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Prevalence of persistent pain after endodontic treatment: a systematic review and meta-analysis

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Aim: To determine the prevalence of persistent pain in endodontic patients. **Methods:** Six electronic databases (EMBASE, LILACS, LIVIVO, PubMed/MEDLINE, Scopus, and Web of Science) were searched, along with the gray literature (Google Scholar, ProQuest Dissertations and Theses). The review used a random-effects model for meta-analysis of proportions and assessed the risk of bias based on the Joanna Briggs Institute Critical Appraisal tool. **Results:** The review included 16 articles (seven cohort studies and nine cross-sectional studies) published in English from 1994 to 2022. Fifteen of them were selected for meta-analysis. The combined prevalence estimate was 5% (95% CI = 0.01 – 0.10). The risk of bias was moderate in four studies and low in the others. **Conclusion:** The estimated prevalence of persistent pain after endodontic treatment was approximately one in every 25 patients.

Keywords: Root canal therapy. Pain. Tooth. Systematic reviews as topic.

Introduction

Endodontic treatment addresses conditions that may affect the pulp, aiming to preserve the function of the treated tooth, with the ultimate goal of promoting periapical tissue regeneration and restoring the function of the dental element[1-3]. This procedure is among the most frequently performed, with a prevalence of approximately 60% in the population[4]. The outcome of initial endodontic treatment has been widely investigated, especially regarding the persistence of pain after treatment completion[5,6]. It is estimated that between 5% and 24% of patients undergoing endodontic treatment experience persistent pain[7].

Prolonged postoperative pain is relatively common after endodontic procedures[8]. However, a small portion of patients may experience persistent pain for months or even years after endodontic treatment[9-11]. Meta-analyses suggest a 5.4% prevalence of dental pain 6 months after treatment[3]. Observational studies report variations in prevalence, indicating 25% persistent pain between 5 and 14 months[12], 10% at 6 months[10], and 5% between 3 and 5 years after the procedure[11].

Postoperative pain may be influenced by factors such as over-instrumentation, irrigation solutions, infected debris, and bacteria in the periapical tissues[13]. It may also involve non-odontogenic causes, such as neuropathic pain resulting from nerve injuries during the endodontic procedure[8]. Non-odontogenic tooth pain can result from other structures, such as muscles, joints, the maxillary sinus, and adjacent cranial nerves, including trigeminal neuralgia[7]. Non-odontogenic causes include etiologies such as referred myofascial pain, headaches, neuropathic disorders, and other pathological conditions[3]. Orofacial pain can occur simultaneously with odontogenic pain[7]. However, these causes are often not easily distinguishable during clinical evaluation[10].

Factors associated with the development of persistent pain after endodontic treatment include preoperative dental pain, pain upon tooth percussion, preexisting chronic pain disorder, and a history of orofacial pain treatment[10]. The persistence of pain 6 months after endodontic treatment may require additional care, such as retreatments, medical consultations, and analgesics. Most studies on the prevalence of persistent pain have been conducted in specialized settings, which makes it difficult to compare with the results in general clinical practice[11].

A significant portion of referrals to endodontists involves the treatment of ongoing pain after beginning the endodontic treatment[14]. Quantifying the prevalence of persistent pain after endodontic treatment is essential for dentists and patients, as it contributes to a more informed approach regarding the risks and benefits of the treatment[3]. A systematic review and meta-analysis by Nixdorf et al.[3] (2010) measured the prevalence of persistent pain after endodontic treatment, highlighting the relevance of this phenomenon for patients health and quality of life. Klasser et al.[15] (2011) reviewed clinical information to update prevalence data. No recent reviews on the subject were found, although new studies have been published since the last review.

Hence, this review aimed to estimate the prevalence of persistent pain in patients undergoing endodontic treatment.

Material and Methods

This systematic review followed the guidelines of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA)[16].

Eligibility Criteria

The study used the PEOS strategy[17] to mediate the searches and study eligibility criteria:

- Population [P]: Individuals with all permanent teeth.
- Exposure [E]: Individuals undergoing surgical or nonsurgical endodontic treatment or retreatment, with at least 6 months of endodontic therapy follow-up.
- Outcome [O]: Self-reported persistent pain.
- Study design [S]: Observational studies.

The review included studies with adults who underwent endodontic treatment or retreatment, with a minimum follow-up of 6 months after the procedure, and whose outcome involved the assessment of self-reported persistent pain. It considered only observational studies, cohort studies, and cross-sectional studies.

The following exclusion criteria were taken into consideration:

1. Studies that included patients with comorbidities.
2. Studies involving individuals who did not undergo endodontic treatment or who were treated endodontically and reported pain in less than 6 months of endodontic therapy.
3. Studies with no pain assessment or that did not exclude odontogenic pain diagnosis.
4. Secondary studies, letters, books, conference abstracts, case reports, case series, case-control studies, opinion articles, technical articles, guidelines, randomized or non-randomized methods, and clinical trials.
5. Studies with unavailable full texts, even after requesting it from the authors.

Sources of Information and Search Strategy

All searches were conducted in May 2023, with an update in April 2024, in the EMBASE, Latin American and Caribbean Health Sciences Literature (LILACS), LIVIVO, PubMed/MEDLINE, Scopus, and Web of Science databases. The gray literature was also a source of information through Google Scholar and ProQuest Dissertations and Theses. MeSH terms were combined to search for potentially relevant articles in all databases (Table 1, Supplement). Furthermore, a manual search was conducted in the references of included studies, and an expert was consulted to check for any studies that had not been included. EndNote® software [EndNote® X7 Thomson Reuters, Philadelphia, PA] managed the references and removed duplicates.

Study Selection

The studies were selected in two phases. In the first phase, two researchers independently evaluated the relevance of each retrieved reference based on the title and abstract, using predefined inclusion and exclusion criteria. The articles selected in this phase were read in full during the second phase, following the same eligibility criteria. In both stages, a third researcher was consulted for the final decision regarding disagreements that could not be resolved by consensus between the two reviewers.

Rayyan [http://rayyan.qcri.org] ensured the review anonymity and allowed for an independent and confidential assessment. Additionally, the Kappa Coefficient of Agreement was calculated to ensure consistency among the reviewers. The study selection process only commenced when the Kappa value exceeded 0.8[18], indicating good agreement.

When data were missing or incomplete, efforts were made to contact the authors for important unpublished information. Authors were contacted via email three times, with 1-week intervals, whenever additional information was needed.

Data collection

The same two researchers who participated in the selection process independently extracted the following information using standardized electronic forms: surname of the first author, year of publication, study type, endodontic procedure, total number of teeth analyzed, teeth with persistent pain, and follow-up time.

Data Items

The review extracted data on the presence or absence of self-reported persistent pain, the maximum duration of pain recorded after endodontic treatment, and the source of the pain.

Assessment of Risk of Bias

The included studies were assessed for methodological quality using the Joanna Briggs Institute assessment[19]. "Yes" responses up to 49% of the total score indicated a high risk of bias in the study. When the study received "yes" responses between 50% and 69%, it was characterized as having a moderate risk of bias. "Yes" responses above 70% indicated a low risk of bias[20]. Funnel plots were generated using the RobVis Tool web app (https://mcguinlu.shinyapps.io/robvis/). Two reviewers conducted this process independently, and a third reviewer was involved in cases of disagreement.

Summary Method

The quantitative synthesis approached articles that observed the prevalence of odontogenic pain in a population initially unaffected by the outcome. Thus, a meta-analysis of proportions with a random-effects model was conducted using the DerSimonian and Laird estimator to calculate tau-squared[21]. Heterogeneity was assessed using Higgins' inconsistency index (I^2)[22]. The Freeman-Tukey double arcsine transformation was applied to ensure the data followed an approximately normal distribution[23]. Each

study's effect size was weighted to estimate their weight in the analysis, using the inverse variance method, and calculating the estimate based on the inverse proportion of the study's variance[23]. The study used 95% confidence intervals (CI), calculated with the Clopper-Pearson method. All analyses and graphs were conducted using the R programming language version 1.2.1335, with the RStudio interface (RStudio Inc., Boston, USA).

A sensitivity analysis enhanced the robustness of the estimates, including only studies with a sufficient sample size to ensure adequate statistical power. The necessary sample size was calculated based on the overall effect estimate, considering all studies included in the analysis. This calculation used a 2% margin of error and a 95% CI.

Results

Study Selection

This study searched the databases comprehensively, retrieving 1,924 articles. After removing duplicates, 1,782 records remained. The articles were then screened according to the inclusion criteria, selecting 31 articles for eligibility assessment. At this stage, 15 articles were excluded (Table 2), and 16 were included in the review (Figure 1).

Table 2. Excluded studies and reasons for exclusion (n=15)

Author, year	Reason for exclusion
Wright[24], 2000	2
Alonso and Nixdorf[25], 2006	2
Baad-Hansen[26], 2008	4
Israel et al.[27], 2003	2
Linn et al.[28], 2007	2
Ferreira et al.[29], 2020	2
Machado et al.[30], 2022	2
Pigg et al.[31], 2013	2
Renton[32], 2019	2
Sjögren et al.[33], 2019	3
Arias et al.[34], 2013	2
Macrae[35], 2008	2
Battrum et al.[36], 1996	2
Pasqualini et al.[37], 2012	2
Nasri-Heir et al.[17], 2015	2

*1. Studies that included patients with comorbidities; 2. Studies involving individuals who did not undergo endodontic treatment or who were treated endodontically and reported pain in less than 6 months of endodontic therapy; 3. Studies with no pain assessment or that did not exclude odontogenic pain diagnosis; 4. Secondary studies, letters, books, conference abstracts, case reports, case series, case-control studies, opinion articles, technical articles, guidelines, randomized or non-randomized methods, and clinical trials; 5. Studies with unavailable full texts, even after requesting it from the authors.

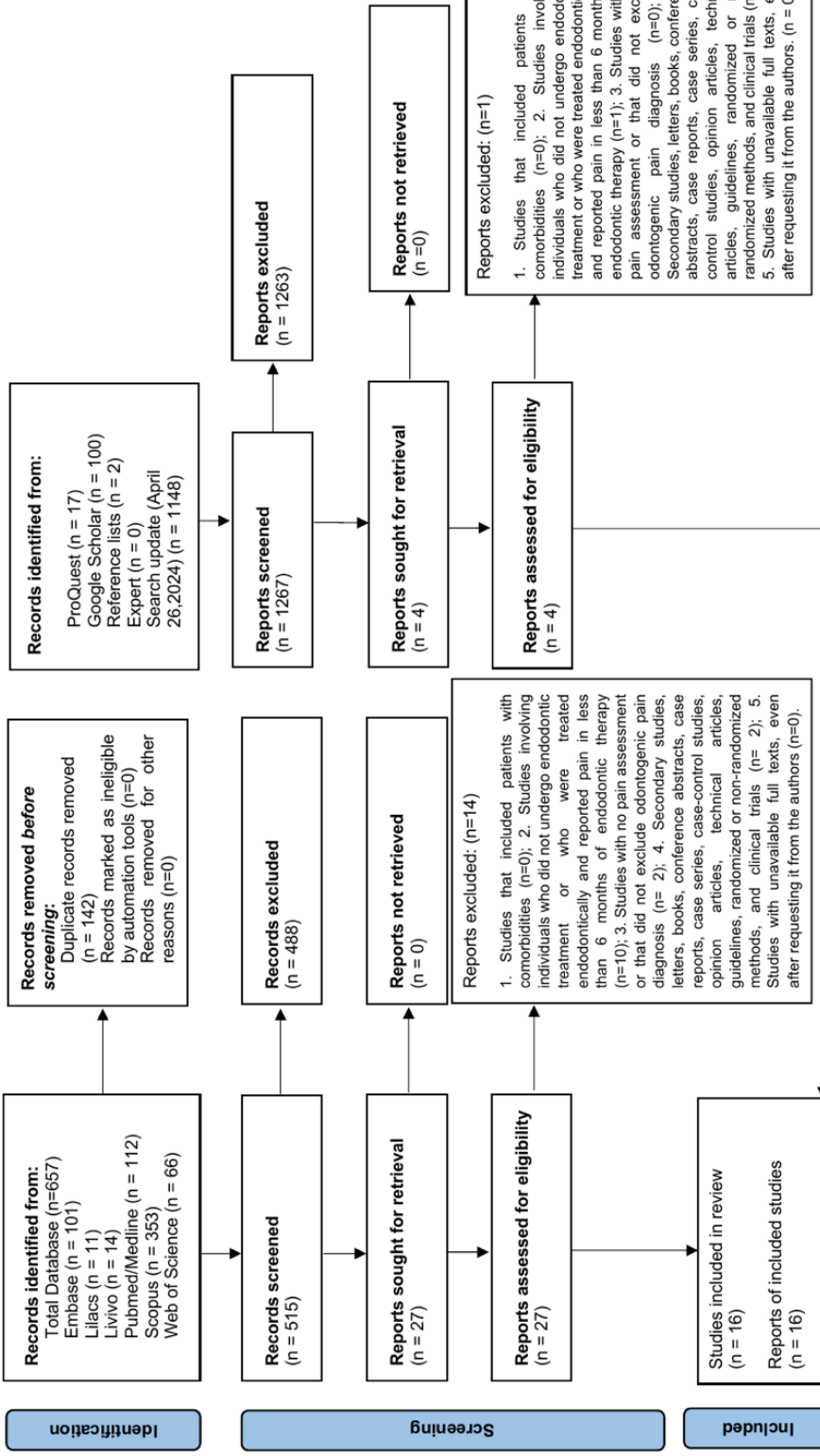

Figure 1. Flowchart of literature search and selection criteria.

Characteristics of the Studies

All 16 selected studies were published in English. They were conducted in various countries, including one study from Singapore, one from Sweden, one from Switzerland, one from the United Kingdom, one from Japan, one from Australia, five from Canada, and six from the United States. Their publication years ranged from 1994 to 2022, with an equivalent distribution across the last three decades.

Table 3. Characteristics of the included studies (n=16).

Author, years, country	Sample size and (sex)	Mean ages	Endodontic Procedure	Teeth Enrolled	Follow-up n (%)	Non-odontogenic tooth pain	Follow-up (y)	Study type
Abbott[14], 1994, Australia	100 26 (men) 74 (women)	39.3 years	Nonsurgical root canal therapy	110	110	110	NR	Cross-sectional
Daline et al.[9], 2020, United States	NR	NR	Initial nonsurgical root canal therapy	45	45 (100)	45	3,4	Cohort
Danin et al.[38], 1999, Sweden	10 4 (men) 6 (women)	55 years	Periapical Surgery	50	43 (86)	1	1-1	Cohort
de Chevigny et al.[39], 2008, Canada	137 63 (men) 74 (women)	NR	Initial nonsurgical root canal therapy	582	137 (24)	6	4-6	Cross-sectional
de Chevigny et al.[2], 2008, Canada	126 40 (men) 86 (women)	NR	Retreatment nonsurgical root canal therapy	477	122 (26)	6	4-6	Cross-sectional
Erdogan et al.[7], 2022, United States	35 7 (men) 28 (women)	48 years	Review of eletronic dental records	60	35 (83)	29	3,6	Cross-sectional
Farzaneh et al.[40], 2004, Canada	103 40 (men) 63 (women)	NR	Initial nonsurgical root canal therapy	523	103 (20)	0	4-6	Cohort
Farzaneh et al.[41], 2004, Canada	122 65 (men) 57 (women)	NR	Initial nonsurgical root canal therapy	422	122 (28)	3	4-6	Cohort
Klasser et al.[15], 2011, United States	18 9 (men) 9 (women)	50.6 years	Initial nonsurgical root canal therapy	250	18 (7)	18	3m-4y	Cross-sectional
Lobb et al.[42], 1996, United States	NR	NR	Initial nonsurgical root canal therapy	165	36 (21,8)	36	1	Cross-sectional

Continue

Continuation

Marquis et al.[5], 2006, Canada	132 54 (men) 78 (women)	21% patients with even 45 years; 77% over to 45 years	Initial nonsurgical root canal therapy	532	132 (25)	7	4-4	Cohort
Nixdorf et al.[43], 2015, United States	19 3 (men) 16 (women)	49 years	Initial nonsurgical root canal therapy	651	65 (10)	65	6-6	Cohort
Oshima et al.[8], 2009, Japan	16 3 (men) 13 (women)	46.8 years	Initial nonsurgical root canal therapy	271	16 (5.9)	16	9,8 m	Cross-sectional
Polycarpou et al.[44], 2005, United Kingdom	175 73 (men) 102 (women)	45,1 years	Combined Treatments	400	175 (44)	21	1-1	Cross-sectional
Vena et al.[11], 2014, United States	1257 528 (men) 729 (women)	51 years	Initial nonsurgical root canal therapy	1257	63 (5)	39	0,6-3,9	Cross-sectional
Von Arx and Kurt[1], 1999, Switzerland	NR	42 years	Periapical Surgery	43	10 (100)	0	1-1	Cohort

Legend: NR: Not Reported

In the cohort studies[1,5,9,38,40,41,43], the sample size ranged from 10 to 523 evaluated teeth, with follow-up periods ranging from 1 to 6 years. In the cross-sectional studies[2,7,8,11,14,15,39,42,44], the sample size ranged from 16 to 175 teeth (M = 79.1), with evaluation periods ranging from 6 months to 6 years.

Studies with similar methodologies grouped the patients' ages into two categories: up to 45 years and over 45 years[2,5,39-41]. Seven studies included patients aged 14 to 77 years[1,8,11,15,38,43]. Most patients in the studies were 30 to 40 years old[14,44], ranging from 11 to 71 years old.

The study by Klasser et al.[15] had a balanced distribution of sexes in their populations, with three and nine patients of each sex, respectively. Only Farzaneh et al.[41] (2004) included more men than women in their analysis. Except for this study, all other ones had more females, as observed in Farzaneh et al.[40] (2004) (62%), de Chevigny et al.[2] (2008) (68%), Abbott[14] (74%), Erdogan et al.[7] (80%) and Nixdorf et al.[43] (2015) (84%). The studies by von Arx and Kurt[1], Daline et al.[9], and Lobb et al.[42] did not report the patients' sex.

Individual Study Results

Five studies followed patients for 4 to 6 years post-endodontic treatment[2,5,39-41]. Marquis et al.[5] examined 131 endodontically treated teeth, of which seven experienced pain. De Chevigny et al.[39] examined 137 teeth that underwent non-surgical endodontic treatment, with only six of the evaluated teeth feeling pain. In another study conducted in the same year, the same authors evaluated 122 teeth treated with the same technique, and again, only six teeth had pain[2]. In contrast, Farzaneh et al.[40] identified persistent pain in only three of the 122 teeth that underwent non-surgical endodontic treatment. These studies demonstrate a relatively low prevalence, ranging from 5.3% to 2.5%.

In another study conducted one year after endodontic treatment, Polycarpou et al.[44] analyzed 175 teeth that underwent surgical and non-surgical treatment, finding 21 cases of persistent pain, representing approximately 12% of the cases. Danin et al.[38] investigated 43 teeth that underwent periapical surgery, with only one tooth feeling pain after 1 year, corresponding to 2.3%. Von Arx and Kurt[1] examined 10 teeth that underwent the same procedure but did not record any case of pain during follow-up.

Farzaneh et al.[41], in your analyses of teeth undergoing non-surgical endodontic therapy, did not report any cases of persistent pain in the 103 teeth evaluated, respectively. On the other hand, Vena, in a follow-up ranging from 6 months to 3 years and 9 months, examined 63 endodontically treated teeth and found that 39 of them reported pain, resulting in a prevalence of approximately 61.9%[11].

The study by Klasser et al.[15] followed patients for 3 months to 4 years, and 18 out of 250 consulted patients reported persistent pain throughout the period following treatment.

Similarly, Erdogan, in a follow-up of 3 years and 6 months involving 35 teeth, found that 29 of these teeth had pain, corresponding to a prevalence of approximately 82.9%[7].

The studies by Daline et al.[9], and Abbott[14] included only teeth that already felt pain at the outset. Daline et al.[9] analyzed 45 teeth over 3 years and 4 months, Lobb et al.[42] examined 36 teeth over 1 year, Oshima et al.[8] followed 16 teeth for 9.8 months and 65 teeth for 6 years, while Abbott evaluated 110 affected teeth, identifying factors associated with the condition[14].

Risk and etiological factors

The following factors stand out among those involved in persistent pain after endodontic treatment: lack of adequate isolation, inadequate provisional restorations, incorrect use of intracanal medication for the condition treated, traumatic occlusion, inadequate obturation, inadequate access to the canal, excessively extended preparation, symptoms during root obturation, excessively extended root fillings or with open apices, fracture of instruments[14], nerve injury caused by intracanal injection[45], perforations[7,45], reactions to foreign bodies such as gutta-percha, inadequate length of filling[40], persistence of periapical disease[2,30], and the effectiveness of anesthesia during treatment[44].

A potential cause of failure can be explained by over-instrumentation, which can cause direct trauma to the tissues surrounding the tooth, such as cementum, periodontal ligament, nerve endings, and bone[14,45], leading to persistent inflammation and consequently ongoing pain[7,40].

Disruption of the myelin sheath and axons may develop a traumatic neuroma. There can also be sympathetic nerve ingrowth into the injured sensory nerves, which may physiologically explain the ongoing post-endodontic pain associated with over-instrumentation[45].

Some systemic conditions can also be related to persistent pain after endodontic treatment[46], such as fibromyalgia, tension headache, temporomandibular dysfunction, migraine, irritable bowel syndrome[7,9,17], psychiatric illnesses[7,44,46], fear of dental procedures[10], and sleep disorders[46].

Another factor associated with the outcome is "phantom tooth pain", a condition in which the patient feels pain in a tooth that has already been extracted or endodontically treated, even though it is no longer present in the oral cavity[45].

Four studies[11,14,43,44] correlated preexisting pulpitis pain with ongoing pain after endodontic treatment, pointing to this condition as a predisposing factor. One of the studies found that for every 1-day increase in pain duration in the week prior to treatment, the risk of developing pain 6 months after the procedure increased significantly by 19%[43].

Risk of Bias in Studies

Regarding the risk of bias, three studies were classified as moderate risk[1,38,42], while all other studies had a low risk of bias[2,5,7-9,11,14,39-44] (Figure 2).

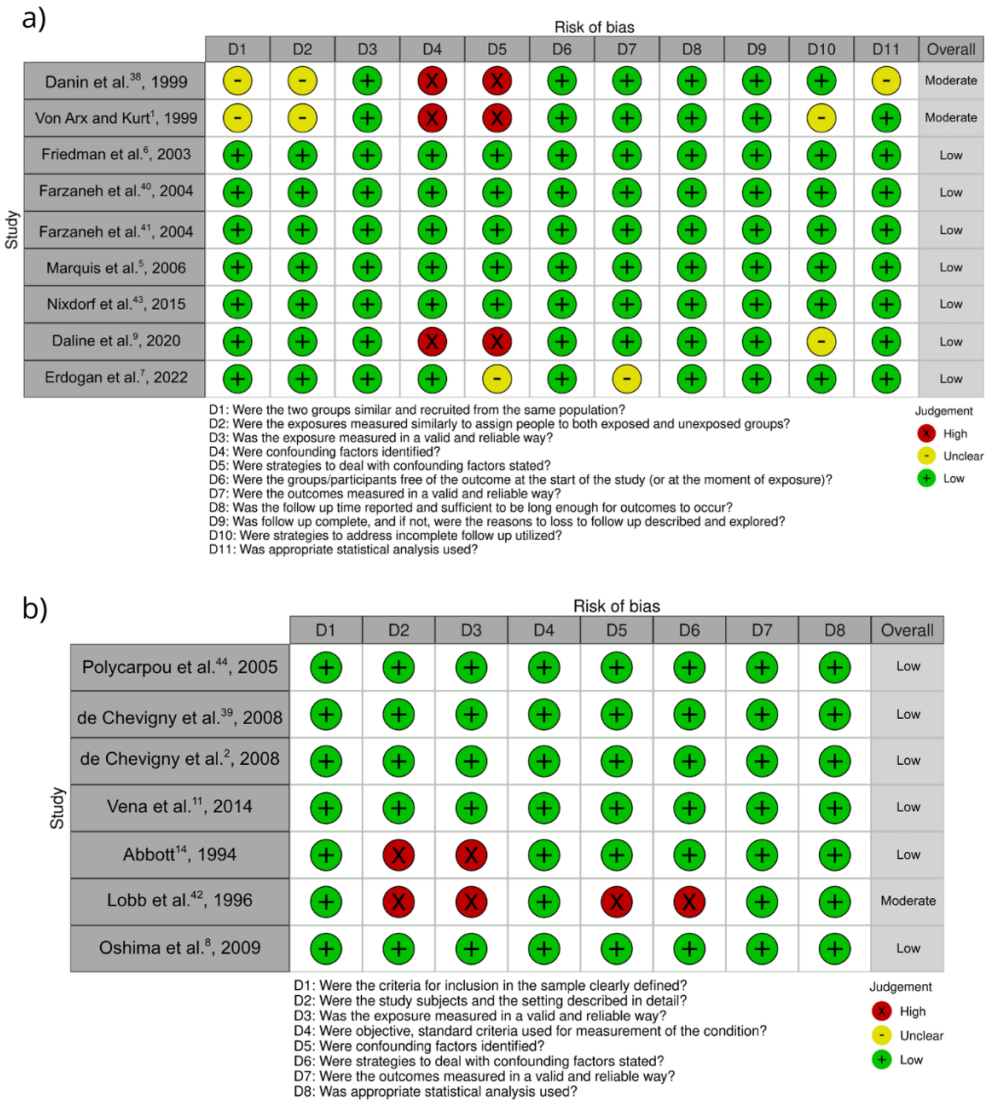

Figure 2. Risk of bias for cross-sectional (a), and cohort studies (b), assessed by JBI.

Summary of results

A meta-analysis was performed with studies that evaluated the prevalence of persistent pain in populations initially exempt from this outcome[1,2,5,7,8,11,15,38-44]. In total, 5,703 endodontically treated teeth were included in the analysis. The pooled prevalence of nonodontogenic pain was 5% (95% CI: 1% - 10%; I^2 = 96%) (Figure 3).

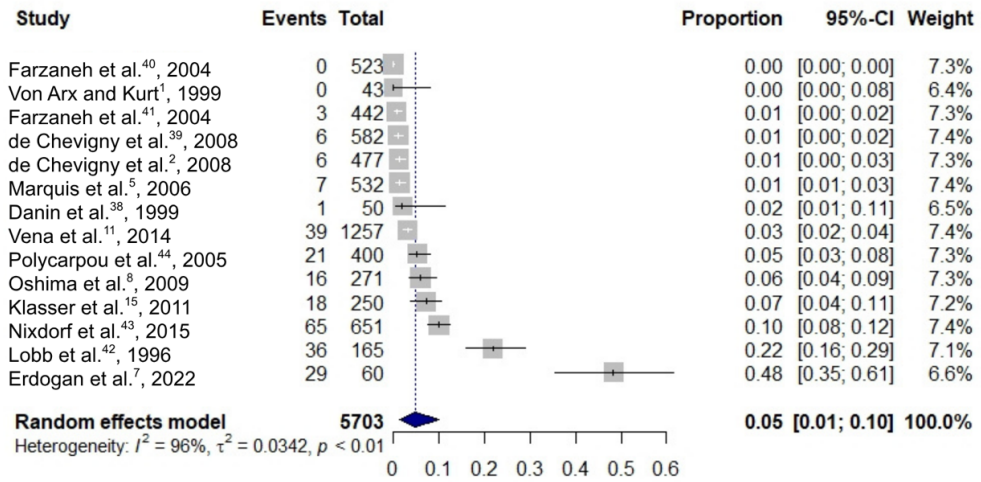

Figure 3. Forest plot the overall prevalence of persistent pain.

A sample size of 369 teeth would be necessary to obtain reliable estimates for an infinite population, with a 2% margin of error and a 95% confidence level. Considering only studies with this sample size, the prevalence was 2% (95% CI: 0% - 4%; I^2 = 95%) (Figure 4).

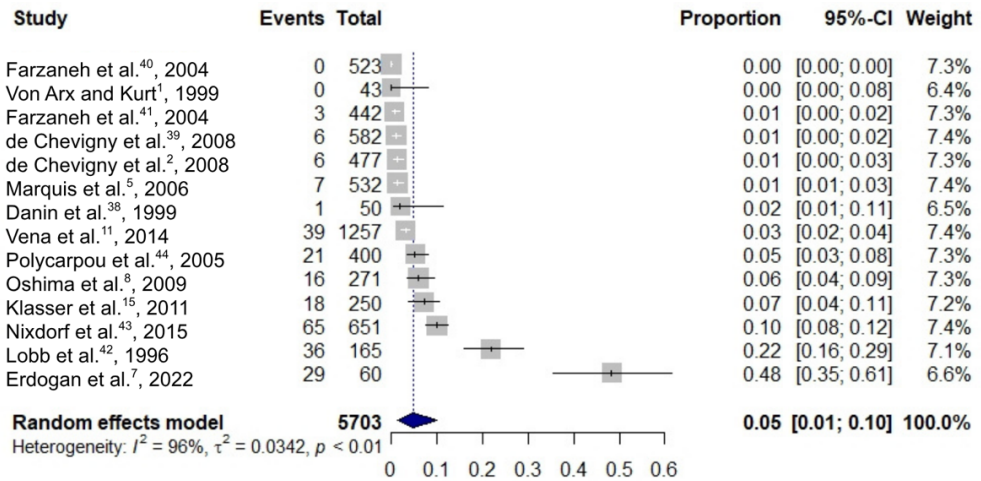

Figure 4. Forest plot of the sensitivity analysis by sample size.

Discussion

Dental professionals need to be prepared to understand and explain persistent pain, especially after endodontic treatment[47]. The continuous pain following endodontic treatment is characterized by its persistence for at least 1 month after the

procedure[46]. This symptom can manifest in different ways, depending on the person's self-perception of pain[43]. Recurrent pain is distinct from pain associated with pulpitis[45], and the diagnosis is based on the appropriate recognition of referred pain and the understanding of its temporality[7]. However, this pain is difficult to diagnose because it is still poorly understood[3]. The variation in the prevalence of odontogenic pain among studies[1,7,11,38,44] can be attributed to these diagnostic and understanding difficulties.

Persistent pain following endodontic treatment differs from the commonly encountered dental pain because it does not involve an apparent cause, making it impossible to remove the stimulus and provide appropriate treatment. This makes its clinical approach more complex, potentially requiring management that also considers neurological factors[47].

To improve pain diagnosis, it is important to recognize that pain is subjective and can be measured based on its intensity, location, and duration[48].

According to Lobb et al.[42], pain can range from mild sensitivity during chewing and temporary pressure to moderate, constant, dull, burning, and deep pain that develops after dental procedures, even in the absence of significant pathology. Asking the patient if the current pain is similar to that experienced before treatment can be helpful. If the answer is affirmative, there may have been an incorrect diagnosis, or the pain was not associated with the treated tooth[45]. Additionally, it is important to consider that the pain may originate from more than one tooth, which can complicate the analysis if appropriate methods are not used[12].

The meta-analysis revealed significantly variable proportions, reflecting discrepancies in prevalence and high heterogeneity, even when considering only studies with adequate statistical power. However, the CI remained narrow, with limits ranging from 0% to 4% in the sensitivity analysis. Due to the non-comparative nature of the proportion data, they are subject to considerable variation, contributing to the high heterogeneity in the estimates[49]. Additionally, differences in pain rates after treatment may be influenced by characteristics of the study populations, poorly specified questionnaires, inclusion of cases with periapical surgeries, exclusions without clear justification, and low follow-up rates.

Continuous pain following endodontic treatment is a complex and multifaceted condition, influenced by factors related to the operator, the technique[14], and the patient[7,9,14]. However, it is still unclear why some patients develop chronic pain after the underlying condition has been treated, while others do not[46]. The persistence of symptoms after technically adequate treatment may be attributed to non-odontogenic causes, such as neuropathic pain, which requires the presence of injury or another pathology in the nervous tissue[43].

Persistent dentoalveolar pain disorder is probably neuropathic in origin[50]. Peripheral and central sensitizations of the trigeminal nervous system are the main mechanisms to promote the development and maintenance of chronic orofacial pain characterized by allodynia, hyperalgesia, and ectopic pain[51]. Hyperexcitability, the main mechanism of central sensitization, is defined as an increase in the responsiveness of nociceptive neurons in the central nervous system to their normal or sub-

threshold afferent input[52]. These mechanisms may help explain why some patients develop persistent pain even after technically adequate endodontic treatment. In the case of endodontic therapy, there is a risk of deafferentation injury, a lesion in the nervous system that can trigger neuropathic pain in some patients[11]. The differential diagnosis should consider this condition when pain persists, even with clinical and radiographic confirmation of treatment quality[15].

The most common age range for this pain is from 30 to 49 years. However, it is not exclusively associated with age, but rather with the higher frequency of dental visits among patients in this range[14]. Moreover, women tend to have a higher incidence of persistent pain[30,46], possibly due to a higher number of dental appointments[14]. In one study, most patients with this outcome were white women with higher education, high income, and dental insurance[9]. In most of the included studies, age, sex, and tooth type do not appear to be directly related to the incidence of continuous pain after endodontics[11,14,41,43,44]. The type of professional who performed the treatment can also influence the results, as specialists tend to handle more complex cases, possibly affecting the prevalence of pain[11]. Regarding the teeth, lower first molars, upper central incisors, and upper first molars are the most frequently associated with continuous pain, possibly due to being the most commonly treated endodontically[8,14].

The duration of pain varies widely, with spontaneous resolutions occurring in up to 3 years[9]. However, while the pain persists, it significantly impacts the patient's quality of life[11,43]. Patients with long-lasting pain may develop associated masticatory muscle pain due to avoidance of chewing in the painful area or muscle tension induced by stress, leading to a diagnosis of temporomandibular dysfunction secondary to dental pain[7].

Patients suffering from persistent pain are more likely to undergo additional radiographs, submit to retreatments, seek extra consultations, and consume more pain medications than those who do not report pain. When considering both the direct and indirect costs of these additional care measures, the financial impact of experiencing persistent pain at 6 months can be significant[43].

Although preclinical studies indicate that some strategies may reduce pain[46], the factors contributing to continuous pain following endodontic treatment are diverse and complex, requiring careful diagnosis and, in some cases, a multidisciplinary approach. Despite these contributions, some limitations must be acknowledged, as the heterogeneous methodologies of the analyzed studies hindered the summary of results. Although all investigated the same outcome, the authors used different sample recruitment criteria, follow-up time, treatment types, and assessment methods. Another limiting factor was the sample size, which varied considerably among studies, being insufficient in some cases. Furthermore, some studies did not implement adequate strategies to control for confounding factors.

The results of this systematic review and meta-analysis indicate that approximately one in 25 patients may experience persistent pain after endodontic treatment. When considering only studies with higher statistical power, this proportion is even lower, at about one in 100 patients. However, quantifying the prevalence of persistent pain

following endodontic treatment remains a challenge due to the variety of possible diagnoses associated with this condition.

Other Information

Registration The protocol for this systematic review was registered at the PROSPERO® website (International Prospective Register of Systematic Review - Center for Reviews and Dissemination University of York) under no. CRD 42023427127.

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Data Availability

No research data was used.

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Conflict of Interest

The authors declare that they have no conflict of interest.

Use of Artificial Intelligence-Assisted Technology

The authors declare that no artificial intelligence tools were used in the design, analysis, writing, or revision of this manuscript.

Authors' Contributions

Edmundo Duarte Martins: Conceptualization, Formal analysis, Data curation, Writing – Original Draft. **Allya Francisca Marques Borges**: Data curation. **Lidiane Oliveira Leão**: Conceptualization, Formal analysis, Data curation, Investigation, Writing – Original Draft. **Bianca Marques de Mattos de Araujo**: Investigation, Writing – Original Draft, Visualization. **José Stechman Neto**: Investigation, Supervision. **Tatiana Carvalho Kowaltschuk**: Investigation, Writing – Original Draft, Visualization. **Camila de Castro Corrêa**: Investigation, Writing – Original Draft. **Cristiano Miranda de Araújo**: Investigation, Supervision, Writing – Original Draft, Visualization. **Karinna Veríssimo Meira Taveira**: Conceptualization, Methodology, Validation, Formal analysis, Investigation, Resources, Data curation, Writing – Review & Editing, Visualization, Supervision, Project administration. All authors actively revised and approved the final version of the manuscript.

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