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Olfactory Stimulation and the Mendelsohn Manoeuvre for Neurogenic Oropharyngeal Dysphagia: A Systematic Review, Meta-Analysis, and Outcome Domain Mapping

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ADMINISTRATIVE INFORMATION

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Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 18 March 2026 and was last updated on 18 March 2026.

INTRODUCTION

Review question / Objective In adults with neurogenic oropharyngeal dysphagia, including those with Alzheimer's disease (P), do structured swallowing interventions incorporating olfactory stimulation and/or the Mendelsohn manoeuvre (I), compared with standard care or sham (C), improve swallowing function, airway protection, and nutritional status (O), as assessed in controlled studies (S)?/Aim 1: To quantify the pooled effect of structured swallowing interventions (incorporating olfactory stimulation and/or the Mendelsohn manoeuvre) on swallowing function in adults with neurogenic dysphagia, measured by the Water Swallowing Test.
→ Addressed by: Section 4.4.1 — Forest plot, 8 RCTs, SMD = −0.93

Aim 2: To quantify the pooled effect of structured swallowing interventions on swallowing safety, measured by the Penetration–Aspiration Scale.
→ Addressed by: Section 4.4.2 — Forest plot, 6 studies, MD = −0.59

Aim 3: To quantify the pooled effect of structured swallowing interventions on nutritional status, measured by the Mini Nutritional Assessment–Short Form.
→ Addressed by: Section 4.4.3 — Forest plot, 6 studies, MD = 1.82

Aim 4: To examine whether intervention duration (≤4 weeks versus >4 weeks) moderates the effect on swallowing function.
→ Addressed by: Section 4.4.4 — Subgroup forest plot, $\chi^2 = 2.32$, $p = 0.128$

Aim 5: To map all outcome domains employed in clinical trials of dysphagia interventions for Alzheimer's disease and neurogenic populations, using the Dodd et al. (2018) taxonomy.
→ Addressed by: Section 4.3 — 247 outcomes → 52 unique → 15 domains; pie chart + bar chart

Aim 6: To identify under-represented outcome domains, with particular attention to caregiver-related outcomes, and to assess the certainty of the evidence using the GRADE framework.
→ Addressed by: Section 4.3 (caregiver = 5.7%) + Section 4.5 (GRADE table).

Rationale Oropharyngeal dysphagia is among the most consequential complications of Alzheimer's disease (AD), affecting 32–45% of mild-stage patients and 84–93% in moderate-to-severe stages (Sura et al., 2012; Mira et al., 2022). Aspiration pneumonia—the principal sequela—accounts for 30–50% of AD-related mortality (Marik & Kaplan, 2003). Beyond mortality, dysphagia drives malnutrition, dehydration, and premature institutionalisation, imposing substantial burden on both patients and their informal caregivers.
Two non-pharmacological techniques have accumulated independent evidence. Olfactory stimulation (OS) with black pepper oil activates olfactory-brainstem pathways, shortening swallowing reflex latency (Ebihara et al., 2006, 2021). The Mendelsohn manoeuvre (MM) strengthens suprahyoid musculature and extends upper oesophageal sphincter opening (Kahrilas et al., 1991; Byeon, 2020). Both are low-cost, non-invasive, and feasible for home-based delivery by trained caregivers—a critical advantage given that most AD patients are community-dwelling and reliant on informal care.
However, five interrelated evidence gaps persist. First, no meta-analysis has isolated the pooled effect of aromatic OS specifically—prior reviews aggregate diverse sensory modalities (Dai et al., 2025). Second, no pooled estimate exists for MM (Adzimová et al., 2025). Third, no study has tested combined OS + MM protocols in AD populations, despite theoretical justification from sensorimotor priming (Huckabee et al., 2022). Fourth, existing interventions overwhelmingly neglect caregiver competency: De Stefano et al. (2020) found that only 53.8% of caregivers managed dysphagia adequately, yet fewer than 11% of trials measure caregiver outcomes. Fifth, no outcome domain mapping exists for AD dysphagia interventions—leaving the measurement landscape uncharted (Hirschwald et al., 2023 identified this problem for Parkinson's disease).
This review addresses all five gaps by combining quantitative meta-analysis (pooling OS, MM, and combined effects), qualitative synthesis of caregiver competency evidence, and comprehensive outcome domain mapping. The findings will directly inform the development and evaluation of the COMBI-OSiMM (Combined Olfactory Stimulation and Mendelsohn Manoeuvre) intervention module—a structured, caregiver-led protocol guided by the Omaha System framework—currently under quasi-experimental evaluation.

Condition being studied The condition under study is oropharyngeal dysphagia in patients with mild-to-moderate Alzheimer's disease (AD) and the associated caregiving burden experienced by their informal caregivers. This dual focus reflects the dyadic nature of AD care, where patient health outcomes and caregiver wellbeing are interdependent.
Alzheimer's disease is the most common form of dementia, accounting for 60–70% of cases globally. Oropharyngeal dysphagia in AD results from three converging pathophysiological mechanisms: (1) cortical degeneration in the insula, orbitofrontal cortex, and anterior cingulate, impairing volitional swallowing initiation (Humbert et al., 2010); (2) progressive sarcopenia and suprahyoid muscle atrophy weakening pharyngeal propulsion (Özsürekci et al., 2020); and (3) olfactory epithelial degeneration—present in up to 80% of early-stage AD—diminishing the sensory drive that primes swallowing motor programmes (Murphy, 2019).
In mild AD (CDR 1), dysphagia manifests as prolonged oral phase, reduced lingual movement, delayed swallowing reflex, and mastication inefficiency. In moderate AD (CDR 2), pharyngeal phase impairments emerge: incomplete airway clearance, bolus stasis, and visible aspiration. The prevalence ranges from 32–45% in mild stages to 84–93% in moderate-to-severe stages (Mira et al., 2022). Clinical consequences include aspiration pneumonia (leading cause of death in AD), malnutrition, dehydration, and accelerated cognitive decline.
Critically, dysphagia management in AD is inseparable from caregiver competency. Most AD patients are community-dwelling and reliant on informal caregivers for mealtime assistance, medication administration, and aspiration monitoring. Yet caregivers receive minimal structured training: De Stefano et al. (2020) found that only 53.8% demonstrated acceptable mealtime management skills. Caregivers of dysphagic AD patients report elevated psychological burden, including fear of aspiration, frustration with mealtime difficulties, and emotional distress (Perry et al., 2022). This caregiver burden, in turn, undermines intervention adherence and patient outcomes—creating a vicious cycle.
This review therefore examines dysphagia as a dyadic condition affecting both the patient (swallowing function, nutritional status, quality of life) and the caregiver (self-efficacy, burden, competency). For the broader meta-analytic

component, evidence from stroke, Parkinson's disease, and other neurogenic dysphagia populations is also synthesised, as these conditions share common mechanisms of cortical swallowing disruption and provide the statistical power necessary for reliable pooled estimates.

METHODS

Participant or population Two populations are included:
(a) Patients: Adults (≥18 years) with oropharyngeal dysphagia. The primary population is patients with mild-to-moderate Alzheimer's disease (MMSE 10–26 or CDR 1–2). For the broader meta-analysis, adults with neurogenic dysphagia secondary to stroke, Parkinson's disease, vascular dementia, or other CNS pathology are also included. Dysphagia must be confirmed by clinical screening (e.g., WST ≥ Grade III, EAT-10 ≥ 3) or instrumental assessment (VFSS, FEES).
(b) Caregivers: Informal caregivers (family members, spouses, non-professional carers) providing regular mealtime assistance or dysphagia management for the above patient populations. No restrictions on age, sex, education, or caregiving experience.
No restrictions on care setting (hospital, community, institutional, home-based).

Intervention (a) Aromatic olfactory stimulation (OS): Inhalation of volatile essential oils (black pepper oil, lemon oil, cedar oil, lavender oil, menthol, or comparable agents) via nasal inhalation, diffuser, or impregnated cotton swab, before or during mealtimes. Any concentration, frequency, and duration eligible.
(b) Mendelsohn manoeuvre (MM): Volitional prolongation of laryngeal elevation during pharyngeal swallowing. Self-performed or caregiver-assisted. Any training protocol eligible (in-person, video-guided, biofeedback-assisted).
(c) Combined OS + MM protocols: Interventions integrating both modalities within a single programme (e.g., COMBI-OSiMM).
(d) Structured caregiver training programmes: Programmes targeting caregiver competencies in dysphagia assessment, intervention delivery, complication monitoring, or mealtime management. Includes Train-the-Trainer models.
(e) Broader swallowing interventions: Nurse-delivered stepwise swallowing training, neuromuscular electrical stimulation (NMES), or multimodal rehabilitation protocols incorporating OS and/or MM components.

Comparator (a) Standard nursing care (diet and posture management, general health education about dysphagia, without specific OS, MM, or structured competency training). (b) Sham stimulation (distilled water or odourless carrier oil). (c) Conventional dysphagia interventions without OS/MM. (d) Routine caregiver education without structured competency-based training. (e) Waitlist control. (f) Alternative active control.

Study designs to be included For meta-analysis: RCTs (parallel, crossover, cluster), quasi-RCTs, controlled before–after studies (≥10 per arm). For narrative synthesis and outcome domain mapping: cohort, cross-sectional, qualitative, and mixed-methods studies with empirical data.

Eligibility criteria Additional inclusion criteria:
• Published in peer-reviewed journals or registered trials with available results.
• Outcomes measured with validated instruments.
• Follow-up ≥2 weeks for intervention studies.
• No restriction on publication date, language, or country.
• Studies addressing caregiver competencies, training models, or the Omaha System framework in dysphagia care contexts are eligible for narrative synthesis.
Exclusion criteria:
• Non-neurogenic or structural dysphagia (head/neck cancer, oesophageal stricture).
• Pharmacological interventions as sole treatment.
• Single-arm pre–post without concurrent control (for meta-analysis).
• Case reports, case series (n < 10), editorials, conference abstracts without full data.
• Studies where AD/neurogenic dysphagia subgroup data cannot be extracted.

Information sources Electronic databases: (1) PubMed/MEDLINE; (2) Embase via Ovid; (3) CINAHL via EBSCOhost; (4) Web of Science; (5) Cochrane CENTRAL; (6) Scopus.
Trial registries: ClinicalTrials.gov; WHO ICTRP.
Grey literature: ProQuest Dissertations & Theses; Google Scholar (first 200 results).
Hand-searching: Reference lists of all included studies and prior reviews (Tong et al., 2025; Chan et al., 2024; Adzimová et al., 2025; Hirschwald et al., 2023; Dai et al., 2025; Mira et al., 2022).
Author contact: Corresponding authors contacted for unpublished data where necessary.

Main outcome(s) Patient primary outcomes:
(1) Swallowing function: Water Swallowing Test (WST; 5-grade) and/or Standard Swallowing Assessment (SSA). Effect measure: SMD (Hedges' g) via random-effects model.

(2) Swallowing safety: Penetration-Aspiration Scale (PAS; 8-point ordinal). Effect measure: mean difference (MD).
Caregiver primary outcome:
(3) Caregiver self-efficacy: Self-Efficacy Questionnaire for Chinese Family Caregivers (SEQCFC) or equivalent validated instrument. Effect measure: MD or narrative synthesis.

Quality assessment / Risk of bias analysis RCTs: Cochrane RoB 2.0 (Sterne et al., 2019) across 5 domains (randomisation, deviations, missing data, measurement, reporting). Non-randomised: ROBINS-I across 7 domains. Qualitative studies: JBI Critical Appraisal Checklist for Qualitative Research. Two independent reviewers; consensus for discordances. Traffic-light plot and summary bar chart via robvis (R). Risk-of-bias incorporated into GRADE certainty ratings. No studies excluded solely on quality; all retained with bias acknowledged.

Strategy of data synthesis Quantitative synthesis: Random-effects meta-analysis in R v4.4.0 (meta, metafor packages). DerSimonian–Laird τ^2 with Knapp–Hartung adjustment. SMD (Hedges' g) for different-scale continuous outcomes; MD for same-instrument outcomes; RR for dichotomous. Prediction intervals computed. Heterogeneity: I^2, τ^2, Q-test (significance $p < 0.10$).
Outcome domain mapping: Verbatim extraction, merging, and classification using adapted Dodd et al. (2018) taxonomy extended with caregiver-specific domains (CG1: self-efficacy; CG2: burden). Follows COMET Handbook and Hirschwald et al. (2023) methodology. Frequency tabulation presented as bar chart and pie chart.
Qualitative synthesis: Thematic analysis of caregiver competency evidence using Braun & Clarke's (2006) six-step framework, organised within the Omaha System Knowledge–Behaviour–Status (KBS) model. Integration with quantitative findings via triangulation.
Evidence certainty: GRADE framework across 5 domains (risk of bias, inconsistency, indirectness, imprecision, publication bias). Summary of Findings table for each primary outcome. Where pooling unfeasible: SWiM guideline (Campbell et al., 2020).

Subgroup analysis Pre-specified for primary outcome (swallowing function):
(1) Intervention duration: ≤4 weeks vs >4 weeks.
(2) Neurological aetiology: AD/dementia vs stroke vs Parkinson's vs other.
(3) Intervention modality: OS alone vs MM alone vs combined OS + MM.
(4) Delivery model: clinician-delivered vs caregiver-delivered.
(5) AD severity: mild (CDR 1) vs moderate (CDR 2) vs mixed/severe.
Subgroup differences tested with χ^2 interaction test (significance $p < 0.10$). All subgroup analyses are hypothesis-generating.

Sensitivity analysis (1) Leave-one-out: Sequential omission of each study; pooled effect recalculated. (2) Exclusion of high RoB studies: Re-run excluding 'high risk' studies; >20% SMD change considered meaningful. (3) Fixed vs random effects comparison. (4) Publication bias: Funnel plot + Egger's test (≥7 studies; $p < 0.10$); trim-and-fill for missing studies estimation.

Country(ies) involved China; Malaysia.

Keywords dysphagia; olfactory stimulation; Mendelsohn manoeuvre; Alzheimer's disease; caregiver; meta-analysis; outcome domains; GRADE; nursing; Omaha System.

Contributions of each author
Author 1 - TINGTING ZHANG - Conceptualised the review; designed the search strategy; conducted database searching, screening, and data extraction; performed all meta-analyses and outcome domain mapping in R; drafted the manuscript; and prepared all figures and tables.
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Author 2 - WANLING LEE - Supervised the overall study design and methodology; verified the eligibility criteria and PICOS framework; reviewed and validated the risk-of-bias assessments; critically revised all manuscript drafts; and approved the final version.
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Author 3 - YANGYANG SHANG - Contributed to the development of the inclusion and exclusion criteria and the risk-of-bias assessment strategy; served as the second independent reviewer for title/abstract and full-text screening; resolved inter-rater disagreements; and reviewed the final manuscript.
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Author 4 - CHONGCHIN CHE - Provided clinical expertise on dysphagia assessment and intervention protocols; assisted with the adaptation of the Dodd et al. outcome taxonomy for Alzheimer's disease populations; validated the GRADE certainty assessments; and approved the final manuscript.
Author 5 - XIAONA ZHENG - Assisted with grey literature searching and reference list hand-searching; independently verified data extraction accuracy; contributed to the outcome domain

mapping classification process; read, provided feedback, and approved the final manuscript.
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