergoing orthognathic surgery	**Cohort study available**[256,280]

Abbreviations. PONV: postoperative nausea and vomiting; NSD: neurosensory disturbances; LLL: low-level laser therapy; RCT: randomized controlled trial; SR: systematic review.

–221,234,236,246,260,268,274,299,300], no SR has been published on those issues, although we did identify an ongoing SR that aims to address them [310]. Note that studies that compared different anesthetic regimens were grouped in the co-interventions bubble map, as analysis of this issue was beyond the scope of this mapping review.

Regarding different OS surgical modalities, SRs more frequently evaluated the use of resorbable versus titanium plates or screws, bicortical versus monocortical osteosynthesis, the use of piezoelectric devices, and low-level laser therapy. Identified were a large number of primary studies not included in the SRs that analyzed bicortical fixation. Furthermore, those primary studies recorded a wider variety of outcomes for this intervention, including neurosensory disturbances, function, occlusion status, etc, whereas the SRs focused exclusively on relapse as an outcome. It would be useful to synthesize observational studies in future SRs to be able to draw conclusions regarding outcomes for bicortical screws. Similarly, while hybrid fixation was reviewed by seven primary studies [163,209,262,292,293], no SR has to date synthesized their results.

Primary studies assessed other variations in fixation methods, such as the use of L-shaped plates [248], modified L-shaped plates [213], slotplates 1.0 [307], 2.0, or 3.0 [308], sliding plates [230], and 4-screw compared to 3-screw osteosynthesis [177]. However, few studies exist of each method in isolation that combine their results.

One SR evaluated additional suturing techniques, such as alar base cinch suture and VY closure compared to placebo or a control group [40]. Several primary studies not included in an SR also evaluated this procedure, although some focus on comparing different modifications of the cinch suture. In addition, the outcome assessed by the SR was incisor exposure, while most of the primary studies evaluated alar base width. This outcome needs to be considered in a future SR so as to obtain more specific conclusions regarding this suturing technique.

To our knowledge, this is the first mapping review performed for OS co-interventions and surgical modalities. A broader mapping review of the oral and maxillofacial surgery field, published in 2017, and aiming to identify knowledge gaps [311], included SRs from several domains, including reconstructive surgery, surgical tooth removal, tumors, orofacial infections, maxillofacial and dental trauma, and OS. Of the nine SRs included in that mapping review, four were also included in our review [27,37,49]; the five excluded SRs did not fulfill our selection criteria: orthopedic surgery [312], orthodontic surgery, no control group [313,314], and postoperative treatment for nerve injuries [315]. In our mapping review, we included 31 SRs not included in the 2017 mapping, which, additionally, did not represent results graphically.

The information obtained from our evidence maps enabled us to identify several OS research gaps (summarized in Table 3) that should help direct future secondary research efforts in resolving unresolved questions regarding OS.

4.1. Strengths

Among the strengths of this study, we highlight the sensitive search strategy implemented without language or date restrictions, meaning that relevant studies were not likely to be omitted. Furthermore, the evidence matrix, which identified primary studies that responded to our inclusion criteria not included in identified SRs, identifies knowledge gaps in topics covered by primary studies but not synthesized in an SR. In addition, the fact that our mapping

approach identified relevant primary studies addressing OS that were excluded from recent SRs has important implications for the results of SRs on OS.

Our mapping approach was designed to ensure confidence in the results. Selection and quality evaluation procedures were performed independently and in duplicate, and data extraction was double-checked by a content expert in the subject. In addition, our use of the PICO format to organize information and results ensured a simplified and effective display of evidence regarding OS co-interventions and surgical modalities. Even though the evidence mapping methodology does not usually include this step [14], we evaluated the methodological quality of the SRs, as this will help identify topics requiring new high-quality SRs to answer clinical questions, and will also help stakeholders determine the quality of the evidence for clinical decision-making. Finally, the graphical display developed for this review is a user-friendly visual presentation of the quality of existing evidence on OS.

4.2. Limitations

Conference abstracts and primary study registries were not included in this mapping due to the very large volume of studies detected; nevertheless, we are confident that their incorporation would have not substantially modified the results due to the large quantity of information compiled. Quality of life was not included as an outcome, due to the complexity of this subject and the extensive evidence available; we are of the opinion that a systematic mapping review should focus exclusively on this topic to ensure a more thorough analysis. The exclusion of studies not published because of their unfavorable results incurs a risk of possible publication bias. Finally, a limitation of the mapping methodology is that it merely organizes and describes evidence as reported by the original authors of studies, so bias may arise from authors describing results as beneficial even though based on low-quality evidence. The mapping approach is therefore not an appropriate tool for healthcare clinical decision-making.

5. Conclusions

This evidence mapping review was based on SRs, RCTs, and observational studies that assessed co-interventions and different surgical modalities used in OS. 16 PICOs were identified in the SRs, primarily addressing the effects of fixation methods, surgical cutting devices, and use of antibiotics, corticosteroids, and induced hypotension. Also identified were 15 research gaps that need to be addressed in future SRs. The methodological quality of most SRs included in this mapping review was rated as critically low. These findings highlight the need for further high-quality primary and secondary research to evaluate OS co-interventions and surgical modalities.

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Authors contributions

JB: Conceptualization, Methodology, Validation, Investigation, Data curation, Writing – Original Draft, Writing – Review & Editing, Visualization, Supervision, Project administration; **MU**: Investigation, Data curation, Writing – Review & Editing; **MB**: Investigation, Data curation, Writing – Review & Editing; **JPV**: Investigation, Data curation, Writing – Review & Editing; **EV**: Data curation, Writing – Review & Editing; **IA**: Data curation, Writing – Review & Editing **JV**: Validation, Resources, Investigation, Writing – Review & Editing, Supervision **GU**: Validation, Resources, Investigation, Writing – Review & Editing, Supervision; **XB**: Validation, Resources, Writing – Review & Editing, Supervision.

Ethics and dissemination

As researchers will not access information that could lead to identifying an individual participant, obtaining ethical approval was waived.

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Declaration of Competing Interest

There are no conflicts of interest.

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.jormas.2022.05.011.

Appendix A. Search strategy for MEDLINE

Search number	Study design	Query
12	Case control	#11 AND #10
11		"Case-Control Studies"[mesh] OR (case[ti] AND control[ti]) OR case control[tiab] OR nested [tiab] OR match*[tiab]
10		#1 NOT (#3 OR #6 OR #9)
9	Cohort	#7 AND #8
8		"Cohort Studies"[mesh] OR cohort*[tiab] OR prospective*[tiab] OR propensity[tiab]
7		#1 NOT (#3 or #6)
6	RCT	#4 AND #5
5		("randomized controlled trial"[Publication Type] OR "controlled clinical trial"[Publication Type] OR "randomized"[Title/Abstract] OR "placebo"[Title/Abstract] OR "drug therapy" [MeSH Subheading] OR "randomly"[Title/ Abstract] OR "trial"[Title/Abstract] OR "groups"[Title/Abstract]) NOT ("animals" [MeSH Terms] NOT "humans"[MeSH Terms])
4		#1 NOT #3
3	SR	#1 AND #2
2		Systematic[sb]
1		"orthognathic surgery"[Title] OR "orthognathic surgical procedures"[Title] OR "sagittal split" [Title] OR "bsso"[Title] OR "ivro"[Title] OR "genioplasty"[Title] OR "mandibular advancement"[Title] OR "orthognathic surgical procedures"[MeSH Terms] OR "orthognathic surgery"[MeSH Terms]

Appendix B. Search strategy for EMBASE

No.	Query
#9	#7 AND #8
#8	'case-control studies'/exp OR (case:ab,ti AND control:ab,ti) OR 'case control':ab,ti OR nested:ab,ti OR match*:ab,ti
#7	#1 NOT (#2 OR #4 OR #6)
#6	#12 AND #5

(*continued*)

#5	'cohort studies'/exp OR cohort*:ab,ti OR prospective*:ab,ti OR propensity:ab,ti
#4	#1 NOT (#2 OR #4)
#4	#3 AND ('clinical trial'/de OR 'controlled clinical trial'/de OR 'randomized controlled trial'/de OR 'randomized controlled trial topic'/de)
#3	#1 NOT #2
#2	#1 AND 'systematic review'/de
#1	'orthognathic surgical':ti OR (orthognathic:ti AND surgical:ti AND procedure*:ti) OR 'orthognathic surgery'/exp OR 'orthognathic surgery' :ti OR 'sagittal split':ti OR orthognathic*:ti OR bsso:ti OR ivro:ti OR 'genioplasty'/exp OR genioplasty:ti

Appendix C. Search strategy for World of Science

#1 TI=(('orthognathic surgery') OR ('orthognathic surgical procedure*') OR ('sagittal split') OR bsso OR ivro OR genioplasty OR ('mandibular advancement'))
#2 TS="systematic review"
#3 TS=pool*
#4 TS="inclusion criteria"
#5 #2 or #3 or #4
#6 #1 and #5
#7 TS='randomized Controlled trial'
#8 ts=randomized
#9 ts=placebo
#10 ts='drug therapy'
#11 ts=randomly
#12 ts=groups
#13 #7 or #8 or #9 or #10 or #11 or #12
#14 #1 not #6
#15 #13 and #14
#16 #1 not (#6 or #15)
#17 ts=cohort*
#18 ts=prospective*
#19 ts=propensity*
#20 #17 or #18 or #19
#21 #16 and #20
#22 ts='case control'
#23 ti=(case AND control)
#24 ts=nested
#25 ts=match*
#26 #22 or #23 or #24 or #25
#27 #1 not (#6 or #15 or #21)
#28 #26 and #27

Appendix D. Search strategy for CENTRAL

#1 "orthognathic surgery":Ti OR "orthognathic surgical procedures":ti OR "sagittal split":ti OR "bsso":ti OR "ivro":ti OR "genioplasty":ti OR "mandibular advancement":ti
#2 MeSH descriptor: [Orthognathic Surgical Procedures] explode all trees
#3 MeSH descriptor: [Orthognathic Surgery] explode all trees
#4 MeSH descriptor: [Osteotomy, Sagittal split Ramus] explode all trees
#5 MeSH descriptor: [Osteotomy, Le Fort] explode all trees
#6 #1 OR #2 OR #3 OR #4 OR #5

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5.2 RESULTADOS DEL SEGUNDO ESTUDIO

Bendersky, J., Uribe, M., Bravo, M., Vargas, J. P., Villanueva, J., Urrutia, G., & Bonfill, X. (2023). Systematic mapping review of interventions to prevent blood loss, infection and relapse in orthognathic surgery. Medicina oral, patología oral y cirugía bucal, 28(2), e116–e125. https://doi.org/10.4317/medoral.25530

Factor de impacto: 2.1

5.2.1 SELECCIÓN DE ESTUDIOS

Dentro de los 290 estudios incluidos en el primer artículo, se seleccionaron 177 que evaluaban los desenlaces de sangrado, infección o recidiva, de los cuales 27 fueron revisiones sistemáticas (RS; 15,3%) y 150 estudios primarios (84,7%). De estos últimos, 91 (51,4%) ya estaban contenidos en las RS, mientras que 59 (33,3%) fueron identificados de manera independiente.

5.2.2 DISEÑO DE LOS ESTUDIOS PRIMARIOS

De los 59 estudios primarios adicionales, 28 (47,5%) correspondieron a ECAs, 25 (42,4%) a cohortes retrospectivos y 6 (10,2%) a cohortes prospectivos.

5.2.3 RESULTADOS POR DESENLACE

PÉRDIDA SANGUÍNEA

El desenlace “pérdida sanguínea” fue evaluado por 11 RS (31,4%) y 27 estudios primarios (18,0%), de los cuales 16 fueron ECA (10,7%), 7 cohortes retrospectivos (4,7%) y 3 cohortes prospectivos (2,0%).

Las intervenciones con efecto beneficioso/probablemente beneficioso incluyeron:

- Ácido tranexámico intravenoso (5 RS, n=1.621; 1 ECA, n=36).
- Hipotensión inducida (2 RS, n=560; 2 cohortes, n=150).
- Piezoeléctrico (2 RS, n=1.680; 1 cohorte, n=44).

- Escalpelo ultrasónico (1 ECA, n=34).

Otros fármacos evaluados fueron Yunnan Baiyao (1 ECA, n=95), haemocoagulasa (1 ECA, n=46) y clonidina (1 ECA, n=30).

INFECCIÓN POSTOPERATORIA

Este desenlace fue analizado en 9 RS (25,7%) y 7 estudios primarios (4,7%), que incluyeron 4 ECA (2,7%), 1 cohorte prospectivo (0,7%) y 3 cohortes retrospectivos (2,0%). Las intervenciones que analizaron este desenlace fueron las siguientes:

- El uso de piezoeléctrico mostró reducción de infecciones (1 RS, n=996).
- Slotplates 3.0 redujo infecciones frente a Slotplates 2.0 (1 ECA, n=186).
- Comparaciones entre osteosíntesis reabsorbible vs titanio arrojaron resultados inconsistentes: 1 RS, n=1.384 y 1 ECA, n=101 sin diferencias; otro RS (n=1.092) fue inconcluso.
- Para antibióticos perioperatorios, los resultados fueron heterogéneos: beneficiosos (1 RS alta calidad, n=788; 3 RS baja/calidad crítica, n=1.150), sin diferencias (2 cohortes, n=178) o inconclusos (1 RS, n=132).

5.2.4 RECIDIVA

La recidiva fue reportada en 9 RS (25,7%), 10 ECA (6,7%), 14 cohortes retrospectivos (9,3%) y 4 cohortes prospectivos (2,7%).

La mayoría de los estudios indicaron ausencia de efecto diferencial entre:

- Osteosíntesis reabsorbible vs titanio (3 RS críticamente bajas, n=3.823; 1 RS baja, n=420; 1 RS moderada, n=120; 2 ECA, n=141; 2 cohortes, n=108).
- Fijación bicortical vs monocortical (2 RS, n=513; 1 ECA, n=76; 2 cohortes, n=78).
- Fijación híbrida vs monocortical/bicortical (2 cohortes, n=114; 1 ECA, n=76).

- Otros co-intervenciones como placas deslizantes (1 cohorte, n=23), minitornillos (1 cohorte, n=74), toxina botulínica A (1 cohorte, n=16) y PRF (1 ECA, n=44) no mostraron diferencias significativas.

En contraste, la comparación entre fijación rígida y con alambre mostró hallazgos heterogéneos:

- Sin diferencias (1 RS moderada, n=187; 1 ECA, n=127; 3 cohortes, n=92).
- Beneficiosos/probablemente beneficiosos (3 ECA, n=345; 4 cohortes, n=105).

Inconclusos (1 cohorte, n=54).

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Systematic mapping review of interventions to prevent blood loss, infection and relapse in orthognathic surgery

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Abstract

Background: This systematic mapping review aims to identify, describe, and organize the currently available evidence in systematic reviews (SR) and primary studies regarding orthognathic surgery (OS) co-interventions and surgical modalities, focusing on the outcomes blood loss, infection and relapse.

Material and Methods: A comprehensive search strategy was performed to identify all SRs, randomized controlled trials and observational studies that evaluate surgical modalities and perioperative co-interventions in OS that evaluate the outcomes blood loss, infection and relapse, regardless of language or publication date. Searches were conducted in MEDLINE, EMBASE, Epistemonikos, Lilacs, Web of Science, and CENTRAL. In addition, grey literature was screened.

Results: 27 SRs and 150 primary studies fulfilled the inclusion criteria, 91 from SRs, and 59 from our search strategy. Overall, the quality of the SRs was graded as "Critically low," and only two SRs were rated as "High" quality. 11 PICO questions were extracted from SRs and 31 from primary studies, which focused on osteosynthesis methods, surgical cutting devices, use of antibiotics, and induced hypotension. In addition, evidence bubble maps for each outcome were created to analyze in a visual manner the existing evidence.

Conclusions: Future primary and secondary high-quality research should be addressed focused on the eight knowledge gaps identified in this mapping review. We concluded that the evidence mapping approach is a practical methodology for organizing the current evidence and identifying knowledge gaps in OS, helping to reduce research waste and canalize future efforts in developing studies for unsolved questions.

Key words: *Orthognathic surgery, mapping review, le fort, blood loss, infection, relapse.*

Introduction

Orthognathic surgery (OS), is frequently used to treat dentofacial deformities that affect 20% of the population (1), restoring anatomic and functional relationships (2). According to the American Association of Oral and Maxillofacial Surgeons (AAOMS), conditions with an indication for orthognathic surgery include anteroposterior, vertical or transverse discrepancies, asymmetries, dysfunctions, temporomandibular joint disorders, speech impairments and airway dysfunctions. An increase in the frequency of OS performed each year has been shown, reaching a total of 8755 OSs performed in the United States in 2007 (3).

The production of scientific literature in the field of OS has increased significantly, however, resolved research questions and specific topics continue to produce a high flow of both primary and secondary research, meanwhile unresolved questions are not being addressed by researchers.

Although OS is considered a safe procedure, a variety of complications exists, which alter in accordance to different surgical modalities and perioperative co-interventions applied for the optimization of surgical results (1,2). Most include blood loss, infection and relapse (4-6). The reason for blood loss is the extensive vascularization of the maxillofacial region and access difficulty in terms of cauterization or ligation of the vessels involved (7). Regarding post operative infection, the proportion of patients developing surgical site infection after OS is estimated to be about 7%. It can cause localized pain, swelling, surface redness (erythema), pus formation and restricted movement (8). Moreover, relapse of the surgical movement has been associated with planning errors, intraoperative difficulties, anatomical variations, or limitations in the postoperative orthodontics (4). Though reported complications are limited, their occurance may suppose a risk for permanent deficiencies, need for reoperations, and impact the patient's quality of life.

To facilitate evidence-informed decision making by making evidence available and presenting it in an accessible format, and to guide future research on blood loss, infection and relapse in OS, it is crucial to identify and analyze all the available evidence regarding co-interventions and surgical modalities which have an effect on these complications. Thus, the emerging synthesis method of mapping reviews constitutes a valuable mechanism for this particular area (9,10). To our knowledge, this is the first evidence synthesis that scopes all the existing evidence regarding blood loss, infection and relapse in OS.

Evidence mapping provides an innovative, friendly and didactic approach that illustrates the existing evidence in extensive research areas (9,11), leading to systematic characterization of evidence, identification of knowledge gaps, and prioritization of new research questions (9-11). Therefore, it can be the first step to conduct future systematic reviews (SRs) or the framework to inform policy development (9-11). Moreover, it allows the identification of resolved research questions, avoiding unnecessary effort of researchers in developing primary studies or SRs in the subject.

This mapping aims to identify, describe, and organize the currently available evidence in SRs and primary studies regarding OS co-interventions and surgical modalities, focusing on the outcomes blood loss, infection and relapse. Moreover, it assesses the quality of the existing evidence present and its claimed effectiveness and unveiled all the clinical questions regarding this topic. This review facilitates the identification of research gaps, allowing for new studies to develop.

Material and Methods

This work is part of a broader mapping review of OS published elsewhere (12). It was drafted using the Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA)-Extension for Scoping Reviews. It adheres to the Global Evidence Mapping Initiative methods (GEM) (13), incorporating the quality of the supporting evidence. All methods are specified a priori in a published protocol (14).

- Mapping boundaries and context

To frame this mapping review, a preliminary search was performed and maxillofacial surgeons experts in OS were consulted, to establish eligibility criteria for study inclusion.

- Eligibility criteria

The population, intervention, comparison, and outcomes (PICO) framework was used to guide the eligibility criteria.

Studies: Included were SRs, as well as RCTs, prospective and retrospective observational studies (case-control and cohort studies). Only studies published as full texts and publications ahead of print were included. Excluded were narrative reviews, case series, case reports, qualitative and cross-sectional studies.

Population. Adult and adolescent participants (aged over 10 years) undergoing OS were included. Syndromic patients were excluded.

Interventions: Perioperative co-intereventions and different surgical modalities of OS were considered. Studies regarding distraction osteogenesis and those which focus relied on orthodontic procedures or surgical planning were excluded.

Comparators: Different approaches to performing OS, different co-interventions, and use of placebo or no treatment (control group) associated with co-interventions were included. Excluded were studies with no comparison group or studies in which the comparison group did not undergo OS.

Outcomes: Studies that assessed blood loss, infection and relapse were included.

- Literature search

A literature search was conducted from inception to March 2021 in the following databases: MEDLINE (via PubMed), EMBASE (via OVID), Epistemonikos, Lilacs, Web of Science, and CENTRAL. The search strategy, adapted for each database considering differences in controlled vocabulary and syntax rules, is available elsewhere (12). No date or language restrictions were applied. Unpublished SRs were also searched in the PROSPERO protocol registration platform. A snowball approach was used for screening reference lists to identify potentially eligible studies. Although the protocol stated that a search would be conducted in ClinicalTrials.gov to detect ongoing primary studies, due to the large quantity of studies identified, it was decided not to include articles from this platform, as the benefits would have been marginal given the extensive data already compiled.

- Data collection and analysis

Two independent reviewers performed a title/abstract screening for results obtained from the search, followed by a full-text screening, independently and in duplicate. Reasons for exclusion were recorded. Any disagreements were resolved by consensus or, if necessary, by a third author. As recommended in the Cochrane Handbook for Systematic Reviews of Interventions, the selection process was documented in sufficient detail to generate a PRISMA flowchart.

- Data extraction and management

Data was extracted and tabulated by one author, using a previously piloted data extraction form, and was double-checked by a content expert in the subject. The following information was extracted from each SR: search date, year of publication, country, objective, number of primary studies included, number of participants, population, co-interventions, comparisons, and outcomes measured. Research PICO questions of the SRs were also identified. For primary studies not included in any identified SRs, the following data were extracted: year of publication, study design, objective, number of patients included, population, interventions, comparisons, and outcomes. Author's conclusions were recorded and classified for descriptive purposes as "beneficial," "probably beneficial," "no differential effect," "harmful," or "inconclusive". Supplement 1 indicates the criteria that was used for this categorization.

- Methodological quality evaluation

Methodological quality was independently evaluated for all the included SRs by two authors. Disagreements were resolved by consensus, or if necessary, by a third author. The AMSTAR-2 instrument (15) was used to evaluate the included SRs, which critically appraises SRs in 16 domains. The overall rating was based on weaknesses in critical domains, namely, items 2, 3, 7, 9, 11, 13, and 15. Global confidence in SR results - used for the mapping diagrams - was rated in the following four quality categories: critically low (more than one critical flaw), low (one critical flaw), moderate (more than one non-critical flaw), and high (no flaw or one non-critical flaw). The included primary studies were not critically appraised since they were included to identify knowledge gaps rather than to inform clinical or policy decisions.

- Data synthesis and analysis

Results, summarized in tabular formats, describe the included study characteristics and all the identified PICO questions. An evidence matrix to link primary studies with their SRs was created using the Epistemonikos platform to identify primary studies not included in the SRs. Evidence bubble maps were also created.

Results

- Search results

8531 records were obtained. In the title/abstact phase, 5373 records were screened. Of the latter, 4476 records were excluded. 863 articles were assessed by full-text reading, resulting in 262 included articles. Reasons for exclusion at detailed in Fig. 1. Moreover, throughout hand-searching, 28 articles, 1 SR, and 27 primary studies were identified and included in the review. A total of 290 studies were included in the general mapping review. For this specific mapping review, 113 studies were excluded for not reporting on the three outcomes of interest (bloos loss, infection, relapse). Thus, a final total of 177 studies were included, 27 SRs and 150 primary studies (91 included and 59 not included in the SRs). Kappa value was 0.81, thus considered excellent agreement. A PRISMA flowchart details this process in Fig. 1.

- Study characteristics

A general description of the study characteristics, including design, aim, population, interventions, comparators, outcomes, and number of primary studies and participants is presented in Supplement 2.

- Study designs

Of the 177 included articles, 27 (27/177; 15.3%) referred to SRs and 150 (150/177; 84.7%) to primary studies. Of the latter, 91 (91/177; 51.4%) were studies included in the identified SRs. The remaining 59 (59/177; 33.3%), identified through the Covidence platform screening, were not included in the SRs. Their designs were as follows: prospective cohort (6/59; 10.2%), retrospective cohort (25/59; 42.4%), and RCT (28/59; 47.5%). Supplement 3 organizes included studies according to their design and outcome assessed.

- Participant characteristics

Age: Seven SRs (25.9%) included only adult populations, two (7.4%) included patients of all ages, and 18 (66.7%) did not mention age.

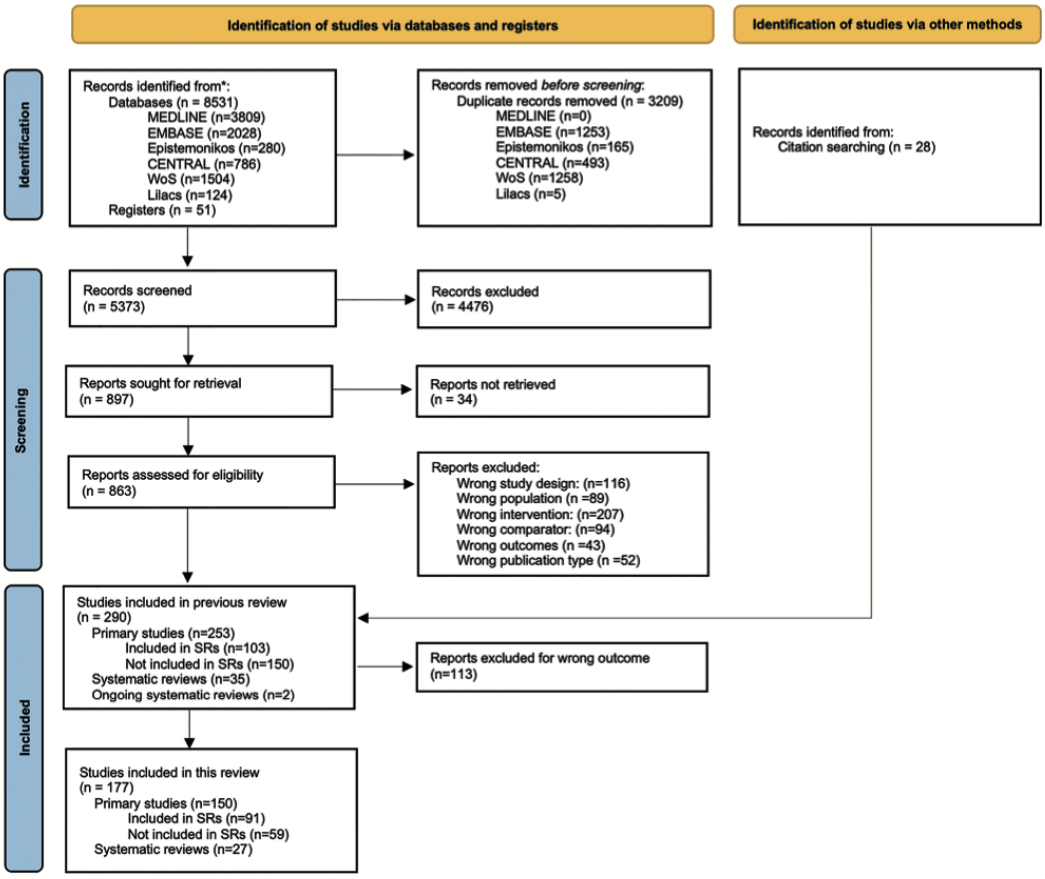


Fig. 1: PRISMA flow chart.

Regarding the age of participants in the 59 primary studies not included in SRs, 15 studies (25.4%) included adolescent and adult patients, 34 studies (57.6%) included only results for adults >16 years, one study (1.7%) included participants of all ages, and 9 studies (15.3%) did not specify age.

Deformity: The type of deformity of participants was recorded in a simplified manner, grouped as either skeletal class II (mandibular retrognathism, mandibular hypoplasia, maxillary prognathism, and maxillary hyperplasia) or class III (mandibular prognathism, mandibular hyperplasia, maxillary retrognathism, and maxillary hypoplasia). Facial asymmetries in participants was also documented. Of the 27 SRs, one (3.7%) included patients with skeletal class III diagnosis and one (3.7%) with skeletal class II, while the remaining 25 (92.6%) did not specify skeletal classes as inclusion or exclusion criteria. Of the 59 primary studies, 13 (22%) included patients with skeletal class III diagnoses (one with facial asymmetry), three (5.1%) included patients with skeletal class II and class III diagnoses, 13 (22%) included results for patients with skeletal class II diagnoses, and 30 (50.8%) did not specify deformity inclusion criteria.

OS type: As for the type of surgery performed, one of the 27 SRs (3.7%) included patients undergoing bimaxillary surgery, four (14.8%) undergoing mandibular surgery, one (3.7%) maxillary surgery, one (3.7%) genioplasty, and 20 (74.1%) did not specify the type of intervention. Of the 59 primary studies, 13 (22%) included patients undergoing bimaxillary OS, four (6.8%) bimaxillary and genioplasty, one (1.7%) genioplasty alone, one (1.7%) genioplasty and other orthognathic procedures, 17 (28.8%) mandibular surgery, nine (15.3%) maxillary surgery, 10 (16.9%) a combination of the procedures mentioned above and four (6.8%) did not specify a type of orthognathic procedure.

- Methodological quality assessment

Based on AMSTAR-2 scores, 16 SRs (16/27; 59.3%) were rated as "Critically low", four as "Low" (4/27; 14.8%), five as "Moderate" (5/27; 18.5%) and two were rated as "High" methodological quality (2/27; 7.4%) (see Supplement 4) The SRs were mainly downgraded as the authors did not state the development of a pre-existing protocol (16/27; 59.3%), nor did they explain their selection of study designs for inclusion in the review (18/27; 66.7%). Moreover, sources of funding of primary studies were not clearly stated (25/27; 92.6%), and the authors did not perform a study selection (12/27; 44.4%) and data extraction (12/27; 44.4%) in duplicate. The best-rated items were attributed to search strategy, description of included studies in adequate detail, and investigation for publication bias.

- PICO questions

11 PICO questions were retrieved from the SRs and 31 from the primary studies (Supplement 5, Supplement 6). For the SRs, the PICO questions were grouped according to the OS type: all types of surgery, mandibular surgery, maxillary surgery, or genioplasty. For practical matters regarding classification, primary study questions were grouped by intervention, leaving aside their population.

- Evidence matrix

The identified SRs were linked with their included primary studies which fulfilled our selection criteria, to create an evidence matrix with the platform Epistemonikos. It is worth mentioning that one SR was not included in the matrix, as it was an update to an already included Cochrane review. Furthermore, one SR could not be added because of technical issues of the platform. The complete matrix is available in the following link: http://www.epistemonikos.org/matrixes/61f044727db23a0765984cfb

- Evidence bubble maps

Evidence bubble maps were created per outcome to graphically depict the available evidence (Fig. 2, Fig. 3, Fig. 4).

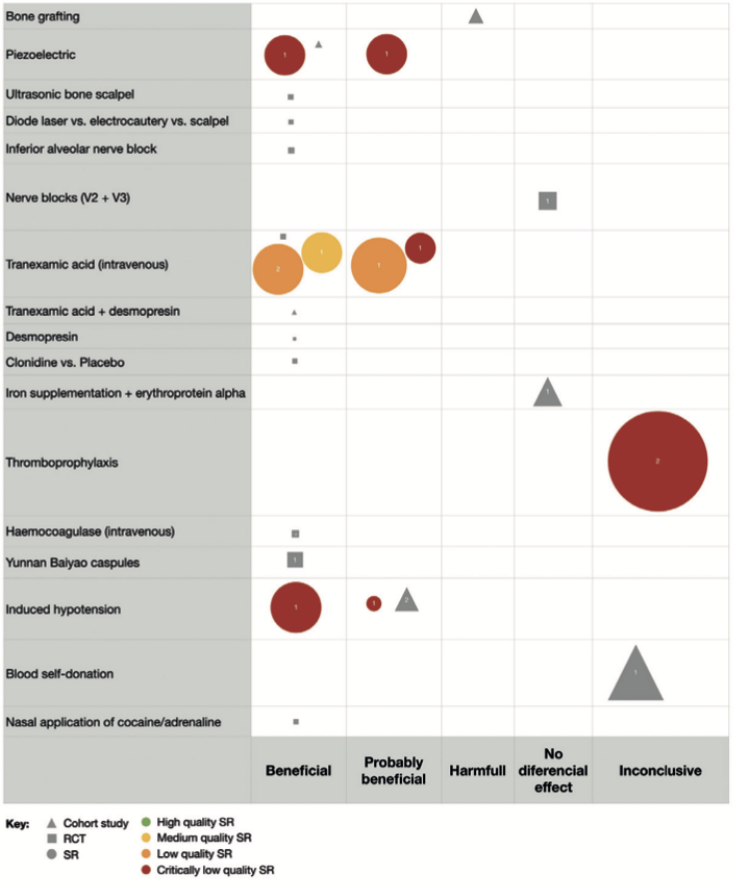


Fig. 2: Bubble map for blood loss in OS.

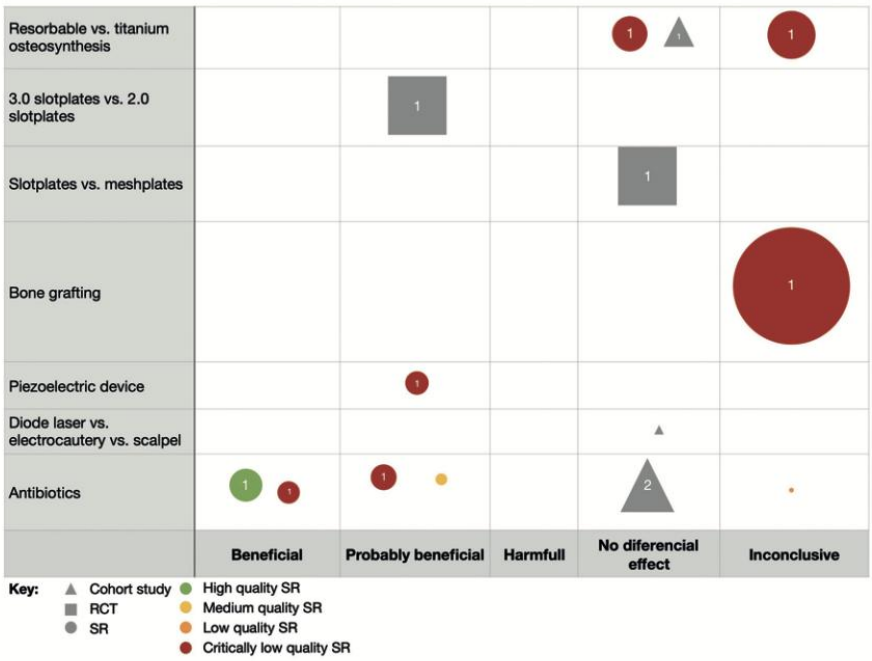


Fig. 3: Bubble map for infection in OS.

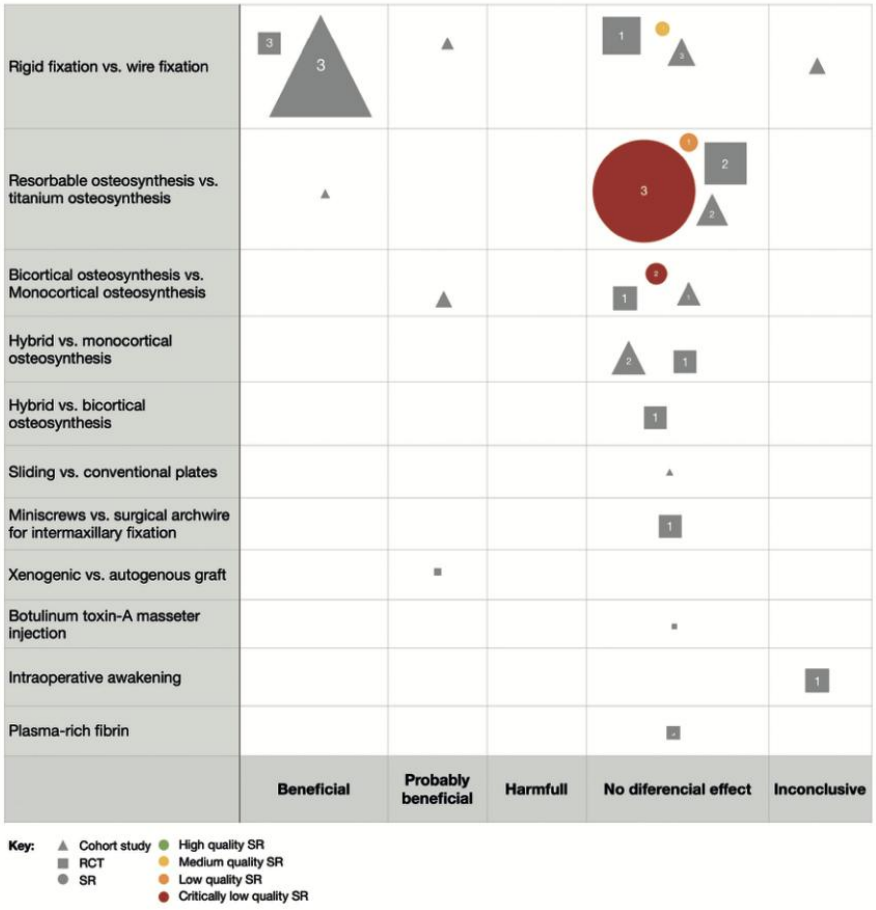


Fig. 4: Bubble map for relapse in OS.

All interventions reviewed in the included studies are listed in rows, and the direction of the results are listed in columns. Symbols indicate the study design (circles for SRs, squares for RCTs, and triangles for observational studies), and bubble size represents the number of primary studies included in the SRs or the number of participants included in the primary studies. A number positioned over each bubble indicates the number of studies. Colors indicate confidence in SR findings (based on the AMSTAR-2 evaluation). The primary studies included in the maps are those not included in any of the identified SRs.

- Blood loss

The outcome blood loss was evaluated by 11 SRs (11/35; 31.4%) and reported by 27 primary studies (27/150; 18%), 16 RCTs (16/150; 10.70%), seven retrospective cohort (7/150, 4.7%) and three prospective cohort (3/150; 2%) (Fig. 2).

Co-interventions which demonstrated a beneficial/probably beneficial effect consisted in IV administration of tranexamic acid (five SR of medium, low and critically low quality, n=1621; one RCT, n=36), induced hypotension (two low quality SR, n=560; two cohort studies, n=150), nasal application of cocaine/adrenaline (one RCT, n=30), administration of Yunnan Baiyao capsules (one RCT, n=95), IV haemocoagulase (one RCT, n=46) and clonidine (one RCT, n=30). On the other hand, the surgical modalities that showed a beneficial/probably beneficial reduction in blood loss were the use of a piezoelectric device (two critically low-quality SRs, n=1680; one cohort study, n=44), ultrasonic bone scalpel (one RCT, n=34), the use of diode laser compared to electrocautery and scalpel (one RCT, n=30), and blockage of inferior alveolar nerve with local anesthesia (one RCT, n=38). Only one observational study assessed blood loss in bone grafting, and concluded its use increased blood loss. Moreover, nerve blocks were performed in the maxillary and mandibular ramus of the trigeminal nerve (one observational study, n=110), and iron plus erythropoietin alpha supplementation (one RCT, n=178) were considered as having no differential effect on blood loss. Inconclusive results were reported for the administration of thromboprophylaxis (two SR of critically low quality, n=9707) and preoperative blood self-donation 7 days before surgery (one observational study, n=345). Note that studies that compared different anesthetic regimens were grouped in the co-interventions bubble map, as analysis of this issue was beyond the scope of this mapping review.

- Infection

Postoperative infection was assessed by nine SRs (9/35; 25.7%) and seven primary studies (7/150; 4.7%) not included in the mentioned SRs: four RCTs (4/150; 2.7%), one prospective cohort (1/150; 0.7%) and three retrospective cohort (3/150; 2%) (Fig. 3).

The use of piezoelectric, compared to conventional rotatory devices, demonstrated a beneficial/probably beneficial effect on infection (one critically low SR, n=996). Regarding fixation method, the use of Slotplates 3.0 compared to Slotplates 2.0 (one RCT, n=186) showed a beneficial effect on infection. However, Slotplates compared to Meshplates as a fixation method showed no differential effect in a cohort study of 190 participants. Furthermore, studies evaluating resorbable osteosynthesis compared to titanium osteosynthesis acquired the same conclusion (one critically low-quality SR, n=1384, one RCT, n=101), whereas other SR from the same authors showed inconclusive results (n=1092). Finally, studies reporting infection for the use of antibiotics in the perioperative surgical period had heterogeneous conclusions, from beneficial/probably beneficial (one high quality SR, n=788; two critically low-quality SR, n=698; one medium quality SR, n=452), no differential effect (two cohort studies, n=178) to inconclusive (one low quality SR, n=132).

- Relapse

Nine SRs (9/35; 25.7%) assessed the outcome relapse, as well as four prospective (4/150; 2.7%), 14 retrospective cohort studies (14/150; 9.3) and 10 RCTs (10/150; 6.7) (Fig. 4).

The majority of the studies concluded that co-interventions and surgical modalities had no differential effect on relapse. This was the case for resorbable compared to titanium osteosynthesis (three critically low quality SRs, n=3823; one low quality SR, n=420, one moderate quality SR, n=120, two RCTs, n=141, two cohort, n=108, one ongoing SR), bicortical compared to monocortical osteosynthesis (two critically low quality SRs, n=513; one RCT, n=76; two cohort, n=78), hybrid compared to monocortical osteosynthesis (two cohort, n=114; one RCT, n=76) and to bicortical osteosynthesis (one RCT, n=76), sliding plates (one cohort, n=23), miniscrews (one cohort, n=74), injection of Botulinum toxin-A into the masseter muscle (one cohort, n=16) and the use of platelet-rich fibrin (one RCT, n=44). Heterogeneous conclusions were observed in rigid compared to the wire fixation method. A recent SR of moderate quality (n=187) and primary studies (one RCT, n=127; three cohort, n=92) concluded no differential effect on the use of rigid fixation on relapse. Nevertheless, other primary studies of considerable population size, reported beneficial/probably beneficial (three RCT, n=345; four cohort, n=105) and inconclusive findings (one cohort, n=54).

- Research gaps

Supplement 7 lists eight identified research gaps that remain unanswered by evidence synthesis, either because they were identified in primary studies and not in SRs, or because of the low or critically low quality of the existing evidence.

Discussion

This review aimed to identify, describe, and organize currently available evidence in SRs and primary studies regarding OS co-interventions, surgical modalities, focusing on the outcomes blood loss, infection and relapse. We therefore performed a systematic mapping review, a relatively new methodological approach focused on the identification of knowledge gaps, prioritization of future research needs in broad fields and displaying the obtained results in a user-friendly format (9). Our mapping review was based on 27 published SRs that included 91 individual studies, and an additional 59 primary studies that were not included in the identified SRs.

Methodological quality assessment using the AMSTAR-2 tool classified most of the SRs as critically low quality (16/27; 59.3%), and only identified two SRs as high quality. Domains that should be improved in future reviews are primarily: [1] development of an a-priori protocol to state that the methods were established previous to the conduct of the SR; [2] an explanation of the selection of study designs for inclusion in the review; [3] reporting the funding sources of primary studies and [4] performing the study selection and data extraction in duplicate. Although quality assessment is not a requirement of mapping reviews, we considered it an advantage in the terms of drawing more accurate conclusions.

Blood loss: Most of the assessed interventions were found to be beneficial for blood loss. For instance, intravenous administration of tranexamic acid has been widely investigated and found favorable for this outcome. Due to the presence of a medium-quality SR and the fact that beneficial conclusions were drawn from all studies, no future efforts should be addressed at answering this question.

Alternatively, even though the use of piezoelectric devices and induced hypotension have also shown beneficial results in SRs with large number of studies, high-quality SRs should be developed to confirm these statements. Unfortunately, no recent RCTs have been developed on these topics. Moreover, the effect on blood loss in interventions such as administration of Yunnan Baiyao capsules, haemocoagulase, nasal application of cocaine, and inferior alveolar nerve blocks should be addressed in future primary studies, as the existing data shows beneficial results on this outcome.

Infection: The outcome of postoperative infection was assessed in fewer interventions. The use of piezoelectric device appears to be probably beneficial for preventing infection, although assessed by a critically low-quality SR (16). No new primary studies have been developed on this topic.

High variability was found in the conclusions of SRs which evaluated the use of antibiotics in OS, ranging from beneficial, probably beneficial, inconclusive, to no differential effect. This phenomenon might be explained because of the high heterogeneity of primary studies, which compare different antibiotics and regimens. Moreover, Brignardello-Petersen *et al.* (8), the only SR evaluating perioperative antibiotics with a high methodological quality, reported moderate and low confidence in their results, mainly because of unclear risk of bias in allocation concealment and blinding phases of the included RCTs. Thus, future research should focus on high-quality RCTs to determine the real effect of perioperative antibiotics in OS.

Relapse: Different osteosynthesis methods, such as resorbable compared to titanium and bicortical compared to monocortical fixation, did not seem to have a differential effect on postoperative relapse. Only one study for resorbable (n=30) and one for bicortical osteosynthesis (n=50) reported beneficial and probably beneficial results, respectively. Nevertheless, these correspond to cohort designs with a low number of patients. For rigid versus wire fixation, contradictory results were found. One SR reported no differential effect of both techniques (17), whereas three RCTs (18-20) and four cohort (21-24) refer a beneficial or probable beneficial effect for relapse. It is worth mentioning that the SR only included patients undergoing genioplasty procedures. Therefore, this mapping suggests that future evidence synthesis should be carried out on the effect of rigid compared to wire fixation in orthognathic patients undergoing mandibular, maxillary, or bimaxillary procedures. Nevertheless, as wire fixation requires a period of maxillomandibular fixation, over the past years its use has been widely replaced for rigid fixation regarding practical reasons. Hence, addressing this research gap is not a priority. Moreover, the effects of hybrid fixation (use of bicortical and monocortical screws) on relapse have only been reported by two cohort (25,26) and one RCT (27). No SRs have been carried out on this topic due to the low number of primary studies. Yet, no superior efficacy has been shown.

To our knowledge, this is the first mapping review performed for blood loss, infection and relapse in OS. However, a broader mapping review aimed at identifying knowledge gaps within the field of oral and maxillofacial surgery, was published in 2017 (28). This mapping included SRs from several domains, including reconstructive surgery, surgical tooth removals, tumors, orofacial infections, maxillofacial and dental trauma, OS, among others. Of the nine SRs included in the mentioned mapping, two were also present in our review (29,30). The seven excluded SRs did not fulfill our selection criteria: reports on orthopedic surgery (31), orthodontic SR, no control group (32,33), postoperative treatment for nerve injuries (34) and wrong outcomes (35-37). Additionally, no graphical representation of their results was illustrated. The information obtained

from our evidence maps enabled us to identify several OS research gaps (summarized in Supplement 7) that should help direct future secondary research efforts in resolving unresolved questions regarding OS.

- Strengths

We highlight the sensitive search strategy implemented without language or date restrictions. Thus, relevant studies were unlikely missed. Furthermore, the evidence matrix allowed us to identify primary studies that responded to our inclusion criteria but were not included in the identified SRs. Therefore, knowledge gaps in topics covered by primary studies without a synthesis of the results performed by a SR were identified. Moreover, selection process and quality assessment were performed independently and in duplicate. Likewise, extraction data was checked by a content expert in the subject, thus, there is confidence in the results. In addition, to organize the obtained information, we used the PICO format to arrange the results, ensuring a simplified yet thorough approach of displaying the evidence on procedures and co-interventions in OS. Even though the evidence mapping methodology does not include a quality assessment of SRs (10), we performed this analysis. This advantage will enable the identification of topics in which new high-quality SRs should be performed to answer clinical questions. Moreover, it will help stakeholders to identify the quality of evidence on which clinical decisions are based. Finally, the graphical display developed for this review provides a user-friendly, visual approach to identify all the existing evidence of this topic and its quality.

- Limitations

First, conference abstracts and primary studies registries were not included in this mapping due to the extended volume of studies found. Nevertheless, we are confident that their incorporation would have not substantially modified the obtained results due to the large quantity of information compiled. Also, the imminent risk of a possible publication bias is present, which would have limited the inclusion of studies that were not published because of their non-favorable results. Finally, this methodology only organizes and describes evidence as reported by the original authors of studies, describing results as beneficial even if they are based on low-quality evidence. Therefore, this is not an appropriate tool for healthcare clinical decision-making.

Conclusions

This evidence map was developed on SRs, RCTs, and observational studies, which assessed blood loss, infection and relapse in OS. 11 PICOs were identified in the SRs and 31 from primary studies, which primarily addressed the effects of fixation methods, surgical cutting devices, antibiotics, and induced hypotension. The methodological quality of most included SRs in this mapping review was rated as "Critically low." Moreover, bubble maps allowed the identification of eight research gaps, including: to evaluate the effect of thromboprophylaxis and the efficacy of piezoelectric in blood loss, to compare the efficacy of resorbable vs. titanium fixation in infection, to assess the use of bone graftings in infection, to compare the use of rigid vs. wire fixation and bicortical vs. monocortical osteosynthesis in relapse, and to assess the efficacy of hybrid fixation in relapse in patients undergoing orthognathic surgery. This research gaps should be addressed in future high-quality research, both primary and secondary.

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Conflict of interest
There are no conflicts of interest.

Ethics
As researchers will not access information that could lead to identifying an individual participant, obtaining ethical approval was waived.

Authors contributions
JB: Conceptualization, Methodology, Validation, Investigation, Data curation, Writing - Original Draft, Writing - Review and Editing, Visualization, Supervision, Project administration; MU: Investigation, Data curation, Writing - Review and Editing; MB: Investigation, Data curation, Writing - Review and Editing; JPV: Investigation, Data curation, Writing - Review and Editing; EV: Data curation, Writing - Review and Editing; IA: Data curation, Writing - Review and Editing JV: Validation, Resources Investigation, Writing - Review and Editing, Supervision GU: Validation, Resources, Investigation, Writing - Review and Editing, Supervision; XB: Validation, Resources, Writing - Review and Editing, Supervision.
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5.3 RESULTADOS DEL TERCER ESTUDIO

Bendersky, J., Zapata, S., Uribe, M., Villanueva, J., Bonfill, X., & Souper, R. (2025). Evidence gaps in orthognathic surgery: an international Delphi study. International journal of oral and maxillofacial surgery, 54(5), 430–437. https://doi.org/10.1016/j.ijom.2024.11.001

Factor de impacto: 2.7

5.3.1 CARACTERÍSTICAS DE LOS PARTICIPANTES

En la primera ronda participaron 74 cirujanos maxilofaciales de 17 países y 4 continentes. La media de experiencia profesional fue de 13,4 años (rango: 1–43). En cuanto al ámbito laboral: 35/74 (47%) trabajaban en universidades, 27/74 (36%) en hospitales, 10/74 (14%) en práctica privada y 2/74 (3%) en otros lugares.

La segunda ronda fue completada por 55 cirujanos, lo que representó una tasa de retención del 74%.

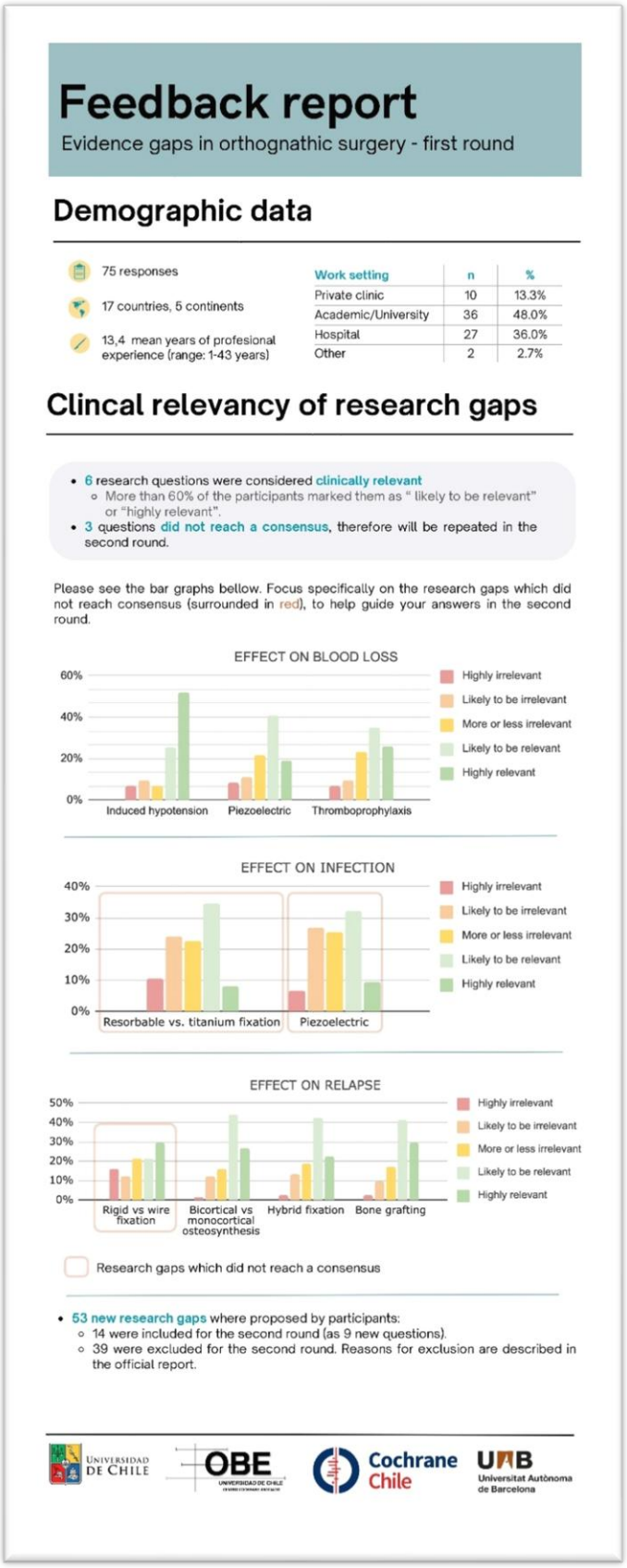
5.3.2 PRIMERA RONDA

En la primera ronda, 6 de las 9 preguntas iniciales fueron consideradas clínicamente relevantes (≥60% de acuerdo). Para todas las preguntas, los puntajes oscilaron entre 1 (“altamente irrelevante”) y 5 (“altamente relevante”).

Además, los participantes propusieron 55 nuevos vacíos de evidencia, de los cuales 11 (20%) fueron aceptados tras aplicar los criterios de inclusión, mientras que 44 (80%) fueron excluidos (27% por no evaluar intervenciones, 16% por referirse a planificación, 16% repetidos, 14% sólo resultados, 9% ya resueltos, 5% población sindrómica, entre otras razones).

Al finalizar la primera ronda, para aumentar la transparencia, se distribuyó un informe de retroalimentación a los participantes con los resultados de la primera ronda (Figura 8).

Figura 8. Informe gráfico de los resultados de la primera ronda del Delphi distribuido a los participantes



Feedback report

Evidence gaps in orthognathic surgery - first round

Demographic data

75 responses

17 countries, 5 continents

13,4 mean years of profesional experience (range: 1-43 years)

Work setting	n	%
Private clinic	10	13.3%
Academic/University	36	48.0%
Hospital	27	36.0%
Other	2	2.7%

Clincal relevancy of research gaps

- 6 research questions were considered clinically relevant
  - More than 60% of the participants marked them as " likely to be relevant" or "highly relevant".
- 3 questions did not reach a consensus, therefore will be repeated in the second round.

Please see the bar graphs bellow. Focus specifically on the research gaps which did not reach consensus (surrounded in red), to help guide your answers in the second round.

EFFECT ON BLOOD LOSS

EFFECT ON INFECTION

EFFECT ON RELAPSE

Research gaps which did not reach a consensus

- 53 new research gaps where proposed by participants:
  - 14 were included for the second round (as 9 new questions).
  - 39 were excluded for the second round. Reasons for exclusion are described in the official report.

5.3.3 SEGUNDA RONDA

De los 11 nuevos gaps, 9 (82%) fueron considerados clínicamente relevantes.

Se alcanzó un listado final de 15 vacíos de evidencia clínicamente relevantes, distribuidas según desenlace: 7 (47%) relacionados con recidiva, 6 (40%) con pérdida sanguínea, y 2 (13%) con infección.

Los ítems con mayor relevancia clínica fueron:

1. Número de placas de osteosíntesis en la recidiva (media 4,20; DE 0,96).
2. Eficacia del ácido tranexámico en la inducción anestésica para reducir sangrado (media 4,18; DE 0,81).
3. Eficacia de la hipotensión inducida en la pérdida sanguínea (media 4,05; DE 1,26).

Otros vacíos de evidencia destacados incluyeron infiltración anestésica previa (media 3,95), desprogramación muscular (media 3,95), fijación intermaxilar postoperatoria con elásticos (media 3,93), cirugía mínimamente invasiva en infección (media 3,91), e injertos óseos en recidiva (media 3,85).

5.3.4 FIABILIDAD DE LAS RESPUESTAS

El análisis de correlación intraclase mostró “acuerdo casi perfecto” en ambas rondas:

- Primera ronda: kappa = 0,77 (IC95% 0,66–0,83; $p < 0,05$).
- Segunda ronda: kappa = 0,86 (IC95% 0,81–0,91; $p < 0,05$).

Para las preguntas repetidas (por bajo consenso en ronda 1), el acuerdo fue más bajo:

- Reabsorbible vs titanio en infección: kappa = 0,43 ($p = 0,023$).
- Fijación rígida vs alambre en recidiva: kappa = 0,50 ($p = 0,012$).
- Piezoeléctrico en infección: kappa = 0,30 ($p = 0,10$, no significativo).

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Research Paper
Orthognathic Surgery

Evidence gaps in orthognathic surgery: an international Delphi study

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Abstract. The aim of this study was to assess the evidence gaps identified in a recent mapping review of orthognathic surgery by evaluating them through consultation with maxillofacial surgeons. Using the Delphi technique, a panel of surgeons who regularly perform orthognathic surgery was engaged. Potential participants were identified through articles included in the mapping review, peer nominations, and social media platforms . Two rounds of surveys, incorporating Likert-type and open-ended questions, were conducted to gauge the clinical relevance of evidence gaps. Questions were refined based on responses from the initial round, with a consensus threshold set at 60%. Seventy-four surgeons participated in the first round and 55 in the second round (retention rate of 74%) . The intra-class correlation analysis revealed 'almost perfect' agreement in each round. Participants in the first round proposed 11 new evidence gaps. A list of 15 potentially clinically relevant research questions was compiled to guide future investigations in orthognathic surgery. This collaborative Delphi study between researchers and clinicians has explored the existing understanding of the clinical relevance of potential evidence gaps in orthognathic surgery. The study findings offer others a pathway to address information gaps and guide future research endeavours.

Keywords: Delphi technique; Orthognathic surgery; Evidence gaps; Oral and maxillofacial surgeons; Surveys and questionnaires.

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Orthognathic surgery is frequently used to treat dentofacial deformities such as skeletal discrepancies, asymmetry, airway dysfunction, speech impairments, and temporomandibular joint disorders[1,2], which affect approximately 20% of the population, with the aim of restoring anatomical and functional relationships[3]. An increase in the frequency of orthognathic surgery performed each year has been observed, with 8755 surgeries performed in the United States in 2007, over 2230 procedures performed in England in 2014[4], and 1000 in Denmark in 2015[5] . This has concomitantly led to an increase in the scientific literature on the subject . However, a high flow of primary and secondary research continues to be produced on certain resolved research questions and specific topics. Meanwhile, there is a need for researchers to address unresolved questions .

While orthognathic surgery is generally considered a safe procedure, a diverse array of complications exist, and their incidence varies depending on the specific surgical modalities employed and

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perioperative co-interventions applied to optimize surgical outcomes[1,3,6]. Common complications include issues such as blood loss, infection, and relapse[6–8]. The significant vascularity of the maxillofacial region contributes to blood loss during orthognathic surgery, which is exacerbated by challenges in cauterizing or ligating the vessels involved[9]. Postoperative infections, which are estimated to occur in approximately 7% of cases, manifest with symptoms such as localized pain, swelling, erythema, pus formation, and restricted movement[10]. The relapse of surgical corrections is associated with factors such as planning errors, intraoperative challenges, anatomical variations, or limitations in postoperative orthodontic management[6]. While the reported incidence of complications is relatively low, their occurrence poses potential risks of permanent deficiencies, necessitating reoperations and impacting the patient's overall quality of life.

A recent mapping review that identified, described, and analysed the available evidence on co-interventions and procedures in orthognathic surgery revealed evidence gaps that need to be addressed to improve the outcomes of blood loss, infection, and relapse[11,12]. Yet, these knowledge gaps only portray what is available in the published literature; they do not consider the views of clinicians who perform the procedures daily.

The aim of this exploratory Delphi study was to assess and compare the results provided in the mapping review through their appraisal by maxillofacial surgeons. It was considered that complementing the available literature with a clinical appraisal would reveal a list of potential evidence gaps that could help guide future investigations in orthognathic surgery .

Materials and methods

All methods have been specified a priori in a protocol published in a peer-reviewed journal[13].

This study used the Delphi technique. The study design was chosen to assess the results of a mapping review of orthognathic surgery through a collaborative approach by maxillofacial surgeons, consequently identifying potentially essential evidence gaps in the literature and guiding future investigations.

A research steering group was formed to undertake this research. This group was responsible for preparing and circulating the content of the Delphi rounds. The group comprised investigators with backgrounds in general dentistry, oral surgery, maxillofacial surgery, and research methodology. The research steering group did not participate in the surveys; they only supervised and monitored the process.

Selection and identification of participants

Participants selected for this study were maxillofacial surgeons who regularly perform orthognathic surgery daily. They were recruited through the following methods: (1) extraction of contact information: the contact information of corresponding authors was obtained from articles included in the mapping review; (2) peer nomination: identified peers nominated other potential participants; and (3) social media: LinkedIn was used to reach out to suitable candidates.

Participants were excluded if they (1) had less than 1 year of experience in the field; (2) had not performed orthognathic surgery for more than 1 year; or (3) could not commit to being available for the entire study process. No restriction was placed on age, country, or gender for participation in this study.

Identified individuals were sent a personalized invitation letter via email. This email included a user-friendly information poster and the study protocol. The invitation provided detailed information on the study objectives, design, and required commitment. Participants were provided with a clear explanation of the anticipated process and were asked to commit to all rounds of the Delphi technique. The invitation also contained a link to the study survey, which included questions regarding the inclusion criteria and had a section to nominate peers. The same invitation email was sent to those nominated peers. After receiving all responses, only surveys from participants who met the inclusion criteria were considered for analysis. Fig. 1 shows details of the recruitment process.

A minimum requirement of 20 participants was established, with no upper limit, as larger panels increase the reliability of the outcomes[14,15]. Following the iterative nature of the Delphi technique, this process was performed anonymously[16].

Design, content, and development of the survey

The survey consisted of 5-point Likert scales and open-ended questions regarding evidence gaps identified in a previous study. The questionnaires were developed in Google Forms. Each round of the survey included an introductory paragraph that stated the intentions of the round. The second round provided details and feedback concerning the results of the first round.

Questions were developed by the principal investigator (J.B.) based on the evidence gaps identified in a previous study[11,12]. Subsequently, they were piloted by the research steering group and adapted according to the feedback received. A 60% consensus was chosen for the results to be considered valid, following the suggestion of some authors[17–19]. Several methods were used to enhance the response rate. Initially, participants were invited to participate via personalized email, explaining the objectives and importance of the study. They were presented with the survey in the same email to decrease drop-outs. Reminders were emailed to participants who did not answer the survey, at a frequency of 7 days. Participants were also offered a participation certificate and their acknowledgment in future publications with Delphi results if they participated in both rounds.

Rounds

Recent evidence shows that the preferred number of rounds is either two or three[18,20,21]. In this study, two rounds were undertaken, allowing participants to receive feedback and revise previous responses, reducing the number of attritions. Results were not considered valid if consensus was below 60% for a specific question.

The round 1 questionnaire consisted of 5-point Likert scale questions, where participants selected the clinical relevance of the identified evidence gaps in orthognathic surgery. These evidence gaps were extracted from a previous mapping review[12] and were categorized according to the outcome: blood loss, infection, or relapse. Also, a final open-ended question asked participants to point out any evidence gap not mentioned in the previous questions.

After the first round, to enhance transparency, feedback reports were distributed to the participants, which included (1) the

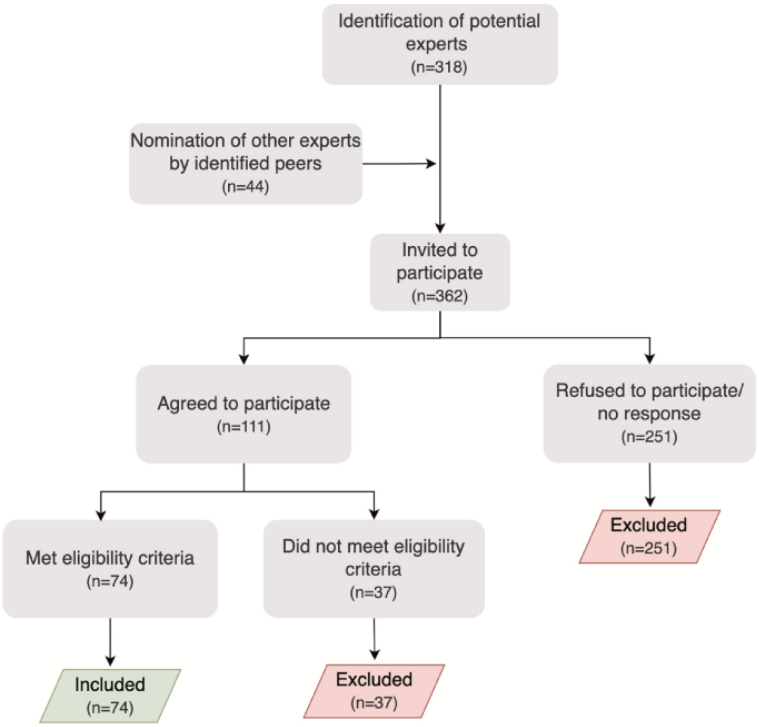


Fig. 1. Recruitment process.

mean and standard deviation (SD) score for each item, (2) the number of responses in the previous round, (3) the current level of consensus, and (4) a summary of the results from the previous round. These results were presented in a narrated and graphical manner.

For the second round, past questions were modified depending on the answers obtained. Questions with low clinical relevance and high agreement between participants (above 60%) were eliminated for the second round. Questions with low agreement (below 60%) were repeated for the second round. Evidence gaps proposed by participants in the previous rounds that fulfilled the inclusion criteria (Table 1) were added as new questions, or previous questions were modified.

Questions defined as relevant, which included the categories 'question is likely to be relevant' and 'question is highly relevant', with a consensus between participants of 60% or higher, were listed as evidence gaps that should be addressed in future research.

Statistical analysis

A descriptive statistical analysis was performed after each round. First, mean and SD values, the range, and numbers and percentages were obtained for the following variables: years of experience in the field, work setting, and country . Histograms were developed for each question in each round, showing the category frequencies. Moreover, the mean and SD were calculated for each question using Jamovi software[22], which converted the Likert scale as a continuous variable. Intra-class correlation coefficients were computed to assess the level of agreement within the subject and between participants.

Results

Participant characteristics

For the first round of the study, 74 participants from 17 countries and four continents agreed to be part of the Delphi process; 55 of these participants (74%) completed both rounds. The mean years of professional experience in orthognathic surgery of the participants was 13.4 years (range 1–43 years). Most worked in an academic setting (35/74, 47%), followed by a hospital (27/74, 36%), private clinic (10/74, 14%), and other (2/75, 3%). The participant characteristics are presented in Table 2.

First round

Seventy-four responses were collected in round 1. Six out of nine research questions were considered clinically relevant, as more than 60% of the participants marked them as 'question is likely to be relevant' or 'question is highly relevant'. A consensus was not reached for three questions and these were repeated in the second round . For all questions, the minimum score recorded was 1 ('question is highly irrelevant'), while the maximum score attained was 5 ('question is highly relevant'). Results are detailed in Fig. 2.

Evidence gaps proposed by the participants

A total of 55 knowledge gaps were proposed by 41 participants in round 1; of these, 11 (20%) were included according to the inclusion and exclusion criteria, while 44 (80%) were excluded. Reasons for exclusion were as follows: no co-interventions or surgical modalities evaluated (12/44, 27%), regarding planning (7/44, 16%), repeated (7/44, 16%), only outcome presented (6/44, 14%), resolved gap (4/44, 9%), syndromic population (2/44, 5%), wrong outcome (2/44, 5%), wrong population (2/44, 5%), regarding orthodontic treatment (1/44, 2%), commentary (1/44, 2%) (Supplementary Material Table S1).

Second round

The retention rate was 74% (55/74 participants). A final consensus was not reached for any of the questions repeated from the first round . Nine of the 11 new evidence gaps presented by participants were considered clinically relevant (82%) (Fig. 3). In all questions in the second round, the minimum score recorded was 1 ('question is highly irrelevant') and the maximum score was 5 ('question is highly relevant'). However, regarding the clinical relevance of the effect of tranexamic acid on blood loss, the minimum score obtained was 2 ('question is likely to be irrelevant').

A final list of 15 clinically relevant evidence gaps to address blood loss, infection, and relapse in orthognathic surgery was achieved (Table 3). The primary outcome addressed was relapse (47%, 7/15), followed by blood loss (40%, 6/15) and infection (13%, 2/15). Knowledge gaps achieving the highest scores for clinical relevance were (1) the

Table 1. Selection criteria for evidence gaps proposed by participants.

Inclusion criteria	Exclusion criteria
Evidence gap regarding co-interventions or surgical modalities used during the perioperative period in the adolescent or adult orthognathic surgery population	Evidence gap regarding surgical planning or quality of life Evidence gap regarding syndromic patients Evidence gap regarding economic outcomes

Table 2. Participant characteristics.

Variable		First round ($n = 74$)	All rounds ($n = 55$)
Work setting	Academic/university	35 (47%)	23 (42%)
	Hospital	27 (36%)	26 (47%)
	Private practice	10 (14%)	6 (11%)
	Other	2 (3%)	0 (0%)
Continent	Asia	6 (8%)	3 (5%)
	Europe	15 (20%)	9 (16%)
	South America	50 (68%)	41 (75%)
	North America	3 (4%)	2 (4%)
Years of professional practice	1–5	16 (22%)	12 (22%)
	6–10	20 (27%)	14 (25%)
	11–15	15 (20%)	11 (20%)
	16–20	8 (11%)	6 (11%)
	21–25	8 (11%)	7 (13%)
	26–30	5 (7%)	3 (5%)
	> 30	2 (3%)	2 (4%)

effect of the number of osteosynthesis plates on relapse (mean score 4.20, SD 0.96), (2) the efficacy of tranexamic acid in anaesthetic induction for blood loss (mean score 4.18, SD 0.81), and (3) the efficacy of induced hypotension in blood loss (mean score 4.05, SD 1.26). A flow diagram was developed to illustrate the results of the process (Supplementary Material Fig. S1).

Intra-class correlation

For the first round, the intra-class correlation coefficient was computed to assess agreement between the 74 maxillofacial surgeons in answering nine questions related to orthognathic surgery. According to the interpretation as described by Landis and Koch[23], there was 'almost perfect' agreement among the 74 surgeons using the two-way random-effects model and single rater unit: kappa = 0.77 (95% CI 0.66–0.83), $P < 0.05$. For the second round, 55 responses were analysed. There was also 'almost perfect' agreement between the 55 surgeons, using the two-way random-effects model and single rater unit: kappa = 0.86 (95% CI 0.81–0.91), $P < 0.05$.

The intra-class correlation was further analysed for the questions with low agreement in the first round that were repeated in the second round. The results showed a moderate agreement on the clinical relevance of the efficacy of resorbable vs titanium fixation on infection (kappa = 0.43, $P = 0.023$), as well as for the use of rigid vs wire fixation on relapse (kappa = 0.50, $P = 0.012$). Additionally, there was a fair agreement on the clinical relevance of the efficacy of piezoelectric devices on infection, although this was not statistically significant (kappa = 0.30, $P = 0.10$) (Table 4) .

Discussion

The aim of this exploratory study was to evaluate evidence gaps in orthognathic surgery identified in a recent mapping review[5,6] through evaluation by maxillofacial surgeons, leading to a potentially clinically relevant list of evidence gaps. Using the Delphi technique, 74 surgeons identified 15 potentially clinically relevant evidence gaps to address blood loss, infection, and relapse in orthognathic surgery.

Intra-class correlation was evaluated throughout the study. An 'almost perfect' agreement was observed in each round, demonstrating consistency in results across all participants. Furthermore, three evidence gaps for which consensus on their clinical relevance was not reached in the first round were included in the second round. The intra-class correlation for these questions, comparing both rounds, indicated moderate to fair agreement. Even though participants' answers to these questions varied from round 1 to round 2, their mean clinical relevance was not ranked as high.

This study is novel in exploring the clinical relevance of identified evidence gaps in orthognathic surgery through examination by maxillofacial surgeons. This Delphi study suggests a potentially clinically relevant list of evidence gaps to be addressed in future research in the participating countries. Moreover, the results suggest future research directed mainly towards obtaining stable results over time (relapse 47%) and haemostatic control of the patients (blood loss 40%), given the degree of agreement among the participants. This reflects the importance that surgeons attribute to aspects directly related to the perioperative patient experience, constantly searching for alternatives that will improve results and reduce the need for new interventions to achieve the stated objectives.

The impact of new techniques on the outcome of infection, such as minimally invasive orthognathic surgery and the concomitant use of multilayer sutures,

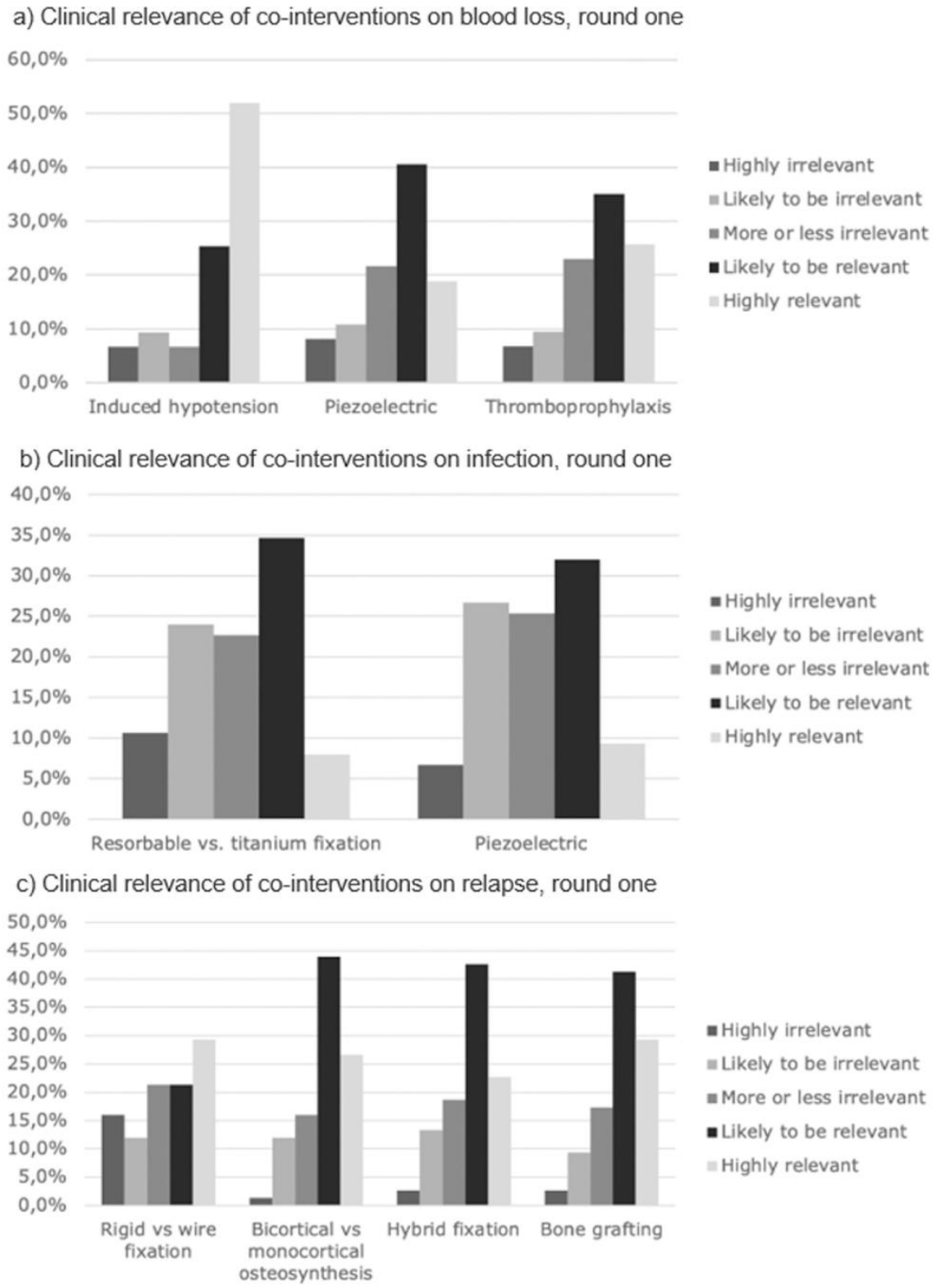


Fig. 2. (A) Clinical relevance of co-interventions on blood loss, round 1. (B) Clinical relevance of co-interventions on infection, round 1. (C) Clinical relevance of co-interventions on relapse, round 1.

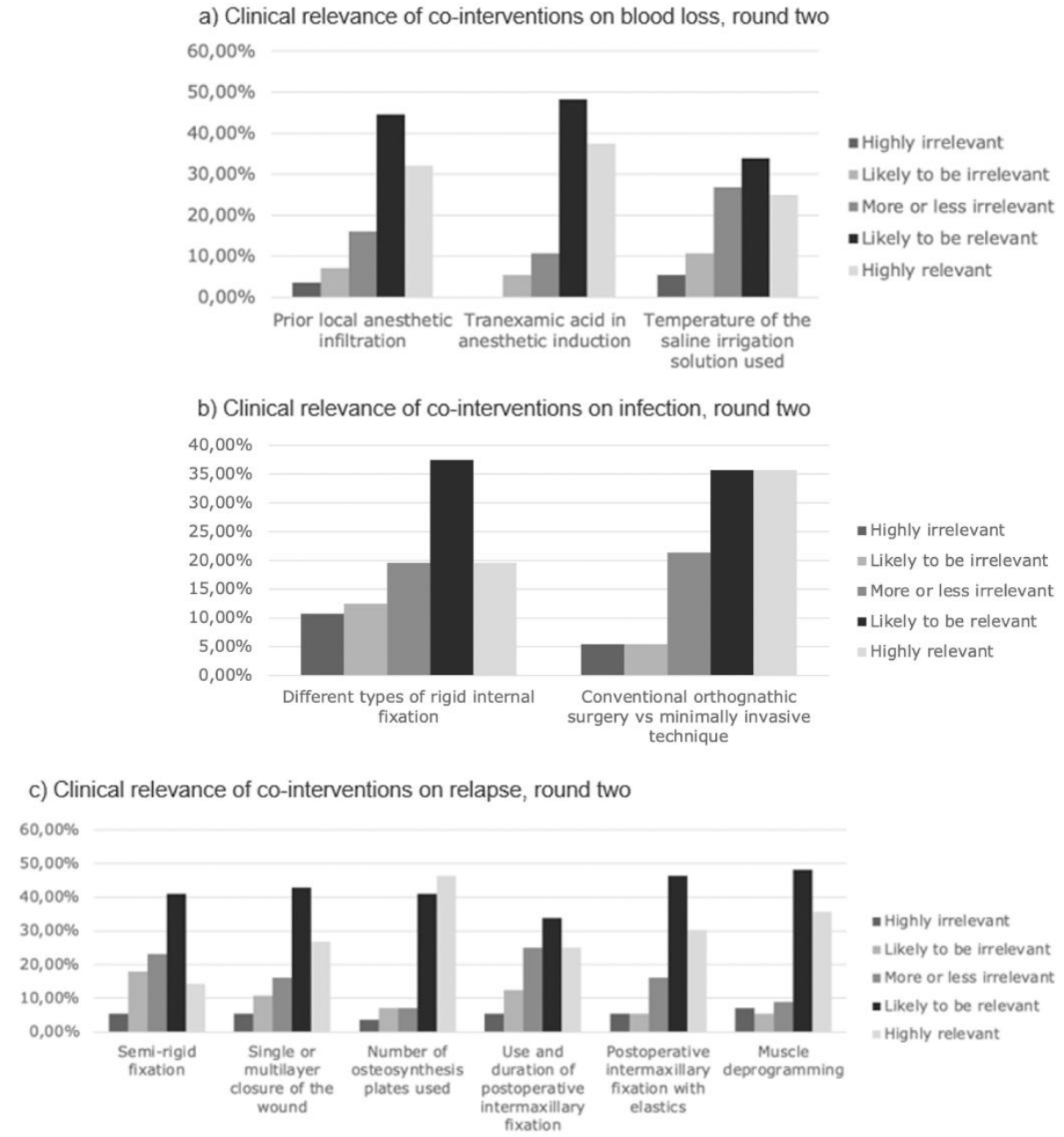


Fig. 3. (A) Clinical relevance of co-interventions on blood loss, round 2. (B) Clinical relevance of co-interventions on infection, round 2 . (C) Clinical relevance of co-interventions on relapse, round 2.

also stands out as a concern for surgeons from the participating countries. Even though infection is a widely studied outcome in orthognathic surgery, research has mainly focused on pharmacological management[24], and it continues to be of constant interest to the consulted professionals, given the impact that infections have on the perception of the results of the surgery and the patient's postoperative quality of life .

This study has several strengths. First, the Delphi technique was used, which is a reliable method for assessing evidence gaps and achieving consensus among a panel of clinicians. Second, the findings revealed a high level of agreement among participants, and the retention rate was high (74%), suggesting that the responses were well-focused and grounded in the collective experience and knowledge of the maxillofacial surgery community, providing confidence in the results. Moreover, according to the methodological standards established in the Delphi

Table 3. Clinically relevant evidence gaps[a].

#	Evidence gap	Mean	SD
1	To compare the number of osteosynthesis plates used in relapse	4.20	0.96
2	To evaluate tranexamic acid in anaesthetic induction in blood loss	4.18	0.81
3	To assess the efficacy of induced hypotension in blood loss	4.05	1.26
4	To evaluate prior local anaesthetic infiltration in blood loss	3.95	0.96
5	To determine muscle deprogramming in relapse	3.95	1.13
6	To assess postoperative intermaxillary fixation with elastics in relapse	3.93	1.04
7	To compare conventional orthognathic surgery vs minimally invasive technique in infection	3.91	1.12
8	To assess the use of bone grafting on relapse	3.85	0.99
9	To compare the use of bicortical vs monocortical osteosynthesis on relapse	3.83	1.01
10	To compare single and multilayer closure of the wound in infection	3.75	1.13
11	To assess the efficacy of hybrid fixation on relapse	3.72	1.04
12	To evaluate the effect of thromboprophylaxis on blood loss	3.64	1.17
13	Temperature of the saline irrigation solution used in blood loss	3.63	1.14
14	To assess the use and duration of postoperative intermaxillary fixation in relapse	3.61	1.15
15	To determine the efficacy of piezoelectric devices on blood loss	3.51	1.16

SD, standard deviation.
[a]A higher score represents higher clinical relevance; maximum score 5 .

Table 4. Intra-class correlation coefficient for repeated questions in both rounds.

Evidence gaps repeated in both rounds	Round 1 Mean (SD) score	Round 2	Kappa value	*P*-value
Resorbable vs titanium fixation on infection	3.05 (1.16)	3.32 (1.27)	0.43	0.023
Efficacy of piezoelectric devices on infection	3.11 (1.51)	3.23 (1.21)	0.30	0.10
Rigid vs wire fixation on relapse	3.36 (1.43)	3.00 (1.66)	0.50	0.012

methods literature, the number of participants who completed both parts of the research is statistically robust[15]. Indeed, numerous previous Delphi studies with fewer participants have been published in well-rated, high impact factor journals, ensuring significant and reliable results[15,25–30]. Finally, the study builds on a recent mapping review of orthognathic surgery, ensuring objective selection criteria encompassing all relevant literature.

However, this study also has some limitations. First, the nationality of the participants was not equally distributed, as most were from South America (68%). This may have implications for the generalizability of the results, as there may be cultural and regional variations in the practice of orthognathic surgery that were not fully captured by the participant panel. Additionally, the sample size of participants from other regions may have needed to be greater to provide a representative perspective . Therefore, the potential evidence gaps identified should be interpreted with caution, as they may reflect regional practices and concerns rather than universally applicable issues. It is important to note the predominance of younger, less experienced surgeons in hospital and academic settings within the dataset. This demographic bias may influence the interpretation of the findings and warrants careful consideration in the broader context of this research. While the potential impact of a more diverse cohort of surgeons is recognized, the methodological approach and the systematic extraction of evidence gaps strengthen the validity and clinical relevance of the findings. Finally, the study may be limited by the use of the Delphi technique, as it is a subjective process that can be influenced by the opinions and biases of the participants .

The findings of this Delphi study may have meaningful implications for future research and clinical practice in orthognathic surgery. This study provides a valuable guide for future investigations by identifying and prioritizing potentially clinically relevant evidence gaps. The evidence gaps identified in this study, which focus on blood loss, infection, and relapse, may allow researchers and clinicians to direct future investigations towards critical areas of concern. By addressing these potential gaps in knowledge and developing more effective clinical decision-making tools, patient outcomes in orthognathic surgery will ultimately improve and this critical field will continue to progress.

Ethical approval

Not applicable.

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Competing interests

None.

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Patient consent

Obtained.

Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.ijom.2024.11.001.

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6. DISCUSIÓN

La cirugía ortognática ha evidenciado un crecimiento sostenido en términos de volumen y atención científica durante los últimos años, reflejado en un número creciente de publicaciones que abordan diversas técnicas complementarias y factores coadyuvantes para optimizar los resultados quirúrgicos y minimizar complicaciones asociadas como la pérdida sanguínea, infecciones y recidivas (66). Esta tendencia pone de manifiesto un interés creciente tanto desde la perspectiva clínica como investigativa, consolidando esta área como una disciplina dinámica y en constante evolución dentro de la cirugía maxilofacial.

El conjunto de los tres estudios desarrollados en esta tesis doctoral conforma una línea de trabajo progresiva y complementaria que permitió identificar, organizar y priorizar los vacíos de evidencia en cirugía ortognática, avanzando desde la caracterización general del cuerpo de literatura disponible hasta la valoración experta de su relevancia clínica. A través de este enfoque secuencial, se logró integrar la síntesis cuantitativa y cualitativa de la evidencia existente con la perspectiva clínica de especialistas del área, contribuyendo así a orientar la investigación futura hacia las áreas de mayor impacto potencial en la práctica quirúrgica. En este sentido, los estudios realizados permitieron no solo sistematizar el conocimiento disponible y evaluar su calidad metodológica, sino también transformar los vacíos detectados en prioridades de investigación concretas, respondiendo de manera coherente a los objetivos planteados en el marco de esta tesis.

6.1 RESULTADOS PRINCIPALES

En primer lugar, la revisión de mapeo inicial (67) constituyó la base metodológica del proyecto, al identificar, describir y organizar toda la evidencia disponible —tanto primaria como secundaria— relacionada con procedimientos quirúrgicos y cointervenciones en cirugía ortognática. En total, se identificaron 290 estudios (27 revisiones sistemáticas y 263 estudios primarios), abarcando una

amplia gama de diseños y enfoques metodológicos. El análisis permitió elaborar matrices de evidencia y mapas de burbujas que facilitaron la visualización de las áreas de mayor y menor densidad de conocimiento. Los resultados revelaron una distribución desigual de la evidencia, concentrada en tópicos ya resueltos, junto con múltiples vacíos de evidencia aún no explorados, entre los cuales se identificaron ocho lagunas críticas relacionadas principalmente con la prevención de la pérdida sanguínea, la infección y la recidiva postoperatoria. Asimismo, se observó una calidad metodológica globalmente baja en las revisiones sistemáticas incluidas, con más del 50% clasificadas como de nivel "críticamente bajo" según AMSTAR-2, lo que puso en evidencia la necesidad de fortalecer la rigurosidad metodológica en las síntesis de evidencia del área.

Sobre esta base, el segundo trabajo —la revisión de mapeo enfocada en las cointervenciones y modalidades quirúrgicas para prevenir pérdida sanguínea, infección y recidiva (66)— permitió profundizar en tres desenlaces clínicamente críticos. Se incluyeron 27 revisiones sistemáticas y 150 estudios primarios, de los cuales la mayoría correspondió a estudios observacionales y ensayos clínicos de calidad variable. El análisis sugirió que la administración intravenosa de ácido tranexámico es la intervención más consistentemente beneficiosa para reducir la pérdida sanguínea, mientras que la hipotensión inducida y el uso de dispositivos piezoeléctricos mostraron resultados prometedores pero sustentados en evidencia de calidad limitada. En cuanto a la prevención de infecciones, los resultados fueron heterogéneos, con falta de consenso respecto al beneficio del uso de antibióticos profilácticos. Por último, en relación con la recidiva quirúrgica, no se observó superioridad clara entre los diferentes métodos de osteosíntesis (resorbible vs. titanio, monocortical vs. bicortical), lo que refleja la persistencia de incertidumbre en torno a la estabilidad postoperatoria. A través de los mapas de burbujas elaborados, se identificaron ocho vacíos de evidencia prioritarios, que constituyeron el punto de partida para orientar nuevas líneas de investigación.

Finalmente, el tercer estudio —el Delphi internacional sobre vacíos de evidencia en cirugía ortognática (68)— abordó la etapa de validación y priorización clínica de estos vacíos mediante la consulta estructurada a un panel de 74 cirujanos maxilofaciales de 17 países. Este proceso permitió contrastar los vacíos identificados en la literatura con la percepción y experiencia de quienes realizan estas intervenciones en la práctica. El panel logró un consenso robusto ("casi perfecto" en los coeficientes de correlación intraclase) y una tasa de retención del 74%, lo que refuerza la consistencia de los resultados. Se obtuvieron 15 brechas de evidencia consideradas clínicamente relevantes, de las cuales un 47% correspondió al desenlace recidiva, un 40% a pérdida sanguínea y un 13% a infección. Las prioridades mejor valoradas incluyeron el efecto del número de placas de osteosíntesis en la recidiva, la eficacia del ácido tranexámico en la reducción de la pérdida sanguínea, y el uso de la hipotensión inducida como estrategia hemostática. Estos hallazgos reflejan una convergencia entre la evidencia científica y las preocupaciones clínicas actuales, subrayando la necesidad de generar estudios colaborativos, multicéntricos y metodológicamente sólidos que respondan a estas prioridades.

6.2 ANÁLISIS DE VACÍOS DE EVIDENCIA CON MAYOR RELEVANCIA CLÍNICA

Los vacíos de evidencia que alcanzaron mayor relevancia clínica en el ejercicio Delphi correspondieron a tres preguntas centrales: la comparación del efecto del número de placas de osteosíntesis sobre la recidiva, la evaluación del uso de ácido tranexámico en la inducción anestésica para la reducción de la pérdida sanguínea y la valoración de la eficacia de la hipotensión controlada en el control del sangrado. Con el objetivo de profundizar en el análisis de estos vacíos, se llevó a cabo una actualización de la literatura publicada desde la primera búsqueda de la revisión de mapeo (marzo 2021–mayo 2025), con el propósito de identificar si habían surgido nuevos estudios en torno a estas áreas prioritarias señaladas por los cirujanos maxilofaciales participantes.

6.2.1 EFECTO DEL NÚMERO DE PLACAS DE OSTEOSÍNTESIS EN LA RECIDIVA

El vacío de evidencia que obtuvo la mayor puntuación en términos de relevancia clínica fue propuesto directamente por los participantes del estudio Delphi, ya que no había sido identificado en la búsqueda bibliográfica realizada previamente en el mapping. Este vacío corresponde a la incertidumbre sobre el impacto del número de placas de osteosíntesis en la estabilidad postoperatoria, específicamente en relación con la recidiva esquelética.

Esta pregunta clínica cobra especial relevancia en el contexto del desarrollo de técnicas quirúrgicas emergentes, en particular la cirugía ortognática mínimamente invasiva. Hunter describió esta disciplina como aquella que incorpora procedimientos innovadores con el propósito de minimizar las secuelas derivadas de la cirugía ortognática convencional. En este ámbito, la técnica mínimamente invasiva ha introducido el uso de dos placas de osteosíntesis en el maxilar superior, en contraste con las cuatro placas tradicionalmente utilizadas en la fijación convencional (69).

Sin embargo, la estabilidad quirúrgica de esta técnica ha sido objeto de controversia. En la literatura identificada en la búsqueda actualizada, se encontraron tres estudios retrospectivos (70–72), además de una revisión sistemática con enfoque de métodos mixtos (73) que aborda esta interrogante. No obstante, los estudios primarios presentan importantes limitaciones en cuanto a su comparabilidad, ya que la localización de las fijaciones difiere entre ellos. En los estudios de Beyler et al. y Murray et al., la fijación se realizó exclusivamente en la apertura piriforme, mientras que en el estudio de Fujio se empleó fijación en el pilar cigomático (70,72). Sin embargo, para obtener resultados más íntegros, la revisión sistemática de Grillo et al. incluyó tanto estudios clínicos como análisis in vitro y modelaciones mediante elementos finitos (73). Aunque el metanálisis no encontró diferencias estadísticamente significativas en términos de estabilidad esquelética entre las fijaciones con dos y cuatro placas, el análisis biomecánico reveló un mayor riesgo de recidiva asociado al uso de dos placas, incluso con avances maxilares limitados (3 mm)

(73). En cambio, en los casos en que se utilizaron cuatro placas, este riesgo sólo aumentó con desplazamientos más amplios (10 mm).

En síntesis, aunque se han identificado algunos estudios exploratorios sobre esta temática, persiste la necesidad de investigaciones primarias de alta calidad metodológica que evalúen de forma directa la estabilidad quirúrgica en relación con el número de placas de osteosíntesis utilizadas. Estos estudios serían fundamentales para sustentar o refutar la adopción generalizada de la técnica mínimamente invasiva en cirugía ortognática.

6.2.2 USO DE ÁCIDO TRANEXÁMICO EN LA INDUCCIÓN ANESTÉSICA PARA DISMINUIR EL SANGRADO

El segundo vacío de evidencia con mayor relevancia clínica corresponde a la efectividad del ácido tranexámico administrado durante la inducción anestésica para la reducción del sangrado en cirugía ortognática. En la actualización de la búsqueda bibliográfica realizada para esta pregunta clínica, se identificaron ocho estudios; tres de los cuales eran estudios observacionales (74–76), dos ensayos clínicos aleatorizados (77,78), así como un protocolo de una revisión sistemática (79) y una revisión sistemática valorizada con alta calidad metodológica según la herramienta AMSTAR II (80). Los hallazgos de esta última indican que el uso de ácido tranexámico reduce de manera estadísticamente y clínicamente significativa el sangrado intraoperatorio, evidenciando una diferencia media de 135,6 mL entre los grupos comparados ($p < 0,00001$; IC 95%: -177,51 a -93,70 mL) (80), con un alto grado de certeza según la evaluación del nivel de evidencia mediante el enfoque GRADE. Además, no se reportaron efectos adversos asociados al uso de este fármaco en el contexto quirúrgico evaluado.

Dado el nivel de evidencia alcanzado y la solidez metodológica de la revisión sistemática disponible, se considera que este vacío de evidencia ha sido adecuadamente resuelto. Cabe destacar, sin embargo, que tras la publicación de dicha revisión (noviembre de 2024), se han seguido publicando estudios observacionales sobre esta temática (74,78), los cuales probablemente fueron

desarrollados de forma paralela. No obstante, se espera que a futuro no se continúen destinando recursos a esta línea de investigación, considerando que la interrogante ha sido respondida con evidencia de alta calidad y relevancia clínica.

6.2.3 HIPOTENSIÓN CONTROLADA PARA REDUCIR EL SANGRADO

El tercer vacío de evidencia clasificado con mayor relevancia clínica corresponde al uso de la hipotensión controlada como estrategia para reducir el sangrado intraoperatorio en cirugía ortognática. En la actualización de la búsqueda bibliográfica se identificaron dos ECR (81,82), cuatro estudios retrospectivos (83–86), una revisión sistemática (87), además de un resumen estructurado de evidencia FRISBEE (88). Este último concluye que la hipotensión controlada podría disminuir el sangrado intraoperatorio; sin embargo, la certeza de la evidencia es baja de acuerdo con el análisis GRADE.

La revisión sistemática identificada concluyó que la hipotensión controlada durante la anestesia en cirugía ortognática puede considerarse un método seguro para disminuir la pérdida sanguínea intraoperatoria, mejorar el campo quirúrgico y reducir la necesidad de transfusiones de sangre (87). Sin embargo, la calidad de la revisión sistemática fue evaluada como críticamente baja al aplicar la herramienta AMSTAR II.

Por otro lado, los resultados del estudio FRISBEE concluyen que el uso de anestesia hipotensiva en la cirugía ortognática podría reducir la pérdida sanguínea intraoperatoria, con una diferencia de medias de 168.68 ml (IC 95%: 228.19 ml a 109.77ml), sin embargo, la evidencia es de certeza baja según el análisis GRADE (88). Este FRISBEE sigue sistemáticamente la metodología preestablecida por el Proyecto de Síntesis de Evidencia de Epistemonikos, siguiendo rigurosos estándares metodológicos y un proceso interno de revisión por pares.

Cabe señalar que el resumen FRISBEE se basa en las mismas revisiones sistemáticas previamente identificadas en el mapping review de esta tesis, pero aplica una evaluación metodológica más rigurosa que los estudios secundarios considerados inicialmente. Por otro lado, los ensayos clínicos aleatorizados identificados en la actualización de la búsqueda no fueron incluidos en el FRISBEE debido a que fueron publicados con posterioridad al periodo cubierto por dicho resumen. Esto resalta la pertinencia de realizar un nuevo análisis que incorpore estos estudios recientes, lo que podría mejorar la precisión de los resultados disponibles.

A pesar de estas limitaciones, todas las síntesis de evidencia identificadas coinciden consistentemente en que el uso de la hipotensión controlada se asocia con una reducción del sangrado intraoperatorio en cirugía ortognática.

La actualización del estado de los vacíos de evidencia con mayor relevancia clínica a través de búsquedas en la literatura trajo varios análisis. Se pudo confirmar que el vacío de evidencia identificado con la mayor relevancia clínica de la lista sigue siendo un área sin resolver, lo que resalta la necesidad de destinar recursos para llevar a cabo estudios primarios de alta calidad que aborden dicha pregunta. Fue alentador descubrir que el segundo y el tercer vacío de evidencia ya han sido resueltos, con estudios que demuestran la alta eficacia del ácido tranexámico y de la hipotensión controlada en la reducción del sangrado en cirugía ortognática, aunque la confianza en los resultados sea baja de este último. Con esta actualización, se pretende avanzar en la cobertura de los vacíos de evidencia, mejorando los resultados en cirugía ortognática y reduciendo complicaciones mediante el uso de evidencia de alta calidad.

6.3 DESEQUILIBRIO TEMÁTICO EN LA LITERATURA CIENTÍFICA Y DESCONEXIÓN CON LAS PRIORIDADES CLÍNICAS

A pesar del notable incremento de publicaciones de artículos científicos sobre cirugía ortognática, el análisis derivado del mapping review (89) pone en evidencia un claro desequilibrio en la atención

investigativa otorgada a diferentes tópicos clínicos. Se observa una considerable cantidad de publicaciones dedicadas a ciertos aspectos específicos con limitada relevancia clínica, tales como el efecto del dispositivo piezoeléctrico o la comparación entre placas de osteosíntesis reabsorbibles versus placas de titanio sobre la incidencia de infecciones. Este fenómeno contrasta con la escasa evidencia disponible sobre preguntas clínicas consideradas de mayor relevancia para los especialistas, resaltadas mediante el estudio Delphi realizado con expertos internacionales (68). Específicamente, la investigación reiterada en torno a fijaciones rígidas comparadas con alambradas respecto a la recidiva es otro ejemplo de sobreinvestigación en tópicos que clínicamente han sido considerados de baja prioridad por la comunidad quirúrgica internacional.

Estos hallazgos enfatizan la importancia crítica de incluir la valoración clínica en el diseño y desarrollo de investigaciones futuras en cirugía ortognática. Las brechas de evidencia identificadas exclusivamente a través del análisis bibliográfico no siempre se alinean con las necesidades y prioridades clínicas. De hecho, algunas preguntas relevantes propuestas por los especialistas en el estudio Delphi, como el efecto del número de placas de osteosíntesis utilizadas, la deprogramación muscular y la influencia de la fijación intermaxilar sobre la recidiva, fueron completamente omitidas en la literatura científica disponible. Esta desconexión sugiere la necesidad de un enfoque más integrado y colaborativo entre la investigación académica y la experiencia clínica para mejorar la pertinencia y aplicabilidad de la evidencia generada.

En este contexto, las living reviews y la estrategia de data-sharing emergen como herramientas fundamentales para optimizar los recursos en investigación clínica y mejorar la eficiencia de la síntesis de evidencia (90). El concepto de living evidence implica la actualización continua de revisiones sistemáticas, permitiendo la incorporación oportuna y eficiente de nuevos hallazgos científicos, y evitando así la realización reiterada de revisiones sistemáticas desde cero, lo que resulta en un gasto considerable de tiempo y recursos económicos y humanos. Esta metodología

se torna especialmente relevante ante la prevalencia de revisiones sistemáticas inconclusas, como se observó en el análisis mediante mapas de burbujas sobre resultados relacionados con el uso de injerto óseo o placas reabsorbibles versus placas de titanio en la recidiva, o la eficacia de la tromboprofilaxis en la reducción de pérdida sanguínea (66).

La adopción extendida de revisiones sistemáticas vivas implicaría también un cambio significativo en los procesos editoriales tradicionales, promoviendo sistemas más abiertos, colaborativos y transparentes, que faciliten una difusión rápida y precisa de la información científica actualizada (90). Este enfoque no sólo permitiría un mejor aprovechamiento de los recursos de investigación disponibles, sino que contribuiría significativamente a resolver de manera más expedita y certera interrogantes clínicas críticas, mejorando así la práctica clínica basada en evidencia en cirugía ortognática.

En resumen, esta tesis doctoral destaca la necesidad urgente de redirigir esfuerzos investigativos hacia preguntas clínicas de alta relevancia y no suficientemente abordadas, considerando integralmente la valoración clínica como guía primordial para la identificación y priorización de vacíos de evidencia. Asimismo, la implementación sistemática de metodologías de living evidence se perfila como una estrategia indispensable para mejorar la eficiencia, pertinencia y aplicabilidad clínica de la investigación en cirugía ortognática, con el potencial último de optimizar resultados quirúrgicos y la calidad de vida de los pacientes intervenidos.

6.4 CALIDAD METODOLÓGICA

El análisis realizado evidencia de manera consistente la baja calidad metodológica de la mayoría de los estudios disponibles en cirugía ortognática. Según la evaluación con la herramienta AMSTAR-2, más de la mitad de las revisiones sistemáticas incluidas (57%) fueron clasificadas como de calidad “críticamente baja”, un 14,3% como de calidad “baja” y solo un 8,6% alcanzaron el nivel de “alta calidad”. Estos resultados revelan limitaciones sustanciales en aspectos centrales de la

investigación clínica, lo que repercute directamente en la confianza que se puede depositar en las conclusiones disponibles para guiar la práctica quirúrgica.

Entre las principales deficiencias metodológicas identificadas destacan la ausencia de protocolos predefinidos en más de la mitad de las revisiones (51,4%), la falta de justificación de los criterios de inclusión o del diseño de estudio (60%) y la omisión de procedimientos fundamentales como la selección de estudios y la extracción de datos en duplicado, prácticas que solo se realizaron en el 54,3% y 57,1% de las revisiones respectivamente. Asimismo, en la gran mayoría de los casos (91,4%) no se informó la fuente de financiamiento de los estudios primarios incluidos, lo que limita la transparencia y dificulta evaluar el riesgo de sesgo asociado a potenciales conflictos de interés. Aunque algunos ítems, como la exhaustividad de las estrategias de búsqueda y la descripción detallada de los estudios incluidos, obtuvieron mejores valoraciones, las falencias en dominios críticos comprometen de manera significativa la validez interna y externa de los resultados.

Estos hallazgos reflejan retos estructurales y metodológicos propios de la investigación en odontología y, particularmente, en cirugía maxilofacial. En primer lugar, la complejidad de los procedimientos quirúrgicos y la gran variabilidad de técnicas, protocolos anestésicos y co-intervenciones utilizadas dificultan la estandarización de comparadores y resultados, lo que redunda en una heterogeneidad considerable entre estudios. A ello se suma la dificultad para reclutar un número adecuado de pacientes, debido a que las indicaciones de cirugía ortognática suelen estar circunscritas a poblaciones específicas y a centros altamente especializados, lo que reduce el poder estadístico de los ensayos clínicos y favorece el predominio de estudios observacionales de menor nivel de evidencia (91,92).

Otro desafío relevante es la medición y estandarización de los desenlaces clínicos. Como se observa en la literatura, existe una amplia variedad de resultados reportados (recidiva, pérdida sanguínea, infecciones, alteraciones neurosensoriales, dolor, cambios en tejidos blandos, entre otros),

muchos de ellos medidos de forma heterogénea o con instrumentos poco validados. Esta dispersión dificulta la síntesis de la evidencia y la realización de metaanálisis comparativos robustos. La ausencia de un core outcome set consensuado para cirugía ortognática representa, en este sentido, una de las principales prioridades metodológicas para futuros estudios.

Asimismo, deben considerarse las barreras éticas y logísticas para la conducción de ensayos clínicos aleatorizados en esta disciplina. La asignación aleatoria de pacientes a determinadas intervenciones quirúrgicas puede ser percibida como poco factible, tanto por los profesionales como por los pacientes, dado el carácter invasivo e irreversible de muchos procedimientos (93). Ello favorece la preferencia por diseños menos exigentes metodológicamente, como cohortes retrospectivas, pero al costo de incrementar el riesgo de sesgos de selección y de confusión.

La situación descrita no es exclusiva de la cirugía ortognática, sino que refleja limitaciones ampliamente documentadas en la investigación clínica en odontología. En un contexto donde las decisiones terapéuticas requieren cada vez más sustentarse en evidencia sólida, la carencia de estudios de alta calidad representa un obstáculo significativo para la implementación de prácticas basadas en evidencia (94,95). Superar estas limitaciones exige una agenda de investigación coordinada, que fomente la realización de ensayos multicéntricos con protocolos estandarizados, la adherencia estricta a guías metodológicas internacionales y la inclusión de resultados clínicamente relevantes y centrados en el paciente.

En la publicación del mapping review se muestra que la base de evidencia actual en cirugía ortognática es débil y fragmentada, condicionada por fallas metodológicas recurrentes y por retos estructurales propios de la especialidad. El camino hacia una investigación clínica de mayor calidad requiere no sólo fortalecer la formación metodológica de los equipos quirúrgicos y de investigación, sino también generar colaboraciones internacionales y plataformas de registro prospectivo que permitan superar las limitaciones de tamaño muestral y heterogeneidad.

6.5 PRIORIZACIÓN DE EVIDENCIA Y LOS GRUPOS COLABORATIVOS

Un aspecto fundamental que emerge de este análisis es la necesidad de establecer procesos formales de priorización de evidencia en cirugía ortognática y, más ampliamente, en odontología y cirugía maxilofacial. La gran cantidad de preguntas clínicas potenciales, sumada a los recursos limitados para la realización de estudios de alta calidad, obliga a desarrollar mecanismos sistemáticos que permitan identificar cuáles son los vacíos de conocimiento más relevantes y urgentes. La priorización basada en criterios explícitos —como el impacto clínico esperado, la frecuencia de la condición, la variabilidad en la práctica clínica y la factibilidad metodológica— constituye una herramienta esencial para orientar los esfuerzos de investigación hacia áreas donde la generación de evidencia pueda tener un mayor beneficio para pacientes y profesionales (58,59).

En este sentido, la experiencia de Cochrane Oral Health constituye un ejemplo paradigmático de cómo la investigación colaborativa y los procesos de priorización estructurados pueden guiar la agenda científica. Este grupo ha desarrollado marcos de trabajo participativos que integran a clínicos, investigadores y pacientes en la identificación de preguntas prioritarias para revisiones sistemáticas y ensayos clínicos. Mediante consultas amplias y transparentes, Cochrane Oral Health ha logrado definir líneas de investigación con alto impacto potencial en la práctica odontológica y ha favorecido la producción de revisiones de alta calidad metodológica, con rigor estandarizado y orientadas a problemas clínicos relevantes (96,97). No obstante, dentro de las prioridades de investigación del grupo Cochrane Oral Health del 2021-2024, no se especificaba ninguna pregunta sobre cirugía ortognática.

La relevancia de este modelo radica en que no se limita a sintetizar la evidencia existente, sino que también influye directamente en la producción de nueva investigación, al señalar vacíos críticos de conocimiento y estimular a equipos de investigación a diseñar ensayos clínicos en esas áreas. Así, la priorización sistemática se transforma en un puente entre la práctica clínica y la agenda investigadora, evitando la duplicación de esfuerzos en áreas marginales y promoviendo la eficiencia

en el uso de recursos. Por ende, aplicar un enfoque similar en esta área permitiría superar una de las principales limitaciones detectadas en esta tesis: la dispersión y heterogeneidad de los estudios disponibles.

6.6 RECOMENDACIONES PARA LA IMPLEMENTACIÓN DE PROCESOS DE PRIORIZACIÓN EN CIRUGÍA ORTOGNÁTICA

Para trasladar estas experiencias al ámbito de la cirugía ortognática, se proponen varias recomendaciones. En primer lugar, resulta fundamental el uso de métodos participativos y transparentes de priorización, tales como la técnica Delphi o las consultas en línea a expertos y pacientes. Estos métodos permiten alcanzar consenso en torno a las preguntas de investigación más relevantes, considerando tanto la perspectiva clínica como la experiencia de los pacientes, quienes aportan información clave sobre los desenlaces de mayor impacto en su calidad de vida (98,99).

Un segundo paso esencial es la definición de core outcome sets (COS) para cirugía ortognática. La heterogeneidad observada en los desenlaces reportados por los estudios revisados limita la posibilidad de realizar síntesis comparativas sólidas. El desarrollo de COS consensuados garantizaría que todos los ensayos clínicos futuros incluyan un conjunto mínimo de resultados estandarizados y clínicamente significativos, facilitando la comparación entre estudios y la elaboración de metaanálisis con mayor poder estadístico (100).

Asimismo, es recomendable fomentar la colaboración multicéntrica a nivel nacional e internacional. La cirugía ortognática es un procedimiento que suele realizarse en centros altamente especializados, lo que limita el tamaño muestral de estudios individuales. La creación de redes colaborativas y registros clínicos prospectivos permitiría superar esta barrera, aumentando la validez externa de los resultados y reduciendo la duplicación de esfuerzos (101,102).

Otra estrategia relevante consiste en la integración de pacientes y decisores en el diseño de estudios, no solo como participantes, sino como agentes activos en la definición de preguntas, selección de desenlaces y evaluación de la relevancia clínica de los hallazgos. Este enfoque de investigación centrada en el paciente asegura que los resultados generados respondan a necesidades reales y promueve una mayor aplicabilidad de la evidencia en la práctica quirúrgica (103,104).

Finalmente, la implementación de plataformas de registro y seguimiento de proyectos de investigación, similares a PROSPERO para revisiones sistemáticas o ClinicalTrials.gov para ensayos clínicos, contribuiría a mejorar la transparencia y reducir el sesgo de publicación. La inscripción obligatoria de protocolos fortalecería la confianza en los resultados publicados y permitiría un mejor monitoreo de las prioridades establecidas.

En síntesis, la aplicación de procesos formales de priorización en cirugía ortognática debe sustentarse en metodologías participativas, estandarización de desenlaces, colaboración multicéntrica, involucramiento de pacientes y transparencia en el registro de protocolos. Estas estrategias, inspiradas en experiencias exitosas de otros campos de la salud, ofrecen un camino concreto y viable para elevar la calidad metodológica de la investigación en cirugía ortognática y maximizar su impacto clínico.

6.7 FORTALEZAS Y LIMITACIONES

El presente trabajo doctoral presenta diversas fortalezas metodológicas y conceptuales que sustentan la solidez, pertinencia y originalidad de sus resultados. En primer lugar, los estudios de mapeo de evidencia se desarrollaron bajo un enfoque sistemático, transparente y reproducible, conforme a las guías metodológicas internacionales vigentes para este tipo de revisiones. Todas las etapas —desde la formulación de la pregunta de investigación hasta la selección, extracción y síntesis de los datos— fueron exhaustivamente documentadas, garantizando la trazabilidad y la posibilidad de replicación futura. La estrategia de búsqueda bibliográfica, amplia y exhaustiva, abarcó múltiples bases de datos sin restricciones de idioma ni fecha de publicación, con el propósito de identificar la totalidad de la literatura relevante sobre cirugía ortognática. Este abordaje permitió no solo caracterizar el volumen y la naturaleza de la investigación existente, sino también analizar su distribución temática y detectar vacíos de evidencia de relevancia clínica.

Una fortaleza central de este trabajo radica en su diseño metodológico secuencial e integrador, en el que los resultados del mapeo de evidencia sirvieron como base empírica para la formulación del estudio Delphi. Esta articulación permitió vincular la identificación sistemática de vacíos de evidencia con la definición participativa de prioridades de investigación, asegurando la coherencia interna del proyecto y reforzando su aplicabilidad práctica. A su vez, la tesis representa una contribución metodológica innovadora en el campo de la cirugía oral y maxilofacial, al combinar por primera vez un enfoque de evidence mapping con un proceso de consenso internacional tipo Delphi. Este modelo interdisciplinario constituye un referente metodológico replicable que puede servir de guía para futuras investigaciones orientadas a la planificación estratégica de la evidencia en otras áreas de la odontología y las ciencias de la salud.

Otra fortaleza relevante fue la evaluación crítica de la calidad metodológica de las revisiones sistemáticas incluidas, realizada mediante la herramienta AMSTAR II, ampliamente reconocida y validada a nivel internacional. Este análisis permitió trascender la mera descripción cuantitativa del

cuerpo de evidencia, aportando una valoración cualitativa de la solidez, consistencia y fiabilidad de los estudios. En complemento, la construcción de la matriz de evidencia constituyó un aporte metodológico significativo, al vincular revisiones sistemáticas y estudios primarios para identificar investigaciones no sintetizadas previamente. Esta aproximación favoreció una visión integral y actualizada del panorama de investigación, contribuyendo a delimitar con mayor precisión los vacíos de conocimiento vigentes y a orientar el diseño de futuros estudios.

Asimismo, la utilización de mapas de burbujas (bubble maps) representó una herramienta de síntesis visual innovadora, que permitió representar gráficamente la relación entre las intervenciones quirúrgicas, los desenlaces clínicos y la densidad de la evidencia disponible. Este recurso no solo facilitó la interpretación de los resultados, sino que también fortaleció la transferencia del conocimiento científico hacia la práctica clínica y la toma de decisiones informadas, al ofrecer un formato de visualización claro, accesible y de alta utilidad comunicacional para distintos públicos.

En relación con el estudio Delphi, este se diseñó y ejecutó conforme a las recomendaciones internacionales para métodos de consenso, garantizando un proceso metodológicamente robusto y transparente. El carácter anónimo de las rondas redujo la influencia de jerarquías o sesgos de autoridad, y se implementaron estrategias activas de retención, logrando mantener una elevada tasa de respuesta entre rondas. La inclusión de cirujanos maxilofaciales de 17 países y 5 continentes aportó una amplia diversidad geográfica, cultural y profesional, fortaleciendo la validez externa y la aplicabilidad internacional de los resultados.

No obstante, el trabajo presenta ciertas limitaciones que deben ser reconocidas. En primer lugar, los estudios de mapeo poseen un carácter eminentemente descriptivo, lo que impide establecer relaciones causales o realizar comparaciones cuantitativas de efectividad entre intervenciones. Este tipo de revisión proporciona una visión panorámica y estructural del campo, pero no permite

extraer conclusiones sobre la magnitud o dirección de los efectos clínicos, lo que limita parcialmente la capacidad de inferencia directa.

Otra limitación de este trabajo es que las guías de práctica clínica no fueron consideradas de manera explícita en una fase complementaria de análisis de los resultados. Se optó por mantener la inclusión únicamente de revisiones sistemáticas y estudios primarios con el fin de estandarizar las fuentes, evitar la duplicación de información y facilitar su organización y síntesis. No obstante, las guías de práctica clínica podrían haberse identificado e incorporado en una etapa posterior, orientada a contextualizar los hallazgos, contribuir a la priorización de preguntas clínicamente relevantes y contrastar si los vacíos de evidencia detectados persistían desde la perspectiva de la toma de decisiones en salud. Su integración en futuras investigaciones podría fortalecer la interpretación de los resultados y la relevancia clínica de las brechas de conocimiento identificadas.

Un aspecto metodológico a considerar es que no se incluyeron de manera explícita desenlaces reportados por pacientes, tales como la calidad de vida, la satisfacción estética o la percepción funcional. Esta decisión se fundamentó principalmente en la amplitud, complejidad y heterogeneidad de estos desenlaces, los cuales constituyen un ámbito de investigación relevante y suficientemente amplio como para ser abordado de manera específica y sistemática como un cuerpo de evidencia independiente. No obstante, su exclusión puede limitar la alineación del estudio con un enfoque centrado en el paciente y reducir la aplicabilidad clínica de las prioridades identificadas. En este sentido, futuros estudios deberían considerar el análisis integral de estos desenlaces mediante metodologías similares de mapeo de evidencia, con el fin de complementar y enriquecer la identificación de brechas de conocimiento en cirugía ortognática.

Desde una perspectiva metodológica, cabe señalar que, durante el proceso de priorización, las preguntas de investigación fueron vinculadas a un único desenlace específico. Esta decisión respondió a la necesidad de simplificar y estandarizar el análisis, facilitando la organización,

comparación y síntesis de la información dentro del mapeo de evidencia, así como una clasificación más clara y reproducible de los vacíos de evidencia identificados. Además, los desenlaces considerados fueron seleccionados por expertos en el área como temas de alto interés en la investigación en cirugía ortognática, lo que aporta pertinencia y relevancia al enfoque adoptado. No obstante, este esquema puede no reflejar completamente la complejidad de la práctica clínica, donde la toma de decisiones implica una evaluación simultánea de múltiples desenlaces, incluyendo tanto efectos deseables como indeseables de las intervenciones. En este sentido, la reducción de las preguntas a desenlaces individuales podría limitar la integralidad y aplicabilidad de las prioridades identificadas.

En cuanto al estudio Delphi, aunque se alcanzó una tasa de participación elevada y un bajo porcentaje de pérdidas, la representatividad de la muestra podría haberse visto afectada por la concentración de participantes en determinados países (principalmente Chile y Francia), lo que podría introducir sesgos culturales o contextuales en la priorización de los temas. Además, el panel de expertos incluyó exclusivamente a cirujanos maxilofaciales, sin la participación de otros actores clave —como ortodoncistas, anestesiólogos, pacientes o gestores sanitarios—, lo que limita una visión más multidimensional y centrada en el paciente sobre las prioridades de investigación identificadas.

Adicionalmente, aunque se contempló mantener una actualización continua de la búsqueda bajo un modelo de evidencia viva, esta no pudo sostenerse por limitaciones de recursos, si bien se realizó una actualización puntual y exhaustiva que permitió incorporar los estudios más recientes.

7. CONCLUSIONES

Esta tesis doctoral permitió identificar, sintetizar y organizar de manera sistemática los vacíos de evidencia clínicamente relevantes en cirugía ortognática, integrando métodos de mapeo y consenso que demostraron ser herramientas eficaces para orientar la investigación futura hacia áreas de mayor impacto clínico.

Mediante las revisiones de mapeo, se logró sistematizar y representar gráficamente la literatura disponible, evidenciando una marcada concentración de estudios en temas ya resueltos y la presencia de ocho vacíos críticos de evidencia en torno a la prevención de la pérdida sanguínea, la infección y la recidiva postoperatoria. El análisis de la calidad metodológica calificó al 60% de las revisiones sistemáticas con calidad críticamente baja, lo que refuerza la necesidad de fortalecer los estándares de rigor en las síntesis de evidencia del área.

Posteriormente, a través del estudio Delphi internacional, se determinó la relevancia clínica de los vacíos de evidencia identificados, estableciendo 15 prioridades de investigación consideradas esenciales por cirujanos maxilofaciales de distintos países. Entre ellas, destacan el efecto del número de placas de osteosíntesis sobre la recidiva, la eficacia del ácido tranexámico en la reducción del sangrado y el uso de la hipotensión controlada como estrategia hemostática, configurándose como las tres áreas de mayor prioridad clínica.

Con respecto a estos vacíos de mayor relevancia clínica, podemos concluir que 1) falta elaborar estudios primarios sobre el efecto del número de placas de osteosíntesis en la recidiva de la cirugía ortognática; 2) el ácido tranexámico es efectivo para disminuir el sangrado en la cirugía ortognática; y 3) la hipotensión controlada podría disminuir el sangrado en la cirugía ortognática.

En conjunto, los resultados obtenidos confirman que la aplicación combinada de métodos de evidencia mapeada y consenso clínico estructurado constituye un enfoque sólido y reproducible para definir prioridades de investigación basadas en necesidades reales de la práctica quirúrgica, optimizando así la pertinencia y el impacto de la producción científica futura en cirugía ortognática.

8. ANEXOS

8.1 ANEXO 1: ESTRATEGIAS DE BÚSQUEDA PARA LA ACTUALIZACIÓN DE LOS VACÍOS DE EVIDENCIA CON MAYOR RELEVANCIA CLÍNICA

Tabla 1.1. Estrategia de búsqueda para eficacia de ácido tranexámico en cirugía ortognática

#1	fixation*[tiab] or plate*[tiab] or osteosynthesis[tiab] or OTS[tiab]
#2	"orthognathic surgery"[tiab] OR "orthognathic surgical procedures"[tiab] OR "orthognathic surgical procedures"[MeSH Terms] OR "orthognathic surgery"[MeSH Terms] OR bimaxillary osteotom*[tiab] OR maxillary osteotom*[tiab] OR lefort[tiab]
#3	Relapse*[tiab] or stabilit*[tiab]
#4	#1 AND #2 AND #3

Tabla 1.2. Estrategia de búsqueda número de placas de osteosíntesis

#1	tranexamic acid[mesh] OR tranexamic acid[tiab] OR Antifibrinolytic Agents[mesh] OR antifibrinolytic*[tiab] OR TXA[tiab] OR Transamin[tiab] OR Exacyl[tiab] OR Lysteda[tiab] OR Cyklokapron[tiab] OR AMCHA[tiab]
#2	"orthognathic surgery"[tiab] OR "orthognathic surgical procedures"[tiab] OR "sagittal split"[tiab] OR "bsso"[tiab] OR "ivro"[tiab] OR "genioplasty"[tiab] OR "mandibular advancement"[tiab] OR "orthognathic surgical procedures"[MeSH Terms] OR "orthognathic surgery"[MeSH Terms] OR bimaxillary osteotom*[tiab] OR maxillary osteotom*[tiab]

#1	tranexamic acid[mesh] OR tranexamic acid[tiab] OR Antifibrinolytic Agents[mesh] OR antifibrinolytic*[tiab] OR TXA[tiab] OR Transamin[tiab] OR Exacyl[tiab] OR Lysteda[tiab] OR Cyklokapron[tiab] OR AMCHA[tiab]
#3	("randomized controlled trial"[Publication Type] OR "controlled clinical trial"[Publication Type] OR "randomized"[Title/Abstract] OR "placebo"[Title/Abstract] OR "drug therapy"[MeSH Subheading] OR "randomly"[Title/Abstract] OR "trial"[Title/Abstract] OR "groups"[Title/Abstract]) NOT ("animals"[MeSH Terms] NOT "humans"[MeSH Terms])
#4	#1 AND #2 AND #3

Tabla 1.3. Estrategia de búsqueda hipotensión controlada

#1	hypotens*[tiab] OR "Hypotension, Controlled"[Mesh]
#2	"orthognathic surgery"[tiab] OR "orthognathic surgical procedures"[tiab] OR "sagittal split"[tiab] OR "bsso"[tiab] OR "ivro"[tiab] OR "genioplasty"[tiab] OR "mandibular advancement"[tiab] OR "orthognathic surgical procedures"[MeSH Terms] OR "orthognathic surgery"[MeSH Terms] OR bimaxillary osteotom*[tiab] OR maxillary osteotom*[tiab]
#3	#1 AND #2

8.2 ANEXO 2: PUBLICACIÓN ADICIONAL

Bendersky J, Auladell-Rispau A, Urrútia G, Rojas-Reyes MX. Methods for developing and reporting living evidence synthesis. J Clin Epidemiol. 2022 Dec;152:89–100. doi:10.1016/j.jclinepi.2022.09.020. Epub 2022 Oct 8.

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REVIEW

Methods for developing and reporting living evidence synthesis

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Abstract

Background and Objectives: Identify currently methodological aspects proposed for planning, conducting, and reporting living evidence (LE) synthesis. Develop a preliminary checklist of key LE synthesis elements.

Methods: A survey of methodological articles describing or analyzing methods for the design, conduction, or reporting of LE synthesis.

Results: Twelve methodological articles were identified and analyzed. Key elements were related to: i) definition of LE and characteristics of LE synthesis, ii) methods and tools for the living process, iii) new evidence integration (methods and considerations), iv) updates dissemination and publication, v) revisiting living parameters, and vi) protocol considerations for LE synthesis.

Conclusion: This survey displays basic methodological concepts that can drive the development of LE synthesis and identifies specific aspects with opportunities for development. The potential impact of the LE approach calls for a change in the current evidence synthesis updating processes to more open, collaborative, transparent, and efficient systems. LE approaches also challenge journal editors to shift toward more efficient processes for synthesis update dissemination, which minimizes the risks of reliability of published information. © 2022 Elsevier Inc. All rights reserved.

Keywords: Living evidence; Survey; Update; Methods; Planning and reporting; Evidence synthesis

1. Introduction

Elliot et al. developed the foundations of the living evidence (LE) model in 2014, in response to the need for incorporating and summarizing emerging evidence in systematic reviews (SRs) efficiently [1]. LE is the methodological approach that allows new research findings to be continuously incorporated into evidence syntheses. Following Elliot, authors within and outside the Cochrane Collaboration have described methods for conducting living systematic reviews (LSRs) [1–4], which were defined as SRs that are continuously updated as new evidence emerges [4]. Presently, several review groups have adopted the initial LE model for evidence synthesis (LE synthesis) in overviews and network meta-analysis (NMA). Many of these groups have introduced changes and/or developed different proposals for this approach. It has also been used as basis for developing living guidelines [5].

LE became increasingly relevant during the COVID-19 pandemic in face of the urgent need to summarize and constantly update emerging evidence on diagnostics, treatments, and vaccines.

Knowledge of available methodological proposals for developing and reporting LE synthesis will provide information to address methodological decisions in LE synthesis, support developments in conducting and reporting LE synthesis, and guide scientific journal editors' assessments.

This survey aims to identify and summarize the methods currently available for developing and reporting LE

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Declaration of interests: The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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What is new?

Key findings

- Twelve articles were identified presenting methods for living evidence (LE) synthesis. The key elements presented by authors are related to: i) definition of living evidence and the characteristics of living evidence synthesis, ii) methods and tools for the living process, iii) new evidence integration (methods and considerations), iv) updates dissemination and publication, v) revisiting parameters, and vi) protocol considerations for LE synthesis.

What this adds to what was known?

- This survey maps and summarizes methodological studies that guide and address the conduction of LE synthesis. It presents a preliminary checklist for the planning and conduction of LE synthesis based on the results of this review.

What is the implication and what should change now?

- Authors of systematic reviews (SRs) and developers of evidence synthesis aimed to inform decisions must be aware of the methodological approaches and tools currently available to conduct LE synthesis that address relevant topics in which evidence is constantly changing.
- From a methodological point of view, there are opportunities for improvement on how to carry out, inform, and evaluate evidence synthesis developed following the LE approach.
- A summary of the methodological aspects for conducting and reporting living evidence syntheses proposed by different groups is an important contribution toward an international consensus of key criteria.

synthesis; its results will contribute to developing a list of items to be considered by authors when planning to conduct and report an LE synthesis. This survey is being conducted as part of a larger knowledge transfer project entitled "Living Evidence to Inform Health Decisions" [4].

2. Methods

We conducted a survey of methodological articles. We used systematic approaches for searching electronic databases. The results of these searches constituted the sampling frame from which eligible studies were drawn.

2.1. Articles identification and sampling

A highly sensitive Boolean literature search strategy to identify all articles referring to LE synthesis was devised and supported by an information specialist (see Table 1). We ran searches in MEDLINE (via PubMed) and EMBASE from January 2010 to August 2021. No language restriction was applied. The references of included articles were reviewed, and methodological experts in evidence synthesis were consulted to identify additional relevant articles.

We included peer reviewed articles that fulfill the "methodological research article" criteria proposed by Mbuagbaw et al. [6]. All identified articles describing or analyzing methods for the design, conduction, analysis, or reporting of LE synthesis were included. We excluded review articles, commentaries, editorials, letters to editors, articles or abstracts reporting results of LSRs, or any other type of LE synthesis (e.g., living NMA). Two reviewers independently screened the titles and abstracts and full-texts of all references retrieved using Covidence. A third reviewer was consulted when consensus was not reached.

2.2. Data collection and synthesis

We extracted data related to the definition of LE, characteristics of the LE synthesis approach, aspects included in a LE synthesis protocol, proposed methods, and tools to set up and maintain the LE process and considerations for updates publication.

Data extraction was independently conducted by two reviewers using Google Spreadsheets. Data were grouped and analyzed descriptively into five categories identified by this survey authors. For this, each author after reviewing the extracted data independently proposed up to five categories according to the type of information and/or the phase in the synthesis process in which the obtained information can be applied. An initial list of proposed categories was developed and presented to all authors by email with the instructions to approve/disapprove the categories proposed or to propose new categories, if necessary. Up to three rounds were planned and aimed to reach 80% consensus among authors. Data were then grouped into the categories resulting from this process and shared with authors in an additional verification round.

2.3. Development of a checklist

The categorized results were used for drafting a preliminary check list that was later revised in face-to-face working meetings by all the authors to develop a list of items to be considered when planning the conduction and reporting of an LE synthesis. The final checklist presented as a planning aid for authors of LE synthesis was approved independently by all authors.

Table 1. Search strategy

MEDLINE
(Continuous updat*[tiab] OR continually updat*[tiab] OR constant updat*[tiab]) and (systematic[sb] OR review[tiab] OR meta- analysis*[tiab] OR evidence[tiab] OR synthes*[tiab])
([living systematic review*[tiab]] OR [living meta-analysis*[tiab]] OR [living rapid review*[tiab]] OR [living rapid evidence[tiab]] OR [living review[tiab]] OR [living network[tiab]] OR [living evidence[tiab]]) OR ([continuous itera*[tiab] OR continually itera*[tiab] OR constant itera*[tiab]])
([systematic[sb] OR review[tiab] OR meta-analysis*[tiab] OR evidence[tiab] OR synthes*[tiab]]OR [synthes* OR review* OR network* OR evidenc* OR "systematic-review" OR ''meta-analysis'' OR ''meta-analysis'' OR "meta-analyses'' OR meta-analysis* OR "rapid-review'' OR ''rapid-evidence" OR overview* OR scoping*])
EMBASE
(continuous updat*.ti,ab. OR continually updat*.tiab. OR constant updat*.tiab.) AND (systematic[sb] OR review.tiab. OR meta analys*.tiab. OR evidence.tiab. OR synthes*.tiab.)
([living systematic review*.tiab.] OR [living meta-analysis*.ti,ab.] OR [living rapid review*.tiab.] OR [living rapid evidence.tiab.] OR [living review.ti,ab.] OR [living network.ti,ab.] OR [living evidence.ti,ab.]) OR ([continuous itera*.ti,ab. OR continually itera*.ti,ab. OR constant itera*.ti,ab.])
([systematic[sb] OR review.ti,ab. OR meta analys*.ti,ab. OR evidence.ti,ab. OR synthes*.ti,ab.] OR [synthes* OR review* OR network* OR evidenc* OR systematic-review OR meta-analysis OR meta-analysis OR meta-analyses OR meta-analysis* OR rapid-review OR rapid-evidence OR overview* OR scoping*])

3. Results

After removing duplicates of references identified by searches, 1,520 records were screened, 1,180 were excluded at title and abstract screening, and 340 were assessed in full text. Of these, 321 did not fulfill the eligibility criteria and were excluded. 19 were included [1–4,6,5,7–18]. Seven articles were later excluded at the data extraction [6,8,11,13,15,17,18]. Finally, 12 articles about methodologies or tools for the LE synthesis development were assessed [1–4,5,7,9,10,12,14,16] (see Fig. 1).

3.1. Characteristics of included articles

The characteristics of the 12 articles included and analyzed in this survey are presented in Table 2.

Two rounds were necessary to reach 90% consensus in five initial categories used to group data. After data were grouped, an additional category was identified and agreed upon by all authors in a face-to-face meeting. We grouped data into six categories: i) definition of LE and characteristics of LE synthesis, ii) methods and tools for the living process, iii) new evidence integration (methods and

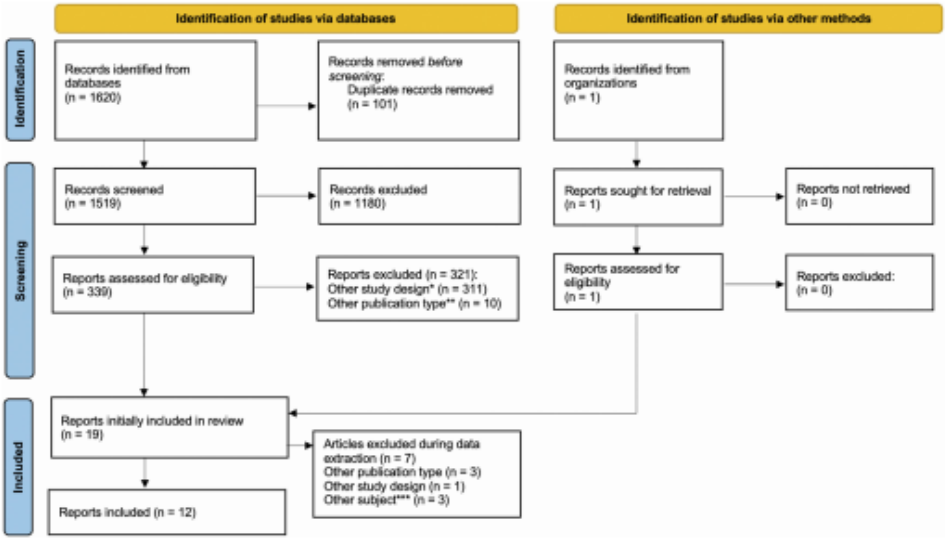


Fig. 1. PRISMA flow diagram. Legend: *Other study design: other than methodological study (e.g., living SRs, living network meta-analysis [NMA]). **Other publication type: e.g., workshops, study protocols, and commentaries. *** Other subject: methodological articles referring to subjects other than living evidence.

Table 2. Description of included articles

Author, year	Title	Aim	Relevant topics addressed
Elliot et al. 2014 [1]	Living Systematic Reviews: An Emerging Opportunity to narrow the evidence-practice gap	Proposing living evidence (LE) to address the challenges facing contemporary evidence synthesis, while retaining the strengths of systematic reviews (SRs) that have been a critical underpinning of knowledge for health over the last quarter century.	Definition and characteristics of living systematic reviews (LSRs) Production of LSRs Workflow and collaboration tools Data repositories and linked data Publication of LSRs LSRs and a new evidence ecosystem
Elliott et al. 2017 [19]	Living systematic review: 1. Introduction the why, what, when, and how	To provide an overview of the LE approach for LSRs	Keeping evidence up to date Continual updating What is an LSR? When is an LSR appropriate? How to perform an LSR Detailed description of the approach for review production Implications for implications of this approach for review publication
Thomas et al. 2017 [2]	Living systematic reviews: 2. Combining human and machine effort	To present and reflect on the use of new human and machine "technologies" to make the standard SR process more efficient.	Opportunities for a different workflow The micro tasks (i.e., searching, eligibility assessment, data extraction, RoB assessment etc.) of an LSR, and how they may be automated or made more efficient New research evidence surveillance systems
Simmonds et al. 2017 [3]	Living systematic reviews: 3. Statistical methods for updating meta-analyses	To review methods for updating meta-analysis (MA) as part of the LE approach and how to correct for potential type 1 and 2 errors when updating an MA.	Analysis methods for repeated MA Methods for network MA Commentary on the methods/conclusions and recommendations
Akl et al.2017 [20]	Living systematic reviews: 4. Living guideline recommendations	To define living guidelines and discuss when they are appropriate, the workflows required to support them, the collaboration between LSR and living guideline teams, the thresholds for changing recommendations, and potential approaches to publication and dissemination.	Definition of living guidelines When are living guidelines appropriate? Workflows required to support living guidelines Collaboration between LSRs and living guideline teams Thresholds for changing recommendations Approaches to publication and dissemination
Nikolakopoulou et al. 2018 [5]	Living network meta-analysis(NMA) compared with pairwise MA in comparative effectiveness research: empirical study	To examine whether living NMA would have provided strong evidence against the null hypothesis more often and earlier than the corresponding updated pairwise MA.	Comparison of living pairwise and NMA Unanswered questions and future work
Crèquit et al. 2019 [7]	Living NMA was feasible when considering the pace of evidence generation	To assess the feasibility of living NMA considering the pace of evidence generation across different medical areas.	Pace of evidence generation Feasibility assessment of living NMA Workload for an update
Ravaud et al. 2020 [8]	Future of evidence ecosystem series: 3. From an evidence synthesis ecosystem to an evidence ecosystem	To rethink the evidence synthesis ecosystem, its infrastructure, and management to move toward producing LE syntheses (i.e., comprehensive, based on rigorous methods, and up to date).	Encouraging communities to work together and concrete to allow for continuous refreshing of synthesized evidence Rethinking evidence synthesis Developing a harmonized international work plan

(*Continued*)

Table 2. Continued

Author, year	Title	Aim	Relevant topics addressed
Cochrane 2019 [9]	Guidance for the production and publication of Cochrane living systematic Reviews: Cochrane Reviews in living mode Version December 2019	To provide a guidance of the methods, production and publication processes for LSRs of interventions published in the Cochrane Database of SRs.	When to conduct an LSR Planning and publishing LSR methods Producing and publishing an LSR Informing readers about the currency of LSRs Implications of LSRs for peer review, copy-editing, and screening Periodic review of LSRs LSR enablers Managing searches for LSRs Authorship and LSRs Transitioning an LSR out of living mode
Tendal et al. 2020 [10]	Weekly updates of national living evidence-based guidelines: methods for the Australian living guidelines for care of people with COVID-19	To describe the methods used to develop and maintain the living, evidence-informed guidelines for primary, hospital and critical care of people with suspected or confirmed COVID-19.	Search and selection methods Assessment of evidence and formulation of recommendations Data extraction and RoB assessment Evidence synthesis Development of the recommendations Consumer involvement Considering the needs of specific populations Dissemination and evaluation
Iannizzi et al. 2021 [11]	Methodological challenges for living systematic reviews conducted during the COVID-19 pandemic: A concept paper	To discuss some challenges faced when conducting LSRs in the context of the COVID-19 pandemic, and to provide methodological guidance for others doing similar work.	Considerations regarding a living PICO – Interventions and comparators How to deal with changes in outcome measures Developing the search strategy When to update, or rather when not to update Policy relevance Important studies Transparency in the reporting of changes Lessons learned and conclusion
Kahale et al. 2021 [12]	Tailored PRISMA 2020 flow diagrams for living systematic reviews: a methodological survey and a proposal	To assess how published LSRs report on the flow of studies through the different phases of the review for the different updates and to propose an approach to reporting on that flow.	Documenting LSR study flow Reporting LSR study flow

Abbreviations: LE, living evidence; LSR, living systematic review; SR, systematic review; MA, meta-analysis; NMA, network meta-analysis; PICO, population,intervention,comparator, outcome

considerations), iv) updates dissemination and publication, v) revisiting living parameters, and vi) protocol considerations for LE synthesis (Table 3).

3.2. Definition of living evidence and characteristics of living systematic reviews

Eight articles provided a definition of LE or mentioned their characteristics [1,3,9,11,19,20]. The most frequently presented definition of LE was "high-quality, up-to-date summary of health research or guideline recommendation, which is continually updated, incorporating relevant new evidence as it becomes available" [1–3,9,10,19,20]. Four articles added to the definition that "the living evidence approach uses standard SR methods, can be applied to any type of review, has to have an explicit and a priori commitment to a predetermined frequency of search and review updating" [2,3,9,19]. Ianizzi et al. additionally added that LE syntheses are most suitable for high-priority topics with substantial uncertainty, and when new evidence is published regularly [11].

Five [1,9,10,19,20] provided information on the pertinence of using an LE synthesis approach to solve a given question. All authors agreed the decision should be based on the four aspects illustrated in Figure 2.

3.3. Methods and tools for the living process

Five articles provided information on procedures for evidence searching (who, when, and how) [2,9–11,19].

Table 3. Variables identified in methodological papers

Categories	Variables
Definition and characteristics of LE	What is LE? When it is pertinent to set up an LE approach?
Methods and tools for the living process	Search strategy design and maintenance Procedures for evidence searching (who, when, and how) Evidence surveillance related tasks (screening, selection, and definition of inclusion) Quality/RoB assessment Criteria to transition out of living mode
New evidence integration	Update report of searching/selection results (PRISMA) Trigger of the new evidence integration Methods and statistical considerations for updating MA
Updates dissemination and publication	Update content Editorial and peer review considerations Citation/DOI (digital object identifier) Strategies to alert readers (what to do and how frequently)
Revisiting living parameters	Which parameters to revisit during the "living mode" When and how to revisit Criteria to transition out of living mode
Considerations for an LE synthesis protocol	Authorship (for baseline vs. updates) Statements of the search and screening frequency Methods to incorporate new evidence Timelines to revisit parameters Criteria for transitioning out the question from the living mode

Abbreviations: LE, living evidence; RoB, risk of bias.

According to three articles, including the Cochrane guidance, an information specialist should be responsible for designing and maintaining the search strategy [9,10,19]. Three authors suggested monthly searches for evidence identification [9,11,19]. This frequency should be applied to major bibliographic sources and clinical trial registries and extended to 3 months for other sources [9,19]. Two articles [2,10] suggested daily and continuous searches, respectively, while 1 proposed weekly searches [11]. The Cochrane guidance states that searches should always be up to date for newly published versions of LSRs [9].

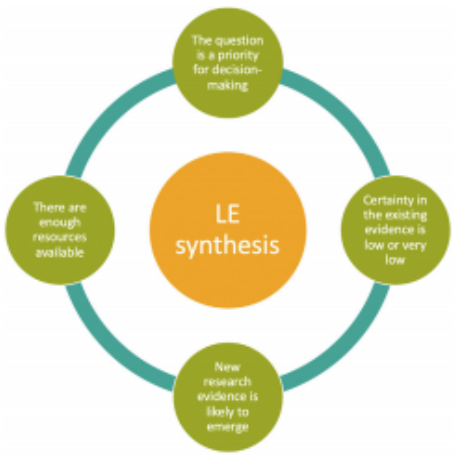


Fig. 2. When to conduct an LE synthesis.

Regarding surveillance methods, three articles suggested using auto-alerts or notifications from databases and clinical trial registries [2,10,19]. Periodic manual searching in databases is proposed when alerts cannot be made [2]. Thomas et al. suggested using database aggregators (i.e., process in which information is gathered, compiled as required, and expressed together to prepare combined datasets for data processing) [13]. Cochrane and Tendal et al. proposed information specialists also be in charge of evidence surveillance [9,10]; Tendal et al. adds that the evidence team (review authors) should also be tasked with evidence surveillance [10]. (See Table SM1 in supplementary material).

3.3.1. Use of technological enablers

Five out of twelve included articles reported on using technological enablers for conducting LE synthesis [1,2,9,12,19]. Tools proposed to increase efficiency in producing and maintaining LE synthesis are presented in Table 4.

3.4. Integration of new evidence and reporting of updates

Different time intervals for integrating new evidence into LE syntheses have been proposed. Some authors suggest a fixed-interval schedule, integrating new evidence

Table 4. Technological enablers proposed for living evidence (LE) synthesis

Review phase	Technological enabler	Proposed by
Team formation	Crowdsourcing	Thomas 2017, Cochrane [2,9]
	Task-sharing platforms	Thomas 2017, Cochrane [2,9]
Searching	Automatic, continuous database search with push notification	Thomas 2017 [2]
	Database aggregators (e.g., HDAS, Epistemonikos)	Thomas 2017 [2]
	Notification from clinical trial registries	Thomas 2017 [2]
	randomized clinical trial classifier	Cochrane [9]
	Text-mining technologies	Elliot 2014, Elliot 2017 [1,19]
	Automatic retrieval of full-text papers	Thomas 2017, Cochrane [2,9]
Data extraction or collection	Machine-learning information-extraction systems	Thomas 2017, Cochrane [2,9]
	Automated structured data extraction tools for PDFs	Thomas 2017, Cochrane [2,9]
	Machine learning assisted RoB tool	Thomas 2017, Elliot 2014, Elliot 2017 [1,2,19]
	Data repositories and linked data	Elliot 2014, Thomas 2017 [1,2]
Synthesis	Structured data extraction tools, which automatically provide data in suitable format for statistical analysis	Thomas 2017 [2]
	Continuous analysis updating based on availability of structured extracted data	Thomas 2017 [2]
	Templated reporting of some report items	Thomas 2017 [2]
	Statistical surveillance of key analysis results, with threshold set for potential conclusion change	Thomas 2017 [2]
	Automatic text generation tools for synthesis and writing	Cochrane, Elliot 2014, Elliot 2017 [1,9,19]
Dissemination	Automatization in the identification of changes between LSR versions for peer review and editorial process (e.g., Archie).	Cochrane [9]
For reduction of duplication of effort	Using standard descriptors for studies across all systematic reviews (e.g., linkeddata.cochrane.org)	Thomas 2017 [2]

Abbreviations: RCT, randomized clinical trial; LE, living evidence; LSR, living systematic review.

every 4–6 months, irrespective of its impact [9,11], especially when high volumes of new evidence are anticipated [9]. When ordinary volumes are anticipated [7], authors suggest integrating evidence every 6–12 months or when new evidence has the potential to impact review conclusions [9,11,19].

Simmonds et al. [3] reported the most appropriate statistical approach for integrating new evidence into an updated MA. Authors distinguish between the "continued integration" of new evidence, expected when the LE synthesis is aimed to inform health decision-making, and the "periodic integration" of evidence conducted to provide an up-to-date evidence summary. In the first case, four approaches were presented to avoid potential type 1 and 2 errors when updating MA. Pros and cons of each method were discussed by authors without stating clear guidance on a preferred approach [3]. Conversely, when the LE purpose is presenting an evidence summary at the time of the update, authors recommend repeating and updating each MA, adding new studies through traditional methods (fixed or random effects models) [3]. All other components of the MA (forest plots, summary estimates, and among others) should also be updated, regardless of the LE synthesis's purpose [3].

Regarding reports of updates resulting from the living process, only one article [12] addressed how to handle "living" updates data on the PRISMA flow diagram. Authors propose four approaches: i) presenting results from baseline and each update separately; ii) presenting combined search results for baseline and all updates; iii) presenting search results for the baseline version separately and combining results of all other updates; and iv) presenting results of the latest update separately, and results of all previous versions combined [12]. Kahale et al. suggest that authors performing LE synthesis should keep a record of the results of all searches [12].

3.5. Communication and publication of updates

Eight articles addressed aspects related to communication of updates [1,5,8–11,19,20]. Three scenarios related to the identified evidence and its potential impact on the synthesis conclusions were discussed as presented in Table 5.

Table 5. Dissemination and publication of living evidence

Scenarios	No new evidence	New evidence unlikely to impact on conclusions	New evidence likely to impact conclusions
Communication content	Communicate statement with search date [19,9]	Communicate search date and number of studies pending for inclusion [19,9]	Update the whole report (RoB, data extraction, MA update, etc.) [19,9,11]
Editorial review	Yes [19,9]	Yes [1,19,9]	Yes [1,19,9]
	Not necessary [1]		
Peer review	Not necessary [1,19,9]	Not necessary [1,9]	Yes [1,19,9]
		Optional [19]	Selective [9]
Ways of dissemination	Website [19,5,10]	Website [19,5,10]	Publication in peerreviewed journal [1,5,8]
	Digital online document [20,8]	Appended to existing entry in bibliographic database/ presented alongside published articles [1,19]	Website [10]
	What's new table [9]	Digital online document [20,8]	
		What's new table [9]	

Abbreviations: LE, living evidence; RoB, risk of bias; MA, meta-analysis.

Regarding managing citations for new updates, two articles [1,19] suggest that no DOI or citation changes are necessary if the frequently updated information is presented alongside published articles. New DOIs, database listings, and citable publications would be required if content is frequently updated and published in a more unified form [1,19].

Authors have proposed several mechanisms to alert end-users about review updates, including: push mechanism and linking living guidelines to information systems at the point of care [20], social media, email communications [10], advanced information technology [12], and online communities with alerts for practice-changing updates [8]. Elliot et al. stated that end-users should be alerted as soon as possible about the date of the last search, details of the new evidence, whether or not the evidence has been incorporated into the review, and a transparent justification for this decision [19].

Regarding the frequency of update communication, Créquit et al. [7] proposed a frequency of 4–6 months for fast-paced evidence generation and 6–12 months for slow-paced. Tendal et al. used weekly periodicity [10], and Iannizzi et al. reported this as context dependent [11], while other authors recommend a maximum of 6 months [19]. The Cochrane guidance suggested monthly updates in the What's New table with a full LSR update every 4 months [9].

3.6. Revisiting living parameters

Five articles described the review components that should be reassessed periodically while a question is in "living mode", which include: search strategy [9–11], population, intervention, comparator, outcome (PICO) components of the question [9], outcome measures [11], and author team [1,9,19]. The Cochrane guidance recommended the reassessment of the aforementioned aspects once the question has been in "living mode" for 12 months [9].

Three studies reported on the timing and criteria for transitioning the question out of "living mode" [8,9,20] authors suggested using the same criteria that drive the decision to initiate an LE approach (Table SM2)

3.7. Protocol considerations for living evidence synthesis

Elliot et al. and the Cochrane guidance provide information on protocol considerations for LE synthesis [9,19] (Table 6). Both emphasize that an LSR should come from a methodologically rigorous SR, which should be taken as the "baseline review".

Three included articles recommended considering the project team membership and authorship as part of the LE synthesis planning phase and protocol. Authors encourage the participation of a project manager, an information specialist, and the number of reviewers necessary for completing screening, data extraction, and assessment efficiently [1,2,9]. Elliot 2014 and 2017 et al. propose that team members can join, contribute, and leave as needed, and once authors' contributions no longer fulfill criteria for authorship, they can be acknowledged as former contributors [1,19].

3.8. Preliminary checklist of methodological items for living evidence synthesis

Based on the aspects proposed in the included articles, we developed a list of items to be considered by authors when planning the conduction and report of LE syntheses (Table 7). This list can be used as a starting point for further developments and by interested reviewers.

Table 6. Protocol considerations for a living evidence synthesis

Protocol considerations	Reported by
Justification for the review/question being maintained in a living mode	Elliot 2017 [19]
Frequency of searches and screening	Elliot 2017 [19]
Time for incorporation of new evidence into review	Elliot 2017, Cochrane [9,19]
Planned statistical approach to updating MA	Elliot 2017 [19]
Use of technological enablers	Elliot 2017 [19]
Frequency to review the scope and methods (search methods and strategies)	Elliot 2017, Cochrane [9,19]
Thresholds and criteria for transitioning the question out of living mode	Elliot 2017, Cochrane [9,19]

Abbreviations: MA, meta-analysis.

4. Discussion

Our survey aimed to identify and summarize published methodological articles focused on developing and reporting an LE synthesis. To our knowledge, this is the first survey that summarizes the key methodological articles focused on the LE approach.

The high sensitivity of the searches carried out to identify methodological articles on the subject and the detailed review we performed on each of them allowed us to achieve an exhaustive review of the items that have been proposed to date to carry out evidence synthesis under the LE approach. We believe that the preliminary checklist derived from this exercise can be considered valid and exhaustive while new developments are published. It will be used to develop a framework to aid the development of trustworthy LE synthesis to inform health decisions.

As a result, we also identified key aspects in which there are opportunities to continue methodological research aimed at facilitating the development and publication of LE syntheses and update dissemination.

Authors of the included articles agreed on four well-established criteria that justify setting up an LE approach: i) when the question is a priority for decision-making, ii) when there is a low or very low certainty in the existing evidence, iii) when it is probable that new evidence likely to impact decisions or conclusion emerge, and iv) when feasible. Evidence arising from the COVID-19 pandemic checked all these boxes, but there are many other topics in which evidence is constantly changing and will benefit from this methodology (e.g., biological treatments for cancer).

Evidence surveillance is the key for the LE approach and is recommended as a process that should be established frequently depending on a high or low flow of evidence. Nevertheless, other factors such as practicality and feasibility based on time and personnel organizational resources should also be considered. To increase evidence monitoring efficiency, the correct indexation of SRs is crucial for their prompt identification by technological enablers and to facilitate evidence matrices creation [14].

The process of integrating new evidence and the criteria used for its implementation has important implications for the way evidence teams work. The LE approach involves incorporating new studies constantly or more frequently than a standard review. This process could change drastically if studies were available in formats that facilitated their use; for example, allowing automated data extraction and other artificial intelligence-supported tasks. In this regard, initiatives such as the open research data initiative proposed by the European Commission [15], which promotes individual research data availability through open-access registers, may contribute to the improvement and efficacy of evidence synthesis generation and to the implementation of LE approach to solve key questions.

Only 1 article focused on the statistical elements to be considered in an LE synthesis. It is worth highlighting that it has not been empirically proved that sequential MA yields better results than an updated MA. Controversial aspects of the statistical approach in LSRs, such as the implications of constant new data aggregation into the MA remain and necessitate further methodological research.

As LE syntheses persist during a continuous period, parameters such as the PICO question components must be revisited periodically to keep up with the current evidence. Nevertheless, re-examining the PICO components becomes more fundamental in broader rather than specific synthesis, as evidence on subgroups can vary during the monitoring process. In contrast, the focus of specific synthesis should rely on evaluating whether enough certainty in the results of the outcomes of interest already exists. Moreover, it is essential that global organizations (e.g., Cochrane, WHO) performing LE synthesis do not set aside a universal perspective when revisiting these parameters. A challenge for them will be to produce LE synthesis reports in a clear and structured manner so the knowledge user can identify the portions of evidence that are useful to them.

The LE syntheses require communicating new evidence in a prompt manner, regardless of whether it changes the conclusions. Thus, a heightened need emerges for an open access repository that easily identifies new available evidence, keeping users continuously up to date. This dynamic process will also require reassessing editorial criteria regarding authorship acknowledgment. Additionally, there is an urgent need to transform and streamline the editorial process by incorporating more flexible, dynamic, and

Table 7. Checklist of items to be considered when planning the conduction and report of living evidence syntheses

Checklist of items to be considered when planning the conduction and report of LE syntheses	Verification
Verifying the justification for the question to be included/maintained in living mode	
Is the problem addressed in the research question relevant for health decision-making?	☐
Is there an important level of uncertainty in the evidence for critical and important outcomes (e.g., low or very low certainty of evidence)?	☐
Is it probable that new evidence that may impact the conclusions will emerge?	☐
Are there (in your group) enough resources (financial, personnel, and time) available to maintain an LE approach for this question?	☐
Planning the living evidence (process and steps)	
Search strategy and evidence surveillance	
Include in the search strategy all relevant sources for the topic and for the living approach (e.g., bibliographic databases, trial registries, and web-based repositories)	☐
Define the frequency for: • Searching major bibliographic sources (e.g., bibliographic databases and trial registries) • Searching other sources (e.g., repositories, gray literature) • Screening search results	☐
Assign a qualified person/role in charge of: • Creating and maintaining the search strategy (e.g., an information specialist) • Performing the screening of search results • Assessing the eligibility of new evidence • Performing the RoB assessment of new eligible studies	☐
Define and describe the use or the "nonuse" of technological enablers for synthesis tasks (e.g., searching, screening, eligibility assessment, data extraction, and RoB assessment)	☐
Incorporation of new evidence	
For the incorporation of new eligible studies into the synthesis, define and/or describe: • The frequency (e.g., fixed interval schedule; as soon as new evidence emerges) according to the evidence flow and resources (feasibility) • The criteria (e.g., impact of new evidence on conclusions) • The process (e.g., who, when, and how the decision will be made) • The statistical approach and/or methods to be used for updating the MA	☐
Assign a qualified person/role in charge to assess the certainty of new evidence (i.e., after integration of new studies) for important outcomes (e.g., who will conduct the GRADE assessment)	☐
Revisiting living parameters	
For reviewing the following aspects during the living mode (search strategy; PICO components; outcome measures and author team required to continue performing the LE related tasks (e.g., searches, screening, selection) • Define the frequency • Describe the process to be followed	☐
Assign a qualified person/team/role in charge of revisiting living parameters and making the decisions	
For transitioning the question out of the "living mode": • Define the criteria/thresholds • Determine the frequency with which this review will be carried out	☐
Planning the updates communications and publication	
Update content	
Consider the inclusion of information related to the entire process planned above as part of the methods section of any report	☐
Consider recording and reporting the date of searches and dates of all other surveillance tasks (e.g., screening, data extraction, and RoB assessment).	☐
Plan to record the results of all searches during the living mode for their inclusion in the adapted PRISMA flow chart, including: • Identified references • Deduplicated references • Included references at title and abstract screening • Included references at full-text screening	☐

(*Continued*)

Table 7. Continued

Checklist of items to be considered when planning the conduction and report of LE syntheses	Verification
Define the information to be included as results in updates (e.g., date of the last search, details of the new evidence, whether or not the evidence has been incorporated/postpone incorporation into the synthesis and justification)	☐
Dissemination of updates	
Plan the report or publication of the "baseline synthesis" (e.g., actual/future publication; where it was/will be published, or results disseminated). If it has been done already, specify where it was published.	☐
Describe the plan to disseminate synthesis updates resulting from the evidence surveillance (e.g., when and how results are going to be disseminated or published/communication strategy)	☐
Describe how readers will be alerted of updates (e.g., social media, email communications to users, advanced information technology, etc.)	☐
Describe how publications, editorial and peer review processes for updates will be managed (e.g., agreement with a specific journal, including the published baseline report alongside the update)	☐

Abbreviations: LE, living evidence; RoB, risk of bias; GRADE, Grading of Recommendations, Assessment, Development and Evaluation system

transparent models that maintain quality and facilitate the immediate incorporation of peer-review comments and discussions. One example of an efficient proposal for this process is open research Europe, which facilitates postpublication peer review for both living and traditional evidence synthesis [16].

The LE approach sets a new paradigm by supporting organizations in health policy decision-making to produce less competitive and more collaborative work throughout a networking strategy, while avoiding duplication. The contribution of numerous authors from different backgrounds will likely enrich the production of evidence synthesis. Furthermore, this model brings us closer to recovering the primal sense of SRs, as it attempts to reduce the "mass production of redundant, misleading, and conflicted SRs" [17]. We echo the call made by authors [18] for researchers in all scientific fields, such as cardiology, oncology, dentistry, among others, to test the LE approach, as it should no longer be acceptable for evidence to be out of date, biased, or selective.

Some of our methods have potential limitations. First, our literature searches were limited to a 10-year period as the evolvement of LE synthesis and concepts have occurred mainly over the last decade. Of note, there were challenges in the search strategy due to the lack of suitable filters to identify methodological articles. Second, we did not assess the quality of the methodological articles included in this review due to the absence of quality assessment tools for this purpose.

5. Conclusions

Our survey reveals that there are basic methodological concepts that can drive the development of LE synthesis; nevertheless, specific aspects could be improved to help their authors.

The LE approach will eventually change the structure with which evidence syntheses are currently conducted toward a more open, transparent, efficient, and collaborative system in areas where evidence is rapidly changing.

There are many challenges that scientific journal editors face with this new way of updating evidence syntheses. It is time to rethink the editorial processes and move quickly to another model for disseminating evidence synthesis updates with minimal risks for the reliability of the information that is published.

Our survey enabled the generation of a preliminary checklist of items that can guide authors when planning the conduction and report of LE synthesis.

CRediT authorship contribution statement

Josefina Bendersky: Conceptualization; Data curation; Formal analysis; Investigation; Methodology; Project administration; Validation; Visualization; Roles/Writing - original draft; Writing - review & editing. **Ariadna Auladell:** Conceptualization; Data curation; Investigation; Methodology; Project administration; Validation; Roles/Writing - original draft; Writing - review & editing. **Gerard Urrútia:** Conceptualization; Validation; Roles/Writing - original draft; Writing - review & editing. **María Ximena Rojas-Reyes:** Conceptualization; Data curation; Formal analysis; Funding acquisition; Investigation; Methodology; Project administration; Supervision; Validation; Visualization; Roles/Writing - original draft; Writing - review & editing.

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Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jclinepi.2022.09.020.

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8.3 PROTOCOLOS PUBLICADOS

8.3.1 Bendersky J, Uribe M, Bravo M, Vargas JP, Villanueva J, Urrutia G, Bonfill X. Systematic mapping review of orthognathic surgery (protocol). Craniomaxillofac Trauma Reconstr. 2023;16:147-53. doi:10.1177/19433875221078385.

Review

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Systematic Mapping Review of Orthognathic Surgery (Protocol)

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Abstract

Study Design: This document details the planning phase of a systematic mapping review.
Objective: The objective of this mapping review is to identify, describe, and organize evidence currently available from systematic reviews and primary studies regarding different co-interventions and surgical modalities used in orthognathic surgery (OS) and their outcomes.
Methods: Systematic reviews (SRs), randomized controlled trials (RCTs), and observational studies that evaluate perioperative OS co-interventions and surgical modalities will be identified in an exhaustive search of MEDLINE, EMBASE, Epistemonikos, Lilacs, Web of Science, and CENTRAL. Grey literature will also be screened.
Results: Expected results include identification of all PICO questions available in the evidence regarding OS and generation of evidence bubble maps, involving a matrix of all identified co-interventions, surgical modalities, and outcomes presented in the studies. This will achieve identification of research gaps and prioritization of new research questions.
Conclusions: The significance of this review will result in a systematic identification and characterization of the available evidence, leading to a reduction in research waste and a guidance of future efforts in developing studies for unsolved questions.

Keywords
orthognathic surgery, mapping review, orthognathic co-interventions, orthognathic procedures, le fort surgery, sagittal split osteotomy

Introduction

Orthognathic surgery (OS), a widely used procedure to correct dentofacial deformities that affects 20% of the population,[1] involves surgical manipulation of facial skeletal elements.[1-6] The repositioning of maxillar and mandibular bones improves function, facial architecture,[7] facial harmony, and esthetics.[6,8] According to the American Association of Oral and Maxillofacial Surgeons (AAOMS),[5] conditions that indicate the need for OS include anteroposterior, vertical, or transverse discrepancies, asymmetries, dysfunctions, temporomandibular joint disorders, speech impairments, airway dysfunctions, and psychosocial disorders.[5] Although data is scant, the records of the American Dental Association (ADA) and the AAOMS[9] would indicate that the number of OS procedures performed each year is increasing; in 2007, for instance, 8755 OS procedures were performed in the USA.[9]

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8.3.2 Bendersky J, Zapata S, Uribe M, Pilar J, González C, Villanueva J, Souper R. Evidence gaps in orthognathic surgery: a Delphi study protocol. Int J Interdiscip Dent. 2023;16(2):169-71. doi:10.4067/s2452-55882023000200169.

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PROTOCOL

Evidence gaps in orthognathic surgery, a Delphi study protocol.

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ABSTRACT

Aim: To assess the research gaps identified in a recent mapping review of orthognathic surgery through their evaluation by clinical experts, leading to a clinically relevant list of research gaps. This will guide future investigations of the topic, focusing on the outcomes of blood loss, infection, and relapse. **Methods:** The Delphi technique will be used to appraise the identified research gaps. The expert panel will include maxillofacial surgeons who regularly perform orthognathic surgery. Potential participants will be identified through various methods, including contact information from articles in the mapping review, nominations from peers, and social media platforms. Two rounds of surveys will be undertaken with Likert-type and open-ended questions to assess the clinical relevance of research gaps. For the second round, participants will receive a report of the results of the first round. Questions will be modified depending on the answers obtained in the first round. A consensus of 60% will be considered valid. **Conclusions:** Through this Delphi study, in a collaborative effort between researchers and clinical experts, a comprehensive understanding of the clinical relevance of research gaps in orthognathic surgery will be achieved. The outcomes will guide future investigations, ultimately improving the outcomes and practices in this field.

KEY WORDS:

Delphi study; Orthognathic surgery; Evidence gaps; Mapping review; Research gaps; Maxillofacial surgery.

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INTRODUCTION

Orthognathic surgery (OS) is frequently used to treat dentofacial deformities that affect 20% of the population, such as skeletal discrepancies, asymmetries, airway dysfunctions, speech impairments, and temporomandibular disorders[1,2], restoring anatomic and functional relationships[3]. There has been an increase in the frequency of OS performed each year, reaching a total of 8755 OSs performed in the United States in 2007[4], concomitantly leading to an increase in the production of scientific literature on the subject. However, resolved research questions and specific topics continue to produce a high flow of both primary and secondary research, meanwhile, unresolved questions are not being addressed by researchers.

A recent mapping review that identified, described, and analyzed the available evidence on co-interventions and procedures in orthognathic surgery, revealed a series of research gaps that should be addressed to improve the outcomes of blood loss, infection, and relapse[5,6]. Yet, these knowledge gaps only portray what is available in the published literature but do not consider the views of clinicians who perform this procedure on a daily matter.

The objective of this Delphi study is to assess and compare the results provided in the mapping review through their appraisal by clinical experts in the subject. Therefore, by complementing the available literature with clinical appraisal, a thorough, clinically relevant, and pertinent list of research gaps will be exposed to help guide future investigations in orthognathic surgery.

METHODS

Justification for study design

This study will use the Delphi technique. We have chosen this design as it is the most appropriate to appraise research gaps identified in a mapping review of orthognathic surgery, consequently establishing the most essential research gaps in the literature assessed by clinicians, and guiding future investigations.

Research steering group

A research steering group will be formed to undertake this research. They will be responsible for preparing and circulating the content of the Delphi rounds. It will comprise investigators with backgrounds in general dentistry, oral surgery, maxillofacial surgery, and research methodology. The research steering group will not participate in the surveys; rather, they will supervise and monitor the process.

Selection and identification of the expert panel

Potential participants must be maxillofacial surgeons who perform orthognathic surgery in their daily practice. They will be identified by the following methods:

1. Extraction of contact information of corresponding authors of articles

8.4 ANEXO 4. OTRAS PUBLICACIONES DESARROLLADAS EN EL DOCTORADO

8.4.1 Martín C, Delgado I, Rojo R, Souper R, Véliz C, Salazar J, Díaz M, Cuéllar J, Dallaserra M, Bofill X, Bendersky J, Zapata S, Villanueva J. Risk of bias in dentistry-related randomized controlled trials in Spanish language journals. Int J Interdiscip Dent. 2023;16(2):137-41. doi:10.4067/s2452-55882023000200137

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ORIGINAL ARTICLE

Risk of bias in dentistry-related randomized controlled trials in spanish language journals.

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ABSTRACT

Objectives: To assess the risk of bias (RoB) of randomized controlled trials (RCTs) published in dental journals in the Spanish language. **Methods:** A systematic retrospective survey was conducted of all RCTs published from 1980 to 2019 in dentistry Spanish and Latin American journals. We extracted data and performed RoB assessments using the Cochrane Risk of Bias tool. **Results:** 292 RCTs published in 51 journals were included. The best-rated domains were incomplete outcome data, selective reporting, and other biases. The domains assessed with higher proportions of an unclear or high risk of bias were sequence generation, allocation concealment, and blinding of outcome assessment. There is a low proportion of RCTs published in Spanish language journals. However, the number has been increasing over the years, and the low risk of bias assessment rates across domains show an increasing trend. **Conclusions:** A low percentage of Spanish-language dental journals issue RCTs. Our assessment of these RCTs' RoB suggests higher difficulties in the design and conduction phase than in the posterior reporting stage.

KEY WORDS
Randomized clinical trial; Dentistry; Risk of bias; Reporting.

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INTRODUCTION

Randomized controlled trials (RCTs) are considered the best approach to assess the effects, benefits, and harms of therapeutic intervention, drug, device, or technique in human beings[1–3]. RCTs are also the foundation of systematic reviews and other evidence synthesis documents[4,5]. Evidence-based hierarchies place RCTs just below systematic reviews as the highest form of evidence[6,7] that could be achieved from an in vivo/clinical trial. RCTs are widely accepted as the "gold standard" for obtaining unbiased estimates of treatment effects[8]. However, the reliability of individual test conclusions depends largely on internal validity, based on the quality of the research methodology and execution 6. Therefore, high-quality reporting of the details of such research is essential[1,4,9].

RCTs can have weaknesses in the design or analyses that could lead to underestimating or overestimating the intervention; this is known as bias and can affect in any direction[10]. It is usually impossible to know the extent to which biases have affected a particular study's results. Consequently, to draw reliable conclusions, reviewers should consider the possible limitations of the studies, which relate to the extent to which their design, conduct, analysis, and presentation were appropriate to answer your research question[7,11]. Therefore, assessing the validity of included studies is a fundamental component of any systematic review and should influence the review's analysis, interpretation, and conclusions.

Many tools have been proposed to assess RCTs' quality in the context of systematic reviews or other evidence syntheses. Most of them are

8.4.2 Al-Sakkaf AM, Bonfill X, Ardiles-Ruesjas S, Bendersky-Kohan J, Solà I, Masia J. Risk of bias assessment of the randomised clinical trials and systematic reviews on surgical treatments for breast cancer-related lymphedema: a mapping review. J Plast Reconstr Aesthet Surg. 2023 May 6. doi:10.1016/j.bjps.2023.05.002

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Review

Risk-of-bias assessment of the randomized clinical trials and systematic reviews on surgical treatments for breast cancer-related lymphedema: A mapping review

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KEYWORDS
Evidence mapping;
Risk-of-bias assessment;
Breast cancer-related lymphedema

Abstract *Background:* Breast cancer treatment is the principal cause of lymphedema in the upper extremities. Breast cancer-related lymphedema (BCRL) treatments were previously based on conservative therapy; surgical treatments are alternative options that could be highly beneficial, especially for patients who are not responsive to conservative therapy. The main aim of this study was to describe and critically assess the risk of bias of randomized clinical trials (RCTs) and systematic reviews (SRs) on surgical treatment for BCRL.
Methods: We conducted an evidence mapping review according to the methodology proposed by Global Evidence Mapping (GEM). An update was done for our previous systematic search in MEDLINE, EMBASE, CENTRAL (Cochrane), and Epistemonikos from the year 2000 onward. We assessed the risk of bias for the RCTs and SRs using the RoB-2 and ROBIS tools, respectively.
Results: Two surgical RCTs and eight SRs were found among the 47 surgical studies that met the eligibility criteria. The overall risk-of-bias assessments of these studies were rated as some concerns (six outcomes) and high risk (three outcomes) for the measured outcomes among the RCTs and as a high risk of bias (five studies) and low risk (three studies) for the included SRs.

Abbreviations: BCRL, Breast cancer-related lymphedema; RCTs, Randomized control trials; SRs, Systematic reviews; GEM, Global Evidence Mapping; LVA, lymphaticovenular anastomosis; VLNT, vascularized lymph node transfers

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8.4.3 Salas GA, Lai SA, Verdugo-Paiva F, Requena RA. Platelet-rich fibrin in third molar surgery: systematic review and meta-analysis protocol. Craniomaxillofac Trauma Reconstr. 2022 Jun;15(2):164-8. 10.1177/19433875211016203.

Review

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SAGE

Platelet-Rich Fibrin in Third Molar Surgery: Systematic Review and Meta-Analysis Protocol

Gaston A. Salas, DDS[1,2], Shuheng A. Lai, DDS[1], Francisca Verdugo-Paiva, MSc[3,4], and Roberto A. Requena, OMFS[5,6,7]

Abstract

Objective: The objective of this systematic review is to assess the effectiveness and safety of platelet-rich fibrin (PRF) in third molar surgery.

Data Sources: A comprehensive search strategy is meant to be used in an attempt to identify all relevant randomized controlled trials (RCTs), ongoing investigation reported in specialty congresses and trials regardless of language or publication status (published, unpublished, in press and in progress). Searches will be conducted in the Cochrane Central Register of Controlled Trials (CENTRAL), PUBMED, Embase, Lilacs, the International Clinical Trials Registry Platform (ICTRP), ClinicalTrials.gov, US National Institutes of Health (NIH), grey literature and in specialized congresses and conferences.

Eligibility Criteria: We will include randomized trials evaluating the effect of PRF on wound healing after third molar surgery. Two reviewers will independently screen each study for eligibility, data extraction and risk of bias assessment using Cochrane "risk of bias" tool. We will pool the results using meta-analysis and will apply the GRADE system to assess the certainty of the evidence for each outcome.

Ethics and Dissemination: As researchers will not access information that could lead to the identification of an individual participant, obtaining ethical approval was waived.

Keywords

platelet-rich fibrin, third molars, wound healing, systematic review, protocol

Introduction

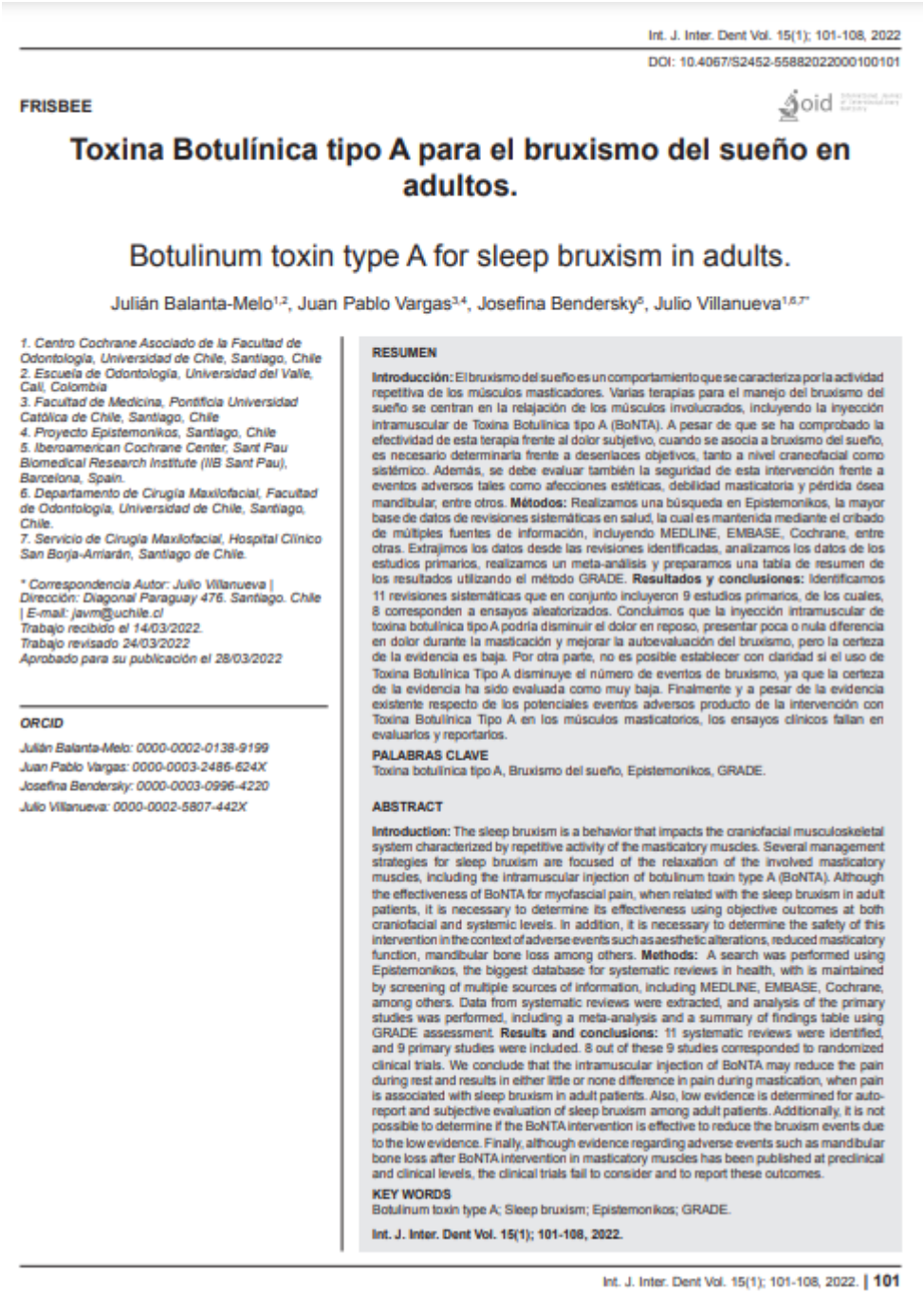
Third molars are completely developed usually between 17 and 26 years of age.[1,2] There are 3 common scenarios for third molar eruption: complete eruption reaching functionality, partial exposition of the crown or full inclusion. Prevalence of third molars impaction rounds 24%[3] which can be due to obstruction by another structure or abnormal path of development.[2] Specifically, impacted ones have been linked with diverse conditions such as pericoronitis, root resorption, periodontal disease, caries, cysts and tumors.[4] Diagnosis is generally made by a combination of clinical and radiographic assessment and its main course of treatment is surgical removal.[5]

In the last stages of the surgical procedure for third molars, the socket is prepared for healing in several ways. Standard care calls for socket conditioning and copious irrigation with saline solution, and closure by first or second intention. Multiple techniques have been proposed to

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8.4.4 Balanta-Melo J, Vargas J, Verdugo F, Bendersky J, Villanueva J. Toxina botulínica tipo A para el bruxismo del sueño en adultos. Int J Interdiscip Dent. 2022;15(1):101-8. doi:10.4067/S2452-55882022000100101.



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DOI: 10.4067/S2452-55882022000100101

FRISBEE

Toxina Botulínica tipo A para el bruxismo del sueño en adultos.

Botulinum toxin type A for sleep bruxism in adults.

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RESUMEN

Introducción: El bruxismo del sueño es un comportamiento que se caracteriza por la actividad repetitiva de los músculos masticadores. Varias terapias para el manejo del bruxismo del sueño se centran en la relajación de los músculos involucrados, incluyendo la inyección intramuscular de Toxina Botulínica tipo A (BoNTA). A pesar de que se ha comprobado la efectividad de esta terapia frente al dolor subjetivo, cuando se asocia a bruxismo del sueño, es necesario determinarla frente a desenlaces objetivos, tanto a nivel craneofacial como sistémico. Además, se debe evaluar también la seguridad de esta intervención frente a eventos adversos tales como afecciones estéticas, debilidad masticatoria y pérdida ósea mandibular, entre otros. **Métodos:** Realizamos una búsqueda en Epistemonikos, la mayor base de datos de revisiones sistemáticas en salud, la cual es mantenida mediante el cribado de múltiples fuentes de información, incluyendo MEDLINE, EMBASE, Cochrane, entre otras. Extrajimos los datos desde las revisiones identificadas, analizamos los datos de los estudios primarios, realizamos un meta-análisis y preparamos una tabla de resumen de los resultados utilizando el método GRADE. **Resultados y conclusiones:** Identificamos 11 revisiones sistemáticas que en conjunto incluyeron 9 estudios primarios, de los cuales, 8 corresponden a ensayos aleatorizados. Concluimos que la inyección intramuscular de toxina botulínica tipo A podría disminuir el dolor en reposo, presentar poca o nula diferencia en dolor durante la masticación y mejorar la autoevaluación del bruxismo, pero la certeza de la evidencia es baja. Por otra parte, no es posible establecer con claridad si el uso de Toxina Botulínica Tipo A disminuye el número de eventos de bruxismo, ya que la certeza de la evidencia ha sido evaluada como muy baja. Finalmente y a pesar de la evidencia existente respecto de los potenciales eventos adversos producto de la intervención con Toxina Botulínica Tipo A en los músculos masticatorios, los ensayos clínicos fallan en evaluarlos y reportarlos.

PALABRAS CLAVE
Toxina botulínica tipo A, Bruxismo del sueño, Epistemonikos, GRADE.

ABSTRACT

Introduction: The sleep bruxism is a behavior that impacts the craniofacial musculoskeletal system characterized by repetitive activity of the masticatory muscles. Several management strategies for sleep bruxism are focused of the relaxation of the involved masticatory muscles, including the intramuscular injection of botulinum toxin type A (BoNTA). Although the effectiveness of BoNTA for myofascial pain, when related with the sleep bruxism in adult patients, it is necessary to determine its effectiveness using objective outcomes at both craniofacial and systemic levels. In addition, it is necessary to determine the safety of this intervention in the context of adverse events such as aesthetic alterations, reduced masticatory function, mandibular bone loss among others. **Methods:** A search was performed using Epistemonikos, the biggest database for systematic reviews in health, with is maintained by screening of multiple sources of information, including MEDLINE, EMBASE, Cochrane, among others. Data from systematic reviews were extracted, and analysis of the primary studies was performed, including a meta-analysis and a summary of findings table using GRADE assessment. **Results and conclusions:** 11 systematic reviews were identified, and 9 primary studies were included. 8 out of these 9 studies corresponded to randomized clinical trials. We conclude that the intramuscular injection of BoNTA may reduce the pain during rest and results in either little or none difference in pain during mastication, when pain is associated with sleep bruxism in adult patients. Also, low evidence is determined for auto-report and subjective evaluation of sleep bruxism among adult patients. Additionally, it is not possible to determine if the BoNTA intervention is effective to reduce the bruxism events due to the low evidence. Finally, although evidence regarding adverse events such as mandibular bone loss after BoNTA intervention in masticatory muscles has been published at preclinical and clinical levels, the clinical trials fail to consider and to report these outcomes.

KEY WORDS
Botulinum toxin type A; Sleep bruxism; Epistemonikos; GRADE.

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8.4.5 Bravo Valenzuela M, Bendersky Kohan J, Uribe Monasterio M. Effectiveness of glucocorticoids in orthognathic surgery: an overview of systematic reviews. Br J Oral Maxillofac Surg. 2021;59(8):e1–e9. doi:10.1016/j.bjoms.2021.04.011.

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Review

Effectiveness of glucocorticoids in orthognathic surgery: an overview of systematic reviews

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Abstract

For decades, short-term glucocorticoids have been advocated to reduce postoperative swelling, pain, trismus, and nausea and vomiting in patients experiencing maxillofacial surgeries. The purpose of this systematic overview was to identify and assess the best evidence regarding the efficacy of glucocorticoid administration in patients who undergo orthognathic surgery. Five databases (Medline, Embase, The Cochrane Library, Web of Science, and Epistemonikos) were searched from their inception to October 2020. The risk of bias assessment was performed using the ROBIS tool, and the quality of the evidence reported was rated using the GRADE approach. Six systematic reviews were identified, of which three were included in this overview (n=527). According to the rating of the overall risk of bias, one achieved a low score and two were rated as high. The quality of the evidence reported ranged from very low to moderate. Corticoids may reduce the incidence of moderate or severe postoperative nausea and vomiting in the early postoperative period (0-6 hours) compared to metoclopramide, but the evidence is very uncertain. Some significant therapeutic effects on neurosensory recovery have been reported, but there was inconsistency across the studies. Finally, based on a moderate quality of evidence, it is possible to establish that the administration of glucocorticoids is likely to reduce oedema in the early postoperative period (0-48 hours) in patients who undergo orthognathic surgery, and to have no significant adverse effects. Further quantitative syntheses based on well-designed and standardised clinical studies are suggested to determine direction and strength of the intervention on the other outcomes.
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Keywords: Orthognathic surgery; Orthognathic surgical procedures; Glucocorticoids; Steroids

Introduction

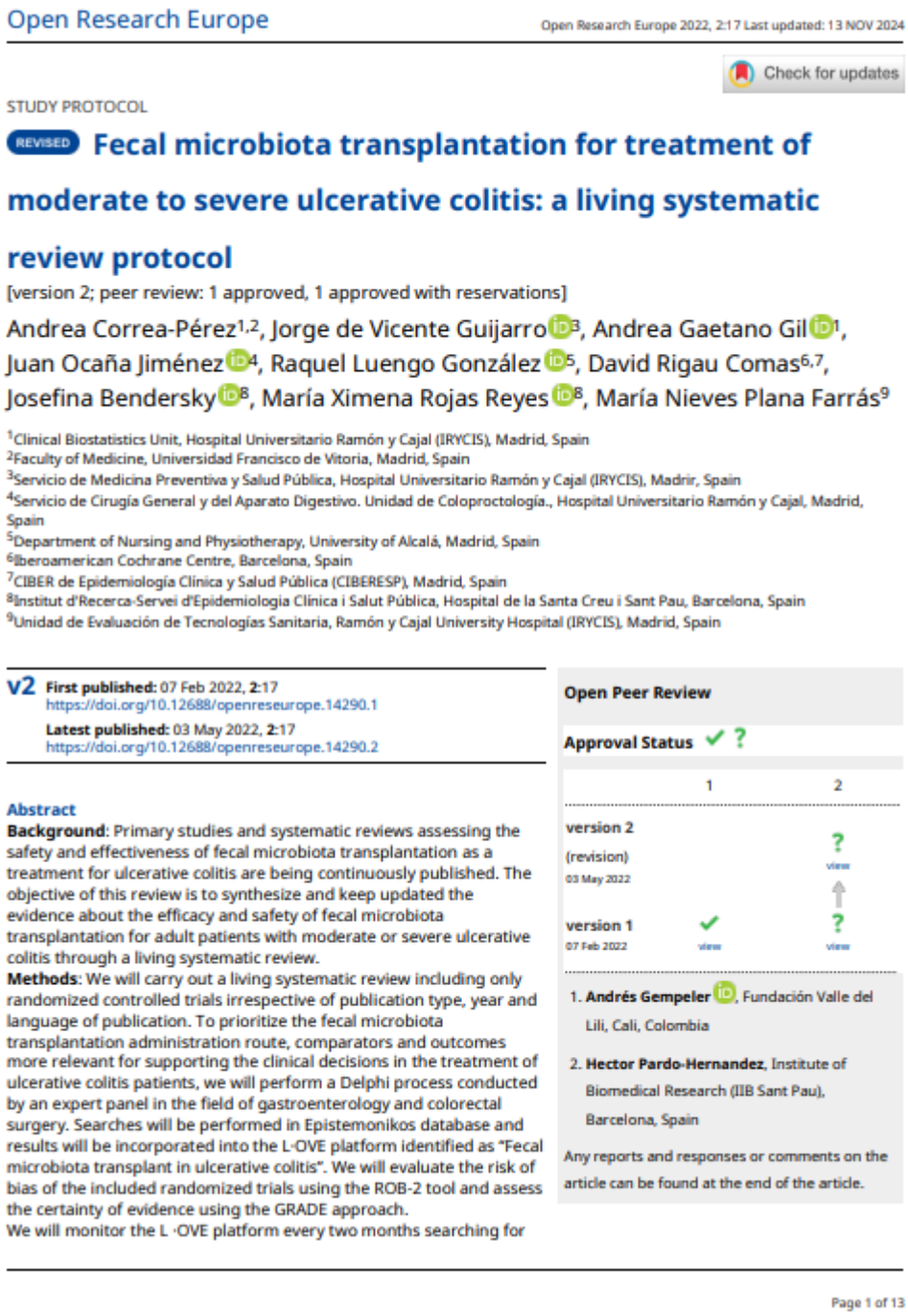
Currently, orthognathic surgery techniques are well-refined and reliable procedures that are used to achieve a harmonious jaw relation. Although it is a well-known safe intervention, it is not exempt from complications or inconveniences, or both,[1–3] and due to its highly traumatic characteristics, a long period of recovery is expected. Although inflammation is an essential biological process in wound healing, massive swelling is a significant problem, as it can compromise the airway, intensify pain, and delay recovery or disturb optimal outcomes.[4] Short-term high doses of glucocorticoids (CSs) have been advocated and used for decades to reduce postoperative pain, swelling, trismus, and nausea and vomiting in patients who have orthognathic surgery.[5,6] However, the ideal regimen remains contentious, as do certain effects regarding neurosensory disturbance and other consequences, largely due to the heterogeneity of the current literature and conflicting evidence.[4,7]

Evidence-based medical research is essential for the improvement of conscientious, judicious and reasonable

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8.4.6 Correa-Pérez A, de Vicente Guijarro J, Gaetano Gil A, et al. Fecal microbiota transplantation for treatment of moderate to severe ulcerative colitis: a living systematic review protocol Open Res Europe. 2022;2:17. doi:10.12688/openreseurope.14290.1.



Open Research Europe

Open Research Europe 2022, 2:17 Last updated: 13 NOV 2024

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STUDY PROTOCOL

REVISED Fecal microbiota transplantation for treatment of moderate to severe ulcerative colitis: a living systematic review protocol

[version 2; peer review: 1 approved, 1 approved with reservations]

Andrea Correa-Pérez[1,2], Jorge de Vicente Guijarro[3], Andrea Gaetano Gil[1], Juan Ocaña Jiménez[4], Raquel Luengo González[5], David Rigau Comas[6,7], Josefina Bendersky[8], María Ximena Rojas Reyes[8], María Nieves Plana Farrás[9]

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Abstract

Background: Primary studies and systematic reviews assessing the safety and effectiveness of fecal microbiota transplantation as a treatment for ulcerative colitis are being continuously published. The objective of this review is to synthesize and keep updated the evidence about the efficacy and safety of fecal microbiota transplantation for adult patients with moderate or severe ulcerative colitis through a living systematic review.

Methods: We will carry out a living systematic review including only randomized controlled trials irrespective of publication type, year and language of publication. To prioritize the fecal microbiota transplantation administration route, comparators and outcomes more relevant for supporting the clinical decisions in the treatment of ulcerative colitis patients, we will perform a Delphi process conducted by an expert panel in the field of gastroenterology and colorectal surgery. Searches will be performed in Epistemonikos database and results will be incorporated into the L·OVE platform identified as "Fecal microbiota transplant in ulcerative colitis". We will evaluate the risk of bias of the included randomized trials using the ROB-2 tool and assess the certainty of evidence using the GRADE approach.
We will monitor the L ·OVE platform every two months searching for

Open Peer Review

Approval Status ✔ ?

	1	2
version 2 (revision) 03 May 2022		? view
version 1 07 Feb 2022	✔ view	? view

1. **Andrés Gempeler**, Fundación Valle del Lili, Cali, Colombia

2. **Hector Pardo-Hernandez**, Institute of Biomedical Research (IIB Sant Pau), Barcelona, Spain

Any reports and responses or comments on the article can be found at the end of the article.

8.4.7 Auladell-Rispau A, Bendersky J, Santafé A, et al. Methods for living evidence synthesis: a systematic review protocol. Open Res Europe. 2021;1:113. doi:10.12688/openreseurope.14044.1.



Open Research Europe

Open Research Europe 2021, 1:113 Last updated: 13 NOV 2024

Check for updates

STUDY PROTOCOL

Methods for living evidence synthesis: a systematic review protocol

[version 1; peer review: 2 approved with reservations]

Ariadna Auladell-Rispau[1], Josefina Bendersky[2], Angie Santafe[2], Cecilia Buchanan[3], David Rigau Comas[4], Francisca Verdugo[5], Camila Ávila[5], Pablo Alonso[1,4,6], Gerard Urrutia[1,4,6], Gabriel Rada[5,7], María Ximena Rojas-Reyes[1,4]

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Abstract

Background: Living evidence (LE) refers to the methodological process that permits new research findings to be continually incorporated to evidence synthesis as they become available. This approach is of great value in the resolution of relevant and rapidly changing clinical questions. To date, the methods to carry out this type of synthesis are not completely defined, and great variability is observed in the approaches used by different groups of authors.
Objective: To identify and summarise the current methods used for living evidence synthesis.
Methods: We will conduct a systematic literature review of systematic reviews, overviews, and network metanalyses that have used "living evidence synthesis" as part of their methods. The search will be conducted in Medline (via PubMed) and the Epistemonikos database. Two reviewers will independently screen each article for eligibility, extract data, and assess the methodological quality standards of the study accordingly. This protocol is being registered in Prospero.

Keywords
Systematic review, Living Systematic Review, Evidence-based medicine, Evidence Synthesis, Living Evidence Synthesis, Living network metanalysis

Open Peer Review

Approval Status ✓ ✓

	1	2
version 2 (revision) 21 Mar 2022	✓ view	✓ view
version 1 28 Sep 2021	? view	? view

1. **Juan Erviti**, Navarre Health Service, Pamplona, Spain
2. **Nancy Santesso**, McMaster University, Hamilton, Canada

Any reports and responses or comments on the article can be found at the end of the article.

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