Systematic Review

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Olfactory Training for COVID-19-Related Olfactory Dysfunction: A Systematic Review and Meta-Analysis of Randomized Controlled Trials

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Abstract

The coronavirus disease-2019 (COVID-19) pandemic has led to a high prevalence of olfactory dysfunction (OD), a debilitating condition that significantly impacts quality of life (QoL). While most patients recover their sense of smell, a substantial number experience persistent COVID-OD. Olfactory training (OT) has emerged as a leading, non-invasive therapeutic strategy. A systematic review and meta-analysis were conducted on evidence retrieved from Web of Science, PubMed, Scopus, CENTRAL, and Embase through June 2025 for randomized controlled trials (RCTs) evaluating OT in patients with COVID-OD. The primary outcome was the change in objective olfactory scores, and the secondary outcome was the change in QoL scores. We used STATA software to pool outcomes using standardized mean differences (SMD) with 95% confidence intervals (CI). Ten RCTs involving 628 patients were included in the analysis. Compared to the control group, OT was associated with a significant improvement in objective olfactory scores [SMD=0.30, 95% CI (0.08, 0.51), p=0.01] and QoL [SMD=-0.40, 95% CI (-0.65, -0.15), p<0.001]. The heterogeneity among studies was low for both outcomes (I^2=33.69% and I^2=37.47%, respectively). OT significantly improves objective olfactory function and QoL in patients with COVID-OD. Despite these positive findings, the results should be interpreted with caution due to heterogeneity in OT protocols and variability among the included studies. Future large-scale, rigorously designed RCTs with standardized OT protocols are necessary to establish definitive clinical practice guidelines.

Keywords: Anosmia, COVID-19, olfactory training, quality of life, meta-analysis

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Introduction

The coronavirus disease-2019 (COVID-19) pandemic has presented a diverse range of clinical symptoms; notably, the abrupt onset of olfactory dysfunction (OD), encompassing anosmia and hyposmia, quickly became a significant diagnostic indicator of COVID-19 (1). The high predictive value of COVID-OD, exceeding that of fever or cough, has led major health organizations and otolaryngology societies to recognize it as a key diagnostic indicator warranting self-isolation (2,3). Early pandemic meta-analyses revealed a substantial pooled prevalence of COVID-OD, affecting approximately 47%; some studies employing objective psychophysical testing reported rates as high as 98% (4,5). Despite a reduction in prevalence with variants such as Omicron, the underlying pathophysiological mechanisms and optimal treatment strategies remain unclear (6).

COVID-OD, unlike the majority of postviral anosmia cases, does not typically arise from direct viral infection of the olfactory sensory neurons (OSNs). Evidence from molecular and autopsy studies suggest that SARS-CoV-2 predominantly infects non-neuronal support cells, particularly sustentacular cells expressing ACE2 and TMPRSS2, leading to secondary disruption of OSN function through inflammatory mechanisms (7-9). The initial insult initiates a cascade of localized tissue damage, an inflammatory response, and non-cell-autonomous disruption of OSN function, including the downregulation of odorant receptor genes, resulting in functionally silent neurons (10). Although most patients recover within weeks to months, approximately 10-20% develop persistent OD, a key feature of long COVID-19 syndrome (11,12). Persistent chemosensory dysfunction significantly impairs quality of life (QoL), affecting nutrition, safety, and psychosocial well-being, and is associated with increased depression and anxiety (13,14).

Lacking proven, effective pharmacotherapies for postviral OD, olfactory training (OT) has become the foremost evidence-based, non-invasive treatment modality (15). OT is a structured rehabilitative intervention involving repeated exposure to predefined odorants, based on the olfactory system's neuroplastic capacity at both peripheral and central levels (16). Pre-pandemic studies have confirmed its effectiveness in treating postviral OD (17).

Accordingly, the substantial global prevalence of persistent OD following COVID-19 necessitates a thorough assessment of the evidence supporting OT to direct clinical practice and future research. Therefore, this systematic review and meta-analysis study aimed to critically synthesize the current evidence from randomized controlled trials (RCTs) on the efficacy of OT for the treatment of COVID-OD.

Methods

Protocol Registration

We registered this systematic review with the International Prospective Register of Systematic Reviews (PROSPERO) with the CRD420251127095. The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement and the Cochrane Handbook for Systematic Reviews of Interventions guided the conduction of this systematic review and meta-analysis (18,19).

Data Sources and Search Strategy

On June 2025, an electronic search was conducted on the following databases: Web of Science (WoS), PubMed, Scopus, CENTRAL, and Embase. The search strategy included the following search entries: ("COVID-19" OR "2019 nCoV" OR "2019nCoV" OR "COVID 19" OR "COVID19" OR "new coronavirus" OR "novel coronavirus" OR "novel corona virus" OR "SARS-CoV-2" OR "SARSCoV2" OR "2019-novel CoV" OR "ncov19" OR "ncov-19" OR "nCov 2019" OR "coronavirus" OR "coronavirus disease 2019" OR "long COVID" OR "coronavirus disease" OR "COVID") AND ("olfactory dysfunction" OR "anosmia" OR "hyposmia" OR "parosmia" OR "olfactory loss" OR "loss of smell" OR "smell disorder*" OR "smell dysfunction" OR "olfaction" OR "olfactory" OR "dysosmia*" OR "phantosmia*" OR "cacosmia*" OR "microsmia*" OR "absent smell" OR "olfactory impairment" OR "smell impairment" OR "sense of smell" OR "smell loss") AND ("olfactory training" OR "smell training" OR "odor exposure" OR "odorants" OR "olfactory rehabilitation" OR "olfactory stimulation" OR "smell therapy" OR "smell retraining" OR "scent training" OR "olfactory retraining" OR "odor retraining" OR "nasal smell training" OR "smell recovery training"). Table S1 provides detailed information on the specific search terms and results for each database. To ensure that no relevant studies were omitted, we comprehensively reviewed the reference lists of all included trials.

Eligibility Criteria

RCTs conducted using the following PICO criteria were included: population (P), patients with post-COVID-19 OD; intervention (I), OT; control (C), placebo or no OT; and outcomes (O): the primary outcome was the change in objective olfactory scores, including the University of Pennsylvania Smell Identification test, Sniffin' Sticks test (threshold, discrimination, and identification score), Connecticut Chemosensory Clinical Research Center olfaction test, and Brief Smell Identification test. The secondary outcome was the change in the QoL scores. Furthermore, our analysis excluded quasi-randomized trials, active comparators like nasal corticosteroids, conference presentations and proceedings, observational studies, *in vitro* research, and review articles.

Study Selection

A thorough screening was performed by two independent reviewers (E.A. and G.A.). Following the elimination of duplicate records, a two-stage screening procedure was executed. The process included an initial screening of titles and abstracts, followed by a full-text review of the remaining articles. The reviewers resolved their disagreements through discussion.

Data Extraction

To design an Excel extraction form, we first conducted a preliminary extraction of eligible publications. This preliminary extraction informed the design of the final extraction form, which included three sections: (1) summary characteristics of the included trials (study ID, country, study

design, sample size, treatment protocols, main inclusion criteria, assessment scores, and OT duration); (2) baseline characteristics of the included participants (age, gender, smoking, diabetes mellitus, and type of OD); and (3) the outcomes sheet (change in objective olfactory scores and change in subjective QoL scores).

Data were independently extracted by two reviewers (G.A. and M.A.), and disagreements were resolved through consultation with a senior author (A.A.). Event rates were used to summarize dichotomous data, while continuous data were summarized using means and standard deviations. Mean and standard deviation were computed using conversion formulas from Wan et al. (20), based on median and interquartile range (or range) data reported in some included studies. According to the Cochrane guideline, we included trials that have not yet been published or are in preprint form (19).

Risk of Bias Assessment

The risk of bias in the included studies was evaluated using the revised Cochrane collaboration tool for RCTs (RoB-2) (21). Each study was reviewed by two independent reviewers (G.A. and M.A.), who assessed aspects such as selection, performance, reporting, and attrition biases, as well as other potential sources of bias. Disputes were resolved through consensus.

Effect Measures and Meta-analysis

Data analysis was conducted with STATA MP version 18 (StataCorp). Continuous outcomes were analyzed using the standardized mean difference (SMD), which was presented with the corresponding 95% confidence intervals (CIs). The SMD was used for both objective and subjective endpoints due to the variability in the scoring systems and the assessment tools used across the included trials. The fixed-effect model constituted the primary methodology. Heterogeneity was assessed among the included studies via the chi-squared test and the I-squared statistic (I^2), where a p-value <0.1 for the chi-square test and an I^2 value of ≥50% suggested noteworthy heterogeneity. Publication bias was not evaluated, given that all assessed outcomes involved fewer than ten RCTs (22). To evaluate the robustness of the pooled estimates, a leave-one-out sensitivity analysis was performed, systematically removing each study to determine its influence on the overall effect size.

Results

Search Results and Study Selection

Following a search of the WoS, Scopus, PubMed, CENTRAL, and Embase databases, 1,486 records were identified. An additional two studies were identified through manual search. After 458 duplicates were removed, 1,030 records were screened. Of these, 993 studies failed to meet the inclusion criteria and were excluded based on their titles and abstracts, leaving 37 full-text articles for further assessment. Following a full-text review, 27 studies were excluded (Table S2), leaving 10 studies (23-32) to be included in the final quantitative and qualitative assessments (Figure 1).

Characteristics of Included Studies

Ten trials and 628 participants were included in our analysis (23-32). Two trials were conducted in Brazil (30,32), two in Canada (24,26), and two in Iran (23,31), with single trials in Denmark (29), China (reference 25), Malaysia (27), and the United Kingdom (28). The follow-up duration ranged from four weeks to 12 months. Intervention details and trial characteristics are given in Table 1. Also, the baseline data of the included patients are outlined in Table 2.

Risk of Bias Summary

Four RCTs showed an overall low risk of bias (23,27,29,31). Still, five studies showed a high overall risk of bias (25,26,28,30,32) due to various issues, including high risk of selection bias (26,32), performance bias (25,28), attrition bias (30,32), and detection bias (24,26,28) (Figure 2).

Objective Olfactory Score

OT significantly improved objective olfactory scores [n=7 RCTs, SMD=0.30, 95% CI (0.08, 0.51), p=0.01] (Figure 3A). Pooled studies showed low heterogeneity (I^2=33.69%), and the leave-one-out sensitivity analysis showed a consistent and significant effect after the exclusion of each individual study, confirming the robustness of our findings (Figure 3B).

Quality of Life

OT significantly improved QoL scores [n=5 RCTs, SMD=-0.40, 95% CI (-0.65, -0.15), p<0.001] (Figure 4A). Pooled studies showed low heterogeneity (I^2=37.47%), and the leave-one-out sensitivity analysis showed the results were significantly affected by a single study, as after the exclusion of Akbarpour et al. (23), there was no significant difference between the two groups (p=0.097) (Figure 4B).

Discussion

This systematic review and meta-analysis of ten RCTs and 628 patients showed that OT was effective in improving olfactory function and QoL. These results align with previous studies supporting OT as an effective, evidence-based treatment for postviral OD (17). OT promotes recovery through peripheral and central neuroplastic mechanisms and is widely recommended as a safe, first-line treatment (16,33).

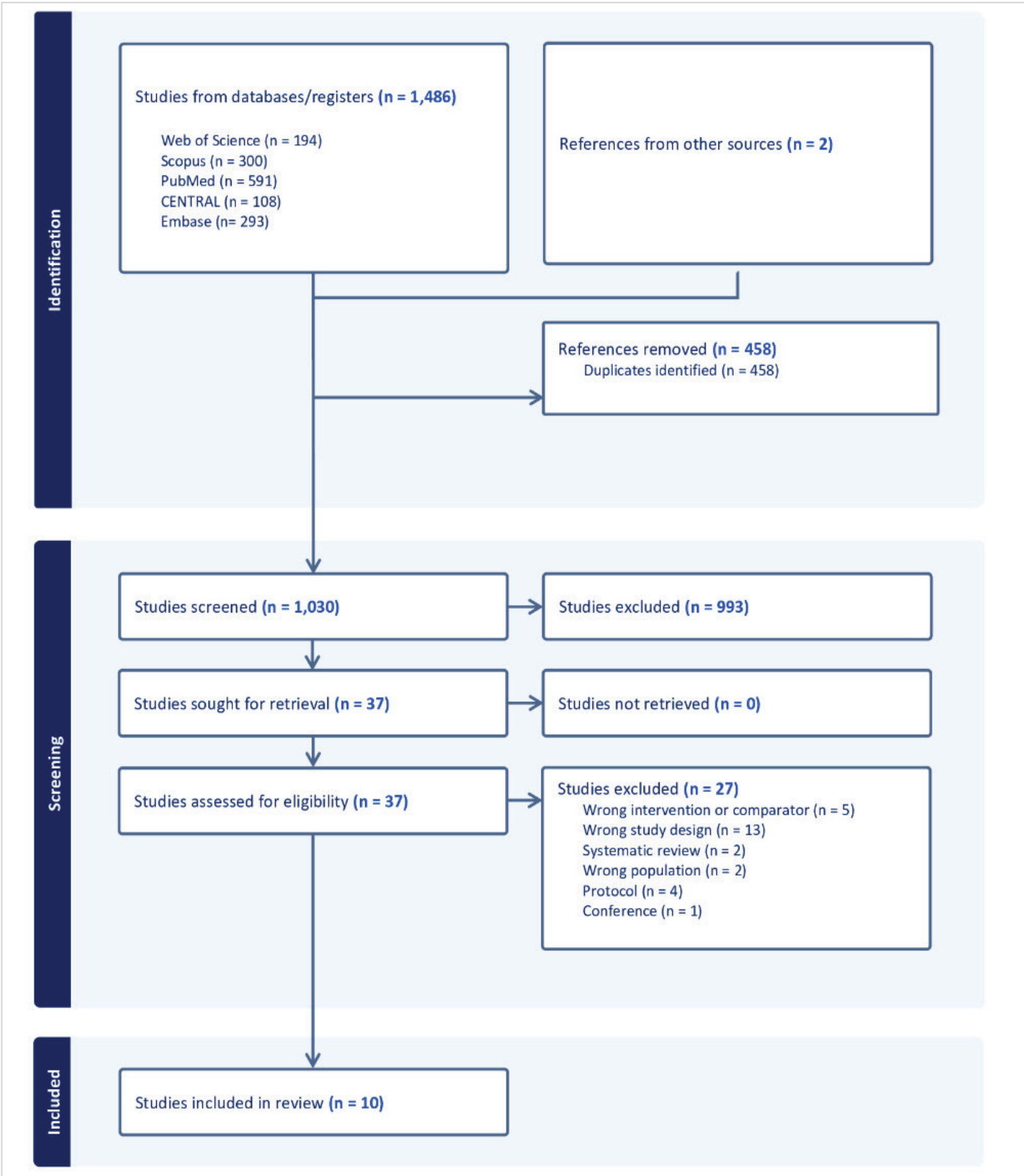

Figure 1. The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow diagram illustrates the systematic study selection process

Table 1. Summary information of the included randomized controlled trials

Study ID	Study design	Country	Recruitment	Sample size, n	Patient criteria	Intervention	Control	Olfactory training duration
Akbarpour et al. 2024 (23)	RCT	Iran	Not reported	n=95	Post-COVID-19 olfactory dysfunction	Olfactory training: twice-daily exposure to 4 scents—rose, eucalyptus, lemon, and clove—each for 20 seconds with 10-second intervals.	No olfactory training	6 weeks
Bérubé et al. 2023 (24)	RCT	Canada	May 2021-October 2021	n=50	Post-COVID-19 olfactory dysfunction (≥4 weeks)	Olfactory training: twice-daily training with 4 scents—rose, orange, clove, and eucalyptus—each for 10 seconds with 10-second intervals, using amber vials. Sessions lasted ~5 minutes.	Placebo (odorless vials with propylene glycol)	12 weeks
Chung et al. 2023 (25)	RCT	China	August 2020-11 June 2021	n=13	Post-COVID-19 olfactory dysfunction (≥12 weeks)	Olfactory training: three-times-daily training using diffuser-delivered essential oils—lemon, eucalyptus, geranium, and cedarwood—each for 20 seconds.	No olfactory training	4 weeks
Filiz et al. 2024 (26)	RCT	Canada	Not reported	n=40	Post-COVID-19 olfactory dysfunction (≥8 weeks)	Olfactory training: twice-daily training with 4 scents—rose, orange, clove, and eucalyptus—each for 10 seconds with 10-second intervals, using amber vials. Sessions lasted ~5 minutes.	Placebo (odorless vials with propylene glycol)	12 weeks
Ho et al. 2024 (27)	RCT	Malaysia	January 2022-November 2022	n=21	Post-COVID-19 olfactory dysfunction (≥4 weeks)	Olfactory training: twice-daily exposure to essential oils—rose, lemon, clove, eucalyptus—each for 10 seconds with 10-second intervals; stored in 50 mL jars with cotton pads.	No olfactory training	12 weeks
Lechner et al. 2022 (28)	RCT	UK	May 2020-January 2021	n=63	Post-COVID-19 olfactory dysfunction	Olfactory training delivered using Sniffin' Sticks (Duft-Quartett).	No olfactory training	12 weeks
Mogensen et al. 2025 (29)	RCT	Denmark	June 2022-December 2023	n=49	Post-COVID-19 olfactory dysfunction (≥12 weeks)	Olfactory training: twice-daily exposure to 4 essential oils—orange, lavender, clove, and peppermint—each for 20 seconds with 10-second intervals.	Placebo (odor-free oils)	12 weeks
Paranhos et al. 2025 (32)	RCT	Brazil	May 2021-May 2024	n=114	Post-COVID-19 olfactory dysfunction (≥3 weeks)	Olfactory training: twice-daily inhalation of 4 scents—rose, lemon, eucalyptus, and clove—each for 30 seconds with 30-second intervals.	No olfactory training	12 weeks
Serrano et al. 2025 (30)	RCT	Brazil	June 2020-December 2020	n=123	Post-COVID-19 olfactory dysfunction	Olfactory training: twice-daily 5-minute training with 4 labeled vials—clove, lemon, eucalyptus, and rose—rotating scents every 15 seconds.	Placebo (vials without essential oils)	180 days or until recovery
Taheri et al. 2024 (31)	RCT	Iran	March 2020-March 2021	n=60	Post-COVID-19 olfactory dysfunction (≥2 weeks)	Olfactory training: twice-daily exposure to 4 standard-concentration odors—rose, eucalyptus, lemon, and clove—each for 10 seconds.	No olfactory training	12 weeks

RCT: Randomized controlled trial, COVID-19: Coronavirus disease 2019

Table 2. Baseline characteristics of the included participants and trials

Study ID	Group	Sample size, n	Age (years)	Sex, n [male/female]	Smoking, n	DM, n	Type of OD, n (%)			Assessment tools
							Anosmia	Hyposmia	Parosmia	
Akbarpour et al. 2024 (23)	OT	47	38±12.45	[26/21]	19	NR	47	0	0	QOD-NS
	Control	48	39.1±13.76	[29/19]	16	NR	48	0	0	
Bérubé et al. 2023 (24)	OT	25	44.9±7.4	[9/16]	0	NR	5	20	16	UPSIT, NOSE, and QOD
	Control	25	44.5±10.1	[8/17]	0	NR	5	20	19	
Chung et al. 2023 (25)	OT	8	47.53±14.07	[2/6]	0	0	5	2	3	BTT, and SIT
	Control	5	56.33±8.15	[2/3]	0	1	2	3	0	
Filiz et al. 2024 (26)	OT	20	39.5±9.6	[5/15]	NR	NR	NR	NR	18	UPSIT, SQOD-NS, and QOD
	Control	20	43.5±10.1	[5/15]	NR	NR	NR	NR	16	
Ho et al. 2024 (27)	OT	10	20-60 (range)	NR	3	NR	NR	NR	NR	TIBSIT, and eODQ
	Control	11	20-60 (range)	NR	1	NR	NR	NR	NR	
Lechner et al. 2022 (28)	OT	33	46.25±13.75	NR	NR	NR	NR	NR	NR	BSIT
	Control	30		NR	NR	NR	NR	NR	NR	
Mogensen et al. 2025 (29)	OT	25	47.33±16.30	[6/19]	2	NR	2	7	16	Sniffin Sticks extended TDI test, and NRS
	Control	24	48±27	[8/16]	2	NR	4	8	12	
Paranhos et al. 2025 (32)	OT	70	45.9±12.4	[16/54]	1	5	20	50	10	CCCRC
	Control	44	47.3±13.1	[15/29]	0	2	13	21	2	
Serrano et al. 2025 (30)	OT	68	38.03±10.67	[21/47]	2	4	24	99	NR	CCCRC, QOD-NS, and VAS
	Control	55	37.13±7.93	[10/45]	3	2			NR	
Taheri et al. 2024 (31)	OT	30	42.26±10.98	[14/16]	3	3	9	21	3	UPSIT
	Control	30	40.40±11.84	[14/16]	2	2	21	9	1	

NR: Not reported, DM: Diabetes mellitus, OT: Olfactory training, n: Number, OD: Olfactory dysfunction, UPSIT: University of Pennsylvania Smell Identification Test, CCCRC: Connecticut Chemosensory Clinical Research Center olfactory test, QOD-NS: Brief version of the questionnaire of olfactory disorders-negative statements, VAS: Visual analogue scale, TDI: Threshold, discrimination, identification, NRS: Numeric rating scale, BSIT: Brief smell identification test, TIBSIT: Top international biotech smell identification test, eODQ: English Olfactory Disorder Questionnaire, SQOD-NS: Shortened questionnaire of olfactory disorders-negative statements, QOD: Questionnaire for olfactory disorders, BTT: Butanol threshold test, SIT: Smell identification test, NOSE: Nasal obstruction symptom evaluation

However, these findings should be interpreted with caution.

Our rigorous analysis showed significant improvements in objective smell tests. The mechanism of this improvement arises from the distinct pathophysiology of COVID-19 and the olfactory system's restorative potential. The primary target of SARS-CoV-2 infection in the olfactory epithelium differs from that of other respiratory viruses, as it infects non-neuronal support cells that possess ACE2 receptors, thereby minimizing direct viral damage to OSNs (8). The resulting inflammatory cascade and damage to support cells lead to a secondary, non-cell-autonomous disruption of OSN function, including the loss of cilia and downregulation of odorant receptor genes (8).

OT, involving structured, repetitive exposure to odors, is proposed as a targeted neurorehabilitation method. Peripheral stimulation is thought to promote the regeneration of the damaged olfactory neuroepithelium; this is achieved by activating basal stem cells and guiding the maturation of new OSNs (34). Centrally, the consistent sensory input drives neuroplastic changes. Neuroimaging studies suggest that OT induces structural and functional changes in olfactory pathways, enhancing odor processing (35). Therefore, the olfactory improvements observed are likely attributable to a confluence of peripheral tissue regeneration and central neural plasticity.

Furthermore, our analysis showed a substantial improvement in QoL. Considerable evidence confirms the profoundly debilitating impact of OD on activities of daily living (5). COVID-19-related OD has a significant impact on daily functioning, including nutrition, safety, and psychosocial well-being (5,14). Impaired gustatory perception may result in nutritional deficiencies or poor dietary habits, while an inability to detect hazards such as smoke, gas leaks, or spoiled food presents a significant safety concern (13). Restoration of olfactory function through OT may improve these domains and reduce associated psychological distress (36). OT directly ameliorates these deficits by restoring, even

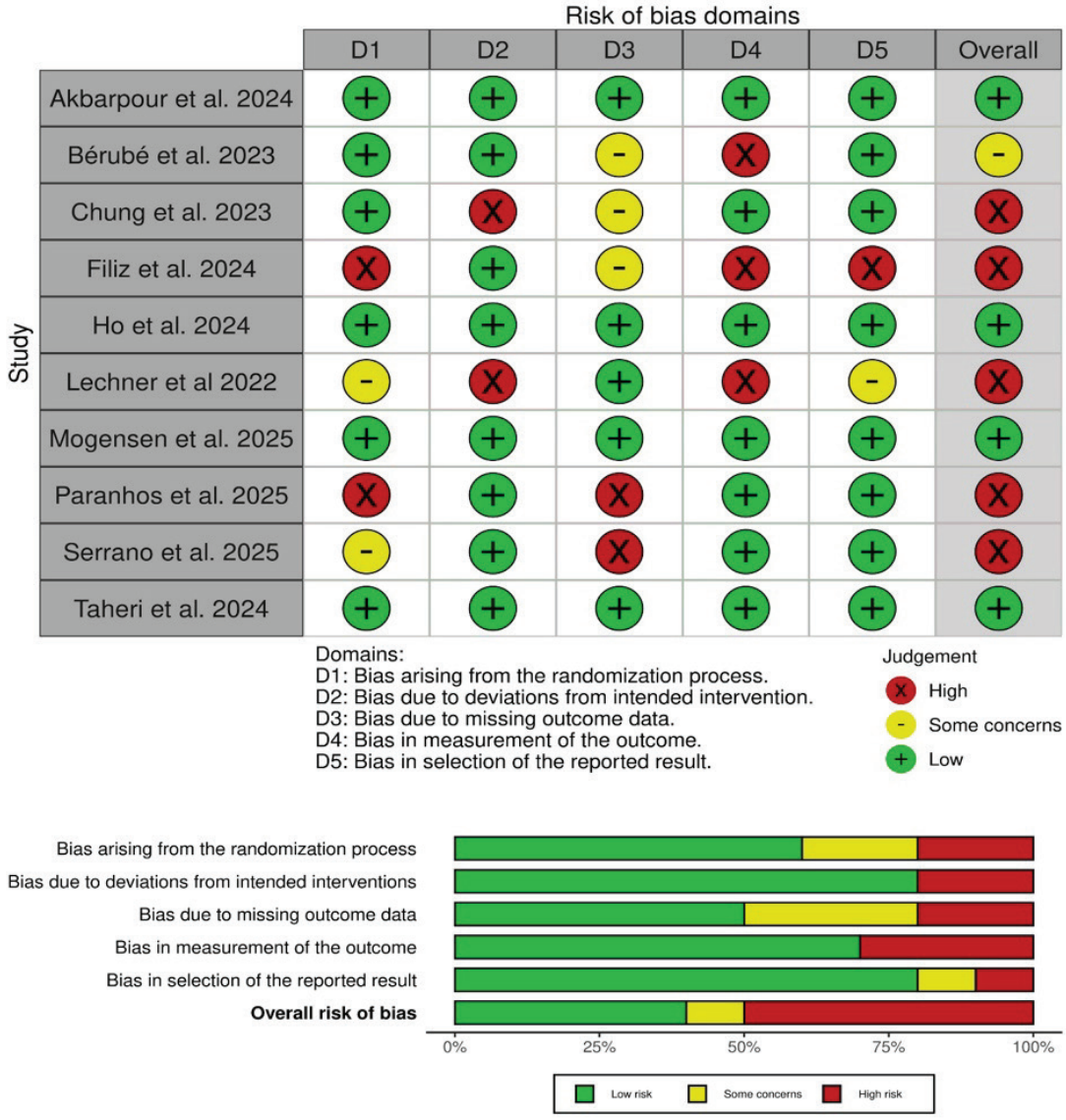

Figure 2. Risk of bias graph and summary of the included randomized controlled trials. The upper panel presents a schematic representation of risks (low=green, some concerns=yellow, and high=red) for specific types of biases of each study in the review. The lower panel presents risks (low=green, some concerns=yellow, and high=red) for the subtypes of biases of the combination of studies included in this review

if partially, olfactory function. Recovery of the sense of smell can lead to renewed enjoyment of food, a restored sense of safety, and improved social confidence, consequently reducing related psychological distress (37).

Moreover, a significant advantage of OT is its remarkably safe profile. Unlike pharmacological interventions, this non-invasive, non-pharmacological approach avoids systemic side effects (38). Neither the trials included in this study nor broader research have shown any significant adverse side effects from smelling essential oils as administered in OT protocols (39). The excellent safety profile supports its suitability as a first-line treatment for persistent post-COVID-OD. Still, the primary challenge associated with OT is not safety, but rather patient adherence, as data from real-world settings and clinical trials reveal poor adherence (17). Non-adherence remains a challenge, with patients either discontinuing early after partial improvement or abandoning therapy due to perceived lack of benefit (40). The dose-dependent nature of OT's benefits, coupled with the need for prolonged treatment (often 12 weeks or longer) to see results, means that poor adherence significantly hinders its

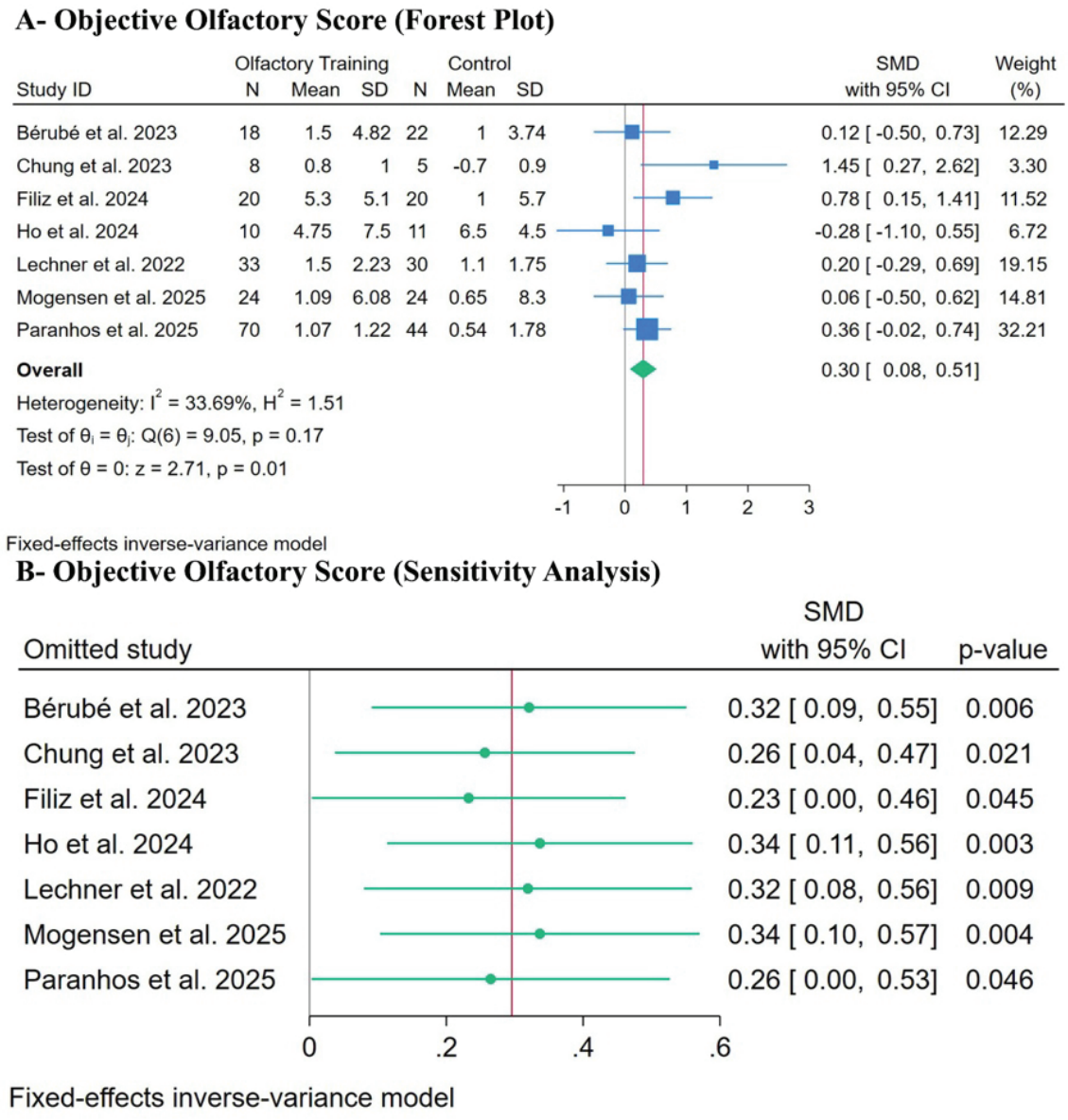

Figure 3. Forest plot and leave-one-out sensitivity analysis of objective olfactory score
SMD: Standardized mean difference, CI: Confidence interval, SD: Standard deviation

real-world efficacy and likely contributes to the small effect sizes reported in certain studies (41).

Study Limitations

This review has several limitations, largely related to the included studies. First, several of the included RCTs had methodological limitations, which may affect the reliability of the estimated effect size. Second, the scores used for olfactory function and QoL varied among the included trials; however, we addressed this limitation by implementing the SMD. Third, there is substantial clinical heterogeneity in the OT protocols employed in the included trials. The studies revealed significant heterogeneity in OT protocols, including duration (ranging from 4 to more than 24 weeks),

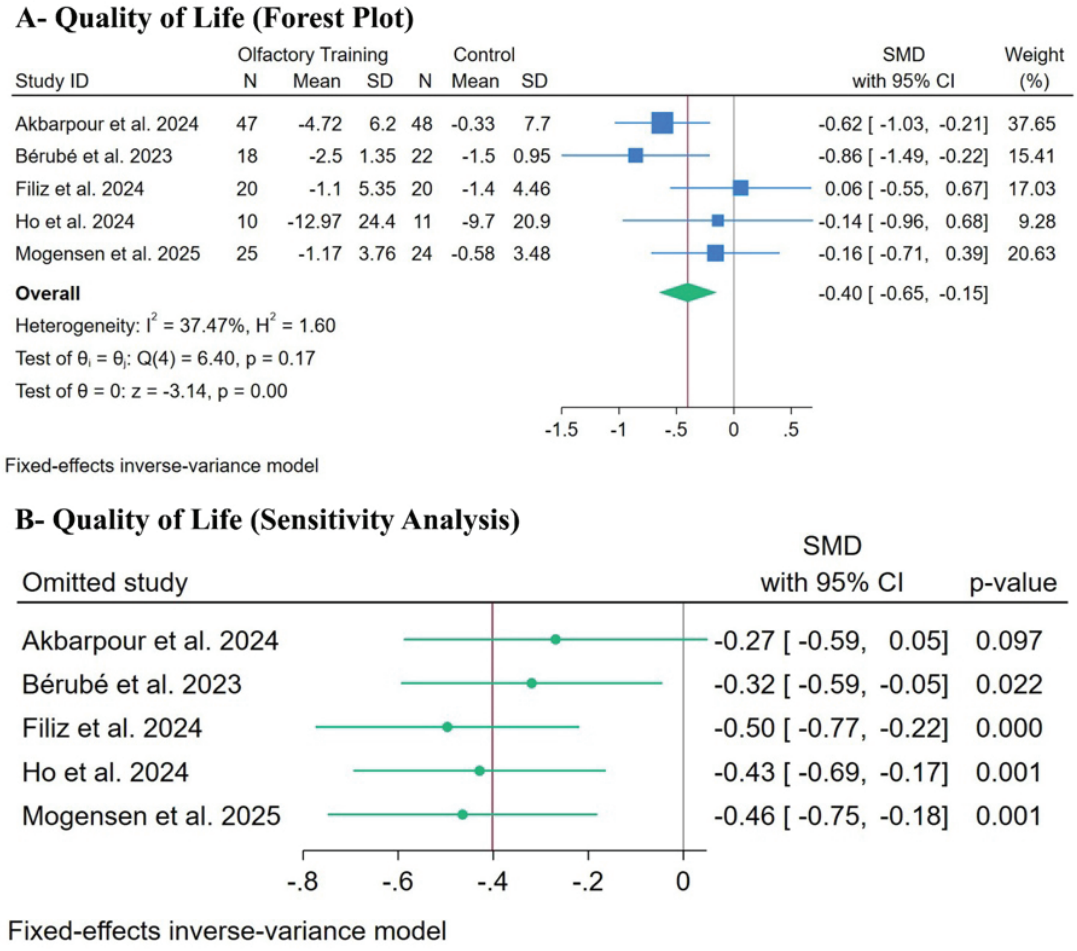

Figure 4. Forest plot and leave-one-out sensitivity analysis of quality of life
SMD: Standardized mean difference, CI: Confidence interval, SD: Standard deviation

the types of odorants used, and the delivery methods employed. The absence of a standardized protocol hinders the recommendation of a definitive, optimized OT protocol, potentially obscuring OT's true potential. Finally, a formal assessment of publication bias was not possible given the limited number of studies per outcome (<10).

Conclusion

OT significantly improved objective olfactory function and QoL in patients with COVID-OD. However, the current evidence should be interpreted with caution due to heterogeneity in OT protocols and the variability among the included studies. Therefore, the development of conclusive, evidence-based clinical practice guidelines urgently requires future research focusing on large-scale, rigorously designed, and standardized RCTs.

Footnotes

Authorship Contributions

Concept: E.A., G.A., M.A., A.H.A., A.A., Design: E.A., A.A., Data Collection and/or Processing: E.A., G.A., M.A., A.H.A., Analysis or Interpretation: E.A., G.A., M.A., Literature Search: E.A., G.A., A.H.A., A.A., Writing: E.A., G.A., M.A., A.H.A., A.A.

Conflict of Interest: The authors declare that they have no conflict of interest.

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Main Points

- Olfactory training (OT) has emerged as a leading, non-invasive therapeutic strategy.
- This systematic review and meta-analysis study aims to critically synthesize the current evidence from randomized controlled trials (RCTs) on the efficacy of OT for the treatment of coronavirus disease (COVID)-olfactory dysfunction (OD).
- OT significantly improves objective olfactory function and quality of life in patients with COVID-OD.
- However, these findings should be interpreted with caution due to the heterogeneity of the OT protocols and the variability among the included studies.
- Future large-scale, rigorously designed RCTs with standardized OT protocols are necessary to establish definitive clinical practice guidelines.

Tables S1-2: https://d2v96fxpocvxx.cloudfront.net/d363ec1e-9e5e-4591-a00a-d656bfcabb80/content-images/bb7f969c-6ee8-4379-9c2c-3668dd27cf13.pdf

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