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EXPLORANDO CONEXÕES ENTRE ALTERAÇÕES ÓSSEAS DEGENERATIVAS E INFLAMATÓRIAS E AS PATOLOGIAS PULPO-PERIAPICAIS

SÃO LUÍS
2026

ANA PAULA NÓBREGA CAETANO DA SILVA

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Dissertação apresentada ao Programa de Pós-Graduação em Odontologia como parte dos requisitos para a obtenção do título de Mestre em Odontologia.

Orientador: Profa. Dra. Soraia de Fátima Carvalho Souza
Coorientador: Profa. Dra. Erika Bárbara Abreu Fonseca Thomaz

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A Comissão julgadora da Defesa do Trabalho Final de Mestrado em Odontologia, em sessão pública realizada no dia 29/01/2026, considerou a candidato(a).

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Epígrafe

"Se você não tivesse capacidade, Deus não te daria a oportunidade. Seus medos você já conhece, experimente suas coragens"
- Santa Terezinha

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RESUMO

Introdução: As patologias pulpo-periapicais são doenças inflamatórias crônicas de alta prevalência global, majoritariamente resultantes da progressão da cárie dentária não tratada. Além do impacto local, essas condições contribuem com a carga inflamatória sistêmica do indivíduo. Inversamente, desordens sistêmicas que afetam o metabolismo ósseo podem modular a resposta do hospedeiro a essas infecções bucais. Esta dissertação investigou as conexões entre duas classes de alterações ósseas sistêmicas: uma degenerativa (osteoporose) e a outra inflamatória (doenças autoimunes reumáticas) com as patologias pulpo-periapicais. Os objetivos foram avaliar as evidências sobre: 1) a associação entre osteoporose e a ocorrência de patologias pulpo-periapicais; e 2) a associação entre doenças autoimunes reumáticas e a ocorrência de patologias pulpo-periapicais.

Métodos: Esta dissertação é composta por duas revisões sistemáticas e metanálises, seguindo as recomendações do PRISMA 2020. Foram realizadas buscas abrangentes nas bases de dados MEDLINE/PubMed, Embase, Scopus, BVS-Bireme, Web of Science, SciELO e Cochrane Library, além da literatura cinza. Foram incluídos estudos observacionais (transversais, coorte e caso-controle) que compararam a ocorrência de patologias pulpo-periapicais em indivíduos com osteoporose (primeiro estudo) ou com doenças autoimunes reumáticas (segundo estudo) *versus* grupos controle saudáveis, em ambos os estudos. Os dados foram extraídos por revisores independentes. O risco de viés foi avaliado pela ferramenta do Joanna Briggs Institute (JBI) e a certeza da evidência pelo sistema GRADE. As metanálises foram conduzidas utilizando modelos de efeitos aleatórios para calcular as Razões de Chance [Odds Ratio (OR)] com Intervalos de Confiança de 95% (IC95%).

Resultados: No primeiro estudo (Capítulo II), a metanálise de efeito aleatório de seis estudos não identificou associação significativa entre osteoporose e a presença de patologias pulpo-periapicais (OR não ajustado= 1,65; IC95%: 0,80 a 3,41; I^2=98,5%). O resultado manteve-se na análise ajustada (OR= 1,96; IC95%: 0,68 a 5,66). No segundo estudo (Capítulo III), a metanálise de efeito aleatório de treze estudos demonstrou uma associação positiva e significativa entre as doenças autoimunes reumáticas e as patologias pulpo-periapicais. A associação foi encontrada tanto na análise em nível individual (OR ajustado= 1,60; IC95%: 1,20 a 2,12; I^2=95,2%) quanto na análise em nível dentário (OR não ajustado= 1,74; IC95%: 1,28 a 2,37; I^2=69,4%). Em ambas as revisões, a certeza da evidência foi classificada como "Muito Baixa" (GRADE), devido principalmente ao alto risco de viés dos estudos primários, elevada heterogeneidade e imprecisão dos resultados.

Conclusão: O resultado desta dissertação para os desfechos investigados assumiu um caráter antagônico: no primeiro estudo (Capítulo II), a revisão sistemática e metanálise não mostrou associação entre a osteoporose (condição degenerativa) e as patologias pulpo-periapicais; no entanto, no segundo estudo (Capítulo III), foi observada uma associação positiva com as doenças autoimunes reumáticas (condições inflamatórias). A plausibilidade biológica desse resultado sugere a necessidade de uma abordagem clínica integrada para a prevenção das patologias pulpo-periapicais em indivíduos com doenças autoimunes reumáticas. Ademais, sugerimos futuros estudos longitudinais com maior rigor metodológico a fim de elucidar possíveis conexões entre a osteoporose e os desfechos endodônticos.

Palavras-chave: Osteoporose. Doenças Autoimunes. Doenças Reumáticas. Doenças da Polpa Dentária. Doenças Periapicais. Revisão Sistemática.

ABSTRACT

Introduction: Pulpo-periapical pathologies are chronic inflammatory diseases with high global prevalence, mostly resulting from the progression of untreated dental caries. Beyond their local impact, these conditions contribute to the individual's systemic inflammatory burden. Conversely, systemic disorders affecting bone metabolism may modulate the host response to these oral infections. This dissertation investigated the connections between two classes of systemic bone alterations: one degenerative (osteoporosis) and the other inflammatory (rheumatic autoimmune diseases), and pulpo-periapical pathologies. The objectives were to assess the evidence regarding: 1) the association between osteoporosis and the occurrence of pulpo-periapical pathologies; and 2) the association between rheumatic autoimmune diseases and the occurrence of pulpo-periapical pathologies.

Methods: This dissertation comprises two systematic reviews and meta-analyses, following the PRISMA 2020 recommendations. Comprehensive searches were conducted in MEDLINE/PubMed, Embase, Scopus, BVS-Bireme, Web of Science, SciELO, and Cochrane Library databases, as well as in the grey literature. Observational studies (cross-sectional, cohort, and case-control) comparing the occurrence of pulpo-periapical pathologies in individuals with osteoporosis (first study) or rheumatic autoimmune diseases (second study) versus healthy control groups were included in both studies. Data were extracted by independent reviewers. Risk of bias was assessed using the Joanna Briggs Institute (JBI) tool, and the certainty of evidence was evaluated using the GRADE system. Meta-analyses were conducted using random-effects models to calculate Odds Ratios (OR) with 95% Confidence Intervals (95% CI).

Results: In the first study (Chapter II), the random-effects meta-analysis of six studies identified no significant association between osteoporosis and the presence of pulpo-periapical pathologies (unadjusted OR= 1.65; 95% CI: 0.80 to 3.41; I^2=98.5%). The result remained insignificant in the adjusted analysis (OR= 1.96; 95% CI: 0.68 to 5.66). In the second study (Chapter III), the random-effects meta-analysis of thirteen studies demonstrated a positive and significant association between rheumatic autoimmune diseases and pulpo-periapical pathologies. This association was found in both the patient-level analysis (adjusted OR= 1.60; 95% CI: 1.20 to 2.12; I^2=95.2%) and the tooth-level analysis (unadjusted OR= 1.74; 95% CI: 1.28 to 2.37; I^2=69.4%). In both reviews, the certainty of evidence was classified as "Very Low" (GRADE), mainly due to the high risk of bias in primary studies, high heterogeneity, and imprecision of results.

Conclusion: The findings of this dissertation regarding the investigated outcomes yielded contrasting results: in the first study (Chapter II), the systematic review and meta-analysis showed no association between osteoporosis (a degenerative condition) and pulpo-periapical pathologies; however, in the second study (Chapter III), a positive association was observed with rheumatic autoimmune diseases (inflammatory conditions). The biological plausibility of this result suggests the need for an integrated clinical approach for the prevention of pulpo-periapical pathologies in individuals with rheumatic autoimmune diseases. Furthermore, we suggest future longitudinal studies with greater methodological rigor to elucidate possible connections between osteoporosis and endodontic outcomes.

Keywords: Osteoporosis. Autoimmune Diseases. Rheumatic Diseases. Dental Pulp Diseases. Periapical Diseases. Systematic Review.

SUMÁRIO

1. INTRODUÇÃO

As Doenças Crônicas Não Transmissíveis (DCNTs) representam o maior desafio de saúde do século XXI, englobando condições como doenças cardiovasculares, os cânceres, as doenças respiratórias crônicas, o diabetes, as doenças autoimunes reumáticas e a osteoporose, todas caracterizadas por uma etiologia multifatorial, longa duração e desenvolvimento lento (Global Burden of Disease Collaborative Network, 2024; World Health Organization, 2022a). O entendimento dessas enfermidades consolidou-se sob a perspectiva de um *continuum*, descrito como uma cascata de eventos metabólicos e fisiopatológicos interligados, que evolui a partir da exposição a fatores de risco, seguido de alterações subclínicas e culminando com danos estruturais graves do órgão-alvo (World Health Organization, 2022a). É dentro desta perspectiva de *continuum* que as principais doenças bucais - a cárie e a doença periodontal - foram integradas ao grupo das DCNTs, superando a visão histórica de eventos isolados para reconhecer seu impacto sistêmico na saúde geral do indivíduo (FDI World Dental Federation *et al.*, 2017).

Nessa linha de pensamento, consolida-se a compreensão de que a saúde bucal está intrinsecamente ligada à saúde sistêmica, onde a cárie e as doenças periodontais são classificadas como DCNTs devido à sua cronicidade e ao compartilhamento de fatores de risco comuns com outras doenças sistêmicas - uma ideia que remonta à *Teoria da Infecção Focal* (Wolf *et al.*, 2021;Miller, 1891; Hunter, 1921; Niazi e Bakhsh, 2022). Há evidências de que a cárie dentária afeta cerca de 2,5 bilhões de pessoas (World Health Organization, 2022b), resultado de um *continuum* iniciado por um biofilme disbiótico, que pode evoluir da desmineralização subclínica até o colapso do órgão pulpar (Featherstone, 2004) e a consequente infecção do sistema de canais radiculares. Como estágio final dessa cascata, desenvolvem-se as patologias periapicais (American Association of Endodontists; European Society of Endodontology, 2025; Bjørndal, 2008). Em virtude do caráter crônico dessas patologias e do histórico de intervenções endodônticas prévias, estima-se que a prevalência global das periodontites apicais seja elevada - cerca de 52% da população adulta mundial possui pelo menos um dente acometido por essa condição, refletindo a doença não tratada, os insucessos endodônticos prévios e lesões que, mesmo em fase de cicatrização, ainda apresentam radiolucidez, e por isso foram consideradas periodontites apicais (Tibúrcio-Machado *et al.*, 2021).

A persistência da infecção do sistema de canais radiculares desencadeia uma resposta imune local que leva à destruição do ligamento periodontal e do osso alveolar periapical. Além

disso, há uma liberação de mediadores pró-inflamatórios, como interleucinas (IL-1, IL-6) e Fator de Necrose Tumoral Alfa (TNF-α), que podem entrar na circulação sanguínea. Revisões sistemáticas demonstraram que a periodontite apical está associada a níveis séricos elevados de marcadores inflamatórios, sugerindo que infecções endodônticas contribuem com a carga inflamatória sistêmica crônica do indivíduo (Georgiou *et al.*, 2019; Gomes *et al.*, 2013). Assim, partindo da premissa, de que as patologias periapicais são moduladas por condições sistêmicas e, ao mesmo tempo, modulam a resposta inflamatória do indivíduo, esta dissertação explorou duas classes de desordens ósseas sistêmicas (1) uma degenerativa (osteoporose) e (2) a outra inflamatória (doenças autoimunes reumáticas) — com o objetivo de investigar se elas se conectam com as doenças pulpares e periapicais.

A osteoporose é uma doença osteometabólica degenerativa sistêmica que afeta mais de 200 milhões de pessoas, ou 18,3% da população mundial (Salari *et al.*, 2021). É caracterizada pela diminuição da massa óssea e pela deterioração da microarquitetura do tecido ósseo, o que resulta em um aumento da fragilidade esquelética e da predisposição às fraturas (Aibar-Almazán *et al.*, 2022; Khandelwal e Lane, 2023). A doença pode ser classificada em duas categorias principais: primária e secundária. A osteoporose primária, sua forma mais comum, está associada à perda óssea relacionada à idade e, principalmente em mulheres, às alterações hormonais do período pós-menopausa. Já a osteoporose secundária é uma consequência de outras condições médicas, como doenças autoimunes (artrite reumatoide e lúpus eritematoso sistêmico), ou do uso de certos medicamentos (corticosteroides, antiepilépticos, inibidores da bomba de prótons e imunossupressores) ou de mudanças súbitas no estilo de vida, podendo afetar ambos os sexos (Aibar-Almazán *et al.*, 2022; Ebeling *et al.*, 2022; Khandelwal e Lane, 2023; Sheu e Diamond, 2016; Stanev e Vasileva, 2024).

A hipótese de que há associação entre a osteoporose (primária e secundária) e as patologias periapicais tem plausibilidade biológica, uma vez que ambas as condições envolvem perda óssea mediada por processos inflamatórios. Especialmente a osteoporose secundária, caracterizada por um estado inflamatório sistêmico e pela redução da densidade mineral óssea, pode de fato comprometer a resposta imune local e a capacidade de reparação tecidual diante de infecções pulpares e periapicais. Essa relação é ainda mais convincente quando consideramos que tanto a osteoporose quanto a periodontite apical são doenças que envolvem perda óssea induzida por inflamação. Dessa forma, a osteólise, uma característica da osteoporose, pode atuar como um fator sistêmico agravante para o desenvolvimento e progressão da periodontite apical (Stanev e Vasileva, 2024). Apesar dessa lógica, as evidências

clínicas são contraditórias. Alguns estudos mostram uma associação positiva (Kamalı e Turkaydın, 2024; Katz e Rotstein, 2021), enquanto outros não encontram tal relação (Cadoni *et al.*, 2022; López-López *et al.*, 2015), evidenciando uma falta de consenso entre os pesquisadores.

A síntese dessas evidências na literatura apresenta lacunas significativas. Duas revisões sistemáticas prévias (Freitas *et al.*, 2025; Pestana de Vasconcelos *et al.*, 2024) foram limitadas pela inclusão de poucos estudos e por estratégias de busca restritas, além da ausência de uma metanálise para consolidar os resultados. Uma metanálise mais recente (Areal-Quecuty *et al.*, 2024) abordou o tema, mas focou apenas em mulheres na pós-menopausa (osteoporose primária) e apresentou uma busca limitada a poucas bases de dados. Diante deste cenário, o **segundo capítulo** desta dissertação - **Existe associação entre osteoporose e patologias pulpo-periapicais? Uma Revisão Sistemática e Metanálise,** busca preencher essa lacuna por meio de uma revisão sistemática e metanálise, utilizando uma estratégia de busca mais ampla, atualizada e abrangente, incluindo múltiplas bases de dados e investigando todas as patologias pulpo-periapicais, e não apenas a periodontite apical. Desta forma, nosso primeiro estudo buscou responder à seguinte questão de pesquisa: **Indivíduos com osteoporose apresentam maior ocorrência de patologias pulpo-periapicais em comparação a indivíduos sem osteoporose?**

As doenças autoimunes, por sua vez, afetam aproximadamente 10% da população global e resultam de uma resposta imune desregulada contra os próprios tecidos do corpo (Conrad *et al.*, 2023; Pisetsky, 2023). Dentre elas, as doenças autoimunes reumáticas são as mais prevalentes, incluindo condições como artrite reumatoide, espondilite anquilosante, lúpus eritematoso sistêmico, artrite idiopática juvenil, doença mista do tecido conjuntivo, síndrome de Sjögren, artrite psoriática, polimialgia reumática e esclerose sistêmica. Essas doenças, também classificadas como DCNTs, afetam primariamente o sistema musculoesquelético e são caracterizadas por um estado de inflamação crônica sistêmica (Abrão *et al.*, 2016; Fragoulis *et al.*, 2023).

A possível conexão entre as doenças autoimunes reumáticas e as patologias pulpo-periapicais é fundamentada em uma robusta plausibilidade biológica, que ocorre de forma bidirecional. Por um lado, a desregulação imune e a imunossupressão, características das doenças autoimunes podem ampliar a suscetibilidade do hospedeiro a infecções de origem endodôntica. Por outro lado, a própria infecção endodôntica crônica ultrapassa seu caráter local ao liberar mediadores pró-inflamatórios na circulação sanguínea, o que pode exacerbar a carga

inflamatória sistêmica já existente (Cintra *et al.*, 2021a; Segura-Egea *et al.*, 2023). Subjacente a essa inter-relação existe um mecanismo inflamatório comum, mediado por citocinas como IL-1, IL-6 e TNF-α, e pelo sistema RANK/RANKL (Aringer, 2020; Georgiou *et al.*, 2019a; Gomes *et al.*, 2013; Niazi e Bakhsh, 2022a; Párkányi *et al.*, 2018).

Apesar de um estudo recente ter identificado uma alta prevalência de periodontite apical em pacientes com doenças autoimunes (Allihaibi *et al.*, 2023), a evidência geral ainda apresenta resultados contraditórios e limitações importantes. Duas revisões sistemáticas prévias focaram apenas na associação com artrite reumatoide e apresentaram resultados inconclusivos devido às limitações metodológicas (Guerrero-Girones *et al.*, 2021; Karataş *et al.*, 2023). Uma revisão mais recente, com metanálise (do Nascimento *et al.*, 2025), embora tenha indicado uma associação positiva entre periodontite apical e doenças autoimunes em geral, carece de um foco específico nas doenças autoimunes reumáticas como um grupo, e de estratégias de busca mais robustas. Portanto, ainda não há uma revisão sistemática abrangente que tenha investigado a associação entre as diversas doenças autoimunes reumáticas e desfechos endodônticos.

Considerando essa lacuna, o **terceiro capítulo** desta dissertação **– Existe associação entre doenças autoimunes reumáticas e patologias pulpo-periapicais? Uma Revisão Sistemática e Metanálise,** visa elucidar essa questão por meio de uma nova revisão sistemática e metanálise, com uma abordagem metodológica abrangente. Assim, nosso segundo estudo foi desenhado para responder à seguinte questão de pesquisa: **Indivíduos com doenças autoimunes reumáticas têm maior ocorrência de patologias pulpo-periapicais em comparação àqueles sem essas condições?**

2. OBJETIVOS

2.1 Geral

Investigar as conexões entre as alterações ósseas degenerativas (osteoporose) e inflamatórias (doenças autoimunes reumáticas) e as patologias pulpares e periapicais.

2.2 Específicos

Capítulo II:

1) Investigar as evidências sobre a associação entre osteoporose e a ocorrência de patologias pulpares e periapicais.

Capítulo III:

1) Investigar as evidências sobre a associação entre doenças autoimunes reumáticas e a ocorrência de patologias pulpares e periapicais, considerando os dados em nível individual;
2) Investigar as evidências sobre a associação entre doenças autoimunes reumáticas e a ocorrência de patologias pulpares e periapicais, considerando os dados em nível dentário.

3. CAPÍTULO I

FUNDAMENTAÇÃO TEÓRICA

3.1 Da Teoria da Infecção Focal a Medicina Endodôntica

No final do século 19 e início do século 20 havia uma teoria de que focos de infeção dental e dos tecidos bucais estariam associados à saúde geral do indivíduo (Niazi; Bakhsh, 2022). Desse modo, com a intenção de "combater doenças" causadas por esses focos de infecção, vários dentes e tecidos bucais foram removidos de forma generalizada (Price, 1925). Tal assertiva já havia sido confirmada pela descoberta dos microrganismos nas lesões de cárie e nos canais radiculares com polpa necrótica por Miller em 1891. Ele defendia que esses microrganismos e seus produtos poderiam atingir outras partes do corpo, distantes da cavidade bucal. Seguindo esse mesmo raciocínio, no início do século 20, Hunter (1921) propôs que, além dos microrganismos se espalharem por outras partes do corpo, poderiam causar uma série de comprometimentos sistêmicos, dando força para a *Teoria da Infecção Focal*.

Com o passar dos anos, percebeu-se que as extrações dentárias múltiplas não resolviam os problemas de saúde dos indivíduos e que, doenças supostamente causadas pela infecção dental, também eram comuns em indivíduos com dentes hígidos. Assim, essa teoria foi refutada. Depois disso, o interesse por esse tema diminuiu por um longo tempo, mas parece estar ressurgindo nas últimas duas décadas (Niazi e Bakhsh, 2022).

Atualmente, tem-se estudado cada vez mais a relação entre patologias pulpares e periapicais e desordens sistêmicas, bem como seu impacto na saúde geral dos indivíduos (Cintra *et al.*, 2021; Niazi; Bakhsh, 2022; Segura-Egea *et al.*, 2023; Segura-Egea *et al.*, 2015). Uma recente revisão sistemática e metanálise concluiu que a periodontite apical está associada a níveis séricos elevados de proteína C reativa (PCR) e interleucina (IL) 6, sugerindo que a resposta inflamatória local pode ter repercussões na saúde geral do indivíduo, o que pode contribuir para um aumento global da carga inflamatória sistêmica (Georgiou *et al.*, 2019).

A inflamação sistêmica está associada às doenças crônicas não transmissíveis (DCNTs), incluindo a osteoporose e as doenças autoimunes reumáticas, podendo influenciar a progressão de condições bucais ósseas, como as patologias periapicais, e interferir na reparação óssea, após o tratamento endodôntico (Cintra *et al.*, 2021a; Segura-Egea *et al.*, 2023; Stanev e Vasileva, 2024).

3.2 Relação entre Osteoporose e Patologias Pulpares e Periapicais

A osteoporose é uma doença osteometabólica degenerativa sistêmica que afeta mais de 200 milhões de pessoas em todo o mundo. É caracterizada por baixa massa óssea e deterioração da microarquitetura, com aumento da fragilidade óssea e suscetibilidade às fraturas (Aibar-Almazán *et al.*, 2022; Khandelwal e Lane, 2023). Destacamos que processos inflamatórios crônicos podem desempenhar um papel secundário na etiologia e progressão da osteoporose, especialmente em indivíduos com doenças autoimunes reumáticas como artrite reumatoide, espondilite anquilosante e lúpus eritematoso sistêmico, possivelmente porque a inflamação tem uma grande influência no metabolismo ósseo, levando ao aumento da reabsorção óssea e ao risco de fraturas (Ebeling *et al.*, 2022; Lacativa e Farias, 2010; Rotta *et al.*, 2020).

Devido a essa peculiaridade de sua etiologia, pode ser classificada em dois grupos: a osteoporose primária e a osteoporose secundária (Ebeling *et al.*, 2022; Khandelwal e Lane, 2023; Lacativa e Farias, 2010). A osteoporose primária é a perda óssea relacionada à idade, sendo mais comum em mulheres pós-menopáusicas, devido à diminuição dos níveis de estrogênio e aumento dos níveis do hormônio folículo-estimulante (FSH). O FSH pode agravar a inflamação periapical, aumentando a expressão e secreção de citocinas pró-inflamatórias, como IL-1β, IL-6 e TNF-α, sugerindo que mulheres no período de pós-menopausa podem estar mais propensas ao desenvolvimento de inflamação e perda óssea associadas à osteoporose (Qian *et al.*, 2020).

Já a osteoporose secundária é causada por condições subjacentes, como distúrbios endócrinos, uso de certos medicamentos, como corticosteroides, alguns antiepilépticos, inibidores da bomba de prótons e imunossupressores, e doenças inflamatórias, como artrite reumatoide, lúpus eritematoso sistêmico e espondilite anquilosante. Nessas condições, está relacionada à inflamação crônica e ao desequilíbrio entre a atividade dos osteoclastos e osteoblastos (Ebeling *et al.*, 2022; Lacativa e Farias, 2010; Rotta *et al.*, 2020; Sheu e Diamond, 2016).

Um estudo transversal mostrou que a baixa densidade mineral óssea pode estar associada a uma maior severidade da doença periodontal, especificamente relacionada à perda de inserção clínica em mulheres na pós-menopausa (Brennan *et al.*, 2007). Por outro lado, já se sabe que um fator de risco para o desenvolvimento futuro da osteoporose é a baixa densidade mineral óssea (Weaver *et al.*, 2016). Reforçando essa conexão, nosso grupo de pesquisa identificou, em um estudo transversal com uma amostra representativa de adolescentes do estado do Maranhão, que a baixa densidade mineral óssea está associada à periodontite severa (Costa *et al.*, 2021).

Ademais, dois recentes estudos apontam para uma conexão relevante entre condições sistêmicas, como a osteoporose, e a progressão de doenças inflamatórias crônicas, incluindo as lesões periapicais (Kamalı e Turkaydın, 2024; Katz e Rotstein, 2021). A osteoporose afeta todo o esqueleto, e seus efeitos nos ossos maxilares podem exacerbar a reabsorção óssea na região periapical. O mecanismo proposto envolve a desregulação do metabolismo ósseo, frequentemente associada a baixos níveis de estrogênio, que ativa vias moleculares como o aumento da expressão de RANKL e a cascata inflamatória NLRP3/Caspase-1/IL-1β, acelerando a destruição óssea (Stanev e Vasileva, 2024).

Nesse contexto, a plausibilidade biológica se fortalece ao considerarmos a osteoimunologia. A deficiência de estrogênio não apenas reduz a massa óssea, mas altera o "ponto de equilíbrio" da resposta inflamatória (Rossetti *et al.,* 2022). Em um indivíduo com osteoporose, o osso alveolar periapical já se encontra em um estado de *turnover* acelerado e com trabeculado mais poroso. Isso cria um ambiente biologicamente mais vulnerável, onde as toxinas bacterianas do canal radicular encontram menor resistência física e uma resposta osteoclástica desproporcionalmente maior do que a osteoblástica, facilitando a expansão da lesão periapical (Stanev e Vasileva, 2024).

Apesar dessa forte plausibilidade biológica, a literatura carece de evidências consolidadas que confirmem essa hipótese. Revisões sistemáticas prévias (Freitas *et al.*, 2025; Pestana de Vasconcelos *et al.*, 2024) e uma metanálise focada em mulheres na pós-menopausa (Areal-Quecuty *et al.*, 2024) apresentaram limitações significativas, como a inclusão de poucos estudos e estratégias de busca restritas.

3.3 Relação entre Doenças Autoimunes Reumáticas e Patologias Pulpares e Periapicais

Com a persistência da infecção bacteriana no sistema de canais radiculares, os produtos e subprodutos bacterianos destroem o ligamento periodontal e degradam o osso periapical, além de estimular a liberação de mediadores pró-inflamatórios, como as IL-1, IL-6 e TNF-α, que induzem a atividade dos osteoclastos e inibem a formação óssea pelos osteoblastos (Cintra *et al.*, 2021; Niazi; Bakhsh, 2022; Segura-Egea *et al.*, 2023; Segura-Egea *et al.*, 2015).

Além disso, a revisão sistemática e metanálise de Gomes *et al.* (2013) trouxe evidências de que os níveis séricos elevados de PCR, IL-1, IL-2, IL-6, imunoglobulina (Ig) A, Ig G e Ig M estão associados a periodontite apical. Isso sugere que a infecção periapical de origem endodôntica e certos marcadores moleculares de inflamação sistêmica podem estar intimamente

relacionados, levando a crer que há um mecanismo inflamatório comum entre as patologias periapicais e as doenças autoimunes reumáticas.

Essa correlação reforça a hipótese de um mecanismo inflamatório compartilhado. A elevação de citocinas pró-inflamatórias na circulação não restringe seus efeitos aos órgãos-alvo das doenças autoimunes reumáticas, mas gera uma carga inflamatória sistêmica que repercute na região periapical. Nesse cenário, o sistema imunológico, já desregulado pela condição autoimune, pode apresentar uma deficiência funcional na resposta aos patógenos endodônticos, gerando um ambiente biologicamente vulnerável, onde a capacidade do hospedeiro de conter a infecção local e promover o reparo ósseo é suprimida pela condição sistêmica (Segura-Egea et al., 2023; Cintra et al., 2021).

Um recente estudo identificou e avaliou a qualidade metodológica de todas as revisões sistemáticas publicadas que avaliaram a associação entre lesão periapical e DCNTs, incluindo algumas doenças autoimunes, como diabetes mellitus tipo 1, artrite reumatoide e doença inflamatória intestinal. Os autores concluíram que há evidências moderada e inconclusivas associando a periodontite apical às doenças autoimunes e alertaram que não se sabe se as doenças autoimunes reumáticas podem aumentar a suscetibilidade do hospedeiro às alterações pulpares e periapicais ou apenas prejudicar o reparo ósseo periapical, mantendo o processo inflamatório e a reabsorção óssea após o tratamento endodôntico (Pinto *et al.*, 2023).

Nesse sentido para buscar elucidar essas dúvidas e compreendermos como essas conexões são estabelecidas destacamos a ocorrência e a fisiopatologia das doenças autoimunes reumáticas que foram exploradas em nossa segunda questão de pesquisa, por serem as mais prevalentes no contexto global:

(1) *Artrite Reumatoide* é a doença autoimune que envolve inflamação articular mais comum no mundo, afetando mais de 18 milhões de pessoas em 2019, sendo 70% mulheres. É uma doença que pode afetar vários órgãos e sistemas, sendo caracterizada por uma inflamação na membrana sinovial permanente acompanhada de destruição de ossos e cartilagens, ocasionando mobilidade reduzida, inchaço, rigidez e dor (World Health Organization, 2023). Indivíduos com artrite reumatoide têm níveis elevados de citocinas, as quais desempenham um papel importante na inflamação da membrana sinovial e na infiltração de células inflamatórias e imunológicas, como os linfócitos B e T, macrófagos e células dendríticas, além das citocinas pró-inflamatórias, como as IL -1, IL-6, IL-12, IL-17, TNF-α, e moléculas como o receptor ativador do fator nuclear kappa beta (RANK) e seu ligante (RANKL). Essas citocinas também estão

envolvidas no processo de reabsorção óssea inflamatória da periodontite apical assintomática (Karataş, Kul e Tepecik, 2020; Párkányi *et al.*, 2018).

(2) *Espondilite Anquilosante* afeta principalmente a coluna vertebral e as articulações sacroilíacas, causando dor, rigidez e eventual fusão das vértebras. É uma condição debilitante, mais incidente em homens abaixo dos 40 anos, com uma prevalência estimada de 0,1% a 0,5% da população geral (Chen *et al.*, 2021; Smith, 2015). Além dos sintomas musculoesqueléticos característicos, essa doença pode estar associada a várias complicações sistêmicas, incluindo uveíte, doença inflamatória intestinal e aumento do risco de osteoporose (Smith, 2015).

(3) *Lúpus Eritematoso Sistêmico* é caracterizado pela desregulação do sistema imunológico, resultando em inflamação e danos a vários órgãos e tecidos do corpo, como pele, rins, pulmões, articulações, coração e sistema nervoso central (Fortuna e Brennan, 2013; Tsokos, 2024). Apresenta uma prevalência global estimada em 43,7 por 100.000 pessoas, totalizando aproximadamente 3,41 milhões de pessoas afetadas mundialmente. Sua epidemiologia é influenciada por sexo e idade, com a prevalência sendo significativamente mais alta em mulheres do que em homens (Tian *et al.*, 2023).

(4) *Síndrome de Sjögren* (SS) também é uma doença autoimune com repercussões reumáticas. O fenômeno autoimune envolve a invasão de linfócitos em órgãos e glândulas, incluindo as glândulas lacrimais e salivares, desencadeando um processo inflamatório que compromete suas funções normais. Essa patologia pode ocasionar secura ocular, xerostomia, inflamação das glândulas salivares, presença de autoanticorpos, como os anticorpos anti-SSA e anti-SSB, dentre outros sintomas. Além disso, pode ter manifestações extra glandulares, podendo afetar órgãos como pele, pulmões, coração, rins e sistema nervoso (Beydon *et al.*, 2024). Sua prevalência é extremamente variável, com estimativas de 12,4 a 770,0 por 100.000 pessoas, refletindo a escassez de dados globais e inconsistências metodológicas. A doença é mais prevalente em mulheres e em grupos etários mais velhos (≥75 anos) (Thurtle *et al.*, 2024).

(5) *Doença do Tecido Conjuntivo* é uma doença autoimune rara caracterizada por combinar características clínicas de várias doenças autoimunes, como lúpus eritematoso sistêmico e escleroderma sistêmico, e está associada à presença de níveis elevados de anticorpos anti-ribonucleoproteína U1 (U1-RNP). A presença desses autoanticorpos é uma característica definidora da doença e tem sido foco de pesquisas para compreender as respostas imunes e a patogênese da doença (Ortega-Hernandez; Shoenfeld, 2012; Berard; Laxer, 2016). É classificada como uma doença rara, e sua prevalência global, embora incerta, é estimada entre 1 e 9 casos por 100.000 pessoas, afetando majoritariamente mulheres (Ungprasert *et al.*, 2016).

Assim, esta dissertação, composta por dois estudos, explorou e sintetizou qualitativamente as evidências disponíveis sobre as conexões entre alterações ósseas degenerativas (osteoporose) e inflamatórias (doenças autoimunes reumáticas) e as patologias pulpares e periapicais.

4. CAPÍTULO II

Existe associação entre osteoporose e patologias pulpo-periapicais? Uma revisão sistemática e metanálise

(Artigo científico a ser submetido à Revista *Oral Diseases*)

Resumo:

Objetivo: Investigar se indivíduos com osteoporose apresentam maior ocorrência de patologias pulpo-periapicais em comparação a indivíduos sem a doença. **Métodos:** Esta revisão sistemática seguiu as recomendações PRISMA. Foram incluídos estudos observacionais que compararam a ocorrência de patologias pulpo-periapicais em indivíduos com osteoporose e controles sem a doença. Foi realizada uma busca sistemática nas bases de dados PubMed, SciELO, BVS/Bireme, Embase, Scopus, Web of Science, Cochrane Library e na literatura cinza em julho de 2024 e atualizada em junho de 2025. Dois revisores independentes realizaram a seleção dos estudos, extração de dados e avaliação do risco de viés utilizando a ferramenta do Joanna Briggs Institute. Foi realizada metanálise de efeitos aleatórios. A qualidade da evidência dos resultados da metanálise foi aferida pelo sistema GRADE**. Resultados:** Seis estudos foram incluídos na análise. Foram calculadas as razões de chance [Odds Ratio, (OR)] e os respectivos Intervalos de Confiança a 95% (IC95%) dos dados primários. A metanálise de efeito aleatório com dados brutos não identificou associação significativa entre osteoporose e patologias pulpo-periapicais. (OR= 1.65; IC95%: 0.80 a 3.41). A análise ajustada também não foi significativa (OR= 1.96; IC95%: 0.68 a 5.66). A heterogeneidade foi muito alta ($I^2 > 98\%$) e a qualidade da evidência, avaliada pelo GRADE, foi classificada como "muito baixa". **Conclusões:** Não há evidências que associem osteoporose à maior ocorrência de patologias pulpo-periapicais.

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Introdução

A osteoporose é uma doença crônica não transmissível (DCNT) osteometabólica degenerativa sistêmica, caracterizada pela redução da massa óssea e deteriorização da microarquitetura, o que aumenta a fragilidade óssea e a predisposição a fraturas (Sözen, Özışık, & Çalık Başaran, 2017); comum em humanos e um significativo problema de saúde pública que afeta 18,3% da população mundial (Salari *et al.*, 2021). É classificada em primária e secundária, sendo a primária associada ao envelhecimento e a fatores hormonais como a deficiência de estrogênio, razão pela qual é mais prevalente em mulheres; e a secundária é consequência de outras condições de saúde, como doenças autoimunes (artrite reumatoide e lúpus eritematoso sistêmico), do uso de certos medicamentos (corticosteroides, antiepilépticos, inibidores da bomba de prótons e imunossupressores) ou de mudanças súbitas no estilo de vida, podendo afetar ambos os sexos (Aibar-Almazán *et al.*, 2022; Ebeling *et al.*, 2022; Khandelwal & Lane, 2023; Sheu & Diamond, 2016; Stanev & Vasileva, 2024).A osteoporose tem sido associada a complicações orais, como perda de inserção periodontal e perda dentária (Brennan, Genco, Hovey, Trevisan, & Wactawski-Wende, 2007).

A cárie dentária, uma das DCNTs mais prevalentes na cavidade bucal, é considerada a condição de saúde mais comum do mundo, afetando um número estimado em 2,5 bilhões de pessoas (World Health Organization, 2022), e quando não tratada, evolui para pulpites severas e infecções de origem endodôntica, como a necrose pulpar e as periodontites apicais (American Association of Endodontists; European Society of Endodontology, 2025; Bjørndal, 2008). Em virtude do caráter crônico dessas patologias e do histórico de intervenções endodônticas prévias, estima-se que a prevalência global de periodontite apical seja elevada - com cerca de 52% da população adulta mundial possuindo ao menos um dente acometido (Tibúrcio-Machado *et al.*, 2021). Esse estudo considerou realidades clínicas distintas, incluiu na contagem como periodontite apical, além dos insucessos endodônticos verdadeiros, as lesões que, mesmo em fase de cicatrização, ainda apresentavam radiolucidez no momento da avaliação. Há evidências de que em longo prazo, essas lesões podem destruir os ligamentos periodontais, o osso alveolar periapical e liberar mediadores pró-inflamatórios, sugerindo que a infecção crônica de origem endodôntica pode ter repercussões sistêmicas (Georgiou, Crielaard, Armenis, de Vries, & van der Waal, 2019; Gomes *et al.*, 2013).

Estudos recentes sugerem que a osteoporose, pode desempenhar um papel importante na progressão de processos inflamatórios crônicos de origem endodôntica (Kamalı & Turkaydın, 2024; Katz & Rotstein, 2021). O mecanismo envolvido entre essas duas condições

demonstra que a alteração no metabolismo ósseo, frequentemente associada a baixos níveis de estrogênio, intensifica a reabsorção óssea na região periapical. Isso ocorre por duas vias: pelo aumento da expressão de RANKL e da cascata inflamatória NLRP3/Caspase-1/IL-1β, levando a uma progressão mais rápida das lesões periapicais em pacientes com osteoporose (Stanev & Vasileva, 2024).

Apesar da plausibilidade biológica da relação entre osteoporose e desfechos endodônticos, a literatura ainda carece de evidências robustas e abrangentes para suportar essa hipótese. Até o momento, duas revisões sistemáticas (Freitas *et al.*, 2025; Pestana de Vasconcelos, Martins, Afonso, Braga, & Pina-Vaz, 2024) avaliaram a prevalência de periodontite apical em pacientes com osteoporose. No entanto, ambas foram limitadas pela inclusão de apenas três estudos, por estratégias de busca restritas a poucas bases de dados, e sem a realização de metanálise para consolidar os resultados. Mais recentemente, uma metanálise (Areal-Quecuty *et al.*, 2024) investigou a prevalência da periodontite apical em mulheres na pós-menopausa, mas também restringiu as bases de dados estudadas.

Baseado nisso, nosso estudo buscou avançar a fronteira do conhecimento, apresentando uma busca mais ampla e atualizada em um maior número de bases de dados, além de investigar todas as patologias pulpo-periapicais, e não apenas a periodontite apical.

Assim, propusemo-nos a responder à seguinte questão de pesquisa: *Indivíduos com osteoporose apresentam maior ocorrência de patologias pulpo-periapicais em comparação a indivíduos sem osteoporose?*

Material e Métodos

Protocolo e registro

Esta revisão sistemática e metanálise seguiu as diretrizes do Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA 2020) (Nagendrababu *et al.*, 2019; Page *et al.*, 2021). Seu protocolo está registrado no banco de dados do PROSPERO sob o número de registro CRD42024559563. Os checklists PRISMA para o resumo e o texto completo estão na Tabela Suplementar 1 e Tabela Suplementar 2, respectivamente.

Critérios de elegibilidade

A estratégia **PECOs** (Methley, Campbell, Chew-Graham, McNally, & Cheraghi-Sohi, 2014) foi empregada para definir os critérios de elegibilidade: **População** (P)**:** Adultos e idosos, independentemente do sexo, raça/cor ou qualquer outra condição; **Exposição** (E): Osteoporose; **Comparação** (C): Indivíduos sem o diagnóstico de osteoporose (grupo controle); **Desfecho** (O): Presença de patologias pulpo-periapicais; **Desenhos de estudo** (s): Estudos observacionais (transversais, coorte e caso-controle).

Foram incluídos estudos observacionais (transversais, coorte e caso-controle) em humanos que compararam a ocorrência de patologias pulpo-periapicais em indivíduos com osteoporose (grupo de exposição) com um grupo de indivíduos sem essas condições (grupo controle). Não houve restrições quanto à raça/etnia, sexo ou condição socioeconômica, nem quanto ao idioma ou ano de publicação dos trabalhos.

Foram excluídos estudos cujo escopo se limitasse a subpopulações com condições sistêmicas ou fisiológicas específicas capazes de atuar como fatores de confusão para os desfechos investigados (confundidores primários). Adicionalmente, foram descartadas publicações duplicadas ou análises redundantes baseadas na mesma coorte de pacientes de estudos já incluídos.

Seleção dos descritores, bases de dados e estratégia de busca

Para a composição da equação de busca foram considerados todos os termos MeSH (Medical Subject Headings), DeCS (Descritores em saúde) e Emtree equivalentes que descrevem a estratégia **PECOs**: P*opulação* **(P)** - Adult; Aged; *Exposição* **(E) –** Osteoporosis; Osteoporosis, Postmenopausal; Bone Diseases, Metabolic; *Comparação* **(C)**: Não foram utilizados termos de pesquisa específicos para o grupo de controle, uma vez que os critérios de inclusão foram restritos a desenhos de estudo que, por definição, incluem um grupo

comparador; *Desfecho* **(O) –** Periapical Diseases; Dental Pulp Diseases; Dental Pulp Necrosis; Pulpitis; Periapical Periodontitis; Periapical Abscess; Periapical Granuloma; Tooth, Nonvital; Dental Pulp Devitalization; Periapical Tissue; Radicular Cyst; Root Canal Therapy; Root Canal Obturation; *Desenhos de estudo* **(s) -** Observational Study; Cross-Sectional Studies; Cohort Studies; Case-Control Studies; Clinical Trial; Randomized Controlled Trial; Controlled Clinical Trial; Intervention Study].

Estes termos foram conectados pelos operadores booleanos (*OR, AND e NOT*) a fim de garantir a abrangência da busca. A equação de busca referente a cada base de dados está detalhada na Tabela Suplementar 3.

Foram utilizadas as bases de dados online: *MEDLINE/PubMed, Embase, Scopus, BVS-Bireme, Web of Science, SciELO* e *Biblioteca Cochrane.* A literatura cinza também foi consultada no *Google Scholar, Biblioteca Digital Brasileira de Teses e Dissertações (BDTD) e o Catálogo de Teses e Dissertações da CAPES*. Também foram examinadas listas de referências e feito contato com especialistas. As buscas foram realizadas inicialmente em julho de 2024 e atualizadas em junho de 2025. No Google Scholar, apenas os 100 primeiros resultados mais relevantes da busca foram considerados para avaliação.

Seleção dos artigos

Os resultados das buscas foram importados para o *software Rayyan* (Ouzzani, Hammady, Fedorowicz, & Elmagarmid, 2016), onde as duplicatas foram identificadas e excluídas. Os títulos e resumos foram analisados por dois avaliadores independentes, considerando os critérios de elegibilidade pré-estabelecidos. Os estudos pré-selecionados foram lidos na íntegra e os critérios de elegibilidade foram novamente aplicados. Em caso de discordância, um terceiro avaliador atuou como árbitro.

Extração de dados

Após a seleção dos artigos, os dados foram extraídos por dois revisores independentes utilizando formulários de extração de dados personalizados *[autores, ano de publicação, revista, país do estudo, desenho do estudo, população, tamanho da amostra, faixa etária da amostra, diagnóstico da osteoporose, tipo de patologia pulpar/periapical, diagnóstico da patologia pulpar/periapical, medida de efeito não ajustada e ajustada (odds ratio), intervalo de confiança de 95% (IC 95%) e principais resultados]*. As discrepâncias foram resolvidas em

reunião de consenso com a arbitragem do terceiro avaliador. Em alguns casos, foi necessário entrar em contato com os autores correspondentes para obter as informações adicionais.

Avaliação do risco de viés dos estudos incluídos

A avaliação foi conduzida por dois revisores independentes utilizando a ferramenta do Instituto Joanna Briggs (JBI) (Moola *et al.*, 2020) apropriada para cada desenho de estudo, sendo as discordâncias resolvidas por um terceiro revisor. O risco de viés foi classificado como baixo (>75% dos critérios preenchidos), moderado (51–75%) ou alto (≤50%), e os resultados foram apresentados visualmente em um gráfico de semáforo gerado na plataforma robvis (https://www.riskofbias.info/welcome/robvis-visualization-tool).

Análise qualitativa e quantitativa dos dados

Todas as informações extraídas foram compiladas e estão apresentadas em formato estruturado e comparativo em tabelas. Para a metanálise, os dados primários foram extraídos para calcular as razões de chance (odds ratio) e os respectivos IC95%. Quando disponíveis, foram extraídas tanto as razões de chance não ajustadas quanto as ajustadas. O modelo que apresentou o melhor ajuste foi selecionado, e as variáveis de ajuste foram devidamente registradas. Foi adotado o modelo de efeito aleatório conforme o método de Dersimonian & Laird (1986), para o cálculo da estimativa padronizada. A metanálise de efeito aleatório é recomendada quando há heterogeneidade significativa entre os estudos incluídos, definida por um valor de $p < 0,10$ no teste de heterogeneidade ou um valor de $I^2 \geq 50\%$. Considerando que a heterogeneidade entre os estudos foi superior a 50%, optou-se pelo uso deste modelo.

Análise de subgrupo foi conduzida com o objetivo de explorar potenciais fontes de heterogeneidade, sendo realizada a comparação entre medidas de associação não ajustadas e ajustadas. Para avaliar a robustez dos resultados, uma análise de sensibilidade foi feita excluindo-se o estudo de Thanakun, Pornprasertsuk-Damrongsri, Na Mahasarakham, Techatanawat, & Izumi (2019). A exclusão justifica-se porque este estudo não utilizou o exame padrão-ouro para o diagnóstico da osteoporose, baseando-se apenas em sinais clínicos, radiográficos e laboratoriais que são sugestivos, mas não confirmatórios, de baixa densidade mineral óssea. O procedimento garantiu a comparabilidade dos dados com os demais estudos, que seguiram critérios diagnósticos padronizados.

O gráfico de funil (*funnel plot*) não foi analisado por haver trabalhos (n = 6) em número inferior ao mínimo de 10 recomendado para a análise (Debray, Moons, & Riley, 2018; Sterne

& Egger, 2001) Todas as análises estatísticas foram realizadas utilizando os softwares Stata (versão 14.0) (StataCorp, 2015) e RevMan (versão 5.3) (The Cochrane Collaboration, 2014).

Avaliação da qualidade da evidência

A qualidade da evidência dos resultados da metanálise foi aferida pelo sistema GRADE, que classificou cada estudo em alta, moderada, baixa ou muito baixa qualidade da evidência (Guyatt *et al.*, 2008; Ryan & Hill S, 2016).

Resultados

Seleção dos estudos

A busca inicial em 7 bases de dados identificou 803 artigos, enquanto a pesquisa na literatura cinza e em listas de referências encontrou 187 registros adicionais. Após as etapas de remoção de duplicatas e triagem, de acordo com os critérios de elegibilidade, 15 artigos foram selecionados para avaliação do texto completo. Destes, 6 estudos foram considerados elegíveis e incluídos na revisão sistemática e metanálise. Todo o processo de busca e seleção, incluindo as justificativas para as exclusões, está detalhado no fluxograma da Figura 1.

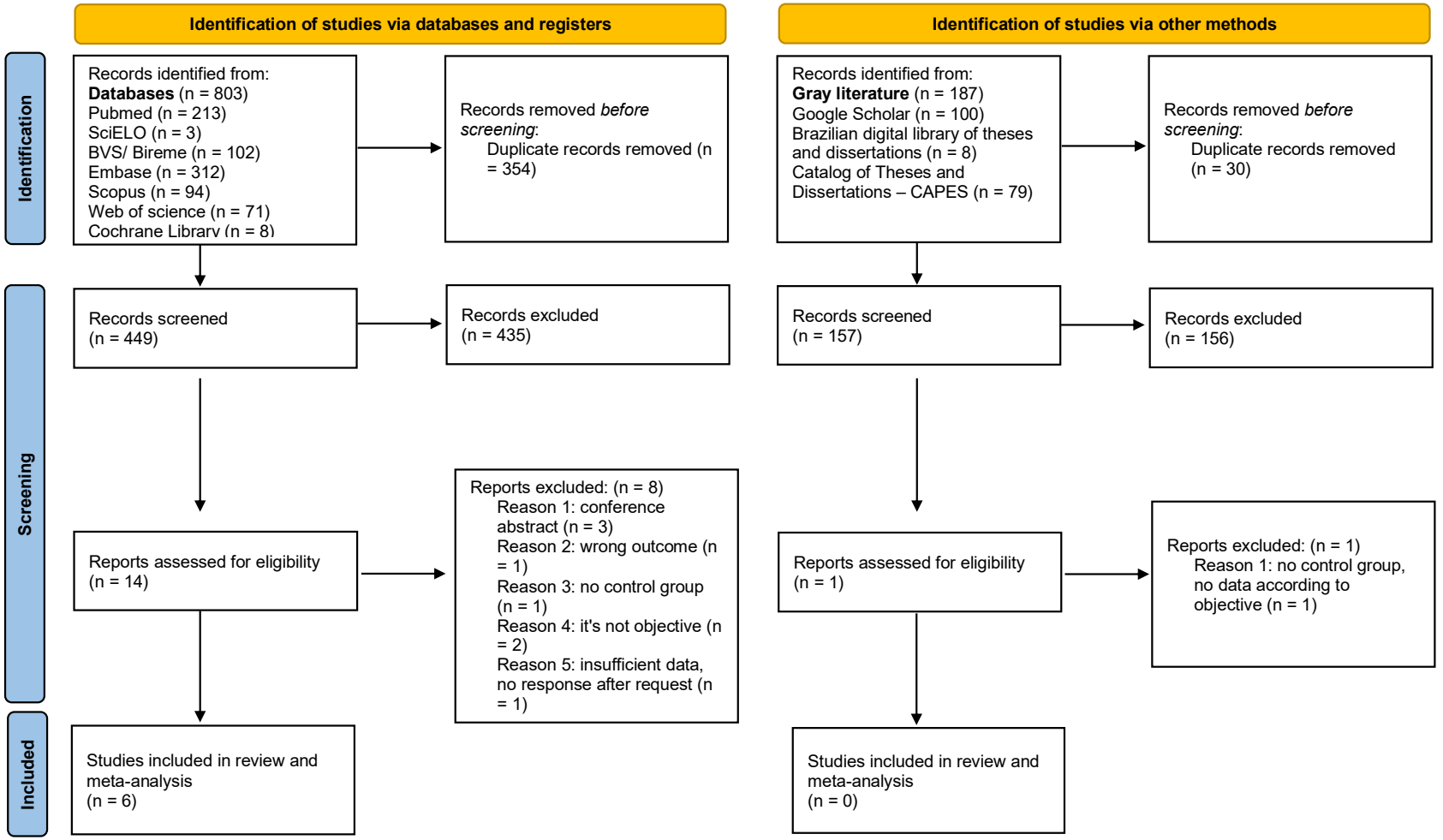

Figura 1. Fluxograma da estratégia de busca da revisão sistemática e metanálise seguindo as diretrizes PRISMA 2020 (Page *et al.*, 2021).

Características dos estudos

As características dos seis estudos incluídos estão descritas na Tabela Suplementar 4. Todos os artigos foram publicados em inglês, com datas de publicação variando entre 2015 (López-López *et al.*, 2015) e 2024 (Kahm & Yang, 2024; Kamalı & Turkaydın, 2024) e amostras de 39 (López-López *et al.*, 2015) a 1.644.954 indivíduos (Katz & Rotstein, 2021).

Em relação aos desfechos endodônticos, observou-se heterogeneidade nas condições investigadas e nos métodos de diagnóstico. A maioria dos estudos avaliou a presença de periodontite apical ou lesões periapicais diagnosticadas por meio de exames radiográficos, utilizando radiografias panorâmicas ou a combinação destas com periapicais (Cadoni et al., 2022; Kamalı & Turkaydın, 2024; López-López et al., 2015; Thanakun et al., 2019). Já os estudos baseados em registros hospitalares utilizaram códigos da Classificação Internacional de Doenças (ICD-10) para identificar desfechos como necrose pulpar (Kahm & Yang, 2024) e lesões periapicais (Katz & Rotstein, 2021).

Avaliação do risco de viés

Dois estudos foram classificados como de baixo risco, três de risco moderado e um de alto risco. A análise detalhada para cada estudo está apresentada na Figura Suplementar 1. As limitações metodológicas mais frequentes concentraram-se nos domínios de mensuração do desfecho e da exposição, refletindo a utilização de métodos diagnósticos com sensibilidade variável, como radiografias panorâmicas isoladas ou ICD-10. Adicionalmente, estudos classificados com maior risco de viés apresentaram fragilidades na análise estatística e no controle de fatores de confusão, não realizando os ajustes necessários para variáveis importantes.

Metanálise

Seis estudos foram incluídos na metanálise considerando associações não ajustadas (Figura 2a). Não foi identificada associação significativa entre osteoporose e a presença de patologias pulpo-periapicais (OR= 1.65; IC95%: 0.80 a 3.41). Somente dois estudos apresentaram medidas ajustadas (Figura 2b), mas a metanálise também não evidenciou associação significativa entre osteoporose e patologias pulpo-periapicais (OR= 1.96; IC95%: 0.68 a 5.66). Na análise de sensibilidade (Figura 2c), ao excluir o estudo de Thanakun, Pornprasertsuk-Damrongsri, Na Mahasarakham, Techatanawat, & Izumi (2019), o único que avaliou exclusivamente mulheres na pós-menopausa, sem o exame padrão-ouro para o

diagnóstico da osteoporose, os resultados permaneceram semelhantes (OR= 1.52; IC95%: 0.69 a 3.35).

Avaliação da qualidade da evidência

A qualidade da evidência para todos os desfechos foi classificada como "muito baixa" (Tabela Suplementar 5). O rebaixamento inicial deveu-se à inclusão exclusiva de estudos observacionais. Adicionalmente, a certeza foi diminuída em todas as análises por três motivos consistentes: um risco de viés "muito grave" (pela predominância de estudos com risco moderado a alto), uma inconsistência "muito grave" com heterogeneidade (I^2) sempre superior a 98%, e uma imprecisão "grave" (intervalos de confiança amplos que cruzaram a linha de nulidade). Essas graves limitações indicam que os resultados devem ser interpretados com extrema cautela.

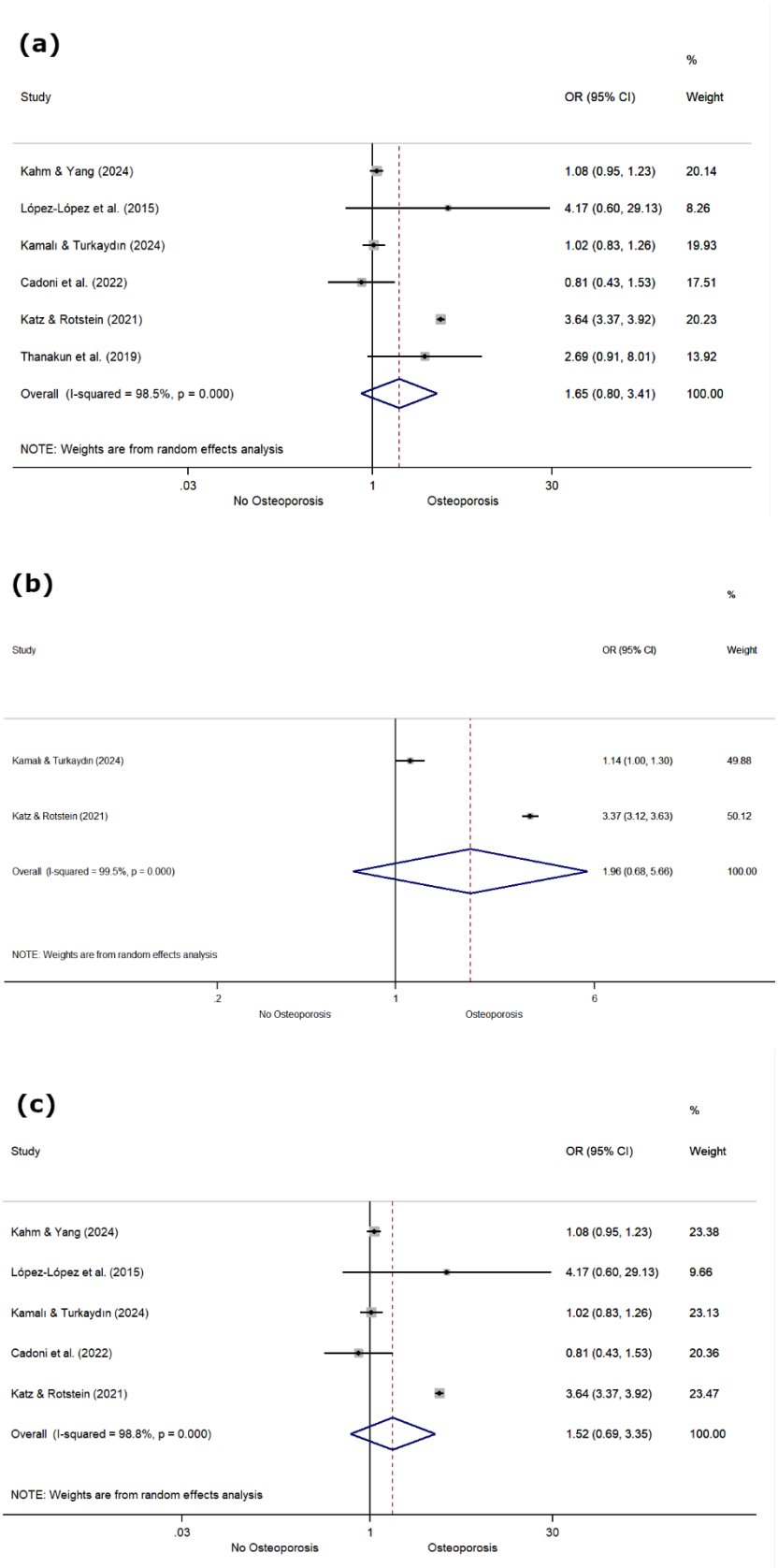

Figura 2. Gráficos Forest Plot da associação entre osteoporose e patologias pulpo-periapicais: **(a)** análise com OR não ajustadas; **(b)** análise com OR ajustadas; e **(c)** análise de sensibilidade com exclusão do estudo de Thanakun *et al.* (2019).

Discussão

Esta revisão sistemática e metanálise teve como objetivo principal investigar a associação entre a osteoporose e a ocorrência de patologias pulpo-periapicais. Ao contrário de revisões anteriores, este estudo apresenta a primeira síntese quantitativa baseada em uma busca abrangente na literatura, englobando todo o espectro das patologias pulpares e periapicais, e não apenas a periodontite apical. Os resultados demonstraram que, embora tenha sido observada uma tendência de maior ocorrência dos desfechos endodônticos no grupo exposto, a associação não foi significativa nas análises brutas (Figura 2a) nem nas ajustadas (Figura 2b). Esses achados permaneceram consistentes mesmo após a análise de sensibilidade (Figura 2c), sugerindo que, com as evidências disponíveis, não é possível confirmar a osteoporose como um fator de risco isolado para essas condições.

Destaca-se que revisões sistemáticas anteriores (Freitas *et al.*, 2025; Pestana de Vasconcelos, Martins, Afonso, Braga, & Pina-Vaz, 2024) foram limitadas por estratégias de busca restritas e ausência de metanálise. A metanálise de Areal-Quecuty *et al.*, (2024), embora mais recente, não encontrou significância estatística (OR 2,16; IC 95%: 0,94 a 4,97), concentrou-se exclusivamente em mulheres pós-menopáusicas e periodontite apical. O presente estudo amplia essas investigações, incorporando uma busca abrangente em múltiplas bases de dados e literatura cinza, além de considerar um espectro mais amplo de patologias pulpo-periapicais, oferecendo uma síntese mais robusta e atualizada.

Quatro dos estudos incluídos nesta metanálise apresentaram resultados consistentes com as conclusões gerais, indicando a ausência de associação significativa entre osteoporose e patologias pulpo-periapicais em ambas as análises não ajustada e ajustada (Cadoni *et al.*, 2022; Kahm & Yang, 2024; López-López *et al.*, 2015; Thanakun *et al.*, 2019). Embora Kamalı & Turkaydın (2024) tenham identificado uma associação significativa após ajuste (OR=1,14; IC95% 1,00 a 1,30), esta foi fraca e marginal. A ausência de associação se manteve tanto em nível individual quanto dentário (Cadoni *et al.*, 2022), bem como na população em geral (Cadoni *et al.*, 2022; Kahm & Yang, 2024; Kamalı & Turkaydın, 2024; López-López *et al.*, 2015), e exclusivamente em mulheres pós-menopausa (Thanakun *et al.*, 2019). Esses achados fortalecem a conclusão de que, até o momento, não há evidência robusta de uma associação entre essas duas condições. Somente um estudo revelou associação em ambas as análises, não ajustada e ajustada, entre osteoporose e patologias pulpo-periapicais (Katz & Rotstein, 2021).

Portanto, embora esta metanálise e a de Areal-Quecuty *et al.* (2024) não tenham encontrado uma associação entre os eventos estudados, é necessário destacar os estudos

individuais que demonstraram achados divergentes, sugerindo uma possível associação entre osteoporose e patologias pulpo-periapicais (Kamalı & Turkaydın, 2024; Katz & Rotstein, 2021). Uma relação significativa foi observada, em uma amostra populacional massiva (n = 1.644.953), com um OR de 3,36 (IC95%: 3,12 a 3,62; $p < 0,0001$), indicando uma probabilidade maior de lesões periapicais em pacientes com osteoporose (Katz & Rotstein, 2021). É sabido que as associações tendem a ser significativas em amostras extraordinariamente grandes, como neste caso, bem como tendem a ser superestimadas quando o desfecho tem prevalência superior a 15%, entretanto neste estudo a prevalência de lesões pulpo-periapicais foi de 0,52%. O estudo de Kamalı & Turkaydın (2024), por sua vez, também indicou associação, porém fraca e marginal (OR = 1,142; IC95%: 1,003 a 1,300; $p = 0,045$).

Esses resultados, embora não sejam suficientes para alterar o efeito combinado da metanálise, reforçam a plausibilidade biológica da hipótese investigada. A osteoporose, quando caracterizada por um estado inflamatório sistêmico e pela redução da densidade mineral óssea, pode de fato comprometer a resposta imune local e a capacidade de reparação tecidual diante de infecções pulpares e periapicais. Essa relação é ainda mais convincente quando consideramos que tanto a osteoporose quanto a periodontite apical são doenças que envolvem perda óssea induzida por inflamação. Dessa forma, a osteólise, uma característica central da osteoporose, poderia atuar como um fator sistêmico agravante para o desenvolvimento e progressão da periodontite apical (Stanev & Vasileva, 2024)

Uma revisão sistemática (Rossetti *et al.*, 2022), que investigou em modelos animais a influência da deficiência de estrogênio na progressão da periodontite apical, fornece um suporte biológico adicional. Todos os 12 estudos incluídos nessa revisão demonstraram que a deficiência de estrogênio influencia a progressão da periodontite apical. Isso pode ser explicado pelo fato de que condições hipoestrogênicas exacerbam a expressão de diversas citocinas pró-inflamatórias, como a interleucina-1, interleucina-6 e fatores de necrose tumoral, que estão intimamente ligadas à periodontite apical. Os autores sugerem que os profissionais de saúde devem estar atentos na prática clínica diária ao tratar mulheres pós-menopáusicas e com deficiência de estrogênio, dada essa plausibilidade biológica e às evidências emergentes.

Apesar do rigor metodológico empregado, esta metanálise apresenta limitações relevantes. A elevada heterogeneidade observada ($I^2 > 98\%$) reflete a grande diversidade clínica e metodológica entre os estudos primários. Essa variabilidade decorre de diferenças nas definições de exposição e desfecho, nos métodos diagnósticos empregados e na vasta amplitude dos tamanhos amostrais, que variaram de 39 a mais de 1.600.000 participantes. Ademais, a

combinação de diferentes desenhos de estudo (transversal, coorte e caso-controle), somada à discrepância nas variáveis de confusão utilizadas para ajuste nos modelos, contribuiu significativamente para a dispersão dos dados.

Consequentemente, a certeza da evidência foi classificada como “muito baixa” pelo sistema GRADE. Esse rebaixamento já era esperado, dada a predominância de estudos observacionais e inconsistências nos resultados. Ressalta-se que, embora a estratégia de busca tenha sido ampla e desenhada para capturar também ensaios clínicos, nenhum estudo com esse delineamento foi identificado. A impossibilidade de randomização da exposição (osteoporose) restringe o nível de evidência possível. Além disso, apenas dois estudos forneceram dados ajustados, limitando análises mais refinadas. Por fim, o pequeno número de estudos (n = 6) impossibilitou a avaliação formal do viés de publicação via funnel plot.

Cabe ressaltar que, embora incluído como um estudo de coorte, o trabalho de Kahm & Yang (2024) apresentou seus resultados em OR devido à utilização de modelos de regressão logística. Isso possibilitou a síntese quantitativa com os demais estudos transversais e caso-controle, que também utilizam o OR como medida de associação.

A ausência de associação estatisticamente significativa, apesar da plausibilidade biológica subjacente, pode ser atribuída, em grande parte, à elevada heterogeneidade entre os estudos incluídos. Essa variabilidade foi evidenciada pelos altos valores de I^2 observados na metanálise, justificando a adoção do modelo de efeitos aleatórios. Tal inconsistência, decorrente de divergências metodológicas e populacionais, limita o poder desta metanálise para detectar um efeito verdadeiro. Um dos motivos dessa heterogeneidade é a diversidade dos métodos utilizados para o diagnóstico da osteoporose. Enquanto alguns estudos empregaram a absorciometria de raios X de dupla energia para avaliar a densidade mineral óssea (Cadoni *et al.*, 2022; Kamalı & Turkaydın, 2024; López-López *et al.*, 2015), considerada o padrão-ouro, outros se basearam em códigos da Classificação Internacional de Doenças (ICD-10) (Kahm & Yang, 2024; Katz & Rotstein, 2021) ou até mesmo em indicadores indiretos, como achados clínicos, radiográficos e laboratoriais, que sugerem, sem no entanto confirmar uma baixa densidade mineral óssea (Thanakun *et al.*, 2019). Essa disparidade diagnóstica da osteoporose pode ter introduzido vieses e comprometido a comparabilidade dos dados entre as diferentes pesquisas. Além disso, a ampla variedade das patologias pulpo-periapicais investigadas também contribuiu para essa complexidade. A metanálise englobou desfechos como necrose pulpar (Kahm & Yang, 2024), periodontite apical (Cadoni *et al.*, 2022; Kamalı & Turkaydın,

2024; López-López *et al.*, 2015) e lesão periapical (Katz & Rotstein, 2021; Thanakun *et al.*, 2019).

Ademais, a variabilidade dos métodos diagnósticos para as patologias pulpo-periapicais representam um fator de confusão relevante. Três dos estudos analisados, por exemplo, empregaram radiografias panorâmicas digitais para o diagnóstico de periodontite apical (Kamalı & Turkaydın, 2024; López-López *et al.*, 2015; Thanakun *et al.*, 2019). Desses, apenas um estudo utilizou o índice radiográfico periapical (PAI), uma ferramenta já validada, em conjunto com a radiografia panorâmica, aumentando a acurácia diagnóstica para detectar lesões periapicais (Kamalı & Turkaydın, 2024). É crucial reconhecer as limitações da radiografia panorâmica nesse contexto. Embora útil para uma triagem inicial, a sua sensibilidade na detecção de lesões periapicais é notavelmente baixa quando comparada à tomografia computadorizada de feixe cônico (CBCT). Estudos demonstram que a CBCT possui uma acurácia diagnóstica superior, sendo frequentemente considerada o padrão-ouro para a identificação e avaliação de lesões periapicais (Estrela, Bueno, Leles, Azevedo, & Azevedo, 2008; Uraba, Ebihara, Komatsu, Ohbayashi, & Okiji, 2016).

Por fim, a grande variação no tamanho das populações dos estudos incluídos (de 39 a 1.644.954 indivíduos) foi um fator importante, com impacto na representatividade e no poder estatístico. Portanto, é plausível concluir que a combinação dessas inconsistências metodológicas e da heterogeneidade amostral tenha tornado o conjunto de evidências insuficiente para confirmar ou descartar de forma definitiva a associação entre osteoporose e patologias pulpo-periapicais.

Apesar das limitações, esta revisão destaca-se pelo rigor metodológico. O uso das diretrizes PRISMA 2020 (Page *et al.*, 2021) e a amplitude da estratégia de busca em sete bases de dados, complementada por literatura cinza, asseguram abrangência e transparência. A dupla avaliação independente dos estudos, a análise de sensibilidade e a avaliação do risco de viés com ferramentas padronizadas (JBI) conferem solidez aos achados, com base nas evidências disponíveis até o momento. Diante do exposto, é lícito afirmar que a existência de evidências em estudos primários e a fundamentação biológica para uma possível influência da osteoporose na saúde óssea periapical sugerem que indivíduos com osteoporose podem ser mais propensos a desenvolver patologias pulpo-periapicais. Entretanto, esta revisão sistemática e metanálise não identificou uma associação significativa entre osteoporose e patologias pulpo-periapicais, possivelmente devido à alta heterogeneidade dos estudos primários e da baixa certeza da evidência, indicando que são necessárias pesquisas com maior rigor metodológico.

Conclusão

Não há evidência robusta que associe osteoporose à maior ocorrência de patologias pulpo-periapicais, possivelmente pela qualidade da evidência disponível ser "muito baixa" devido a limitações metodológicas, heterogeneidade extrema e à natureza observacional dos estudos. Apesar disso, a plausibilidade biológica desta relação sugere que os cirurgiões-dentistas considerem essa condição óssea no planejamento de tratamentos odontológicos.

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5. CAPÍTULO III

Existe associação entre doenças autoimunes reumáticas e patologias pulpares e periapicais? Uma revisão sistemática e metanálise.

(Artigo científico a ser submetido à Revista *Journal of Endodontics*)

Resumo:

Introdução: As evidências sobre a associação entre doenças autoimunes reumáticas e desfechos endodônticos ainda não estão totalmente compreendidas. Assim, esse estudo buscou esclarecer essa associação, considerando dados tanto em nível individual quanto em nível dentário. **Métodos:** Uma busca sistemática nas bases de dados PubMed, SciELO, BVS/Bireme, Embase, Scopus, Web of Science, Cochrane Library e na literatura cinza foi realizada em junho de 2024 e atualizada em maio de 2025. Foram incluídos estudos observacionais que avaliaram a ocorrência de patologias pulpares e periapicais em indivíduos com artrite reumatoide, espondilite anquilosante, síndrome de Sjögren, lúpus sistêmico eritematoso e doença do tecido conjuntivo. Dois revisores independentes (Kappa= 0,8) realizaram a seleção dos estudos, extração de dados e avaliação do risco de viés utilizando a ferramenta do Joanna Briggs Institute. Foram calculadas as razões de chance [Odds Ratio, (OR)] e os respectivos Intervalos de Confiança a 95% (IC95%). As metanálises foram realizadas com modelos de efeitos aleatórios, e a certeza da evidência avaliada pelo GRADE. **Resultados:** A metanálise de treze estudos mostrou associação significativa entre as doenças autoimunes reumáticas e as patologias pulpares e periapicais. Em nível individual, a associação foi observada tanto nas análises brutas (OR=1,80; IC95%:1,57 a 2,05) quanto nas ajustadas (OR=1,60; IC95%:1,20 a 2,12), exceto para a espondilite anquilosante. Em nível dentário, a associação também foi significativa (OR=1,74; IC95%:1,28 a 2,37). **Conclusão:** Existe associação positiva entre as doenças autoimunes reumáticas e as patologias pulpares e periapicais, apesar da baixa certeza das evidências.

Introdução

As doenças autoimunes afetam aproximadamente 10% da população global, resultam de uma resposta imune desregulada, na qual o corpo ataca seus próprios tecidos, levando à inflamação e ao dano tecidual (1,2). Dentre elas, destacam-se as doenças autoimunes reumáticas - como a artrite reumatoide, espondilite anquilosante, lúpus eritematoso sistêmico, artrite idiopática juvenil, doença mista do tecido conjuntivo, síndrome de Sjögren, artrite psoriática, polimialgia reumática e esclerose sistêmica - que afetam o sistema musculoesquelético e são categorizadas como doenças crônicas não transmissíveis (DCNTs) (3,4).

A cárie dentária, uma das DCNTs mais prevalentes em humanos, afeta um terço da população mundial, com mais de 2 bilhões de casos (5). Lesões cariosas não tratadas frequentemente progridem para pulpites severas, podendo culminar em necrose pulpar e infecção periapical, como as periodontites apicais (6,7). Em virtude do caráter crônico dessas patologias e do histórico de intervenções endodônticas prévias, estima-se que a prevalência global de periodontite apical seja elevada - aproximadamente 52% da população adulta mundial possui pelo menos um dente afetado por esta condição (8). É importante esclarecer que esses índices podem superestimar a doença ativa, uma vez que agrupam as lesões decorrentes de insucessos e aquelas que se encontram em processo de reparo tecidual, mas que ainda foram classificadas como periodontite apical pelos critérios radiográficos.

As infecções periapicais podem levar à destruição dos ligamentos periodontais, degradação óssea e à liberação de mediadores pró-inflamatórios, contribuindo para a carga inflamatória sistêmica crônica (9,10). Por sua vez, a resposta inflamatória exacerbada e a imunossupressão inerentes às doenças autoimunes reumáticas podem aumentar a suscetibilidade à essas infecções, caracterizando uma relação bidirecional entre essas condições (11,12).

Apesar de um estudo recente ter identificado uma prevalência de 89,9% de periodontite apical em pacientes com doenças autoimunes (13), a evidência atual ainda apresenta resultados conflitantes sobre a associação entre as doenças autoimunes reumáticas e as patologias pulpo-periapicais (14–18). Até o momento, duas revisões sistemáticas (19,20) investigaram a associação entre artrite reumatoide e patologias pulpo-periapicais. No entanto, ambas apresentaram resultados inconclusivos devido às limitações metodológicas, como o número limitado de estudos incluídos, o risco de viés moderado, estratégias de busca restritas e a ausência de síntese quantitativa. Entretanto, uma revisão mais recente, que integrou metanálise

e análise de randomização mendeliana de duas amostras, não apenas reforçou essa associação, mas também sugeriu uma possível relação causal (21).

Adicionalmente, uma revisão sistemática e metanálise (22) sugeriu associação entre as doenças autoimunes em geral e periodontite apical. Contudo, essa revisão ainda carece de um foco específico nas doenças autoimunes reumáticas e de estratégias de busca mais robustas. Dessa forma, acreditamos que uma nova revisão que inclua múltiplas bases de dados e literatura cinza, investigue a ocorrência dos desfechos endodônticos e assegure a inclusão de estudos com diferentes delineamentos observacionais, possa elucidar essa possível associação. Assim, propusemo-nos a realizar uma revisão sistemática e metanálise para responder à seguinte questão de pesquisa: *Indivíduos com doenças autoimunes reumáticas têm maior ocorrência de patologias pulpo-periapicais em comparação a aqueles sem essas condições?*

Material e Métodos

Protocolo e Registro

O relato desta revisão sistemática e metanálise seguiu as recomendações do *Preferred Reporting Items for Systematic Reviews and Meta-Analyses* (PRISMA) (23,24). O protocolo do estudo foi pré-registrado na PROSPERO sob o número de registro CRD42024559527. Os checklists PRISMA para o resumo e o texto completo são apresentados na Tabela Suplementar 1 e Tabela Suplementar 2, respectivamente.

Critérios de Elegibilidade

A estratégia **PECOs** foi utilizada para definir os critérios de elegibilidade (25): **População (P):** Indivíduos de qualquer idade, sexo ou raça/etnia; **Exposição (E):** Doenças autoimunes reumáticas (artrite reumatoide, espondilite anquilosante, lúpus eritematoso sistêmico, artrite idiopática juvenil, doença mista do tecido conjuntivo, síndrome de Sjögren, artrite psoriática, polimialgia reumática e esclerose sistêmica); **Comparação (C):** Indivíduos sem diagnóstico de doenças autoimunes reumáticas (grupo controle); **Desfecho (O):** Presença de patologias pulpares e periapicais; **Desenhos de estudo (s):** Estudos observacionais (transversal, coorte, caso-controle).

Foram incluídos estudos em humanos que compararam a ocorrência de patologias pulpares e periapicais entre um grupo com doenças autoimunes reumáticas e um grupo controle. Não houve restrições quanto à idade, sexo, raça ou status socioeconômico.

Foram excluídos estudos cujo escopo se limitasse a subpopulações com condições sistêmicas ou fisiológicas específicas que pudessem atuar como confundidores primários. Publicações duplicadas ou aquelas que analisaram a mesma coorte de pacientes de um estudo previamente incluído também foram excluídas.

Seleção de Descritores, Bases de Dados e Estratégia de Busca

Para compor a equação de busca, consideramos todos os termos equivalentes do MeSH (*Medical Subject Headings*), DeCS (Descritores em Ciências da Saúde) e Emtree que descrevem a estratégia PECOs: **População (P):** Child, Adolescent, Adult, Aged, Humans; **Exposição (E):** Autoimmune Diseases, Rheumatic Diseases, Arthritis, Rheumatoid, Spondylitis, Ankylosing, Lupus Erythematosus Systemic, Mixed Connective Tissue Disease, Arthritis, Juvenile, Sjögren's Syndrome, Polymyalgia Rheumatica, Scleroderma Systemic, Arthritis, Psoriatic; **Comparação (C):** Termos de busca específicos para o grupo controle não

foram utilizados, uma vez que os critérios de inclusão foram restritos a desenhos de estudo que, por definição, incluem um comparador; **Desfecho (O):** Periapical Diseases, Dental Pulp Diseases, Dental Pulp Necrosis, Pulpitis, Periapical Periodontitis, Periapical Abscess, Periapical Granuloma, Tooth Nonvital, Dental Pulp Devitalization, Periapical Tissue, Radicular Cyst, Root Canal Therapy, Root Canal Obturation; **Desenhos de estudo (s):** Observational Study, Cross-Sectional Studies, Cohort Studies, Case-Control Studies, Clinical Trial, Randomized Controlled Trial, Controlled Clinical Trial, Intervention Study

Esses termos foram conectados por operadores booleanos (OR, AND e NOT) para garantir uma cobertura de busca abrangente. A equação de busca específica para cada base de dados está detalhada na Tabela Suplementar 3.

As seguintes bases de dados online foram utilizadas: MEDLINE/PubMed, Embase, Scopus, BVS-Bireme, Web of Science, SciELO e Cochrane Library. A literatura cinza também foi consultada através do Google Scholar, da Biblioteca Digital Brasileira de Teses e Dissertações (BDTD) e do Catálogo de Teses e Dissertações da CAPES. As listas de referências dos estudos incluídos também foram rastreadas. As buscas foram realizadas em julho de 2024 e atualizadas em maio de 2025. Não foram aplicadas restrições de idioma, data ou status de publicação. Para o Google Scholar, apenas os 100 primeiros resultados mais relevantes foram avaliados.

Processo de Seleção

Os artigos foram importados para o software Rayyan (26), onde as duplicatas foram removidas. Em seguida, dois revisores independentes selecionaram os estudos em duas fases: primeiro, pela triagem de títulos e resumos, seguida pela leitura do texto completo dos artigos pré-selecionados. Um terceiro revisor foi consultado para resolver quaisquer discrepâncias. Ao final do processo, a concordância entre os revisores foi considerada excelente, com um coeficiente Kappa de 0,8.

Processo de Coleta de Dados

A extração de dados foi realizada de forma independente por dois revisores, utilizando um formulário padronizado para coletar as informações. Os dados extraídos incluíram detalhes do estudo (autor, ano, país), características da amostra (tamanho, idade), diagnósticos de doenças autoimunes e patologias pulpo-periapicais, e os principais desfechos estatísticos (como medidas de efeito e seus intervalos de confiança). As divergências foram resolvidas por

consenso por um terceiro revisor. Em casos de dados ausentes, os autores dos artigos originais foram contatados para obter informações adicionais.

Avaliação do Risco de Viés dos Estudos Incluídos

A avaliação foi conduzida por dois revisores independentes utilizando a ferramenta do Joanna Briggs Institute (JBI) (27) para cada desenho de estudo, com quaisquer desacordos resolvidos por um terceiro revisor. O risco de viés foi classificado como baixo (>75% dos critérios atendidos), moderado (51–75%) ou alto (≤50%), e os resultados foram apresentados visualmente em um gráfico de semáforo (*traffic-light plot*) gerado na plataforma robvis.

Análise de Dados Qualitativa e Quantitativa

Dois revisores independentes extraíram dados dos artigos, coletando informações sobre as características do estudo, detalhes da amostra, diagnósticos e principais desfechos estatísticos. As divergências foram resolvidas por um terceiro revisor. Todas as informações extraídas foram compiladas e são apresentadas em formato estruturado e comparativo na Tabela 1.

Para a metanálise, foram extraídos os dados primários para calcular as razões de chance [Odds Ratios – (OR)] e seus respectivos Intervalos de Confiança (IC95%). Foram extraídos tanto os OR brutos quanto os ajustados, quando disponíveis. Para os estudos de coorte que reportaram originalmente a razão de taxas de incidência (IRR), foi realizada a conversão destas medidas para OR, viabilizando a síntese quantitativa conjunta com os estudos transversais e caso-controle. O modelo com melhor ajuste foi selecionado e as variáveis de ajuste foram registradas. Um modelo de efeitos aleatórios, especificamente o método de DerSimonian-Laird (28), foi adotado para calcular a estimativa padronizada. Uma metanálise de efeitos aleatórios é recomendada quando há heterogeneidade significativa entre os estudos incluídos, definida por um valor de $p < 0,10$ no teste de heterogeneidade ou um valor de $I^2 \geq 50\%$. Dado que a heterogeneidade entre os estudos excedeu 50%, este modelo foi escolhido.

Diferentes análises de subgrupo foram conduzidas para explorar potenciais fontes de heterogeneidade. Essas análises consideraram: (1) as doenças autoimunes reumáticas analisadas de forma coletiva e individual; e (2) a comparação entre medidas de associação brutas e ajustadas. Além disso, foram realizadas análises de sensibilidade para avaliar a robustez dos resultados, excluindo um estudo que relatou lesões mistas e radiolúcidas separadamente como desfechos (29).

O potencial viés de publicação foi avaliado por meio da inspeção visual do gráfico de funil (*funnel plot*), seguindo a metodologia descrita por Sterne & Egger (30) e Debray *et al.* (31). As análises estatísticas foram realizadas utilizando o Review Manager (RevMan), versão 5.3 (32), e o software Stata, versão 14.0 (33).

Avaliação da Certeza da Evidência

A ferramenta *GRADEpro Guideline Development Tool* foi utilizada para classificar a certeza da evidência em quatro níveis: muito baixa, baixa, moderada e alta. Essa avaliação permitiu uma análise crítica da robustez dos resultados e da confiabilidade das conclusões do estudo (34,35).

Resultados

Seleção dos Estudos

Um total de 803 artigos foi identificado por meio de buscas em 7 bases de dados. Adicionalmente, 198 registros foram identificados pela busca na literatura cinza e nas listas de referências. Após a remoção de duplicatas e a triagem de títulos e resumos de ambos os processos, 29 artigos de texto completo foram selecionados para avaliação de elegibilidade. Ao final, 13 estudos foram incluídos. Os detalhes da busca e da seleção dos estudos são apresentados na Figura 1.

Características dos Estudos Incluídos

Todos os artigos foram publicados em inglês entre 2017 (15) e 2024 (36). As características dos 13 estudos incluídos estão detalhadas na Tabela 1. O tamanho das amostras apresentou ampla variação, estendendo-se de 96 participantes (14) a coortes populacionais massivas com mais de 1,6 milhão de indivíduos (16).

Em relação à exposição, a condição mais investigada foi a artrite reumatoide, abordada em nove dos treze estudos incluídos (36, 13, 16, 14, 37, 15, 38, 39 e 29). As demais condições analisadas compreenderam a espondilite anquilosante (29, 40) , a síndrome de Sjögren (41 e 17), o lúpus eritematoso sistêmico (18) e a doença do tecido conjuntivo (39), refletindo um espectro abrangente de desordens reumáticas.

Quanto aos desfechos endodônticos, observou-se heterogeneidade nas condições clínicas investigadas. A periodontite apical (ou lesão periapical radiolúcida) configurou-se como o desfecho mais frequente, sendo diagnosticada na maioria dos estudos por meio de exames de imagem, como radiografias panorâmicas e periapicais (13–15, 29, 38, 40). Paralelamente, outras patologias pulpares e periapicais foram exploradas, predominantemente em estudos baseados em registros de grandes bancos de dados e códigos da Classificação Internacional de Doenças. Nesses casos, os diagnósticos incluíram necrose pulpar (36), pulpites (37, 41) e abscesso periapical (16–18), ampliando o escopo da associação para além das lesões ósseas crônicas detectáveis radiograficamente.

Avaliação do Risco de Viés

Oito estudos apresentaram risco de viés moderado, enquanto cinco apresentaram alto risco (Figura 2). As principais fragilidades metodológicas concentraram-se nos domínios de identificação e controle de fatores de confusão, visto que diversos estudos não realizaram

ajustes estatísticos para variáveis importantes. Além disso, a mensuração da exposição e do desfecho foi frequentemente pontuada como incerta ou de alto risco, refletindo o uso extensivo de registros médicos secundários (códigos CID) e autorrelato, em detrimento de diagnósticos clínicos padronizados.

Metanálise

Treze estudos foram incluídos na metanálise para as associações brutas em nível individual (Figura 3a). Foi encontrada uma associação significativa entre as doenças autoimunes reumáticas (artrite reumatoide, espondilite anquilosante, síndrome de Sjögren, lúpus sistêmico eritematoso e doença do tecido conjuntivo) e a presença de patologias pulpares e periapicais (OR=1,80; IC 95%:1,57 a 2,05). Sete estudos forneceram medidas ajustadas (Figura 3b), mostrando uma chance 60% maior de patologias pulpares e periapicais em indivíduos com doenças autoimunes reumáticas em comparação com os controles (OR=1,60; IC 95%:1,20 a 2,12). Na análise de sensibilidade (Figura 4a), que excluiu o estudo de Yilmaz e Tunc (29), o único estudo que relatou lesões mistas e radiolúcidas como desfechos separados, o resultado permaneceu semelhante (OR=1,60; IC 95%:1,16 a 2,22).

Analisando cada doença autoimune reumática separada, confirma-se uma associação significativa para todas, exceto para a espondilite anquilosante (Figura 3a). Este achado persistiu nas associações ajustadas (Figura 3b). No entanto, para a artrite reumatoide, a exclusão do estudo de Yilmaz e Tunc (29) levou à perda de significância estatística (OR=1,64, IC 95%:1,01 a 2,67 *versus* OR=1,57, IC 95%:0,88 a 2,79) (Figura 4a).

A análise por nível dentário (Figura 4b) revelou uma associação significativa entre as doenças autoimunes reumáticas avaliadas e as patologias pulpares e periapicais (OR=1,74; IC 95%:1,28 a 2,37). Em todas as análises, os valores de I^2 foram superiores a 50%, indicando heterogeneidade significativa. Para verificar a robustez desses achados, realizou-se uma análise de sensibilidade (Figura 4c) excluindo os estudos que não ajustaram estatisticamente a dependência entre dentes do mesmo indivíduo (14, 15, 40). Mesmo após a remoção desses estudos, que tendem a superestimar a significância ao tratar dentes como amostras independentes, a associação permaneceu estatisticamente significativa (OR= 1,93, IC 95%:1,55 a 2.42), confirmando a consistência da evidência obtida.

Viés de Publicação

Embora o gráfico de funil (funnel plot) (Figura Suplementar 1) tenha apresentado leve assimetria, o teste de Egger não significativo (p=0,904) sugere a ausência de viés de publicação, sendo a assimetria provavelmente devida ao acaso ou à heterogeneidade.

Certeza da Evidência

A certeza da evidência foi classificada como "Muito Baixa" pela abordagem GRADE (Tabela 2). Partindo de um nível de certeza "Baixo", padrão para estudos observacionais, a evidência foi rebaixada em dois níveis devido a duas preocupações sérias: 1) risco de viés alto (proveniente do controle inadequado de fatores de confusão e da mensuração indireta do desfecho) e 2) inconsistência séria (confirmada pela heterogeneidade estatística muito alta). Nenhuma preocupação séria em relação à imprecisão, evidência indireta ou viés de publicação justificou um rebaixamento adicional. As avaliações detalhadas do GRADE estão disponíveis na Tabela Suplementar 4.

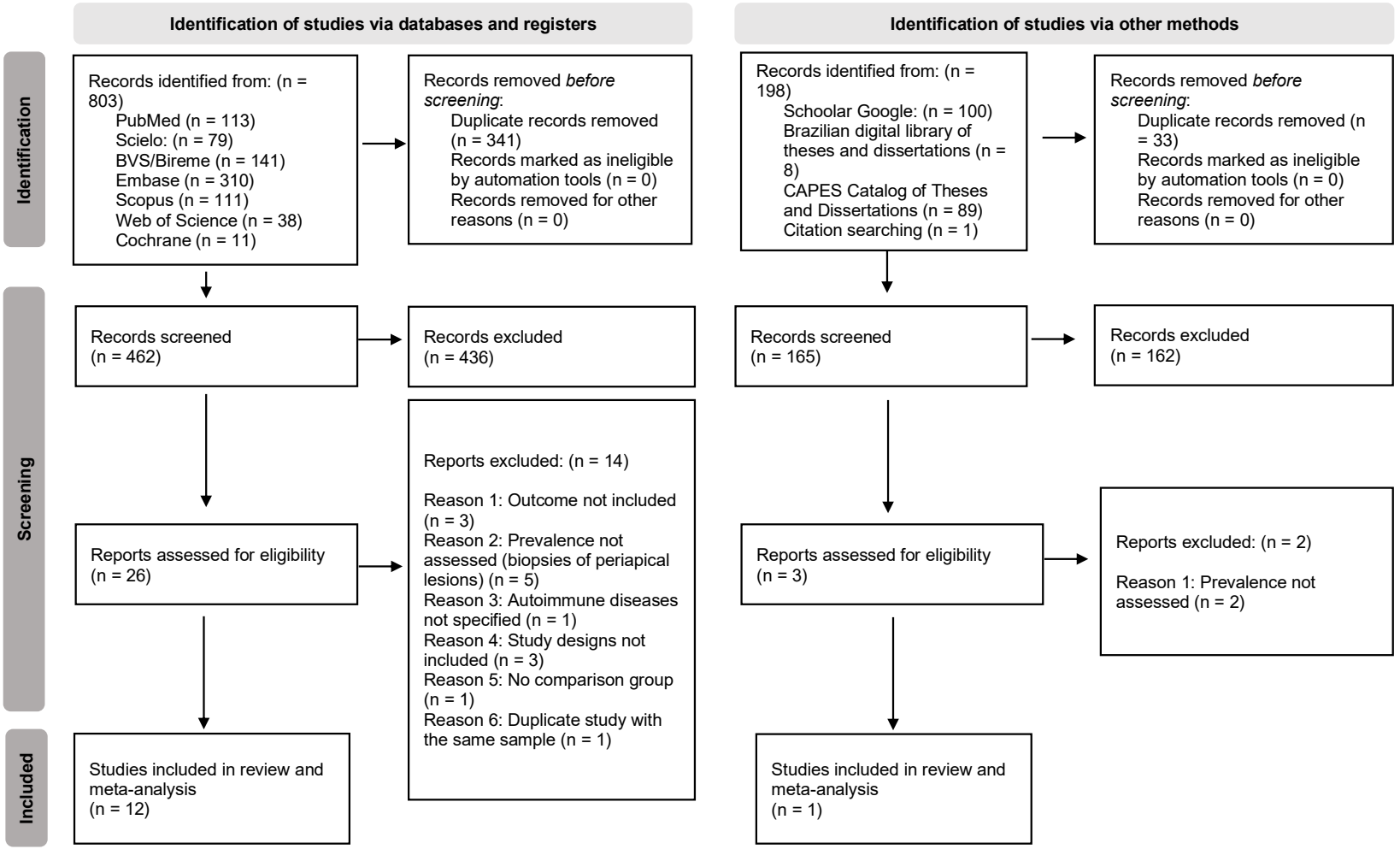

FIGURA 1. Fluxograma da estratégia de busca da revisão sistemática e metanálise, seguindo as diretrizes do PRISMA 2020 (23).

TABELA 1. Síntese Qualitativa dos Estudos Incluídos.

Author/Year	Country	Journal	Study Design	Sample Size	Sample Age Range	Type of Rheumatic Autoimmune Disease	Diagnosis of Rheumatic Autoimmune Diseases	Type of Pulpal-periapical Pathology	Diagnosis of Pulpal-periapical Pathology	Main Findings
Kahm & Yang, 2024 (36)	South Korea	Medicina	Cohort	Exposed: 3.418 individuals Non-exposed: 1.361 individuals	20-80+ years	Rheumatoid Arthritis	Hospital Electronic Health Records - International Classification of Diseases (ICD-10) Code	Pulpal Necrosis	Hospital Electronic Health Records - International Classification of Diseases (ICD-10) Code	A marginally significant association was observed (OR=1.157; 95% CI: 1.012 to 1.322)
Allihaibi *et al.*, 2023 (13)	United Kingdom	International Endodontic Journal	Case-control	Exposed: 24 individuals (536 teeth) Non-exposed: 89 individuals (2.329 teeth)	18-80 years	Rheumatoid Arthritis	Hospital electronic health records	Apical Periodontitis	Full panoramic dental tomographies	An association was observed at the individual level (OR=17.32; 95% CI: 1.01 to 296.22), but not at the tooth level (adjusted OR=1.20; 95% CI: 0.75 to 1.91)
Rotstein & Katz, 2021 (16)	United States	American Journal of Dentistry	Cross-sectional	Exposed: 10.072 individuals Non-exposed: 1.669.904 individuals	Not specified	Rheumatoid Arthritis	Hospital Electronic Health Records - International Classification of Diseases (ICD-10) Code	Periapical Abscess	Clinical and Imaging Examination - International Classification of Diseases (ICD-10 K04.7) Code	The association was significant (adjusted OR=2.60; 95% CI: 2.21 to 3.05)
Karataş *et al.*, 2020a (14)	Turkey	European Endodontic Journal	Cross-sectional	Exposed: 48 individuals (1.026 teeth)	18-65 years	Rheumatoid Arthritis	Hospital Electronic Health Records	All types of apical periodontitis	Clinical and imaging examination	An association was observed at the individual

				Non-exposed: 48 individuals (1.025 teeth)				(symptomatic, asymptomatic, chronic abscess, and acute abscess)	(periapical radiography)	level (adjusted OR=3.08; 95% CI: 1.33 to 7.16) and at the tooth level (OR=2.19; 95% CI: 1.30 to 3.71)
Juan *et al.*, 2022 (37)	Taiwan	BMC Oral Health	Cohort	Exposed: 1.337 individuals Non-exposed: 13.370 individuals	20-80 years	Rheumatoid Arthritis	National Health Insurance Research Database (NHIRD) - International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) Code	Pulpitis	National Health Insurance Research Database (NHIRD) - International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) Code	The association was marginally significant (adjusted OR=1.08; 95% CI: 1.00 to 1.16); aIRR = 1.12 (IC 95%: 1.00 to 1.24)
Jalali *et al.*, 2017 (15)	United States	Journal of Endodontics	Cross-sectional	Exposed: 131 individuals (3.260 teeth) Non-exposed: 131 individuals (3.395 teeth)	22-83 years	Rheumatoid Arthritis	Self-reported disease	Periapical Rarefying Osteitis	Digital periapical radiography and Periapical Index (PAI)	No association was observed at the individual level (OR=0.83; 95% CI: 0.51 to 1.35) or at the tooth level (OR=1.12; 95% CI: 0.87 to 1.45)
Ideo *et al.*, 2022 (38)	Italy	Journal of Endodontics	Cohort	Exposed: 24 individuals (531 teeth)	18-90 years	Rheumatoid Arthritis	Hospital Health Records	Apical Periodontitis	Panoramic and periapical radiography, and Periapical Index (PAI)	An association was observed at the individual level (OR=3.46; 95% CI: 1.27 to

				Non-exposed: 99 individuals (2.655 teeth)						9.44), but not at the tooth level (adjusted OR=0.55; 95% CI: 0.32 to 0.96)
Heikkilä *et al.*, 2022 (39)	Finland	Frontiers in Oral Health	Cohort	Exposed: 47.681 individuals Non-exposed: 20.592 individuals	29+ years	Rheumatoid Arthritis and Connective Tissue Disease	Finnish National Institute for Health and Welfare Data - International Classification of Diseases (ICD-10) System	Apical Periodontitis	Dental treatment procedure codes	The associations between rheumatoid arthritis (adjusted OR=0.87; 95% CI: 0.64 to 1.12) and connective tissue disease (adjusted OR=0.96; 95% CI: 0.84 to 1.08) with apical periodontitis were not significant. Rheumatoid arthritis: aIRR = 0.77 (IC 95%: 0.47 to 1.27). Connective tissue disease: aIRR = 0.93 (IC 95%: 0.73 to 1.18)
Yilmaz & Tunc, 2023 (29)	Turkey	BMC Oral Health	Cross-sectional	Exposed: 97 individuals with ankylosing spondylitis and 327 individuals with	18-80 years	Rheumatoid Arthritis and Ankylosing Spondylitis	Hospital Electronic Health Records	Radiolucent and Mixed Periapical Lesions	Digital panoramic radiography and Periapical Index (PAI)	For rheumatoid arthritis, no association was found with radiolucent periapical lesions (adjusted

				rheumatoid arthritis Non-exposed: 284 individuals						OR=1.25; 95% CI: 0.84 to 1.87), but a significant association was observed with mixed lesions (adjusted OR=11.86; 95% CI: 1.52 to 92.29). For ankylosing spondylitis, there was no association with either radiolucent (adjusted OR=1.03; 95% CI: 0.57 to 1.85) or mixed (adjusted OR=8.93; 95% CI: 0.91 to 87.27) periapical lesions
Karataş *et al.*, 2020b (40)	Turkey	Dental and Medical Problems	Cross-sectional	Exposed: 50 individuals (1.283 teeth) Non-exposed: 50 individuals (1.305 teeth)	18-65 years	Ankylosing Spondylitis	Hospital Electronic Health Records	Apical Periodontitis	Panoramic radiography and clinical examination	An association was observed at both the individual level (OR=2.53; 95% CI: 1.11 to 5.74) and the tooth level (OR=2.25; 95% CI: 1.26 to 4.02)

Chuang *et al.*, 2020 (41)	Taiwan	PLOS ONE	Cohort	Exposed: 709 individuals Non-exposed: 7.090 individuals	20-80 years	Sjögren's Syndrome	National Health Insurance Research Database (NHIRD) - International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) Code	Pulpitis	National Health Insurance Research Database (NHIRD) - International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) Code	Sjögren's syndrome was associated with pulpitis (adjusted OR=1.29; 95% CI: 1.16 to 1.41); aIRR = 1.42 (IC 95%: 1.22 to 1.64).
Rotstein & Katz, 2022b (17)	United States	Endodontology	Cross-sectional	Exposed: 2.675 individuals Non-exposed: 1.146.978 individuals	Not specified	Sjögren's Syndrome	Hospital electronic health records - International Classification of Diseases (ICD-10) Code	Periapical Abscess	Clinical and imaging examination - International Classification of Diseases (ICD-10 K04.7) Code	The association was significant (OR=3.24; 95% CI: 2.45 to 4.29)
Rotstein & Katz, 2022a (18)	United States	Special Care Dentistry	Cross-sectional	Exposed: 3.233 individuals Non-exposed: 984.616 individuals	Not specified	Systemic Lupus Erythematosus	Hospital electronic health records - International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) Code	Periapical Abscess	Clinical and imaging examination - International Classification of Diseases (ICD-10 K04.7) Code	The association was significant (adjusted OR=4.27; 95% CI: 3.23 to 5.65)

OR: Odds ratio; 95% CI: 95% Confidence Interval; ICD-10: International Classification of Diseases and Related Health Problems (10th Revision); NHIRD: National Health Insurance Research Database; ICD-9-CM: International Classification of Diseases, Ninth Revision, Clinical Modification; PAI: Periapical Index; aIRR: adjusted Incidence Rate Ratio.

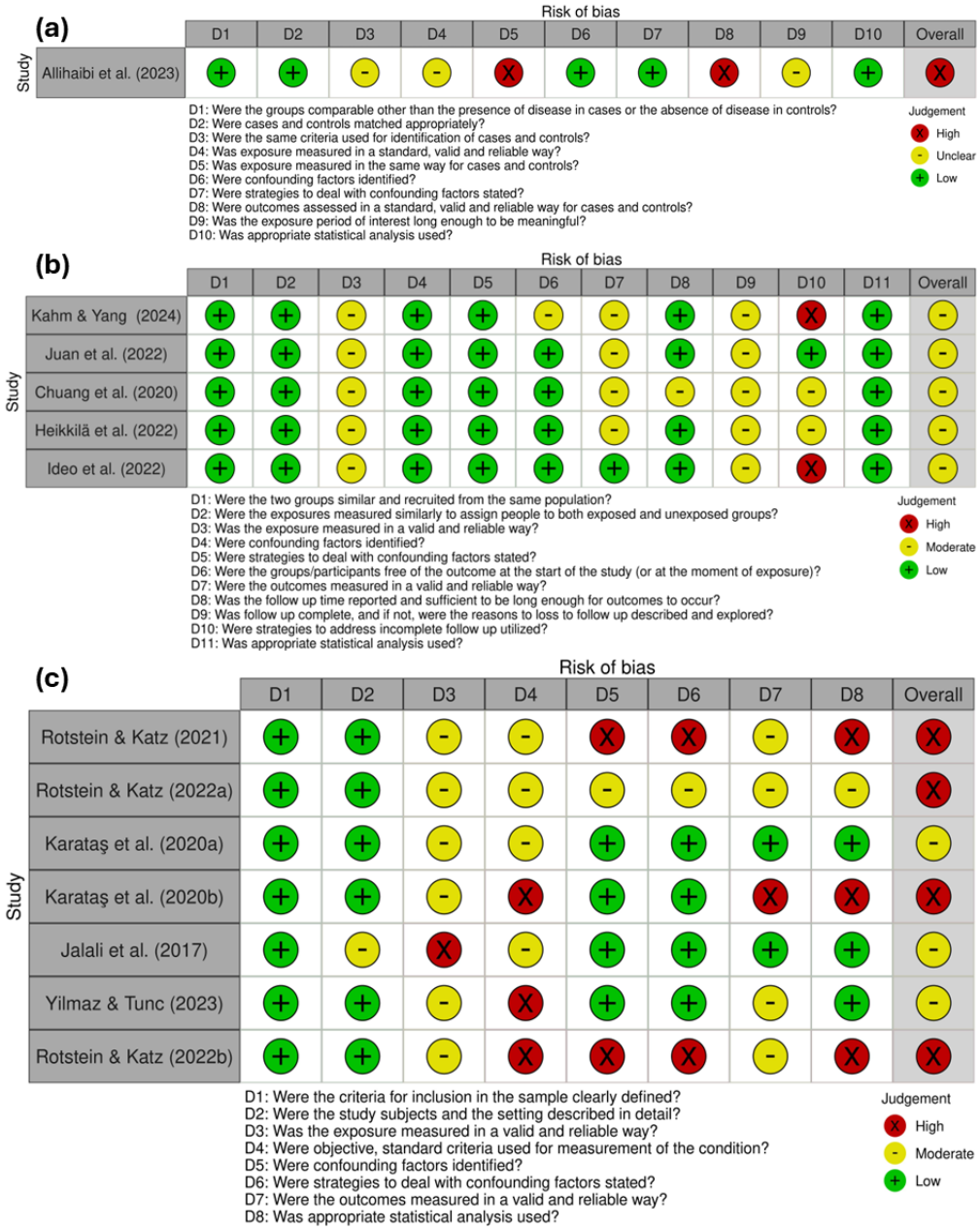

FIGURA 2. Gráfico de semáforo do risco de viés, utilizando as ferramentas do Joanna Briggs Institute para estudos (a) caso-controle, (b) de coorte e (c) transversais.

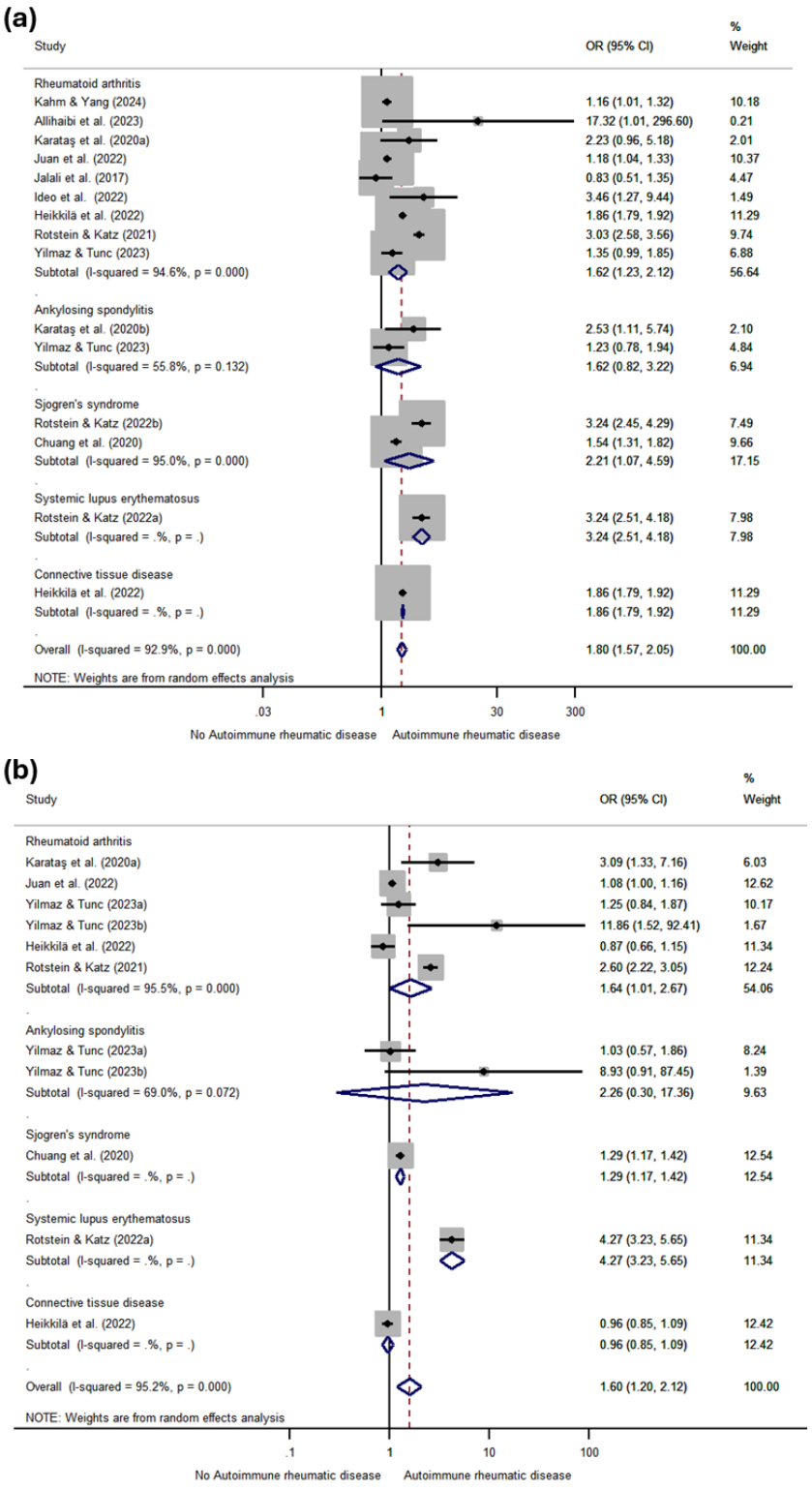

FIGURA 3. Gráfico de Floresta (Forest Plot) — Doenças autoimunes reumáticas *versus* patologias pulpo-periapicais, considerando o nível individual: (a) OR não ajustado, (b) OR ajustado.

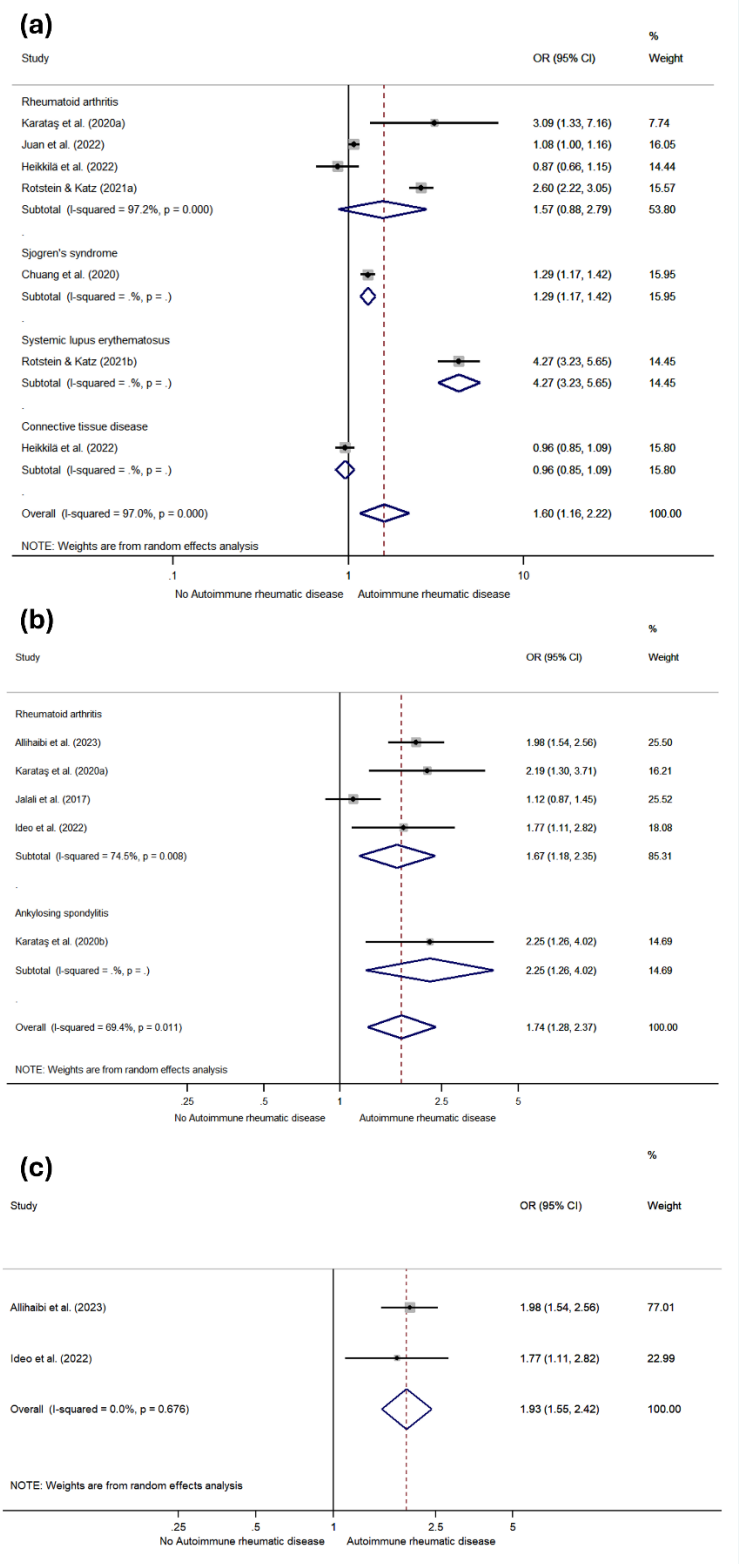

FIGURA 4. Gráfico de Floresta (Forest Plot) — Doenças autoimunes reumáticas versus patologias pulpo-periapicais: (a) análise de sensibilidade para o nível individual (OR ajustado), excluindo o estudo de Yilmaz & Tunc (29); (b) análise para o nível dentário (OR não ajustado); (c) análise de sensibilidade para o nível dentário (OR não ajustado), excluindo os estudos de Karataş, Kul & Tepecik (14), Jalali et al (15) e Karataş, Kul & Tepecik (40).

TABELA 2. Avaliação da certeza da evidência para todas as doenças autoimunes reumáticas incluídas no estudo, considerando o indivíduo e o número de dentes como unidade de medida.

Certainty assessment							Summary of Results				
							Event rates from the study (%)			Potential absolute effects	
Participants (studies)	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall certainty of evidence	Diseased/Non-exposed	Diseased/Exposed	Relative effect (95% CI)	Risk in diseased/non-exposed	Risk difference in diseased/exposed
INDIVIDUAL LEVEL (CRUDE OR)											
3914438 (13 observational studies)	Very serious[a]	Very serious[b]	Not serious	Not serious	None	⨁◯◯◯ Very low[a,b]	39807/3844612 (1.0%)	37597/69826 (53.8%)	OR 1.80 (1.57 to 2.05)	39807/3844612 (1.0%)	**8 more per 1.000** (from 6 more to 11 more)
INDIVIDUAL LEVEL (ADJUSTED OR)											
2759408 (7 observational studies)	Very serious[c]	Very serious[d]	Not serious	Not serious	None	⨁◯◯◯ Very low[c,d]	32468/2695904 (1.2%)	36355/63504 (57.2%)	OR 1.60 (1.20 to 2.12)	32468/2695904 (1.2%)	**7 more per 1.000** (from 2 more to 13 more)
TOOTH LEVEL (CRUDE OR)											
17345 (5 observational studies)	Very serious[e]	Serious[f]	Not serious	Not serious	None	⨁◯◯◯ Very low[e,f]	474/10709 (4.4%)	337/6636 (5.1%)	OR 1.74 (1.28 to 2.37)	474/10709 (4.4%)	**30 more per 1.000** (from 12 more to 55 more)

CI: Confidence interval; **OR:** Odds ratio; **a:** 5 studies with high risk of bias and 8 with moderate risk of bias; **b:** I^2= 91.4%; **c:** 2 studies with high risk of bias and 5 with moderate risk of bias; **d:** I^2= 95.2%; **e:** 2 studies with high risk of bias and 3 with moderate risk of bias; **f:** I^2= 69.4%.

Discussão

Esta revisão sistemática e metanálise investigou as evidências sobre a associação entre doenças autoimunes reumáticas (artrite reumatoide, espondilite anquilosante, síndrome de Sjögren, lúpus sistêmico eritematoso e doença do tecido conjuntivo) e patologias pulpo-periapicais. Este estudo inova ao apresentar a primeira síntese quantitativa abrangente da literatura que analisa o impacto desse grupo diversificado de desordens sistêmicas, superando as limitações de revisões anteriores focadas em doenças isoladas. Os resultados demonstraram de forma consistente uma associação positiva e significativa, indicando que indivíduos com essas condições apresentaram 60% mais chance de desenvolver desfechos endodônticos nas análises ajustadas em nível individual, um padrão de risco elevado que se confirmou também na análise em nível dentário (OR = 1,74). Essa evidência sugere que os processos inflamatórios sistêmicos crônicos, típicos das doenças autoimunes reumáticas, aumentam a predisposição para patologias pulpo-periapicais. Isso provavelmente se deve aos perfis pró-inflamatórios compartilhados por essas condições (9,10,14,42–45), que podem interferir na resposta imune local, favorecendo a progressão dos desfechos endodônticos (11,12,46).

Uma revisão sistemática anterior (19) sugeriu uma possível associação entre algumas doenças autoimunes (artrite reumatoide, doença inflamatória intestinal e diabetes mellitus tipo 1) e patologias periapicais. No entanto, esse estudo tinha limitações significativas, como pequeno número de trabalhos incluídos, o que resultou em baixo poder para identificar associações significativas, além do risco de viés moderado. Nossa revisão expandiu o escopo da busca e foi a primeira a incorporar metanálises considerando diferentes doenças autoimunes reumáticas.

Nesta metanálise, indivíduos com artrite reumatoide apresentaram um risco aumentado para patologias pulpo-periapicais (Figura 3a). Esse risco elevado persistiu mesmo após os ajustes (Figura 3b), e a análise considerando o número de dentes reforçou ainda mais essa associação (Figura 4b). Contudo, a interpretação da análise em nível dentário requer cautela devido a uma limitação metodológica observada em parte dos estudos primários. Enquanto algumas investigações empregaram modelos robustos, como equações de estimativa generalizada (GEE) ou modelos multiníveis, para ajustar a dependência dos dados (efeito de conglomerado) (13, 38), outras utilizaram testes estatísticos convencionais que tratam cada dente como uma unidade independente (14, 15, 40). A ausência de ajuste para a correlação intrabucal nestes últimos, tende a subestimar a variância e estreitar os intervalos de confiança, o que pode ter superestimado a precisão da associação observada. Para reduzir esse viés e testar

a robustez dos nossos achados, realizamos uma análise de sensibilidade excluindo os estudos com erro na unidade de análise (Figura 4c). Os resultados demonstraram que, mesmo removendo os trabalhos que potencialmente superestimam a significância (14, 15, 40), a associação permaneceu estatisticamente significativa (OR= 1,93, IC 95%:1,55 a 2.42). Dessa forma, valida-se a existência da associação mesmo após a remoção dos estudos com limitações analíticas, sustentando a hipótese de maior vulnerabilidade endodôntica nestes pacientes.

Corroborando nossos achados, um estudo recente (21), que integrou metanálise com a técnica de randomização mendeliana de duas amostras, confirmou maior prevalência de periodontite apical em nível dentário em pacientes com artrite reumatoide (OR=1,67; IC 95%: 1,18 a 2,35). Esse resultado é semelhante ao nosso (Figura 4b). Ademais, a análise genética também sugeriu uma possível relação causal, especialmente com a periodontite periapical crônica. Tais achados apoiam a plausibilidade biológica de nossas observações, reforçando a hipótese de que a inflamação sistêmica crônica característica da artrite reumatoide pode comprometer a resposta imune local e predispor estes indivíduos às patologias pulpo-periapicais.

A evidência atual sugere que indivíduos com artrite reumatoide têm um aumento marginalmente significativo para o risco de pulpite (37), necrose pulpar (36) e razões de chance três vezes maior para desenvolverem periodontite apical (14). Entretanto, alguns estudos mostraram resultados conflitantes – (1) um estudo observacional, limitado pelo tamanho da amostra e pela dependência de registros médicos secundários potencialmente imprecisos, não encontrou associação entre artrite reumatoide e periodontite apical (39). Isso pode ser devido a diagnósticos autorrelatados da artrite reumatoide, falta de informação sobre a gravidade e duração da doença, controle limitado de fatores de confusão e análises estatísticas simplificadas; e (2) uma revisão sistemática (20) observou possível associação entre artrite reumatoide e patologias pulpo-periapicais, mas concluiu que a evidência era limitada devido a vários fatores, incluindo a ausência de uma metanálise. Embora a nossa revisão preencha essa lacuna fornecendo síntese quantitativa, nossos achados reforçam a conclusão destes autores quando afirmaram que as evidências disponíveis ainda são muito marcadas por limitações metodológicas e alto risco de viés.

Em relação a espondilite anquilosante, encontramos uma possível associação com as patologias pulpo-periapicais apenas na análise em nível dentário (Figura 4b). As análises em nível individual, bruta (Figura 3a) e ajustada (Figura 3b), mostraram ampla variabilidade, refletindo incerteza nas estimativas. Esse achado confirma a falta de consenso entre os

pesquisadores sobre essa associação, que relataram resultados conflitantes dependendo da unidade de análise ou critérios diagnósticos utilizados (20,40).

Apesar dessa incerteza estatística, existe uma forte plausibilidade biológica para essa relação. A espondilite anquilosante é uma doença inflamatória sistêmica que eleva os níveis séricos de citocinas pró-inflamatórias, como o TNF-α e a IL-6, que estão diretamente ligadas à atividade da doença (44). Além disso, estudos mais recentes destacam também o papel central do eixo IL-23/IL-17 na inflamação crônica e nas alterações ósseas características dessa condição (47, 48). Considerando que a periodontite apical é uma lesão osteolítica impulsionada pelas mesmas citocinas (TNF-α, IL-6 e IL-17) em resposta à infecção endodôntica (9, 10), é provável que o estado inflamatório sistêmico "pré-ativado" do paciente com espondilite poderia exacerbar a resposta imune local ou dificultar o reparo ósseo, embora a evidência clínica atual ainda não tenha confirmado essa relação.

Nossos resultados mostram que tanto a síndrome de Sjögren quanto o lúpus eritematoso sistêmico estão associados a um risco aumentado para as patologias pulpo-periapicais (Figura 3), indicando maior vulnerabilidade da saúde endodôntica em indivíduos com essas condições, com risco aproximadamente três (17,) e quatro (18) vezes maior, respectivamente. Por outro lado, a falta de dados impediu a análise em nível dentário para ambas as condições.

A plausibilidade biológica para a associação com a síndrome de Sjögren é justificada pela disfunção das glândulas exócrinas. A redução do fluxo salivar e as alterações qualitativas na saliva comprometem sua capacidade tampão e antimicrobiana, resultando em um ambiente oral propício ao desenvolvimento de cáries (41). Esse aumento na suscetibilidade à cárie dentária leva, consequentemente, a uma maior incidência de comprometimento pulpar e necrose, culminando no desenvolvimento de periodontite apical (17).

Já no lúpus eritematoso sistêmico, o mecanismo parece ultrapassar a via da cárie e envolver fatores sistêmicos e vasculares. Estudos apontam que a alta carga inflamatória sistêmica, mediada por citocinas como IL-6 e TNF-α, frequentemente elevadas em pacientes com doença ativa, pode potencializar a reabsorção óssea periapical (45,18). Além disso, a deposição de complexos imunes e a vasculite, manifestações comuns do lúpus, podem comprometer a microcirculação pulpar, dificultando a resposta defensiva da polpa frente a agressões e prejudicando o reparo tecidual (49,18).

Destacamos que apenas um estudo incluído nesta revisão avaliou a associação entre doença do tecido conjuntivo e periodontite apical (39). Essa relação não demonstrou significância estatística após os ajustes, provavelmente, porque essa condição agrupa

características comuns de três outras doenças autoimunes (lúpus eritematoso sistêmico, esclerose sistêmica e polimiosite ou dermatomiosite), o que pode ter diluído a força de associação. Portanto, a atual escassez de evidências impede conclusões definitivas e evidencia uma lacuna na literatura que necessita ser preenchida por investigações futuras.

Entre os estudos de coorte incluídos, observou-se uma alteração nas medidas de associação reportadas originalmente. Três estudos (37, 39, 41) apresentaram seus resultados em IRR, refletindo a análise longitudinal. No entanto, para viabilizar a síntese quantitativa unificada na presente metanálise, esses valores foram convertidos para OR. Essa padronização metodológica permitiu o agrupamento estatístico robusto dos dados provenientes dos estudos de coorte com aqueles oriundos dos delineamentos transversal e caso-controle, que utilizam o OR como medida de associação.

Uma das limitações desta revisão é a heterogeneidade diagnóstica dos estudos primários. Essa variabilidade reflete a diversidade metodológica e clínica encontrada na literatura, decorrente de diferenças nas definições de exposição e desfecho, nos métodos diagnósticos empregados, na vasta amplitude dos tamanhos amostrais e nos desenhos dos estudos (transversal, caso-controle e coorte), além das discrepâncias nas variáveis de confusão utilizadas para ajuste. Para verificar o impacto dessa heterogeneidade, realizamos uma análise de sensibilidade, excluindo três estudos que usaram critérios diagnósticos mais fracos (13, 15, 40), e mostramos que a associação entre as exposições e os desfechos permaneceu significativa, tanto em nível individual (Figura Suplementar 2a) quanto em nível dentário (Figura Suplementar 2b), o que reforça a robustez dos nossos achados.

Outra limitação importante desta revisão que destacamos é o foco restrito dos estudo primários incluído apenas na artrite reumatoide. A maioria deles utilizaram registros hospitalares (13,14,16–18,29,36,38,40), o que pode ter introduzido viés de seleção, já que esses indivíduos frequentemente têm maior gravidade da doença, comprometendo a generalização dos nossos resultados. Da mesma forma, um estudo (15) em que o diagnóstico de artrite reumatoide foi autorrelatado também pode ser considerado uma preocupação metodológica devido ao alto risco de viés de aferição, afetando a validade da exposição.

Por fim, deve-se notar que a certeza da evidência foi classificada como “muito baixa” pelo sistema GRADE. Esse nível de confiança já era esperado, dada a natureza exclusivamente observacional dos estudos incluídos. Ressalta-se que, embora a estratégia de busca tenha sido desenhada para incluir ensaios clínicos, nenhum estudo com esse delineamento foi identificado.

A impossibilidade ética de randomizar a condição sistêmica (exposição) restringe o corpo da evidência a estudos observacionais, o que limita a inferência de causalidade direta.

Apesar das limitações identificadas nesta revisão, destacamos os nossos avanços metodológicos e as repercussões positivas de nossos achados tanto para a prática clínica quanto para pesquisas futuras. Os nossos resultados sugerem que dentistas e reumatologistas conheçam a potencial associação entre as doenças autoimunes reumáticas e os desfechos endodônticos para adoção de medidas integradas preventivas capaz de evitar as infecções endodônticas e/ou modular a resposta inflamatória local destes indivíduos. Por outro lado, estudos primários futuros com maior rigor metodológico, delineamento longitudinal, amostras que incluam um espectro mais amplo das doenças autoimunes reumáticas e controle eficaz de fatores de confusão são necessários para confirmar a magnitude dessa associação. Recomenda-se que investigações futuras, que utilizem o dente como unidade de análise, apliquem métodos estatísticos apropriados para dados correlacionados, como modelos multiníveis ou equações de estimativa generalizada, a fim de evitar a superestimação da precisão dos resultados e garantir estimativas de risco mais confiáveis.

Conclusão

Esta metanálise sugere uma associação positiva entre doenças autoimunes reumáticas (artrite reumatoide, síndrome de Sjögren, lúpus eritematoso sistêmico e doença do tecido conjuntivo) e patologias pulpo-periapicais, reforçando a importância da abordagem integrada em saúde nestas populações. No entanto, os resultados devem ser interpretados com cautela, dada a certeza da evidência classificada como “muito baixa”.

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6. CONSIDERAÇÕES FINAIS

Esta dissertação partiu da premissa de que as patologias pulpo-periapicais, embora iniciadas por uma infecção local, em alguns casos não devem ser vistas como eventos isolados, mas sim como parte do *continuum* de algumas Doenças Crônicas Não Transmissíveis (DCNTs). Nossa investigação buscou explorar como DCNTs, tais como as desordens sistêmicas que afetam o metabolismo ósseo, podem influenciar a ocorrência ou progressão das patologias pulpo-periapicais, seguindo duas vias distintas: uma degenerativa (osteoporose) e outra inflamatória (doenças autoimunes reumáticas).

Na investigação da via degenerativa (Capítulo II), não encontramos evidência que associe a osteoporose a uma maior ocorrência de patologias pulpo-periapicais, embora exista uma forte plausibilidade biológica, visto que ambas as condições envolvem perda óssea. Entretanto, os estudos incluídos na revisão sistemática e metanálise são marcados por limitações metodológicas e alta heterogeneidade, não nos permitindo confirmar essa conexão.

Inversamente, a investigação da via inflamatória (Capítulo III) revelou uma associação positiva e estatisticamente significativa entre as doenças autoimunes reumáticas (artrite reumatoide, lúpus eritematoso sistêmico, síndrome de Sjögren e doença do tecido conjuntivo) e as patologias pulpo-periapicais, tanto em nível individual quanto dentário. Este achado reforça a hipótese de que o estado inflamatório sistêmico crônico, característico dessas doenças autoimunes reumáticas, atua como um fator modulador, aumentando a suscetibilidade do hospedeiro às alterações ósseas periapicais decorrentes das infecções endodônticas.

Contudo, a principal conclusão que permeia ambos os estudos é a de "Muito Baixa" certeza da evidência (GRADE). Esta classificação, decorrente do alto risco de viés, das inconsistências metodológicas e da imprecisão dos estudos observacionais disponíveis, deve ser vista não como uma invalidação do nosso estudo, mas como um alerta, apontando que a Endodontia carece de estudos longitudinais robustos, com critérios diagnósticos precisos e controle rigoroso de fatores de confusão, para que a sistematização dos resultados de futuros estudos possam fortalecer a certeza da evidência avaliada.

Para além disso, nossos resultados convocam a Endodontia a um reposicionamento da prática terapêutica curativa hegemônica para uma prática preventiva integrativa nestas populações. Ou seja, a prática clínica, atualmente focada em um modelo tecnicista centrado no tratamento da infecção endodôntica, precisa avançar para uma visão integrada de saúde global, considerando a necessidade de modular a resposta inflamatória dos indivíduos sistemicamente comprometidos, reforçando assim o conceito de "Medicina Endodôntica".

7. TRANSFERÊNCIA DO CONHECIMENTO CIENTÍFICO

Como parte das ações de transferência do conhecimento científico para a sociedade gerado nesta dissertação, foi produzido um material informativo em formato de vídeo, com duração de 1 minuto e 46 segundos destinado à divulgação científica nas redes sociais institucionais do PPGO|UFMA (Programa de Pós-graduação em Odontologia - Universidade Federal do Maranhão).

O vídeo apresenta, em linguagem acessível ao público não especializado, os principais achados desta pesquisa, que investigou as conexões entre as alterações ósseas degenerativas (osteoporose) e inflamatórias (doenças autoimunes reumáticas) e as patologias pulpo-periapicais (infecções de origem endodôntica), destacando a relevância da integração entre a saúde bucal e a saúde geral.

Essa iniciativa tem como objetivo ampliar o alcance social dos resultados desta pesquisa, contribuindo: (1) para a conscientização da população geral, (2) com a orientação de profissionais da área da saúde (médicos reumatologistas e dentistas) para o cuidado integral da saúde sistêmica e bucal destes indivíduos e (3) com o fortalecimento do diálogo entre a academia e a sociedade. Trata-se, portanto, de uma ação alinhada aos princípios de *inserção social* e *impacto do conhecimento científico na sociedade*, conforme preconizado pela CAPES (Coordenação de Aperfeiçoamento de Pessoal de Nível Superior) no âmbito da avaliação dos programas de pós-graduação.

Link do vídeo:

https://drive.google.com/file/d/1REitNp7EaADrXj2bU5jvN77RoG_9nqsx/view?usp=sharing

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APÊNDICE A

Capítulo II

(Capítulo II): Tabela Suplementar 1. Lista de verificação PRISMA para o resumo.

Section and Topic	Item #	Checklist item	Reported (Yes/No)
TITLE			
Title	1	Identify the report as a systematic review.	YES
BACKGROUND			
Objectives	2	Provide an explicit statement of the main objective(s) or question(s) the review addresses.	YES
METHODS			
Eligibility criteria	3	Specify the inclusion and exclusion criteria for the review.	YES
Information sources	4	Specify the information sources (e.g. databases, registers) used to identify studies and the date when each was last searched.	YES
Risk of bias	5	Specify the methods used to assess risk of bias in the included studies.	YES
Synthesis of results	6	Specify the methods used to present and synthesise results.	YES
RESULTS			
Included studies	7	Give the total number of included studies and participants and summarise relevant characteristics of studies.	YES
Synthesis of results	8	Present results for main outcomes, preferably indicating the number of included studies and participants for each. If meta-analysis was done, report the summary estimate and confidence/credible interval. If comparing groups, indicate the direction of the effect (i.e. which group is favoured).	YES
DISCUSSION			
Limitations of evidence	9	Provide a brief summary of the limitations of the evidence included in the review (e.g. study risk of bias, inconsistency and imprecision).	N/A
Interpretation	10	Provide a general interpretation of the results and important implications.	N/A
OTHER			

Section and Topic	Item #	Checklist item	Reported (Yes/No)
Funding	11	Specify the primary source of funding for the review.	YES
Registration	12	Provide the register name and registration number.	YES

Not applicable: N/A

(Capítulo II): Tabela Suplementar 2. Lista de verificação PRISMA para o texto completo.

Section and Topic	Item #	Checklist item	Location where item is reported
TITLE			
Title	1	Identify the report as a systematic review.	Page 1
ABSTRACT			
Abstract	2	See the PRISMA 2020 for Abstracts checklist.	Supplemental Table 1
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of existing knowledge.	Pages 4 and 5
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	Page 5
METHODS			
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	Page 6
Information sources	6	Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted.	Supplemental table 3 Pages 6 and 7
Search strategy	7	Present the full search strategies for all databases, registers and websites, including any filters and limits used.	Supplemental table 3
Selection process	8	Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process.	Page 7
Data collection process	9	Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process.	Pages 7 and 8
Data items	10a	List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect.	Pages 8 and 9
	10b	List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information.	Pages 8 and 9
Study risk of bias assessment	11	Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process.	Page 8
Effect measures	12	Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results.	Pages 8 and 9

Section and Topic	Item #	Checklist item	Location where item is reported
Synthesis methods	13a	Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item #5)).	Pages 8 and 9
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions.	Pages 8 and 9
	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	Pages 8 and 9
	13d	Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used.	Pages 8 and 9
	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression).	Pages 8 and 9
	13f	Describe any sensitivity analyses conducted to assess robustness of the synthesized results.	Pages 8 and 9
Reporting bias assessment	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).	N/A
Certainty assessment	15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.	Page 9
RESULTS			
Study selection	16a	Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram.	Figure 1
	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.	Figure 1
Study characteristics	17	Cite each included study and present its characteristics.	Supplemental table 4
Risk of bias in studies	18	Present assessments of risk of bias for each included study.	Supplemental figure 1
Results of individual studies	19	For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (e.g. confidence/credible interval), ideally using structured tables or plots.	Supplemental figure 4
Results of syntheses	20a	For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies.	Supplemental table 4 Page 11
	20b	Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect.	Figure 2 Pages 11 and 12

Section and Topic	Item #	Checklist item	Location where item is reported
	20c	Present results of all investigations of possible causes of heterogeneity among study results.	Figure 2
	20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results.	Figure 2 Pages 11 and 12
Reporting biases	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.	N/A
Certainty of evidence	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.	Supplemental table 5
DISCUSSION			
Discussion	23a	Provide a general interpretation of the results in the context of other evidence.	Page 13
	23b	Discuss any limitations of the evidence included in the review.	Pages 14-16
	23c	Discuss any limitations of the review processes used.	Pages 16 and 17
	23d	Discuss implications of the results for practice, policy, and future research.	Page 17
OTHER INFORMATION			
Registration and protocol	24a	Provide registration information for the review, including register name and registration number, or state that the review was not registered.	Page 6
	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.	Page 6
	24c	Describe and explain any amendments to information provided at registration or in the protocol.	N/A
Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review.	Page 2 Abstract
Competing interests	26	Declare any competing interests of review authors.	N/A
Availability of data, code and other materials	27	Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review.	Supplemental tables and figures.

Not applicable: N/A

(Capítulo II): Tabela Suplementar 3. Descrição das estratégias de busca realizadas nas bases de dados PubMed, SciELO, Google Acadêmico, Biblioteca Virtual em Saúde (BVS), Embase, Scopus, Web of Science, Cochrane, Biblioteca Digital Brasileira de Teses e Dissertações (BDTD) e Catálogo de Teses e Dissertações da CAPES.

DATABASE	SEARCH EQUATION	DATE
Pubmed	(((Osteoporosis) OR (Osteoporoses)) OR ("Osteoporosis, Age-Related")) OR ("Osteoporosis, Age Related")) OR ("Age-Related Osteoporosis")) OR ("Age-Related Osteoporoses")) OR ("Age Related Osteoporosis")) OR ("Osteoporoses, Age-Related")) OR ("Bone Loss, Age-Related")) OR ("Age-Related Bone Loss")) OR ("Age-Related Bone Losses")) OR ("Bone Loss, Age Related")) OR ("Bone Losses, Age-Related")) OR ("Osteoporosis, Senile")) OR ("Osteoporoses, Senile")) OR ("Senile Osteoporoses")) OR ("Senile Osteoporosis")) OR ("Osteoporosis, Involutional")) OR ("Osteoporosis, Post-Traumatic")) OR ("Osteoporosis, Post Traumatic")) OR ("Post-Traumatic Osteoporoses")) OR ("Post-Traumatic Osteoporosis")) OR ("Osteoporosis, Postmenopausal")) OR ("Osteoporosis, Post-Menopausal")) OR ("Osteoporoses, Post-Menopausal")) OR ("Osteoporosis, Post Menopausal")) OR ("Post-Menopausal Osteoporoses")) OR ("Post-Menopausal Osteoporosis")) OR ("Postmenopausal Osteoporosis")) OR ("Osteoporoses, Postmenopausal")) OR ("Postmenopausal Osteoporoses")) OR ("Perimenopausal Bone Loss")) OR ("Bone Loss, Postmenopausal")) OR ("Bone Losses, Postmenopausal")) OR ("Postmenopausal Bone Losses")) OR ("Postmenopausal Bone Loss")) OR ("Bone Loss, Perimenopausal")) OR ("Bone Losses, Perimenopausal")) OR ("Perimenopausal Bone Losses")) OR ("Bone Diseases, Metabolic")) OR ("Metabolic Bone Diseases")) OR ("Bone Disease, Metabolic")) OR ("Metabolic Bone Disease")) OR (Osteopenia)) OR (Osteopenias)) OR ("Low Bone Density")) OR ("Bone Density, Low")) OR ("Low Bone Densities")) OR ("Low Bone Mineral Density")) AND ((("Dental Pulp") OR ("Dental Pulps")) OR ("Pulp, Dental")) OR ("Pulps, Dental")) OR ("Dental Pulp Diseases")) OR ("Dental Pulp Disease")) OR ("Disease, Dental Pulp")) OR ("Diseases, Dental Pulp")) OR ("Pulp Disease, Dental")) OR ("Pulp Diseases, Dental")) OR ("Dental Pulp Necrosis")) OR ("Dental Pulp Necroses")) OR ("Necroses, Dental Pulp")) OR ("Pulp Necroses, Dental")) OR ("Necroses, Pulp")) OR ("Necrosis, Dental Pulp")) OR ("Pulp Necroses")) OR ("Pulp Necrosis")) OR ("Necrosis, Pulp")) OR ("Pulp Necrosis, Dental")) OR ("Dental Pulp Autolysis")) OR ("Autolyses, Dental Pulp")) OR ("Dental Pulp Autolyses")) OR ("Pulp Autolyses, Dental")) OR ("Autolysis, Dental Pulp")) OR ("Pulp Autolysis, Dental")) OR ("Gangrene, Dental Pulp")) OR ("Dental Pulp Gangrene")) OR ("Pulp Gangrene")) OR ("Gangrene, Pulp")) OR ("Gangrenes, Pulp")) OR ("Pulp Gangrenes")) OR ("Pulp Gangrene, Dental")) OR ("Pulp Mummification")) OR ("Mummification, Pulp")) OR ("Mummifications, Pulp")) OR ("Pulp Mummifications")) OR (Pulpitis)) OR (Pulpitides)) OR ("Inflammation, Endodontic")) OR ("Endodontic Inflammation")) OR ("Endodontic Inflammations")) OR ("Inflammations, Endodontic")) OR ("Periapical Diseases")) OR ("Disease, Periapical")) OR ("Diseases, Periapical")) OR ("Periapical Disease")) OR ("Periapical Periodontitis")) OR ("Periapical Periodontitides")) OR ("Periodontitides, Periapical")) OR ("Periodontitis, Periapical")) OR ("Periodontitis, Apical")) OR ("Apical Periodontitides")) OR ("Apical Periodontitis")) OR ("Periodontitides, Apical")) OR ("Periodontitis, Acute Nonsuppurative")) OR ("Acute Nonsuppurative Periodontitides")) OR ("Acute Nonsuppurative Periodontitis")) OR ("Nonsuppurative Periodontitides, Acute")) OR ("Nonsuppurative Periodontitis, Acute")) OR ("Periodontitides, Acute Nonsuppurative")) OR ("Periapical Abscess")) OR ("Alveolar Abscess, Apical")) OR ("Abscess, Apical Alveolar")) OR ("Abscesses, Apical Alveolar")) OR ("Alveolar Abscesses, Apical")) OR ("Apical Alveolar Abscess")) OR ("Apical Alveolar Abscesses")) OR ("Dentoalveolar Abscess, Apical")) OR ("Abscess, Apical Dentoalveolar")) OR ("Abscesses, Apical Dentoalveolar")) OR ("Apical Dentoalveolar Abscess")) OR ("Apical Dentoalveolar Abscesses")) OR ("Dentoalveolar Abscesses, Apical")) OR ("Abscess, Periapical")) OR ("Abscesses, Periapical")) OR ("Periapical Abscesses")) OR ("Periapical Periodontitis, Suppurative")) OR ("Periapical Periodontitides, Suppurative")) OR ("Periodontitides, Suppurative Periapical")) OR ("Periodontitis, Suppurative Periapical")) OR ("Suppurative Periapical Periodontitides")) OR ("Suppurative Periapical Periodontitis")) OR ("Periodontitis, Apical, Suppurative")) OR ("Periapical Granuloma")) OR ("Granuloma, Periapical")) OR ("Granulomas,	06/2025

	Periapical")) OR ("Periapical Granulomas")) OR ("Periapical Periodontitis, Chronic Nonsuppurative")) OR ("Periodontitis, Apical, Chronic Nonsuppurative")) OR ("Dental Granulomas")) OR ("Granuloma, Dental")) OR ("Granulomas, Dental")) OR ("Dental Granuloma")) OR ("Tooth, Nonvital")) OR ("Nonvital Tooth")) OR ("Teeth, Devitalized")) OR ("Devitalized Teeth")) OR ("Tooth, Devitalized")) OR ("Devitalized Tooth")) OR ("Teeth, Nonvital")) OR ("Nonvital Teeth")) OR ("Teeth, Pulpless")) OR ("Pulpless Teeth")) OR ("Tooth, Pulpless")) OR ("Pulpless Tooth")) OR ("Teeth, Endodontically-Treated")) OR ("Endodontically-Treated Teeth")) OR ("Teeth, Endodontically Treated")) OR ("Tooth, Endodontically-Treated")) OR ("Endodontically-Treated Tooth")) OR ("Tooth, Endodontically Treated")) OR ("Dental Pulp Devitalization")) OR ("Devitalization, Dental Pulp")) OR ("Pulp Devitalization, Dental")) OR ("Periapical Tissue")) OR ("Periapical Tissues")) OR ("Tissue, Periapical")) OR ("Tissues, Periapical")) OR ("Periodontium, Apical")) OR ("Apical Periodontium")) OR ("Apical Periodontiums")) OR ("Periodontiums, Apical")) OR ("Radicular Cyst")) OR ("Cyst, Radicular")) OR ("Cysts, Radicular")) OR ("Radicular Cysts")) OR ("Periapical Cyst")) OR ("Cyst, Periapical")) OR ("Cysts, Periapical")) OR ("Periapical Cysts")) OR ("Periodontal Cyst, Apical")) OR ("Apical Periodontal Cyst")) OR ("Apical Periodontal Cysts")) OR ("Cyst, Apical Periodontal")) OR ("Cysts, Apical Periodontal")) OR ("Periodontal Cysts, Apical")) OR ("Root Canal Therapy")) OR ("Canal Therapies, Root")) OR ("Canal Therapy, Root")) OR ("Root Canal Therapies")) OR ("Therapies, Root Canal")) OR ("Therapy, Root Canal")) OR ("Root Canal Obturation")) OR ("Canal Obturation, Root")) OR ("Canal Obturations, Root")) OR ("Obturation, Root Canal")) OR ("Obturations, Root Canal")) OR ("Root Canal Obturations")) OR ("Endodontic Obturation")) OR ("Endodontic Obturations")) OR ("Obturation, Endodontic")) OR ("Obturations, Endodontic"))	
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Google Scholar	Pulpitis OR "Apical Periodontitis" OR "Dental Pulp Disease" OR "Pulp Necrosis" OR "Periapical Disease" OR "Periapical Periodontitis" OR "Periapical Abscess" AND Osteoporosis OR Osteopenia OR "Metabolic Bone Disease" OR "Low Bone Mineral Density"	06/2025
BVS/Bireme	(((Osteoporosis) OR (Osteoporoses) OR (“Osteoporosis, Age-Related”) OR (“Osteoporosis, Age Related”) OR (“Age-Related Osteoporosis”) OR (“Age-Related Osteoporoses”) OR (“Age Related Osteoporosis”) OR (“Osteoporoses, Age-Related”) OR (“Bone Loss, Age-Related”) OR (“Age-Related Bone Loss”) OR (“Age-Related Bone Losses”) OR (“Bone Loss, Age Related”) OR (“Bone Losses, Age-Related”) OR (“Osteoporosis, Senile”) OR (“Osteoporoses, Senile”) OR (“Senile Osteoporoses”) OR (“Senile Osteoporosis”) OR (“Osteoporosis, Involutional”) OR (“Osteoporosis, Post-Traumatic”) OR (“Osteoporosis, Post Traumatic”) OR (“Post-Traumatic Osteoporoses”) OR (“Post-Traumatic Osteoporosis”) OR (“Osteoporosis, Postmenopausal”) OR (“Osteoporosis, Post-Menopausal”) OR (“Osteoporoses, Post-Menopausal”) OR (“Osteoporosis, Post Menopausal”) OR (“Post-Menopausal Osteoporoses”) OR (“Post-Menopausal Osteoporosis”) OR (“Postmenopausal Osteoporosis”) OR (“Osteoporoses, Postmenopausal”) OR (“Postmenopausal Osteoporoses”) OR (“Perimenopausal Bone Loss”) OR (“Bone Loss, Postmenopausal”) OR (“Bone Losses, Postmenopausal”) OR (“Postmenopausal Bone Losses”) OR (“Postmenopausal Bone Loss”) OR (“Bone Loss, Perimenopausal”) OR (“Bone Losses, Perimenopausal”) OR (“Perimenopausal Bone Losses”) OR (“Bone Diseases, Metabolic”) OR (“Metabolic Bone Diseases”) OR (“Bone Disease, Metabolic”) OR (“Metabolic Bone Disease”) OR (Osteopenia) OR (Osteopenias) OR (“Low Bone Density”) OR (“Bone Density, Low”) OR (“Low Bone Densities”) OR (“Low Bone Mineral Density”)) AND ((“Dental Pulp”) OR (“Dental Pulps”) OR (“Pulp, Dental”) OR (“Pulps, Dental”) OR (“Dental Pulp Diseases”) OR (“Dental Pulp Disease”) OR (“Disease, Dental Pulp”) OR (“Diseases, Dental Pulp”) OR (“Pulp Disease, Dental”) OR (“Pulp Diseases, Dental”) OR (“Dental Pulp Necrosis”) OR (“Dental Pulp Necroses”) OR (“Necroses, Dental Pulp”) OR (“Pulp Necroses, Dental”) OR (“Necroses, Pulp”)	06/2025

	OR (“Necrosis, Dental Pulp”) OR (“Pulp Necroses”) OR (“Pulp Necrosis”) OR (“Necrosis, Pulp”) OR (“Pulp Necrosis, Dental”) OR (“Dental Pulp Autolysis”) OR (“Autolyses, Dental Pulp”) OR (“Dental Pulp Autolyses”) OR (“Pulp Autolyses, Dental”) OR (“Autolysis, Dental Pulp”) OR (“Pulp Autolysis, Dental”) OR (“Gangrene, Dental Pulp”) OR (“Dental Pulp Gangrene”) OR (“Pulp Gangrene”) OR (“Gangrene, Pulp”) OR (“Gangrenes, Pulp”) OR (“Pulp Gangrenes”) OR (“Pulp Gangrene, Dental”) OR (“Pulp Mummification”) OR (“Mummification, Pulp”) OR (“Mummifications, Pulp”) OR (“Pulp Mummifications”) OR (Pulpitis) OR (Pulpitides) OR (“Inflammation, Endodontic”) OR (“Endodontic Inflammation”) OR (“Endodontic Inflammations”) OR (“Inflammations, Endodontic”) OR (“Periapical Diseases”) OR (“Disease, Periapical”) OR (“Diseases, Periapical”) OR (“Periapical Disease”) OR (“Periapical Periodontitis”) OR (“Periapical Periodontitides”) OR (“Periodontitides, Periapical”) OR (“Periodontitis, Periapical”) OR (“Periodontitis, Apical”) OR (“Apical Periodontitides”) OR (“Apical Periodontitis”) OR (“Periodontitides, Apical”) OR (“Periodontitis, Acute Nonsuppurative”) OR (“Acute Nonsuppurative Periodontitides”) OR (“Acute Nonsuppurative Periodontitis”) OR (“Nonsuppurative Periodontitides, Acute”) OR (“Nonsuppurative Periodontitis, Acute”) OR (“Periodontitides, Acute Nonsuppurative”) OR (“Periapical Abscess”) OR (“Alveolar Abscess, Apical”) OR (“Abscess, Apical Alveolar”) OR (“Abscesses, Apical Alveolar”) OR (“Alveolar Abscesses, Apical”) OR (“Apical Alveolar Abscess”) OR (“Apical Alveolar Abscesses”) OR (“Dentoalveolar Abscess, Apical”) OR (“Abscess, Apical Dentoalveolar”) OR (“Abscesses, Apical Dentoalveolar”) OR (“Apical Dentoalveolar Abscess”) OR (“Apical Dentoalveolar Abscesses”) OR (“Dentoalveolar Abscesses, Apical”) OR (“Abscess, Periapical”) OR (“Abscesses, Periapical”) OR (“Periapical Abscesses”) OR (“Periapical Periodontitis, Suppurative”) OR (“Periapical Periodontitides, Suppurative”) OR (“Periodontitides, Suppurative Periapical”) OR (“Periodontitis, Suppurative Periapical”) OR (“Suppurative Periapical Periodontitides”) OR (“Suppurative Periapical Periodontitis”) OR (“Periodontitis, Apical, Suppurative”) OR (“Periapical Granuloma”) OR (“Granuloma, Periapical”) OR (“Granulomas, Periapical”) OR (“Periapical Granulomas”) OR (“Periapical Periodontitis, Chronic Nonsuppurative”) OR (“Periodontitis, Apical, Chronic Nonsuppurative”) OR (“Dental Granulomas”) OR (“Granuloma, Dental”) OR (“Granulomas, Dental”) OR (“Dental Granuloma”) OR (“Tooth, Nonvital”) OR (“Nonvital Tooth”) OR (“Teeth, Devitalized”) OR (“Devitalized Teeth”) OR (“Tooth, Devitalized”) OR (“Devitalized Tooth”) OR (“Teeth, Nonvital”) OR (“Nonvital Teeth”) OR (“Teeth, Pulpless”) OR (“Pulpless Teeth”) OR (“Tooth, Pulpless”) OR (“Pulpless Tooth”) OR (“Teeth, Endodontically-Treated”) OR (“Endodontically-Treated Teeth”) OR (“Teeth, Endodontically Treated”) OR (“Tooth, Endodontically-Treated”) OR (“Endodontically-Treated Tooth”) OR (“Tooth, Endodontically Treated”) OR (“Dental Pulp Devitalization”) OR (“Devitalization, Dental Pulp”) OR (“Pulp Devitalization, Dental”) OR (“Periapical Tissue”) OR (“Periapical Tissues”) OR (“Tissue, Periapical”) OR (“Tissues, Periapical”) OR (“Periodontium, Apical”) OR (“Apical Periodontium”) OR (“Apical Periodontiums”) OR (“Periodontiums, Apical”) OR (“Radicular Cyst”) OR (“Cyst, Radicular”) OR (“Cysts, Radicular”) OR (“Radicular Cysts”) OR (“Periapical Cyst”) OR (“Cyst, Periapical”) OR (“Cysts, Periapical”) OR (“Periapical Cysts”) OR (“Periodontal Cyst, Apical”) OR (“Apical Periodontal Cyst”) OR (“Apical Periodontal Cysts”) OR (“Cyst, Apical Periodontal”) OR (“Cysts, Apical Periodontal”) OR (“Periodontal Cysts, Apical”) OR (“Root Canal Therapy”) OR (“Canal Therapies, Root”) OR (“Canal Therapy, Root”) OR (“Root Canal Therapies”) OR (“Therapies, Root Canal”) OR (“Therapy, Root Canal”) OR (“Root Canal Obturation”) OR (“Canal Obturation, Root”) OR (“Canal Obturations, Root”) OR (“Obturation, Root Canal”) OR (“Obturations, Root Canal”) OR (“Root Canal Obturations”) OR (“Endodontic Obturation”) OR (“Endodontic Obturations”) OR (“Obturation, Endodontic”) OR (“Obturations, Endodontic”)))	
Embase	('osteoporosis'/exp OR 'decalcification, pathologic' OR 'endocrine osteoporosis' OR 'osteoporosis' OR 'osteoporotic decalcification' OR 'pathologic decalcification' OR 'osteopenia'/exp OR 'osteopenia' OR 'postmenopause osteoporosis'/exp OR 'osteoporosis, postmenopausal' OR 'post-menopausal bone loss' OR 'post-menopausal osteoporosis' OR 'post-menopause bone loss' OR 'post-menopause osteoporosis' OR 'postmenopausal bone loss' OR 'postmenopausal osteoporosis' OR 'postmenopause bone loss' OR 'postmenopause osteoporosis' OR 'type 1 osteoporosis' OR 'type i osteoporosis' OR 'metabolic bone disease'/exp OR 'bone disease, metabolic' OR 'bone diseases, metabolic' OR 'metabolic bone disease' OR 'metabolic bone diseases' OR 'metabolic disease, bone') AND ('tooth pulp'/exp OR 'dental pulp' OR 'dental pulpa' OR 'pulp vitality' OR 'pulp, tooth' OR 'pulpa' OR 'pulpa dens vitality' OR 'pulpa dentis' OR 'pulpal tissue' OR 'tooth pulp' OR 'tooth pulp vitality' OR 'tooth pulpa' OR 'tooth, pulp' OR 'tooth pulp disease'/exp OR 'dental pulp autolysis' OR 'dental pulp calcification' OR 'dental pulp disease' OR 'dental pulp diseases' OR 'dental pulp exposure' OR 'dental pulp gangrene' OR 'dental pulp necrosis' OR 'dental pulp test' OR 'nonvital tooth' OR 'reactionary dentin (disease)' OR 'tertiary dentin (disease)' OR 'tooth pulp disease' OR 'tooth pulp gangrene' OR 'tooth, nonvital' OR 'pulpitis'/exp OR 'acute dental pulpitis' OR 'dental pulp inflammation' OR 'endodontal infections' OR 'endodontal	06/2025

	inflammation' OR 'endodontic infection' OR 'endodontic inflammation' OR 'pulp infection' OR 'pulpal infection' OR 'pulpal inflammation' OR 'pulpitis' OR 'tooth pulp infection' OR 'tooth pulp inflammation' OR 'tooth pulpitis' OR 'tooth periapical disease'/exp OR 'dental granuloma' OR 'dentin granuloma' OR 'dentine granuloma' OR 'periapical disease' OR 'periapical diseases' OR 'periapical granuloma' OR 'periapical infection' OR 'periapical lesion' OR 'periapical periodontitis' OR 'tooth granuloma' OR 'tooth periapical disease' OR 'tooth periapical granuloma' OR 'tooth periapical infection' OR 'periapical abscess'/exp OR 'alveolar abscess' OR 'apical abscess (dental)' OR 'dento alveolar abscess' OR 'dentoalveolar abscess' OR 'periapical abscess' OR 'periapical abscesses' OR 'suppurative apical periodontitis' OR 'suppurative periapical periodontitis' OR 'dental pulp devitalization'/exp OR 'dental devitalisation' OR 'dental devitalization' OR 'dental pulp devitalization' OR 'devitalization (dental)' OR 'pulp devitalization' OR 'tooth devitalization' OR 'periapical tissue'/exp OR 'periapical tissue' OR 'radicular cyst'/exp OR 'apical cyst' OR 'apical periodontal cyst' OR 'apical radicular cyst' OR 'dental root cyst' OR 'periapical cyst' OR 'periradicular cyst' OR 'radicular cyst' OR 'radiculodental cyst' OR 'residual radicular cyst' OR 'root end cyst' OR 'endodontic procedure'/exp OR 'endodontic method' OR 'endodontic procedure' OR 'endodontic technique' OR 'pulp canal therapy' OR 'root canal procedure' OR 'root canal therapy' OR 'root canal obturation'/exp OR 'canal obturation (dental)' OR 'dental canal filling' OR 'dental root canal filling' OR 'dental root filling' OR 'root canal filling' OR 'root canal obturation' OR 'tooth root canal filling' OR 'tooth root filling')	
Scopus	TITLE-ABS (osteoporosis OR osteoporoses OR "Osteoporosis, Age-Related" OR "Osteoporosis, Age Related" OR "Age-Related Osteoporosis" OR "Age-Related Osteoporoses" OR "Age Related Osteoporosis" OR "Osteoporoses, Age-Related" OR "Bone Loss, Age-Related" OR "Age-Related Bone Loss" OR "Age-Related Bone Losses" OR "Bone Loss, Age Related" OR "Bone Losses, Age-Related" OR "Osteoporosis, Senile" OR "Osteoporoses, Senile" OR "Senile Osteoporoses" OR "Senile Osteoporosis" OR "Osteoporosis, Involutional" OR "Osteoporosis, Post-Traumatic" OR "Osteoporosis, Post Traumatic" OR "Post-Traumatic Osteoporoses" OR "Post-Traumatic Osteoporosis" OR "Osteoporosis, Postmenopausal" OR "Osteoporosis, Post-Menopausal" OR "Osteoporoses, Post-Menopausal" OR "Osteoporosis, Post Menopausal" OR "Post-Menopausal Osteoporoses" OR "Post-Menopausal Osteoporosis" OR "Postmenopausal Osteoporosis" OR "Osteoporoses, Postmenopausal" OR "Postmenopausal Osteoporoses" OR "Perimenopausal Bone Loss" OR "Bone Loss, Postmenopausal" OR "Bone Losses, Postmenopausal" OR "Postmenopausal Bone Losses" OR "Postmenopausal Bone Loss" OR "Bone Loss, Perimenopausal" OR "Bone Losses, Perimenopausal" OR "Perimenopausal Bone Losses" OR "Bone Diseases, Metabolic" OR "Metabolic Bone Diseases" OR "Bone Disease, Metabolic" OR "Metabolic Bone Disease" OR osteopenia OR osteopenias OR "Low Bone Density" OR "Bone Density, Low" OR "Low Bone Densities" OR "Low Bone Mineral Density") AND TITLE-ABS ("Dental Pulp" OR "Dental Pulps" OR "Pulp, Dental" OR "Pulps, Dental" OR "Dental Pulp Diseases" OR "Dental Pulp Disease" OR "Disease, Dental Pulp" OR "Diseases, Dental Pulp" OR "Pulp Disease, Dental" OR "Pulp Diseases, Dental" OR "Dental Pulp Necrosis" OR "Dental Pulp Necroses" OR "Necroses, Dental Pulp" OR "Pulp Necroses, Dental" OR "Necroses, Pulp" OR "Necrosis, Dental Pulp" OR "Pulp Necroses" OR "Pulp Necrosis" OR "Necrosis, Pulp" OR "Pulp Necrosis, Dental" OR "Dental Pulp Autolysis" OR "Autolyses, Dental Pulp" OR "Dental Pulp Autolyses" OR "Pulp Autolyses, Dental" OR "Autolysis, Dental Pulp" OR "Pulp Autolysis, Dental" OR "Gangrene, Dental Pulp" OR "Dental Pulp Gangrene" OR "Pulp Gangrene" OR "Gangrene, Pulp" OR "Gangrenes, Pulp" OR "Pulp Gangrenes" OR "Pulp Gangrene, Dental" OR "Pulp Mummification" OR "Mummification, Pulp" OR "Mummifications, Pulp" OR "Pulp Mummifications" OR pulpitis OR pulpitides OR "Inflammation, Endodontic" OR "Endodontic Inflammation" OR "Endodontic Inflammations" OR "Inflammations, Endodontic" OR "Periapical Diseases" OR "Disease, Periapical" OR "Diseases, Periapical" OR "Periapical Disease" OR "Periapical Periodontitis" OR "Periapical Periodontitides" OR "Periodontitides, Periapical" OR "Periodontitis, Periapical" OR "Periodontitis, Apical" OR "Apical Periodontitides" OR "Apical Periodontitis" OR "Periodontitides, Apical" OR "Periodontitis, Acute Nonsuppurative" OR "Acute Nonsuppurative Periodontitides" OR "Acute Nonsuppurative Periodontitis" OR "Nonsuppurative Periodontitides, Acute" OR "Nonsuppurative Periodontitis, Acute" OR "Periodontitides, Acute Nonsuppurative" OR "Periapical Abscess" OR "Alveolar Abscess, Apical" OR "Abscess, Apical Alveolar" OR "Abscesses, Apical Alveolar" OR "Alveolar Abscesses, Apical" OR "Apical Alveolar Abscess" OR "Apical Alveolar Abscesses" OR "Dentoalveolar Abscess, Apical" OR "Abscess, Apical Dentoalveolar" OR "Abscesses, Apical Dentoalveolar" OR "Apical Dentoalveolar Abscess" OR "Apical Dentoalveolar Abscesses" OR "Dentoalveolar Abscesses, Apical" OR "Abscess, Periapical" OR "Abscesses, Periapical" OR "Periapical Abscesses" OR "Periapical Periodontitis, Suppurative" OR "Periapical Periodontitides, Suppurative" OR "Periodontitides, Suppurative Periapical" OR "Periodontitis, Suppurative Periapical" OR "Suppurative Periapical Periodontitides" OR "Suppurative Periapical Periodontitis" OR "Periodontitis, Apical, Suppurative" OR "Periapical Granuloma" OR	06/2025

	"Granuloma, Periapical" OR "Granulomas, Periapical" OR "Periapical Granulomas" OR "Periapical Periodontitis, Chronic Nonsuppurative" OR "Periodontitis, Apical, Chronic Nonsuppurative" OR "Dental Granulomas" OR "Granuloma, Dental" OR "Granulomas, Dental" OR "Dental Granuloma" OR "Tooth, Nonvital" OR "Nonvital Tooth" OR "Teeth, Devitalized" OR "Devitalized Teeth" OR "Tooth, Devitalized" OR "Devitalized Tooth" OR "Teeth, Nonvital" OR "Nonvital Teeth" OR "Teeth, Pulpless" OR "Pulpless Teeth" OR "Tooth, Pulpless" OR "Pulpless Tooth" OR "Teeth, Endodontically-Treated" OR "Endodontically-Treated Teeth" OR "Teeth, Endodontically Treated" OR "Tooth, Endodontically-Treated" OR "Endodontically-Treated Tooth" OR "Tooth, Endodontically Treated" OR "Dental Pulp Devitalization" OR "Devitalization, Dental Pulp" OR "Pulp Devitalization, Dental" OR "Periapical Tissue" OR "Periapical Tissues" OR "Tissue, Periapical" OR "Tissues, Periapical" OR "Periodontium, Apical" OR "Apical Periodontium" OR "Apical Periodontiums" OR "Periodontiums, Apical" OR "Radicular Cyst" OR "Cyst, Radicular" OR "Cysts, Radicular" OR "Radicular Cysts" OR "Periapical Cyst" OR "Cyst, Periapical" OR "Cysts, Periapical" OR "Periapical Cysts" OR "Periodontal Cyst, Apical" OR "Apical Periodontal Cyst" OR "Apical Periodontal Cysts" OR "Cyst, Apical Periodontal" OR "Cysts, Apical Periodontal" OR "Periodontal Cysts, Apical" OR "Root Canal Therapy" OR "Canal Therapies, Root" OR "Canal Therapy, Root" OR "Root Canal Therapies" OR "Therapies, Root Canal" OR "Therapy, Root Canal" OR "Root Canal Obturation" OR "Canal Obturation, Root" OR "Canal Obturations, Root" OR "Obturation, Root Canal" OR "Obturations, Root Canal" OR "Root Canal Obturations" OR "Endodontic Obturation" OR "Endodontic Obturations" OR "Obturation, Endodontic" OR "Obturations, Endodontic")	
Web of Science	(ALL=(Osteoporosis OR osteoporosis OR “Age Related Osteoporosis” OR “Senile osteoporosis” OR “Senile Osteoporosis” OR “Osteoporosis, Postmenopausal” OR “Postmenopausal Osteoporosis” OR “Postmenopausal osteoporosis” OR “Perimenopausal Bone Loss” OR “Bone Diseases, Metabolic” OR “Metabolic Bone Diseases” OR Osteopenia OR osteopenia OR “Low Bone Density” OR “Low Bone Mineral Density”)) AND ALL=(“Dental Pulp” OR “Dental Pulp Diseases” OR “Dental Pulp Necrosis” OR Pulpitis OR “Periapical Diseases” OR “Periapical Periodontitis” OR “Periapical Abscess” OR “Periapical Granuloma” OR “Tooth, Nonvital” OR “Dental Pulp Devitalization” OR “Periapical Tissue” OR “Radicular Cyst” OR “Root Canal Therapy” OR “Root Canal Obturation”)	06/2025
Cochrane Library	(Osteoporosis OR Osteoporoses OR “Osteoporosis, Age-Related” OR “Osteoporosis, Age Related” OR “Age-Related Osteoporosis” OR “Age-Related Osteoporoses” OR “Age Related Osteoporosis” OR “Osteoporoses, Age-Related” OR “Bone Loss, Age-Related” OR “Age-Related Bone Loss” OR “Age-Related Bone Losses” OR “Bone Loss, Age Related” OR “Bone Losses, Age-Related” OR “Osteoporosis, Senile” OR “Osteoporoses, Senile” OR “Senile Osteoporoses” OR “Senile Osteoporosis” OR “Osteoporosis, Involutional” OR “Osteoporosis, Post-Traumatic” OR “Osteoporosis, Post Traumatic” OR “Post-Traumatic Osteoporoses” OR “Post-Traumatic Osteoporosis” OR “Osteoporosis, Postmenopausal” OR “Osteoporosis, Post-Menopausal” OR “Osteoporoses, Post-Menopausal” OR “Osteoporosis, Post Menopausal” OR “Post-Menopausal Osteoporoses” OR “Post-Menopausal Osteoporosis” OR “Postmenopausal Osteoporosis” OR “Osteoporoses, Postmenopausal” OR “Postmenopausal Osteoporoses” OR “Perimenopausal Bone Loss” OR “Bone Loss, Postmenopausal” OR “Bone Losses, Postmenopausal” OR “Postmenopausal Bone Losses” OR “Postmenopausal Bone Loss” OR “Bone Loss, Perimenopausal” OR “Bone Losses, Perimenopausal” OR “Perimenopausal Bone Losses” OR “Bone Diseases, Metabolic” OR “Metabolic Bone Diseases” OR “Bone Disease, Metabolic” OR “Metabolic Bone Disease” OR Osteopenia OR Osteopenias OR “Low Bone Density” OR “Bone Density, Low” OR “Low Bone Densities” OR “Low Bone Mineral Density”) AND ("Dental Pulp" OR "Dental Pulps" OR "Pulp, Dental" OR "Pulps, Dental" OR "Dental Pulp Diseases" OR "Dental Pulp Disease" OR "Disease, Dental Pulp" OR "Diseases, Dental Pulp" OR "Pulp Disease, Dental" OR "Pulp Diseases, Dental" OR "Dental Pulp Necrosis" OR "Dental Pulp Necroses" OR "Necroses, Dental Pulp" OR "Pulp Necroses, Dental" OR "Necroses, Pulp" OR "Necrosis, Dental Pulp" OR "Pulp Necroses" OR "Pulp Necrosis" OR "Necrosis, Pulp" OR "Pulp Necrosis, Dental" OR "Dental Pulp Autolysis" OR "Autolyses, Dental Pulp" OR "Dental Pulp Autolyses" OR "Pulp Autolyses, Dental" OR "Autolysis, Dental Pulp" OR "Pulp Autolysis, Dental" OR "Gangrene, Dental Pulp" OR "Dental Pulp Gangrene" OR "Pulp Gangrene" OR "Gangrene, Pulp" OR "Gangrenes, Pulp" OR "Pulp Gangrenes" OR "Pulp Gangrene, Dental" OR "Pulp Mummification" OR "Mummification, Pulp" OR "Mummifications, Pulp" OR "Pulp Mummifications" OR pulpitis OR pulpitides OR "Inflammation, Endodontic" OR "Endodontic Inflammation" OR "Endodontic Inflammations" OR "Inflammations, Endodontic" OR "Periapical Diseases" OR "Disease, Periapical" OR "Diseases, Periapical" OR "Periapical Disease" OR "Periapical Periodontitis" OR "Periapical Periodontitides" OR "Periodontitides, Periapical" OR "Periodontitis, Periapical" OR "Periodontitis, Apical" OR "Apical Periodontitides" OR "Apical Periodontitis" OR "Periodontitides, Apical" OR "Periodontitis, Acute Nonsuppurative" OR "Acute Nonsuppurative	06/2025

	Periodontitides" OR "Acute Nonsuppurative Periodontitis" OR "Nonsuppurative Periodontitides, Acute" OR "Nonsuppurative Periodontitis, Acute" OR "Periodontitides, Acute Nonsuppurative" OR "Periapical Abscess" OR "Alveolar Abscess, Apical" OR "Abscess, Apical Alveolar" OR "Abscesses, Apical Alveolar" OR "Alveolar Abscesses, Apical" OR "Apical Alveolar Abscess" OR "Apical Alveolar Abscesses" OR "Dentoalveolar Abscess, Apical" OR "Abscess, Apical Dentoalveolar" OR "Abscesses, Apical Dentoalveolar" OR "Apical Dentoalveolar Abscess" OR "Apical Dentoalveolar Abscesses" OR "Dentoalveolar Abscesses, Apical" OR "Abscess, Periapical" OR "Abscesses, Periapical" OR "Periapical Abscesses" OR "Periapical Periodontitis, Suppurative" OR "Periapical Periodontitides, Suppurative" OR "Periodontitides, Suppurative Periapical" OR "Periodontitis, Suppurative Periapical" OR "Suppurative Periapical Periodontitides" OR "Suppurative Periapical Periodontitis" OR "Periodontitis, Apical, Suppurative" OR "Periapical Granuloma" OR "Granuloma, Periapical" OR "Granulomas, Periapical" OR "Periapical Granulomas" OR "Periapical Periodontitis, Chronic Nonsuppurative" OR "Periodontitis, Apical, Chronic Nonsuppurative" OR "Dental Granulomas" OR "Granuloma, Dental" OR "Granulomas, Dental" OR "Dental Granuloma" OR "Tooth, Nonvital" OR "Nonvital Tooth" OR "Teeth, Devitalized" OR "Devitalized Teeth" OR "Tooth, Devitalized" OR "Devitalized Tooth" OR "Teeth, Nonvital" OR "Nonvital Teeth" OR "Teeth, Pulpless" OR "Pulpless Teeth" OR "Tooth, Pulpless" OR "Pulpless Tooth" OR "Teeth, Endodontically-Treated" OR "Endodontically-Treated Teeth" OR "Teeth, Endodontically Treated" OR "Tooth, Endodontically-Treated" OR "Endodontically-Treated Tooth" OR "Tooth, Endodontically Treated" OR "Dental Pulp Devitalization" OR "Devitalization, Dental Pulp" OR "Pulp Devitalization, Dental" OR "Periapical Tissue" OR "Periapical Tissues" OR "Tissue, Periapical" OR "Tissues, Periapical" OR "Periodontium, Apical" OR "Apical Periodontium" OR "Apical Periodontiums" OR "Periodontiums, Apical" OR "Radicular Cyst" OR "Cyst, Radicular" OR "Cysts, Radicular" OR "Radicular Cysts" OR "Periapical Cyst" OR "Cyst, Periapical" OR "Cysts, Periapical" OR "Periapical Cysts" OR "Periodontal Cyst, Apical" OR "Apical Periodontal Cyst" OR "Apical Periodontal Cysts" OR "Cyst, Apical Periodontal" OR "Cysts, Apical Periodontal" OR "Periodontal Cysts, Apical" OR "Root Canal Therapy" OR "Canal Therapies, Root" OR "Canal Therapy, Root" OR "Root Canal Therapies" OR "Therapies, Root Canal" OR "Therapy, Root Canal" OR "Root Canal Obturation" OR "Canal Obturation, Root" OR "Canal Obturations, Root" OR "Obturation, Root Canal" OR "Obturations, Root Canal" OR "Root Canal Obturations" OR "Endodontic Obturation" OR "Endodontic Obturations" OR "Obturation, Endodontic" OR "Obturations, Endodontic")	
Brazilian digital library of theses and dissertations	(Todos os campos:Osteoporosis OR Osteoporoses OR “Osteoporosis, Age-Related” OR “Osteoporosis, Age Related” OR “Age-Related Osteoporosis” OR “Age-Related Osteoporoses” OR “Age Related Osteoporosis” OR “Osteoporoses, Age-Related” OR “Bone Loss, Age-Related” OR “Age-Related Bone Loss” OR “Age-Related Bone Losses” OR “Bone Loss, Age Related” OR “Bone Losses, Age-Related” OR “Osteoporosis, Senile” OR “Osteoporoses, Senile” OR “Senile Osteoporoses” OR “Senile Osteoporosis” OR “Osteoporosis, Involutional” OR “Osteoporosis, Post-Traumatic” OR “Osteoporosis, Post Traumatic” OR “Post-Traumatic Osteoporoses” OR “Post-Traumatic Osteoporosis” OR “Osteoporosis, Postmenopausal” OR “Osteoporosis, Post-Menopausal” OR “Osteoporoses, Post-Menopausal” OR “Osteoporosis, Post Menopausal” OR “Post-Menopausal Osteoporoses” OR “Post-Menopausal Osteoporosis” OR “Postmenopausal Osteoporosis” OR “Osteoporoses, Postmenopausal” OR “Postmenopausal Osteoporoses” OR “Perimenopausal Bone Loss” OR “Bone Loss, Postmenopausal” OR “Bone Losses, Postmenopausal” OR “Postmenopausal Bone Losses” OR “Postmenopausal Bone Loss” OR “Bone Loss, Perimenopausal” OR “Bone Losses, Perimenopausal” OR “Perimenopausal Bone Losses” OR “Bone Diseases, Metabolic” OR “Metabolic Bone Diseases” OR “Bone Disease, Metabolic” OR “Metabolic Bone Disease” OR Osteopenia OR Osteopenias OR “Low Bone Density” OR “Bone Density, Low” OR “Low Bone Densities” OR “Low Bone Mineral Density” E Todos os campos:“Dental Pulp” OR “Dental Pulp Diseases” OR “Dental Pulp Disease” OR “Pulp Disease, Dental” OR “Pulp Diseases, Dental” OR “Dental Pulp Necrosis” OR “Pulp Necrosis” OR “Dental Pulp Autolysis” OR Pulpitis OR “Inflammation, Endodontic” OR “Endodontic Inflammation” OR “Periapical Diseases” OR “Periapical Disease” OR “Periapical Periodontitis” OR “Periodontitis, Periapical” OR “Periodontitis, Apical” OR “Apical Periodontitis” OR “Acute Nonsuppurative Periodontitis” OR “Nonsuppurative Periodontitis, Acute” OR “Periapical Abscess” OR “Alveolar Abscess, Apical” OR “Apical Alveolar Abscess” OR “Dentoalveolar Abscess, Apical” OR “Periapical Periodontitis, Suppurative” OR “Periodontitis, Suppurative Periapical” OR “Periapical Granuloma” OR “Periapical Granulomas” OR “Periapical Periodontitis, Chronic Nonsuppurative” OR “Dental Granuloma” OR “Tooth, Nonvital” OR “Nonvital Tooth” OR “Teeth, Devitalized” OR “Devitalized Teeth” OR “Devitalized Tooth” OR “Nonvital Teeth” OR “Endodontically-Treated Teeth” OR “Endodontically-Treated Tooth” OR “Dental Pulp Devitalization” OR “Devitalization, Dental Pulp” OR “Pulp Devitalization, Dental” OR “Periapical Tissue” OR “Periapical Tissues” OR	06/2025

	“Apical Periodontium” OR “Radicular Cyst” OR “Radicular Cysts” OR “Periapical Cyst” OR “Root Canal Therapy” OR “Root Canal Therapies” OR “Root Canal Obturation” OR “Endodontic Obturation”)	
CAPES Theses and Dissertations Catalog	Osteoporose E Oral	06/2025

(Capítulo II): Tabela Suplementar 4. Síntese Qualitativa dos Estudos Incluídos.

Autor/ Ano	País	Revista	Desenho do estudo	Tamanho da amostra	Faixa etária da amostra	Diagnóstico-Osteoporose	Tipo de patologia pulpar/periapical	Diagnóstico-patologia pulpar/ periapical	Principais resultados
Kahm e Yang, 2024	Coreia do Sul	Medicina	Coorte	Osteoporose: 4688 indivíduos Grupo controle: 1361 indivíduos	20-80 anos	Osteoporose: Diagnósticos identificados, classificados e extraídos utilizando o ICD-10	Necrose Pulpar	Diagnósticos identificados, classificados e extraídos utilizando o ICD-10	Não houve uma associação significativa entre osteoporose e necrose pulpar (OR= 1.078; IC95%: 0.9477 a 1.226; p= 0.253)
López-López *et al.*, 2015	Espanha	Gerodontology	Transversal	Osteopenia: 36 indivíduos Osteoporose: 12 indivíduos Grupo controle: 27 indivíduos	59-68 anos	Osteopenia e osteoporose: mensuração da densidade mineral óssea utilizando a técnica de absorciometria de raios-X de dupla energia, nas regiões do pescoço do fêmur e da coluna lombar	Periodontite Apical	Radiografias panorâmicas digitais	Osteopenia: A associação entre osteopenia e periodontite apical não foi significativa (OR= 4.167; IC95%:0.8198 a 21.18). Osteoporose: Não houve associação significativa entre osteoporose e periodontite apical (OR= 4.167; IC95%: 0.5961 a 29.13)

Kamalı e Turkaydın, 2024	Turquia	JADA	Transversal	Osteoporose: 711 indivíduos Grupo controle: 711 indivíduos	18-75 anos	Osteoporose: mensuração da densidade mineral óssea utilizando a técnica de absorciometria de raios-X de dupla energia	Periodontite Apical	Radiografias panorâmicas e índice periapical	Não houve associação significativa entre osteoporose e periodontite apical (OR= 1.024; IC95%: 0.8285 a 1.264). Com dados ajustados, houve associação significativa (OR= 1.142, IC95%: 1.003 a 1.300)
Cadoni *et al.*, 2022	Itália	Clinical and Experimental Dental Research	Caso-controle	Osteoporose: 76 indivíduos (1.691 dentes) Grupo controle: 76 indivíduos (1.867 dentes)	40-80 anos	Osteoporose: A absorciometria de raios X de dupla energia foi usada para avaliar a densidade mineral óssea e diagnosticar a osteoporose.	Periodontite Apical	Radiografia panorâmica e periapical seletiva nos dentes anteriores superiores e em todos os dentes que apresentavam restaurações, periodontite apical ou tratamento endodôntico.	Não foi encontrada uma associação significativa entre osteoporose periodontite apical tanto em nível individual (OR= 0.8081; IC95%: 0.4259 a 1.533) quanto em nível dentário (OR= 1.009; IC95%: 0.6913 a 1.473)
Katz e Rotstein, 2021	Estados Unidos	Journal of Endodontics	Transversal	Com osteoporose:	Não informa	Osteoporose: Código de diagnóstico correspondente para osteoporose	Lesão Periapical	Classificação Internacional de Doenças, Décima	Houve associação significativa entre osteoporose e lesões periapicais

				42.292 indivíduos Grupo controle: 1.602.661 indivíduos		(Classificação Internacional de Doenças 9-733 e Classificação Internacional de Doenças 10-M81)		Revisão K04.7 e Classificação Internacional de Doenças, Nona Revisão 522.5. O diagnóstico foi feito por exames clínicos e radiográficos.	(OR ajustado= 3.3651; IC95%: 3.1219 a 3.6273)
Thanakun *et al.*, 2019	Tailândia	International Journal of Dentistry	Transversal	Pré menopausa: 43 mulheres Pós menopausa: 32 mulheres	35-75 anos	Pós menopausa: definido como ausência de menstruação por um período mínimo de 12 meses consecutivos, conforme relato das participantes durante a entrevista clínica	Lesão Periapical	Radiografias panorâmicas digitais	Não houve associação entre mulheres na pós menopausa e periodontite apical (OR= 2.694; IC95%: 0.906 a 8.01)

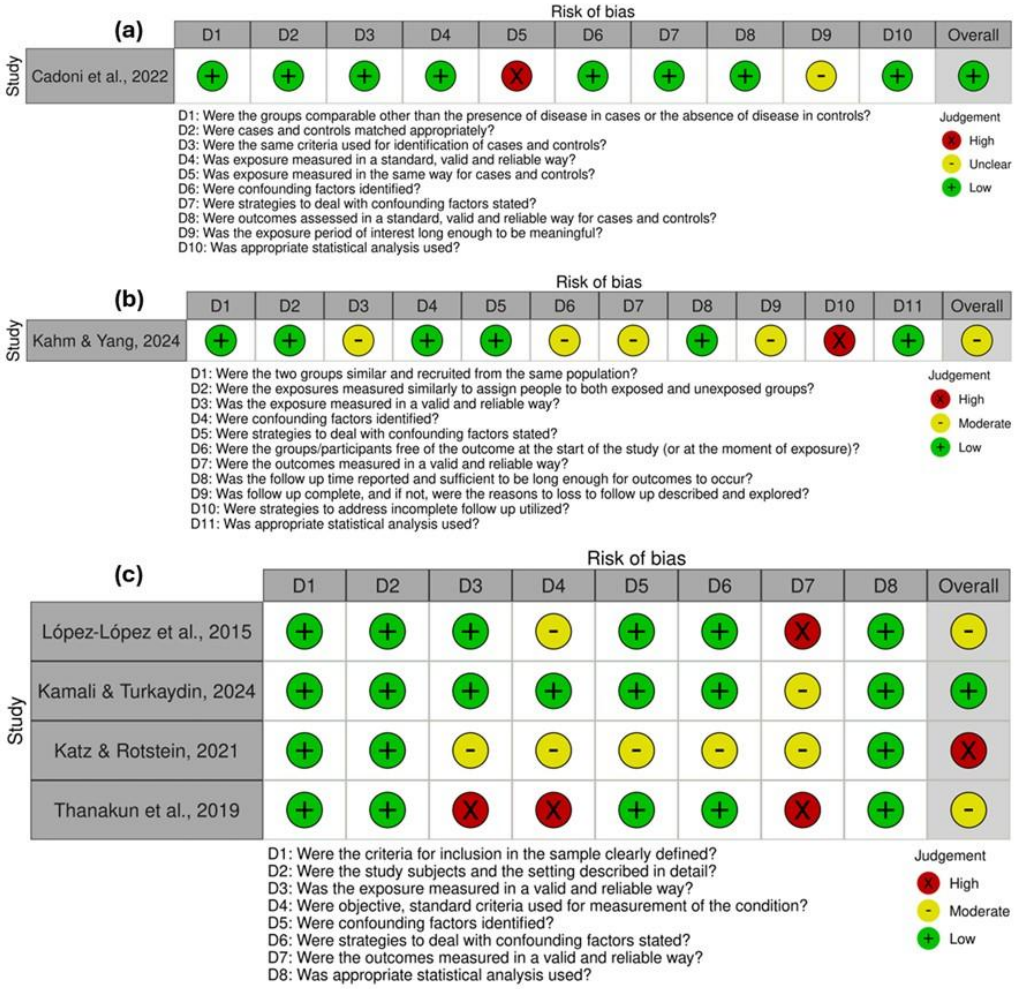
ICD-10: Classificação Internacional de Doenças, Décima Revisão; OR: Odds Ratio; IC95%: Intervalo de Confiança de 95%.

(Capítulo II): Tabela Suplementar 5. Avaliação da certeza da evidência para cada desfecho analisado nas metanálises, segundo a ferramenta GRADE.

Certainty assessment							Sumário de Resultados				
Participantes (estudos) Seguimento	Risco de viés	Inconsistência	Evidência indireta	Imprecisão	Viés de publicação	Overall certainty of evidence	Taxas de eventos do estudo (%)		Efeito relativo (95% CI)	Efeitos absolutos potenciais	
							Com controle	Com osteoporose		Risco com controle	Diferença de risco com osteoporose
Osteoporosis versus pulpal-periapical pathologies (unadjusted OR)											
1652690 (6 estudos observacionais)	muito grave[a]	muito grave[b]	não grave	grave[c]	nenhum	⨁◯◯◯ Muito baixa[a,b,c]	8734/1604879 (0.5%)	2683/47811 (5.6%)	OR 1.65 (0.80 para 3.41)	8734/1604879 (0.5%)	**4 mais por 1.000** (de 1 menos para 13 mais)
Osteoporosis versus pulpal-periapical pathologies (adjusted OR)											
1646375 (2 estudos observacionais)	muito grave[d]	muito grave[e]	não grave	grave[f]	nenhum	⨁◯◯◯ Muito baixa[d,e,f]	8250/1603372 (0.5%)	1047/43003 (2.4%)	OR 1.96 (0.68 para 5.66)	8250/1603372 (0.5%)	**5 mais por 1.000** (de 2 menos para 23 mais)
Osteoporosis versus pulpal-periapical pathologies - sensitivity analysis											
1652615 (5 estudos observacionais)	muito grave[g]	muito grave[h]	não grave	grave[i]	nenhum	⨁◯◯◯ Muito baixa[g,h,i]	8727/1604836 (0.5%)	2672/47779 (5.6%)	OR 1.52 (0.69 para 3.35)	8727/1604836 (0.5%)	**3 mais por 1.000** (de 2 menos para 13 mais)

CI: Confidence interval; **OR:** Odds ratio; **a**: three studies presented a moderate risk of bias, while one presented a high risk; **b:** I^2= 98.5%; **c:** OR= 1.65; IC95%: 0.80 to 3.41; **d:** one study with high risk of bias; **e:** I^2= 99.5%; **f:** OR= 1.96; IC95%: 0.68 to 5.66; **g:** two studies presented a moderate risk of bias, while one presented a high risk; **h:** I^2= 98.8%; **i:** OR= 1.52; IC95%: 0.69 to 3.35.

(Capítulo II): Figura suplementar 1. Risco de viés – Ferramenta de Avaliação Crítica do Instituto Joanna Briggs: (a) estudos caso-controle, (b) estudos de coorte e (c) estudos transversais.



(Capítulo II): PROTOCOLO DE PESQUISA – PROSPERO

NIHR | National Institute for Health and Care Research

PROSPERO
International prospective register of systematic reviews

Impact of osteopenia and osteoporosis on the prevalence of pulpal and periapical pathologies: a systematic review and meta-analysis

Soraia de Fátima Carvalho Souza , Ana Paula Nóbrega Caetano da Silva, Rodrigo Costa Mendes, Randerson Silva Araújo, Erika Bárbara Abreu Fonseca Thomaz

Citation
Soraia de Fátima Carvalho Souza , Ana Paula Nóbrega Caetano da Silva, Rodrigo Costa Mendes, Randerson Silva Araújo, Erika Bárbara Abreu Fonseca Thomaz. Impact of osteopenia and osteoporosis on the prevalence of pulpal and periapical pathologies: a systematic review and meta-analysis. PROSPERO 2024 Available from https://www.crd.york.ac.uk/PROSPERO/view/CRD42024559563

REVIEW TITLE AND BASIC DETAILS

Review title
Impact of osteopenia and osteoporosis on the prevalence of pulpal and periapical pathologies: a systematic review and meta-analysis

Review objectives
We will address the following research question:
Do individuals with osteopenia or osteoporosis have a higher prevalence of pulp and periapical pathologies compared to those without osteopenia or osteoporosis?
Three secondary questions are:
Do both types of osteopenia/osteoporosis (primary and secondary) interfere with the prevalence of pulpal and periapical pathologies?
Does the degree of severity of osteoporosis affect the prevalence of pulpal and periapical pathologies?
Do osteopenia and osteoporosis interfere with bone repair in individuals with pulpal and periapical pathologies after endodontic treatment?

Keywords
Adult, Aged, Dental Pulp Diseases, meta-analysis, Osteopenia, Osteoporosis, Osteoporosis, Postmenopausal, Periapical Diseases, Systematic review

SEARCHING AND SCREENING

Searches

We will search 11 online databases: MEDLINE/PubMed, Embase, Scopus, BVS-Bireme, Web of Science, LILACS, Google Scholar, SciELO, Cochrane Library, ProQuest and the Brazilian digital library of theses and dissertations. Experts will also be consulted about other studies on the subject, as well as reference lists and suggestions for similar work on the articles identified We will not apply any language, date or publication status restrictions. We will search for the entry terms available in each database without filters (All Fields). We will update the search before publishing the results. In addition, we will contact the authors in case of missing information in conference proceedings, manuscripts or abstracts in order to obtain the full papers.

The search will follow the PEOS strategy:

P: Adults and elderly regardless of age, gender, race/color or any other condition (Adult; Aged; Humans).

E: Osteopenia and osteoporosis (Osteoporosis; Osteoporosis, Postmenopausal; Osteopenia)

O: Presence of pulpal and periapical pathology (Periapical Diseases; Dental Pulp Diseases)

S: Study design (Observational Study; Cross-Sectional Studies; Cohort Studies; Case-Control Studies; Clinical Trial; Randomized Controlled Trial; Controlled Clinical Trial; Intervention Study).

Study design

We will include observational studies (cross-sectional, cohort and case-control) and randomized and non-randomized clinical trials. These study designs will be considered given the existence of a comparison group, allowing for a more adequate analysis of the effect of an intervention/exposure on the outcomes of interest. Case reports, expert opinions, technical reports, letters to the editor and reviews of any kind will not be included.

ELIGIBILITY CRITERIA

Condition or domain being studied

Osteoporosis is a systemic degenerative osteometabolic disease that affects more than 200 million people worldwide. It is characterized by low bone mass and deterioration of microarchitecture, with increased bone fragility and susceptibility to fracture (Aibar-Almazán et al, 2022; Khandelwal; Lane, 2023).

Dental caries is one of the most common non-communicable diseases and, when left untreated, can develop into pulp inflammation and serious infections, affecting the periapical tissues and potentially having systemic repercussions. Studies suggest that chronic inflammation from endodontic infections can interact with other inflammatory diseases, such as osteoporosis, increasing susceptibility to infections and impairing tissue repair (Georgiou et al., 2019; Cintra et al., 2021; Segura-Egea et al., 2023).

There is biological plausibility to the evidence of a relationship between osteoporosis and pulp and periapical pathologies. Both diseases are characterized by the presence of inflammation-induced bone loss. Thus, osteolysis, characteristic of osteoporosis, can be an aggravating systemic factor for pulp and periapical pathologies (López-López et al., 2015). We believe that systemic inflammation associated with osteoporosis can influence the progression of local inflammatory conditions, such as pulp and periapical pathologies. Furthermore, this systemic inflammation may interfere with bone repair after endodontic treatment, impacting on the increased prevalence of periapical pathologies in this population.

Population

Adults and elderly regardless of age, gender, race/color or any other condition

Intervention(s) or exposure(s)

Osteopenia and osteoporosis

Comparator(s) or control(s)

No osteopenia or osteoporosis

Context

The search for studies will be carried out by two independent researchers (APNCS and RCM), following the PEOS search strategy, from July to September 2024. In case of disagreement, a third researcher will be consulted (SFCS). The studies will then be pre-selected by reading the titles and abstracts. The pre-selected studies will be read in full (PDF), applying the inclusion and exclusion criteria. For the selected studies, data extraction will be carried out for a period of three months, followed by qualitative synthesis and meta-analysis. The search will be updated every 12 months until this study is published. The entire process of selecting papers and extracting data will also be carried out in duplicate and blinded (APNCS and RCM). Discrepancies will be resolved in a consensus meeting and, if necessary, with the arbitration of the third evaluator (SFCS).

OUTCOMES TO BE ANALYSED

Main outcomes

The main result will be an analysis of the relationship between osteopenia/osteoporosis and pulpal and periapical pathologies.

Measures of effect

The study characteristics and results will be presented in tables. For the meta-analysis, primary data will be extracted to calculate relative risk, prevalence ratio or odds ratios and corresponding 95% confidence intervals. Whenever available, unadjusted and adjusted measures of association will also be extracted. The adjusted model with the best fit will be selected and the adjustment variables recorded. If the outcomes are presented as numerical variables, the association will be estimated using the mean (or median) of the differences between exposed and non-exposed people. Parametric and/or non-parametric tests may be used. Random-effects meta-analysis according to DerSimonian-Laird will be used if the heterogeneity between the studies is significant (considering $p<0.10$) or the I^2 test is greater than or equal to 50% (Lechner, 2010). Otherwise, a fixed-effect meta-analysis will be used.

We will assess potential publication bias by visually interpreting funnel plots for the primary outcomes when ten or more studies are included in a meta-analysis (Sterne et al., 2007). All analyses will be carried out using Stata (version 14.0) and RevMan (version 5.3).

Additional outcomes

In addition, we will analyze whether the types of osteopenia/osteoporosis (primary and secondary) and the degree of severity of exposure interfere with the outcomes of interest. Finally, we will analyze whether exposure interferes with bone repair of periapical lesions after endodontic treatment.

Measures of effect

The same strategy adopted for the primary outcome will be used for the secondary outcomes.

DATA COLLECTION PROCESS

Data extraction (selection and coding)

Data will be extracted by two independent reviewers (APNCS and RCM) using customized data extraction forms [authors, year of publication, country of study, study design, population, sample size, age range of sample, severity of osteoporosis (normal, osteopenia, osteoporosis and severe osteoporosis), classification of osteopenia/osteoporosis (primary and secondary), type of pulp/periapical pathology (reversible pulpitis, symptomatic irreversible pulpitis, asymptomatic irreversible pulpitis, pulp necrosis, acute apical periodontitis, chronic apical periodontitis, acute apical abscess and chronic apical abscess), unadjusted and adjusted measure of effect (RR, PR, OR or other), 95%CI, variables used to adjust the model,

conclusion]. We will contact the corresponding authors for additional information when necessary. Data extraction will be carried out in duplicate, blinded (APNCS and RCM). Discrepancies will be resolved in a consensus meeting and, if necessary, with the arbitration of the third evaluator (SFCS).

Risk of bias (quality) assessment

Two reviewers (APNCS and RCM) will assess quality independently and disagreements will be resolved in a consensus meeting and, if necessary, with the arbitration of the third reviewer (SFCS). The included studies will be assessed according to their design, using the Joanna Briggs Institute (JBI) tool.

PLANNED DATA SYNTHESIS

Strategy for data synthesis

We will carry out a narrative/descriptive synthesis of the data from each included study (systematic review). In the presence of two or more studies with the same research question, a quantitative synthesis will be included (meta-analysis).

Analysis of subgroups or subsets

Different sensitivity analyses will be carried out considering: different classifications of pulp and periapical pathologies; crude and adjusted associations; and risk of bias.
Whenever possible, we will carry out meta-analyses with subgroup analyses according to the study design; the degree of severity of osteoporosis; and the type of osteopenia/osteoporosis (primary or secondary).

REVIEW AFFILIATION, FUNDING AND PEER REVIEW

Review team members

- Professor Soraia de Fátima Carvalho Souza , Federal University of Maranhão
- Ana Paula Nóbrega Caetano da Silva, Federal University of Maranhão
- Rodrigo Costa Mendes, Federal University of Maranhão
- Randerson Silva Araújo, Federal University of Maranhão
- Professor Erika Bárbara Abreu Fonseca Thomaz, Federal University of Maranhão

Review affiliation

Federal University of Maranhão

Funding source

CAPES (Coordenação de Aperfeiçoamento de Pessoal de Nível Superior), FAPEMA (Fundação de Amparo à Pesquisa e ao Desenvolvimento Científico e Tecnológico do Maranhão) e CNPq (Conselho Nacional de Desenvolvimento Científico e Tecnológico).

Named contact

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endosoraia@gmail.com

TIMELINE OF THE REVIEW

Review timeline

Start date: 17 July 2024. End date: 17 July 2025

Date of first submission to PROSPERO

20 June 2024

Date of registration in PROSPERO
05 July 2024

CURRENT REVIEW STAGE

Publication of review results
The intention is to publish the review once completed.The review will be published in English

Stage of the review at this submission

Review stage	Started	Completed
Pilot work		
Formal searching/study identification		
Screening search results against inclusion criteria		
Data extraction or receipt of IP		
Risk of bias/quality assessment		
Data synthesis		

Review status
The review is currently planned or ongoing.

ADDITIONAL INFORMATION

PROSPERO version history

- Version 1.1 published on 05 Jul 2024
- Version 1.0 published on 05 Jul 2024

Review conflict of interest
None known

Country
Brazil

Medical Subject Headings
Bone Diseases, Metabolic; Humans; Osteoporosis; Prevalence

Disclaimer
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Any enquiries about the record should be referred to the named review contact

APÊNDICE B

Capítulo III

(Capítulo III): Tabela Suplementar 1. Lista de verificação PRISMA para o resumo.

Section and Topic	Item #	Checklist item	Reported (Yes/No)
TITLE			
Title	1	Identify the report as a systematic review.	YES
BACKGROUND			
Objectives	2	Provide an explicit statement of the main objective(s) or question(s) the review addresses.	YES
METHODS			
Eligibility criteria	3	Specify the inclusion and exclusion criteria for the review.	YES
Information sources	4	Specify the information sources (e.g. databases, registers) used to identify studies and the date when each was last searched.	YES
Risk of bias	5	Specify the methods used to assess risk of bias in the included studies.	YES
Synthesis of results	6	Specify the methods used to present and synthesise results.	YES
RESULTS			
Included studies	7	Give the total number of included studies and participants and summarise relevant characteristics of studies.	YES
Synthesis of results	8	Present results for main outcomes, preferably indicating the number of included studies and participants for each. If meta-analysis was done, report the summary estimate and confidence/credible interval. If comparing groups, indicate the direction of the effect (i.e. which group is favoured).	YES
DISCUSSION			
Limitations of evidence	9	Provide a brief summary of the limitations of the evidence included in the review (e.g. study risk of bias, inconsistency and imprecision).	N/A
Interpretation	10	Provide a general interpretation of the results and important implications.	N/A
OTHER			
Funding	11	Specify the primary source of funding for the review.	N/A

Section and Topic	Item #	Checklist item	Reported (Yes/No)
Registration	12	Provide the register name and registration number.	N/A

Not applicable: N/A

(Capítulo III): Tabela Suplementar 2. Lista de verificação PRISMA para o texto completo.

	Item #	Checklist item	Location where item is reported
TITLE			
Title	1	Identify the report as a systematic review.	Page 1
ABSTRACT			
Abstract	2	See the PRISMA 2020 for Abstracts checklist.	Page 2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of existing knowledge.	Pages 3 and 4
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	Page 4
METHODS			
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	Page 5
Information sources	6	Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted.	Pages 6 and 7 Supplemental Table 3
Search strategy	7	Present the full search strategies for all databases, registers and websites, including any filters and limits used.	Supplemental Table 3
Selection process	8	Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process.	Page 7
Data collection process	9	Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process.	Page 7
Data items	10a	List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect.	Page 8
	10b	List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information.	Page 8
Study risk of bias assessment	11	Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process.	Page 8
Effect measures	12	Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results.	Pages 8 and 9
Synthesis methods	13a	Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item #5)).	Pages 8 and 9
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary	Pages 8 and 9

	Item #	Checklist item	Location where item is reported
		statistics, or data conversions.	
	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	Pages 8 and 9
	13d	Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used.	Pages 8 and 9
	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression).	Pages 8 and 9
	13f	Describe any sensitivity analyses conducted to assess robustness of the synthesized results.	Pages 8 and 9
Reporting bias assessment	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).	Page 9
Certainty assessment	15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.	Page 9
RESULTS			
Study selection	16a	Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram.	Page 9 Figure 1
	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.	Figure 1
Study characteristics	17	Cite each included study and present its characteristics.	Table 1
Risk of bias in studies	18	Present assessments of risk of bias for each included study.	Pages 9 e 10 Figure 2
Results of individual studies	19	For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (e.g. confidence/credible interval), ideally using structured tables or plots.	Table 1
Results of syntheses	20a	For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies.	Table 1 Figure 2
	20b	Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect.	Page 10 Figures 3 and 4
	20c	Present results of all investigations of possible causes of heterogeneity among study results.	Page 10 Figures 3 and 4
	20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results.	Page 10 Figure 4a Supplemental Figure 2
Reporting biases	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.	Pages 10 e 11

	Item #	Checklist item	Location where item is reported
			Supplemental Figure 1
Certainty of evidence	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.	Page 11 Table 2 Supplemental Table 4
DISCUSSION			
Discussion	23a	Provide a general interpretation of the results in the context of other evidence.	Pages 11 to 14
	23b	Discuss any limitations of the evidence included in the review.	Pages 15 to 16
	23c	Discuss any limitations of the review processes used.	Pages 15 to 16
	23d	Discuss implications of the results for practice, policy, and future research.	Page 16
OTHER INFORMATION			
Registration and protocol	24a	Provide registration information for the review, including register name and registration number, or state that the review was not registered.	Pages 4 and 5
	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.	Pages 4 and 5
	24c	Describe and explain any amendments to information provided at registration or in the protocol.	N/A
Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review.	ACKNOWLEDGEMENTS
Competing interests	26	Declare any competing interests of review authors.	ACKNOWLEDGEMENTS
Availability of data, code and other materials	27	Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review.	N/A

Not applicable: N/A

(Capítulo III): Tabela Suplementar 3. Descrição das estratégias de busca realizadas nas bases de dados PubMed, SciELO, Google Acadêmico, Biblioteca Virtual em Saúde (BVS), Embase, Scopus, Web of Science, Cochrane, Biblioteca Digital Brasileira de Teses e Dissertações (BDTD) e Catálogo de Teses e Dissertações da CAPES.

DATABASE	SEARCH EQUATION	DATE
Pubmed	((" Autoimmune Diseases"[Title/Abstract]) OR ("Disease, Autoimmune"[Title/Abstract])) OR ("Diseases, Autoimmune"[Title/Abstract])) OR ("Autoimmune Disease"[Title/Abstract])) OR ("Rheumatic Diseases"[Title/Abstract])) OR ("Disease, Rheumatic"[Title/Abstract])) OR ("Diseases, Rheumatic"[Title/Abstract])) OR ("Rheumatic Disease"[Title/Abstract])) OR (Rheumatism[Title/Abstract])) OR ("Arthritis, Rheumatoid"[Title/Abstract])) OR ("Rheumatoid Arthritis"[Title/Abstract])) OR ("Lupus Erythematosus, Systemic"[Title/Abstract])) OR ("Lupus Erythematosus Disseminatus"[Title/Abstract])) OR ("Systemic Lupus Erythematosus"[Title/Abstract])) OR ("Libman-Sacks Disease"[Title/Abstract])) OR ("Disease, Libman-Sacks"[Title/Abstract])) OR ("Libman Sacks Disease"[Title/Abstract])) OR ("Spondylitis, Ankylosing"[Title/Abstract])) OR ("Bechterew's Disease"[Title/Abstract])) OR ("Bechterews Disease"[Title/Abstract])) OR ("Marie-Struempell Disease"[Title/Abstract])) OR ("Marie Struempell Disease"[Title/Abstract])) OR ("Spondylarthritis Ankylopoietica"[Title/Abstract])) OR ("Rheumatoid Spondylitis"[Title/Abstract])) OR ("Spondylitis, Rheumatoid"[Title/Abstract])) OR ("Ankylosing Spondylitis"[Title/Abstract])) OR ("Ankylosing Spondylarthritis"[Title/Abstract])) OR ("Ankylosing Spondylarthritides"[Title/Abstract])) OR ("Spondylarthritides, Ankylosing"[Title/Abstract])) OR ("Spondylarthritis, Ankylosing"[Title/Abstract])) OR ("Ankylosing Spondyloarthritis"[Title/Abstract])) OR ("Ankylosing Spondyloarthritides"[Title/Abstract])) OR ("Spondyloarthritides, Ankylosing"[Title/Abstract])) OR ("Spondyloarthritis, Ankylosing"[Title/Abstract])) OR ("Spondylitis Ankylopoietica"[Title/Abstract])) OR ("Bechterew Disease"[Title/Abstract])) OR ("Spondyloarthritis Ankylopoietica"[Title/Abstract])) OR ("Arthritis, Psoriatic"[Title/Abstract])) OR ("Psoriasis Arthropathica"[Title/Abstract])) OR ("Psoriasis, Arthritic"[Title/Abstract])) OR ("Arthritic Psoriasis"[Title/Abstract])) OR ("Psoriatic Arthropathy"[Title/Abstract])) OR ("Arthropathies, Psoriatic"[Title/Abstract])) OR ("Arthropathy, Psoriatic"[Title/Abstract])) OR ("Psoriatic Arthropathies"[Title/Abstract])) OR ("Psoriatic Arthritis"[Title/Abstract])) OR ("Arthritis, Juvenile"[Title/Abstract])) OR ("Juvenile Arthritis"[Title/Abstract])) OR ("Juvenile Idiopathic Arthritis"[Title/Abstract])) OR ("Idiopathic Arthritis, Juvenile"[Title/Abstract])) OR ("Arthritis, Juvenile Idiopathic"[Title/Abstract])) OR ("Juvenile Chronic Arthritis"[Title/Abstract])) OR ("Chronic Arthritis, Juvenile"[Title/Abstract])) OR ("Juvenile Rheumatoid Arthritis"[Title/Abstract])) OR ("Childhood Arthritis"[Title/Abstract])) OR ("Arthritides, Childhood"[Title/Abstract])) OR ("Arthritis, Childhood"[Title/Abstract])) OR ("Childhood Arthritides"[Title/Abstract])) OR ("Arthritis, Juvenile Rheumatoid"[Title/Abstract])) OR ("Rheumatoid Arthritis, Juvenile"[Title/Abstract])) OR ("Arthritis, Juvenile Chronic"[Title/Abstract])) OR ("Juvenile-Onset Still Disease"[Title/Abstract])) OR ("Juvenile Onset Still Disease"[Title/Abstract])) OR ("Juvenile-Onset Stills Disease"[Title/Abstract])) OR ("Juvenile Onset Stills Disease"[Title/Abstract])) OR ("Stills Disease, Juvenile-Onset"[Title/Abstract])) OR ("Still's Disease, Juvenile-Onset"[Title/Abstract])) OR ("Juvenile-Onset Still's Disease"[Title/Abstract])) OR ("Still's Disease, Juvenile Onset"[Title/Abstract])) OR ("Still Disease, Juvenile-Onset"[Title/Abstract])) OR ("Still Disease, Juvenile Onset"[Title/Abstract])) OR ("Systemic Arthritis, Juvenile"[Title/Abstract])) OR ("Arthritis, Juvenile Systemic"[Title/Abstract])) OR ("Juvenile Systemic Arthritis"[Title/Abstract])) OR ("Oligoarthritis, Juvenile"[Title/Abstract])) OR ("Juvenile Oligoarthritis"[Title/Abstract])) OR ("Enthesitis-Related Arthritis, Juvenile"[Title/Abstract])) OR ("Arthritis, Juvenile Enthesitis-Related"[Title/Abstract])) OR ("Enthesitis Related Arthritis, Juvenile"[Title/Abstract])) OR ("Juvenile Enthesitis-Related Arthritis"[Title/Abstract])) OR ("Psoriatic Arthritis, Juvenile"[Title/Abstract])) OR ("Arthritis, Juvenile Psoriatic"[Title/Abstract])) OR ("Juvenile Psoriatic Arthritis"[Title/Abstract])) OR ("Polyarthritis, Juvenile, Rheumatoid Factor Negative"[Title/Abstract])) OR ("Polyarthritis, Juvenile, Rheumatoid Factor Positive"[Title/Abstract])) OR ("Polyarticular Juvenile Idiopathic Arthritis"[Title/Abstract])) OR (PCJIA[Title/Abstract])) OR ("PJIA Polyarticular Juvenile	05/2025

Idiopathic Arthritis"[Title/Abstract])) OR ("Polyarticular-Course Juvenile Idiopathic Arthritis"[Title/Abstract])) OR ("Mixed Connective Tissue Disease"[Title/Abstract])) OR (MCTD[Title/Abstract])) OR ("Connective Tissue Disease, Mixed"[Title/Abstract])) OR ("Sharp Syndrome"[Title/Abstract])) OR ("Syndrome, Sharp"[Title/Abstract])) OR ("Polymyalgia Rheumatica"[Title/Abstract])) OR ("Forestier-Certonciny Syndrome"[Title/Abstract])) OR ("Forestier Certonciny Syndrome"[Title/Abstract])) OR ("Syndrome, Forestier-Certonciny"[Title/Abstract])) OR ("Rheumatism, Peri-Extra-Articular"[Title/Abstract])) OR ("Peri-Extra-Articular Rheumatism"[Title/Abstract])) OR ("Rheumatism, Peri Extra Articular"[Title/Abstract])) OR ("Pseudopolyarthritis, Rhizomelic"[Title/Abstract])) OR ("Pseudopolyarthritides, Rhizomelic"[Title/Abstract])) OR ("Rhizomelic Pseudopolyarthritides"[Title/Abstract])) OR ("Rhizomelic Pseudopolyarthritis"[Title/Abstract])) OR ("Scleroderma, Systemic"[Title/Abstract])) OR ("Sclerosis, Systemic"[Title/Abstract])) OR ("Systemic Scleroderma"[Title/Abstract])) OR ("Systemic Sclerosis"[Title/Abstract])) OR ("Sjogren's Syndrome"[Title/Abstract])) OR ("Sjogrens Syndrome"[Title/Abstract])) OR ("Syndrome, Sjogren's"[Title/Abstract])) OR ("Sjogren Syndrome"[Title/Abstract])) OR ("Sicca Syndrome"[Title/Abstract])) OR ("Syndrome, Sicca"[Title/Abstract])) AND ((("Dental Pulp"[Title/Abstract]) OR ("Dental Pulps"[Title/Abstract])) OR ("Pulp, Dental"[Title/Abstract])) OR ("Pulps, Dental"[Title/Abstract])) OR ("Dental Pulp Diseases"[Title/Abstract])) OR ("Dental Pulp Disease"[Title/Abstract])) OR ("Disease, Dental Pulp"[Title/Abstract])) OR ("Diseases, Dental Pulp"[Title/Abstract])) OR ("Pulp Disease, Dental"[Title/Abstract])) OR ("Pulp Diseases, Dental"[Title/Abstract])) OR ("Dental Pulp Necrosis"[Title/Abstract])) OR ("Dental Pulp Necroses"[Title/Abstract])) OR ("Necroses, Dental Pulp"[Title/Abstract])) OR ("Pulp Necroses, Dental"[Title/Abstract])) OR ("Necroses, Pulp"[Title/Abstract])) OR ("Necrosis, Dental Pulp"[Title/Abstract])) OR ("Pulp Necroses"[Title/Abstract])) OR ("Pulp Necrosis"[Title/Abstract])) OR ("Necrosis, Pulp"[Title/Abstract])) OR ("Pulp Necrosis, Dental"[Title/Abstract])) OR ("Dental Pulp Autolysis"[Title/Abstract])) OR ("Autolyses, Dental Pulp"[Title/Abstract])) OR ("Dental Pulp Autolyses"[Title/Abstract])) OR ("Pulp Autolyses, Dental"[Title/Abstract])) OR ("Autolysis, Dental Pulp"[Title/Abstract])) OR ("Pulp Autolysis, Dental"[Title/Abstract])) OR ("Gangrene, Dental Pulp"[Title/Abstract])) OR ("Dental Pulp Gangrene"[Title/Abstract])) OR ("Pulp Gangrene"[Title/Abstract])) OR ("Gangrene, Pulp"[Title/Abstract])) OR ("Gangrenes, Pulp"[Title/Abstract])) OR ("Pulp Gangrenes"[Title/Abstract])) OR ("Pulp Gangrene, Dental"[Title/Abstract])) OR ("Pulp Mummification"[Title/Abstract])) OR ("Mummification, Pulp"[Title/Abstract])) OR ("Mummifications, Pulp"[Title/Abstract])) OR ("Pulp Mummifications"[Title/Abstract])) OR (Pulpitis[Title/Abstract])) OR (Pulpitides[Title/Abstract])) OR ("Inflammation, Endodontic"[Title/Abstract])) OR ("Endodontic Inflammation"[Title/Abstract])) OR ("Endodontic Inflammations"[Title/Abstract])) OR ("Inflammations, Endodontic"[Title/Abstract])) OR ("Periapical Diseases"[Title/Abstract])) OR ("Disease, Periapical"[Title/Abstract])) OR ("Diseases, Periapical"[Title/Abstract])) OR ("Periapical Disease"[Title/Abstract])) OR ("Periapical Periodontitis"[Title/Abstract])) OR ("Periapical Periodontitides"[Title/Abstract])) OR ("Periodontitides, Periapical"[Title/Abstract])) OR ("Periodontitis, Periapical"[Title/Abstract])) OR ("Periodontitis, Apical"[Title/Abstract])) OR ("Apical Periodontitides"[Title/Abstract])) OR ("Apical Periodontitis"[Title/Abstract])) OR ("Periodontitides, Apical"[Title/Abstract])) OR ("Periodontitis, Acute Nonsuppurative"[Title/Abstract])) OR ("Acute Nonsuppurative Periodontitides"[Title/Abstract])) OR ("Acute Nonsuppurative Periodontitis"[Title/Abstract])) OR ("Nonsuppurative Periodontitides, Acute"[Title/Abstract])) OR ("Nonsuppurative Periodontitis, Acute"[Title/Abstract])) OR ("Periodontitides, Acute Nonsuppurative"[Title/Abstract])) OR ("Periapical Abscess"[Title/Abstract])) OR ("Alveolar Abscess, Apical"[Title/Abstract])) OR ("Abscess, Apical Alveolar"[Title/Abstract])) OR ("Abscesses, Apical Alveolar"[Title/Abstract])) OR ("Alveolar Abscesses, Apical"[Title/Abstract])) OR ("Apical Alveolar Abscess"[Title/Abstract])) OR ("Apical Alveolar Abscesses"[Title/Abstract])) OR ("Dentoalveolar Abscess, Apical"[Title/Abstract])) OR ("Abscess, Apical Dentoalveolar"[Title/Abstract])) OR ("Abscesses, Apical Dentoalveolar"[Title/Abstract])) OR ("Apical Dentoalveolar Abscess"[Title/Abstract])) OR ("Apical Dentoalveolar Abscesses"[Title/Abstract])) OR ("Dentoalveolar Abscesses, Apical"[Title/Abstract])) OR ("Abscess, Periapical"[Title/Abstract])) OR ("Abscesses, Periapical"[Title/Abstract])) OR ("Periapical Abscesses"[Title/Abstract])) OR ("Periapical Periodontitis, Suppurative"[Title/Abstract])) OR ("Periapical Periodontitides, Suppurative"[Title/Abstract])) OR ("Periodontitides, Suppurative Periapical"[Title/Abstract])) OR ("Periodontitis, Suppurative Periapical"[Title/Abstract])) OR ("Suppurative Periapical Periodontitides"[Title/Abstract])) OR ("Suppurative Periapical Periodontitis"[Title/Abstract])) OR ("Periodontitis, Apical, Suppurative"[Title/Abstract])) OR ("Periapical Granuloma"[Title/Abstract])) OR ("Granuloma, Periapical"[Title/Abstract])) OR ("Granulomas, Periapical"[Title/Abstract])) OR ("Periapical

	Granulomas"[Title/Abstract])) OR ("Periapical Periodontitis, Chronic Nonsuppurative"[Title/Abstract])) OR ("Periodontitis, Apical, Chronic Nonsuppurative"[Title/Abstract])) OR ("Dental Granulomas"[Title/Abstract])) OR ("Granuloma, Dental"[Title/Abstract])) OR ("Granulomas, Dental"[Title/Abstract])) OR ("Dental Granuloma"[Title/Abstract])) OR ("Tooth, Nonvital"[Title/Abstract])) OR ("Nonvital Tooth"[Title/Abstract])) OR ("Teeth, Devitalized"[Title/Abstract])) OR ("Devitalized Teeth"[Title/Abstract])) OR ("Tooth, Devitalized"[Title/Abstract])) OR ("Devitalized Tooth"[Title/Abstract])) OR ("Teeth, Nonvital"[Title/Abstract])) OR ("Nonvital Teeth"[Title/Abstract])) OR ("Teeth, Pulpless"[Title/Abstract])) OR ("Pulpless Teeth"[Title/Abstract])) OR ("Tooth, Pulpless"[Title/Abstract])) OR ("Pulpless Tooth"[Title/Abstract])) OR ("Teeth, Endodontically-Treated"[Title/Abstract])) OR ("Endodontically-Treated Teeth"[Title/Abstract])) OR ("Teeth, Endodontically Treated"[Title/Abstract])) OR ("Tooth, Endodontically-Treated"[Title/Abstract])) OR ("Endodontically-Treated Tooth"[Title/Abstract])) OR ("Tooth, Endodontically Treated"[Title/Abstract])) OR ("Dental Pulp Devitalization"[Title/Abstract])) OR ("Devitalization, Dental Pulp"[Title/Abstract])) OR ("Pulp Devitalization, Dental"[Title/Abstract])) OR ("Periapical Tissue"[Title/Abstract])) OR ("Periapical Tissues"[Title/Abstract])) OR ("Tissue, Periapical"[Title/Abstract])) OR ("Tissues, Periapical"[Title/Abstract])) OR ("Periodontium, Apical"[Title/Abstract])) OR ("Apical Periodontium"[Title/Abstract])) OR ("Apical Periodontiums"[Title/Abstract])) OR ("Periodontiums, Apical"[Title/Abstract])) OR ("Radicular Cyst"[Title/Abstract])) OR ("Cyst, Radicular"[Title/Abstract])) OR ("Cysts, Radicular"[Title/Abstract])) OR ("Radicular Cysts"[Title/Abstract])) OR ("Periapical Cyst"[Title/Abstract])) OR ("Cyst, Periapical"[Title/Abstract])) OR ("Cysts, Periapical"[Title/Abstract])) OR ("Periapical Cysts"[Title/Abstract])) OR ("Periodontal Cyst, Apical"[Title/Abstract])) OR ("Apical Periodontal Cyst"[Title/Abstract])) OR ("Apical Periodontal Cysts"[Title/Abstract])) OR ("Cyst, Apical Periodontal"[Title/Abstract])) OR ("Cysts, Apical Periodontal"[Title/Abstract])) OR ("Periodontal Cysts, Apical"[Title/Abstract])) OR ("Root Canal Therapy"[Title/Abstract])) OR ("Canal Therapies, Root"[Title/Abstract])) OR ("Canal Therapy, Root"[Title/Abstract])) OR ("Root Canal Therapies"[Title/Abstract])) OR ("Therapies, Root Canal"[Title/Abstract])) OR ("Therapy, Root Canal"[Title/Abstract])) OR ("Root Canal Obturation"[Title/Abstract])) OR ("Canal Obturation, Root"[Title/Abstract])) OR ("Canal Obturations, Root"[Title/Abstract])) OR ("Obturation, Root Canal"[Title/Abstract])) OR ("Obturations, Root Canal"[Title/Abstract])) OR ("Root Canal Obturations"[Title/Abstract])) OR ("Endodontic Obturation"[Title/Abstract])) OR ("Endodontic Obturations"[Title/Abstract])) OR ("Obturation, Endodontic"[Title/Abstract])) OR ("Obturations, Endodontic"[Title/Abstract]))) NOT (animal[Title/Abstract])	
SciELO	((“Dental Pulp”) OR (“Pulpa Dental”) OR (“Polpa Dentária”) OR (“Dental Pulp Diseases”) OR (“Enfermedades de la Pulpa Dental”) OR (“Doenças da Polpa Dentária”) OR (“Dental Pulp Necrosis”) OR (“Necrose da Polpa Dentária”) OR (“Necrosis de la Pulpa Dental”) OR (Pulpitis) OR (Pulpite) OR (Pulpitis) OR (“Periapical Diseases”) OR (“Doenças Periapicais”) OR (“Enfermedades Periapicales”) OR (“Periapical Periodontitis”) OR (“Periodontite Periapical”) OR (“Periodontitis Periapical”) OR (“Periapical Abscess”) OR (“Abscesso Periapical”) OR (“Absceso Periapical”) OR (“Periapical Granuloma”) OR (“Granuloma Periapical”) OR (“Granuloma Periapical”) OR (“Tooth, Nonvital”) OR (“Dente não Vital”) OR (“Diente no Vital”) OR (“Dental Pulp Devitalization”) OR (“Desvitalização da Polpa Dentária”) OR (“Desvitalización de la Pulpa Dental”) OR (“Periapical Tissue”) OR (“Tecido Periapical”) OR (“Tejido Periapical”) OR (“Radicular Cyst”) OR (“Cisto Radicular”) OR (“Quiste Radicular”) OR (“Root Canal Therapy”) OR (“Tratamento do Canal Radicular”) OR (“Tratamiento del Conducto Radicular”) OR (“Root Canal Obturation”) OR (“Obturação do Canal Radicular”) OR (“Obturación del Conducto Radicular”)) OR ((“Autoimmune Diseases”) OR (“Doenças Autoimunes”) OR (“Enfermedades Autoinmunes”) OR (“Rheumatic Diseases”) OR (“Doenças Reumáticas”) OR (“Enfermedades Reumáticas”) OR (“Arthritis, Rheumatoid”) OR (“Artrite Reumatoide”) OR (“Artritis Reumatoide”) OR (“Lupus Erythematosus, Systemic”) OR (“Lúpus Eritematoso Sistêmico”) OR (“Lupus Eritematoso Sistémico”) OR (“Spondylitis, Ankylosing”) OR (“Espondilite Anquilosante”) OR (“Espondilitis Anquilosante”) OR (“Arthritis, Psoriatic”) OR (“Artrite Psoriásica”) OR (“Artritis Psoriásica”) OR (“Arthritis, Juvenile”) OR (“Artrite Juvenil”) OR (“Artritis Juvenil”) OR (“Mixed Connective Tissue Disease”) OR (“Doença Mista do Tecido Conjuntivo”) OR (“Enfermedad Mixta del Tejido Conjuntivo”) OR (“Polymyalgia Rheumatica”) OR (“Polimialgia Reumática”) OR (“Polimialgia Reumática”) OR (“Scleroderma, Systemic”) OR (“Escleroderma Sistêmico”) OR (“Esclerodermia Sistémica”) OR (“Sjogren's Syndrome”) OR (“Síndrome de Sjogren”) OR (“Síndrome de Sjögren”))	05/2025

Google Scholar	Pulpitis Periodontitis Periapical Autoimmune Rheumatic	05/2025
BVS/Bireme	(((“Autoimmune Diseases”) OR (“Rheumatic Diseases”) OR (“Arthritis, Rheumatoid”) OR (“Lupus Erythematosus, Systemic”) OR (“Spondylitis, Ankylosing”) OR (“Arthritis, Psoriatic”) OR (“Arthritis, Juvenile”) OR (“Mixed Connective Tissue Disease”) OR (“Polymyalgia Rheumatica”) OR (“Scleroderma, Systemic”) OR (“Sjogren's Syndrome”)) AND ((“Dental Pulp”) OR (“Dental Pulps”) OR (“Pulp, Dental”) OR (“Pulps, Dental”) OR (“Dental Pulp Diseases”) OR (“Dental Pulp Disease”) OR (“Disease, Dental Pulp”) OR (“Diseases, Dental Pulp”) OR (“Pulp Disease, Dental”) OR (“Pulp Diseases, Dental”) OR (“Dental Pulp Necrosis”) OR (“Dental Pulp Necroses”) OR (“Necroses, Dental Pulp”) OR (“Pulp Necroses, Dental”) OR (“Necroses, Pulp”) OR (“Necrosis, Dental Pulp”) OR (“Pulp Necroses”) OR (“Pulp Necrosis”) OR (“Necrosis, Pulp”) OR (“Pulp Necrosis, Dental”) OR (“Dental Pulp Autolysis”) OR (“Autolyses, Dental Pulp”) OR (“Dental Pulp Autolyses”) OR (“Pulp Autolyses, Dental”) OR (“Autolysis, Dental Pulp”) OR (“Pulp Autolysis, Dental”) OR (“Gangrene, Dental Pulp”) OR (“Dental Pulp Gangrene”) OR (“Pulp Gangrene”) OR (“Gangrene, Pulp”) OR (“Gangrenes, Pulp”) OR (“Pulp Gangrenes”) OR (“Pulp Gangrene, Dental”) OR (“Pulp Mummification”) OR (“Mummification, Pulp”) OR (“Mummifications, Pulp”) OR (“Pulp Mummifications”) OR (Pulpitis) OR (Pulpitides) OR (“Inflammation, Endodontic”) OR (“Endodontic Inflammation”) OR (“Endodontic Inflammations”) OR (“Inflammations, Endodontic”) OR (“Periapical Diseases”) OR (“Disease, Periapical”) OR (“Diseases, Periapical”) OR (“Periapical Disease”) OR (“Periapical Periodontitis”) OR (“Periapical Periodontitides”) OR (“Periodontitides, Periapical”) OR (“Periodontitis, Periapical”) OR (“Periodontitis, Apical”) OR (“Apical Periodontitides”) OR (“Apical Periodontitis”) OR (“Periodontitides, Apical”) OR (“Periodontitis, Acute Nonsuppurative”) OR (“Acute Nonsuppurative Periodontitides”) OR (“Acute Nonsuppurative Periodontitis”) OR (“Nonsuppurative Periodontitides, Acute”) OR (“Nonsuppurative Periodontitis, Acute”) OR (“Periodontitides, Acute Nonsuppurative”) OR (“Periapical Abscess”) OR (“Alveolar Abscess, Apical”) OR (“Abscess, Apical Alveolar”) OR (“Abscesses, Apical Alveolar”) OR (“Alveolar Abscesses, Apical”) OR (“Apical Alveolar Abscess”) OR (“Apical Alveolar Abscesses”) OR (“Dentoalveolar Abscess, Apical”) OR (“Abscess, Apical Dentoalveolar”) OR (“Abscesses, Apical Dentoalveolar”) OR (“Apical Dentoalveolar Abscess”) OR (“Apical Dentoalveolar Abscesses”) OR (“Dentoalveolar Abscesses, Apical”) OR (“Abscess, Periapical”) OR (“Abscesses, Periapical”) OR (“Periapical Abscesses”) OR (“Periapical Periodontitis, Suppurative”) OR (“Periapical Periodontitides, Suppurative”) OR (“Periodontitides, Suppurative Periapical”) OR (“Periodontitis, Suppurative Periapical”) OR (“Suppurative Periapical Periodontitides”) OR (“Suppurative Periapical Periodontitis”) OR (“Periodontitis, Apical, Suppurative”) OR (“Periapical Granuloma”) OR (“Granuloma, Periapical”) OR (“Granulomas, Periapical”) OR (“Periapical Granulomas”) OR (“Periapical Periodontitis, Chronic Nonsuppurative”) OR (“Periodontitis, Apical, Chronic Nonsuppurative”) OR (“Dental Granulomas”) OR (“Granuloma, Dental”) OR (“Granulomas, Dental”) OR (“Dental Granuloma”) OR (“Tooth, Nonvital”) OR (“Nonvital Tooth”) OR (“Teeth, Devitalized”) OR (“Devitalized Teeth”) OR (“Tooth, Devitalized”) OR (“Devitalized Tooth”) OR (“Teeth, Nonvital”) OR (“Nonvital Teeth”) OR (“Teeth, Pulpless”) OR (“Pulpless Teeth”) OR (“Tooth, Pulpless”) OR (“Pulpless Tooth”) OR (“Teeth, Endodontically-Treated”) OR (“Endodontically-Treated Teeth”) OR (“Teeth, Endodontically Treated”) OR (“Tooth, Endodontically-Treated”) OR (“Endodontically-Treated Tooth”) OR (“Tooth, Endodontically Treated”) OR (“Dental Pulp Devitalization”) OR (“Devitalization, Dental Pulp”) OR (“Pulp Devitalization, Dental”) OR (“Periapical Tissue”) OR (“Periapical Tissues”) OR (“Tissue, Periapical”) OR (“Tissues, Periapical”) OR (“Periodontium, Apical”) OR (“Apical Periodontium”) OR (“Apical Periodontiums”) OR (“Periodontiums, Apical”) OR (“Radicular Cyst”) OR (“Cyst, Radicular”) OR (“Cysts, Radicular”) OR (“Radicular Cysts”) OR (“Periapical Cyst”) OR (“Cyst, Periapical”) OR (“Cysts, Periapical”) OR (“Periapical Cysts”) OR (“Periodontal Cyst, Apical”) OR (“Apical Periodontal Cyst”) OR (“Apical Periodontal Cysts”) OR (“Cyst, Apical Periodontal”) OR (“Cysts, Apical Periodontal”) OR (“Periodontal Cysts, Apical”) OR (“Root Canal Therapy”) OR (“Canal Therapies, Root”) OR (“Canal Therapy, Root”) OR (“Root Canal Therapies”) OR (“Therapies, Root Canal”) OR (“Therapy, Root Canal”) OR (“Root Canal Obturation”) OR (“Canal Obturation, Root”) OR (“Canal Obturations, Root”) OR (“Obturation, Root Canal”) OR (“Obturations, Root Canal”) OR (“Root Canal Obturations”) OR (“Endodontic Obturation”) OR (“Endodontic Obturations”) OR (“Obturation, Endodontic”) OR (“Obturations, Endodontic”)))	05/2025
Embase	('autoimmune disease'/exp OR 'auto immune disease' OR 'auto immunologic disease' OR 'auto-immune disorder' OR 'auto-immune disorders' OR 'autoaggression, immune' OR 'autoaggressive disease' OR 'autoantibody disease' OR 'autoimmune disease' OR 'autoimmune diseases' OR 'autoimmune disorder' OR 'autoimmune disorders' OR 'autoimmune disturbance' OR 'autoimmune pathology' OR 'autoimmuno disease' OR 'autoimmunologic disease' OR 'rheumatic disease'/exp	05/2025

OR 'chronic rheumatic disease' OR 'chronic rheumatism' OR 'rheumatic disease' OR 'rheumatic diseases' OR 'rheumatic syndrome' OR 'rheumatism' OR 'rheumatoid disease' OR 'rheumatoid inflammation' OR 'rheumatoid syndrome' OR 'rheumatoid arthritis'/exp OR 'beauvais disease' OR 'arthritis deformans' OR 'arthritis, rheumatoid' OR 'arthrosis deformans' OR 'chronic articular rheumatism' OR 'chronic polyarthritis' OR 'chronic rheumatoid arthritis' OR 'disease, beauvais' OR 'infantile rheumatoid arthritis' OR 'inflammatory arthritis' OR 'polyarthritis rheumatica' OR 'polyarthritis, primary chronic' OR 'primary chronic polyarthritis' OR 'rheumarthritis' OR 'rheumatic arthritis' OR 'rheumatic polyarthritis' OR 'rheumatism, chronic articular' OR 'rheumatoid arthritis' OR 'rheumatoid polyarthritis' OR 'systemic lupus erythematosus'/exp OR 'osler libman sacks disease' OR 's.l.e.' OR 'sle' OR 'dermatovisceritism, malignant' OR 'disseminated lupus' OR 'disseminated lupus erythematodes' OR 'disseminated lupus erythematosis' OR 'disseminated lupus erythematosus' OR 'erythematodes visceralis' OR 'lupovisceritis' OR 'lupus erythematodes disseminatus' OR 'lupus erythematosus disseminatus' OR 'lupus erythematosus visceralis' OR 'lupus erythematosus, systemic' OR 'systemic le' OR 'systemic lupus' OR 'systemic lupus erythematodes' OR 'systemic lupus erythematosis' OR 'systemic lupus erythematosus' OR 'systemic lupus erythematous' OR 'lupus erythematosus'/exp OR 'chronic lupus erythematosus' OR 'lupus (erythematosis)' OR 'lupus erythematodes' OR 'lupus erythematosis' OR 'lupus erythematosus' OR 'lupus erythematosus treatment' OR 'lupus syndrome' OR 'ankylosing spondylitis'/exp OR 'bechterew disease' OR 'ankylating spondylitis' OR 'ankylopoietic spondylarthritis' OR 'ankylopoietic spondylitis' OR 'ankylosing spine' OR 'ankylosing spondilitis' OR 'ankylosing spondylarthritis' OR 'ankylosing spondylarthrosis' OR 'ankylosing spondylitis' OR 'ankylosis spondylitis' OR 'ankylotic spondylitis' OR 'bekhterev disease' OR 'morbus bechterew' OR 'spinal ankylosis' OR 'spine ankylosis' OR 'spondylarthritis ankylopoietica' OR 'spondylarthritis ankylosans' OR 'spondylarthrosis ankylopoietica' OR 'spondylitis ankylopoetica' OR 'spondylitis ankylopoietica' OR 'spondylitis, ankylosing' OR 'spondyloarthritis ankylopoietica' OR 'vertebral ankylosis' OR 'psoriatic arthritis'/exp OR 'arthritic psoriasis' OR 'arthritis psoriatica' OR 'arthritis, psoriasis' OR 'arthritis, psoriatic' OR 'arthropathic psoriasis' OR 'arthropathy, psoriatic' OR 'polyarthritis, psoriatic' OR 'psoriasis arthropathica' OR 'psoriasis pustulosa arthropathica' OR 'psoriasis, arthritis' OR 'psoriatic arthritis' OR 'psoriatic arthropathy' OR 'psoriatic polyarthritis' OR 'psoriatic rheumatism' OR 'psoriatic rheumatoid arthritis' OR 'rheumatoid arthritis, psoriatic' OR 'juvenile rheumatoid arthritis'/exp OR 'jia (juvenile idiopathic arthritis)' OR 'arthritis deformans juvenilis' OR 'arthritis, juvenile' OR 'arthritis, juvenile rheumatoid' OR 'arthropathy, juvenile' OR 'chronic arthritis, juvenile' OR 'chronic juvenile arthritis' OR 'juvenile arthritis' OR 'juvenile arthritis deformans' OR 'juvenile arthropathy' OR 'juvenile chronic arthritis' OR 'juvenile idiopathic arthritis' OR 'juvenile rheumatoid arthritis' OR 'polyarthritis, progressive splenoadenomegalic' OR 'rheumatoid arthritis, juvenile' OR 'mixed connective tissue disease'/exp OR 'mctd' OR 'mctd syndrome' OR 'sharp syndrome' OR 'sharp`s syndrome' OR 'sharps syndrome' OR 'connective tissue disease overlap syndrome' OR 'connective tissue disease, mixed' OR 'mixed collagen disease' OR 'mixed collagen vascular disease' OR 'mixed connective tissue disease' OR 'mixed connective tissue disease syndrome' OR 'mixed connective tissue disorder' OR 'rheumatic polymyalgia'/exp OR 'forestier certonciny syndrome' OR 'polymyalgia arteritica' OR 'polymyalgia rheumatica' OR 'pseudopolyarthritis rhizomelica' OR 'rheumatic myalgia' OR 'rheumatic polymyalgia' OR 'rheumatism, inflammatory rhizomelic' OR 'rhizomelic pseudopolyarthritis' OR 'systemic sclerosis'/exp OR 'generalised scleroderma' OR 'generalized scleroderma' OR 'progressive scleroderma' OR 'progressive sclerodermia' OR 'progressive sclerosis, systemic' OR 'progressive systemic sclerosis' OR 'scleroderma, generalised' OR 'scleroderma, generalized' OR 'scleroderma, progressive' OR 'scleroderma, systemic' OR 'sclerosis, progressive systemic' OR 'sclerosis, systemic' OR 'sclerosis, systemic progressive' OR 'systemic progressive sclerosis' OR 'systemic scleroderma' OR 'systemic sclerosis' OR 'systemic sclerosis, progressive' OR 'sjoegren syndrome'/exp OR 'gougerot houwer sjoegren syndrome' OR 'gougerot mulock houwer sjoegren syndrome' OR 'gougerot sjoegren disease' OR 'gougerot sjoegren syndrome' OR 'gougerot sjogren disease' OR 'gougerot sjogren syndrome' OR 'gougerot-sjogren syndrome' OR 'mikulicz gougerot sjoegren syndrome' OR 'mikulicz radecki syndrome' OR 'mukilicz radecki syndrome' OR 'sjoegren disease' OR 'sjoegren syndrome' OR 'sjoegren`s syndrome' OR 'sjogren disease' OR 'sjogren syndrome' OR 'sjogren`s syndrome' OR 'dacryosialoadenopathia atrophicans' OR 'dyssecretosis, mucoserous' OR 'mucoserous dyssecretosis' OR 'oculobuccopharyngeal dryness' OR 'rheumatic sialosis' OR 'sialosis, rheumatic' OR 'sicca syndrome' OR 'xerodermosteosis') AND ('tooth pulp'/exp OR 'dental pulp' OR 'dental pulpa' OR 'pulp vitality' OR 'pulp, tooth' OR 'pulpa' OR 'pulpa dens vitality' OR 'pulpa dentis' OR 'pulpal tissue' OR 'tooth pulp' OR 'tooth pulp vitality' OR 'tooth pulpa' OR 'tooth, pulp' OR 'tooth pulp disease'/exp OR 'dental pulp autolysis' OR 'dental pulp calcification' OR 'dental pulp disease' OR 'dental pulp diseases' OR 'dental pulp exposure' OR 'dental pulp gangrene' OR 'dental pulp necrosis' OR 'dental pulp test' OR 'nonvital tooth' OR 'reactionary dentin (disease)' OR 'tertiary dentin (disease)' OR 'tooth pulp disease' OR 'tooth pulp gangrene' OR 'tooth, nonvital' OR 'pulpitis'/exp OR 'acute dental pulpitis' OR 'dental

	pulp inflammation' OR 'endodontal infections' OR 'endodontal inflammation' OR 'endodontic infection' OR 'endodontic inflammation' OR 'pulp infection' OR 'pulpal infection' OR 'pulpal inflammation' OR 'pulpitis' OR 'tooth pulp infection' OR 'tooth pulp inflammation' OR 'tooth pulpitis' OR 'tooth periapical disease'/exp OR 'dental granuloma' OR 'dentin granuloma' OR 'dentine granuloma' OR 'periapical disease' OR 'periapical diseases' OR 'periapical granuloma' OR 'periapical infection' OR 'periapical lesion' OR 'periapical periodontitis' OR 'tooth granuloma' OR 'tooth periapical disease' OR 'tooth periapical granuloma' OR 'tooth periapical infection' OR 'periapical abscess'/exp OR 'alveolar abscess' OR 'apical abscess (dental)' OR 'dento alveolar abscess' OR 'dentoalveolar abscess' OR 'periapical abscess' OR 'periapical abscesses' OR 'suppurative apical periodontitis' OR 'suppurative periapical periodontitis' OR 'dental pulp devitalization'/exp OR 'dental devitalisation' OR 'dental devitalization' OR 'dental pulp devitalization' OR 'devitalization (dental)' OR 'pulp devitalization' OR 'tooth devitalization' OR 'periapical tissue'/exp OR 'periapical tissue' OR 'radicular cyst'/exp OR 'apical cyst' OR 'apical periodontal cyst' OR 'apical radicular cyst' OR 'dental root cyst' OR 'periapical cyst' OR 'periradicular cyst' OR 'radicular cyst' OR 'radiculodental cyst' OR 'residual radicular cyst' OR 'root end cyst' OR 'endodontic procedure'/exp OR 'endodontic method' OR 'endodontic procedure' OR 'endodontic technique' OR 'pulp canal therapy' OR 'root canal procedure' OR 'root canal therapy' OR 'root canal obturation'/exp OR 'canal obturation (dental)' OR 'dental canal filling' OR 'dental root canal filling' OR 'dental root filling' OR 'root canal filling' OR 'root canal obturation' OR 'tooth root canal filling' OR 'tooth root filling')	
Scopus	TITLE-ABS ("Autoimmune Diseases" OR "Disease, Autoimmune" OR "Diseases, Autoimmune" OR "Autoimmune Disease" OR "Rheumatic Diseases" OR "Disease, Rheumatic" OR "Diseases, Rheumatic" OR "Rheumatic Disease" OR rheumatism OR "Arthritis, Rheumatoid" OR "Rheumatoid Arthritis" OR "Lupus Erythematosus, Systemic" OR "Lupus Erythematosus Disseminatus" OR "Systemic Lupus Erythematosus" OR "Libman-Sacks Disease" OR "Disease, Libman-Sacks" OR "Libman Sacks Disease" OR "Spondylitis, Ankylosing" OR "Bechterew's Disease" OR "Bechterews Disease" OR "Marie-Struempell Disease" OR "Marie Struempell Disease" OR "Spondylarthritis Ankylopoietica" OR "Rheumatoid Spondylitis" OR "Spondylitis, Rheumatoid" OR "Ankylosing Spondylitis" OR "Ankylosing Spondylarthritis" OR "Ankylosing Spondylarthritides" OR "Spondylarthritides, Ankylosing" OR "Spondylarthritis, Ankylosing" OR "Ankylosing Spondyloarthritis" OR "Ankylosing Spondyloarthritides" OR "Spondyloarthritides, Ankylosing" OR "Spondyloarthritis, Ankylosing" OR "Spondylitis Ankylopoietica" OR "Bechterew Disease" OR "Spondyloarthritis Ankylopoietica" OR "Arthritis, Psoriatic" OR "Psoriasis Arthropathica" OR "Psoriasis, Arthritic" OR "Arthritic Psoriasis" OR "Psoriatic Arthropathy" OR "Arthropathies, Psoriatic" OR "Arthropathy, Psoriatic" OR "Psoriatic Arthropathies" OR "Psoriatic Arthritis" OR "Arthritis, Juvenile" OR "Juvenile Arthritis" OR "Juvenile Idiopathic Arthritis" OR "Idiopathic Arthritis, Juvenile" OR "Arthritis, Juvenile Idiopathic" OR "Juvenile Chronic Arthritis" OR "Chronic Arthritis, Juvenile" OR "Juvenile Rheumatoid Arthritis" OR "Childhood Arthritis" OR "Arthritides, Childhood" OR "Arthritis, Childhood" OR "Childhood Arthritides" OR "Arthritis, Juvenile Rheumatoid" OR "Rheumatoid Arthritis, Juvenile" OR "Arthritis, Juvenile Chronic" OR "Juvenile-Onset Still Disease" OR "Juvenile Onset Still Disease" OR "Juvenile-Onset Stills Disease" OR "Juvenile Onset Stills Disease" OR "Stills Disease, Juvenile-Onset" OR "Still's Disease, Juvenile-Onset" OR "Juvenile-Onset Still's Disease" OR "Still's Disease, Juvenile Onset" OR "Still Disease, Juvenile-Onset" OR "Still Disease, Juvenile Onset" OR "Systemic Arthritis, Juvenile" OR "Arthritis, Juvenile Systemic" OR "Juvenile Systemic Arthritis" OR "Oligoarthritis, Juvenile" OR "Juvenile Oligoarthritis" OR "Enthesitis-Related Arthritis, Juvenile" OR "Arthritis, Juvenile Enthesitis-Related" OR "Enthesitis Related Arthritis, Juvenile" OR "Juvenile Enthesitis-Related Arthritis" OR "Psoriatic Arthritis, Juvenile" OR "Arthritis, Juvenile Psoriatic" OR "Juvenile Psoriatic Arthritis" OR "Polyarthritis, Juvenile, Rheumatoid Factor Negative" OR "Polyarthritis, Juvenile, Rheumatoid Factor Positive" OR "Polyarticular Juvenile Idiopathic Arthritis" OR pcjia OR "PJIA Polyarticular Juvenile Idiopathic Arthritis" OR "Polyarticular-Course Juvenile Idiopathic Arthritis" OR "Mixed Connective Tissue Disease" OR mctd OR "Connective Tissue Disease, Mixed" OR "Sharp Syndrome" OR "Syndrome, Sharp" OR "Polymyalgia Rheumatica" OR "Forestier-Certonciny Syndrome" OR "Forestier Certonciny Syndrome" OR "Syndrome, Forestier-Certonciny" OR "Rheumatism, Peri-Extra-Articular" OR "Peri-Extra-Articular Rheumatism" OR "Rheumatism, Peri Extra Articular" OR "Pseudopolyarthritis, Rhizomelic" OR "Pseudopolyarthritides, Rhizomelic" OR "Rhizomelic Pseudopolyarthritides" OR "Rhizomelic Pseudopolyarthritis" OR "Scleroderma, Systemic" OR "Sclerosis, Systemic" OR "Systemic Scleroderma" OR "Systemic Sclerosis" OR "Sjogren's Syndrome" OR "Sjogrens Syndrome" OR "Syndrome, Sjogren's" OR "Sjogren Syndrome" OR "Sicca Syndrome" OR "Syndrome, Sicca") AND TITLE-ABS ("Dental Pulp" OR "Dental Pulps" OR "Pulp, Dental" OR "Pulps, Dental" OR "Dental Pulp Diseases" OR "Dental Pulp Disease" OR "Disease, Dental Pulp" OR "Diseases, Dental Pulp" OR "Pulp Disease, Dental" OR "Pulp Diseases, Dental" OR "Dental Pulp Necrosis"	05/2025

	OR "Dental Pulp Necroses" OR "Necroses, Dental Pulp" OR "Pulp Necroses, Dental" OR "Necroses, Pulp" OR "Necrosis, Dental Pulp" OR "Pulp Necroses" OR "Pulp Necrosis" OR "Necrosis, Pulp" OR "Pulp Necrosis, Dental" OR "Dental Pulp Autolysis" OR "Autolyses, Dental Pulp" OR "Dental Pulp Autolyses" OR "Pulp Autolyses, Dental" OR "Autolysis, Dental Pulp" OR "Pulp Autolysis, Dental" OR "Gangrene, Dental Pulp" OR "Dental Pulp Gangrene" OR "Pulp Gangrene" OR "Gangrene, Pulp" OR "Gangrenes, Pulp" OR "Pulp Gangrenes" OR "Pulp Gangrene, Dental" OR "Pulp Mummification" OR "Mummification, Pulp" OR "Mummifications, Pulp" OR "Pulp Mummifications" OR pulpitis OR pulpitides OR "Inflammation, Endodontic" OR "Endodontic Inflammation" OR "Endodontic Inflammations" OR "Inflammations, Endodontic" OR "Periapical Diseases" OR "Disease, Periapical" OR "Diseases, Periapical" OR "Periapical Disease" OR "Periapical Periodontitis" OR "Periapical Periodontitides" OR "Periodontitides, Periapical" OR "Periodontitis, Periapical" OR "Periodontitis, Apical" OR "Apical Periodontitides" OR "Apical Periodontitis" OR "Periodontitides, Apical" OR "Periodontitis, Acute Nonsuppurative" OR "Acute Nonsuppurative Periodontitides" OR "Acute Nonsuppurative Periodontitis" OR "Nonsuppurative Periodontitides, Acute" OR "Nonsuppurative Periodontitis, Acute" OR "Periodontitides, Acute Nonsuppurative" OR "Periapical Abscess" OR "Alveolar Abscess, Apical" OR "Abscess, Apical Alveolar" OR "Abscesses, Apical Alveolar" OR "Alveolar Abscesses, Apical" OR "Apical Alveolar Abscess" OR "Apical Alveolar Abscesses" OR "Dentoalveolar Abscess, Apical" OR "Abscess, Apical Dentoalveolar" OR "Abscesses, Apical Dentoalveolar" OR "Apical Dentoalveolar Abscess" OR "Apical Dentoalveolar Abscesses" OR "Dentoalveolar Abscesses, Apical" OR "Abscess, Periapical" OR "Abscesses, Periapical" OR "Periapical Abscesses" OR "Periapical Periodontitis, Suppurative" OR "Periapical Periodontitides, Suppurative" OR "Periodontitides, Suppurative Periapical" OR "Periodontitis, Suppurative Periapical" OR "Suppurative Periapical Periodontitides" OR "Suppurative Periapical Periodontitis" OR "Periodontitis, Apical, Suppurative" OR "Periapical Granuloma" OR "Granuloma, Periapical" OR "Granulomas, Periapical" OR "Periapical Granulomas" OR "Periapical Periodontitis, Chronic Nonsuppurative" OR "Periodontitis, Apical, Chronic Nonsuppurative" OR "Dental Granulomas" OR "Granuloma, Dental" OR "Granulomas, Dental" OR "Dental Granuloma" OR "Tooth, Nonvital" OR "Nonvital Tooth" OR "Teeth, Devitalized" OR "Devitalized Teeth" OR "Tooth, Devitalized" OR "Devitalized Tooth" OR "Teeth, Nonvital" OR "Nonvital Teeth" OR "Teeth, Pulpless" OR "Pulpless Teeth" OR "Tooth, Pulpless" OR "Pulpless Tooth" OR "Teeth, Endodontically-Treated" OR "Endodontically-Treated Teeth" OR "Teeth, Endodontically Treated" OR "Tooth, Endodontically-Treated" OR "Endodontically-Treated Tooth" OR "Tooth, Endodontically Treated" OR "Dental Pulp Devitalization" OR "Devitalization, Dental Pulp" OR "Pulp Devitalization, Dental" OR "Periapical Tissue" OR "Periapical Tissues" OR "Tissue, Periapical" OR "Tissues, Periapical" OR "Periodontium, Apical" OR "Apical Periodontium" OR "Apical Periodontiums" OR "Periodontiums, Apical" OR "Radicular Cyst" OR "Cyst, Radicular" OR "Cysts, Radicular" OR "Radicular Cysts" OR "Periapical Cyst" OR "Cyst, Periapical" OR "Cysts, Periapical" OR "Periapical Cysts" OR "Periodontal Cyst, Apical" OR "Apical Periodontal Cyst" OR "Apical Periodontal Cysts" OR "Cyst, Apical Periodontal" OR "Cysts, Apical Periodontal" OR "Periodontal Cysts, Apical" OR "Root Canal Therapy" OR "Canal Therapies, Root" OR "Canal Therapy, Root" OR "Root Canal Therapies" OR "Therapies, Root Canal" OR "Therapy, Root Canal" OR "Root Canal Obturation" OR "Canal Obturation, Root" OR "Canal Obturations, Root" OR "Obturation, Root Canal" OR "Obturations, Root Canal" OR "Root Canal Obturations" OR "Endodontic Obturation" OR "Endodontic Obturations" OR "Obturation, Endodontic" OR "Obturations, Endodontic")	
Web of Science	(ALL=(“Dental Pulp” OR “Dental Pulp Diseases” OR “Dental Pulp Necrosis” OR Pulpitis OR “Periapical Diseases” OR “Periapical Periodontitis” OR “Periapical Abscess” OR “Periapical Granuloma” OR “Tooth, Nonvital” OR “Dental Pulp Devitalization” OR “Periapical Tissue” OR “Radicular Cyst” OR “Root Canal Therapy” OR “Root Canal Obturation”)) AND ALL=(“Autoimmune Diseases” OR “Rheumatic Diseases” OR “Arthritis, Rheumatoid” OR “Lupus Erythematosus, Systemic” OR “Spondylitis, Ankylosing” OR “Arthritis, Psoriatic” OR “Arthritis, Juvenile” OR “Mixed Connective Tissue Disease” OR “Polymyalgia Rheumatica” OR “Scleroderma, Systemic” OR “Sjogren's Syndrome”)	05/2025
Cochrane Library	("Autoimmune Diseases" OR "Disease, Autoimmune" OR "Diseases, Autoimmune" OR "Autoimmune Disease" OR "Rheumatic Diseases" OR "Disease, Rheumatic" OR "Diseases, Rheumatic" OR "Rheumatic Disease" OR rheumatism OR "Arthritis, Rheumatoid" OR "Rheumatoid Arthritis" OR "Lupus Erythematosus, Systemic" OR "Lupus Erythematosus Disseminatus" OR "Systemic Lupus Erythematosus" OR "Libman-Sacks Disease" OR "Disease, Libman-Sacks" OR "Libman Sacks Disease" OR "Spondylitis, Ankylosing" OR "Bechterew's Disease" OR "Bechterews Disease" OR "Marie-Struempell Disease" OR "Marie Struempell Disease" OR "Spondylarthritis Ankylopoietica" OR "Rheumatoid Spondylitis" OR "Spondylitis, Rheumatoid" OR "Ankylosing Spondylitis" OR "Ankylosing Spondylarthritis" OR "Ankylosing	05/2025

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Brazilian digital library of theses and dissertations	"(Todos os campos:“Dental Pulp” OR “Dental Pulp Diseases” OR “Dental Pulp Disease” OR “Pulp Disease, Dental” OR “Pulp Diseases, Dental” OR “Dental Pulp Necrosis” OR “Pulp Necrosis” OR “Dental Pulp Autolysis” OR Pulpitis OR “Inflammation, Endodontic” OR “Endodontic Inflammation” OR “Periapical Diseases” OR “Periapical Disease” OR “Periapical Periodontitis” OR “Periodontitis, Periapical” OR “Periodontitis, Apical” OR “Apical Periodontitis” OR “Acute Nonsuppurative Periodontitis” OR “Nonsuppurative Periodontitis, Acute” OR “Periapical Abscess” OR “Alveolar Abscess, Apical” OR “Apical Alveolar Abscess” OR “Dentoalveolar Abscess, Apical” OR “Periapical Periodontitis, Suppurative” OR “Periodontitis, Suppurative Periapical” OR “Periapical Granuloma” OR “Periapical Granulomas” OR “Periapical Periodontitis, Chronic Nonsuppurative” OR “Dental Granuloma” OR “Tooth, Nonvital” OR “Nonvital Tooth” OR “Teeth, Devitalized” OR “Devitalized Teeth” OR “Devitalized Tooth” OR “Nonvital Teeth” OR “Endodontically-Treated Teeth” OR “Endodontically-Treated Tooth” OR “Dental Pulp Devitalization” OR “Devitalization, Dental Pulp” OR “Pulp Devitalization, Dental” OR “Periapical Tissue” OR “Periapical Tissues” OR “Apical Periodontium” OR “Radicular Cyst” OR “Radicular Cysts” OR “Periapical Cyst” OR “Root Canal Therapy” OR “Root Canal Therapies” OR “Root Canal Obturation” OR “Endodontic Obturation” E Todos os campos:“Autoimmune Diseases” OR “Disease, Autoimmune” OR “Autoimmune Disease” OR “Rheumatic Diseases” OR “Disease, Rheumatic” OR “Diseases, Rheumatic” OR “Rheumatic Disease” OR Rheumatism OR “Arthritis, Rheumatoid” OR “Rheumatoid Arthritis” OR “Lupus Erythematosus, Systemic” OR “Systemic Lupus Erythematosus” OR “Spondylitis, Ankylosing” OR “Bechterew's Disease” OR “Bechterews Disease” OR “Spondylarthritis Ankylopoietica” OR “Rheumatoid Spondylitis” OR “Spondylitis, Rheumatoid” OR “Spondyloarthritides, Ankylosing” OR “Bechterew Disease” OR “Spondyloarthritis Ankylopoietica” OR “Arthritis, Psoriatic” OR “Psoriasis Arthropathica” OR “Psoriasis, Arthritic” OR “Arthritic Psoriasis” OR “Psoriatic Arthropathy” OR “Arthropathies, Psoriatic” OR “Arthropathy, Psoriatic” OR “Psoriatic Arthropathies” OR “Psoriatic Arthritis” OR “Arthritis, Juvenile” OR “Juvenile Arthritis” OR “Juvenile Idiopathic Arthritis” OR PCJIA OR “PJIA Polyarticular Juvenile Idiopathic Arthritis” OR “Polyarticular-Course Juvenile Idiopathic Arthritis” OR “Mixed Connective Tissue Disease” OR MCTD OR “Sharp Syndrome” OR “Polymyalgia Rheumatica” OR “Forestier-Certonciny Syndrome” OR “Forestier Certonciny Syndrome” OR “Syndrome, Forestier-Certonciny” OR “Rhizomelic Pseudopolyarthritis” OR “Scleroderma, Systemic” OR “Sclerosis, Systemic” OR “Sjogren's Syndrome” OR “Sjogrens Syndrome” OR “Sjogren Syndrome”)"	05/2025
CAPES Theses and Dissertations Catalog	Autoimune Oral	05/2025

(Capítulo III): Tabela Suplementar 4. Avaliação da certeza da evidência para cada desfecho analisado nas metanálises, segundo a ferramenta GRADE.

Certainty assessment							Summary of Results				
							Event rates from the study (%)			Potential absolute effects	
Participants (studies)	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall certainty of evidence	Diseased/Non-exposed	Diseased/Exposed	Relative effect (95% CI)	Risk in diseased/non-exposed	Risk difference in diseased/exposed
INDIVIDUAL LEVEL (CRUDE OR)											
3914438 (13 observational studies)	Very serious[a]	Very serious[b]	Not serious	Not serious	None	⨁◯◯◯ Very low[a,b]	39807/3844612 (1.0%)	37597/69826 (53.8%)	**OR 1.80** (1.57 to 2.05)	39807/3844612 (1.0%)	**8 more per 1.000** (from 6 more to 11 more)
INDIVIDUAL LEVEL - RHEUMATOID ARTHRITIS (CRUDE OR)											
1768940 (9 observational studies)	Very serious[c]	Very serious[d]	Not serious	Not serious	None	⨁◯◯◯ Very low[c,d]	25508/1705878 (1.5%)	37343/63062 (59.2%)	**OR 1.62** (1.23 to 2.12)	25508/1705878 (1.5%)	**9 more per 1.000** (from 3 more to 16 more)
INDIVIDUAL LEVEL - ANKYLOSING SPONDYLITIS (CRUDE OR)											
481 (2 observational studies)	Very serious[e]	Serious[f]	Not serious	Serious[g]	None	⨁◯◯◯ Very low[e,f,g]	91/334 (27.2%)	57/147 (38.8%)	**OR 1.62** (0.82 to 3.22)	91/334 (27.2%)	**105 more per 1.000** (from 38 less to 274 more)
INDIVIDUAL LEVEL - SJÖGREN'S SYNDROME (CRUDE OR)											

1157452 (2 observational studies)	Very serious[e]	Very serious[h]	Not serious	Not serious	None	⨁◯◯◯ Very low[e,h]	8478/1154068 (0.7%)	291/3384 (8.6%)	**OR 2.21** (1.07 to 4.59)	8478/1154068 (0.7%)	**9 more per 1.000** (from 1 more to 26 more)

INDIVIDUAL LEVEL (ADJUSTED OR)

2759408 (7 observational studies)	Very serious[i]	Very serious[j]	Not serious	Not serious	None	⨁◯◯◯ Very low[i,j]	32468/2695904 (1.2%)	36355/63504 (57.2%)	**OR 1.60** (1.20 to 2.12)	32468/2695904 (1.2%)	**7 more per 1.000** (from 2 more to 13 more)

INDIVIDUAL LEVEL - RHEUMATOID ARTHRITIS (ADJUSTED OR)

1763663 (5 observational studies)	Very serious[k]	Very serious[l]	Not serious	Not serious	None	⨁◯◯◯ Very low[k,l]	24886/1704198 (1.5%)	36022/59465 (60.6%)	**OR 1.64** (1.01 to 2.67)	24886/1704198 (1.5%)	**9 more per 1.000** (from 0 less to 23 more)

INDIVIDUAL LEVEL (ADJUSTED OR) - SENSITIVITY ANALYSIS

2758700 (6 observational studies)	Very serious[m]	Very serious[n]	Not serious	Not serious	None	⨁◯◯◯ Very low[m,n]	32392/2695620 (1.2%)	36211/63080 (57.4%)	**OR 1.60** (1.16 to 2.22)	32392/2695620 (1.2%)	**7 more per 1.000** (from 2 more to 14 more)

INDIVIDUAL LEVEL - RHEUMATOID ARTHRITIS (ADJUSTED OR) - SENSITIVITY ANALYSIS

1763052 (4 observational studies)	Very serious[o]	Very serious[p]	Not serious	Serious[q]	None	⨁◯◯◯ Very low[o,p,q]	24810/1703914 (1.5%)	35909/59138 (60.7%)	**OR 1.57** (0.88 to 2.79)	24810/1703914 (1.5%)	**8 more per 1.000** (from 2 less to 25 more)

TOOTH LEVEL (CRUDE OR)

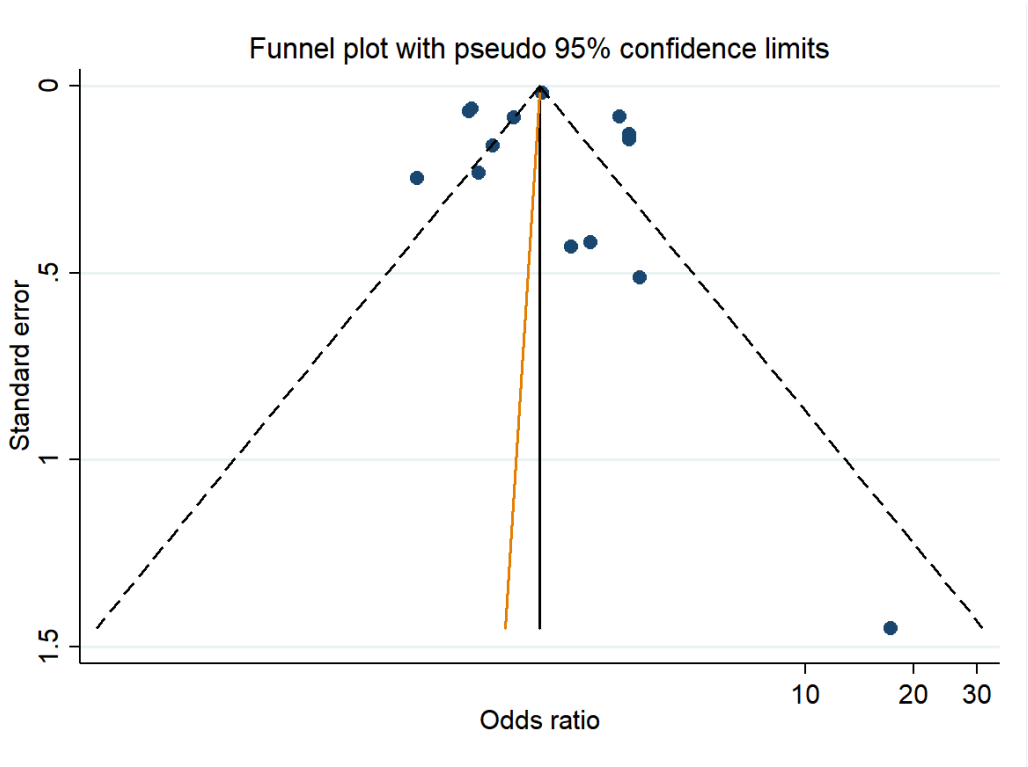
17345 (5 observational studies)	Very serious[r]	Serious[s]	Not serious	Not serious	None	⊕◯◯◯ Very low[r,s]	474/10709 (4.4%)	337/6636 (5.1%)	**OR 1.74** (1.28 to 2.37)	474/10709 (4.4%)	**30 more per 1.000** (from 12 more to 55 more)

TOOTH LEVEL - RHEUMATOID ARTHRITIS (CRUDE OR)

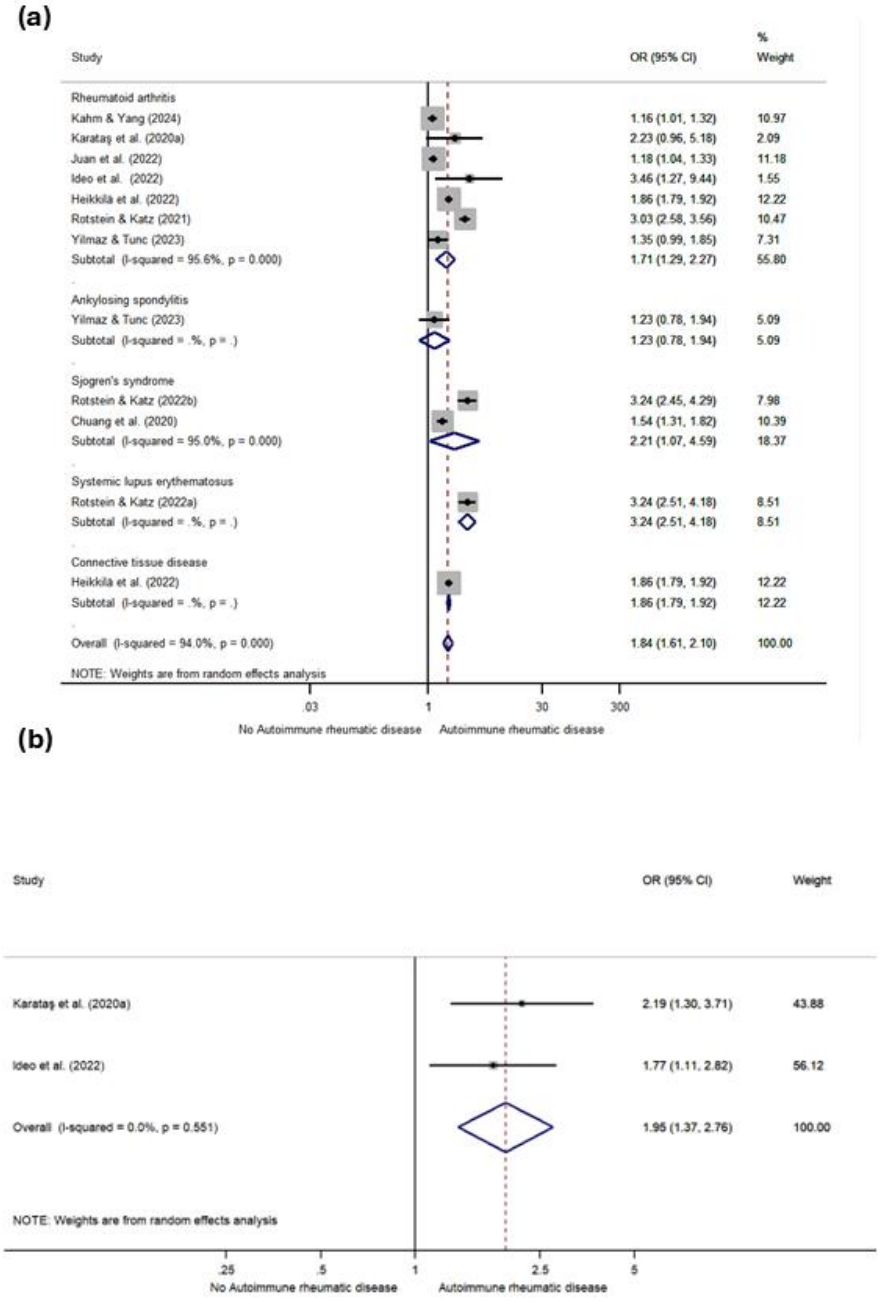
14757 (4 observational studies)	Very serious[o]	Serious[t]	Not serious	Not serious	None	⊕◯◯◯ Very low[o,t]	457/9404 (4.9%)	300/5353 (5.6%)	**OR 1.67** (1.18 to 2.35)	457/9404 (4.9%)	**30 more per 1.000** (from 8 more to 59 more)

CI: Confidence interval; **OR:** Odds ratio; **a:** 5 studies with high risk of bias and 8 with moderate risk of bias; **b:** I^2= 91.4%; **c:** 2 studies with high risk of bias and 7 with moderate risk of bias; **d:** I^2= 93.5%; **e:** 1 study with high risk of bias and 1 with moderate risk of bias; **f:** I^2= 55.8%; **g:** IC 95%= 0.82 a 3.22); **h:** I^2= 95%; **i:** 2 studies with high risk of bias and 5 with moderate risk of bias; **j:** I^2= 95.2%; **k:** 1 study with high risk of bias and 4 with moderate risk of bias; **l:** I^2= 95.5%; **m:** 2 studies with high risk of bias and 4 with moderate risk of bias; **n:** I^2= 97%; **o:** 1 study with high risk of bias and 3 with moderate risk of bias; **p:** I^2= 97.2%; **q:** IC 95%= 0.88 a 2.79; **r:** 2 studies with high risk of bias and 3 with moderate risk of bias; **s:** I^2= 69.4%; **t:** I^2= 74.5%.

(Capítulo III): Figura suplementar 1. Funnel plot para a avaliação do viés de publicação.



(Capítulo III): Figura suplementar 2. Análise de sensibilidade para a associação entre doenças autoimunes reumáticas e patologias pulpo-periapicais, excluindo-se três estudos com critérios mais frágeis [13, 15, 40]. (a) Análise em nível de paciente. (b) Análise em nível dentário.



(Capítulo III): PROTOCOLO DE PESQUISA – PROSPERO

NIHR | National Institute for Health and Care Research

PROSPERO
International prospective register of systematic reviews

Impact of autoimmune rheumatic diseases on the prevalence of pulpal and periapical pathologies: a systematic review and meta-analysis

Soraia de Fátima Carvalho Souza , Ana Paula Nóbrega Caetano da Silva, Rodrigo Costa Mendes, Randerson Silva Araújo, Erika Bárbara Abreu Fonseca Thomaz

Citation
Soraia de Fátima Carvalho Souza , Ana Paula Nóbrega Caetano da Silva, Rodrigo Costa Mendes, Randerson Silva Araújo, Erika Bárbara Abreu Fonseca Thomaz. Impact of autoimmune rheumatic diseases on the prevalence of pulpal and periapical pathologies: a systematic review and meta-analysis. PROSPERO 2024 Available from https://www.crd.york.ac.uk/PROSPERO/view/CRD42024559527

REVIEW TITLE AND BASIC DETAILS

Review title
Impact of autoimmune rheumatic diseases on the prevalence of pulpal and periapical pathologies: a systematic review and meta-analysis

Review objectives
We will address the following research question:
Do individuals with Autoimmune Rheumatic Diseases have a higher prevalence of pulpal and periapical pathologies compared to those without Autoimmune Rheumatic Diseases?
Three secondary questions are:
What is the effect of the different Autoimmune Rheumatic Diseases on the prevalence of Pulpal and Periapical Pathologies?
Does the severity of Autoimmune Rheumatic Diseases affect the prevalence of Pulpal and Periapical Pathologies?
Do Autoimmune Rheumatic Diseases interfere with bone repair in individuals with Pulpal and Periapical Pathologies after endodontic treatment?

Keywords
Adolescent, Adult, Aged, Arthritis, Juvenile, Arthritis, Psoriatic, Arthritis, Rheumatoid, Autoimmune Disease, Autoimmune Diseases, Child, Dental Pulp Diseases, Lupus Erythematosus, Systemic, meta-analysis, Mixed Connective Tissue Disease, Periapical Diseases, Polymyalgia Rheumatica, Rheumatic Diseases, Scleroderma, Systemic, Sjogren's Syndrome, Spondylitis, Ankylosing, Systematic review

SEARCHING AND SCREENING

Searches

We will search 11 online databases: MEDLINE/PubMed, Embase, Scopus, BVS-Bireme, Web of Science, LILACS, Google Scholar, SciELO, Cochrane Library, ProQuest and the Brazilian digital library of theses and dissertations. Experts will also be consulted about other studies on the subject, as well as reference lists and suggestions for similar work on the articles identified We will not apply any language, date or publication status restrictions. We will search for the entry terms available in each database without filters (All Fields). We will update the search before publishing the results. In addition, we will contact the authors in the event of missing information in conference proceedings, manuscripts or abstracts in order to obtain the full papers.
The search will follow the PEOS strategy:
P: Children, adolescents, adults and the elderly regardless of age, gender, race/color or any other condition (Child; Adolescent; Adult; Aged; Humans).
E: Rheumatic Autoimmune Disease (Autoimmune Diseases; Rheumatic Diseases; Arthritis, Rheumatoid; Spondylitis, Ankylosing; Lupus Erythematosus, Systemic; Mixed Connective Tissue Disease; Arthritis, Juvenile; Sjogren's Syndrome; Polymyalgia Rheumatica; Scleroderma, Systemic; Arthritis, Psoriatic)
O: Presence of pulp and periapical pathology (Periapical Diseases; Dental Pulp Diseases)
S: Study design (Observational Study; Cross-Sectional Studies; Cohort Studies; Case-Control Studies; Clinical Trial; Randomized Controlled Trial; Controlled Clinical Trial; Intervention Study)

Study design

We will include observational studies (cross-sectional, cohort and case-control) and randomized and non-randomized clinical trials. These study designs will be considered given the existence of a comparison group, allowing for a more adequate analysis of the effect of an intervention/exposure on the outcomes of interest. Case reports, expert opinions, technical reports, letters to the editor and reviews of any kind will not be included.

ELIGIBILITY CRITERIA

Condition or domain being studied

Autoimmune diseases are disorders where the immune system attacks the body's tissues, causing inflammation and damage, influenced by genetic, environmental, and hormonal factors (Pisetsky, 2023). Autoimmune rheumatic diseases primarily affect the musculoskeletal system and include nine conditions such as rheumatoid arthritis, systemic lupus erythematosus, ankylosing spondylitis, psoriatic arthritis, juvenile arthritis, polymyalgia rheumatica, mixed connective tissue disease, systemic scleroderma, and Sjogren's syndrome (Abrão et al., 2016).

Dental caries is a prevalent non-communicable disease of the oral cavity, with a global prevalence in permanent teeth estimated at around 29% (WHO, 2022). Untreated caries can lead to pulp inflammation and serious infections, affecting the periapical tissues and potentially having systemic repercussions (Bjørndal, 2008; American Association of Endodontics, 2013). Bacterial infection in the root canal system and the degradation of periapical bone and periodontal ligaments stimulate the release of pro-inflammatory mediators such as IL-1, IL-6, and TNF-α, suggesting a common inflammatory mechanism between periapical pathologies and rheumatic autoimmune diseases (Gomes et al., 2013; Georgiou et al., 2019).
Systemic inflammation from rheumatic autoimmune diseases can influence local inflammatory conditions, such as pulpal and periapical pathologies. This inflammation may interfere with bone repair after endodontic treatment, increasing the prevalence of periapical pathologies in this population.

Population
Children, adolescents, adults and elderly regardless of age, gender, race/color or any other condition

Intervention(s) or exposure(s)
Autoimmune Rheumatic Diseases

Comparator(s) or control(s)
No Autoimmune Rheumatic Diseases

Context
The search for studies will be carried out by two independent researchers (APNCS and RCM), following the PEOS search strategy, from July to September 2024. In case of disagreement, a third researcher will be consulted (SFCS). The studies will then be pre-selected by reading the titles and abstracts. The pre-selected studies will be read in full (PDF), applying the inclusion and exclusion criteria. For the selected studies, data extraction will be carried out for a period of three months, followed by qualitative synthesis and meta-analysis. The search will be updated every 12 months until this study is published. The entire process of selecting papers and extracting data will also be carried out in duplicate and blinded (APNCS and RCM). Discrepancies will be resolved in a consensus meeting and, if necessary, with the arbitration of the third evaluator (SFCS).

OUTCOMES TO BE ANALYSED

Main outcomes
The main result will be an analysis of the relationship between Autoimmune Rheumatic Diseases and pulp and periapical pathologies.

Measures of effect
The study characteristics and results will be presented in tables. For the meta-analysis, primary data will be extracted to calculate relative risk, prevalence ratio or odds ratios and corresponding 95% confidence intervals. Whenever available, unadjusted and adjusted measures of association will also be extracted. The adjusted model with the best fit will be selected and the adjustment variables recorded. If the outcomes are presented as numerical variables, the association will be estimated using the mean (or median) of the differences

between exposed and non-exposed people. Parametric and/or non-parametric tests may be used. Random-effects meta-analysis according to DerSimonian-Laird will be used if the heterogeneity between the studies is significant (considering $p<0.10$) or the I^2 test is greater than or equal to 50% (Lechner, 2010). Otherwise, a fixed-effect meta-analysis will be used. Different sensitivity analyses will be carried out considering: the diseases together and separately; different classifications of pulp and periapical pathologies; unadjusted and adjusted associations; and risk of bias.
We will assess potential publication bias by visually interpreting funnel plots for the primary outcomes when ten or more studies are included in a meta-analysis (Sterne et al., 2007). All analyses will be carried out using Stata (version 14.0) and RevMan (version 5.3).

Additional outcomes

In addition, the dose-response effect of autoimmune rheumatic diseases on the outcomes of interest will be analyzed, as well as whether exposure to these diseases can interfere with bone repair of periapical lesions after endodontic treatment.

Measures of effect

The same strategy adopted for the primary outcome will be used for the secondary outcomes.

DATA COLLECTION PROCESS

Data extraction (selection and coding)

Data will be extracted by two independent reviewers using customized data extraction forms [authors, year of publication, country of study, study design, population, sample size, age range of sample, type of autoimmune rheumatic disease, type of pulpal/periapical pathology, unadjusted and adjusted measure of effect (RR, PR, OR or other), 95% CI, variables used in model adjustment, conclusion]. We will contact the corresponding authors for additional information when necessary. Data extraction will be carried out in duplicate, blinded. Discrepancies will be resolved in a consensus meeting and, if necessary, with the arbitration of the third evaluator (SFCS).

Risk of bias (quality) assessment

Two reviewers (APNCS and RCM) will assess quality independently and disagreements will be resolved in a consensus meeting and, if necessary, with the arbitration of the third reviewer (SFCS). The included studies will be assessed according to their design, using the tool of the Joanna Briggs Institute (JBI).

PLANNED DATA SYNTHESIS

Strategy for data synthesis

We will carry out a narrative/descriptive synthesis of the data from each included study (systematic review). In the presence of two or more studies with the same research question, a quantitative synthesis will be included (meta-analysis).

Analysis of subgroups or subsets

Different sensitivity analyses will be carried out:
The analysis of autoimmune rheumatic diseases together and separately
Different classifications of pulp and periapical pathologies

Crude and adjusted associations
All studies regardless of risk of bias and leaving the studies with the lowest risk of bias. Whenever possible, we will carry out meta-analyses with subgroup analyses according to the study design and type of autoimmune rheumatic disease.

REVIEW AFFILIATION, FUNDING AND PEER REVIEW

Review team members

- Professor Soraia de Fátima Carvalho Souza , Federal University of Maranhão
- Ana Paula Nóbrega Caetano da Silva, Federal University of Maranhão
- Rodrigo Costa Mendes, Federal University of Maranhão
- Randerson Silva Araújo, Federal University of Maranhão
- Professor Erika Bárbara Abreu Fonseca Thomaz, Federal University of Maranhão

Review affiliation

Federal University of Maranhão

Funding source

CAPES (Coordenação de Aperfeiçoamento de Pessoal de Nível Superior), FAPEMA (Fundação de Amparo à Pesquisa e ao Desenvolvimento Científico e Tecnológico do Maranhão) e CNPq (Conselho Nacional de Desenvolvimento Científico e Tecnológico).

Named contact

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endosoraia@gmail.com

TIMELINE OF THE REVIEW

Review timeline

Start date: 17 July 2024. End date: 17 July 2025

Date of first submission to PROSPERO

20 June 2024

Date of registration in PROSPERO

05 July 2024

CURRENT REVIEW STAGE

Publication of review results

The intention is to publish the review once completed.The review will be published in English

Stage of the review at this submission

Review stage	Started	Completed
Pilot work		

Review stage	Started	Completed
Formal searching/study identification		
Screening search results against inclusion criteria		
Data extraction or receipt of IP		
Risk of bias/quality assessment		
Data synthesis		

Review status
The review is currently planned or ongoing.

ADDITIONAL INFORMATION

PROSPERO version history

- Version 1.1 published on 05 Jul 2024
- Version 1.0 published on 05 Jul 2024

Review conflict of interest
None known

Country
Brazil

Medical Subject Headings
Arthrodesis; Humans; Periapical Periodontitis; Plastic Surgery Procedures; Prevalence; Rheumatic Diseases

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Any enquiries about the record should be referred to the named review contact

ANEXO A

Capítulo II

Diretrizes para publicação no *Oral Diseases*

1. **Author Guidelines**

Oral Diseases now offers Free Format submission for a simplified and streamlined submission process; More details here

Content of Author Guidelines:

Relevant Documents: **Open Access Order Form**, **Standard Release Form for photographic consent**

Useful Websites: **Submission Site**, **Articles Published in *Oral Diseases***, **Author Services**, **Author Services**, **Guidelines for Figures**

SUBMISSION

Once the submission materials have been prepared in accordance with the Author Guidelines, manuscripts should be submitted online at https://wiley.atyponrex.com/journal/ODI.

Click here for more details on how to use ScholarOne.

For technical help with the submission system, please review our **FAQs** or contact **submissionhelp@wiley.com.**

For general assistance, please contact **odiedoffice@wiley.com**.

1. GENERAL

The editors encourage submissions of original articles, review articles, reports of meetings, book reviews and correspondence in the form of letters to the editor. *Oral Diseases* does not accept case reports.

Please read the instructions below carefully for details on the submission of manuscripts, the journal's requirements and standards as well as information concerning the procedure after a manuscript has been accepted for publication in *Oral Diseases*. Authors are encouraged to visit **Wiley Author Services** for further information on the preparation and submission of articles and figures.

Preprint Policy

Please find the Wiley preprint policy **here**. *Oral Diseases* accepts articles previously published on preprint servers. *Oral Diseases* will consider for review articles previously available as preprints. Authors are requested to update any pre-publication versions with a link to the final published article. Authors may also post the final published version of the article immediately after publication.

Data Sharing and Data Accessibility

Oral Diseases expects data sharing. All accepted manuscripts will need to publish a data availability statement to confirm the presence or absence of shared data. The journal expects authors to share the data and other artefacts supporting the results in the paper by archiving it in an appropriate public repository. Authors should include a data accessibility statement, including a link to the repository they have used, in order that this statement can be published alongside their paper. Review **Wiley's Data Sharing policy** where you will be able to see and select the data availability statement that is right for your submission. If you have shared data, this statement will describe how the data can be accessed, and include a persistent identifier (e.g., a DOI for the data, or an accession number) from the repository where you shared the data. **Sample statements are available here**. If published, statements will be placed in the heading of your manuscript.

2. ETHICAL GUIDELINES

Oral Diseases adheres to the ethical guidelines given below for publication and research.

2.1. Authorship and Acknowledgements

Authorship: *Oral Diseases* adheres to the **International Standards for Authors** published by the Committee on Publication Ethics (COPE). All authors named on a paper should agree to be named on the paper, and all authors so named should agree to the submission of the paper to *Oral Diseases* and approve the submitted and accepted versions of the publication. Any change to the author list should be approved by all authors, including any author who has been removed from the list.

Oral Diseases also adheres to the **definition of authorship** set up by The International Committee of Medical Journal Editors (ICMJE). According to the ICMJE authorship criteria should be based on 1) substantial contributions to conception and design of, or acquisition of data or analysis and interpretation of data, 2) drafting the article or revising it critically for important intellectual content and 3) final approval of the version to be published. Authors should meet conditions 1, 2 and 3.

It is a requirement that the corresponding author submit a short description of each individual's contribution to the research and its publication. Upon submission of a manuscript all co-authors should also be registered with a correct e-mail addresses. If any of the e-mail addresses supplied are incorrect, the corresponding author will be contacted by the Journal Administrator.

For all articles, the journal mandates the CRediT (Contribution Roles Taxonomy), for more information please see **Author Services**.

Acknowledgements: Authors must acknowledge individuals who do not qualify as authors but who contributed to the research. Authors must acknowledge any assistance that they have received (e.g. provision of writing assistance, literature searching, data analysis, administrative support, supply of materials). If/how this assistance was funded should be described and included with other funding information. “Acknowledgements” should be brief and should not include thanks to anonymous referees and editors. Where people are acknowledged, a cover letter demonstrating their consent must be provided.

2.2. Ethical Approvals

Human Subjects: Experimentation involving human subjects will only be published if such research has been conducted in full accordance with ethical principles, including the World Medical Association **Declaration of Helsinki** (version 2002) and the additional requirements, if any, of the country where the research has been carried out. Manuscripts must be accompanied by a statement that the experiments were undertaken with the understanding and written consent of each subject and according to the above mentioned principles. A statement regarding the fact that the study has been independently reviewed and approved by an ethical board should also be included.

Photographs of People: Oral Diseases follows current HIPAA guidelines for the protection of patient/subject privacy. If an individual pictured in a digital image or photograph can be identified, his or her permission is required to publish the image. The corresponding author must either submit a letter signed by the patient authorizing Oral Diseases to publish the image/photo, or complete the 'Standard Release Form for photographic consent' available at the top of this page or by clicking the “instructions and Forms” link on the submission site. The approval must be received by the Editorial Office prior to final acceptance of the manuscript for publication. Otherwise, the image/photo must be altered such that the individual cannot be identified (black bars over eyes, tattoos, scars, etc.). Oral Diseases will not publish patient photographs that will in any way allow the patient to be identified, unless the patient has given their express consent.

Editors reserve the right to reject papers if there are doubts as to whether appropriate procedures have been used.

Animal Study: When experimental animals are used the methods section must clearly indicate that adequate measures were taken to minimize pain or discomfort. Experiments should be carried out in accordance with the Guidelines laid down by the National Institute of Health (NIH) in the USA regarding the care and use of animals for experimental procedures or with the European Communities Council Directive of 24 November 1986 (86/609/EEC) and in accordance with local laws and regulations.

2.3 Clinical Trials

Clinical Trials should be reported using the CONSORT guidelines available at **www.consort-statement.org**. A **CONSORT checklist** and **flowchart** should also be included in the submission material. Clinical trials can be registered in any free, public clinical trials registry such as **http://www.clinicaltrials.gov** or **http://isrctn.org/**. A list of further registries is available at **http://www.who.int/ictrp/network/primary/en/**. As stated in an editorial published in *Oral Diseases* **(12:217-218), 2006)**, all manuscripts reporting results from a clinical trial must indicate that the trial was fully registered at a readily accessible website. The clinical trial registration number and name of the trial register will be published with the paper.

2.4 DNA Sequences and Crystallographic Structure Determinations

Papers reporting protein or DNA sequences and crystallographic structure determinations will not be accepted without a Genbank or Brookhaven accession number, respectively. Other supporting data sets must be made available on the publication date from the authors directly.

2.5 Conflict of Interest and Source of Funding

All sources of institutional, private and corporate financial support for the work within the manuscript must be fully acknowledged, and any potential grant holders should be listed. Authors are also required to disclose any possible conflict of interest. These include financial (for example patent, ownership, stock ownership, consultancies, speaker's fee). Information on sources of funding and any potential conflict of interest should be disclosed at submission under the heading "Acknowledgements".

2.6 Appeal of Decision

The decision on a paper is final and cannot be appealed.

2.7 Avoiding allegations of plagiarism

The journal to which you are submitting your manuscript employs text matching software (iThenticate) to ensure against plagiarism. By submitting your manuscript to this journal you accept that your manuscript may be screened for plagiarism against previously published work. Authors should consider whether their manuscript may raise concerns via iThenticate, which will signal whether a paper is likely in any way to be plagiarized in a formal sense. iThenticate will also, however, signal whether a paper may be plagiarized by repeating work of the submitting authors and thus be regarded as duplicate or redundant publication. Experience shows that, on occasion, large sections of submitted manuscripts can be close to verbatim in

word choice from that seen in other papers from the authors' group. This has nothing to do with simple repetition of names/affiliations, but does involve common (not necessarily "standard") phrases that are more appropriately referenced instead of repeating. Alternatively, they can be rephrased differently. Previously published results, including numerical information and figures or images, should be labeled to make it clear where they were previously reported. Papers that present new analyses of results that have already been published (for example, subgroup analyses) should identify the primary data source, and include a full reference to the related primary publications. *Oral Diseases* will review and publish accepted mansucripts that report data included in conference proceedings in abstract form. In such cases, authors must be clear to readers that part of all of the manuscript's data have already been published in abstract form by so indicating using a footnote to the title that states the confrence proceedings in which the relevant abstract was published. For full guidance on text matching and plagiarism, please refer to Section 3 ('Research Integrity') of Wiley's Ethics Guidelines at **https://authorservices.wiley.com/ethics-guidelines/index.html**.

2.8 Permissions

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3. MANUSCRIPT SUBMISSION PROCEDURE

Oral Diseases only accepts online submission of manuscripts. Manuscripts should be submitted at the online submission site: **https://wiley.atyponrex.com/journal/ODI**. Complete instructions for submitting a manuscript are available at the site upon creating an account. Assistance for submitting papers can be sought with the editorial assistant at: odiedoffice@wiley.com.

Data protection: By submitting a manuscript to or reviewing for this publication, your name, email address, and affiliation, and other contact details the publication might require, will be used for the regular operations of the publication, including, when necessary, sharing with the publisher (Wiley) and partners for production and publication. The publication and the

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3.1. Manuscript Files Accepted

Manuscripts should be uploaded as Word (.doc/.docx) or Rich Text Format (.rft) files (not write-protected) plus separate figure files. GIF, JPEG, PICT or Bitmap files are acceptable for submission, but only high-resolution TIF or EPS files are suitable for printing. The files will be automatically converted to HTML and PDF on upload and will be used for the review process. The text file must contain the entire manuscript including title page, abstract, text, references, acknowledgements, tables, and figure legends, but no embedded figures. In the text file, please reference figures as for instance 'Figure 1', 'Figure 2' etc to match the tag name you choose for individual figure files uploaded. Manuscripts should be formatted as described in the Author Guidelines below.

3.2. Transparent Peer Review

This journal is participating in a Peer Review Transparency initiative. By submitting to this journal, authors agree that the reviewer reports, their responses, and the editor's decision letter will be linked from the published article to where they appear on **Publons** in the case that the article is accepted. Authors have the opportunity to opt out during submission, and reviewers may remain anonymous unless they would like to sign their report. Read more about this initiative **here**.

3.3. Suggest a Reviewer

Oral Diseases attempts to keep the review process as short as possible to enable rapid publication of new scientific data. In order to facilitate this process, you must suggest the names and current e-mail addresses of from 2-4 potential reviewers whom you consider capable of reviewing your manuscript in an unbiased way.

3.4. Suspension of Submission Mid-way in the Submission Process

You may suspend a submission at any phase before clicking the 'Submit' button and save it to submit later. The manuscript can then be located under 'Unsubmitted Manuscripts' and you can click on 'Continue Submission' to continue your submission when you choose to.

3.5. E-mail Confirmation of Submission

After submission you will receive an e-mail to confirm receipt of your manuscript. If you do not receive the confirmation e-mail after 24 hours, please check your e-mail address carefully in the system. If the e-mail address is correct please contact your IT department. The error may be caused by some sort of spam filtering on your e-mail server. Also, the e-mails should be received if the IT department adds our e-mail server (uranus.scholarone.com) to their whitelist.

3.6. Manuscript Status

The average time from submission to first decision for manuscripts submitted to *Oral Diseases* is 20 days. You can access ScholarOne Manuscripts any time to check your 'Author Centre' for the status of your manuscript. The Journal will inform you by e-mail once a decision has been made.

3.7. Submission of Revised Manuscripts

To upload a revised manuscript, locate your manuscript under 'Manuscripts with Decisions' and click on 'Submit a Revision'. Please remember to delete any old files uploaded when you upload your revised manuscript.

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Original Research Articles: Manuscripts reporting laboratory investigations, well-designed and controlled clinical research, and analytical epidemiology are invited. Studies related to aetiology, pathogenesis, diagnosis, prevention and treatment are all of interest, but all papers must be based on rigorous hypothesis-driven research. Areas of interest include diseases affecting any structures of the mouth; cancer and pre-cancerous conditions; saliva and salivary glands; bone and hard tissues; relationship between oral, periodontal, and dental conditions and general health; pain; behavioral dentistry; chemosensory, developmental, geriatric, and motor disorders.

Randomised trials must adhere to the **CONSORT guidelines**, and a **CONSORT checklist** and **flowchart** must be submitted with such papers. Please also refer to the notes under section 2.3 above.
Oral Diseases supports the ALLTRIALS initiative and encourages authors submitting manuscripts reporting a clinical trial to register the trials in any of the following free, public clinical trials registries: **www.clinicaltrials.gov**, **http://clinicaltrials.ifpma.org/clinicaltrials/**, **http://isrctn.org/**. The clinical trial registration number and name of the trial register will then be published with the paper.

Observational studies must adhere to the **STROBE guidelines**, and a **STROBE checklist** must be submitted with such papers. Diagnostic accuracy studies must adhere to the **STARD guidelines**, and a **STARD checklist** must be submitted with such papers.

Review Papers: *Oral Diseases* commissions review papers and also welcomes uninvited reviews. Systematic reviews with or without meta-analyses must adhere to the **PRISMA guidelines**, and a **PRISMA checklist** and **flowchart** must be submitted with such papers. The word limit for Review Papers is 4,000 words, with a maximum of two tables or images and 50 references.

Clinical Image: Clinical Images illustrate a brief presentation of a peculiar case. These include a clinical description, excellent clinical pictures, a multiple choice quiz on the putative diagnosis (no more than 4-5 options), the final diagnosis and a brief discussion, followed by the patient outcome. Clinical Images should be structured as follows:

1.

    1. TITLE describing the case without mentioning the diagnosis
    2. CASE REPORT: 120 words
    3. CASE IMAGE(S): No more than 2 clinical pictures of the case (the legend must not mention the diagnosis). Label image(s) Figure 1 or Figure 1A and 1B.
    4. QUIZ: Provide no more than 4 possible answers. See example here:

WHAT IS YOUR DIAGNOSIS?

Based on the patient's history, physical examination, and laboratory findings, which one of the following is the most suspicious diagnosis?

        1.

            1. Answer A
            2. Answer B
            3. Answer C
            4. Answer D

2.

    1. 5. DIAGNOSIS: Provide the answer along with a 1-2 sentence explanation followed by the subsequent discussion. (350 words).
    2. 6. DIAGNOSIS IMAGE: One picture clarifying the diagnosis (i.e. a histological picture, images, micro, blood tests, ...). Label this Figure
    3. 7. OUTCOME: 1-2 sentences.

4. 8. AUTHOR CONTRIBUTION section: Required.
5. 9. PATIENT CONSENT section: Use standard wording, “The patient reported in this manuscript provided written informed consent for the publication of the case details."
6. 10. CONFLICT OF INTEREST STATEMENTS (COIS): Required section. Default text when no conflicts exist reads “All authors have no conflicts of interest to disclose.”
7. 11. ACKNOWLEDGEMENTS: Optional section.
8. 12. KEYWORDS: Not required as they may give away the answer.
9. 13. FUNDING: Not required for this article type.
10. 14. REFERENCES: Maximum 10.

Letters to the Editors: Letters, if of broad interest, are encouraged. They may deal with material in papers published in *Oral Diseases* or they may raise new issues, but should have important implications. Only one letter may be submitted by any single author or group of authors on any one published paper. Letters to the Editors should not include an abstract and are limited to 500 words, with a maximum of 1 figure and 10 references.

Case Reports: *Oral Diseases* does not accept case reports and instead recommends that authors submit to ***Clinical Case Reports*** an open access journal published by Wiley.

Meeting Reports: Will be considered by the editors for publication only if they are of wide and significant interest.

Short Communications: These are brief papers of any topic within the scope of *Oral Diseases*about significant and novel advances that are complete in research endeavor but not suitable for full publications. Short Communications should not include an abstract and are limited to 1000 words, with a maximum of 3 figures and 20 references. Short Communications **should not** be structured into sections.

Invited Reviews: These may be submitted by invitation of the Senior Editors only, and consist of around 2500-2750 words, with a maximum of one table or image and 25 references.

Commentaries: These may be submitted by invitation of the Senior Editors only.

Invited Editorials: These may be submitted by invitation of the Senior Editors only.

Invited Book Reviews: These may be submitted by invitation of the Senior Editors only.

5. MANUSCRIPT FORMAT AND STRUCTURE

Oral Diseases now offers Free Format submission for a simplified and streamlined submission process.

Before you submit, you will need:

- Your manuscript: this should be an editable file including text, figures, and tables, or separate files – whichever you prefer. All required sections should be contained in your manuscript, including abstract, introduction, methods, results, and conclusions. Figures and tables should have legends. Figures should be uploaded in the highest resolution possible. References may be submitted in any style or format, as long as it is consistent throughout the manuscript. Supporting information should be submitted in separate files. If the manuscript, figures or tables are difficult for you to read, they will also be difficult for the editors and reviewers, and the editorial office will send it back to you for revision. Your manuscript may also be sent back to you for revision if the quality of English language is poor.
- An ORCID ID, freely available at https://orcid.org. *(Why is this important? Your article, if accepted and published, will be attached to your ORCID profile. Institutions and funders are increasingly requiring authors to have ORCID IDs.)*
- The title page of the manuscript, including:
    - Your co-author details, including affiliation and email address. *(Why is this important? We need to keep all co-authors informed of the outcome of the peer review process.)*
    - Statements relating to our ethics and integrity policies, which may include any of the following *(Why are these important? We need to uphold rigorous ethical standards for the research we consider for publication):*
        - data availability statement

- funding statement
- conflict of interest disclosure
- ethics approval statement
- patient consent statement
- permission to reproduce material from other sources
- clinical trial registration

If you are invited to revise your manuscript after peer review, the journal will also request the revised manuscript to be formatted according to journal requirements as described below.

5.1. Page Charge

IMPORTANT: Please note that articles exceeding 8 published pages, including title page, abstract, references, table/figure legends and tables and figures, are subject to a charge of GBP 70 per additional page. As a guide, one published page amounts approximately to 850 words, or two to four small tables/figures. Additional supplementary material (including text and figures), which does not fit within the page limits, can be published online only as supporting information.

Open Access Article Processing Charges (APCs) are billed separately from additional page charges. If your institution or funder is covering your APC, please refer to their guidelines on what additional costs they may be able to cover. For more information on this journal's APCs, please see the Open Access page.

For Special Issue content, **only,** the excessing page charges will be waived for invited reviews that often require greater length, but we still strongly recommend the invited authors to follow the formatting requirements detialed here.

5.2. Format

Language: Authors should write their manuscripts in British English using an easily readable style. Authors whose native language is not English should have a native English speaker read and correct their manuscript. Spelling and phraseology should conform to standard British usage and should be consistent throughout the paper. A list of independent suppliers of editing services can be found at **http://authorservices.wiley.com/bauthor/english_language.asp**. All services are paid for and arranged by the author, and use of one of these services does not guarantee acceptance or preference for publication.

Presentation: Authors should pay special attention to the presentation of their findings so that they may be communicated clearly. The background and hypotheses underlying the study as well as its main conclusions should be clearly explained. Titles and abstracts especially should be written in language that will be readily intelligible to any scientist.

Technical jargon: should be avoided as much as possible and clearly explained where its use is unavoidable.

Abbreviations: Oral Diseases adheres to the conventions outlined in Units, Symbols and Abbreviations: A Guide for Medical and Scientific Editors and Authors. Non-standard abbreviations must be used three or more times and written out completely in the text when first used.

5.3. Structure: All papers submitted to *Oral Diseases* should include:

- Title Page
- Structured Abstract
- Main text
- References
- (Figures)
- (Figure Legends)
- (Tables)

Title Page: should be part of the manuscript uploaded for review and include:

- A title of no more than 100 characters including spaces
- A running title of no more than 50 characters
- 3-6 keywords
- Complete names and institutions for each author
- Corresponding author's name, address, email address and fax number
- Date of submission (and revision/resubmission)

Abstract: is limited to 200 words in length and should contain no abbreviations. The abstract should be included in the manuscript document uploaded for review as well as separately where specified in the submission process. The abstract should convey the essential purpose and message of the paper in an abbreviated form. Structured abstract is an abstract divided into distinct sections such as Objective, Methods, Results, and Conclusions. It is typically maximum 250 words containing no abbreviations. The abstract should be included in the manuscript document uploaded for review as well as separately where specified during the submission process.

The Main Text of Original Research Articles should be organised as follows

Introduction: should be focused, outlining the historical or logical origins of the study and not summarize the results; exhaustive literature reviews are inappropriate. It should close with the explicit statement of the specific aims of the investigation.

Materials and Methods must contain sufficient detail such that, in combination with the references cited, all clinical trials and experiments reported can be fully reproduced. As a condition of publication, authors are required to make materials and methods used freely available to academic researchers for their own use. This includes antibodies and the constructs used to make transgenic animals, although not the animals themselves. Other supporting data sets must be made available on the publication date from the authors directly.

(i) Clinical trials: As noted above, these should be reported using the CONSORT guidelines available at **www.consort-statement.org**. A **CONSORT checklist** should also be included in the submission material. Clinical trials can be registered in any of the following free, public clinical trials registries: **www.clinicaltrials.gov**, **http://clinicaltrials.ifpma.org/clinicaltrials/**, **http://isrct**

n.org/.As stated in an editorial published in *Oral Diseases* (12:217-218), 2006), all manuscripts reporting results from a clinical trial must indicate that the trial was fully registered at a readily accessible website. The clinical trial registration number and name of the trial register will be published with the paper.

(ii)Experimental subjects: As noted above, experimentation involving human subjects will only be published if such research has been conducted in full accordance with ethical principles, including the World Medical Association **Declaration of Helsinki** (version 2002) and the additional requirements, if any, of the country where the research has been carried out. Manuscripts must be accompanied by a statement that the experiments were undertaken with the understanding and written consent of each subject and according to the above mentioned principles. A statement regarding the fact that the study has been independently reviewed and approved by an ethical board should also be included.Editors reserve the right to reject papers if there are doubts as to whether appropriate procedures have been used. When experimental animals are used the methods section must clearly indicate that adequate measures were taken to minimize pain or discomfort. Experiments should be carried out in accordance with the Guidelines laid down by the National Institute of Health (NIH) in the USA regarding the care and use of animals for experimental procedures or with the European Communities Council Directive of 24 November 1986 (86/609/EEC) and in accordance with local laws and regulations.

***(iii) Suppliers*:** Suppliers of materials should be named and their location (town, state/county, country) included.

Results: should present the observations with minimal reference to earlier literature or to possible interpretations.

Discussion: may usually start with a brief summary of the major findings, but repetition of parts of the abstract or of the results sections should be avoided. The section should end with a brief conclusion and a comment on the potential clinical relevance of the findings. Statements and interpretation of the data should be appropriately supported by original references.

Acknowledgements: Should be used to provide information on sources of funding for the research, any potential conflict of interest and to acknowledge contributors to the study that do not qualify as authors. All sources of institutional, private and corporate financial support for

the work within the manuscript must be fully acknowledged, and any potential grant holders should be listed. Acknowledgements should be brief and should not include thanks to anonymous referees and editors. Where people are acknowledged, a cover letter demonstrating their consent must be provided.

5.4. References

References should be prepared according to the *Publication Manual of the American Psychological Association* (6th edition). This means in-text citations should follow the author-date method whereby the author's last name and the year of publication for the source should appear in the text, for example, (Jones, 1998). For references with three to five authors, all authors should be listed only on the first occurrence of the in-text citation, and in subsequent in-text occurrences only the first author should be listed followed by '*et al.*'. The complete reference list should appear alphabetically by name at the end of the paper.

A sample of the most common entries in reference lists appears below. Please note that a DOI should be provided for all references where available. For more information about APA referencing style, please refer to the **APA website**. Please note that for journal articles, issue numbers are not included unless each issue in the volume begins with page one.

Journal article

Example of reference with 2 to 7 authors

Beers, S. R., & De Bellis, M. D. (2002). Neuropsychological function in children with maltreatment-related posttraumatic stress disorder. *The American Journal of Psychiatry, 159*, 483–486. doi: 10.1176/appi.ajp.159.3.483

Ramus, F., Rosen, S., Dakin, S. C., Day, B. L., Castellote, J. M., White, S., & Frith, U. (2003). Theories of developmental dyslexia: Insights from a multiple case study of dyslexic adults. *Brain, 126*(4), 841–865. doi: 10.1093/brain/awg076

Example of reference with more than 7 authors

Rutter, M., Caspi, A., Fergusson, D., Horwood, L. J., Goodman, R., Maughan, B., … Carroll, J. (2004). Sex differences in developmental reading disability: New findings from 4 epidemiological studies. *Journal of the American Medical Association, 291*(16), 2007–2012. doi: 10.1001/jama.291.16.2007

Book edition

Bradley-Johnson, S. (1994). *Psychoeducational assessment of students who are visually impaired or blind: Infancy through high school* (2nd ed.). Austin, TX: Pro-ed.

5.5. Tables, Figures and Figure Legends

Figures: All figures and artwork must be provided in electronic format. Please save vector graphics (e.g. line artwork) in Encapsulated Postscript Format (EPS) and bitmap files (e.g. half-tones) or clinical or in vitro pictures in Tagged Image Format (TIFF).

Detailed information on our digital illustration standards can be found at **http://authorservices.wiley.com/bauthor/illustration.asp**.

Check your electronic artwork before submitting it: **http://authorservices.wiley.com/bauthor/eachecklist.asp**.

Unnecessary figures and parts (panels) of figures should be avoided: data presented in small tables or histograms, for instance, can generally be stated briefly in the text instead. Figures should not contain more than one panel unless the parts are logically connected.

Figures divided into parts should be labelled with a lower-case, boldface, roman letter, a, b, and so on, in the same type size as used elsewhere in the figure. Lettering in figures should be in lower-case type, with the first letter capitalized. Units should have a single space between the number and unit, and follow SI nomenclature common to a particular field. Unusual units and abbreviations should be spelled out in full or defined in the legend. Scale bars should be used rather than magnification factors, with the length of the bar defined in the legend rather than on the bar itself. In general visual cues (on the figures themselves) are preferred to verbal explanations in the legend (e.g. broken line, open red triangles etc).

Guidelines for Cover Submissions

If you would like to send suggestions for artwork related to your manuscript to be considered to appear on the cover of the journal, please **follow these general guidelines.**

6. AFTER ACCEPTANCE

Wiley Author Services

When an accepted article is received by Wiley's production team, the corresponding author will receive an email asking them to login or register with Wiley Author Services. You will be asked to sign a publication license at this point as well as pay for any applicable APCs.

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Proofs must be returned to the Production Editor within **three days** of receipt. As changes to proofs are costly, we ask that you only correct typesetting errors. Excessive changes made by the author in the proofs, excluding typesetting errors, will be charged separately. Other than in exceptional circumstances, all illustrations are retained by the publisher. Please note that the author is responsible for all statements made in their work, including changes made by the copy editor.

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ANEXO B

Capítulo III

Diretrizes para publicação no *Journal of Endodontics*

GUIDE FOR AUTHORS

1. Introduction

The *Journal of Endodontics* is owned by the American Association of Endodontists. Submitted manuscripts must pertain to endodontics and may be original research (eg, clinical trails, basic science related to the biological aspects of endodontics, basic science related to endodontic techniques, case reports, or review articles related to the scientific or applied aspects of endodontics). Clinical studies using CONSORT methods or systematic reviews using meta-analyses are particularly encouraged. Authors of potential review articles are encouraged to first contact the Editor during their preliminary development via e-mail at *JEndodontics@UTHSCSA.edu*. Manuscripts submitted for publication must be submitted solely to *JOE*. They must not be submitted for consideration elsewhere or be published elsewhere.

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2. Before you begin

Ethics in publishing

Please see our information on Ethics in publishing.

Human and Animal Rights

If the work involves the use of animal or human subjects, the author should ensure that the work described has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for experiments involving humans http:// www.wma.net/en/30publications/10policies/ b3/index.html; EU Directive 2010/63/EU for animal experiments http://ec.europa.eu/environment/chemicals/lab_animals/legislation_en.htm; Uniform Requirements for manuscripts submitted to Biomedical journals http://www.icmje.org. Authors should include a statement in the manuscript that informed consent was obtained for experimentation with human subjects. The privacy rights of human subjects must always be observed.

Submission Declaration

Submission of an article implies that the work described has not been published previously (except in the form of an abstract or as part of a published lecture or academic thesis or as an electronic preprint, see http://www.elsevier.com/postingpolicy), that it is not under consideration for publication elsewhere, that its publication is approved by all authors and tacitly or explicitly by the responsible authorities where the work was carried out, and that, if accepted, it will not be published elsewhere including electronically in the same form, in English or in any other language, without the written consent of the copyright-holder

Declaration of generative AI in scientific writing

The below guidance only refers to the writing process, and not to the use of AI tools to analyse and draw insights from data as part of the research process.

Where authors use generative artificial intelligence (AI) and AI-assisted technologies in the writing process, authors should only use these technologies to improve readability and language. Applying the technology should be done with human oversight and control, and authors should carefully review and edit the result, as AI can generate authoritative-sounding output that can be incorrect, incomplete or biased. AI and AI-assisted technologies should not be listed as an author or co-author, or be cited as an author. Authorship implies responsibilities and tasks that can only be attributed to and performed by humans, as outlined in Elsevier's AI policy for authors.

Authors should disclose in their manuscript the use of AI and AI-assisted technologies in the writing process by following the instructions below. A statement will appear in the published work. Please note that authors are ultimately responsible and accountable for the contents of the work.

Disclosure instructions

Authors must disclose the use of generative AI and AI-assisted technologies in the writing process by adding a statement at the end of their manuscript in the core manuscript file, before the References list. The statement should be placed in a new section entitled 'Declaration of Generative AI and AI-assisted technologies in the writing process'

Statement: During the preparation of this work the author(s) used [NAME TOOL / SERVICE] in order to [REASON]. After using this tool/service, the author(s) reviewed and edited the content as needed and take(s) full responsibility for the content of the publication

This declaration does not apply to the use of basic tools for checking grammar, spelling, references etc. If there is nothing to disclose, there is no need to add a statement.

Use of inclusive language

Inclusive language acknowledges diversity, conveys respect to all people, is sensitive to differences, and promotes equal opportunities. Content should make no assumptions about the beliefs or commitments of any reader; contain nothing which might imply that one individual is superior to another on the grounds of age, gender, race, ethnicity, culture, sexual orientation, disability or health condition; and use inclusive language throughout. Authors should ensure that writing is free from bias, stereotypes, slang, reference to dominant culture and/or cultural assumptions. We advise to seek gender neutrality by using plural nouns ("clinicians, patients/clients") as default/wherever possible to avoid using "he, she," or "he/she." We recommend avoiding the use of descriptors that refer to personal attributes such as age, gender, race, ethnicity, culture, sexual orientation, disability or health condition unless they are relevant and valid. When coding terminology is used, we recommend to avoid offensive or exclusionary terms such as "master", "slave", "blacklist" and "whitelist". We suggest using alternatives that are more appropriate and (self-) explanatory such as "primary", "secondary", "blocklist" and "allowlist". These guidelines are meant as a point of reference to help identify appropriate language but are by no means exhaustive or definitive.

Reporting sex-and gender-based analyses

Reporting guidance

For research involving or pertaining to humans, animals or eukaryotic cells, investigators should integrate sex and gender-based analyses (SGBA) into their research design according to funder/sponsor requirements and best practices within a field. Authors should address the sex and/or gender dimensions of their research in their article. In cases where they cannot, they should discuss this as a limitation to their research's generalizability. Importantly, authors should explicitly state what definitions of sex and/or gender they are applying to enhance the precision, rigor and reproducibility of their research and to avoid ambiguity or conflation of terms and the constructs to which they refer (see Definitions section below). Authors can refer to the Sex and Gender Equity in Research (SAGER) guidelines and the SAGER guidelines checklist. These offer systematic approaches to the use and editorial review of sex and gender information in study design, data analysis, outcome reporting and research interpretation - however, please note there is no single, universally agreed-upon set of guidelines for defining sex and gender.

Definitions

Sex generally refers to a set of biological attributes that are associated with physical and physiological features (e.g., chromosomal genotype, hormonal levels, internal and external anatomy). A binary sex categorization (male/female) is usually designated at birth ("sex assigned at birth"), most often based solely on the visible external anatomy of a newborn. Gender generally refers to socially constructed roles, behaviors, and identities of women, men and gender-diverse people that occur in a historical and cultural context and may vary across societies and over time. Gender influences how people view themselves and each other, how they behave and interact and how power is distributed in society. Sex and gender are often incorrectly portrayed as binary (female/male or woman/man) and unchanging whereas these constructs actually exist along a spectrum and include additional sex categorizations and gender identities such as people who are intersex/have differences of sex development (DSD) or identify as non-binary. Moreover, the terms "sex" and "gender" can be ambiguous--thus it is important for authors to define the manner in which they are used. In addition to this definition guidance and the SAGER guidelines, the resources on this page offer further insight around sex and gender in research studies.

Author contributions

For transparency, we encourage corresponding authors to provide co-author contributions to the manuscript using the relevant CRediT roles. The CRediT taxonomy includes 14 different roles describing each contributor's specific contribution to the scholarly output. The roles are: Conceptualization; Data curation; Formal analysis; Funding acquisition; Investigation; Methodology; Project administration; Resources; Software; Supervision; Validation; Visualization; Roles/Writing - original draft; and Writing - review & editing. Note that not all roles may apply to every manuscript, and authors may have contributed through multiple roles. More details and an example.

Changes to authorship

Authors are expected to consider carefully the list and order of authors **before** submitting their manuscript and provide the definitive list of authors at the time of the original submission. Any addition, deletion or rearrangement of author names in the authorship list should be made only **before** the manuscript has been accepted and only if approved by the journal Editor. To request such a change, the Editor must receive the following from the **corresponding author**: (a) the reason for the change in author list and (b) written confirmation (e-mail, letter) from all authors that they agree with the addition, removal or rearrangement. In the case of addition or removal of authors, this includes confirmation from the author being added or removed.

Only in exceptional circumstances will the Editor consider the addition, deletion or rearrangement of authors **after** the manuscript has been accepted. While the Editor considers the request, publication of the manuscript will be suspended. If the manuscript has already been published in an online issue, any requests approved by the Editor will result in a corrigendum.

Reporting clinical trials

Randomized controlled trials should be presented according to the CONSORT guidelines. At manuscript submission, authors must provide the CONSORT checklist accompanied by a flow diagram that illustrates the progress of patients through the trial, including recruitment, enrolment, randomization, withdrawal and completion, and a detailed description of the randomization procedure. The CONSORT checklist and template flow diagram are available online.

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Language

Please write your text in good English (American or British usage is accepted, but not a mixture of these). Authors who feel their English language manuscript may require editing to eliminate possible grammatical or spelling errors and to conform to correct scientific English may wish to use the Language Editing service available from Elsevier's Language Services.

Submission

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Submit Your Article

Please submit your article via https://www.editorialmanager.com/JOE.

3. Preparation

General Points on Composition

Authors are strongly encouraged to analyze their final draft with both software (eg, spelling and grammar programs) and colleagues who have expertise in English grammar. References listed at the end of this section provide a more extensive review of rules of English grammar and guidelines for writing a scientific article. Always remember that clarity is the most important feature of scientific writing. Scientific articles must be clear and precise in their content and concise in their delivery because their purpose is to inform the reader. The Editor reserves the right to edit all manuscripts or to reject those manuscripts that lack clarity or precision or that

have unacceptable grammar or syntax. The following list represents common errors in manuscripts submitted to the Journal of Endodontics:

a. The paragraph is the ideal unit of organization. Paragraphs typically start with an introductory sentence that is followed by sentences that describe additional detail or examples. The last sentence of the paragraph provides conclusions and forms a transition to the next paragraph. Common problems include one-sentence paragraphs, sentences that do not develop the theme of the paragraph (see also section "c," below), or sentences with little to no transition within a paragraph.

b. Keep to the point. The subject of the sentence should support the subject of the paragraph For example, the introduction of authors' names in a sentence changes the subject and lengthens the text. In a paragraph on sodium hypochlorite, the sentence, "In 1983, Langeland et al, reported that sodium hypochlorite acts as a lubricating factor during instrumentation and helps to flush debris from the root canals" can be edited to: "Sodium hypochlorite acts as a lubricant during instrumentation and as a vehicle for flushing the generated debris (Langeland et al, 1983)." In this example, the paragraph's subject is sodium hypochlorite and sentences should focus on this subject.

c. Sentences are stronger when written in the active voice, that is, the subject performs the action. Passive sentences are identified by the use of passive verbs such as "was," "were," "could," etc. For example: "Dexamethasone was found in this study to be a factor that was associated with reduced inflammation," can be edited to: "Our results demonstrated that dexamethasone reduced inflammation." Sentences written in a direct and active voice are generally more powerful and shorter than sentences written in the passive voice.

d. Reduce verbiage. Short sentences are easier to understand. The inclusion of unnecessary words is often associated with the use of a passive voice, a lack of focus, or run-on sentences. This is not to imply that all sentences need be short or even the same length. Indeed, variation in sentence structure and length often helps to maintain reader interest. However, make all words count. A more formal way of stating this point is that the use of subordinate clauses adds variety and information when constructing a paragraph. (This section was written deliberately with sentences of varying length to illustrate this point.)

e. Use parallel construction to express related ideas. For example, the sentence, "Formerly, endodontics was taught by hand instrumentation, while now rotary instrumentation is the

common method," can be edited to "Formerly, endodontics was taught using hand instrumentation; now it is commonly taught using rotary instrumentation." The use of parallel construction in sentences simply means that similar ideas are expressed in similar ways, and this helps the reader recognize that the ideas are related.

f. Keep modifying phrases close to the word that they modify. This is a common problem in complex sentences that may confuse the reader. For example, the statement, "Accordingly, when conclusions are drawn from the results of this study, caution must be used," can be edited to "Caution must be used when conclusions are drawn from the results of this study."

g. To summarize these points, effective sentences are clear and precise, and often are short, simple and focused on one key point that supports the paragraph's theme.

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