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Characteristics of phase 4 clinical trials on Dental Caries registered at Clinicaltrials.gov

Kerim Safa Kul^{1*} and Muhammet Kerim Ayar¹

Abstract

Background Dental caries, a widespread chronic oral disease, is caused by multiple factors including microorganisms, genetic predisposition. Despite being preventable, it poses a significant global burden. This study reviews all phase 4 clinical trials on dental caries registered at ClinicalTrials.gov to provide a comprehensive overview of their characteristics.

Methods A search was conducted on the ClinicalTrials.gov database using keywords. The registration data for all relevant phase 4 studies concerning 'Dental Caries' were retrieved. This search was conducted on the 23rd of January, 2024.

Results The analysis included 58 phase 4 clinical trials, with most studies (67.2%) reporting complete data. The majority (63.8%) had fewer than 100 participants, and the predominant sponsors were medical institutions (77.6%). Geographically, the highest percentage of studies were conducted in South America (24.1%), with the lowest in North America (10.3%). Interventional trials primarily focused on treatment (51.7%) and prevention (41.4%), with a significant portion being randomized (93.1%). Blinding varied, with single and double blinding each used in 25.9% of studies. Drug interventions were the most common (60.6%), followed by other categories such as dietary supplements and procedures. Among drug interventions, agents containing fluoride were the largest category, accounting for 52.6% of the trials. Fluoride varnishes and silver diamine fluoride were the most frequently evaluated. Sedatives and pain relievers constituted 15.7% of the trials, with midazolam and ketamine being predominant. Other drugs accounted for 23.2% of the trials, featuring diverse substances such as inactivated poliovirus vaccine and xylitol. Dental materials and operative treatments made up 29.5% of the trials, with resin and fissure sealants being the most commonly evaluated.

Conclusion This analysis of phase 4 clinical trials highlighted fluoride as the most studied intervention for dental caries prevention. The analysis also revealed a need for further research on non-fluoride interventions and emphasized the importance of using evidence-based practices in dental care for improved oral health outcomes.

Clinical trial number Not applicable.

Keywords Dental caries, Phase 4, Clinical trials, Dentistry

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Background

Dental caries, commonly known as tooth decay, is a prevalent chronic oral disease caused by various factors, such as microorganisms, oral habits, genetics and time. It is a preventable disease that has a significant global burden, affecting both primary and permanent dentition [1]. The prevalence of dental caries varies across different populations and is influenced by factors such as fluoride levels in drinking water, diet and genetic predisposition between races [2]. The multifactorial nature of dental caries highlights the importance of preventive measures such as fluoride varnishes, fluoride gels, and regular daily dental care, in reducing its incidence [3]. As the prevalence of dental caries remains a significant public health concern, ongoing research is essential to understand its etiology and develop effective preventive strategies.

To prevent dental caries, various treatments and preventive measures are available. Silver diamine fluoride (SDF) has been shown to be more effective in preventing dental caries in primary teeth compared to untreated groups, placebo, or other fluoride varnishes [4]. The contemporary philosophy of dental caries management emphasizes noninvasive treatment of caries lesions whenever possible, limiting operative interventions to severe and irreversible cases [5]. Furthermore, interventions such as dental sealants and fluoride varnish have been identified as effective strategies for preventing dental caries [6]. Fluorides, particularly when used in toothpaste containing casein phosphopeptide or sodium mono-fluorophosphate have resulted in a greater reduction in dental caries and prevent dental caries [7]. Moreover, public health measures and other caries-preventive approaches have led to significant reductions in dental caries across populations [8].

It is important to note that the treatment concept for caries has evolved, with a shift toward noninvasive approaches before the lesion reaches dentine [9]. Additionally, the use of glass ionomer cement (GIC) sealants has been found to prevent dental caries on molars affected by molar incisor hypomineralization, although a protective effect was not observed for posteruptive breakdown [10]. Furthermore, maternal mental disorders have been associated with an increased risk of dental caries in children, highlighting the need for enhanced prevention strategies in such cases [2]. Compared with that of the control group, the use of fluoride gel treatment resulted in a 22% reduction in the incidence of caries, indicating its effectiveness in preventing dental caries [11].

Phase 4 clinical studies, also known as postmarketing surveillance studies, are being conducted after a drug or treatment has been approved and is on the market. These studies are crucial for monitoring the long-term safety and effectiveness of treatment in a larger population. In

the context of dental caries, phase 4 clinical studies play a significant role in evaluating preventive care and treatment strategies during the eruption of teeth, as highlighted by Pitts et al. [12]. These studies are essential for understanding the patterns of dental caries at the surface, tooth, and child levels among adolescents and are valuable for both epidemiological surveys and clinical care [13].

The importance of phase 4 clinical studies relevant to dental caries is further underscored by the fact that dental caries not only affects oral health but also correlates with other systemic diseases, such as diabetes, indicating the global health risk associated with this condition [14]. Additionally, these studies are crucial for understanding the interrelationship between dental caries and other noncommunicable diseases, which merits further investigation [15] and emphasizes the significance of clinical studies in establishing the relationship between dental caries and dietary changes, as well as risk factors for cardiovascular disease [16]. Moreover, phase 4 clinical studies are essential for identifying the prevalence and risk factors associated with *Streptococcus mutans* dental caries [17]. Furthermore, these studies are crucial for predicting dental caries among children and assessing the prevalence and associated factors of dental caries in different populations [18].

In 1997, the United States Congress mandated the creation of the ClinicalTrials.gov registry to assist individuals with serious illnesses in finding and accessing clinical trials. In September 2004, the International Committee of Medical Journal Editors (ICMJE) released a statement specifying that only trials registered before the initiation of patient recruitment would qualify for publication [19]. The systematic and transparent registration of clinical trials holds the promise of considerably reducing bias in clinical research and elevating the general quality of such trials. This article describes a thorough examination of all phase 4 clinical trials related to dental caries within the ClinicalTrials.gov database. The objective is to provide a detailed overview of the characteristics of these studies. The primary objective of the present study is to consolidate the current status of phase 4 clinical trials related to dental caries, offer guidance for future research endeavors, and identify any potential research gaps that may exist.

Methods

Data sources and search

A search was conducted on the ClinicalTrials.gov database using keywords. The registration data for all relevant phase 4 studies concerning 'Dental Caries' were retrieved. This search was conducted on the 23rd of January, 2024.

Data collection and analysis

Data from the downloaded registration information files were independently gathered by one researcher (K.S. K) and subsequently verified by another researcher (M.K.A). The collected data from each study included current status, interventions, sponsors and collaborators, estimated enrollment, eligibility criteria (age), study type, study design, (planned) trial start date, trial registration date, and location.

Absolute numbers and percentages are reported for categorical variables, while medians and interquartile ranges (IQRs) are reported for continuous variables. The analysis was performed using IBM SPSS Statistics for Windows, Version 25 (IBM Corp., Armonk, NY, USA).

Table 1 Characteristics of phase 4 trials on Dental Caries registered in ClinicalTrials.gov

Status	Number	Percentage (n = 60)
Not yet recruiting	-	-
Active, not recruiting	3	5.2
Available	-	-
Enrolling by invitation	1	1.7
Recruiting	4	6.9
Completed	39	67.2
Unknown	11	19.0
Total	58	100
Study type		
Interventional	58	100
Observational	-	-
Expanded access	-	-
Total	58	100
Anticipated enrollment		
≤ 100 participants	37	63.8
101–500 participants	19	32.8
501–1000 participants	-	-
> 1000 participants	2	3.4
Total	58	100
Location		
Asia	8	13.8
Europe	12	20.7
North America	6	10.3
South America	14	24.1
Middle East	8	13.8
Africa	10	17.2
Other	-	-
Missing	-	-
Total	58	100
Funding source		
Medical institution	46	77.9
Research institution	1	1.6
Industry	6	10.1
Government	3	5.08
Other	3	5.08
Total	59	100

Three separate analyses were performed, describing the results of all trials and trials on interventions.

The study locations were classified into the following categories: Asia (excluding the Middle East), Europe, North America (including the United States, Canada, and Mexico), South America (including Central America), Africa, the Middle East, and others. Studies with undisclosed locations were omitted from the counts, and studies conducted in multiple locations were considered in each corresponding region.

Funding sources were classified according to the details provided under ‘sponsors’, ‘collaborators’, and ‘funder type’ within the ClinicalTrials.gov database, partially adhering to the criteria established by prior research [20]. The categorization of studies was determined based on the nature of their sponsorship or collaboration. If a government agency served as a sponsor or collaborator, the study fell under the classification of government agency-funded. On the other hand, if industry representatives were sponsors or collaborators without any involvement from a government agency, the study was categorized as industry funded. In cases where the sponsor was a medical institution and there were no affiliations with industry or government collaborators, the study was designated as medical institution-funded. Similarly, if the sponsor was a research institution and there were no ties to industry, government, or medical institutions among collaborators, the study was labeled research institution-funded. The ‘other’ category encompassed all remaining types of funders.

Results

Analysis of the quantity of trial registrations

A total of 58 registrations for phase 4 clinical trials concerning “dental caries” were identified in the ClinicalTrials.gov database. Due to the absence of studies with a “withdrawn” status, all registered studies were included in our analysis.

Trial characteristics

The characteristic features of the studies included in the analysis are summarized in Table 1. Of the 58 studies included, 39 (67.2%) had complete data. Three studies (5.2%) were active but not recruiting. Four studies (6.9%) were actively recruiting patients. The status of eleven studies (19%) was unknown.

All included studies were of the interventional type. The majority of studies (37, 63.8%) had fewer than 100 participants. Nineteen studies (32.8%) had between 101 and 500 participants. Two studies (3.4%) had more than 1000 participants.

A significant portion of the studies, forty-six (77.9%), were sponsored by medical institutions. Six studies (10.1%) were sponsored by industry. The location

percentages of studies conducted worldwide were similar (ranging from 24.1 to 13.8%). The highest percentage of studies, 24.1%, were conducted in the South American region. The lowest percentage of studies, 10.3%, were conducted in the North American region. When ranked by the number of studies per region, the order from highest to lowest was as follows: South America (24.1%), Europe (20.7%), Africa (17.2%), the Middle East (13.8%), Asia (13.8%), and North America (10.3%).

Characteristics of the interventional trials

The characteristic features of the interventional studies are summarized in Table 2. Thirty studies with two primary purposes predominantly emphasized the purpose of treatment (51.7%), followed by 24 studies with the same primary purpose of treatment (41.4%). There were no studies with primary screening or basic science objectives. The allocation status of 54 studies (93.1%)

Table 2 Characteristics of interventional phase 4 trials on Dental Caries registered in ClinicalTrials.gov

Primary purpose	Number	Percentage (n = 58)
Treatment	30	51.7
Prevention	24	41.4
Supportive care	1	1.7
Diagnosis	1	1.7
Health services research	1	1.7
Screening	-	-
Basic science	-	-
Other	1	1.7
Total	58	100
Allocation Status		
Randomized	54	93.1
Nonrandomized	2	3.4
Missing	2	3.4
Total	58	100
Blinding		
Single	15	25.9
Double	15	25.9
Triple	5	8.6
Quadruple	10	17.2
None (open-label)	13	22.4
Total	58	100
Interventions		
Drugs	73	60.6
Biological interventions	3	2.5
Devices	3	2.5
Dietary supplement	9	7.5
Behavioral interventions	3	2.5
Procedure	6	5
Diagnostic test	-	-
Radiation	3	2.5
Combination Product	2	1.7
Other	18	14.9
Total	121	100

was randomized, while the allocation status of 2 studies (3.4%) was not specified. Additionally, the allocation status of 2 studies (3.4%) was nonrandomized.

Single blinding was utilized in 15 studies (25.9%), and double blinding was employed in an equal number of studies (25.9%). Triple blinding was implemented in 5 studies (8.6%), while quadruple blinding was used in 10 studies (17.2%). Blinding was not performed in 13 studies (22.4%).

Due to the presence of multiple interventions in some studies, there are 121 interventions across 58 studies. The most common type of intervention was drugs (60.6%), followed by the "other" category (14.9%). Interventions such as dietary supplements (7.5%) and procedures (5%) came after drugs.

Characteristics of drugs

In interventional studies, drug-type interventions are predominantly utilized, and the list of subcategories is provided in Table 3. Drug-type interventions are divided into subgroups such as agents containing fluoride, sedatives and analgesics, other medications, and dental materials/operative treatments. The largest subgroup was agents containing fluoride, accounting for 52.6% of the trials (50 out of 95). Within this subgroup, fluoride varnishes and silver diamine fluoride were the most frequently evaluated, comprising 12.6% and 10.5% of the total trials, respectively. Other notable fluoride-based interventions included fluoride dentifrice (9.5%), fluoride gel (3.2%), and nano-silver fluoride varnish (2.1%). Several other fluoride products, such as fluoride foam, fluoride water, fluoride salt, and various mouth rinses, each represented 1.1% of the trials.

Sedatives and pain relievers constituted 15.7% of the trials, with midazolam (7.4%) and ketamine (5.3%) being the predominant substances evaluated. The remaining drugs in this category, including analgesic mouth rinses, dexmedetomidine hydrochloride, and meperidine, each accounted for 1.1% of the trials. Other drugs constituted 23.2% of the trials, featuring a diverse array of substances such as inactivated poliovirus vaccine (6.3%), xylitol (3.2%), probiotic lozenges (3.2%), and various unique mouthwashes and vitamins. Dental materials and operative treatments comprised 29.5% of the trials, with resin sealants (4.2%) and fissure sealants (3.2%) being the most commonly evaluated. Other materials, such as glass ionomers, pulp capping agents, and calcium-based liners, each accounted for smaller percentages, reflecting the broad range of materials tested for their efficacy in preventing or treating dental caries.

Table 3 Features of drug intervention trials on dental caries recorded in ClinicalTrials.gov

Drug Category	Drug Types	Number of evaluations of single drugs	Percentage (%)
Agents containing fluoride	Silver diamine fluoride SDF	10	10.5
	Fluoride Varnishes	12	12.6
	Fluoride Dentifrice	9	9.5
	Fluoride gel	3	3.2
	Sodium fluoride/silica and carbopol	3	3.2
	Nano Silver Fluoride varnish	2	2.1
	Fluoride Foam	1	1.1
	Fluoride water	1	1.1
	Fluoride salt	1	1.1
	CPP-ACP 5% sodium fluoride varnish & 900ppm fluoride paste	1	1.1
	CPP-ACP Complex	1	1.1
	0.2% NaF mouth rinse	1	1.1
	0.2% NaF mouth rinse + 0.12% chlorhexidine	1	1.1
	SnF Dentifrice	1	1.1
	NaMFP Dentifrice	1	1.1
	1,100pm F-toothpaste and 0.5%NaF rinse	1	1.1
	5% sodium fluoride gel + Vitamin D soft gel capsules	1	1.1
Subtotal:	50/95	52.6	
Sedatives and Pain Relievers	Ketamine	5	5.3
	Midazolam	7	7.4
	Analgesic mouth rinses (Dissolved aspirin)	1	1.1
	Dexmedetomidine Hydrochloride	1	1.1
	Meperidine	1	1.1
	Subtotal:	15/95	15.7
Other Drugs	Moringa mouthwash	1	1.1
	nanohydroxyapatite varnish	1	1.1
	xylitol	3	3.2
	Xylitol + B12	1	1.1
	Sorbitol	1	1.1
	star anise mouthwash	1	1.1
	Indian Costus mouth wash	1	1.1
	Efavirenz, lamivudine, and tenofovir	1	1.1
	Hydroxyzine	1	1.1
	Enfuvirtide	1	1.1
	Probiotic lozenges	3	3.2
	Vitamin D soft gel capsules	1	1.1
	Inactivated poliovirus vaccine (IPV)	6	6.3
	Subtotal:	22/95	23.2

Table 3 (continued)

Drug Category	Drug Types	Number of evaluations of single drugs	Percentage (%)
Dental Materials and Operative Treatments	ACTIVA™ BioACTIVE	1	1.1
	Theracal LC	1	1.1
	Fissure sealant	3	3.2
	Resin sealant	4	4.2
	GIC Based sealant	1	1.1
	ART sealant	1	1.1
	Light-cured tri-calcium silicate base material	1	1.1
	MTA	1	1.1
	Glass Ionomer	3	3.2
	Indirect pulp treatment using Vitrebond (TM)	1	1.1
	Pulp Capping Agents	2	2.1
	Calcium hydroxide liner	1	1.1
	Calcium silicate liner	1	1.1
	Compomer	1	1.1
	Indirect pulp treatment using Dycal (TM)	1	1.1
	calcium silicate cement (Biodentine™)	2	2.1
	glass ionomer cement (Fuji IX™)	1	1.1
	Formocrezol	1	1.1
	Conventional atraumatic restorative treatment	1	1.1
	Subtotal:	28/95	29.5
Total	95	100	

Discussion

The analysis of phase 4 clinical trials on dental caries revealed that fluoride-based interventions were the most studied, comprising 52.6% of trials, with fluoride varnishes and silver diamine fluoride being the most common. Sedatives and pain relievers accounted for 15.7% of the trials, primarily focusing on midazolam and ketamine. Other drug interventions and dental materials made up 23.2% and 29.5% of the trials, respectively, and included a variety of preventive and treatment approaches (Fig. 1). Most of the trials were completed (67.2%), involved fewer than 100 participants (63.8%), and were sponsored by medical institutions (77.6%). Geographically, South America had the highest concentration of trials (24.1%), while North America had the lowest (10.3%). The trials mainly focused on treatment and prevention, with a significant portion being randomized and employing various levels of blinding.

Fluoride-based interventions stand out as the predominant focus in phase 4 clinical trials on dental caries, constituting over half (52.6%) of the total studies. This dominance underscores the well-established efficacy of fluoride in preventing dental caries and highlights its critical role in public health strategies aimed at reducing the prevalence of this common oral disease [21]. The effectiveness of fluoride in preventing dental caries is primarily attributed to its ability to enhance the remineralization of tooth enamel and inhibit the demineralization

process. It helps in the formation of fluorapatite, a less soluble form of enamel that is more resistant to acid attacks from bacterial metabolism. Additionally, fluoride has antibacterial properties that reduce the acid production of cariogenic bacteria, further protecting the tooth structure [22].

The trials include various fluoride-containing agents, with fluoride varnishes and silver diamine fluoride (SDF) being the most studied. Fluoride varnishes, due to their easy application and prolonged contact with the tooth surface, are effective, particularly in high-risk populations like children and those with limited dental care access. SDF is valued for arresting active caries and preventing new lesions, making it a key tool in minimally invasive dentistry [23]. Other fluoride-based methods, such as dentifrice, gels, and rinses, offer different delivery modes but collectively reduce caries incidence across populations [24]. Community water fluoridation remains one of the most cost-effective caries prevention measures, and ongoing clinical trials continue to assess the efficacy of new fluoride formulations [25]. Fluoride varnishes, in particular, have shown significant effectiveness in reducing caries incidence, especially in high-risk groups, by providing sustained fluoride release and enhanced enamel uptake [26].

Fluoride dentifrices, commonly used in daily oral hygiene routines, have been shown to be effective in preventing caries. The mechanical action of toothbrushing,

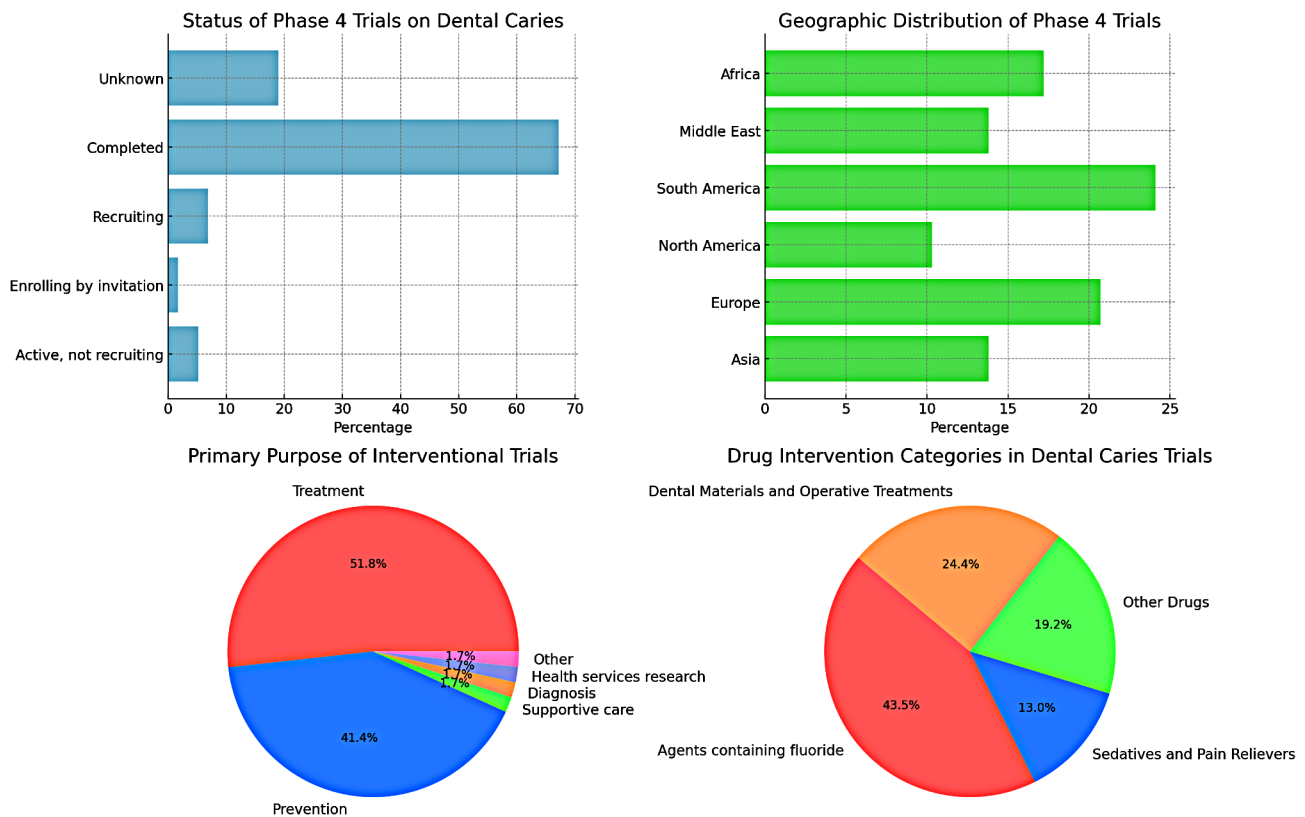


Fig. 1 Summary of the key characteristics of phase 4 clinical trials on dental caries registered in ClinicalTrials.gov. The figure illustrates the distribution of trial status, geographic location, primary purpose of interventions, and drug intervention categories. This visual representation highlights the predominance of completed trials, the geographic focus in South America, the primary focus on treatment and prevention interventions, and the dominance of fluoride-based drugs in these trials

combined with fluoride in dentifrices, helps remineralize enamel and inhibit bacterial growth. Several clinical trials have reported a reduction in caries rates with regular use of fluoride dentifrices, particularly when fluoride concentration is optimized [26].

Fluoride gels, often applied in professional dental settings, offer a high concentration of fluoride for short-term exposure. Although less convenient for daily use than dentifrices, fluoride gels have been shown to provide significant protection against caries, particularly when used as part of professionally administered treatments or home care regimens under dental supervision [27].

The analysis of phase 4 clinical trials highlighted the use of sedatives and pain relievers in dental caries treatment. Midazolam and ketamine were particularly noted for their effectiveness in managing pain and anxiety during procedures. Midazolam, a benzodiazepine, is frequently used for conscious sedation due to its rapid onset and short duration [28]. Its efficacy in reducing anxiety and discomfort has been consistently demonstrated [29]. Ketamine, a dissociative anesthetic, is especially valuable in pediatric dentistry for managing pain and anxiety, with the added benefit of preserving airway reflexes [30]. These sedatives and pain relievers play a crucial

role in improving patient comfort and facilitating dental treatment.

Apart from fluoride-based interventions, phase 4 clinical trials on dental caries have explored various alternative treatments. Xylitol, a sugar alcohol, inhibits cariogenic bacteria and promotes enamel remineralization. Studies on xylitol-containing products such as gums and toothpaste have shown a reduction in caries incidence, especially in high-risk groups [31]. Probiotics, including *Lactobacillus* and *Bifidobacterium* strains, have been evaluated in lozenges and mouth rinses, though further research is needed to determine the most effective strains and dosages [32]. Inactivated poliovirus (IPV) vaccines have also shown promise in reducing caries prevalence, particularly in populations with high baseline rates [33].

Resin sealants and glass ionomer cement (GIC) are two widely studied materials in phase 4 clinical trials for dental caries. Resin sealants are primarily used to seal occlusal pits and fissures, preventing plaque and bacterial accumulation in these areas [34]. Their efficacy in reducing caries risk, especially in children and adolescents with deep fissures, has been well-documented, with long-term protection reported in some studies [35]. GIC, with its

fluoride-releasing properties, promotes remineralization and inhibits caries progression. Its chemical adhesion to tooth structure further reduces bacterial infiltration, making it effective in preventing caries recurrence [36]. Studies support GIC's effectiveness as a restorative material in primary teeth, particularly in noncarious cervical lesions and early carious lesions, especially in high-carries-risk patients [37].

Phase 4 clinical trials on dental caries show a higher concentration in South America and a lower concentration in North America. This may reflect differences in research priorities, funding, and caries prevalence. The higher trial concentration in South America suggests a proactive response to a greater caries burden [38]. In contrast, fewer trials in North America may result from established preventive measures, such as water fluoridation, and strong dental care infrastructure [39].

The predominance of medical institution-funded studies in phase 4 clinical trials on dental caries has several implications for the field. Although the predominance of medical institution-funded studies in dental caries research underscores the recognition of oral health as a critical component of overall health, it also highlights potential limitations and biases introduced by funding patterns. Addressing these challenges requires continued efforts to diversify funding sources, enhance collaboration between medical and dental research communities, and prioritize research that addresses the complex and multifaceted nature of dental caries.

The analysis of phase 4 clinical trials on dental caries highlights several research gaps. One key gap is the need for more studies on nonfluoride-based interventions. While fluoride effectively reduces caries, alternative approaches may be needed for those who cannot tolerate or benefit from fluoride. Investigating nonfluoride options, such as xylitol, probiotics, and novel antimicrobial agents, could offer insights into alternative strategies. Additionally, the analysis emphasizes evaluating various preventive strategies beyond fluoride. A multifaceted approach, including dietary changes, oral hygiene practices, and behavioral interventions, may offer better protection, particularly for high-risk populations [40]. Examining the comparative effectiveness and potential synergy of these strategies could guide the development of comprehensive prevention programs for diverse groups.

The findings from phase 4 clinical trials on dental caries underscore the importance of evidence-based preventive measures in dental practice. With a significant focus on fluoride-based interventions, including varnishes, gels, and mouth rinses, these findings emphasize the efficacy of fluoride in reducing the incidence of dental caries. Incorporating fluoride treatments into routine dental care protocols can significantly benefit patients,

particularly those at high risk for caries development, such as children, individuals with poor oral hygiene, and those with limited access to dental services.

Furthermore, the evaluation of sedatives and pain relievers in dental procedures highlights the importance of patient comfort and satisfaction during treatments. Effective pain management not only improves the patient experience but also promotes better compliance with dental appointments and recommended preventive measures. Dentists can leverage the findings from these trials to optimize pain control strategies and enhance the overall quality of care provided to patients.

Additionally, the exploration of various dental materials and operative treatments underscores the importance of employing evidence-based practices in restorative dentistry. By selecting materials with proven efficacy in caries prevention, such as resin and fissure sealants, dental professionals can ensure long-term success in preserving tooth structure and preventing further decay. Implementing these evidence-based interventions can lead to better treatment outcomes, reduced need for invasive procedures, and improved patient satisfaction.

Despite the valuable insights gained from this analysis, several limitations must be acknowledged. First, reliance on data from the ClinicalTrials.gov database introduces the risk of publication bias, where trials with positive results are more likely to be registered or reported [41]. Additionally, the accuracy and completeness of the database information may vary, affecting the comprehensiveness of the analysis. Second, focusing solely on phase 4 trials may limit the findings, as these trials primarily assess long-term safety and effectiveness in real-world settings, but may not fully reflect the scope of research on dental caries prevention and treatment. Excluding phases 1–3, which address intervention development and efficacy, could overlook important insights. Lastly, the geographical distribution of trials may not represent global dental health patterns, and variations in healthcare infrastructure and access to dental services across regions could affect the applicability of the results. Sponsorship and funding sources may also introduce bias, with industry-funded trials potentially producing more favorable outcomes [42].

However, the limited scope of this study—focusing primarily on dental caries—may have constrained the novelty of its conclusions. Prior literature has explored broader categories of clinical trials, including those that examine various dental conditions, rare diseases, and orthodontics, suggesting that future research could benefit from expanding the scope beyond a singular focus on caries. Notably, a comprehensive cross-sectional analysis conducted in 2016 evaluated all available dental trials across the World Health Organization's clinical trial registry platform, offering more generalized insights

into dental research [43]. However, given that this study is now relatively outdated, it may not reflect the current trends and advancements in dental research. This further underscores the need for updated and comprehensive evaluations in the field.

This study is an analysis of clinical trials' characteristics, and while we did not adhere to specific international guidelines commonly used for systematic reviews, the methodology applied does not hinder the standardization or reproducibility of our results. Our approach allowed for a comprehensive and structured examination of trial data, ensuring the reliability of our findings. Future studies may choose to adopt such frameworks depending on the specific research questions being addressed.

To enhance the scientific impact, future studies should consider broadening the inclusion criteria to incorporate other dental conditions or interventions, potentially offering more significant insights into trends and gaps within dental clinical trials. Additionally, integrating data from other registries, not limited to ClinicalTrials.gov, could provide a more comprehensive understanding of global trends in dental research.

Conclusion

In conclusion, ongoing research plays a pivotal role in advancing dental caries prevention and treatment. By addressing knowledge gaps, refining existing interventions, and developing novel approaches, research contributes to the enhancement of oral health outcomes and the overall well-being of populations worldwide. Translating research findings into practice has the potential to yield substantial benefits in reducing the global burden of dental caries. By embracing evidence-based approaches and fostering collaboration between researchers, policy-makers, healthcare providers, and communities, we can work toward achieving significant improvements in oral health outcomes worldwide.

Supplementary Information

The online version contains supplementary material available at <https://doi.org/10.1186/s12903-025-05662-7>.

Supplementary Material 1

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M.K.A wrote the main manuscript text. K.S.K. performed the statistical analysis and wrote the statistical analysis and the results sections.

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Declarations

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Not applicable.

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Competing interests

The authors declare no competing interests.

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