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**EFEITOS DAS GUIAS DE DESOCLUSÃO EM DISPOSITIVOS OCLUSAIS TOTAIS
NO TRATAMENTO DA DISFUNÇÃO TEMPOROMANDIBULAR E
BRUXISMO DO SONO: UMA REVISÃO SISTEMÁTICA**

Florianópolis

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Efeitos das guias de desoclusão em dispositivos oclusais totais no tratamento da disfunção temporomandibular e bruxismo do sono: uma revisão sistemática

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Orientadora: Prof^ª Dra. Beatriz Dulcineia Mendes de Souza

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O presente trabalho em nível de mestrado foi avaliado e aprovado por banca
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Florianópolis, 21 de outubro de 2020.

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“Educação não transforma o mundo,
Educação muda as pessoas.
Pessoas mudam o mundo.”

PAULO FREIRE

APRESENTAÇÃO

Esta revisão sistemática foi escrita originalmente sob a forma de artigo científico na língua inglesa, com o objetivo de ser submetido ao periódico *Journal of Oral Rehabilitation* em parceria com os pesquisadores, Luiza Pereira do Nascimento (doutoranda na Universidade Federal de Santa Maria), Lígia Figueiredo Valesan (mestranda na Universidade Federal de Santa Catarina), Cecília Doebber da Cas (mestranda na Universidade Federal de Santa Catarina), Patrícia Pauletto (doutoranda na Universidade Federal de Santa Catarina), Roberto Ramos Garanhani (mestre e Prof. da Universidade do sul de Santa Catarina), Eduardo Januzzi (Prof. Dr. da Faculdade de Tecnologia de Sete Lagoas), Leandro Augusto Hilgert (Prof. Dr. da Universidade de Brasília) sob coordenação de Beatriz Dulcineia Mendes de Souza (Prof^a Dra. da Universidade Federal de Santa Catarina).

RESUMO

Objetivo: Avaliar os efeitos dos diferentes tipos de guias de desocclusão utilizadas em dispositivos oclusais totais para o tratamento de disfunção temporomandibular (DTM) e controle de bruxismo do sono (BS).

Metodologia: A busca foi realizada em sete bases de dados principais e três bases de literatura cinzenta, além das referências dos artigos incluídos e contato com especialistas. Dois revisores realizaram, de maneira cegada, a leitura dos artigos em duas fases. A análise do risco de viés foi realizada por meio do Joanna Briggs Institute Critical Appraisal e a qualidade da evidência acessada através do Grading of Recommendations Assessment, Development and Evaluation.

Resultados: 15 artigos foram incluídos na síntese qualitativa. A guia canino (GC) foi a mais estudada (n=12), seguida da oclusão balanceada bilateral (OBB) (n=3), guia molar (n=1), função em grupo (n=1) e guia anterior (n=1). O uso de GC, quando comparado a placa placebo ou ausência de tratamento, apresentou melhorias dos desfechos dor, atividade muscular e conforto. Além disso, diminuição do índice de DTM, aumento da amplitude de abertura bucal e melhora na qualidade do sono também foram observados em pacientes que utilizaram dispositivos com GC, quando comparados aos que não receberam tratamento. No entanto, na comparação realizada entre as placas com diferentes guias (GC, OBB e guia molar) não houve diferença estatística nos desfechos de índice de DTM, nível de dor e atividade muscular. Devido a grande heterogeneidade clínica e metodológica encontrada nos estudos primários não foi possível realizar metanálise. Três estudos apresentaram alto risco de viés, seis moderado e seis baixo risco.

Conclusão: Com base nas limitações encontradas nessa RS sugere-se que as guias avaliadas parecem não desempenhar uma função fundamental na melhora dos desfechos avaliados. Além disso, GC e BBO parecem causar efeitos similares em pacientes com BS e DTM. Recomenda-se a realização de mais estudos que avaliem todos os tipos de guias aqui reportados, a fim de aumentar o nível da evidência.

Palavras-chave: Revisão Sistemática, Placas Oclusais, Bruxismo do Sono, Síndrome da Disfunção da Articulação Temporomandibular.

ABSTRACT

Aim: Evaluate what are the effects of different disocclusion guide on occlusal splints (OS) on Temporomandibular Disorder treatment and Sleep Bruxism control.

Methods: A search was conducted on seven electronic main databases and three databases of gray literature. The list of references of included articles was also checked and experts were contacted. Risk of bias of included articles was assessed through Joanna Briggs Institute Critical Appraisal Checklist. The level of evidence was determined by Grading of Recommendations Assessment, Development and Evaluation.

Results: Fifteen studies were included on qualitative synthesis. Canine guide (CG) was the most studied (n=12), followed by bilateral balanced occlusion (BBO) (n=3). Molar guide (n=1), group function (n=1) and anterior guide (n=1), were reported. CG showed better results when compared with placebo splint or absence of treatment on pain levels, muscle activity and comfort. Improvements on TMD index, mouth opening and sleep quality were also observed in patients wearing devices with CG, when compared with those who did not receive treatment. However, when comparing splints with different guides (CG, BBO and molar guide) there was no statistical difference on TMD index, pain level and muscle activity. Due to high clinical and methodological heterogeneity found between eligible studies, it was not possible to perform a meta-analysis. Three studies had a high risk of bias, six moderate and six low risk.

Conclusion: It is suggested that evaluated guides do not appear to perform a fundamental role on improving assessed outcomes. In addition, CG and BBO appear to cause similar effects in patients with SB and TMD. Accomplishment of further studies is recommended to assess all types of guidance reported, in order to increase the level of evidence.

Keywords: Systematic Review, Occlusal Splint, Sleep Bruxism, Temporomandibular disorders.

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LISTA DE ABREVIATURAS

BS.....	Bruxismo do Sono
DTM.....	Disfunção Temporomandibular
GC.....	Guia canino
MA.....	Metanálise
OBB.....	Oclusão Balanceada Bilateral
RS.....	Revisão sistemática

Do artigo em inglês:

BBO.....	Bilateral balanced occlusion
CG.....	Canine guidance
EMG.....	Electromyography
M.....	Mean
NRCT.....	Nonrandomized clinical trial
OS.....	Occlusal splint
PRISMA.....	Preferred reporting items for systematic reviews and meta-analysis
PROSPERO.....	Prospective Register of Systematic Reviews
PS.....	Placebo splint
PSQI.....	Pittsburgh Sleep Quality Index
RCT.....	Randomized clinical trials
RMS.....	Root mean square
SB.....	Sleep Bruxism
SD.....	Standard deviations
SR.....	Systematic Review
TMD.....	Temporomandibular disorder
vs.....	Versus

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1 INTRODUÇÃO

O Bruxismo do Sono (BS) afeta aproximadamente de 1,1% a 15,3% da população adulta, enquanto sua prevalência entre adolescentes e crianças varia de 3,5% a 49,6% (MELO et al., 2019). Caracteriza-se por movimentos mandibulares gerados a partir de um aumento da atividade muscular dos músculos do sistema estomatognático (LOBBEZOO et al., 2018). O BS é classificado como um hábito comportamental em indivíduos saudáveis. Os métodos de detecção dessa condição são divididos em instrumentais e não-instrumentais (LOBBEZOO et al., 2018). As medidas não-instrumentais consistem no relato positivo do paciente e/ou de uma pessoa próxima a respeito da emissão de sons durante o sono e caracteriza a detecção como possível (LOBBEZOO et al., 2018). Ao adicionarmos ao relato do paciente, a realização de um exame físico, passamos a ter uma detecção provável de BS (SVENSSON et al., 2016; LOBBEZOO et al., 2018). Os métodos instrumentais, fornecem uma detecção definitiva de BS, e sua realização acontece através do exame de polissonografia (LOBBEZOO et al., 2018).

Outra condição orofacial comum que acomete aproximadamente de 5 a 12% (<https://www.nidcr.nih.gov/research/data-statistics/facial-pain>) da população mundial é a Disfunção Temporomandibular (DTM), caracterizada pela Academia Americana de Dor Orofacial como um termo “guarda-chuva” utilizado para definir um conjunto de sinais e sintomas relacionados às estruturas do sistema estomatognático (DE LEEUW e KLASSER, 2008). O diagnóstico de DTM é baseado em exame físico e anamnese do paciente, e algumas diretrizes foram estabelecidas pela Associação Americana de Dor Orofacial, a fim de aumentar a homogeneidade entre os diagnósticos (DE LEW & KLASSER, 2008). Em 1992 foi desenvolvido um critério para a utilização no diagnóstico em pesquisas com essa condição denominado “Research Diagnostic Criteria for Temporomandibular Disorders (RDC/TMD)”. Em 2014 esse critério passou por uma atualização, onde o eixo psicossocial dessa condição ganhou uma posição de destaque a partir da qual foi elaborada o “Diagnostic Criteria for Temporomandibular Disorders (DC/TMD)” (SCHIFMAN et al., 2014). Além disso, o diagnóstico de DTM pode ser realizado de acordo com o índice de Helkymo, o qual possui três eixos, a avaliação do primeiro acontece por meio de anamnese, o segundo através de exame clínico, onde é realizada uma análise das estruturas do sistema estomatognático, e o terceiro através de análise oclusal (da CUNHA et al., 2007).

Devido a etiologia multifatorial do BS e da DTM, e principalmente, a associação dessas condições a fatores psicossociais (SCHIFFMAN et al., 2014; MANFREDINI et al., 2017; LOBBEZOO et al., 2018), múltiplas abordagens terapêuticas podem ser consideradas (MANFREDINI et al., 2015; SU et al., 2018). No entanto, o uso de dispositivos oclusais rígidos e lisos, que envolvem toda a arcada dental têm sido considerada, uma vez que trata-se de uma abordagem minimamente invasiva que pode ser eficaz na redução de sinais de sintomas de BS e DTM (MANFREDINI et al., 2015; SU et al., 2018; AL-MORAISSEI et al., 2020).

O mecanismo de ação dos dispositivos oclusais ainda não é completamente compreendido, mas sabe-se que eles são responsáveis por promover uma relação mais estável às estruturas da articulação temporomandibular (ATM), além de proteger os tecidos dentais de desgastes ocasionados pela atrição e promover uma oclusão ideal (OKESON, 2008). Além disso, alguns autores apontam diminuição transitória da atividade muscular dos músculos mastigatórios, redução no quadro algíco do paciente, melhora na qualidade de vida e qualidade do sono (CONTI et al., 2006; ALAJBEG et al., 2014; ROSAR et al., 2017; CÂMARA-SOUZA et al., 2019).

As guias de desocclusão estabelecidas nas placas oclusais podem variar, dentre elas a Guia Canino (GC), Oclusão Balanceada Bilateral (OBB), função em grupo, guia molar e guia anterior (SOLOW, 2013). A GC é caracterizada pela desocclusão dos dentes posteriores, guiado pelos caninos durante os movimentos de lateralidade, nos lados de trabalho e balanceio, enquanto na BBO são mantidos contatos bilaterais em todos movimentos excêntricos. Já a função em grupo é caracterizada pelo contato entre pelo menos um dente posterior, além dos caninos, no lado de trabalho (OKESON et al., 2008). Os dispositivos confeccionados com guia anterior são caracterizados pela desocclusão dos dentes posteriores guiada pelos dentes anteriores durante os movimentos protrusivos (OKESON et al., 2008). Na guia molar a desocclusão dos dentes ocorre através dos segundos ou primeiros molares (ITO et al., 1986).

Ensaio clínico vêm sendo realizados na tentativa de avaliar os efeitos dessas diferentes guias em pacientes com BS e/ou DTM. Alguns autores não encontraram diferenças significativas na diminuição da dor ou do índice de DTM ao comparar duas placas com diferentes esquemas de desocclusão (BORRROMEO et al., 1995; CONTI et al., 2006; AL-RAFAH et al., 2014), outros apontam pequena diminuição na atividade muscular dos

músculos masseter e temporal quando da utilização de GC (WILLIAMSON e LUNDQUIST, 1983).

Algumas revisões sistemáticas (RS) foram desenvolvidas buscando elucidar quais os efeitos dos dispositivos oclusais no tratamento de BS e DTM (JOKUBAUSKAS et al., 2017; AL-MORAISSI et al., 2020; EBRAHIM et al., 2012). No entanto, até o momento, não foi realizada uma RS a respeito de qual desenho de guia de desocclusão é mais efetivo no tratamento de DTM e BS. Portanto, nosso estudo possui como objetivo responder a seguinte pergunta de pesquisa: “Qual o efeito das guias de desocclusão em dispositivos oclusais totais no tratamento de DTM e controle de BS?”

2 JUSTIFICATIVA

Os dispositivos interoclusais totais são uma das modalidades de manejo amplamente utilizada no tratamento de DTM e BS (MANFREDINI et al., 2015; SU et al., 2019). Apesar dos inúmeros estudos publicados com essa temática, ainda não há um consenso sobre qual seu exato mecanismo de ação e o seu papel na redução de sinais e sintomas dessas duas condições. As guias de desoclusão e seus efeitos nos pacientes têm sido estudada por alguns autores (ITO et al., 1986; BORROMEO et al., 1995; AL-RAFAH et al., 2014; CONTI et al., 2006; WILLIAMSON e LUNDQUIST, 1983). No entanto, ainda não foi realizada uma revisão sistemática a respeito dos efeitos dos tipos de guias de desoclusão utilizadas em dispositivos oclusais.

3 OBJETIVOS

3.1 Objetivo geral

Revisar sistematicamente e avaliar criticamente os efeitos das diferentes guias de desoclusão (guia canino, oclusão balanceada bilateral, função em grupo, guia molar e guia anterior) utilizadas nos dispositivos interoclusais no tratamento de DTM e BS.

3.2 Objetivos específicos

- verificar qual o tipo de guia mais estudada;
- verificar se há alteração no quadro algico de pacientes com BS e DTM;
- verificar se há alteração dos quadros de cefaleia;
- verificar se há alteração nos ruídos articulares e na amplitude de abertura bucal;
- verificar se há alteração no índice de DTM;
- verificar se há alteração na força de mordida;
- verificar se há melhora na qualidade do sono e no conforto dos pacientes;
- verificar se há redução da atividade dos músculos do sistema estomatognático.

4 ARTIGO

Effect of different disocclusion guides of occlusal splint on temporomandibular disorders and sleep bruxism: a systematic review

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ABSTRACT

Background: Occlusal splints (OS) were widely approach used for temporomandibular disorders (TMD) and sleep bruxism (SB).

Aim: Assess what are the effects of different disocclusion guide on OS on treatment of TMD and SB control.

Methods: Search was conduct on seven electronic main databases and gray literature. Risk of bias (Rob) was assessed through Joanna Briggs Institute Critical Appraisal Checklist. Grading of Recommendations Assessment, Development and Evaluation approach was used to determine the level of evidence.

Results: Among 2,603 papers, 15 were eligible to include on qualitative synthesis. Canine guide (CG) was the most studied (n=12), followed by bilateral balanced occlusion (BBO) (n=3). CG showed better results when compared with placebo splint or absence of treatment on pain levels, muscle activity and comfort. Improvements on TMD index, mouth opening and sleep quality were also observed in patients wearing devices with CG, when compared with those did not receive treatment. However, when comparing splints with different guides (GC, OBB and molar guide) there was no statistical difference on TMD index, pain level and muscle activity. Three studies had a high Rob, six moderate and six low. The quality of the evidence was considered very low in majority outcomes.

Conclusion: It is suggested the evaluated guides do not appear to perform a fundamental role on improving assessed outcomes. In addition, CG and BBO appear to cause similar effects in patients with SB and TMD. Accomplishment of further studies is recommended to assess all types of guidance reported, in order to increase the level of evidence.

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Key Words: Systematic Review, Occlusal Splint, Sleep Bruxism, Temporomandibular Disorders.

1. INTRODUCTION

Sleep Bruxism (SB) affects approximately 3,5% to 49,6% of the young population and 1,1% to 15,3% of adults.¹ This condition is characterized by mandibular movements which result in an increase of stomatognathic muscles activity during sleep.² Additionally, temporomandibular disorder (TMD) is a common orofacial condition that affects approximately 5 to 12% of world's population³ and is characterized by the American Academy of Orofacial Pain as an "umbrella", term to define a set of signs and symptoms related to stomatognathic system structures.⁴

Due to the multifactorial etiology of SB and TMD above all, the association of these conditions with psychosocial factors,^{2,5,6} multiple approaches might be considered in their management.^{7,8} However, the use of hard occlusal splints (OS) has been considered a minimally invasive approach that can be effective in reducing signs and symptoms of SB and TMD.^{7,8,9}

The OS action mechanism is not completely explained but, until this moment, these devices are responsible for promoting a stable relationship among the temporomandibular joint structures, as well as to protect dental tissues from wear caused by attrition and to promote an ideal occlusion.¹⁰ In addition, some authors relate a temporary decrease in muscle activity, pain reduction, besides improvements on both life and sleep quality.^{11,12,13,14} The OS design range according to the type of disocclusion guide, such as the canine guidance (CG), bilateral balanced occlusion (BBO), anterior guidance¹⁵ and molar guidance.¹⁶

Studies have been carried out attempting to evaluate the effects of different OS designs,^{11,17,18,19,20,21,22} however, the results remain controversial. Systematic Reviews (SRs) were developed to assess OS effects in the management of SB and TMD.^{9,23,24,25} However, to the best of our knowledge, none SR has been carried out considering the most effective disocclusion guidance for SB and TMD signs and symptoms reduction, muscle activity

decrease and sleep quality improvement. Therefore, this SR aims to answer the following question: “What are the effects of different disocclusion guides of OS on the SB and TMD?”

2. METHODS

2.1 Protocol and registration

This SR was carried out in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyzes (PRISMA).²⁶ The protocol was prepared in accordance with PRISMA-p²⁷ and registered in the “International Prospective Register of Systematic Reviews” (PROSPERO)²⁸ under number CRD42020169797.

2.2 Eligibility criteria

Randomized controlled trials (RCT), nonrandomized clinical trials (NRCT), and before and after studies which investigated OS effects with different guidance in adolescents (12-18 years old), adults and older adults with SB and/or TMD were included in this study. The comparison can occur between CG, BBO, group function, molar guide, anterior guide, placebo or no therapy. This SR included studies of all languages, with no restrictions regarding gender sample, nor time of publication.

P	Adolescents, adults and elderly.
I	Occlusal Splints with disocclusion guide (CG, BBO, group function, molar guide and anterior guide).
C	Occlusal Splints with disocclusion guide (CG, BBO, group function, molar guidance and anterior guidance), placebo or no therapy.
O	<ol style="list-style-type: none"> 1) Mouth opening; 2) TMJ sounds; 3) Pain alteration; 4) Headache; 5) TMD index (according to Helkymo dysfunction index or RDC/TMD); 6) Sleep quality; 7) Splint comfort; 8) Masticatory muscle activity; 9) Bite force.
S	Randomized clinical trials, nonrandomized clinical trials and before and after studies.

2.3 Exclusion criteria

The following exclusion criteria were applied: **1)** studies not performing clinical examination as diagnostic criteria for TMD; **2)** studies not performing instrumental or non-instrumental for SB; **3)** studies not performing follow up for at least seven days; **4)** studies with samples with diagnostic for sleep disturbance, exception for bruxism; **5)** studies that used prefabricated or partially occlusal splints; **6)** studies that used other therapies for SB and TMD management; **7)** studies that included patients with comorbidities; **8)** studies that included edentulous patients; **9)** studies that used only imaging methods to assess outcomes; **10)** studies that did not report the disocclusion guidance of OS; **11)** studies that did not perform selected outcomes; **12)** studies that did not assess sleep quality with validated questionnaires; **13)** studies with same sample; **14)** reviews, letters, books, conference abstracts, cases reports, case series, animal studies, opinions articles, technique articles, posters and guidelines; **15)** full-text not available.

2.4 Information sources and search

The search strategies were performed in the following databases: Cochrane, Embase, Latin American and Caribbean Health Sciences Literature (LILACS), LIVIVO, PubMed (including MedLine), Scopus and Web of Science. Additional search was performed in gray literature (Google Scholar, OpenGrey and ProQuest Dissertation and Thesis). All searches were conducted on April 10th 2020 (Appendix 1). Furthermore, manual searches were also carried out on reference lists of the included manuscripts. Field experts were consulted to improve the research findings, following the recommendations of Greenhalgh and Peacock.²⁹ Reference management software (EndNote X8, Thomson Reuters, Philadelphia, USA) was used to collect references and delete duplicates.

2.5 Study selection

The selection process was carried out in two phases. In phase one, two reviewers (A.C.D. and L.P.N.) independently analyzed titles and abstracts of all identified references and applied the eligibility criteria. In phase two, the same authors applied the eligibility to the full-text studies. A third author (L.V.) was consulted to make a final decision in both phases if any disagreement arose. An online software (Rayyan[®], Qatar Computing Research Institute, Qatar)³⁰ was used to facilitate the study selection process.

2.6 Analysis and data collection

Data of the study were collected independently in duplicate through a previously formulated table by two reviewers (A.C.D. and L.P.N.). Any controversies were discussed and decided by the third reviewer (L.F.V.). The data not found in the articles were requested for each author by e-mail. If at first the reviewers did not get an answer, they requested contact for more three consecutive weeks. In case of absence, if it was possible, data were collected by the authors of this SR. The descriptive characteristics are recorded in table 1

2.7 Risk of Bias in individual studies (RoB)

Two reviewers (A.C.D. and L.P.N.) performed the risk of bias analysis separately and judged the articles included through the Joanna Briggs Institute Critical Appraisal Checklist according to study design (RCT, NRCT).^{32,32} The studies were judged according to: 1) low risk of bias (RoB), if the “yes” score of the studies reached more than 70%; 2) moderate RoB, if “yes” scores ranged between 50% and 69%; and 3) high RoB, if “yes” scores were below 49%.³³ Figures were generated by software RevMan 5.3 (Review Manager 5.3, The Cochrane Collaboration).

2.8 Study outcomes and summary measures

Data were reported in accordance to each outcome, continuous variables (mouth opening, pain, TMD index (TMDi), masticatory muscle activity, bite force and sleep quality) were reported through means (M) and standard deviations (SD). Furthermore, outcomes

expressed with dichotomous variables (TMJ sounds, headache and splint comfort) were reported by percentage.

2.9 Synthesis of results

Qualitative analyses were carried out with regard to effects of disocclusion guidance of OS for TMD and SB management. Due to the impossibility of direct comparison between studies because high sample heterogeneity, we clustered included articles according to comparison. Firstly, we reported OS (CG or BBO) *vs* no treatment, then OS (CG, BBO or anterior guide) *vs* Placebo Splint and finally papers that compared different kinds of disocclusion guidance to each other (CG, BBO, group function and molar guide).

Initially, metanalysis (MA) was planned, however, due to methodological heterogeneity, such as study design, diverse follow-up time, condition of interest (SB and TMD) and different outcomes, it was not possible to perform a quantitative synthesis.

2.10 Confidence in cumulative evidence

The evidence overall quality was assessed using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) criteria. The findings summary was generated using online software (GRADEpro GDT; the GRADE Working Group).³⁴ The following domains were considered: risk of bias, inconsistency, indirectness, imprecision, and others (publication bias).

3. RESULTS

3.1 Study selection

Search in the main databases identified 6,053 citations. In the gray literature were identified 117 studies. After removing duplicates, 2,603 citations remained from the first phase. In the second phase, 63 articles were selected by the two reviewers for full-text reading, among them, 48 were excluded (each manuscript exclusion reason is available on supplementary table 2) and 15 were included in qualitative synthesis. Additional search was

performed on the reference list of the included manuscripts, however no study was selected. A flowchart summarizing the systematic selection process is presented in Figure 1.

3.2 Studies characteristics

In relation to the study design, five NRCT,^{13,14,35,36,37} four RCT^{11,38,39,40} and six before and after studies^{12,18,22,41,42,43} were selected. The sample size ranged from eight³⁷ to eighty participants⁴⁰, accounting a total of 580 participants, of which approximately 66,9% were female and the sample age ranged between 14-73 years. The follow-up time ranged from one week(w)³⁷ to six months(m).^{11,12} Regarding location, the studies were carried out in USA,^{37,41} Israel,³⁵ Singapore,⁴² Brazil,^{11,13,14,22,43} England,³⁸ Croatia,^{12,36} China^{39,40} and Saudi Arabia¹⁸. With regards to condition of interest only two studies assessed SB,^{14,37} while 10 evaluated TMD^{11,18,22,35,36,38,39,40,41,43} and three studies selected participants with SB and TMD.^{12,13,42}

3.3 Risk of bias within studies (RoB)

RoB in individual manuscripts was performed through JBI check list according to study design. One³⁸ RCT study was judged with high RoB levels, while one¹¹ showed low and two^{39,40} moderate risk. On NRCT studies, three^{13,14,35} were judged with low and two^{36,37} with moderate RoB. On before and after studies, two^{18,42} were judged with high RoB while, two^{12,22} with low risk and the latest two^{41,43} with moderate risk. RoB graphs of NRCT and before and after studies are available on figures 2a and 2b. For RCT RoB graphs are represented on figure 3a and 3b. Detailed information on the RoB assessment is available on supplementary tables 2a and 2b.

3.4 Results of individual studies

Fifteen articles were included in the qualitative synthesis, among them the CG was the most investigated, appearing in thirteen of the included articles,^{11,12,13,18,22,35,36,37,39,40,41,42,43} followed by the BBO, which was assessed on four studies.^{11,14,18,22} Two other guidances were evaluated by one manuscript each one, anterior guide³⁸ and molar guide.³⁷ Aiming to make a

detailed results description, the raw data for each included article are presented on supplementary table 3.

3.4.1 Occlusal Splint vs no treatment

In this subgroup, seven studies that evaluated occlusal devices with CG were arranged.^{12,13,37,41,42,43,44} Among them, four manuscripts selected participants with TMD^{37,41,42,44} and three studies included a sample with SB and TMD.^{12,13,43}

Articles that evaluated only TMD patients, when pain levels were assessed through a 0 to 3 scale, showed significant improvements on pain ($p=0,01$)⁴² after four weeks of therapy. Whereas pain assessed through Visual Analogue Scale (VAS), authors that evaluated TMJ pain showed eliminated pain on 42,4% of TMJ, however, insufficient data were presented to conclude if this change was significant.³⁷ Furthermore, a second study showed a significant decrease ($p<0,001$) on VAS between before ($3,22\pm 2,52$) and after 8 weeks ($0,69\pm 1,25$)⁴⁴ of therapy with CG.

When masseter muscle activity was assessed, authors reported decrease on EMG levels on rest position in participants using OS with CG when compared with TMD patients that did not receive treatment, ($p<0,01$).⁴¹ Additionally, after three months of therapy, EMG values in TMD group wearing OS with CG showed similar EMG levels to a third group without TMD.⁴¹ It was observed reduction on TMDi scores after three months of therapy in all participants with TMD who wore OS with CG.⁴¹ Comfort was assessed on patients with TMD wearing OS with CG, and 67% of patients reported improvements with OS use.³⁷

Regarding mouth opening, there was a mean increase of 5.3 mm between before and after four weeks of treatment ($p<0,01$).⁴² In addition, patients wearing CG showed improvements on sleep quality assessed through Pittsburgh Sleep Quality Index (PSQI) ($p=0,04$).⁴⁴

In relation to patients with SB, measures on bite force found significant ($p=0,0003$) increase on right side when patients wearing devices with CG were compared with patients without SB that did not receive treatment.¹³

Three manuscripts included samples with SB and TMD,^{12,13,43} one of them reported significantly reduced pain on palpation ($p<0,05$), after three months of OS therapy with CG⁴³. Similarly, authors of a before and after study, found a significant decrease on VAS ($p<0,001$) in participants wearing a canine guide,¹² moreover, it was observed an improvement on pain levels upon waking on SB participants after 2 months of wearing OS with CG ($p=0,0025$).¹³ Two studies assessed mouth opening on patients wearing devices with CG, and showed an improvement on 80% of participants.⁴³ Similar results were found on a second trial,¹² which observed improvement on maximal mouth opening ($p=0,003$) and on maximal assisted mouth opening [myofascial pain group ($p<0,001$); disc displacement group ($p=0,006$)] after 6 months of therapy. In relation to magnitude of bite force, there was a significant increase ($p=0,003$) in patients with SB, nevertheless, these patients showed improvement in sleep quality measured through PSQI ($p=0,0006$).¹³

3.4.2 Occlusal Splint vs Placebo Splint

Six studies performed a comparison between occlusal device and placebo splints (PS).^{11,14,36,39,40,41} OS with CG was evaluated on four studies,^{11,36,40,41} while BBO was assessed by two studies^{11,14} and only one assessed anterior guide³⁹.

Decreased on pain levels was found in the group using CG ($30,24\pm 32,19$) when compared to PS ($4,75\pm 17,23$), ($p=0,0083$).³⁶ Two RCT reported similar results, as significant reduction on VAS was found on patients that wore CG ($p<0,05$)¹¹ and decreased on pain levels in patients wearing a OS with CG [baseline ($49,0\pm 16,1$); 1 month ($12,0\pm 10,2$)].⁴⁰ One manuscript assessed VAS on participants wearing OS with anterior guide and reported improvements with no significant differences between the patients wearing PS.³⁹ In relation to

BBO, the authors found significant decrease on VAS on participants that wore OS with BBO ($p=0,064$) when compared with PS.¹¹

Muscle activity was evaluated through electromyography activity (EMG) at mandibular position and showed that the devices with CG use when compared with participants wearing PS promoted a significant decreased ($p<0,01$) in amplitude index (RMS values) after one month of therapy, which can indicate a relief on fatigue muscle.⁴⁰ Furthermore, in relation to joint sounds, no significant differences ($p>0,05$) were found between disocclusion guidances evaluated (CG and BBO) in comparison with PS.¹¹

Improvements on sleep quality was observed in patients that wore OS with BBO [baseline ($7,13\pm3,87$); 60 days ($5,87\pm3,23$)], however, no significant difference was found in relation to patients wearing a PS [baseline ($7,00\pm2,56$); 60 days ($5,00\pm2,62$)].¹⁴

Regarding passive mouth opening, authors reported that patients wearing PS and OS with CG presented an increase in amplitude, but without a statistically significant difference among groups.³⁶ Likewise, when the same outcome was assessed on patients wearing OS with anterior guidance and placebo splints, the authors found improvements with no significant difference between groups.³⁹

Comfort was assessed by one study that reported 67% of improvements on patients wearing OS with CG and BBO, independent of disocclusion guidance.¹¹ When headache was evaluated, the authors found a decrease on episodes percentage per week [baseline (39%); 21 weeks (31%)] on patients wearing OS with anterior guide³⁹.

3.4.3 Different type of disocclusion guidances

Among the included studies, three perform a direct comparison between two different disocclusion guidance type.^{18,22,38} One evaluated CG and BBO¹⁸, a second article assessed CG vs molar guide³⁸ and third evaluated CG and group function²². TMDi was evaluated by two studies^{18,38} and showed a decrease on index after using OS. However, there was no significant

difference between the guides evaluating CG vs molar guide ($p=0,654$)³⁸ and CG vs group function [3 weeks ($p=0,102$); 3 months ($p=0,146$)].¹⁸ Regarding to pain, participants that wore molar guide had improvements, but with no significant difference in relation to patients that wore CG ($p=0,221$).³⁸ Muscle activity was assessed in two studies,^{22,38} when evaluated CG vs molar guide³⁸ no significant difference ($p=0,578$) was found on EMG levels between the guidance types. However, on a manuscript that evaluated CG vs group function, it was reported that significant decrease ($p<0,05$) was on EMG levels of Temporalis muscle.²²

3.5 Synthesis of results

A summary of results according to the outcomes can be found on figure 4.

3.5.1 Pain

Eleven studies^{11,12,13,36,37,38,39,40,42,43,44} assessed pain. On patients wearing OS with CG all authors suggested a decrease on pain,^{11,12,13,36,37,38,40,42,43,43} including studies comparing OS with CG and placebo splint.^{11,36,40} However, when comparing molar guide and CG, no significant difference on pain levels was found.³⁸ In relation to pain on palpation, findings showed improvements after treatment with CG.⁴³ Similarly, on patients that used same disocclusion guidance, improvements on pain upon waking was reported on SB patients.¹³ Furthermore, among patients wearing anterior guidance it was reported improvements on pain levels, but with no statistical difference when compared to placebo splint. The use of occlusal device with BBO showed significant improvements on pain level in one clinical trial.¹¹

3.5.2 Maximal mouth opening

Maximal mouth opening was evaluated by five studies,^{12,36,39,42,43} among them, three evaluated patients wearing devices with CG and reported improvements after treatment.^{12,42,43} The authors who measured OS with CG and anterior guide showed no significant improvements when compared to placebo splint.^{36,39}

3.5.3 Temporomandibular joint sounds

Presence of TMJ sounds was evaluated by four studies.^{11,37,39,43} Regardless of the guidance types (CG and BBO),¹¹ there was no significant difference between the patients assessed before and after treatment.¹¹ Moreover, two other authors^{37,43} assessed joint sounds on device with CG and reported no changes on click during reassessment. When evaluating anterior guide, findings showed some decrease on joint sounds, but with no significant difference in relation to patients that used placebo splint.³⁹

3.5.4 Headache

One study evaluated percentage of episodes per week on patients with TMD wearing OS with anterior guide and reported a decrease in headache episodes, when compared with patients that used placebo splint.³⁹

3.5.5 Temporomandibular disorder index (TMDi)

TMDi was evaluated on three studies^{18,41,38} of which two carried out comparisons between two different guidance types.^{18,38} The article that evaluated devices with CG and MG reported no significant differences between the guidance types.³⁸ The same was reported when evaluating OS with CG and BBO, findings showed TMDi decrease on patients that used both splints with no significant differences among the disocclusion guides.¹⁸ Moreover, the use of device with CG showed improvements on TMDi levels in relation to patients that did not receive treatment.⁴¹

3.5.6 Muscle activity

Four studies assessed muscle activity.^{22,38,40,41} Among them, studies that compared molar guide with CG³⁸ or group function with CG²² showed decrease on EMG values with no significant difference between disocclusion guide. However, on a study that compared devices with CG and absence of treatment, there was EMG levels improvement with significant difference between patients who used splint.⁴¹ Similar improvements were observed when comparing patients wearing device with CG and placebo splints.⁴⁰

3.5.7 Bite force

Was observed increased on bite force in patients with SB that wearing OS with CG when compared with participants without SB that no receive treatment¹³.

3.5.8 Sleep quality

Sleep quality was assessed by three studies^{13,14,44} through PSQI and ESS. It was found significant improvements on SB participants that wore devices with CG in relation to patients did not present SB and did not receive treatment.¹³ Similar findings were reported when OS with BBO was compared with placebo splint.¹⁴ One study evaluated participants with TMD and found some sleep quality increase when using device with CG.⁴⁴

3.5.9 Splint comfort

Two clinical trials^{11,37} assessed splint comfort. One of them wore splint with CG and BBO and 67% of patients related improvements on comfort independent of the disocclusion guidance available.¹¹ While, authors that assessed OS with CG found improvements on comfort of patients that used this splint when compared with participants that did not present TMD³⁷.

3.6 Confidence in cumulative evidence

The GRADE was done according to selected outcomes (pain, maximal opening, joint sounds, headache, TMD index, muscle activity, bite force, sleep quality and splint comfort). The confidence in cumulative evidence was very low for the following outcomes: pain, maximal opening, joint sounds, headache, TMD index, muscle activity, sleep quality and splint comfort; and moderate for bite force. The domains that downgrade certainty were the Rob of included studies (-1 point), the inconsistency (-2 points), due to de high methodological and clinical heterogeneity among studies; the indirectness evidence (-1 point), as some studies did not perform this outcomes like a primary outcomes and the imprecision (-1 point), due to absence of sufficient described data for judgment confidence intervals and a

presence of small sample (<400) in all studies. The publication bias was not detected, due to the broad search strategy including gray literature. Complementary information from GRADE evaluation can be found on table 2.

4. DISCUSSION

This SR investigated effects of different disocclusion guide of occlusal splints (OS) on TMD and SB management. Occlusal devices with hard and smoothness surfaces are the only therapy considered a standard reference on SB management⁷ besides being a treatment widely indicated for TMD⁸. It is a non-invasive therapy, does not cause side effects to patients²⁶ and it is considered accessible to clinical and also to patients. However, until this moment have a lack of information regarding the the most appropriate disocclusion guide to be used on OS.

In this SR, five types of guidances were studied. Devices with canine guide (CG), in which, disocclusion of posterior teeth occurs through canines on work and nonworking side, were the most studied guide. This guide promotes a more stable relationship among teeth structures, since as during excursion movements, the loads are transmitted to canines, teeth anatomically prepared to receive them.¹⁰ The bilateral balanced occlusion (BBO) was characterized by maintain of bilateral balanced contact between anterior and posterior teeth during all mandibular movements. The presence of contacts on posterior teeth appears to protect TMJ of overload caused by tooth clenching¹⁶. Furthermore, was related OS with group function, characterized by contact between at least one posterior teeth besides canine, on work side, during lateral movements, these contacts on posterior teeth appear equalize muscle activity²². Molar guidance was characterized by teeth disocclusion guided through first or second molars¹⁶. On devices with anterior guidance disocclusion of posterior teeth occur guided by anterior teeth during protrusive movements.

Besides the different kinds of disocclusion guidances, different comparisons were found among the fifteen eligible studies included. In order to facilitate data interpretation, we

clustered results according to the type of comparison carried out in each study: occlusal splint vs no treatment, occlusal splint vs placebo splint and different types of disocclusion guidances.

Among studies that compared participants wearing OS with participants that did not receive treatment^{13,36,39} or performed before and after studies^{12,40,42,43} only canine guide (CG) was investigated. Some included studies evaluated SB and TMD on patients^{12,13,42} while others studies appraised only TMD.^{36,40,41,43} Therefore, the absence of SB^{36,40,41,43} and/or awake bruxism assessment may have influenced the results. Although there is not enough evidence regarding the association with bruxism and TMD,¹ both types of bruxism can promote an overload on stomatognathic system structures contributing to perpetuation of signs and symptoms of TMD.⁴⁵

In general, participants with only TMD and those with TMD and SB associated, showed significant improvements on outcomes pain levels, muscle activity, TMDi, mouth opening and sleep wuality when wearing OS with CG and perform a compartsion with no-treatment group. Canine guide can promote a stable positioning for TMJ and adjacent structures²⁵ and improved the distribution of load on TMJ during clenching and grinding.⁴⁵ The occlusal stability promoted by devices an normalize the proprioception of periodontal ligament and relieve symptoms, such as dental sensitivity,²⁵ besides promoting an increase on patient comfort.¹⁵ On patients wearing OS with CG were observed reduction on pain levels^{36,41,43} and muscle activity⁴⁰ as well as increase on mouth opening amplitude⁴² and sleep quality^{13,43} were observed. However, we cannot attribute these good results only with the presence of CG, since there was no comparison with other types of guides. The positive effect may be due to the presence of the device itself, independent of disocclusion guide.

Furthermore, in our SR five included articles performed a comparison between OS (with CG and/or BBO) with placebo splints (PS).^{11,14,35,37,38} This device involves palatal and

vestibular surfaces of dental arch and presented a design without coverage at occlusal surface,¹¹ in an attempt to control the placebo effect⁴⁶ assigned by OS. Studies that performed CG^{11,35} and BBO¹¹ with placebo devices, showed significant improvements on pain levels in relation to participants wearing a PS. Reduction on muscle activity with CG in one month was observed and can be attributed to a possible decrease on bite force during lateral movements caused by this guide.^{17,36} However, these results should be interpreted with caution, since the authors evaluated only one guidance type. Beneficial effects may be caused again due to presence of OS and not attributed only to disocclusion guidance. In the same studies^{11,14,35,37,38} that evaluated joint sounds,¹¹ mouth opening³⁵ and sleep quality¹⁴ improvements were observed, however, with no significant difference in relation to control group, independent of guidance type (CG^{11,35} and BBO^{11,14}). The absence of significant improvements on mouth opening can be attributed to fact that studies have used OS such as stand-alone therapy.⁴⁷ Furthermore, although SB and sleep stages are correlated, the use of OS appear did not influence sleep parameters,⁴⁸ such as found in our results.¹⁴

In study that evaluated anterior guide, findings showed improvements on joint sounds, pain level and mouth opening, however, with no significant difference in relation to PS.³⁸ These results suggest that anterior guide was unnecessary on OS design. In addition, it is important to highlight disocclusion guidance on lateral movements were not described by the authors.³⁸

The appropriate study design in order to evaluate effects of disocclusion guides was randomized clinical trials. The inclusion of an adequate control group wearing placebo splint, and more than one experimental group with different kinds of disocclusion guidances are necessary. This study design would enable us to perform a lot of comparisons including among guidance types. In our SR, studies that were included evaluate two types of guidance with each other,^{18,22,37} however absence of control a group was a limitation in these studies.

The finding showed no significant difference between the guides evaluated (molar guide,³⁷ group function²² and BBO¹⁸ and CG^{18, 22, 37}) on TMD index, pain levels and muscle activity.

The results found on our SR highlight the importance of wearing OS on management of TMD and SB. Although the OS can contribute with reducing signals and symptoms of these conditions, the development of personalized therapies, through phenotyping of patients,⁴⁸ in addition to multimodal approach, such as physical therapy, self-management and counseling are widely recommended.^{49,50} Our results suggested the disocclusion guidances evaluated on lateral movements (CG, BBO, group function and molar guide) appear to be an effective choice to use on OS. Since these guidances showed similar improvements on signs and symptoms evaluated. In order to facilitate procedure occlusal adjustment and optimize clinical time, it is suggested that BBO guides and group function may be feasible options to be used on OS.

Findings on our SR may be interpreted with caution since the quality of evidence assessed was very low on majority outcomes (pain, maximal mouth opening, joint sounds, headache, TMD index, muscle activity, sleep quality and splint comfort). High and moderate Rob achieved on some studies included, besides high inconsistency among studies that made it impossible to perform MA. Serious imprecision, assigned to small sample size and an absence of sufficiently described data to analyze imprecision through confidence interval.

4.1 Limitations

Heterogeneity of study design, large amount of variations on follow up time, absence of accurately described raw data and absence of adequate control group, are some limitations of this study. For future studies, the development of better conducted randomized clinical trials with control groups wearing placebo splint is suggested. Moreover, high heterogeneity also observed among conditions of interest (SB and TMD). It is suggested for future studies

the sample included patients with similar conditions, as well as a diagnosis of awake bruxism in order to control this condition. Also is recommended TMD diagnosis in accordance to subtypes, since the results found can be limited according to the type of TMD studied due to the only use of OS like a therapy. It is important highlight the lack of available evidence about all guidance types. Due to it, it is suggested that more studies be carried out with canine guidande, bilateral balanced occlusion, group function, molar guides and anterior guide.

5. CONCLUSION

Thus far, despite the low quality of evidence available in relation to kind of disocclusion guidance, we suggest that both canine guide and bilateral balanced occlusion perform a similar role in relation to TMD and SB management. However, it is recommended that more randomized clinical trials be carried out with canine guide, bilateral balanced occlusion, group function, molar guide and anterior guide.

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Table 1. Summary of descriptive characteristics of included articles (n=15).

STUDY	SAMPLE		MATERIALS AND METHODS				MAIN FINDINGS	
Author, Year, Country	Size/ Gender	Age (mean±SD)	Type of guidance	Group Allocation	Diagnostic criteria (SB/TMD)	Follow-up	Outcomes	Results/Conclusions
Okeson, 1982 USA	Final n=33 (30F) Drop-out n=0	Overall 14-60y (32±NR)	Canine guide	Participants were evaluated before and after treatment	TMD Clinical examination	4w	-Mouth opening -Pain (0-3)	63% of participants showed improvement in pain scores. The mean decrease was 4.4 (p<.01). 84.8% of participants showed an increase in maximal mandibular opening, however, the increase of 1.7 mm was not statistically significant.
Rugh, 1989 USA	Initial n=10 (8F) Final n=8 (6F) Drop-out n=2	Overall 23-46y	Canine guide (CG) and molar guide (MG)	GI- firstly wore CG (7 to 14d); after used MG (7 to 14d) GII- firstly wore MG (7 to 14d); after used CG (7 to 14d)	SB EMG and Clinical Examination	7 to 14d	-Pain (eight-point Likert Scale) -Muscle activity (EMG) -TMD index (according to HDI ₀)	The two appliances provided nearly equivalent effects on nocturnal bruxism in seven of eight subjects. Clinical examination and subjective pain ratings did not differ with the two guidance patterns.
YAP, 1998 Singapore	Final n=21 (15F) Drop-out n=0	Overall 23-63y (39±NR)	Canine guide	Participants were evaluated before and after treatment	SB (n=21) Clinical Examination _b TMD (n=14) Clinical Examination _c	3m	-Mouth opening -TMJ sounds (clicking) -Tenderness on palpation (muscle and TMJ)	With the exception of TMJ clicks, stabilization appliance with canine and bilateral balanced guidance is effective in eliminating the signs of TMD evaluated.

Gavish, 2002 Israel	Final n=37 (29F) Drop-out n=0	Overall 16-45y EG (30.3±9.12) CG (27.5±6.65)	Canine guide	Experimental group (EG) - Michigan splint n=21 (16F) Control group (CG) - placebo splint n=16 (13F)	TMD RDC/TMD	8w	-Mouth opening - Pain (VAS)	At the end of the experiment, the EG had a statistically significant reduction in pain intensity and in mean muscle sensitivity to palpation compared with no change in the controls. A stabilization splint has a therapeutic value beyond its placebo effects.
Landulpho, 2004 Brazil	Final n=22 (15F) Drop-out n=0	Overall 18-53y (NR)	Canine guide and bilateral balanced occlusion _d	Canine guide - 0-30d of therapy n=22 (NR) Group function - 90-150d of therapy n= 22 (NR)	TMD NR	T1) 90d T2) 120d T3) 150d	-Muscle activity (EMG)	Occlusal splint with group function disclusion caused a shorter EMG activity when compared with the canine guidance in rest position for the anterior temporalis muscle.
Conti, 2006 Brazil	Initial n=60 (55F) Final n=57 (52F) Drop out 3	Overall 14-73y GI (28,9±NR) GII (31,3±NR) GIII (29,5±NR)	Bilateral balanced occlusion and canine guide	GI Bilateral balanced occlusion GII Canine Guidance GIII Placebo splint	TMD RDC/TMD	T1) 7d T2)15d T3) 1m T4) 3m T5) 6m	-Joint sounds -Pain (VAS) -TMJ tenderness -Muscle tenderness_e -Comfort	The type of lateral guidance did not influence the subjects' improvement. All of the subjects had a general improvement on the VAS, though subjects in the occlusal splint groups had better results that did subjects in the non-occluding splint group.
Wassell, 2004 England	Initial n=93 Final n=78 (69F) Drop-out n=21	Overall 19-65y Control group 35.9±10.3 Stabilization splint	Stabilization splint Anterior guide Placebo splint	Stabilization splint n=21 (NR) Control splint n=27 (NR) Cross-over_f n=13 (NR)	TMD IHS and AAOP	T1) 3w T2) 6w T3) 12w T4) 21w	-Mouth opening -TMJ sounds (clicking) -Pain (VAS) -Number of tender muscles_e -TMJ tenderness	At 6 weeks, patients that wearing a control and stabilization splints had similar improvements for all outcome variables with no significant differences between groups.

37.9±12.6

-Headache

Wassel, 2006 England	Initial n=72 (63F) Final n=52 (NR) Drop-out n=40	Overall 19-65y Females 37.7±11.9y Males 35.1±8.7y	Stabilization splint Anterior guide Control splint Placebo splint	Stabilization splint n=27 (NR) Control splint n=12 (NR) Cross-over_f n=13 (NR)	TMD IHS and AAOP	T1) 3w T2) 6w T3) 12w T4) 21w T5) 1y	-Mouth opening -TMJ sounds (clicking) -Pain (VAS) -Number of tender muscles_e -TMJ tenderness -Headache	81% of participants rated treatment as either good or excellent in reducing jaw pain. Improvements after initial treatment were maintained at one year for all outcomes, except for TMJ clicking, which returned to pretreatment levels.
Badel, 2008 Croatia	Final n=65 (49F) Drop-out n=0	GI - disc displacement 35.5±NR GII - control 23.4± NR	Canine guide	GI -disc displacement n=40 (31F) GII - without clinical symptoms and signs of TMD n=25 (18F)	TMD RDC/TMD and MRI	3 to 6m	-TMJ pain (VAS) -Comfort	Michigan splint eliminated pain in 42.4% of TMJs, in 35.6% of TMJs pain was eliminated with the joint sound still present, and pain was still present in 22% of TMJs. Comfort: 67% of patients regularly used the Michigan splint, declared carrying the splint was comfortable.
Zhang, 2013 China	Final n=36 (24F) Drop-out n=0	Overall 16-57y GA 31.4±9.0 GB 31.3±8.3	Canine guide	Group A (GA)- stabilization splint n=18 Group B (GB)- placebo splint n=18	TMD RDC/TMD	1 month	-Pain (VAS) -Muscle activity (EMG)	GA: 89% patients showed reductions in subjective pain and pain upon pressure on masseter muscle, as well as increased mouth opening after the treatment, out of which 39% showed complete recovery and 50% showed clinical improvements.

								GB: 22% of patients had a spontaneous improvement
Alajbeg, 2014 Croatia	Final n=30 (23F) Drop out n=0	Myofascial pain (MP) 19-63y (39.4±13.11) Disc displacement (DD) 21-63y (34.7±14.13)	Canine guide	MP n=14 (11F) DD n=16 (12F)	Bruxism IB (based on clinical examination and self-report) TMD RDC/TMD	T1) 1m T2) 3m T3) 6m	-Mouth opening -Pain (VAS)	Significant improvements were observed on pain after the use of occlusal splint with canine guidance in both groups MP and DD.
Al-Rafah, 2014 Saudi Arabia	Final n=16 (0F) Drop out n=0	Overall 32-50y (NR)	GI - Canine Guide GII - Bilateral balanced occlusion	The groups were allocated according to splint design	TMD Clinical examination according to HDI	T0) Baseline T1) 3w T2) 3m	-TMD index (according to HDI)	Significant improvement in TMD symptoms in GII after three months of using the different occlusal design stabilizing splint
Vilanova, 2014 Brazil	Initial n=57 (NR) Final n=50 (50F) Drop out n=7	Overall 26.7±7.1	Canine guide	Participants were evaluated before and after treatment	TMD TMD/RDC	8w	-Pain (VAS) -Sleep quality (PSQI)	Higher pain levels before the stabilization device therapy. Sleep Quality: (ESS) 32% of participants presented excessive daytime sleepiness in baseline. After treatment, ESS total score reduced and 82% of these participants no longer experienced excessive daytime sleepiness. (PSQI) values also were reduced after treatment, with 68% of participants being classified as good

								sleepers.
Rosar, 2017	Initial	Overall	Canine guide	CG - without SB	SB	T1) 1m	-TMD index (according	Decrease in perception of pain in mandibular region upon awakening was observed in SB during treatment, while it remained stable in GC. SBG showed an increase in the bite force magnitude, while in CG these parameters did not differ. SBG showed an increase in the sleep quality indexes, while in GC these parameters did not differ.
Brazil	n=56 (NR)	19-30y (NR)		n=15 (11F)	Self-report;	T2) 2m	to RDC/TMD)	
	Final	Control group (CG)		SBG	clinical examination;		-Sleep quality (PSQI)	
	n=43 (34F)	1.6±1.7		n=28 (23F)	polysomnography exam.		-Bite force (gnatodynamometer)	
	Drop out	Sleep bruxism group (SBG)			TMD			
	n=13	22.6±2.7			RDC/TMD			
He, 2019	Final	Overall	Canine guide	Control group (CG)	TMD	3m	-TMD index (according	The EMG values in E1 decreased significantly for all the muscles at rest and on anterior/lateral movements, post-treatment.
China	n=80 (42F)	18-22y		- no TMD	RDC/TMD		to HDI)	
	Drop out	(NR)		C1 - occlusal splint			-Muscle activity (EMG)	
	n=0			n=34 (8F)				
				n=17 (NR)				
				C2 - no splint				
				n=17 (NR)				
				Experimental group (EG) - TMD				
				n=46 (34F)				
				E1 - occlusal splint				
				n=23 (NR)				
				E2 - no splint				
				n=23 (NR)				

Câmara-Souza, 2019 Brazil	Initial n=37 (NR)	Overall 20-45y	Bilateral balanced	CG - placebo n=15 (8F)	SB Clinical examination according to AASM	T1) 30d T2) 60d	-Sleep Quality (PSQI)	Subjective sleep quality had improved after 30d of using both occlusal and palatal device.
	Final n=30 (17F)	Control group (CG) 32.0 ±6.7	occlusion	EG - occlusal splint n=15 (9F)				
	Drop out n=7	Experimental group (EG) 29.0 ±5.1						

Legend: M, male; F, female; y, years; d, days; IHS, International Headache Society; AAOP, American Academy of Orofacial Pain RDC/TMD, Clinical Diagnostic Criteria for TMD; G, group; DC, Diagnostic Criteria; SB: Sleep Bruxism; TMD, temporomandibular disorder; m, months; w, weeks; TMJ, Temporomandibular Joint; EMG, electromyography; VAS, Visual Analog Scale; IB, bruxism individual index; PSQI, Pittsburgh Sleep Quality Index; HDI, Helkymo Clinical; Dysfunction Index; AASM, American Academy of Sleep Medicine; TMI, Temporomandibular Index; MRI, Magnetic resonance imaging; NR, not reported.

Explanations

- Clinical examination: masticatory muscles, TMJ, mandibular range of motion, and TMJ noises. Relative changes in the severity of the clinical symptoms were estimated using the first four categories of the Helkimo Dysfunction Index;
- SB diagnosis based on: Self-report; generalized incisal and occlusal tooth wear; tooth facets that meet in extreme eccentric mandibular movements; presence of mucosal and/or lateral tongue ridging;
- TMD diagnosis based on: Restricted range of mandibular motion; TMJ clicking; periauricular TMJ tenderness; tenderness of masseter, temporalis and sternocleidomastoid muscles;
- All patients received splints with Canine Guidance at begin, at 30th day the authors change the guide for group function;
- Muscle tenderness performed by authors: Masseter (origin, body and insertion); Deep masseter; Temporalis (anterior, medium and posterior);
- Cross over Group: 13 subjects in the control group were relocated to the stabilization splint group in the 12weeks of treatment.

Table 2. Summary of findings by “Grading of Recommendations Assessment, Development and Evaluation” (GRADE).

“Effect of different disocclusion guide of Occlusal Splint on Sleep Bruxism and Temporomandibular disorders: a systematic review”

Patient or population: Adolescents, adults and elderly with TMD and/or SB

Setting: “What is the effect of different OS disocclusion guides on the SB and TMD?”

Intervention: Occlusal Splints with disocclusion guide (canine guidance, anterior guidance, bilateral balanced occlusion, group function, molar guidance)

Comparison: Occlusal Splints with disocclusion guide (canine guidance, anterior guidance, bilateral balanced occlusion, group function, molar guidance) placebo or no therapy

Certainty assessment							Certainty
No of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	
Pain							
10	RCT; NRCT; before and after	serious ^a	serious ^c	not serious	serious ^b	none	⊕○○○ VERY LOW
Mouth opening							
5	RCT; NRCT; before and after	serious ^a	serious ^c	serious ^d	serious ^b	none	⊕○○○ VERY LOW
Muscle activity							
4	RCT; NRCT; before and after	serious ^a	serious ^c	not serious	serious ^f	none	⊕○○○ VERY LOW
Bite force							
1	NRCT	not serious	not serious	not serious	serious ^f	none	⊕⊕⊕○ MODERATE
TMD index							
4	RCT; NRCT; before and after	serious ^a	serious ^c	serious ^e	serious ^f	none	⊕○○○ VERY LOW
Joint Sounds							
3	RCT; before and after	serious ^a	serious ^c	serious ^e	serious ^f	none	⊕○○○ VERY LOW
Comfort							
2	RCT; NRCT	serious ^a	serious ^c	serious ^e	serious ^f	none	⊕○○○ VERY LOW
Headache							
1	RCT	serious ^b	serious ^d	serious ^e	serious ^f	none	⊕○○○ VERY LOW
Sleep quality							

Certainty assessment							Certainty
No of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	
3	NRCT; before and after	serious ^a	serious ^c	not serious	serious ^f	none	⊕○○○ VERY LOW

Legend: RCT, randomized clinical trial; NRCT, non-randomized clinical trial

Explanations

- a. some studies presented high risk of bias, when Rob check list was applied;
- b. some studies presented moderate risk of bias, when Rob check list was applied;
- c. was observed high heterogeneity between studies designs, as well as among sample and in relation to methodology;
- d. there was a change in some patients from the control group to group that received treatment;
- e. this outcome was not assessed firstly in some studies;
- f. absence of enough data described on articles that enable to judgment this criteria, and small sample size (>400).

Supplementary table 1. Articles excluded and the reasons for exclusion (n=48).

	Author, year	Reasons for exclusion*
1.	Abekura, 1995	3
2.	Ahmed, 2016	10
3.	Alajbeg, 2003	14
4.	Alkan, 2009	10
5.	Amorim, 2012	3
6.	Baad-Hansen, 2007	5
7.	Badel, 2011	10
8.	Carraro, 1978	10
9.	Chandu, 2004	3
10.	Chong, 2007	14
11.	Clark, 1979	10
12.	Costa, 2015	10
13.	Daif, 2012	6
14.	Dao, 1994	4
15.	De Leeuw, 1994	2
16.	Ekberg, 1998	9
17.	Ekberg, 2002	10
18.	Ekberg, 2003	10
19.	Fayed, 2004	7
20.	Ferrario, 2002	10
21.	Garefis, 1994	10
22.	Glaros, 2007	10
23.	Göz, 2013	4
24.	Griffin, 1975	8
25.	Hamada, 1982	9
26.	Harada, 2006	10
27.	Hirata, 2010	10
28.	Holmgren, 1990	10
29.	Kurita, 1997	7
30.	La Mantia, 2018	10
31.	Long, 1995	14
32.	Lundh, 1992	3
33.	Miralles, 1992	3
34.	Nascimento, 2008	10
35.	Nilsson, 2011	10
36.	Qasim, 2006	12
37.	Sheikholeslam, 1993	14

38.	Su, 2010	6
39.	Suganuma, 2013	10
40.	Sung-Wen, 2010	3
41.	Suvinen, 2003	5
42.	Takahashi, 2013	10
43.	Van Zaag, 2005	10
44.	Villalón, 2013	7
45.	Wassel, 2006	13
46.	Willis, 1995	7
47.	Wu, 2013	10
48.	Yustin, 1993	11

Exclusion criteria: **1)** studies that not performing clinical examination as diagnostic criteria for TMD; **2)** studies not performing instrumental or non-instrumental for Bruxism; **3)** studies not performing follow up minimum for seven days; **4)** studies with samples with diagnostic for sleep disturbance, exception for SB; **5)** studies that used prefabricated or partially splints; **6)** studies that used other therapies for management SB and TMD; **7)** studies within patients with comorbidities; **8)** studies that included edentulous patients; **9)** studies that used only imaging methods to assess outcomes; **10)** studies that not report the disocclusion guide of occlusal splint; **11)** studies that not used the selected outcomes; **12)** studies that not assessed sleep quality with validated questionnaires; **13)** studies that used the same sample; **14)** reviews, letters, books, conference abstracts, case report, case series, animal studies, opinion article, technique articles, posters and guidelines; **15)** full-text not available.

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Supplementary table 2a. Risk of bias (RoB) according individual domain (NRCT and before and after studies)

Author, year	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Overall (%)	Rob
Okeson et al., 1982	Y	Y	Y	N	Y	N	Y	Y	U	67%	Moderate
Rugh et al., 1989	Y	N	Y	N	Y	Y	N	U	Y	55%	Moderate
YAP, 1998	U	N	Y	N	Y	U	U	U	Y	33%	High
Gavish et al., 2002	Y	Y	Y	Y	Y	Y	Y	Y	Y	100%	Low
Landulpho et al, 2004	Y	N	Y	N	Y	Y	Y	Y	Y	78%	Low
Badel et al., 2008	Y	N	Y	Y	U	U	U	Y	Y	55%	Moderate
Alajbeg et al., 2014	Y	N	Y	N	Y	Y	Y	Y	Y	78%	Low
Al-Rafah et al., 2014	Y	N	N	N	Y	U	U	Y	Y	44%	High
Vilanova et al., 2014	Y	Y	Y	N	Y	N	N	Y	Y	67%	Moderate
Rosar et al., 2017	Y	Y	Y	Y	Y	Y	Y	Y	Y	100%	Low
Câmara-Souza et al., 2019	Y	Y	Y	Y	Y	Y	Y	Y	Y	100%	Low

Legend: Y, yes; N, no; U, unclear; Q1, “Is it clear in the study what is the ‘cause’ and what is the ‘effect’?”; Q2, “Were the participants included in any comparisons similar?”; Q3, “Were the participants included in any comparisons receiving similar treatment/care, other than the exposure or intervention of interest?”; Q4, “Was there a control group?”; Q5, “Were there multiple measurements of the outcome both pre and post the intervention/exposure?”; Q6, “Was follow up complete and if not, were differences between groups in terms of their follow up adequately described and analyzed?”; Q7, “Were the outcomes of participants included in any comparisons measured in the same way?”; Q8, “Were outcomes measured in a reliable way?; Q9, Was appropriate statistical analysis used?”.

Supplementary table 2b. Risk of bias (RoB) according individual domain (RCT)

Author, year	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10	Q11	Q12	Overall (%)	Rob
Conti et al., 2006	Y	Y		U	N		Y	Y	Y	Y	Y	Y	75%	Low
Wassel et al., 2004	Y	N	N	N	N	U	N	N	N	U	Y	N	17%	High
Zhang et al., 2013	Y	N	U	N	N	Y	Y	Y	Y	Y	Y	Y	67%	Moderate
He et al., 2019	Y	N	N	N	N	U		Y	Y	Y	Y	Y	50%	Moderate

Legend: Y, yes; N, no; U, unclear; Q1, “Was true randomization used for assignment of participants to treatment groups?”; Q2, “Was allocation to treatment groups concealed?”; Q3, “Were treatment groups similar at the baseline?”; Q4, “Were participants blind to treatment assignment?”; Q5, “Were those delivering treatment blind to treatment assignment?; Q6, Were outcomes assessors blind to treatment assignment?”; Q7, “Were treatment groups treated identically other than the intervention of interest?”; Q8, “Was follow up complete and if not, were differences between groups in terms of their follow up adequately described and analyzed?”; Q9, “Were participants analyzed in the groups to which they were randomized?”; Q10, “Were outcomes measured in the same way for treatment groups?”; Q11, “Was appropriate statistical analysis used?”; Q12, “Was the trial design appropriate, and any deviations from the standard RCT design (individual randomization, parallel groups) accounted for in the conduct and analysis of the trial?”.

Supplementary table 3. Outcomes and raw datas of included studies (n=15).

Author, Year Country Study Design	TMD and/or Bruxism	Splint Design	Outcomes/Results												
Okeson, 1982 USA Before and after	TMD	Canine Guidance	<p>- Pain (0-3); mouth opening (mm).</p> <table border="1" data-bbox="1055 478 2130 568"> <thead> <tr> <th></th> <th>Before</th> <th>After (4 weeks)</th> <th>P value</th> </tr> </thead> <tbody> <tr> <td>Pain</td> <td>9.4</td> <td>5</td> <td>0.01*</td> </tr> <tr> <td>Mouth opening</td> <td>40.5</td> <td>42.2</td> <td>>0.05</td> </tr> </tbody> </table> <p>(*) Statistically significant difference (p=0.01).</p>		Before	After (4 weeks)	P value	Pain	9.4	5	0.01*	Mouth opening	40.5	42.2	>0.05
	Before	After (4 weeks)	P value												
Pain	9.4	5	0.01*												
Mouth opening	40.5	42.2	>0.05												
Rugh, 1989 USA NRCT	SB	Canine Guidance (CG) and molar guidance (MG)	<p>- Muscle activity (EMG); HDI index (clinical examination); pain (Likert Scale).</p> <table border="1" data-bbox="1055 655 2130 1026"> <thead> <tr> <th>Muscle activity</th> <th>HDI index</th> <th>Subjective Pain</th> </tr> </thead> <tbody> <tr> <td>- 37.5% (3 participants) of participants reduced SB levels - 37.5% (3 participants) of participants increased SB levels - 12.5% (1 participant) no clear effect - 12.5% (1 participant) increased with CG and no change with MG</td> <td>- 25% (2 participants) of participants had improved on HDI with both OS - 25% of participants had worse HDI index (2 participants) with both OS - 37.5% (3 participants) had improvements with MG - 12.5%(1 participant) of participants no changes with both splints</td> <td>- 25% (2 participants) of participants reduced pain levels with CG - 50% (4 participants) of participants reduced pain levels with MG</td> </tr> <tr> <td>p=0.578</td> <td>p=0.654</td> <td>p=0.221</td> </tr> </tbody> </table>	Muscle activity	HDI index	Subjective Pain	- 37.5% (3 participants) of participants reduced SB levels - 37.5% (3 participants) of participants increased SB levels - 12.5% (1 participant) no clear effect - 12.5% (1 participant) increased with CG and no change with MG	- 25% (2 participants) of participants had improved on HDI with both OS - 25% of participants had worse HDI index (2 participants) with both OS - 37.5% (3 participants) had improvements with MG - 12.5%(1 participant) of participants no changes with both splints	- 25% (2 participants) of participants reduced pain levels with CG - 50% (4 participants) of participants reduced pain levels with MG	p=0.578	p=0.654	p=0.221			
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YAP, 1998 Singapore Before and after	SB and TMD	Canine Guidance	- Tenderness on palpation (NR); mouth opening (mm); TMJ clicking.			
			Outcomes	Pre-treatment (% of patients)	Post-treatment (% of patients)	
			Temporalis tenderness**	55.0	12.5*	
			Masseter tenderness**	97.5	7.5*	
			Sternocleidomastoid tenderness**	42.5	7.5*	
			TMJ tenderness**	47.5	0*	
			Mouth opening<40mm**	47.5	7.5*	
TMJ Clicking**	60.0	60.0				
(*) Statistically significant difference (p< 0.05); (**) Data calculated by authors						
Gavish et al., 2002 Israel NRCT	TMD	Canine guidance	- Pain (VAS); mouth opening (mm).			
				Experimental group	Control group	P value
			Pain	T1) 59.57±27.73 T2) 29.62±22.63	T1) 46.00±26.23 T2) 41.25±30.34	0.0083
Mouth opening	T1) 48.76±8.56 T2) 51.24±8.07	T1) 52.44±5.94 T2) 53.81±6.68				
Landulpho et al., 2004 Brazil Before and after	TMD	Canine Guidance (CG) Group Function (GF)	- Muscle activity (EMG).			
			M±SD	Anterior Temporalis		Masseter
			Baseline (CG)	Left: RMS 3.44±1.75 Right: RMS 2.98±1.46		Left: RMS 2.38±1.62 Right: RMS 2.05±1.15
			90d (GF)	Left: RMS 3.15±0.94 Right: RMS 2.54±0.85		Left: RMS 2.13±1.26 Right: RMS 2.10±1.25
			120d (GF)	Left: RMS 2.76±1.34 Right: RMS 2.81±0.91		Left: RMS 2.13±0.73 Right: RMS 1.98±1.17
			150d (GF)	Left: RMS 2.56±1.00 Right: 2.24±0.81		Left: RMS 2.00±1.11 Right: 1.70±0.99
p value	< 0.05		> 0.05			
Datas were assessed with participants on rest position						
Wassell et al., 2004 England RCT	TMD	Placebo Splint (CS) Cross Over Group (CO) Anterior guide (SS)	- Pain (VAS); mouth opening (mm); number of muscle tenderness; TMJ tenderness; joint click (%); Headaches (% per week)			
			Outcomes M (SD)	Group	Baseline	21 weeks
			Pain	CS	46.7 (28.8)	16.4 (20.9)
				CO	44.2 (24.8)	12.9 (14.1)
SS	54.2 (25.6)	18.6 (23.7)				

			<table border="1"> <tbody> <tr> <td rowspan="3">Mouth opening</td> <td>CS</td> <td>43.0 (10.0)</td> <td>46.6 (7.3)</td> </tr> <tr> <td>CO</td> <td>40.6 (10.2)</td> <td>44.9 (5.6)</td> </tr> <tr> <td>SS</td> <td>41.5 (9.8)</td> <td>45.7 (8.3)</td> </tr> <tr> <td rowspan="3">Number of muscle tenderness</td> <td>CS</td> <td>6.5 (4.5)</td> <td>1.6 (2.7)</td> </tr> <tr> <td>CO</td> <td>7.0 (5.1)</td> <td>2.0 (3.4)</td> </tr> <tr> <td>SS</td> <td>6.2 (4.2)</td> <td>2.8 (3.2)</td> </tr> <tr> <td rowspan="3">Joint tenderness</td> <td>CS</td> <td>1.7 (1.5)</td> <td>0.2 (0.40)</td> </tr> <tr> <td>CO</td> <td>1.8 (1.3)</td> <td>0.8 (1.3)</td> </tr> <tr> <td>SS</td> <td>1.8 (1.4)</td> <td>0.7 (1.2)</td> </tr> <tr> <td rowspan="3">Joint click</td> <td>CS</td> <td>42 (51)</td> <td>19 (40)</td> </tr> <tr> <td>CO</td> <td>65 (49)</td> <td>42 (51)</td> </tr> <tr> <td>SS</td> <td>49 (51)</td> <td>31 (47)</td> </tr> <tr> <td rowspan="3">Headache</td> <td>CS</td> <td>16</td> <td>13</td> </tr> <tr> <td>CO</td> <td>17</td> <td>11</td> </tr> <tr> <td>SS</td> <td>39</td> <td>31</td> </tr> </tbody> </table>	Mouth opening	CS	43.0 (10.0)	46.6 (7.3)	CO	40.6 (10.2)	44.9 (5.6)	SS	41.5 (9.8)	45.7 (8.3)	Number of muscle tenderness	CS	6.5 (4.5)	1.6 (2.7)	CO	7.0 (5.1)	2.0 (3.4)	SS	6.2 (4.2)	2.8 (3.2)	Joint tenderness	CS	1.7 (1.5)	0.2 (0.40)	CO	1.8 (1.3)	0.8 (1.3)	SS	1.8 (1.4)	0.7 (1.2)	Joint click	CS	42 (51)	19 (40)	CO	65 (49)	42 (51)	SS	49 (51)	31 (47)	Headache	CS	16	13	CO	17	11	SS	39	31																																																												
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			Pain free maximal mouth opening M±SD/Min-max (T0) 33.46 ± 8.48/ 20.5-49 (T3) 43.89 ± 6.47/ 35.0-53	(T0) 37.59 ± 10.26/ 22-54 (T3) 44.78 ± 7.27/ 34-59	DD t=-4.46, p<0.001 MP t= -3.66, p=0.003																
			Assisted maximal mouth opening M±SD/Min-max (T0) 40.96 ± 10.1/ 22.5-58 (T3) 49.32 ± 5.7/ 38-59	(T0) 45.41 ± 9.14/ 30-62 (T3) 50.03 ± 6.91/ 38-64	DD t= -4.45, p<0.001 MP t= -3.31, p=0.006																
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AL-Rafah, 2014 Saudi- Arabia Before and after	TMD	Canine Guidance (GI) Bilateral balanced occlusion (GII)	- TMD index (HDI) <table border="1"> <thead> <tr> <th>Group</th> <th>T0</th> <th>T1</th> <th>T2</th> <th>p value</th> </tr> </thead> <tbody> <tr> <td>GI</td> <td>13.0±6.44/6.0-22.0</td> <td>3.88±2.36/1.8-8.0</td> <td>0.5±0.93/0.0-2.0</td> <td><0.001</td> </tr> <tr> <td>GII</td> <td>13.75±7.25/7.0-25.0</td> <td>7.38±4.8/3.0-16.0</td> <td>1.75±1.91/0.0-4.0</td> <td><0.001</td> </tr> </tbody> </table>				Group	T0	T1	T2	p value	GI	13.0±6.44/6.0-22.0	3.88±2.36/1.8-8.0	0.5±0.93/0.0-2.0	<0.001	GII	13.75±7.25/7.0-25.0	7.38±4.8/3.0-16.0	1.75±1.91/0.0-4.0	<0.001
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Vilanova, 2014 Brazil Before and after	TMD	Canine Guidance	- Pain (VAS); sleep quality [ESS (%) and PSQI (%)] <table border="1"> <thead> <tr> <th></th> <th>Pain (M±SD)</th> <th>PSQI (mean)</th> </tr> </thead> <tbody> <tr> <td>Before</td> <td>3.22±2.52</td> <td>Poor sleeper: 38 (76) Good sleeper: 12 (24)</td> </tr> <tr> <td>After</td> <td>0.69±1.25</td> <td>Poor sleeper: 16 (32) Good sleeper: 34 (68)</td> </tr> <tr> <td>P value</td> <td>f=11.31; p<0.001</td> <td>f=4.3; p=0.04</td> </tr> </tbody> </table>					Pain (M±SD)	PSQI (mean)	Before	3.22±2.52	Poor sleeper: 38 (76) Good sleeper: 12 (24)	After	0.69±1.25	Poor sleeper: 16 (32) Good sleeper: 34 (68)	P value	f=11.31; p<0.001	f=4.3; p=0.04			
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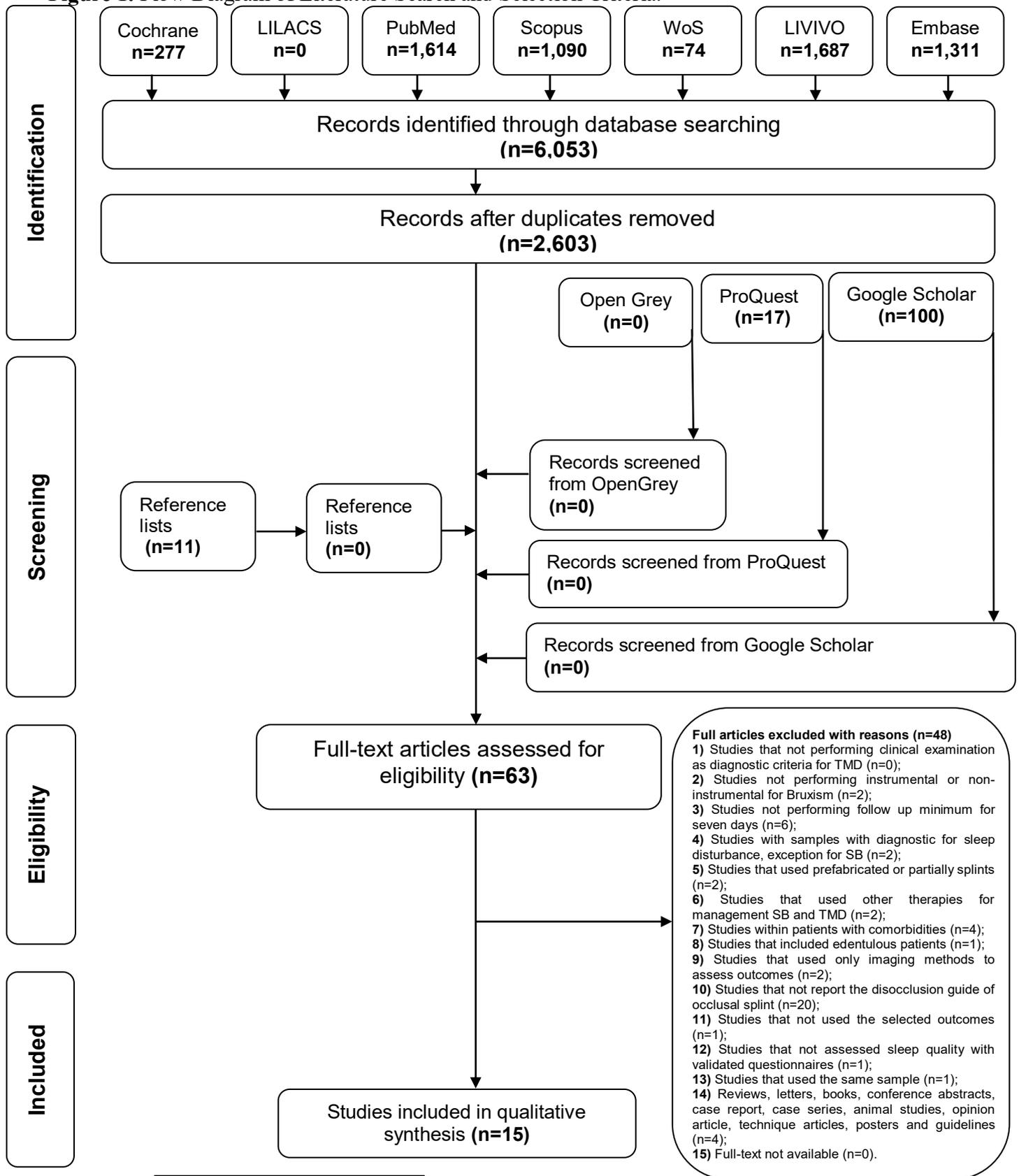
Rosar, 2017 Brazil NRCT	TMD and Sleep Bruxism	Canine Guidance	- Bite force (EMG)						
			Left side (N) M(SD)			Right side (N) M(SD)			
			T0	T1	T2	T0	T1	T2	
			SBG	496.8 (129.1)	546.5 (138.7)*	588.9 (126.2)	476.5 (140.6)	556.3 (149.8)*	596.5 (162.1)*
			CG	452.4 (50.2)	465.3 (49.8)	459.6 (63.2)	471.5 (94.5)	470.0 (96.8)	475.5 (92.2)
			P value	0.0122			0.0003		
			- Sleep quality (PSQI); TMD index (according to RDC/TMD)						
			Sleep Quality (PSQI Index) Median (IQR)			TMI index Median (IQR)			
			T0	T1	T2	T0	T1	T2	
			SBG	7.0 (3.0)	5.0 (3.0)*	6.0 (3.0)	0.32 (0.12)	0.29 (0.15)	0.22 (0.19)
CG	7.0 (3.0)	7.0 (3.0)	7.0 (2.5)	0.14 (0.12)	0.17 (0.07)	0.18 (0.14)			
P value	0.0006			0.0015					
He, 2019 China RCT	TMD	Canine Guidance	- Muscle activity (EMG)						
			Group Experimental 1	T0	T1				
			Left masseter	RMS 26.25± 12.00***	RMS 8.75± 5.25***				
			Right masseter	RMS 22.50± 9.75***	RMS 7.50± 2.50***				
			Left anterior temporal	RMS 13.33± 10.00***	RMS 5.00± 2.50***				
			Right anterior temporal	RMS 20.00± 10.00***	RMS 2.50± 1.25***				
			Group Experimental 2	T0	T1				
			Left masseter	RMS 6.66± 2.00	RMS 5.33± 2.20				
			Right masseter	RMS 6.66± 2.00*	RMS 4.66± 1.40*				
			Left anterior temporal	RMS 6.66± 1.33	RMS 6.33± 3.66				
			Right anterior temporal	RMS 6.00±1.66	RMS 4.66± 2.33				
			Data calculated by authors (*) p < 0.05. (***) p < 0.01; (**); **** EMG data were assessed with participants on rest position						
			- TMD index (according to HDI)						
				Mean scores	0	I (1-4)	II (5-9)	III (10-25)	
E1	T0	0	0	7	16				
	T1	0	1	4	0				

			E2	T0	0	0	8	17
				T1	0	0	8	17
			- Sleep quality (PSQI)					
			Groups	T0	T1	T2		
			Experimental	7.13±3.87	6.60±4.34*	5.87±3.23*		
			Control	7.00±2.56	5.27±1.91*	5.00±2.62*		

(*) Statistically significant difference (p< 0.05).

Legend: SB, sleep bruxism; TMD, temporomandibular disorders; EMG, eletroelectromyography activity; HDI, helkymo dysfunction index; TMD index, temporomandibular dysfunction index; TMJ, temporomandibular joint; NRCT, non-randomized controlled trial; VAS, Visual Analog Scale; RCT, randomized clinical trial; M, mean; SD, standart deviation; Mín, Minimum; Max, maximum; d, days; ESS, epworth sleepiness scale; PSQI: Pittsburgh Sleep Quality Index; f, f-ratio; RDC/TMD, diagnostic criteria for TMD; MMP, mandibular postural position; ICP, intercuspal position.

Figure 1. Flow Diagram of Literature Search and Selection Criteria.¹



¹ Adapted from PRISMA.

Figure 2a. Risk of bias graph: review authors' judgments about each risk of bias item presented as percentages across all included studies (NRCT and before and after studies)

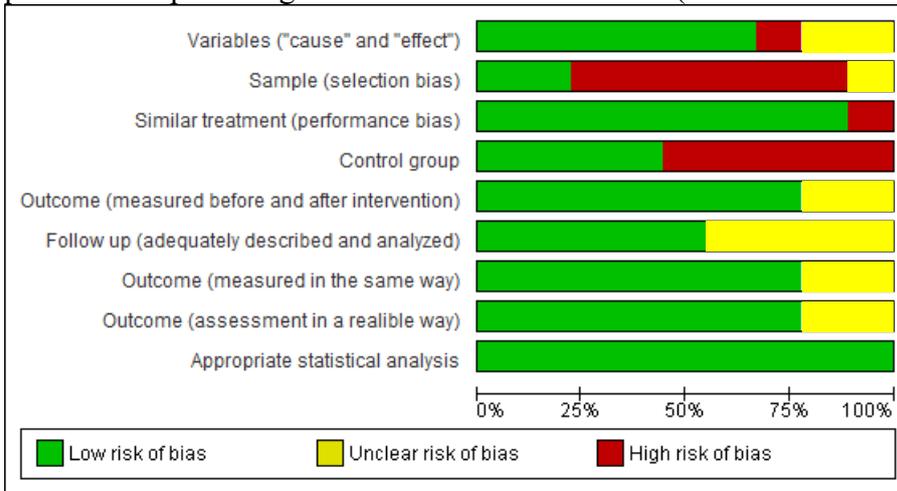


Figure 2b. Risk of bias summary (NRCT and before and after studies)

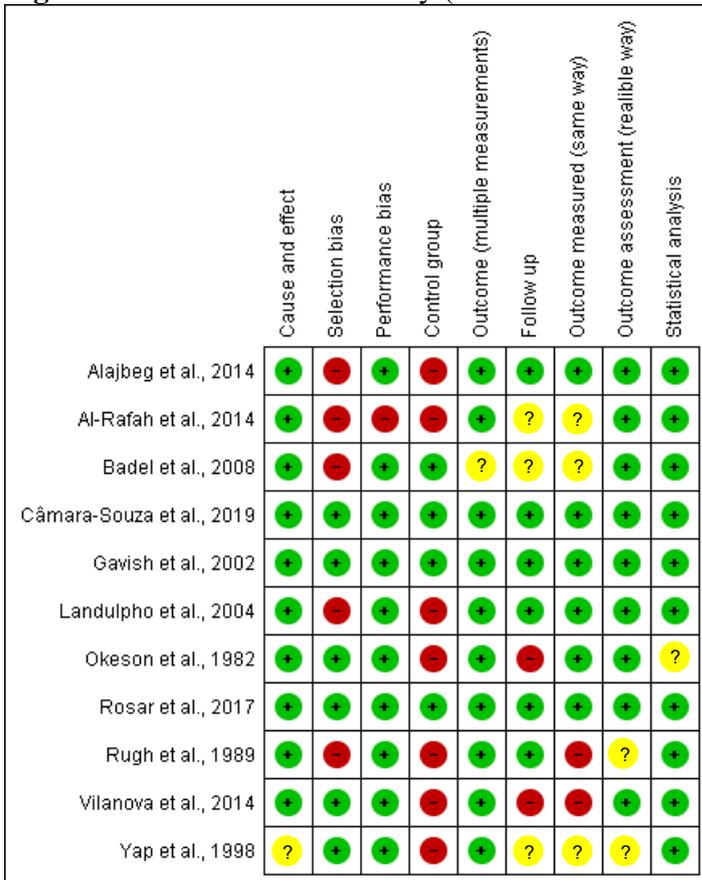


Figure 3a. Risk of bias graph: review authors' judgments about each risk of bias item presented as percentages across all included studies (RCT studies)

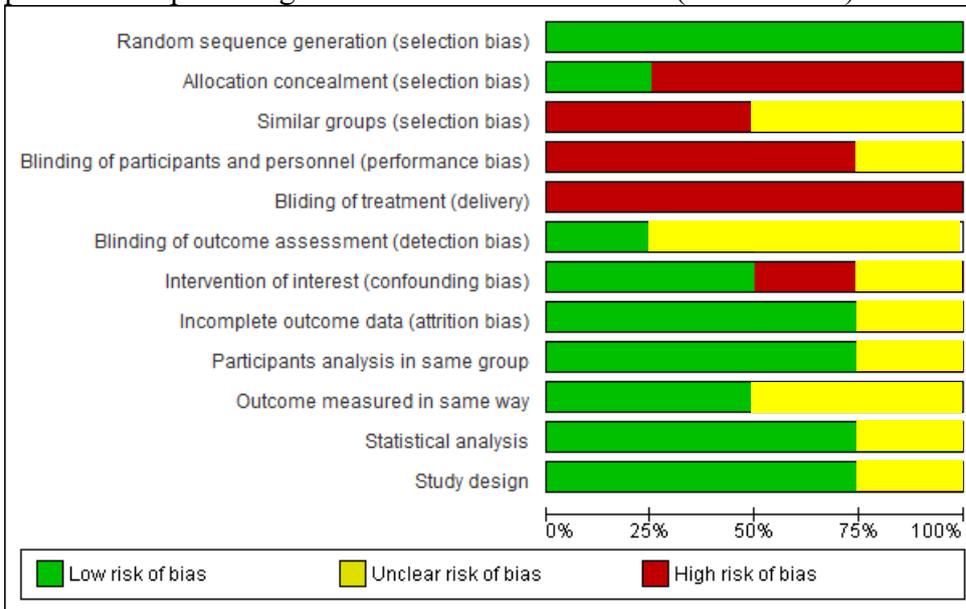


Figure 3b. Risk of Bias summary (RCT studies)

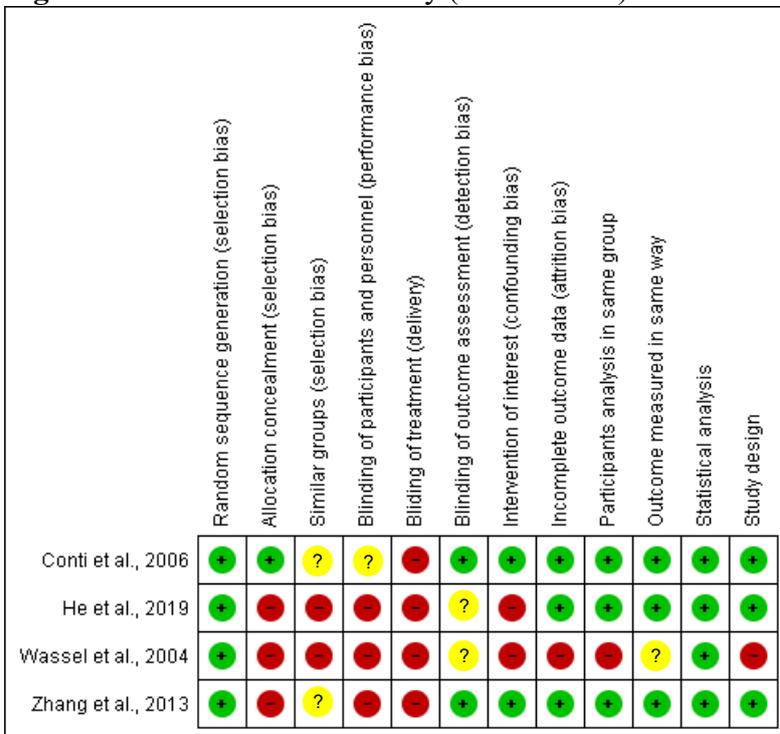


Figure 4. Summary of results according to outcomes. (+) improved; (-) worst; (=) not; (*) statically significance

Author, year	SB and/or TMD	Type of guidance	Mouth opening	TMJ sounds	Pain	Headache	TMD index	Sleep quality	Splint comfort	Muscle activity
Okeson et al., 1982	TMD	CG	63.6% (+)* 30.3% (-)	-	84.8%(+)* 3% (-)	-	-	-	-	-
Rugh et al., 1989	SB	CG	-	-	25% (+)	-	12.5% (=)	-	-	12.5% (-)
		MG	-	-	50% (+)	-	37.5% (+) 50% (-)	-	-	12.5% (=)
YAP, 1998	SB and TMD	CG	80% (+)*	(=)	75% (+) T* 93% (+) M* 83% (+) SCM*	-	-	-	-	-
Gavish et al., 2002	TMD	CG	(+)*	-	(+)*	-	-	-	-	-
Landulpho et al., 2004	TMD	BBO	-	-	-	-	-	-	-	(+)T;(=) M
Conti et al., 2006	TMD	CG	-	30% (+)	86% (+)*	-	-	-	67% (+)	-
		BBO	-	15.79% (+)	83.4% (+)*	-	-	-	67% (+)	-
Wassel et al., 2004	TMD	AG	(+)	(+)	(+)	(+)	-	-	-	-
Badel et al., 2008	TMD	CG	-	35.6% (=)	78% (+) TMJ	-	-	-	67% (+)	-
Zhang et al., 2013	TMD	CG	-	-	89% (+)	-	-	-	-	(+)*
Alajbeg et al., 2014	Bruxism and TMD	CG	(+)*	-	(+)*	-	-	-	-	-
Al-Rafah et al., 2014	TMD	CG	-	-	-	-	(+)	-	-	-
		BBO	-	-	-	-	(+)	-	-	-
Vilanova et al., 2014	TMD	CG	-	-	(+)*	-	-	(+)*	-	-
Rosar et al., 2017	SB and TMD	CG	-	-	-	-	-	(+)*	-	(-)*
He et al., 2019	TMD	CG	-	-	-	-	82% (+)	-	-	(+)*
Câmara-Souza et al., 2019	SB	BBO	-	-	-	-	-	(+)	-	-

Legend: SB, sleep bruxism; TMD, temporomandibular disorder; TMJ, temporomandibular joint; CG, canine guide; BBO, bilateral balanced occlusion; AG, anterior guide; MG, molar guide; SCM, sternocleidomastoid; M, masseter; T, temporalis.

5 CONSIDERAÇÕES FINAIS

A qualidade da evidência encontrada nessa RS foi muito baixa na maioria dos desfechos avaliados, devido à alta heterogeneidade clínica e metodológica entre os estudos primários, o que ocasionou limitações em nossas conclusões. Os resultados encontrados sugerem que, em relação aos desfechos dor, amplitude de abertura bucal, índice de DTM, qualidade do sono e conforto melhorias foram encontradas com a utilização de guia canino, oclusão balanceada bilateral e guia molar. Devido a isso, a utilização de guias com maior facilidade de ajuste, como a oclusão balanceada bilateral, parece ser uma alternativa viável para facilitar esta etapa do processo de confecção dos dispositivos. A guia mais estudada na literatura disponível até o momento foi a guia canino, seguida da oclusão balanceada bilateral. No entanto, há uma carência de estudos primários, para que em estudos futuros possa ser realizada uma metanálise, e a qualidade da evidência seja melhorada, é indicado que sejam realizados mais ensaios clínicos randomizados com guia canino, oclusão balanceada bilateral, função em grupo, guia anterior e guia molar.

Appendix 1. Database search strategy.

Database	Search (April 10 th 2020)
PubMed	("temporomandibular joint disorders"[MeSH Terms] OR "temporomandibular joint disorders"[All Fields] OR "temporomandibular Joint disorder"[All Fields] OR "temporomandibular disorder"[All Fields] OR "temporomandibular disorders"[All Fields] OR "temporomandibular joint disease"[All Fields] OR "temporomandibular joint diseases"[All Fields] OR "temporomandibular dysfunction"[All Fields] OR "temporomandibular dysfunctions"[All Fields] OR "temporomandibular joint dysfunction syndrome"[MeSH Terms] OR "temporomandibular joint dysfunction syndrome"[All Fields] OR "costen syndrome"[All Fields] OR "costens syndrome"[All Fields] OR "costens syndromes"[All Fields] OR "costen syndromes"[All Fields] OR "costen's Syndrome"[All Fields] OR "temporomandibular joint syndrome"[All Fields] OR "temporomandibular joint syndromes"[All Fields] OR "temporomandibular joint dysfunction"[All Fields] OR "tmj disease"[All Fields] OR "tmd"[All Fields] OR "tmj"[All Fields] OR "tmjd"[All Fields] OR "tmj disorders"[All Fields] OR "tmj disorder"[All Fields] OR "tmj diseases"[All Fields] OR "craniomandibular disorders"[MeSH Terms] OR "craniomandibular disorders"[All Fields] OR "craniomandibular disorder"[All Fields] OR "craniomandibular dysfunction"[All Fields] OR "craniomandibular dysfunctions"[All Fields] OR "craniomandibular dysfunction"[All Fields] OR "craniomandibular dysfunctions"[All Fields] OR Bruxism OR "Sleep Bruxism"[MeSH Terms] OR "bruxer" OR "bruxers" OR "tooth grinding"[All Fields] OR "tooth clenching"[All Fields] OR "teeth grinding" [All Fields] OR "teeth clenching" [All Fields] OR Bruxism OR "Sleep Bruxism"[MeSH Terms] OR "bruxer" OR "bruxers" OR "tooth grinding"[All Fields] OR "tooth clenching"[All Fields] OR "teeth grinding" [All Fields] OR "teeth clenching" [All Fields]) AND ("occlusal splint" OR "splint" OR "splints" OR "stabilization devices" OR "stabilization device" OR "splints"[MeSH Terms] OR "oral device" OR "oral devices" OR "intraoral splints" OR "intraoral splint" OR "night guard" OR "bite guard" OR "interocclusal appliances" OR "intraoral orthotic" OR "bite splint" OR "bite splints" OR "interocclusal device" OR "interocclusal devices" OR "nociceptive trigeminal inhibitory" OR "NTI splint" OR "overlay splint" OR "repositioning splint" OR "repositioning appliance") AND ("occlusal guidance" OR "canine guidance" OR "Bilateral balanced occlusion" OR occlusion OR occlusal OR "lateral occlusion" OR "lateral occlusal")
Scopus	(TITLE-ABS-KEY ("temporomandibular joint disorders" OR "temporomandibular joint disorder" OR "tmj disorders" OR "tmj disorder" OR "temporomandibular disorders" OR "temporomandibular disorder" OR "temporomandibular joint diseases" OR "temporomandibular joint disease" OR "tmj" OR "costen's syndrome" OR "costen syndrome" OR "costens syndrome" OR "temporomandibular joint syndrome" OR "tmd" OR

	"temporomandibular dysfunction" OR "temporomandibular dysfunctions" OR "craniomandibular disorders" OR "craniomandibular disorder" OR "craniomandibular dysfunction" OR "craniomandibular dysfunctions" OR "temporomandibular joint dysfunction" OR "temporomandibular joint dysfunctions" OR "bruxism" OR "sleep bruxism")) AND ((TITLE-ABS-KEY) ("occlusal splint" OR splint* OR "stabilization devices" OR "stabilization device" OR "oral device" OR "oral devices" OR "intraoral splints" OR "intraoral splint" OR "night guard" OR "night guards" OR "bite guard" OR "bite guards" OR "interocclusal appliances" OR "intraoral orthotic" OR "bite splint" OR "bite splints" OR "interocclusal device" OR "interocclusal devices" OR "nociceptive trigeminal inhibitory" OR "NTI splint" OR "overlay splint" OR "repositioning splint" OR "repositioning appliance")) AND ((TITLE-ABS-KEY) ("occlusal guidance" OR "canine guidance" OR "Bilateral balanced occlusion" OR "occlusion" OR "occlusal" OR "lateral occlusion" OR "lateral occlusal"))
Cochrane	((("temporomandibular joint disorders" OR "temporomandibular joint disorder" OR "tmj disorders" OR "tmj disorder" OR "temporomandibular disorders" OR "temporomandibular disorder" OR "temporomandibular joint diseases" OR "temporomandibular joint disease" OR "tmj" OR "costen's syndrome" OR "costen syndrome" OR "costens syndrome" OR "temporomandibular joint syndrome" OR "tmd" OR "temporomandibular dysfunction" OR "temporomandibular dysfunctions" OR "craniomandibular disorders" OR "craniomandibular disorder" OR "craniomandibular dysfunction" OR "craniomandibular dysfunctions" OR "temporomandibular joint dysfunction" OR "temporomandibular joint dysfunctions" OR "bruxism" OR "sleep bruxism") AND (pain OR ache)) AND ("occlusal splint" OR "stabilization devices" OR "stabilization device" OR "oral device" OR "oral devices" OR "intraoral splints" OR "intraoral splint" OR "night guard" OR "night guards" OR "bite guard" OR "bite guards" OR "interocclusal appliances" OR "intraoral orthotic" OR "bite splint" OR "bite splints" OR "interocclusal device" OR "interocclusal devices" OR "nociceptive trigeminal inhibitory" OR "NTI splint" OR "overlay splint" OR "repositioning splint" OR "repositioning appliance") AND (pain OR ache)) AND ("occlusal guidance" OR "canine guidance" OR "Bilateral balanced occlusion" OR occlusion OR occlusal OR "lateral occlusion" OR "lateral occlusal") in Title, Abstract, Keywords in Cochrane Reviews'
Web of Science	(TS= ("temporomandibular joint disorders" OR "temporomandibular joint disorder" OR "tmj disorders" OR "tmj disorder" OR "temporomandibular disorders" OR "temporomandibular disorder" OR "temporomandibular joint diseases" OR "temporomandibular joint disease" OR "tmj" OR "costen's syndrome" OR "costen syndrome" OR "costens syndrome" OR "temporomandibular joint syndrome" OR "tmd" OR "temporomandibular dysfunction" OR "temporomandibular dysfunctions" OR "craniomandibular disorders" OR "craniomandibular disorder" OR "craniomandibular dysfunction" OR "craniomandibular dysfunctions" OR "temporomandibular joint dysfunction" OR "temporomandibular joint dysfunctions" OR "bruxism" OR "sleep

	bruxism")) AND (TS= ("occlusal splint" OR splint* OR "stabilization devices" OR "stabilization device" OR "oral device" OR "oral devices" OR "intraoral splints" OR "intraoral splint" OR "night guard" OR "night guards" OR "bite guard" OR "bite guards" OR "interocclusal appliances" OR "intraoral orthotic" OR "bite splint" OR "bite splints" OR "interocclusal device" OR "interocclusal devices" OR "nociceptive trigeminal inhibitory" OR "NTI splint" OR "overlay splint" OR "repositioning splint" OR "repositioning appliance")) AND (TS= ("occlusal guidance" OR "canine guidance" OR "Bilateral balanced occlusion" OR occlusion OR occlusal OR "lateral occlusion" OR "lateral occlusal"))
EMBASE	('temporomandibular joint disorders' OR 'temporomandibular joint disorder' OR 'tmj disorders' OR 'tmj disorder' OR 'temporomandibular disorders' OR 'temporomandibular disorder' OR 'temporomandibular joint diseases' OR 'temporomandibular joint disease' OR 'tmj' OR 'costen syndrome' OR 'costens syndrome' OR 'temporomandibular joint syndrome' OR 'tmd' OR 'temporomandibular dysfunction' OR 'temporomandibular dysfunctions' OR 'craniomandibular disorders' OR 'craniomandibular disorder' OR 'craniomandibular dysfunction' OR 'craniomandibular dysfunctions' OR 'temporomandibular joint dysfunction' OR 'temporomandibular joint dysfunctions' OR bruxism OR 'sleep bruxism') AND ('occlusal splint' OR splint* OR 'stabilization devices' OR 'stabilization device' OR 'oral device' OR 'oral devices' OR 'intraoral splints' OR 'intraoral splint' OR 'night guard' OR 'night guards' OR 'bite guard' OR 'bite guards' OR 'interocclusal appliances' OR 'intraoral orthotic' OR 'bite splint' OR 'bite splints' OR 'interocclusal device' OR 'interocclusal devices' OR 'nociceptive trigeminal inhibitory' OR 'nti splint' OR 'overlay splint' OR 'repositioning splint' OR 'repositioning appliance') AND ('occlusal guidance' OR 'canine guidance' OR 'bilateral balanced occlusion' OR 'occlusion' OR 'occlusal' OR 'lateral occlusion' OR 'lateral occlusal')
LILACS	("desordens da articulação temporomandibular" OR "Transtorno da articulação temporomandibular" OR "Transtornos da ATM" OR "Transtornos da ATM" OR "Transtornos da articulação temporomandibular" OR "Transtornos da articulação temporomandibular" OR "Síndrome da articulação temporomandibular" OR "Síndrome de Costen" OR "Síndrome de Costens" OR "Síndrome da articulação temporomandibular" OR DTM OR "disfunção temporomandibular" OR "disfunção temporomandibular" OR "desordens craniomandibulares" OR "desordem craniomandibular" OR "disfunção craniomandibular" OR "disfunções craniomandibulares" OR Disfunção da articulação temporomandibular OR "Disfunções da articulação temporomandibular" OR Bruxismo OR "Bruxismo do sono" OR "Temporomandibular Joint Disorders" OR "Temporomandibular Joint Disorder" OR "TMJ Disorders" OR "TMJ Disorder" OR "Temporomandibular Disorders" OR "Temporomandibular Disorder" OR "Temporomandibular Joint Diseases" OR "Temporomandibular Joint Disease" OR "TMJ" OR "Costen's Syndrome" OR "Costen Syndrome" OR "Costens Syndrome" OR "Temporomandibular Joint Syndrome" OR "TMD" OR "Temporomandibular Dysfunction" OR "Temporomandibular Dysfunctions" OR "Craniomandibular Disorders" OR "Craniomandibular Disorder" OR

	<p>"Craniomandibular Dysfunction" OR "Craniomandibular Dysfunctions" OR "Temporomandibular Joint Dysfunction" OR "Temporomandibular Joint Dysfunctions" OR "Bruxism" OR "Sleep Bruxism" OR "Trastornos de la articulación temporomandibular" OR "Trastorno de la articulación temporomandibular" OR "Trastornos de la ATM" OR "Trastorno de la ATM" OR "Trastornos temporomandibulares" OR "Trastorno de la articulación temporomandibular" OR "Enfermedades de la Articulación Temporomandibular" OR "Enfermedad de la articulación temporomandibular" OR "Síndrome de Costen" OR "Síndrome de Costen" OR "Síndrome de Costens" OR "Síndrome de la articulación temporomandibular" OR "TMD" OR "Disfunción temporomandibular" OR "Disfunción temporomandibular" OR "Trastornos craneomandibulares" OR "Disfunción craneomandibular" OR "Disfunción craneomandibular" OR "disfunción craneomandibular" OR "Disfunción de la articulación temporomandibular" OR "disfunciones de la articulación temporomandibular" OR "bruxismo" OR "bruxismo del sueño" OR "Apretamiento Dental Nocturno" OR "Nocturno" OR "Trastorno de Rechinamiento Nocturno de los Dientes" OR "Trastorno de Rechinamiento de los Dientes Durante el Sueño" OR "Rechinamiento de los Dientes Durante el Sueño" OR "Rechinamiento Dental Nocturno") AND ("Férula oclusal" OR férula OR "dispositivos de estabilización" OR "dispositivo de estabilización" OR "dispositivo oral" OR "dispositivos orales" OR "férulas intraorales" OR "férula intraoral" OR "guardia nocturna" OR "guardias nocturnos" OR "protectores de mordida" OR "aparatos interoclusales" OR "férula de mordida " OR "férulas de mordida" OR "dispositivo interoclusal" OR "dispositivos interoclusales" OR "inhibidor trigeminal nociceptivo" OR "férula de superposición" OR "férula de reposicionamiento" OR "dispositivo de reposicionamiento" OR "placa oclusal" OR "dispositivos de estabilização" OR "dispositivo de estabilização" OR "dispositivo oral" OR "dispositivos orais" OR "placas intraorais" OR "placa intraoral" OR "placa noturna" OR "placas noturnas" OR "mordida guarda" OR "protetores de mordida" OR "aparelhos interoclusais" OR "placa de mordida" OR "placa de mordida" OR "dispositivo interoclusal" OR "dispositivos de interoclusão" OR "inibidor trigeminal nociceptivo" OR "placa de reposicionamento "OR" aparelho de reposicionamento") AND ("guía oclusal" OR "guía canina" OR "Oclusión equilibrada bilateral" OR "oclusión" OR "oclusal" OR "oclusión lateral" OR "guia oclusal" OR "guia canino" OR "oclusao balanceada bilateral" OR "oclusao" OR "oclusal" OR "oclusao lateral")</p>
LIVIVO	<p>("temporomandibular joint disorders" OR "Temporomandibular Joint Disorder" OR "TMJ Disorders" OR "TMJ Disorder" OR "Temporomandibular Disorders" OR "Temporomandibular Disorder" OR "Temporomandibular Joint Diseases" OR "Temporomandibular Joint Disease" OR TMJ OR "Costen's Syndrome" OR "Costen Syndrome" OR "Costens Syndrome" OR "Temporomandibular Joint Syndrome" OR TMD OR "temporomandibular dysfunction" OR "temporomandibular dysfunctions" OR "craniomandibular disorders" OR "craniomandibular disorder" OR "craniomandibular</p>

	dysfunction" OR "craniomandibular dysfunctions" OR "temporomandibular Joint dysfunction" OR "temporomandibular joint dysfunctions" OR Bruxism OR "Sleep Bruxism") AND ("Occlusal Splint" OR splint* OR "stabilization devices" OR "stabilization device" OR "oral device" OR "oral devices" OR "intraoral splints" OR "intraoral splint" OR "night guard" OR "night guards" OR "bite guard" OR "bite guards" OR "interocclusal appliances" OR "intraoral orthotic" OR "bite splint" OR "bite splints" OR "interocclusal device" OR "interocclusal devices" OR "nociceptive trigeminal inhibitory" OR "NTI splint" OR "overlay splint" OR "repositioning splint" OR "repositioning appliance") AND ("occlusal guidance" OR "canine guidance" OR "Bilateral balanced occlusion" OR occlusion OR occlusal OR "lateral occlusion" OR "lateral occlusal")
Google Scholar	"temporomandibular disorder" OR "TMD" AND "occlusal splint"
OpenGrey	"temporomandibular disorder" OR "temporomandibular disorders" OR "temporomandibular joint disorders"
ProQuest	noft(mandibular joint disorders OR mandibular disorder OR mandibular disorders OR mandibular dysfunction OR mandibular dysfunctions) AND noft("occlusal splint") AND noft(guidance)

Appendix 2. Checklist PRISMA.

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	23
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	24
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	19
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	26
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	26
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	26
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	27
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	75
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	28
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	28

Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	28
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	28
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	29
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	34

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(7): e1000097. doi:10.1371/journal.pmed1000097

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