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شیوع هالیتوزیس در مریضان مبتلا به پریودنتیت: یک مرور سیستماتیک و متاآنالیز

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چکیده

زمینه و هدف: هالیتوزیس یا بوی بدن دهان ۲۲ تا ۵۰ درصد بزرگسالان جهان را مبتلا می‌سازد که پریودنتیت یا التهاب انساج پریودنتال به عنوان یک عامل اتیولوژیک مهم برای هالیتوزیس محسوب می‌شود. با وجود اینکه همبستگی آماری بین آنها ثابت شده است، شیوع گزارش شده در مریضان مبتلا به پریودنتیت دامنه وسیعی (۳۷٪ تا ۸۱٫۷٪) داشته که ناهمسانی میتودولوژیک را نشان می‌دهد. تاکنون هیچ میتاآنالیز با استفاده از سنجش‌های عینی ترکیبات گوگردی فرار (VSC)، شیوع تجمیعی را کمّی‌سازی نکرده است.

روش تحقیق: بر اساس دستورالعمل‌های PRISMA ۲۰۲۰، به‌طور سیستماتیک پایگاه‌های PubMed، Cochrane، Wiley و Google Scholar را در بازه سال‌های ۲۰۰۰ تا ۲۰۲۵ جستجو کردیم. مطالعات مشاهده‌ای که هالیتوزیس را با روش‌های عینی (کروماتوگرافی گازی/ مانیتورهای سولفید) در مریضان مبتلا به پریودنتیت گزارش کرده بودند، وارد مطالعه هذا شدند. خطر سوگیری با استفاده از ابزار هوی (Hoy) ارزیابی شد. متاآنالیز با مدل اثرات تصادفی انجام شد و برای بررسی منابع ایجاد کننده ناهمسانی، تفسیر و تحلیل کیفی صورت گرفت.

یافته‌ها: نه مطالعه (529 مریض) مورد تحلیل قرار گرفت. شیوع تجمیعی هالیتوزیس 95% (CI: 46.6–75.4%) 62.0%بود، اما ناهمسانی قابل‌توجهی وجود داشت (I^2 = 85.77% ، τ^2=0.53، p<0.001). تحلیل کیفی چند منبع مهم ناهمسانی را شناسایی کرد: اول، معیارهای تشخیصی پریودنتیت (طبقه‌بندی AAP/EFP ۲۰۱۸ در مقایسه با آستانه‌های PD)؛ دوم، روش‌های سنجش ترکیبات گوگرد فرار (کروماتوگرافی گازی در مقایسه با مانیتورهای سولفید)؛ سوم، آستانه‌های تشخیصی VSC (140-80 ppb)؛ چهارم، ناسازگاری در ارزیابی پوشش زبان (WTCI در ۴ مورد از ۹ مطالعه استفاده شده بود).

نتیجه‌گیری: تقریباً دوسوم مریضان مبتلا به پریودنتیت دچار هالیتوزیسِ تأییدشده به صورت عینی هستند. ناهمسانی بالا مانع از ارائه یک برآورد قطعی از شیوع هالیتوزس در مریضان نام برده، می‌شود. مسئله اخیرالذکر بیان گر این است که پروتکل‌های تشخیصی استاندارد در زمینه موضوع ضرورت است.

واژه‌گانِ کلیدی: هالیتوزیس، بوی بد دهان، پریودنتیت، ترکیبات گوگرد فرّار.

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Prevalence of halitosis in patients with periodontitis: a systematic review and meta-analysis

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Abstract

Background: Halitosis or bad breath affects 22-50% of adults globally, with periodontitis being an important etiological factor for halitosis. Despite established associations, the reported prevalence in patients with periodontitis varies widely (37%-81.7%), showing methodological heterogeneity. No previous meta-analysis has quantified pooled prevalence using objective volatile sulfur compound (VSC) measures.

Methods: Following the PRISMA 2020 guidelines, we systematically searched PubMed, Cochrane, Wiley, and Google Scholar (2000-2025). Observational studies reporting objectively measured halitosis (gas chromatography/sulfide monitors) in patients with periodontitis were included. The risk of bias was assessed using Hoy's tool. Random-effects meta-analysis was performed, with qualitative synthesis to explore heterogeneity sources.

Results: Nine studies (n=529 patients) were analyzed. The pooled prevalence of halitosis was 62.0% (95% CI: 46.6–75.4%), but with substantial heterogeneity (I^2 = 85.77%, τ^2=0.53, p<0.001). Qualitative synthesis identified several important heterogeneity sources: first, Periodontitis diagnostic criteria (2018 AAP/EFP classification vs. PD thresholds); second, the VSC measurement methods (gas chromatography vs. sulfide monitors); third, VSC diagnostic thresholds (80–140 ppb); fourth, Tongue coating assessment inconsistency (WTCI used in 4/9 studies)

Conclusion: Approximately two-thirds of patients with periodontitis exhibit objectively confirmed halitosis. High heterogeneity prevents a definitive prevalence estimate, highlighting the need for standardized diagnostic protocols.

Key words: Halitosis, Oral malodor, Periodontitis, Periodontal diseases, Volatile sulfur compounds.

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Introduction

Halitosis is an unpleasant or offensive breath odor that occurs in the oral cavity in nearly 80–90% of cases [1-4]. Halitosis primarily arises when gram-negative anaerobic bacteria break down substrates in the oral cavity, producing volatile sulfur compounds (VSCs) as by-products like hydrogen sulfide (H_2S) and methyl mercaptan (CH_3SH)and CH3SCH3 [5, 6]. There are three assessment methods for halitosis diagnosis; i) organoleptic scoring (OLS) , a subjective approach that involves sensory evaluation which is done by a trained examiner; ii) gas chromatography (e.g., OralChroma), an objective approach that measures and differentiates between VSCs and iii) electrochemical sensor (e.g., Halimeter), an objective approach that measures total sulfur levels without differentiating between VSCs [6, 7]. Halitosis prevalence affects 22-50% of the general population globally [2, 3, 8]. This high prevalence has a significant psychosocial impact that causes embarrassment and awkwardness, thereby negatively affecting interpersonal relationships and overall quality of life [4, 9, 10]. On the other hand, periodontitis is a chronic inflammatory disease characterized by the irreversible destruction of tooth-supporting tissues, especially the alveolar bone and periodontal ligaments. Periodontitis is most commonly assessed through periodontal probing to measure pocket depth (PD), with varied cutoff ranges of 3 to 6mm, and clinical attachment loss (CAL), with varied cutoff ranges of 2 to 6mm [11]. The burden of periodontitis is substantial, affecting an estimated 20-50% of people worldwide and 59.9% in Portugal, with nearly half exhibiting moderate or severe forms [2, 10].

Both systemic and oral disorders can cause halitosis; among the oral causes of halitosis, periodontal diseases and tongue coating are the leading [1, 4, 12, 13]. In periodontitis the gram-negative anaerobic bacteria mentioned earlier, especially P. gingivalis and T. forsythia, which reside in periodontal pockets, metabolize sulfur-containing amino acids to produce the VSCs, contributing to halitosis [1, 2, 10, 14, 15]. Despite establishing a strong association between periodontitis and halitosis (OR 3.16-4.52) by more than one systematic review [16, 17], there is a debate on the prevalence of halitosis in patients with periodontitis in clinical settings. We can see that the reported prevalence varies significantly across studies: high (81.7%) [1], moderate (61.9%) [3], and low (37%) [4], suggesting methodological or demographic heterogeneity. The debate demands a consensus on its prevalence and the exploration of sources of heterogeneity that will be helpful for public health and clinical resource allocation.

To inform this debate, a systematic review of existing evidence is crucially needed. Although organoleptic assessment remains the gold standard, objective methods minimize examiner bias and infection risk [6]. These methods are reliable, specific, and sensitive for all three VSCs and demonstrate moderate-to-strong correlations with organoleptic scores, supporting their validity for prevalence assessment and halitosis diagnosis [1, 6, 9, 18-20]. No existing meta-analysis quantifies the pooled prevalence of halitosis objectively in patients with periodontitis using halitometers (e.g., gas chromatographs).

Therefore, this systematic review and meta-analysis aimed to estimate the pooled prevalence of objectively measured halitosis among patients diagnosed with periodontitis and to explore the sources of heterogeneity across the available studies.

Methods

We conducted the current systematic review in accordance with the PRISMA 2020 statement [21] . We didn't register the protocol for this study, but the full protocol can be observed throughout this article.

Search strategy

We searched PubMed, Wiley Online Library, Cochrane Library, and Google Scholar on 26 January 2025 for peer-reviewed articles on halitosis among patients with periodontal diseases. We operationalized different combinations of each keyword by integrating the methodology from 2 systematic reviews on halitosis and periodontal diseases [14, 22]. The full details of the search strategy are written in the table 1.

Our initial search identified 111 articles in PubMed, 5 in Cochrane Library, 65 in Wiley Library, and 196 in Google Scholar which were imported into EndNote reference management software. Of these 377 articles, 54 were identified as duplicates, leaving 323 for the screening and eligibility stages, as in figure 1 (PRISMA Flow Diagram).

Inclusion/exclusion

We applied a series of inclusion and exclusion criteria. Articles were included if they were; i) published in a peer-reviewed journal; ii) written in English; iii) published in 2000 onwards, because there was only one study prior to the time as we found in databases that we searched and the study didn't control extraoral causes of halitosis [23]; iv) Observational studies that reported prevalence of halitosis in patients with periodontitis by using validated diagnostic techniques for periodontitis, measuring PPD and CAL with a

periodontal probe [24]. and v) Studies that used validated diagnostic techniques to assess halitosis objectively either by gas chromatography or sulfide monitoring[25] or follow threshold values for detecting VSC according to the manufacturer's instructions that is equivalent to the cognitive threshold (OLT ≥ 2 meaning clearly noticeable odor or worse) [25-27]. studies were excluded if they were: i) not controlled for extraoral causes of halitosis [12]. and ii) Case reports, editorials, reviews, commentaries, and non-peer-reviewed sources.

Of the 323 records screened, we excluded 289 because they didn't report prevalence of halitosis among patients with periodontal diseases and 9 were not in English, leaving 25 articles for retrieval. We were unable to find the full text for 2 articles, resulting in 23 articles for eligibility. At eligibility, after reviewing the full text, we excluded another 5 articles, which were identified to be reviews. We also further excluded 3 articles because they didn't use validated diagnostic techniques to assess halitosis objectively. In addition, we excluded 3 studies, which were self-reported halitosis, one more study that had no prevalence data, and one study in which participants were selected based on the outcome. This left 9 articles for final review.

Data Extraction Process

We independently extracted data on studies, including author, year, and country into Microsoft Excel. Additional data were extracted to evaluate the prevalence of halitosis in patients with periodontitis including design, diagnostic criteria of periodontitis and halitosis, sample sizes, mean age, VSC thresholds, TC scores, and prevalence data. Finally, for the quality assessment of the included studies, we used the risk of bias (ROB) developed by D. Hoy et al [28], and evaluated ten methodological domains. Each domain was scored as "Yes" (low risk) or "No" (high risk). Studies were categorized into three risk levels based on total "No" responses: Low (0–3), Moderate (4–6), or High (7–10). Two reviewers performed ROB assessment independently, and they agreed after a discussion with a third person.

Analysis

We performed a meta-analysis to estimate the pooled prevalence of halitosis in the 9 studies, using the random-effects model in Meta-Essentials (MEs) with Microsoft Excel 2021, under the assumption of heterogeneity in reported prevalence rates [29, 30].

We entered all 9 studies with their number of observations, the logit-transformed prevalence proportion(pp) as effect size (Formula; =LN(pp/(1 - pp))) and the number of observed halitosis cases (k) within the total sample of periodontal patients (n) as standard error (Formula; =SQRT(1/k + 1/(n - k))) in the input sheet of MEs[29, 30]. To test the overall effect whether the pooled prevalence differed from 50% (i.e., H_o: logit-transformed effect size = 0), we used the two-tailed p-value. Heterogeneity via Cochran's Q and I^2, the forest plot and potential publication bias (Egger's linear regression test and funnel plot) were automatically measured by MEs[29, 30].

Due to substantial heterogeneity from variability in diagnostic criteria for periodontitis/halitosis and differences in VSC thresholds/measurement tools, we supplemented quantitative findings with qualitative synthesis to contextualize heterogeneity sources, thus interpret the results with caution.

Table 1. Full details of the search strategy used to identify studies on halitosis in patients with periodontal disease. Databases (PubMed, Cochrane, Wiley, Google Scholar), search terms, and results are shown. Note that we used an advanced Google Scholar search with the exact phrase in the title of the article and spaces between Boolean Operators and keywords are removed (because spaces are interpreted as AND being a Boolean Operator)

Databases	Search strategy	Result
PubMed	(("Epidemiological Studies"[Title/Abstract] OR "Cross-sectional Studies"[Title/Abstract] OR "Cross-sectional study"[Title/Abstract] OR "Studies, Cross-sectional"[Title/Abstract] OR "Prevalence Studies"[Title/Abstract] OR "Prevalence Study"[Title/Abstract] OR "Studies, Prevalence"[Title/Abstract] OR "Study, Prevalence"[Title/Abstract] OR "Cohort Study"[Title/Abstract] OR "Cohort Studies"[Title/Abstract] OR "Studies, Cohort"[Title/Abstract] OR "Study, Cohort"[Title/Abstract] OR "Longitudinal Study"[Title/Abstract] OR "Longitudinal Studies"[Title/Abstract] OR "Studies, Longitudinal"[Title/Abstract] OR "Study, Longitudinal"[Title/Abstract] OR "Incidence Study"[Title/Abstract] OR "Studies, Incidence"[Title/Abstract] OR "Study, Incidence"[Title/Abstract] OR "Follow up Studies"[Title/Abstract] OR "Follow-up Study"[Title/Abstract] OR "Prevalence"[Title/Abstract] OR "Incidence"[Title/Abstract] OR "Surveys"[Title/Abstract] OR "Questionnaires"[Title/Abstract]) AND ("periodontal disease(s)"[Title/Abstract] OR "periodontitis"[Title/Abstract] OR "gingivitis"[Title/Abstract] OR "Periodontal Disease"[Title/Abstract] OR "Disease, Periodontal"[Title/Abstract] OR "Diseases, Periodontal"[Title/Abstract] OR "Periodontal Diseases"[Title/Abstract])) AND (Halitosis: "halitosis"[Title/Abstract] OR "bad-breath"[Title/Abstract] OR "oral malodour"[Title/Abstract] OR "Oral Malodor"[Title/Abstract] OR "Foetor Ex Ore"[Title/Abstract] OR "Bad Breath"[Title/Abstract])	111
Cochrane Library (5 article) And Wiley Library (65 article)	“halitosis” OR “bad-breath” OR “oral malodour” OR "Oral Malodor" OR "Foetor Ex Ore" OR "Bad Breath" in Title Abstract Keyword AND “periodontal disease(s)” OR “periodontitis” OR “gingivitis” in Title Abstract Keyword AND “Epidemiological Studies” OR “Cross-sectional Studies” OR “Cross-sectional study” OR “Studies, Cross-sectional” OR “Prevalence Studies” OR “Prevalence Study” OR “Studies, Prevalence” OR “Study, Prevalence” OR “Cohort Study” OR “Cohort Studies” OR “Studies, Cohort” OR “Study, Cohort” OR “Longitudinal Study” OR “Longitudinal Studies” OR “Studies, Longitudinal” OR “Study, Longitudinal” OR “Incidence Study” OR “Studies, Incidence” OR “Study, Incidence” OR “Follow up Studies” OR “Follow-up Study” OR “Prevalence” OR “Incidence” OR “Surveys” OR “Questionnaires” in Title Abstract	70
Google scholar	“halitosis”OR“bad-breath”OR“oral malodour”OR"Oral Malodor"OR"Foetor Ex Ore" OR "Bad Breath" “periodontal disease(s)” OR “periodontitis” OR “gingivitis” OR “Periodontal Disease”OR“Disease, Periodontal”OR“Diseases, Periodontal”OR“Periodontal Diseases”	196

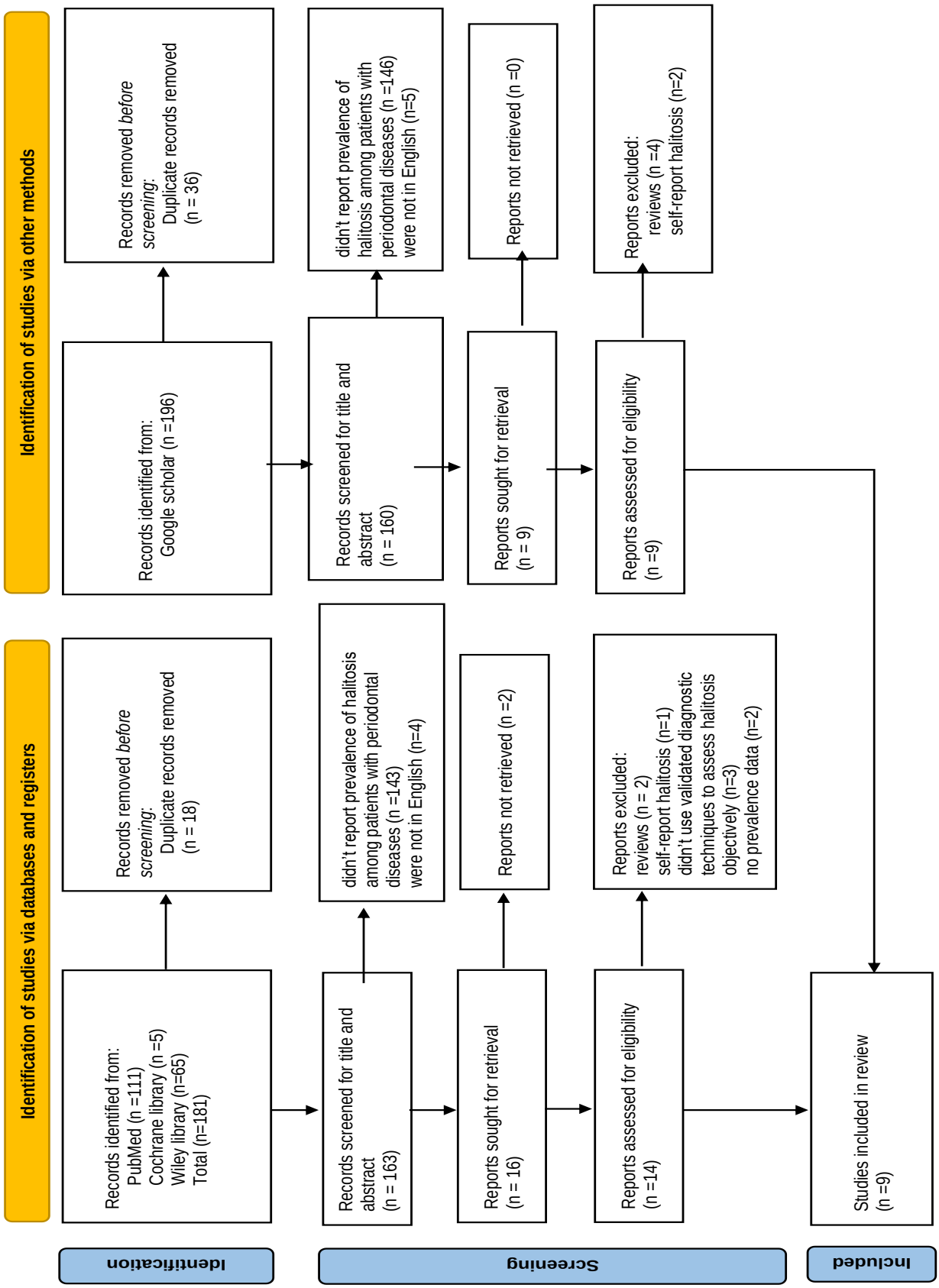


Figure 1. PRISMA flow diagram. The figure visualizes study selection process: 377 records identified, 323 screened after duplicate removal, 9 studies included in the meta-analysis.

Table 2. Data extraction table derived from Microsoft Excel 2021. studies characteristics like author, year, country, sample size, diagnostic tools for halitosis (Halimeter/gas chromatography), and prevalence rates are extracted.

age±SD	methods for Tongue coating scores	mean TC score±SD	significance of TCS on halitosis	halitosis assessed by type of instruments	diagnostic criteria for Halitosis	proportion of halitosis in the sample size	Assessing risk of bias(RoB) in prevalence studies
between 18 and 65	WTCI	3 (±2)	significantly correlated with VSC production	Halimeter	80 or more	0.373	Moderate
between 18 and 65	not measured	-	-	Halimeter	80 or more	0.444	Low
18 years old and older	not measured	-	-	OralChroma-Kyoto(gas chromatography)	equal to the cognitive threshold as follows: H2S≥ 112 PPB, CH3SH ≥ 26 PPB and CH3SCH3 ≥ 8 PPB)	0.817	low
52.75 ± 6.69	WTCI	7±1.58	strong relationship	Halimeter	cut of point of halimeter was 80 ppb	0.750	Low
54±12	WTCI	3.2±2.1	slightly elevated	Halimeter	organoleptic score 2 or more and/or Halimeter exceed 140 p.p.b	0.820	Low
56.79 ± 11.70	not measured	-	-	gas chromatograph-TwinBreasor II(gas chromatography)	The VSC cut-off values 65.79 ppb for women and 79.94 ppb for men	0.429	Moderate
> 16 years	presence of Coating	31% TC - presence	associated with an increased likelihood	Halimeter	halimeter (≥120ppb) and an organoleptic measurement (0-5 point scale) of ≥3.	0.619	Low
56.6 ± 18.0	distribution area	1.65±0.5	increase in the tongue coating influenced the VSCs level	gas chromatograph -G2800(gas chromatography	at or above the organoleptic threshold level [TVSC: (H2S) ≥ 1.5 ng/10 mL or (CH3SH) ≥ 0.4 ng/10 mL]	0.438	Low
not specified	WTCI	8.22±.2.7	very strong positive correlation between TCS	Halimeter	110 ppb was used as a standard above	0.75	Low

Authors year	year	Location	Study Design(CS=cross-sectional, CC=case-control)	definition of exposure (periodontitis)	type of settings	exposure severity	total patients diagnosed by periodontitis
C Izidoro et al 2023	2023	Portugal	CS	Followed AAP/EFP 2018 consensus, (PD) > 3 mm	clinical based	PD>3mm	51
C Izidoro et al 2021	2021	Portugal	CS	Followed AAP/EFP 2018 consensus, (PD) > 3 mm	clinical based	PD>3mm	72
H Alzoman 2021	2021	Saudi Arabia	CS	Chronic periodontitis	clinical based	PD>3mm	60
L. G Soares et al 2015	2015	Brazil	CS	generalized chronic periodontitis	clinical based	PD≥5mm	112
A Apatzidou et al 2013	2013	Greece	CS	having at least one site per quadrant with clinical probing depth (PD) ≥5 mm and radiographic evidence of bone loss	imaginary general population	PD≥5mm	28
Y H Lee et al 2023	2023	South Korea	stated CC, actual CS	criteria defined in the 2017 World Workshop on the Classification of Periodontal Diseases	clinical based	PD≥6mm	28
O A Ayo-Yusuf et al 2011	2011	South Africa	CS	PD≥5mm were ≥5% of the total teeth	clinical based	PD≥5mm	42
H Kurata et al 2008	2008	Japan	CS	PD≥4mm	clinical based	PD≥4mm	16
Bolepalli et al 2015	2015	India	stated CC, actual CS	(CAL of 1–4 mm, and CAL of ≥5 mm)involving at least nine sites of six Ramfjord index teeth.	clinical based	CAL of ≥5 and CAL of 1–4 mm	120

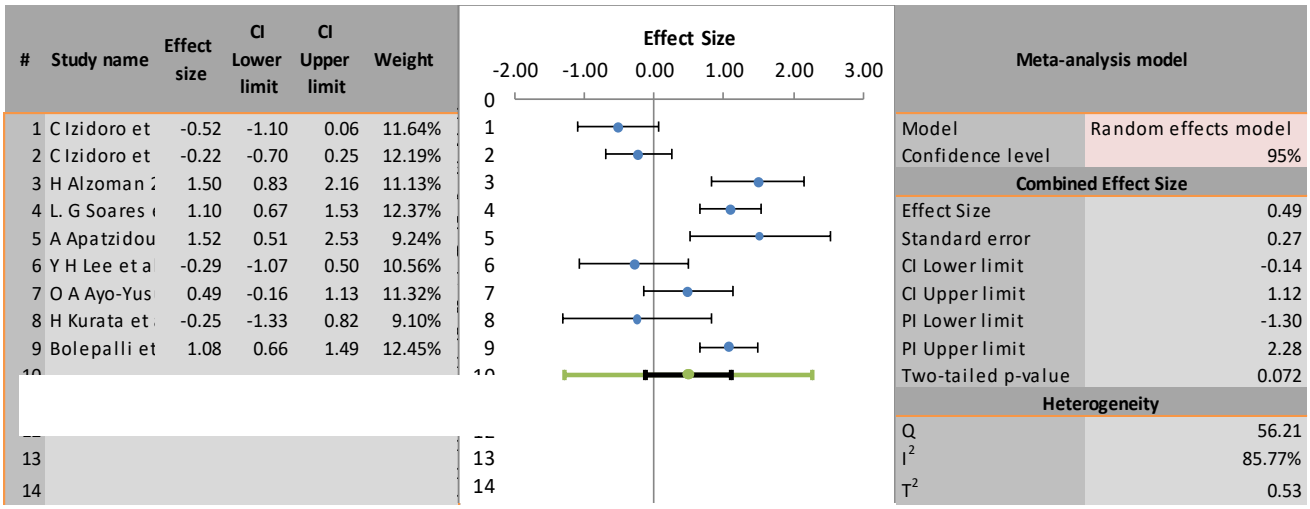
Results

Study descriptive

Among the included studies, four were conducted in Asia [3, 4, 31, 32], three in Europe [2, 11, 14], one in South America [9], and one in South Africa [5]. Altogether, 529 participants diagnosed with periodontitis were enrolled across these studies. Halitosis was evaluated using a halimeter in six studies [2, 5, 9, 11, 14, 31], and gas chromatography was employed in three studies [3, 4, 32].

Quantitative synthesis to estimate the pooled prevalence rate

In the meta-analysis, we found 62% (95% CI: 46.6%–75.4 %), as the pooled prevalence of halitosis among patients with periodontitis when halitosis was measured objectively by halitometers. The two-tailed p-value of the overall effect test was 0.072, which was greater than 0.05, indicating that the pooled estimate did not reach statistical significance (i.e., we cannot reject the null hypothesis that the true prevalence is 50%). We also observed substantial heterogeneity I^2 = 85.77%, Cochran's Q= 56.21, ($p < 0.001$), and between-study variance was $\tau^2 = 0.53$, as shown in the figure 2. For publication bias, Egger's regression revealed a non-significant intercept (p = 0.928), suggesting no evidence of bias as shown in the figure 3 and Funnel plot visualization showed no asymmetry as seen in the figure 4.



#	Study name	Effect size	CI Lower limit	CI Upper limit	Weight
1	C Izidoro et	-0.52	-1.10	0.06	11.64%
2	C Izidoro et	-0.22	-0.70	0.25	12.19%
3	H Alzoman 2	1.50	0.83	2.16	11.13%
4	L. G Soares (	1.10	0.67	1.53	12.37%
5	A Apatzidou	1.52	0.51	2.53	9.24%
6	Y H Lee et a	-0.29	-1.07	0.50	10.56%
7	O A Ayo-Yus	0.49	-0.16	1.13	11.32%
8	H Kurata et	-0.25	-1.33	0.82	9.10%
9	Bolepalli et	1.08	0.66	1.49	12.45%

Figure 2. (Forest plot): meta-analysis 62% (95CI: 46.6%-75.4%)-I2=85.77%, Cochran's Q = 56.21.

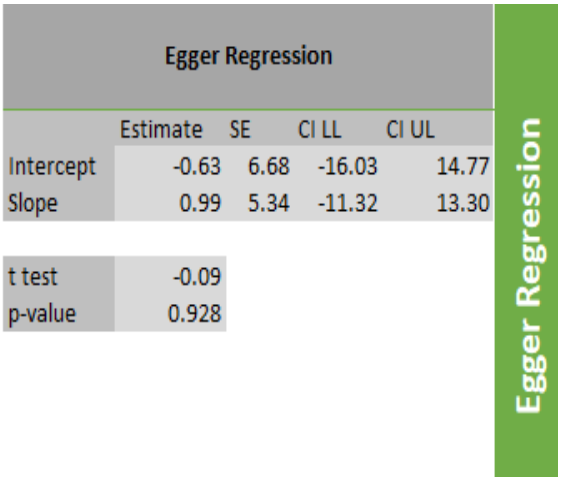


Figure 3. Egger's regression shown non-significant intercept (p=0.928p=0.928), indicates no bias.

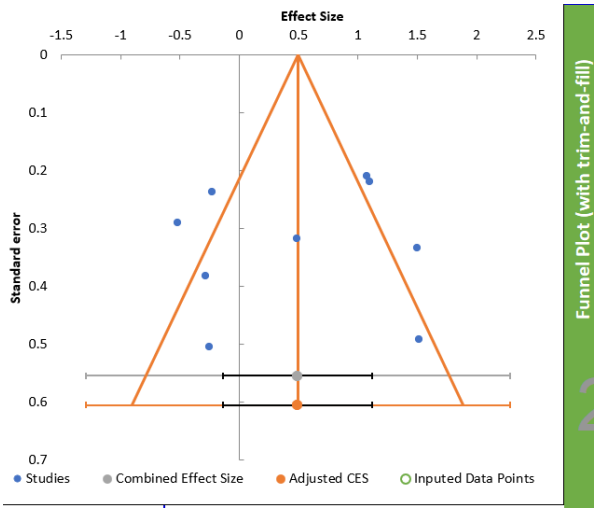


Figure 4. Funnel plot visualization shown symmetric distribution of studies that suggests no bias.

Qualitative synthesis to explore the sources of heterogeneity

1. Diagnostic criteria for periodontal patients and its severity

We found significant heterogeneity in the definition criteria used by studies for periodontitis, namely the 2018 AAP/EFP classification [31], PD ≥4, PD≥5, CAL of ≥5 mm, and 2017 World Workshop [32] that resulted in different kinds of classification of exposure severity and even most of the studies didn't classify the severity of the exposure (table 3). This affected the reported prevalence of halitosis to be different. Generally, we found that with low PD thresholds (>3–4) mm, low prevalence rates reported [4, 10, 33], and with, high PD thresholds (≥5–6 mm) or as classified chronic periodontitis , high prevalence rates reported [1, 3, 8, 13, 34], with the exception of one study, it was considered a potential outlier, isolated in the table [2].

Table 3. studies stratified by exposure severity and compared with outcome prevalence. Higher periodontitis severity (PD ≥5mm) correlates with higher halitosis prevalence (e.g., 75–82%), except one outlier (PD ≥6mm: 42.9%).

Study names	Sample size	Exposure Severity	exposure classifications	Prevalence rates of halitosis
C Izidoro et al 2023	51	PD>3mm	Not defined	37.30%
C Izidoro et al 2021	72	PD>3mm	Not defined	44.40%
H Kurata et al 2008	16	PD≥4mm	Not defined	43.80%
L. G Soares et al 2015	112	PD≥5mm	chronic periodontitis	75%
A Apatzidou et al 2013	28	PD≥5mm	Chronic periodontitis	82%
O A Ayo-Yusuf et al 2011	42	PD≥5mm	Not defined	61.90%
Bolepalli et al 2015	120	CAL≥5mm	Not defined	75%
H Alzoman 2021	60	PD>3mm	Chronic periodontitis	81.7%
Potential Outlier Study				
Study names	Sample size	Exposure Severity	exposure classifications	Outcome prevalence
Y H Lee et al 2023	28	PD≥6mm	Not defined	42.9%

2. Assessment devices for halitosis

We found that halitosis assessment was performed using various of instruments (Table 4). 6 of 9 studies [3, 4, 8, 10, 13, 34] relied on Halimeter. The remaining three studies [1, 2, 33] used different Gas chromatographs. Maybe the variation in devices, their specificity and sensitivity contributed to the heterogeneity in the prevalence rates.

Table 4. studies were stratified by instrument type and compared by outcome proportions.

Study names	Sample size	Method	Prevalence rates
C Izidoro et al 2023	51	Halimeter	0.373
C Izidoro et al 2021	72	Halimeter	0.444
L. G Soares et al 2015	112	Halimeter	0.75
A Apatzidou et al 2013	28	Halimeter	0.82
Bolepalli et al 2015	120	Halimeter	0.75
O A Ayo-Yusuf et al 2011	42	Halimeter	0.619
H Alzoman 2021	60	GC (OralChroma-Kyoto)	0.817
Y H Lee et al 2023	28	GC (TwinBreasor II)	0.429
H Kurata et al 2008	16	GC (G2800)	0.438

3. VSC threshold values for the diagnosis of halitosis

We found that different threshold criteria of VSCs were defined for halitosis diagnosis, as shown in table 5. In studies that used Halimter, 3 out them [4, 8, 10] defined low VSC cut-off values (80ppb), and the other 3 studies [3, 13, 34] defined high VSC cut-off values (110-140 ppb). In the mentioned studies VSC threshold values (80-140) had a neglected impact in the heterogeneity of prevalence rates in context of severe periodontitis (PD≥5mm), and also in studies that gas chromatograph was used, even with different type of scales for measuring VSCs, at cognitive thresholds the defined thresholds had the same impact as Halimeter was used on prevalence rates in context of periodontal status. For example, in a study in Saudi Arabia prevalence rate was high (81.7) [1] in context of severe periodontitis. These findings suggest that the different VSC cut-off values defined the included studies did not moderate the prevalence proportion in the context of periodontal status, with an exception of one study [2].

Table 5. Halitosis defined by different VSC cutoff values (80–140 ppb). No clear threshold effect on prevalence in severe periodontitis.

The VSC cut-off values for diagnosing halitosis	Authors year	exposure severity	halitosis assessed by type of instruments	proportion of halitosis in the sample size
80 ppb	C Izidoro et al 2023	PD>3mm	Halimeter	0.373
	C Izidoro et al 2021	PD>3mm	Halimeter	0.444
	L. G Soares et al 2015	PD≥5mm	Halimeter	0.750
110-140ppb	O A Ayo-Yusuf et al 2011	PD≥5mm	Halimeter	0.619
	Bolepalli et al 2015	CAL of ≥5 and CAL of 1–4 mm	Halimeter	0.75
	A Apatzidou et al 2013	PD≥5mm	Halimeter	0.820
equal to the cognitive threshold as follows: H2S≥ 112 PPB, CH3SH ≥ 26 PPB and CH3SCH3 ≥ 8 PPB)	H Alzoman 2021	PD>3mm-chronic periodontitis	OralChroma-Kyoto(gas chromatography)	0.817
The VSC cut-off values 65.79 ppb for women and 79.94 ppb for men	Y H Lee et al 2023	PD≥6mm	gas chromatograph-TwinBreasor II(gas chromatography)	0.429
at or above the organoleptic threshold level [TVSC: (H2S) ≥ 1.5 ng/10 mL or (CH3SH) ≥ 0.4 ng/10 mL]	H Kurata et al 2008	PD≥4mm	gas chromatograph - G2800(gas chromatography	0.438

4. Assessment of tongue coating (TC)

We found significant heterogeneity in the assessment method of TC, as seen in the table 6. Four studies [4, 8, 13, 34] used the Winkel Tongue Coating Index (WTCI) [35]. Three studies didn't assess TC [1, 2, 10]. The last 2 studies used alternative methods; one assessed the presence/absence of coating [3], and the other assessed the distribution area of coating [33]. Most studies that used WTCI as a TC assessment reported that TC consistently contributed to halitosis prevalence through VSC production in patients with periodontitis.

Table 6. TC consistently contributed to halitosis prevalence through VSC production in patients with periodontitis.

Authors year	methods for TCS	mean scores (±SD)	significance of TCS on VSC production	Proportion of halitosis	exposure severity
C Izidoro et al 2023	WTCI	3 (±2)	correlated significantly with VSC production	0.373	PD>3mm
L. G Soares et al 2015	WTCI	7±1.58	strong relationship	0.750	PD≥5mm
A Apatzidou et al 2013	WTCI	3.2±2.1	no significance, but slightly elevated	0.820	PD≥5mm
Bolepalli et al 2015	WTCI	8.22±.2.7	very strong positive correlation between TCS and VSC levels	0.75	CAL of ≥5 and CAL of 1–4 mm
O A Ayo-Yusuf et al 2011	presence of Coating	31% TC - presence	associated with an increased likelihood	0.619	PD≥5mm

H Kurata et al 2008	distribution area	1.65±0.5	increase in the tongue coating influenced the VSCs level	0.438	PD≥4mm
C Izidoro et al 2021	not measured	-	-	0.444	PD>3mm
H Alzoman 2021	not measured	-	-	0.817	PD>3mm
Y H Lee et al 2023	not measured	-	-	0.429	PD≥6mm

5. Risk of bias assessment

We assessed the quality of the included studies via the Hoy 2012 tool (Table 7). We found a low-risk profile in the overall result of the assessment. However, weaknesses existed in the representation domain (D1), sampling (D2) and random selection domain (D3) across all included studies. Two studies had moderate risk of bias.[2, 4]. The quality of the included studies may have a small contribution to the heterogeneity in prevalence rates.

Table 7. Risk of bias assessment of nine studies conducted using the Hoy 2012 tool. The table shows Low overall bias risk

Author (Year)	1. Representation	2. Sampling	3. Random selection	4. Non response bias	5. Data collection	6. Case Definition	7. Reliability and validity of study tool	8. Method of data collection	9. Prevalence period	10. Numerator and denominator	overall scores	overall risk of bias
C Izidoro et al 2023	No	No	No	No	Yes	Yes	Yes	Yes	Yes	Yes	4	Moderate
C Izidoro et al 2021	No	No	No	yes	Yes	Yes	Yes	Yes	yes	Yes	3	Low
H Alzoman 2021	No	No	No	yes	Yes	Yes	Yes	Yes	Yes	Yes	3	Low
L. G Soares et al 2015	No	No	No	yes	Yes	Yes	Yes	Yes	Yes	Yes	3	Low
A Apatzidou et al 2013	No	No	No	yes	Yes	Yes	Yes	Yes	yes	Yes	3	Low
Y H Lee et al 2023	No	No	No	yes	Yes	Yes	Yes	no	yes	Yes	4	Moderate
O A Ayo-Yusuf et al 2011	No	No	No	yes	Yes	Yes	yes	Yes	yes	Yes	3	Low
H Kurata et al 2008	No	No	No	yes	Yes	Yes	Yes	Yes	yes	Yes	3	Low
Bolepalli et al 2015	No	No	No	yes	Yes	Yes	Yes	Yes	yes	Yes	3	Low
Risk of bias assessment tool (Hoy 2012): Yes (low risk); No (high risk)												
1. Representation: Was the study's target population a close representation of the national population?												
2. Sampling: Was the sampling frame a true or close representation of the target population?												
3. Random selection: Was some form of random selection used to select the sample, OR, was a census undertaken?												
4. Non-response bias: Was the likelihood of non-response bias minimal?												
5. Data collection: Were data collected directly from the subjects?												
6. Case definition: Was an acceptable case definition used in the study?												
7. Reliability and validity of study tool: Was the study instrument that measured the parameter of interest shown to have reliability and validity?												
8. Data collection: Was the same mode of data collection used for all subjects?												
9. Prevalence period: Was the length of the prevalence period for the parameter of interest appropriate?												
10. Numerators and denominators: Were the numerator(s) and denominator(s) for the parameter of interest appropriate?												
Summary on the overall risk of study bias					LOW RISK if ovearall score is between 0 and 3							
					MODERATE RISK if ovearall score is between 4 and 6							
					HIGH RISK if ovearall score is between 7 and 10							

Discussion

Our systematic review highlights some important findings on the prevalence halitosis in patients with periodontitis. First of all, in our analysis, we calculated pooled effect sizes as 62% (95% CI: 46.6–75.4%), this finding suggests a positive association between periodontitis and halitosis as other studies support this [16, 17], but the generalizability of the estimate is limited due to the high heterogeneity (I^2 = 85.77%) found in the studies, which is not unexpected in view of the heterogeneity associated with diagnostic criteria for periodontitis, VSCs measurement devices, and TC involvement. However, a meta-analysis of such studies might still be useful in providing an idea of the overall prevalence and in estimation of the burden of halitosis

in periodontal patients in clinical settings. Second, we found that halitosis was more prevalent in high-stage periodontitis than lower stages which is supported by several other studies [3, 8, 13, 34]. This finding aligns with the understanding that a high severity of periodontitis, characterized by deeper periodontal pockets and greater microbial activities, leads to a high amount of VSC production that can be detected objectively [9, 36, 37]. Third, the variation in devices, their specificity and sensitivity contributed to the heterogeneity in prevalence rates; using gas chromatography-based devices preferred and defined as the gold standard by some studies for its high specificity and sensitivity in detecting the main VSCs [9, 20, 38], although in a systematic review concluded that none of the halitometers demonstrated a clear advantage over the others[6] thus, Standardization of measurement tools and developing better halitometers is critical to minimize heterogeneity in prevalence rates. Fourth, the different threshold criteria of VSCs that were used for halitometers, did not moderate the prevalence proportion in the context of periodontal status. This finding aligns with knowledge-based article defined by Halimeter® company that a range of 80-140 is considered normal cutoff ranges for halitosis diagnosis [27] also, aligns with gas chromatograph manufacturers that halitosis is diagnosed, if levels of H_2S or CH_3SH pass 112 ppb and 26 ppb [19]. Therefore, the findings suggest that this didn't contribute to the heterogeneity of reported prevalence rates across studies, but generally its maybe better to have standard threshold values of VSCs for diagnosis of halitosis. Fifth, heterogeneity in TC assessment methods identified in this review (Table 6), ranges from the use of the WTCI [4, 8, 13, 34] to alternative methods [3, 33] or no assessment at all [1, 2, 10] that poses another challenge for synthesizing a pooled prevalence of halitosis in people with periodontitis. Crucially, studies using the standardized WTCI consistently identified TC as a significant factor associated with halitosis via VSC production [4, 8, 34]. This methodological variation may oppose the true contribution of TC to overall halitosis prevalence estimates in patients with periodontitis and explain the heterogeneity observed in reported prevalence rates across studies. Standardization of TC assessment, particularly using validated indices like the WTCI, is therefore essential for obtaining accurate and reliable estimates of halitosis prevalence in this population.

Our review has important limitations. First, the generalizability of the overall prevalence estimate is limited due to high heterogeneity. To address this limitation, we conducted a qualitative synthesis of the data, thus permitting comparisons across studies and identifying the sources of heterogeneity. Second, the absence of a pre-registered protocol of this study. To address this limitation, we followed and presented the protocol transparently in this article. Third, we didn't include Scopus and Web of science databases in our search strategy and we may have missed some studies. To address this limitation, we extensively used gray literature by using Google Scholar to find more studies and publication bias test was not significant according to our publication bias analysis. Fourth, we didn't dig into the methods that halitosis was assessed by halitometers that may give us insights on the heterogeneity of outcomes that are within studies, but there are many different devices with different sensitivity, specificity, reliability issues and even constantly evolving that they can further complicate the process [6, 39]. Fifth, we couldn't retrieve the full article of two studies as seen in the PRISMA flow chart. Sixth, the final nine studies in our meta-analysis are not high enough with such enormous heterogeneity discussed.

Two main limitations arose from the existing studies included in this review. First, the studies used different definition criteria and parameters for the diagnosis of periodontitis. Second, the studies used different methods and devices for the diagnosis of halitosis.

Our systematic review and meta-analysis have some strengths. First, to our knowledge, this is the first systematic review focusing exclusively on the prevalence of halitosis in patients with periodontitis that is measured objectively using Halimeter or gas chromatography. Second, our pooled prevalence estimation bridges a gap left by association studies [6, 16]. While they confirmed periodontitis-halitosis links, our 62% pool estimate quantifies the clinical burden of halitosis in periodontal patients, providing insight to support its management by healthcare professionals. Third, because there was high heterogeneity among studies, we have a detailed qualitative synthesis. This approach helped us systematically define the main sources of heterogeneity (e.g., diagnostic criteria for periodontitis). It gave us much richer insights than a simple pooled estimate.

Recommendations

Our systematic review points to several promising directions for future research. First, future studies should use a standardized diagnostic criterion like the 2018 AAP/EFP classification [31] for periodontitis severity to reduce heterogeneity. Second, for researching in the field it's better to use gas chromatography as supported by several studies when we assess halitosis objectively [1, 2, 6, 9, 33] although, no device showed superiority over

the others [6]. Third, studies should identify optimal VSC thresholds for halitosis diagnosis. Fourth, future studies should isolate tongue coating's contribution in VSC production. Fifth, use a standardized tongue coating assessment like WTCI [35] in studies to clarify its role in halitosis prevalence. Finally, researchers must pre-register their protocol for a systematic review and include Scopus/Web of Science in the search strategy to minimize selection bias

Conclusion

Based on the evidence shown above, approximately two-thirds of patients with periodontitis were found to have confirmed halitosis following assessment with VSC measuring devices. High heterogeneity and tongue coating involvement prevented a definitive prevalence estimate, highlighting the need for standardized diagnostic protocols.

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