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Influence of tobacco smoking on the development of halitosis

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ABSTRACT

Background: Halitosis is the general term used to describe any disagreeable odor in exhaled air, regardless of whether the odorous substances originate from oral or non-oral sources. Previous research has strongly associated tobacco smoking in the development of halitosis, as it increases the synthesis of toxic volatile sulfur compounds in diseased periodontal pockets. In this review, we summarize the etiopathology and epidemiology of halitosis as well as the current evidence on the impact of smoking by means of a meta-analysis.

Methods: PubMed and Embase were searched to identify publications that reported halitosis in smokers and nonsmokers. Meta-analyses were performed if a sufficient number ($n \geq 3$) of articles were available that evaluated the same outcome.

Results: The meta-analyses showed that there was an increased risk of halitosis in current smokers versus nonsmokers (odds ratios). These results were consistent both in fixed and random effects models. Even though the interstudy heterogeneity was high ($I^2 = 91\%$), sensitivity analysis by limiting the number of studies yielded similar results, with no-to-moderate heterogeneity ($I^2 = 0–65\%$). The analysis comparing ever smokers with never smokers showed no significant difference in the risk of halitosis in ever smokers. The same effect was observed when upon stratifying the analyses on the basis of ascertainment of halitosis (self-reported or measured by a Halimeter).

Conclusions: Halitosis is a common condition which can affect the quality of life of those affected. The results from this literature review and meta-analysis show that current smokers are more likely to suffer from halitosis, even if they are less likely to report it.

1. Introduction

Halitosis is the general term used to describe any disagreeable odor in expired air, regardless of whether the odorous substances originate from oral or non-oral sources. People who have halitosis often feel embarrassed about it and are adversely affected in terms of the social aspects of their life [1]. These social effects of halitosis usually urge compel patients to seek professional care [2]. Halitosis is considered the third most common reason for dentist visits in the United States, after caries and periodontal disease [3]. However, there should be a differentiation between genuine halitosis and pseudo-halitosis or halitophobia. In genuine halitosis, local factors as well as general factors may play a role in the etiology of the problem.

The prevalence of halitosis varies according to the study population, because the perception of halitosis differs among culturally diverse populations [4]. In Japan, population-based studies have reported the prevalence of halitosis to be 6–23% [5,6]. A recent study conducted in Saudi Arabia found that approximately 22% of adults have self-perceived halitosis and that it was significantly associated with waterpipe tobacco smoking [7].

Additionally, approximately 25% of individuals with halitosis experience such a severe problem that it affects their social functioning. For example, individuals may feel nervous and embarrassed in the presence of other people and may avoid social contact and intimate relationships [8].

Reviews in research reports now agree that, in the vast majority of cases (80–90%), halitosis originates within the oral cavity [9], where anaerobic bacteria degrade sulfur-containing amino acids into the foul-smelling volatile sulfur compounds (VSC) hydrogen sulfide and methylmercaptan. These sulfur-containing compounds are produced by microorganisms and are often associated with bad odors. Some investigators believe that, besides VSCs, other volatiles produced by oral

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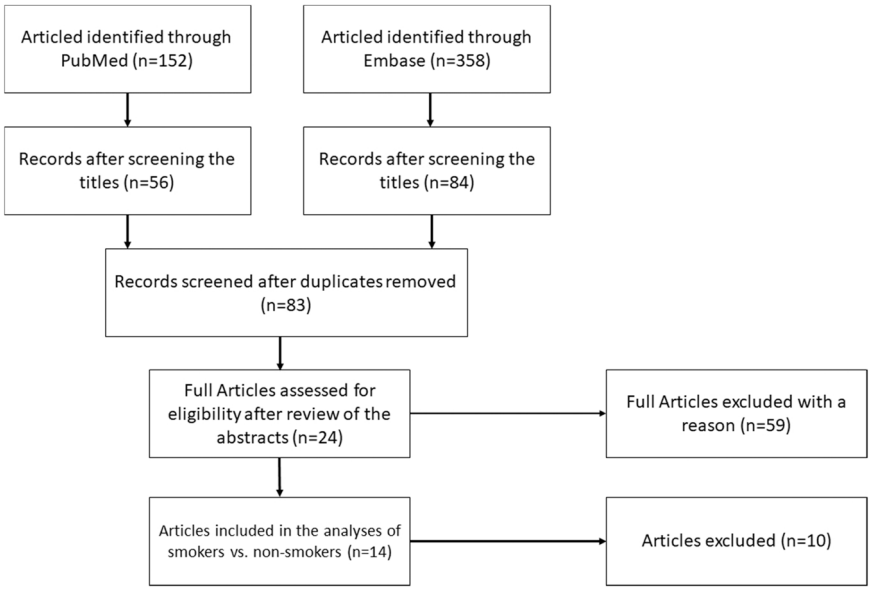

Fig. 1. PRISMA chart detailing the literature search results.

putrefaction processes—such as organic acids, ammonia, and amines—may also cause oral malodor [10,11]. The two major sources for VSCs are periodontal disease and tongue coating, which is a grayish-white deposit on the tongue [12]. On the other hand, an estimated 10–20% of halitosis cases have non-oral causes [13,14].

Previous research has shown that tobacco smoking is the second greatest offender in the development of halitosis, behind periodontal disease and the associated food stagnation. Smoking causes a decrease in the commensal population of normal flora in the oral cavity, leading to an increase in pathogenic microbes [15] as well as enhancement of microbial colonization by biofilm formation on oral epithelial cells. More importantly, a number of studies have reported that smoking increases the probability of extensive disease development [16,17] and causes significant disruption in the oral microbiota, creating an imbalance in the oral environment. Moreover, smoking contributes to halitosis by causing hyposalivation [18,19].

The aim of this study is to summarize of evidence on the effects of smoking on the development of halitosis by means of a meta-analysis.

2. Methods

This was a meta-analysis of interventional and observational studies performed using literature identified through PubMed and Embase. The query used in both search engines was: (halitosis OR bad breath) AND (tobacco OR smoke OR smoking OR smoker OR nicotine OR e-cigarette OR e-cig OR ENDS OR e-vapor OR heated tobacco OR IQOS OR THS OR tobacco heating). The searches were performed in the week of March 1, 2021.

Retrieval of articles was limited to those written in English and considering human populations. To verify that all available relevant publications were retrieved, the reference lists of the publications obtained through the original search were checked for additional citations.

2.1. Study selection

The following criteria were used for including publications in our review: a) case control, cohort, or interventional studies such as randomized controlled trials; b) adult human populations; c) number of patients with halitosis (self-reported or diagnosed by a Halimeter), stratified by smoking status and including sample size; and d) published between 1970 and March 1, 2021.

The exclusion criteria were as follows: a) review articles, case reports, or editorials; b) reports with incomplete data; and c) data reused in a more recent study.

2.2. Data extraction

The following information was extracted from each study: first author's name, year of publication, study design, population characteristics, and number of participants per group.

2.3. Statistical analysis

Meta-analyses were performed when a sufficient number of articles ($n \geq 3$) that evaluating the same outcome were available. The risk comparison between two groups was measured using ORs with 95% confidence intervals (CIs) and visualized using the forest plot. The Mantel–Haenszel method with inverse variance weighting was used in both fixed and random effects models to pool results. The degree of heterogeneity between the study results was tested by the inconsistency statistic (I2). Funnel plots were used to evaluate publication bias [20]. Statistical significance was assessed at $\alpha = 0.05$.

The analyses were implemented using R 4.0.5. Specifically, we used the R library "meta" [21].

3. Results

The searches yielded 152 articles in PubMed and 358 in Embase. The results of both searches can be found in the PRISMA chart in Fig. 1.

A total of 24 publications that assessed the effect of smoking status on halitosis were identified. Of these, 14 studies met the inclusion criteria for the analysis. Table 1 presents the characteristics of these studies. The remaining 10 studies were not included, as 8 of these contained incomplete information [5,22–28], 1 included smokers and former smokers together [29] and 1 had no control group [30].

The meta-analysis assessing the risk of halitosis in current smokers versus nonsmokers included nine comparisons from eight studies. Both fixed and random effects models showed an increased risk for halitosis among current smokers (ORs = 1.46 [95% CI, 1.30–1.64] and OR=2.00 [95% CI, 1.25–3.21], respectively). The interstudy heterogeneity was high ($I^2 = 91\%$). Figs. 2 and 3 present the forest and funnel plots related to this comparison, respectively. Overall, the funnel plots show the odds ratio and standard errors of each study are plotted on the x-axis and y-axis, respectively. The dark and light blue shaded regions represent

Table 1
Characteristics of studies evaluating halitosis in smokers and nonsmokers included in the meta-analyses.

Reference	Country	Study design	Study participants	Smoking definition	Diagnosis of halitosis	Subgroup (halitosis, YES/NO)			
						Patient group	Smokers (n)	Nonsmokers (n)	OR (95% CI)
Al Ansari et al. [31]	Kuwait	Cross-sectional	1551 Kuwaiti adult subjects	Smoking history	Self-reported	All	107/182	249/976	2.30 (1.75–3.04)
Alqatahni et al. [32]	Saudi Arabia	Cross-sectional	100 male participants with peri-implantitis	Current smoking	Self-reported	All	20/15	11/21	2.55 (0.95–6.85)
AlSadhan [7]	Saudi Arabia	Cross-sectional	Male and female students	Smoking history	Self-reported	All	66/173	468/1636	1.33 (0.99–1.80)
Al-Zahrani et al. [33]	Saudi Arabia	Cross-sectional	38 consecutive type 2 diabetic patients were recruited from among patients who presented for treatment at a University hospital	Smoking history	Self-reported	All	3/7	13/15	0.49 (0.11–2.31)
Ayo-Yusuf et al. [34]	South Africa	Cross-sectional	896 patients examined between January and October 2004 were retrospectively analyzed.	Current smoking	Halimeter: No halitosis considered in subjects with halitosis measurement of 0–1	All	119/133	206/431	1.87 (1.39–2.52)
Babazadeh et al. [35]	Iran	Cross-sectional	519 adolescents in Qazvin, Iran	Current smoking	Self-reported	All	57/48	197/219	1.32 (0.86–2.03)
Eldarrat et al. [36]	United Arab Emirates	Cross-sectional	Men and women aged between 19 and 24 years	Smoking history	Self-reported	All	7/27	36/163	1.17 (0.47–2.91)
Jiun et al. [37]	Malaysia	Cross-sectional	100 smokers and 100 nonsmokers aged 18–50 years were recruited	Current smoking	Halimeter	All	75/25	8/92	34.50 (14.71–80.92)
Lee et al. [4]	South Korea	Cross-sectional	54 subjects (male:female = 33:21) with a mean age of 46.0 ± 11.4 years were analyzed	Smoking history	Halimeter: Halitosis was measured as > 100 ppb	All	8/3	23/20	2.32 (0.54–9.94)
Rech et al. [38]	Brazil	Cross-sectional	48 subjects (current tobacco users and never smokers, 24 each)	Current smoking	Self-reported	All	8/16	1/23	11.50 (1.31–101.18)
Romano et al. [39]	Italy	Cross-sectional	736 adults (25- to 75-years-old) in a city in northern Italy	Current smoking	Self-reported	All	76/97	307/256	0.65 (0.46–0.92)
Saadaldina et al. [40]	Saudi Arabia	Cross-sectional	460 adults participated in the study	Smoking	Self-reported	All	16/19	121/304	2.12 (1.05–4.25)
Sanli et al. [41]	Turkey	Cross-sectional	1840 patients (823 men and 1017 women) over 25 years of age, who were admitted to a ear, nose, and throat outpatient clinic were included in the study	Current smoking	Self-reported	All	194/515	237/1058	1.68 (1.35–2.09)
Struch et al. [42]	Germany	Cross-sectional	Halitosis was assessed among 417 edentulous (toothless) subjects aged 40–81 years and among 2588 dentate subjects aged 20–59 years	Current smoking	Self-reported	Dentate	207/787	173/684	1.04 (0.83–1.30)
						Edentulous	10/76	12/129	1.41 (0.58–3.43)

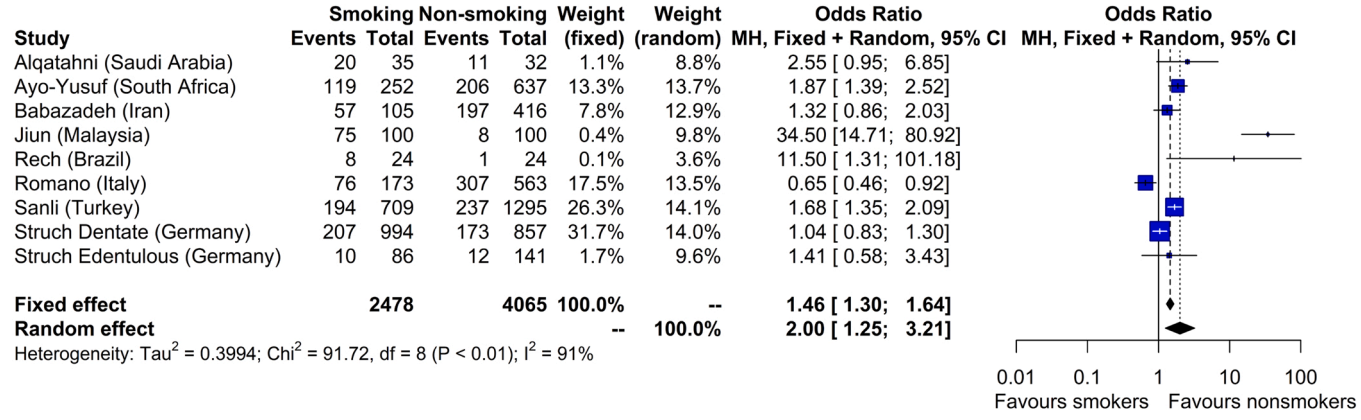

Fig. 2. Forest plot meta-analysis of risk of halitosis in current smokers versus nonsmokers.

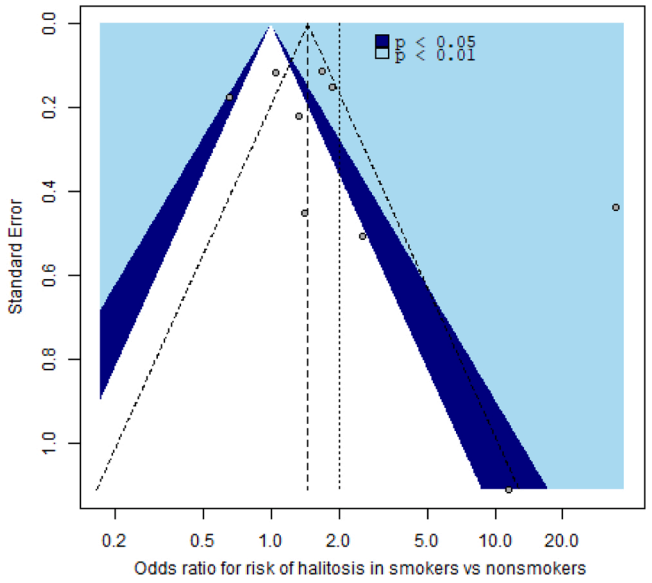

Fig. 3. Funnel plot meta-analysis of risk of halitosis in current smokers versus nonsmokers.

significant effects at p = 0.05 and p = 0.01 levels of significance, respectively.

Visual analysis of the funnel plot showed no evidence of publication bias. Because of the high heterogeneity, we performed sensitivity analysis by excluding those studies that were driving the most heterogeneity. The sensitivity analysis shown in Fig. 4 includes six studies [32,34,35,41,42], as the studies by Rech et al. [38], Jiun et al. [37], and Romano et al. [39] accounted for 20% of all interstudy heterogeneity. The results of this analysis also showed an increased risk of halitosis among current smokers in both fixed and random effects models (ORs = 1.43 [95% CI, 1.26–1.63] and OR = 1.49 [95% CI, 1.15–1.92], respectively; $I^2 = 65\%$).

The meta-analysis of ever smokers versus never smokers included six studies. The fixed effects model showed an increased risk for halitosis in ever smokers versus nonsmokers (OR = 1.74 [95% CI, 1.45–2.10]), while the random effects analysis did not show a statistically significant difference in halitosis risk between the two groups (OR = 1.66 [95% CI, 1.16–2.37]). The interstudy heterogeneity was moderate (I^2 = 53%). Figs. 5 and 6 show the forest and the funnel plots of these analyses, respectively. Visual analysis of the funnel plot did not reveal any evidence of publication bias.

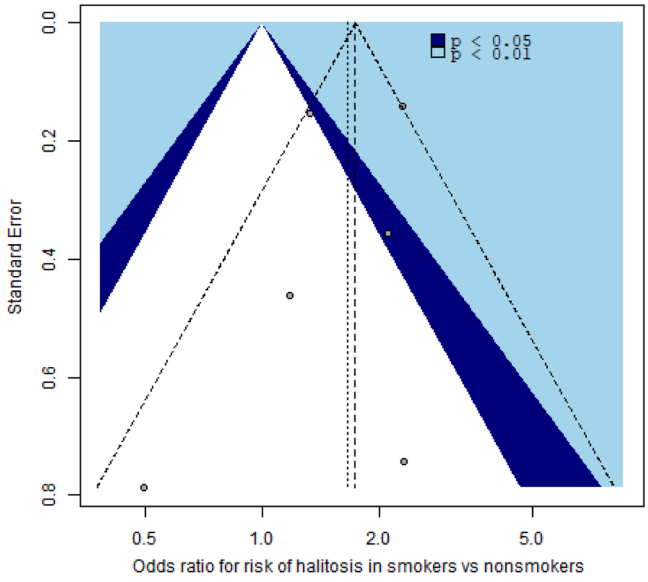

Fig. 6. Funnel plot meta-analysis of risk of halitosis in ever smokers versus nonsmokers.

Study	Smoking Events	Smoking Total	Non-smoking Events	Non-smoking Total	Weight (fixed)	Weight (random)	Odds Ratio MH, Fixed + Random, 95% CI
Alqatahni (Saudi Arabia)	20	35	11	32	1.3%	5.5%	2.55 [0.95; 6.85]
Ayo-Yusuf (South Africa)	119	252	206	637	16.2%	21.7%	1.87 [1.39; 2.52]
Babazadeh (Iran)	57	105	197	416	9.6%	16.5%	1.32 [0.86; 2.03]
Sanli (Turkey)	194	709	237	1295	32.1%	25.1%	1.68 [1.35; 2.09]
Struch Dentate (Germany)	207	994	173	857	38.7%	24.7%	1.04 [0.83; 1.30]
Struch Edentulous (Germany)	10	86	12	141	2.1%	6.6%	1.41 [0.58; 3.43]
Fixed effect		**2181**		**3378**	**100.0%**	**--**	**1.43 [1.26; 1.63]**
Random effect					**--**	**100.0%**	**1.49 [1.15; 1.92]**

Heterogeneity: $Tau^2 = 0.0562$; $Chi^2 = 14.32$, df = 5 (P = 0.01); $I^2 = 65\%$

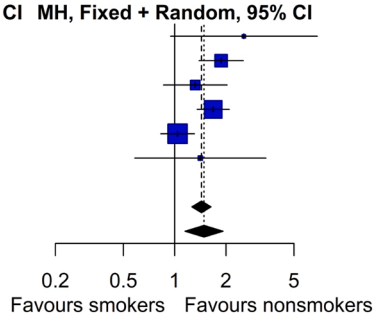

Fig. 4. Forest plot meta-analysis of risk of halitosis in current smokers versus nonsmokers (sensitivity analysis).

Study	Smoking Events	Smoking Total	Non-smoking Events	Non-smoking Total	Weight (fixed)	Weight (random)	Odds Ratio MH, Fixed + Random, 95% CI
Al Ansari (Kuwait)	107	289	249	1225	38.7%	32.1%	2.30 [1.75; 3.04]
AlSadhan (Saudi Arabia)	66	239	468	2104	44.7%	31.0%	1.33 [0.99; 1.80]
Al-Zahrani (Saudi Arabia)	3	10	13	28	3.1%	4.7%	0.49 [0.11; 2.31]
Eldarrat (UAE)	7	34	36	199	5.4%	11.2%	1.17 [0.47; 2.91]
Saadaldina (Saudi Arabia)	16	35	121	425	6.5%	15.8%	2.12 [1.05; 4.25]
Lee (South Korea)	8	11	23	43	1.7%	5.2%	2.32 [0.54; 9.94]
Fixed effect		**618**		**4024**	**100.0%**	**--**	**1.74 [1.45; 2.10]**
Random effect					**--**	**100.0%**	**1.66 [1.16; 2.37]**

Heterogeneity: $Tau^2 = 0.0837$; $Chi^2 = 10.69$, df = 5 (P = 0.06); $I^2 = 53\%$

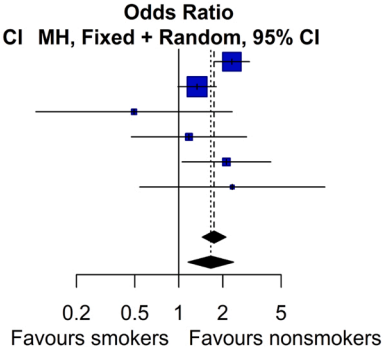

Fig. 5. Forest plot meta-analysis of risk of halitosis in ever smokers versus never smokers.

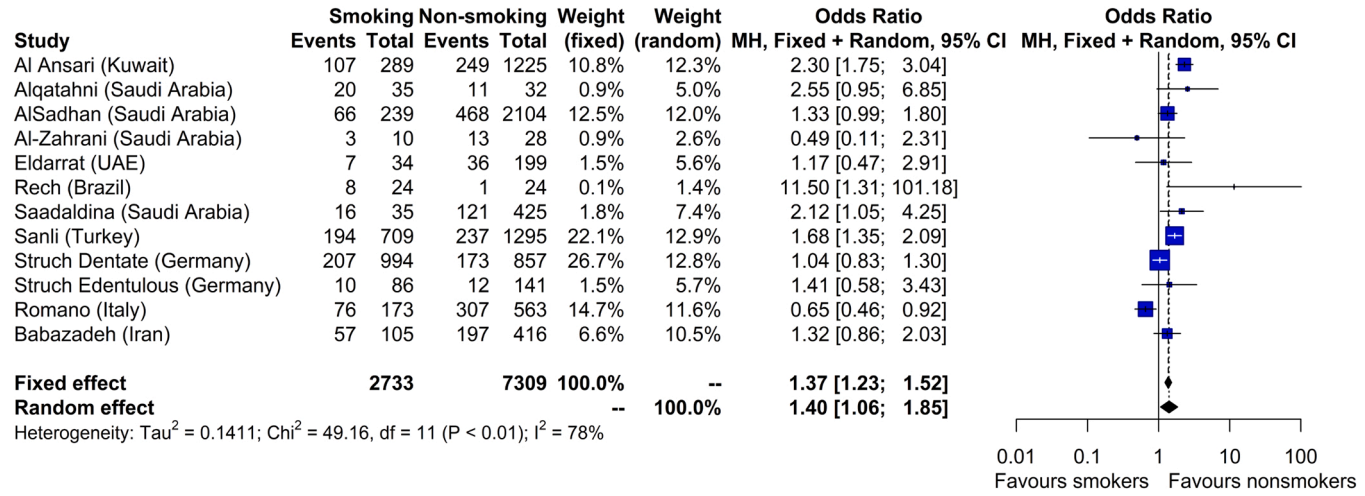

Fig. 7. Forest plot meta-analysis of risk of halitosis in smokers versus nonsmokers (self-reported outcome).

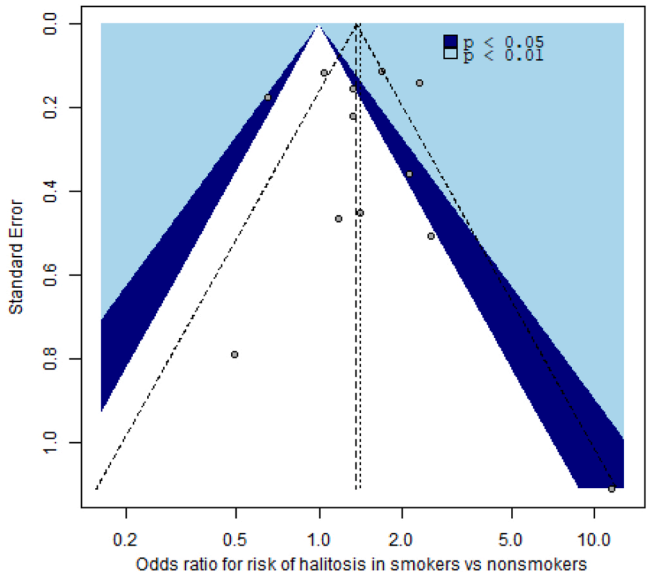

Fig. 8. Funnel plot meta-analysis of risk of halitosis in smokers versus nonsmokers (self-reported outcome).

For meta-analysis of smokers (current and ever smokers) versus nonsmokers including only those studies that used self-reporting of halitosis, 12 of the 14 studies met the inclusion criteria. The fixed effects model showed an increased risk of halitosis in smokers (OR = 1.37 [95% CI, 1.23–1.52]), while the random effects analysis did not show a statistically significant difference in halitosis risk between the two groups (OR = 1.40 [95% CI, 1.06–1.85]). The interstudy heterogeneity was high ($I^2 = 78\%$). Figs. 7 and 8 show the forest and funnel plots related to this analysis, respectively. Visual analysis of the funnel plot did not reveal any evidence of publication bias.

For the meta-analysis of smokers (current and ever smokers) versus nonsmokers including only those studies that used a Halimeter for diagnosis, only three studies met the inclusion criterion. The fixed effects model showed an increased risk for halitosis in smokers (OR = 2.88 [95% CI, 2.22–3.72]), while the random effects analysis did not show a statistically significant difference in halitosis risk between the two

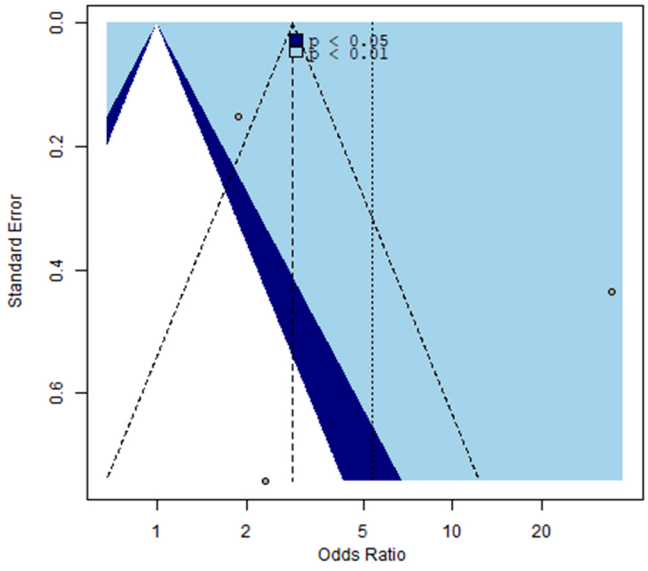

Fig. 10. Funnel plot meta-analysis of risk of halitosis in smokers versus nonsmokers (Halimeter-measured outcome).

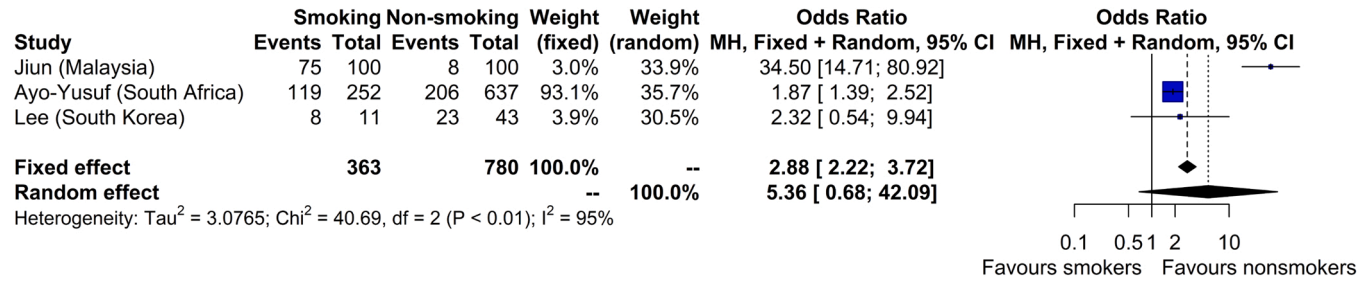

Fig. 9. Forest plot meta-analysis of risk of halitosis in smokers versus nonsmokers (Halimeter-measured outcome).

groups (OR = 5.36 [95% CI, 0.68–42.09]). The interstudy heterogeneity was high (I^2 = 95%). Figs 9 and 10 show the forest and funnel plots of this analysis. Visual analysis of the funnel plot did not reveal any evidence of publication bias.

4. Discussion

Halitosis is commonly defined as an unpleasant or offensive smell that is emitted from the oral cavity [43], and has a long history, dating back to 1500 BCE, as Hippocrates, the ancient Greeks, and the Romans mentioned it in their writings [12]. Halitosis poses a diagnostic problem, probably because there are many methods to measure it and because of its multifactorial etiology [44]. The aim of this manuscript was to summarize the effects of smoking on the development of halitosis by means of a meta-analysis. The meta-analysis assessing risk for halitosis in current smokers relative to nonsmokers found an increased risk for the current smoker group. These results were consistent both in fixed and random effects models. Even though the interstudy heterogeneity was high (I^2 = 91%), sensitivity analysis by limiting the number of studies yielded similar results, with no-to-moderate heterogeneity (I^2 = 0–65%). The analysis comparing ever smokers with never smokers showed a non-significantly increased risk of halitosis in ever smokers, which disappeared when using the random effects model. The same effect was seen when stratifying the analyses by ascertainment of halitosis (self-reported or measured by a Halimeter).

A possible reason for the high interstudy heterogeneity could be that the studies originated from very diverse populations. However, the most probable cause is the ascertainment of halitosis. This is because smokers have a greater probability of being less objective in reporting gingival conditions and halitosis [39], and, therefore, the prevalence of halitosis in these studies might be higher than that reported among the smoking groups.

Cigarette smoking is a public health problem [15] and cigarette smoke contains numerous toxicants to which smokers are regularly exposed on a periodic basis. These toxicants can potentially alter the microbial ecology of the mouth through numerous mechanisms such as antibiotic effects and oxygen deprivation [45].

A characteristic stale odor, difficult to abolish is the hallmark of the tobacco smoker [46]. Previous research has shown that tobacco smoking is the second greatest offender in the development of halitosis, behind periodontal disease and associated food stagnation. Halitosis is often unsuspected by the sufferer because of an adaptation to the smell which occurs within a short period of time (summarized by [46]). The study by Romano et al. [39] also showed that smokers had a greater probability of being less objective in reporting gingival conditions and halitosis.

Some components of tobacco combustion are actually absorbed into the blood stream via the oral mucosa or the mucosa of the lung alveoli. These substances can be exhaled because of the blood-air interchange which occurs in the lungs. The offensiveness of exhaled breath relates to the odor intensity of the tobacco used, so that cigar and pipe tobacco smokers suffer more from halitosis than those who smoke cigarettes.

Other pathways by which smoking can produce halitosis is by decreasing the commensal population of normal flora in the oral cavity, leading to an increase of pathogenic microbes, [15] as well as enhancing microbial colonization by biofilm formation on oral epithelial cells. This may impair host immune responses against pathogens and also disrupt effective nasal mucociliary clearance [47,48]. More importantly, a number of studies have reported that smoking increases the probability of extensive disease development [16,17] and causes a significant disruption in the oral microbiota, creating an imbalance in the oral environment. The study by Ilankizhai and Leelavathi [45] for instance, examined the changes caused by tobacco smoking on the microbial profile and oral health conditions of cigarette smokers compared to non-smokers. They found that smokers had more diverse microbial colonization than non-smokers. Staphylococcus and Bacillus species were the most prevalent bacterial isolates among smokers, followed by Enterococcus and Micrococcus species, while among non-smokers, Streptococcus was the most prevalent isolate followed by Enterococcus and Bacillus species.

Moreover, smoking contributes to halitosis by causing hyposalivation and periodontal diseases [18,19]. The study by Rad et al. [49] evaluated the effect of smoking on salivary flow rate as well as oral and dental health in 100 smokers and 100 non-tobacco users. The authors reported that mean (± SD) salivary flow rates were 0.38 (± 0.13) ml/min in smokers and 0.56 (± 0.16) ml/min in non-smokers. The difference was statistically significant (P = 0.00001). Also, 39% of smokers and 12% of non-smokers reported experiencing at least one xerostomia symptom, with statistically significant difference between groups (p = 0.0001).

Finally, it has been shown that while the oral hygiene habits in nonsmokers and light smokers are comparable, heavy smokers have been found to have worse oral hygiene habits than nonsmokers [50].

Our analyses have some limitations. First of all, all studies included were of cross-sectional design. Also, the majority of these (n = 11) relied on the self-reporting of halitosis and only 3 had objective measurement of halitosis by using a halimeter. Of the 3 studies that used a halimeter, all of them seem to have used different definitions. The study by Ayo-Yusuf [34] measured halitosis as yes/no, the study by Lee et al. [4] used a definition of > 100 ppb while the study by Jiun et al. [37] did not specify a definition.

Our meta-analyses found that smoking is associated with the development of halitosis, most likely because of hyposalivation and periodontal diseases [18,19] as well as by decreasing the commensal population of normal flora in the oral cavity, which leads to an increase in pathogenic microbes [15] and also enhancement of microbial colonization by biofilm formation on oral epithelial cells.

5. Conclusions

Halitosis is a common condition that can affect the quality of life of the affected individual. The results from this meta-analyses show that current smokers are more likely to suffer from halitosis than nonsmokers.

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CRediT authorship contribution statement

Alba Romero Kauss: Formal analysis, Writing – original draft. **Meagan Antunes:** Data curation. **Filippo Zanetti:** Conceptualization, Project administration. **Matthew Hankins:** Supervision, Writing – review & editing. **Julia Hoeng:** Conceptualization. **Annie Heremans:** Supervision. **Angela van der Plas:** Methodology, Investigation, Writing – review & editing.

Declaration of Competing Interest

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References

[1] C.M. Bollen, T. Beikler, Halitosis: the multidisciplinary approach, Int. J. Oral Sci. 4 (2) (2012) 55–63.
[2] A.M. van den Broek, L. Feenstra, C. de Baat, A review of the current literature on aetiology and measurement methods of halitosis, J. Dent. 35 (8) (2007) 627–635.
[3] A.D.A, Council on Scientific Affairs, J. Am. Dent. Assoc. 134 (35) (2003) 209–214.
[4] H.J. Lee, H.M. Kim, N. Kim, J.C. Oh, H.J. Jo, J.T. Lee, et al., Association between halitosis diagnosed by a questionnaire and halimeter and symptoms of gastroesophageal reflux disease, J. Neurogastroenterol. Motil. 20 (4) (2014) 483–490.

[5] H. Miyazaki, S. Sakao, Y. Katoh, T. Takehara, Correlation between volatile sulphur compounds and certain oral health measurements in the general population, J. Periodontol. 66 (8) (1995) 679–684.
[6] R. Seemann, M. Bizhang, C. Djamchidi, A. Kage, S. Nachnani, The proportion of pseudo-halitosis patients in a multidisciplinary breath malodour consultation, Int. Dent. J. 56 (2) (2006) 77–81.
[7] S.A. AlSadhan, Self-perceived halitosis and related factors among adults residing in Riyadh, Saudi Arabia. A cross sectional study, Saudi Dent. J. 28 (3) (2016) 118–123.
[8] L. McKeown, Social relations and breath odour, Int. J. Dent. Hyg. 1 (4) (2003) 213–217.
[9] G. Delanghe, J. Ghyselen, L. Feenstra, D. van Steenberghe, Experiences of a Belgian multidisciplinary breath odour clinic, Acta Otorhinolaryngol. Belg. 51 (1) (1997) 43–48.
[10] S. Goldberg, A. Kozlovsky, D. Gordon, I. Gelernter, A. Sintov, M. Rosenberg, Cadaverine as a putative component of oral malodor, J. Dent. Res. 73 (6) (1994) 1168–1172.
[11] R.B. Greenstein, S. Goldberg, S. Marku-Cohen, N. Sterer, M. Rosenberg, Reduction of oral malodor by oxidizing lozenges, J. Periodontol. 68 (12) (1997) 1176–1181.
[12] K. Seerangaiyan, F. Juch, E.G. Winkel, Tongue coating: its characteristics and role in intra-oral halitosis and general health-a review, J. Breath Res. 12 (3) (2018), 034001.
[13] J. Tonzetich, Production and origin of oral malodor: a review of mechanisms and methods of analysis, J. Periodontol. 48 (1) (1977) 13–20.
[14] T.M. Durham, T. Malloy, E.D. Hodges, Halitosis: knowing when 'bad breath' signals systemic disease, Geriatrics 48 (8) (1993) 55–59.
[15] O.M.E.J. Ogba, O.A. Olorode, M. Mbah, Effect of tobacco smoking on oral microbial flora and the relationship with oral health in Calabar, Nigeria, Int. J. Biomed. Lab. Sci. 6 (2017) 1–5.
[16] P.P. Hujoel, M.A. del Aguila, T.A. DeRouen, J. Bergstrom, A hidden periodontitis epidemic during the 20th century? Commun. Dent. Oral Epidemiol. 31 (1) (2003) 1–6.
[17] D.A. Apatzidou, M.P. Riggio, D.F. Kinane, Impact of smoking on the clinical, microbiological and immunological parameters of adult patients with periodontitis, J. Clin. Periodontol. 32 (9) (2005) 973–983.
[18] B.A.A.-R.A. Al-Atrooshi, Oral halitosis and oral hygiene practices among dental students, J. Bagh. Coll. Dent. 19 (2007) 72–76.
[19] C. Scully, J. Greenman, Halitology (breath odour: aetiopathogenesis and management), Oral Dis. 18 (4) (2012) 333–345.
[20] P. Macaskill, S.D. Walter, L. Irwig, A comparison of methods to detect publication bias in meta-analysis, Stat. Med. 20 (4) (2001) 641–654.
[21] G.C. Schwarzer, J.R. Rucker, G. Fixed, Effect and random effects meta-analysis, Meta-Analysis with R. XII (2015) 252.
[22] C.M. Kayombo, E.G. Mumghamba, Self-reported halitosis in relation to oral hygiene practices, oral health status, general health problems, and multifactorial characteristics among workers in Ilala and Temeke Municipals, Tanzania, Int. J. Dent. 2017 (2017), 8682010.
[23] M.M. Bornstein, K. Kislig, B.B. Hoti, R. Seemann, A. Lussi, Prevalence of halitosis in the population of the city of Bern, Switzerland: a study comparing self-reported and clinical data, Eur. J. Oral Sci. 117 (3) (2009) 261–267.
[24] M.M. Bornstein, B.L. Stocker, R. Seemann, W.B. Burgin, A. Lussi, Prevalence of halitosis in young male adults: a study in swiss army recruits comparing self-reported and clinical data, J. Periodontol. 80 (1) (2009) 24–31.
[25] S.Y. Kim, S. Sim, S.G. Kim, B. Park, H.G. Choi, Prevalence and associated factors of subjective halitosis in Korean adolescents, PLoS One 10 (10) (2015), e0140214.
[26] R.S. Tubaishat, Z.A. Malkawi, Z.S. Albashaireh, The influence of different factors on the oral health status of smoking and nonsmoking adults, J. Contemp. Dent. Pract. 14 (4) (2013) 731–737.
[27] M.F. Silva, G.G. Nascimento, F.R.M. Leite, B.L. Horta, F.F. Demarco, Periodontitis and self-reported halitosis among young adults from the 1982 Pelotas Birth Cohort, Oral Dis. 26 (4) (2020) 843–846.
[28] S. Setia, P. Pannu, R.S. Gambhir, V. Galhotra, P. Ahluwalia, A. Sofat, Correlation of oral hygiene practices, smoking and oral health conditions with self perceived halitosis amongst undergraduate dental students, J. Nat. Sci. Biol. Med. 5 (1) (2014) 67–72.
[29] N.A. Yahya, R. Saub, M.M. Nor, N. Yusoff, Dental patient knowledge about the effects of smoking and attitudes about the role of dentists in smoking cessation, Southeast Asian J. Trop. Med. Public Health 48 (2) (2017) 473–484.
[30] A. Barik, R.K. Rai, A. Chowdhury, Tobacco use and self-reported morbidity among rural Indian adults, Prim. Health Care Res. Dev. 17 (5) (2016) 514–523.
[31] J.M. Al-Ansari, H. Boodai, N. Al-Sumait, A.K. Al-Khabbaz, K.F. Al-Shammari, N. Salako, Factors associated with self-reported halitosis in Kuwaiti patients, J. Dent. 34 (7) (2006) 444–449.
[32] F. Alqahtani, N. Alqhtani, D.D. Divakar, S.B. Shetty, B. Shetty, F. Alkhtani, Self-rated peri-implant oral symptoms and clinicoradiographic characteristics in Narghile-smokers, cigarette-smokers, and nonsmokers with peri-implantitis, Clin. Implant Dent. Relat. Res. 21 (6) (2019) 1235–1240.
[33] M.S. Al-Zahrani, K.H. Zawawi, O.N. Austah, H.S. Al-Ghamdi, Self reported halitosis in relation to glycated hemoglobin level in diabetic patients, Open Dent. J. 5 (2011) 154–157.
[34] O.A. Ayo-Yusuf, T.C. Postma, C. van Wyk, Clinical correlates of oral malodour in a population of patients attending a preventive clinic in Pretoria, South Africa, SADJ 66 (7) (2011) 8–31, 326.
[35] S.Y.R. Babazadeh, A. Pakdaman, S.M. Kambakhsh, Normative and Subjective Oral Health Evaluation among Smoking and Non-Smoking Adolescents of Qazvin, Iran, in 2015, Iran. Red. Crescent Med. J. (2017).
[36] A.H. Eldarrat, Influence of oral health and lifestyle on oral malodour, Int. Dent. J. 61 (1) (2011) 47–51.
[37] I.L. Jiun, S.N. Siddik, S.N. Malik, M.M. Tin-Oo, M.K. Alam, M.M. Khan, Association between oral hygiene status and halitosis among smokers and nonsmokers, Oral Health Prev. Dent. 13 (5) (2015) 395–405.
[38] R.S. Rech, K.W. Santos, M.A. Maahs, D.C. Vidor, Masticatory changes as a result of oral disorders in smokers, Int. Arch. Otorhinolaryngol. 18 (4) (2014) 369–375.
[39] F. Romano, S. Perotto, L. Bianco, F. Parducci, G.M. Mariani, M. Aimetti, Self-perception of periodontal health and associated factors: a cross-sectional population-based study, Int. J. Environ. Res. Public Health 17 (2020) 8.
[40] S.A. Saadaldina, E. Eldwakhly, A.A. Alnazzawi, R.A. Alharbi, B.K. Alghamdi, O. A. Abu Hammad, et al., Awareness and practice of oral health measures in medina, Saudi Arabia: an observational study, Int. J. Environ. Res. Public Health 17 (2020) 23.
[41] A. Sanli, E. Bekmez, G. Yildiz, B.A. Erdogan, H.B. Yilmaz, G. Altin, Relationship between smoking and otorhinolaryngological symptoms, Kulak Burun Bogaz Ihtis Derg. 26 (1) (2016) 28–33.
[42] F. Struch, C. Schwahn, H. Wallaschofski, H.J. Grabe, H. Volzke, M.M. Lerch, et al., Self-reported halitosis and gastro-esophageal reflux disease in the general population, J. Gen. Intern. Med. 23 (3) (2008) 260–266.
[43] A.D. Apatzidou, E. Bakirtzoglou, I. Vouros, V. Karagiannis, A. Papa, A. Konstantinidis, Association between oral malodour and periodontal disease-related parameters in the general population, Acta Odontol. Scand. 71 (1) (2013) 189–195.
[44] R. Sombie, A.J.F. Tiendrebeogo, W.P.L. Guiguimde, A. Guingane, S. Tiendrebeogo, K. Ouoba, et al., Halitosis: multidisciplinary diagnostic and therapeutic approaches, Pan Afr. Med. J. 30 (2018) 201.
[45] R.J.L.L. Ilankizhai, Comparison of oral microbiota among smokers and non-smokers - a pilot study, Drug Invent. Today (2018) 10.
[46] R.J. Bastiaan, P.C. Reade, The effects of tobacco smoking on oral and dental tissues, Aust. Dent. J. 21 (4) (1976) 308–315.
[47] E. Tamashiro, G. Xiong, W.T. Anselmo-Lima, J.L. Kreindler, J.N. Palmer, N. A. Cohen, Cigarette smoke exposure impairs respiratory epithelial ciliogenesis, Am. J. Rhinol. Allergy 23 (2) (2009) 117–122.
[48] L. Arcavi, N.L. Benowitz, Cigarette smoking and infection, Arch. Intern. Med. 164 (20) (2004) 2206–2216.
[49] M. Rad, S. Kakoie, F. Niliye Brojeni, N. Pourdamghan, Effect of long-term smoking on whole-mouth salivary flow rate and oral health, J. Dent. Res. Dent. Clin. Dent. Prospects 4 (4) (2010) 110–114.
[50] A. Santos, A. Pascual, J. Llopis, L. Giner, D.M. Kim, P. Levi Jr., et al., Self-reported oral hygiene habits in smokers and nonsmokers diagnosed with periodontal disease, Oral Health Prev. Dent. 13 (3) (2015) 245–251.