

A clinical study on multidimensional phenotypic parameters of gender and age differences between Chinese dry mouth and non-dry mouth population

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Research Article

Keywords: Dry mouth, Oral moisture, Multidimensional phenotypes, Salivary biomarkers, Objective assessment, Personalized oral care

Posted Date: September 17th, 2026

DOI: <https://doi.org/10.21203/rs.3.rs-10847571/v1>

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Additional Declarations: No competing interests reported.

Abstract

Background

Dry mouth extends beyond mere salivary hypofunction, presenting as a comprehensive multidimensional manifestation. Current diagnostic modalities are largely confined to isolated subjective questionnaires or cumbersome glandular function tests, lacking a comprehensive evaluation of the oral microenvironment and perioral physical barriers. This study aimed to systematically characterize the multidimensional phenotypic profiles of dry mouth and non-dry mouth Chinese adults across different sex and age strata, thereby establishing an objective assessment framework and providing a robust scientific basis for targeted interventions.

Methods

A stratified cross-sectional study was conducted with 164 healthy Chinese adults, evenly distributed across age (30–70 years), sex, and dry mouth status. Through image acquisition, instrumental measurements, clinical assessments, and questionnaires, we systematically evaluated differences between the dry mouth and non-dry mouth groups. The assessment parameters encompassed oral and perioral moisture, gingival blood perfusion, objective salivary flow rate, volatile sulfur compounds (VSCs), human α 1-salivary amylase (AMY1) and epidermal growth factor (EGF), subjective questionnaire scores, and clinical grading.

Results

Individuals with dry mouth demonstrated an overall functional decline, marked by profound oral and perioral dehydration ($P < 0.001$), significantly diminished salivary flow and AMY1 levels, and abnormally elevated VSCs (specifically CH_3SH and $(\text{CH}_3)_2\text{S}$). Cross-stratified subgroup analyses revealed distinct demographic heterogeneity. The subgroup of females aged 51–70 years experienced the most severe lip moisture loss, whereas females aged 30–50 years reported the highest psychosomatic burden alongside severe subjective dry mouth. In contrast, males were highly susceptible to the accumulation of VSCs and angular dehydration, with older males specifically presenting with prominent mucosal atrophy.

Conclusions

This study establishes a multidimensional objective assessment framework, reducing the traditional overreliance on subjective reporting for dry mouth evaluation. The sex and age disparities in clinical phenotypes identified herein provide a robust translational foundation for the development of population-specific, innovative oral care interventions.

Background

Dry mouth extends beyond a mere subjective sensation, presenting as an objective manifestation of reduced salivary secretion and glandular decline, frequently accompanied by abnormal moisture distribution across the oral mucosa [1, 2]. Epidemiological studies indicate that the prevalence of dry mouth ranges from 11% to 64% in adult populations [3, 4], with even higher rates observed among the elderly [5]. Far from being a localized discomfort, dry mouth constitutes a substantial health burden; it predisposes individuals to dental caries, periodontal disease, and oral candidiasis, while also causing difficulties in mastication, swallowing, and speech [6, 7]. Furthermore, the deterioration of the oral microenvironment, driven by increased salivary viscosity and mucosal fragility, severely compromises patients' quality of life and psychological well-being [8–10].

Saliva is a complex biofluid containing essential proteins and electrolytes required to maintain oral homeostasis. Existing studies have identified various biomarkers associated with salivary function, such as human α 1-salivary amylase (AMY1) and epidermal growth factor (EGF). Specifically, AMY1, a major protein secreted by the parotid glands, frequently serves as a surrogate marker for autonomic nervous system activity and glandular secretory reserve [11]. EGF plays a pivotal role in maintaining mucosal integrity and promoting wound healing [12, 13]. Recent investigations have also begun to explore the potential relationships between dry mouth and perioral physiological parameters, such as lip and oral corner moisture [14]. However, current research on dry mouth assessment remains limited. The majority of studies have focused on western populations or specific clinical cohorts (e.g., patients with Sjögren's syndrome or those undergoing radiotherapy) [15–17], resulting in a severe dearth of data concerning Chinese populations with balanced sex and age stratifications. Notably, the lack of epidemiological surveys on dry mouth among community-dwelling older adults in China indicates insufficient awareness and clinical attention given to this condition. Consequently, many affected older individuals fail to proactively seek intervention.

Furthermore, the precise detection and multidimensional assessment of dry mouth are fundamental prerequisites for the rational development of next-generation oral care products. Current assessment methods predominantly rely on subjective questionnaires, with a notable deficit in objective instrumental evaluations. It remains unclear how multidimensional objective physiological parameters, ranging from biomarkers and volatile sulfur compounds (VSCs) to biophysical tissue moisture, intertwine to characterize the highly complex dry mouth phenotypes across different populations [16]. Driven by these limitations, three critical research gaps persist in the evaluation of dry mouth. First, existing studies often rely on isolated subjective metrics, lacking a systematic integration of objective instrumental parameters, biological markers, and professional clinical assessments [18, 19]. Second, insufficient attention has been given to the disparities of these multidimensional indicators across different life stages (particularly the transition from middle to old age) and their potential correlation with the early decline of localized oral function [20, 21]. Finally, there is a lack of authoritative baseline physiological data for "sub-healthy" populations presenting with dry mouth but free from major systemic diseases [22].

This absence impedes the early identification of oral health issues and constrains the mechanism-based development of health products.

To bridge these critical gaps and transcend the limitations of isolated subjective measurements, this study systematically evaluated the multidimensional phenotypic differences between dry mouth and non-dry mouth groups. These dimensions encompassed instrumental measurements of oral and perioral moisture, gingival blood perfusion, objective salivary flow rate, VSCs (H_2S , CH_3SH , and $(\text{CH}_3)_2\text{S}$), salivary biomarkers (AMY1 and EGF), alongside subjective questionnaires and clinical grading. Building upon this multidimensional framework, the present study aimed to elucidate the specific heterogeneity driven by sex and age. Ultimately, this research sought to establish a multidimensional objective assessment framework for dry mouth, reducing the traditional overreliance on subjective perception, thereby providing a rigorous scientific foundation for the implementation of stratified management and the development of population-specific, innovative oral care interventions.

Materials and Methods

Study Design and Setting

This study employed a cross-sectional stratified design to explore the relationships between various indicators and factors such as age and sex. The aim is to obtain an overall understanding of people experiencing dry mouth and to preliminarily investigate evaluation indicators and methods for clinical efficacy testing in people with dry mouth.

Study Participants

A total of 164 participants were enrolled and stratified using a balanced $2 \times 2 \times 2$ factorial design. The stratification variables included sex (male versus female), age group (30–50 versus 51–70 years), and dry mouth status (dry versus non-dry). This approach yielded eight distinct subgroups, with participant allocation carefully controlled to include roughly 21 individuals per group, thereby guaranteeing a minimum effective sample size of 20 for each stratum. Inclusion criteria: (1) 30–70 years old Chinese healthy subjects. (2) Criteria for determining dry mouth: Use Oral moisture Mucus® instrument for screening with the "dry mouth" group defined by a value ≤ 27.9 and the "non-dry mouth" group by a value ≥ 29.6 [23], (3) There are no obvious blemishes (scars, etc.) in the oral cavity that may affect the result, (4) Voluntarily participate in the study and comply with the requirements of the test for visits, and those who are able to respond to any discomfort in a timely manner, (5) A person who is able to accept to complete the test according to the test requirements, (6) Those who can understand and fill in the project questionnaire and co-operate with the staff. Exclusion criteria: (1) Having an allergic constitution, allergic dermatitis and infectious diseases (such as dental caries, periodontitis, oral candidiasis, herpetic stomatitis, hand-foot-mouth disease, syphilis, etc. (2) Patients with a history of diseases (such as depression, diabetes, hyperthyroidism, chronic rhinitis, sinusitis, nasal polyps and other nasal diseases,

cancer patients, AIDS, rheumatoid arthritis, Parkinson's disease, chronic renal failure, burning mouth syndrome), and those who are clinically judged as unsuitable to participate in this project, (3) Subjects using oral saliva moisturizers and saliva stimulants, (4) The test site has large areas of birthmarks, scratches, white patches, pigmented nevus, keloids and other skin manifestations that affect the test. (5) Currently taking drugs that have an impact on the test results and using antibiotics one month before participating in the study, (6) Subjects who in the clinical judgement are considered unsuitable to participate in the study, (7) Subjects who have participated in other oral clinical trials within the last 2 month.

Data Collection

Instrumental measurements

Oral moisture was evaluated using an Oral Moisture Checker Mucus® (Life Co., Ltd., Japan). Measurements were performed in triplicate, with the average values recorded in arbitrary units (a.u.). Moisture levels of the lips and oral corners were quantified using a Corneometer® CM 825 (Courage + Khazaka Electronic GmbH, Germany); three parallel measurements were taken per site to calculate the mean value (a.u.). Volatile sulfur compounds (VSCs)—specifically hydrogen sulfide (H_2S), methanethiol (CH_3SH), and dimethyl sulfide ($(CH_3)_2S$)—were analyzed using an OralChroma™ detector (Nissha FIS, Inc., Japan). Gingival blood perfusion was mapped using a PeriCam PSI NR laser speckle contrast imaging system (Perimed AB, Sweden).

Clinical assessment

A trained clinical dentist performed comprehensive evaluations of the participants' overall condition of the oral mucosa, condition of the teeth, condition of dry mouth, redness of the oral mucosa, atrophy of the oral mucosa, condition of angular stomatitis, and clinical grading of salivary secretion. Each parameter was graded on a scale of 0 to 3. The scores from these individual parameters were summed to yield a total oral condition score, where higher values indicate a more severe deterioration of oral health.

Saliva collection and analysis

Unstimulated whole saliva was collected over a 5-minute period to determine the objective salivary flow rate (mL/min). Participants were seated with their heads tilted slightly forward, resting the tip of the tongue against the lingual surface of the mandibular anterior teeth to allow saliva to pool naturally in the floor of the mouth. The pooled saliva was carefully aspirated using a pipette and transferred into sterile Eppendorf (EP) tubes. Following centrifugation, the saliva samples were analyzed to quantify the concentrations of the salivary biomarkers human α 1-salivary amylase (AMY1) and epidermal growth factor (EGF).

Questionnaires

A multidimensional assessment of the participants' oral and psychological states was conducted using four validated questionnaires. (1) A subjective oral dryness condition scale was utilized to quantify dry mouth severity, with higher scores reflecting more severe symptoms. (2) The Oral Health Impact Profile-14 (OHIP-14) [24–26] was employed to evaluate the impact of oral health on quality of life across seven domains: functional limitation, physical pain, psychological discomfort, physical disability, psychological disability, social disability, and handicap. Higher total scores denote a more profound negative impact. (3) The Oral Health Scale H&N35 [27] assessed oral health symptoms, including oral pain, swallowing difficulties, and dry mouth, where elevated scores indicate worse symptomatology. (4) The Huaxi Emotional Distress Index (HEI) [28], a tool specifically developed for the Chinese population, was used to assess anxiety, depression, and negative cognitions, accurately capturing emotional expression and psychological distress within a Chinese cultural context. Higher HEI scores correspond to elevated levels of emotional distress.

Statistical analysis

Statistical analyses were performed using SAS software, version 9.4 (SAS Institute Inc., Cary, NC, USA). Continuous variables are presented as means $\pm$ standard deviations (SD), whereas categorical variables are expressed as frequencies and percentages. The comparison of continuous variables was guided by normality testing and the number of comparative groups. For two-group comparisons, normally distributed data were analyzed using the independent samples t-test, and non-normally distributed data via the nonparametric Wilcoxon rank-sum test. For comparisons involving three or more groups, a one-way analysis of variance (ANOVA) followed by Fisher's Least Significant Difference (LSD) post-hoc test was applied to normally distributed data, while the Kruskal-Wallis test followed by Dunn's post-hoc test was utilized for non-normally distributed data. Categorical variables were compared using the Chi-square test or the Cochran-Mantel-Haenszel (CMH) test. Confidence intervals (CIs) were set at 95%, with the significance level established at $\alpha = 0.05$. Statistical significance is denoted as follows: n.s. (not significant, $P > 0.05$), $*P < 0.05$, $**P < 0.01$, $***P < 0.001$.

Result

This study enrolled a total of 164 participants, comprising 82 individuals in the dry mouth group and 82 in the non-dry mouth group. Proportional stratification by sex and age yielded eight independent subgroups, each containing 20 to 21 participants (**Figure S1**). Figure 1 outlines the detailed study design, including participant screening, group allocation, and the multidimensional assessment parameters.

Instrumental measurements revealed that oral moisture in the dry mouth group was profoundly lower than that in the non-dry mouth group ($P < 0.001$) (Fig. 2A). Although no significant overall sex or age differences were observed (n.s.), this highly significant discrepancy driven by dry mouth status persisted robustly across all sex and age subgroups (all $P < 0.001$) (Fig. 2D and **Figure S2**). Subsequent cross-

stratified subgroup analyses demonstrated that females aged 30–50 years in the non-dry mouth cohort exhibited the highest oral moisture, whereas males aged 51–70 years with dry mouth presented the lowest levels (**Figure S2**). Regarding lip moisture, the non-dry mouth group maintained significantly higher levels compared to the dry mouth group, this disparity remained statistically significant within the female and the 30–50-year-old subgroups (Fig. 2B, 2E, and **Figure S3**). Cross-stratified evaluations indicated that lip moisture peaked in non-dry mouth females (30–50 years) and non-dry mouth males (51–70 years), but dropped to the lowest values in females aged 51–70 years with dry mouth (**Figure S3**). A similar pattern emerged for moisture at the oral corners, the non-dry mouth group showed significantly higher overall levels than the dry mouth group, a finding that remained consistent among males and the 51–70-year-old subgroup. In the overall comparison, females exhibited significantly greater moisture at the oral corners than males, an advantage that was preserved within the dry mouth group (Fig. 2C, 2F, and **Figure S4**). Moreover, within the dry mouth population, males aged 30–50 years had significantly higher moisture at the oral corners than their 51–70-year-old counterparts, with the latter registering the lowest values across all stratified subgroups (**Figure S4**).

Assessment of objective Unstimulated salivary flow rates (USFR) demonstrated significantly reduced secretion in the dry mouth group compared to the non-dry mouth group. In the overall population, males exhibited significantly higher flow rates than females (Fig. 3A). Cross-stratified subgroup analyses revealed that non-dry mouth males aged 30–50 years achieved the highest USFR (significantly exceeding those of age-matched females), whereas females aged 51–70 years with dry mouth recorded the lowest rates (**Figure S5**). Similarly, quantitative analysis of AMY1 showed significantly diminished levels in the dry mouth group compared to their non-dry mouth counterparts (Fig. 3B). However, AMY1 concentrations displayed no significant main effects for sex or age (Fig. 3B). In further subgroup evaluations, although the non-dry mouth male group exhibited relatively elevated AMY1 levels, pairwise comparisons across the finely stratified subgroups did not reach statistical significance (Fig. 3E and **Figure S6**). Regarding salivary EGF, preliminary assessments found no significant main effects for dry mouth status, sex, or age (Fig. 3C). Within the non-dry mouth group, EGF levels in the 51–70-year-old subgroup were significantly higher than those in the 30–50-year-old subgroup (Fig. 3F). Cross-stratified analyses indicated that males aged 51–70 years with dry mouth had significantly lower EGF levels than age-matched non-dry mouth males. All other observed significant disparities in EGF were confined exclusively within a single clinical status group (either dry mouth or non-dry mouth) (**Figure S7**).

Analysis of VSCs revealed that concentrations of CH_3SH and $(\text{CH}_3)_2\text{S}$ were significantly elevated in the dry mouth group relative to the non-dry mouth group, whereas H_2S levels showed no significant main effect for dry mouth status (Fig. 4A, 4B, and **Figure S8**). Stratification by sex and age indicated that males possessed significantly higher H_2S and CH_3SH levels than females, and individuals aged 30–50 years exhibited significantly greater $(\text{CH}_3)_2\text{S}$ concentrations than those aged 51–70 years. Cross-stratified subgroup analyses of the three VSCs demonstrated that the subgroup of males aged 30–50 years with dry mouth consistently presented the highest concentrations. Specifically, H_2S levels in this subgroup were significantly higher than those in 30–50-year-old females with dry mouth, 30–50-year-old non-dry mouth males, and 51–70-year-old males with dry mouth. Conversely, non-dry mouth females

aged 30–50 years generally displayed the lowest VSC levels (Fig. 4C and 4D). Regarding oral microcirculation, gingival blood perfusion was significantly higher in males than in females, a disparity that persisted within the dry mouth group (Fig. 4E and **Figure S9**). Although cross-stratified evaluations did not yield significant pairwise differences, males aged 30–50 years with dry mouth registered the highest absolute values for gingival blood perfusion (Fig. 4E).

In the subjective Dry Mouth Scale, scores in the dry mouth group were significantly higher than those in the non-dry mouth group across all sex and age strata. Cross-stratified subgroup analyses highlighted that females aged 30–50 years with dry mouth experienced the most severe subjective dry mouth, scoring significantly higher than age-matched non-dry mouth females (Fig. 5A and 5B). Conversely, the OHIP-14 and the H&N35 module exhibited no significant differences across clinical status, sex, or age groups (**Tables S9 and S10**). For the HEI, although overall comparisons and preliminary stratified assessments yielded no significant main effects (**Figure S11**), further three-factor combined analyses revealed that females aged 30–50 years with dry mouth experienced the highest levels of emotional distress, significantly surpassing age-matched males with dry mouth (Fig. 5C). Consistent with the participants' subjective reports, clinical grading for the condition of dry mouth by clinicians was significantly worse (higher scores) in the dry mouth group, particularly among females and the 51–70-year-old demographic (**Table S2**). However, Clinical grading of salivary secretion, overall condition of the oral mucosa, and condition of angular stomatitis showed no significant differences based on dry mouth status, although females scored significantly worse on the clinical salivary secretion assessment than males. Evaluations of redness of the oral mucosa and atrophy of the oral mucosa revealed significant sex and age main effects, with greater severity observed in males and the 51–70-year-old group. The final finely cross-stratified results consistently identified the subgroup of males aged 51–70 years with dry mouth as the specific population presenting with the worst condition of the teeth and the most severe mucosal atrophy (**Tables S3–S8**).

Table 1
Significant clinical assessment results.

Clinical Assessment	Stratification Variable	Significant Pairwise Comparison (Higher vs. Lower)	Mean Scores	Significance
Dry mouth score	Dry mouth status	Dry mouth vs. Non-dry mouth	1.43 vs. 1.15	*
	Age	51–70 years vs. 30–50 years	1.40 vs. 1.17	*
Condition of the teeth	Sex	Male vs. Female	1.62 vs. 1.43	*
	Age	51–70 years vs. 30–50 years	1.71 vs. 1.33	***
	Cross-stratified subgroup	Dry mouth (Male, 51–70) vs. Dry mouth (Male, 30–50)	2.05 vs. 1.30	***
Mucosal redness	Sex	Male vs. Female	0.38 vs. 0.20	*
	Age	51–70 years vs. 30–50 years	0.39 vs. 0.20	*
Mucosal atrophy	Age	51–70 years vs. 30–50 years	1.33 vs. 1.12	**
	Cross-stratified subgroup	Dry mouth (Male, 51–70) vs. Dry mouth (Male, 30–50)	1.55 vs. 0.95	**
Clinical grading of salivary secretion	Sex	Female vs. Male	2.81 vs. 2.56	**

This table summarizes significant primary main effects and representative tertiary extremes from clinical assessments. Higher scores indicate greater severity or slower saliva flow. Non-significant evaluations are detailed in the Supplementary Information. * $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$; n.s., not significant.

Discussion

The present study provides a comprehensive multidimensional phenotypic profiling of dry mouth and non-dry mouth groups within the Chinese population, highlighting distinct sex and age disparities. Historically, the clinical assessment of dry mouth has disproportionately relied on subjective questionnaires or isolated glandular function tests, which often fail to capture the complex objective physiological landscape. To transcend these methodological limitations, we implemented a multidimensional framework integrating instrumental moisture quantification, biomarker analysis, VSCs

measurements, and professional clinical grading. The distinct physiological signatures observed across our evenly stratified groups elucidate that dry mouth extends far beyond a mere reduction in saliva; rather, it manifests as a systemic physiological deterioration that compromises the oral microenvironment, the perioral physical barrier, and psychosomatic homeostasis. Specifically, the significant depletion of AMY1—a critical surrogate marker for parotid parenchymal function and autonomic regulation [11]—not only impairs initial digestive efficacy but also disrupts biofilm homeostasis and the mucosal defense barrier. Concurrently, the marked elevation in VSCs (particularly CH_3SH and $(\text{CH}_3)_2\text{S}$) underscores the severe consequences of microenvironmental dysbiosis. The loss of the mechanical flushing action of saliva allows desquamated epithelial cells and dietary debris to stagnate, providing an ideal substrate for anaerobic bacterial proliferation. These findings successfully bridge existing diagnostic gaps, demonstrating that parameters such as AMY1 depletion and localized oral moisture deficits can serve as reliable, quantifiable clinical metrics, thereby driving a critical paradigm shift toward precise, objective dry mouth evaluation.

Beyond establishing objective indicators, our refined subgroup analyses revealed profound heterogeneity across sex and age strata, underscoring the necessity of transitioning toward highly personalized oral care strategies. The data clearly indicates that interventions must be strategically tailored to address the unique physiological and psychological vulnerabilities of different populations. For instance, males, particularly those aged 51–70 years, exhibited prominent structural atrophy and a markedly high susceptibility to VSC accumulation (specifically CH_3SH and H_2S). Such anomalies likely reflect the cumulative physiological impact of long-term lifestyle factors (e.g., smoking and dietary habits) superimposed on early glandular changes. Consequently, targeted interventions for males must prioritize breath freshening, VSC regulation, and the optimization of the oral microecology. Furthermore, the fluctuations in EGF observed within this older male subgroup may hint at specific compensatory repair mechanisms initiated by the body in response to mucosal barrier impairment. Conversely, females aged 30–50 years demonstrated the highest psychological vulnerability, evidenced by peak HEI scores accompanied by severe subjective dry mouth and lip moisture loss. From a psychosomatic perspective, this acute escalation in emotional distress profoundly reflects the complex, intersecting burdens experienced by this group during this specific life stage—namely, the physiological transitions triggered by perimenopausal endocrine fluctuations, compounded by intense occupational and familial role conflicts. Therefore, holistic management strategies for this specific group cannot be confined to traditional moisturization; they must proactively incorporate psychosocial support, stress mitigation, and emotional regulation.

The comprehensive mapping of these multidimensional phenotypic parameters also establishes a robust scientific foundation for the rational development of next-generation oral care products. Crucially, aligning with the findings of Hyun-Sook Kim et al. [14], the impact of dry mouth traverses the intraoral boundaries, extending to the perioral skin. From a biophysical standpoint, healthy salivary secretion forms a protective hydration film that maintains the moisture of the perioral stratum corneum [29]. When this physical shield deteriorates due to glandular decline, transepidermal moisture loss accelerates dramatically. Our findings reveal pronounced sex and age heterogeneity in localized perioral tissue

moisture. Specifically, females aged 51–70 years experienced severe lip moisture loss, whereas their male counterparts exhibited a distinct propensity for moisture loss at the oral corners. These striking regional characteristics highlight an urgent demand for interventions targeting specific physiological barriers. Future product innovations should pivot toward personalized formulations adapted to varying demographic profiles; for example, female-oriented care regimens could emphasize lip barrier restoration, while male-focused product lines might reinforce targeted protection for vulnerable areas such as the oral corners. Additionally, the ubiquitous decline of AMY1 across the dry mouth group illuminates the broad potential of biomimetic oral care and enzyme-targeted solutions. Advanced formulations designed to replenish or activate key functional salivary constituents could offer a direct, mechanism-based therapeutic pathway to counteract glandular hypofunction. By aligning product design with the distinct multidimensional physiological profiles of specific populations, future interventions can deliver precise, multi-target care to restore oral homeostasis.

Although this study comprehensively delineates the multidimensional phenotypic profiles of dry mouth and presents broad clinical and translational prospects, certain limitations warrant acknowledgment. First, the cross-sectional design precludes definitive causal inferences regarding the temporal relationships among biomarker depletion, escalating psychological distress, and mucosal structural atrophy. Second, while the current sample size ($n = 164$) and the rigorous factorial design framework are entirely sufficient for establishing initial objective metrics and constructing the assessment model, large-scale, multicenter longitudinal cohorts remain necessary. Tracking the longitudinal evolution of these physiological parameters will not only serve to robustly validate the proposed objective metrics; it remains fundamentally indispensable for ultimately achieving highly personalized oral health interventions that address the heterogeneous care demands across distinct populations.

Conclusion

This study establishes a multidimensional objective assessment framework, reducing the traditional overreliance on subjective reporting for dry mouth evaluation. The sex and age disparities in clinical phenotypes identified herein provide a robust translational foundation for the development of population-specific, innovative oral care interventions.

Abbreviations

VSCs Volatile sulfur compounds

AMY1 Human α 1-Salivary Amylase

EGF Epidermal growth factor

H₂S Hydrogen sulfide

CH₃SH Methanethiol

(CH₃)₂S Dimethyl sulfide

USFR Unstimulated salivary flow rate

OHIP-14 The Oral Health Impact Profile-14

HEI The Huaxi Emotional Distress Index

SD Standard deviations

ANOVA Analysis of variance

LSD Least Significant Difference

CMH test Cochran-Mantel-Haenszel test

CI Confidence intervals

n.s not significant

Declarations

Acknowledgements

We would like to express our gratitude to the participants of this study.

Ethics approval and consent to participate

This study was performed in compliance with Good Clinical Practice and the Declaration of Helsinki. Approval was obtained from the Shanghai Clinical Research Ethics Committee (reference number SECCR2025-100-01). Participation was voluntary and based on a signed written informed consent form.

Consent for publication

Not applicable.

Conflict of interest

The authors have no conflicts of interest to declare.

Competing interests

The authors declare no competing interests.

Funding

Not applicable.

Author Contribution

Xuehua Zhao: Conceptualization (Lead), Methodology (Lead), Project administration (Equal), Writing – original draft (Lead), Writing – review & editing (Lead) Hao Chen Methodology (Supporting), Project administration (Equal), Data curation (Lead), Supervision (Lead) Yi Jiang Methodology (Supporting), Clinical assessment (Lead) Jianwei Liu: Methodology (Supporting), Validation (Supporting), Writing – review & editing (Supporting).

Data Availability

The data supporting this study's findings are available upon reasonable request to the corresponding author (Xuehua Zhao)

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Figures

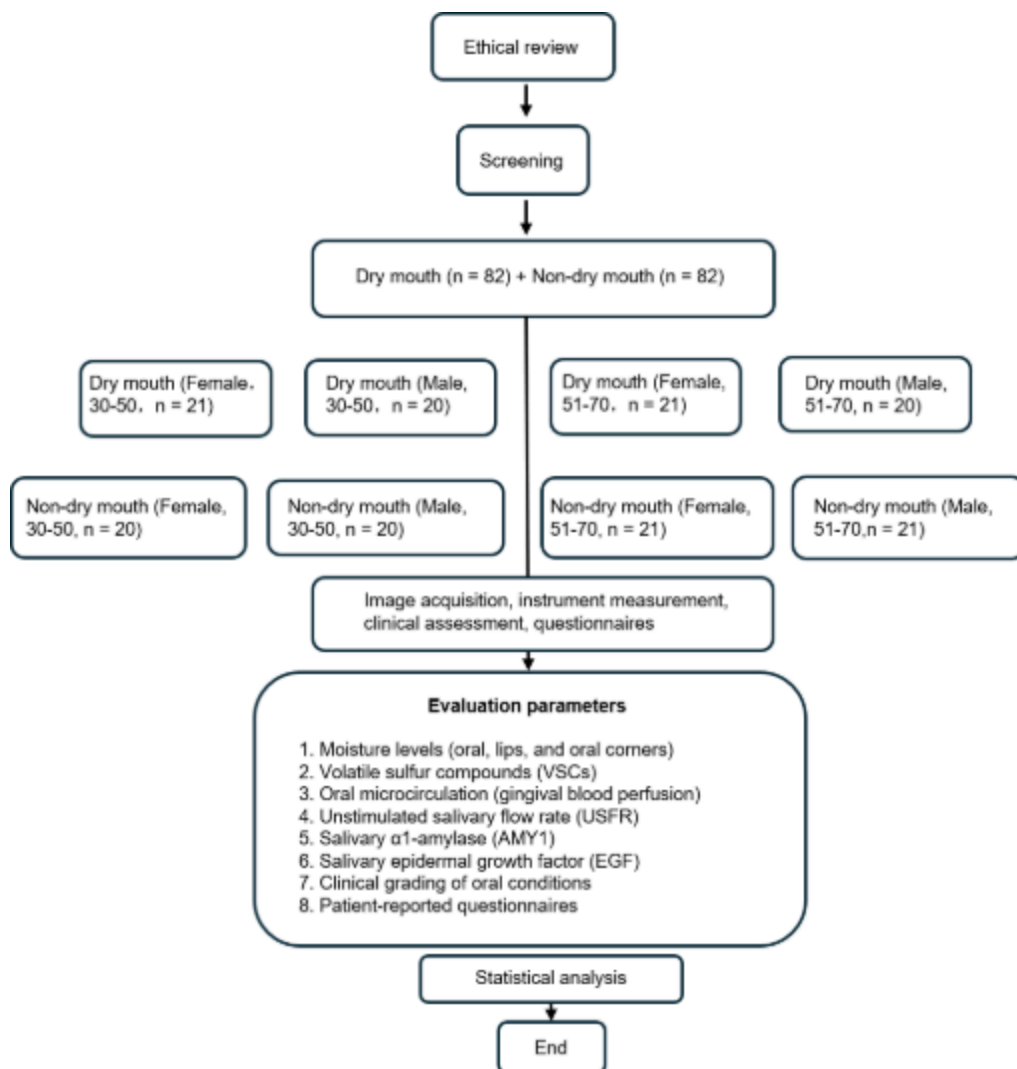


Figure 1

Flow diagram of the study.

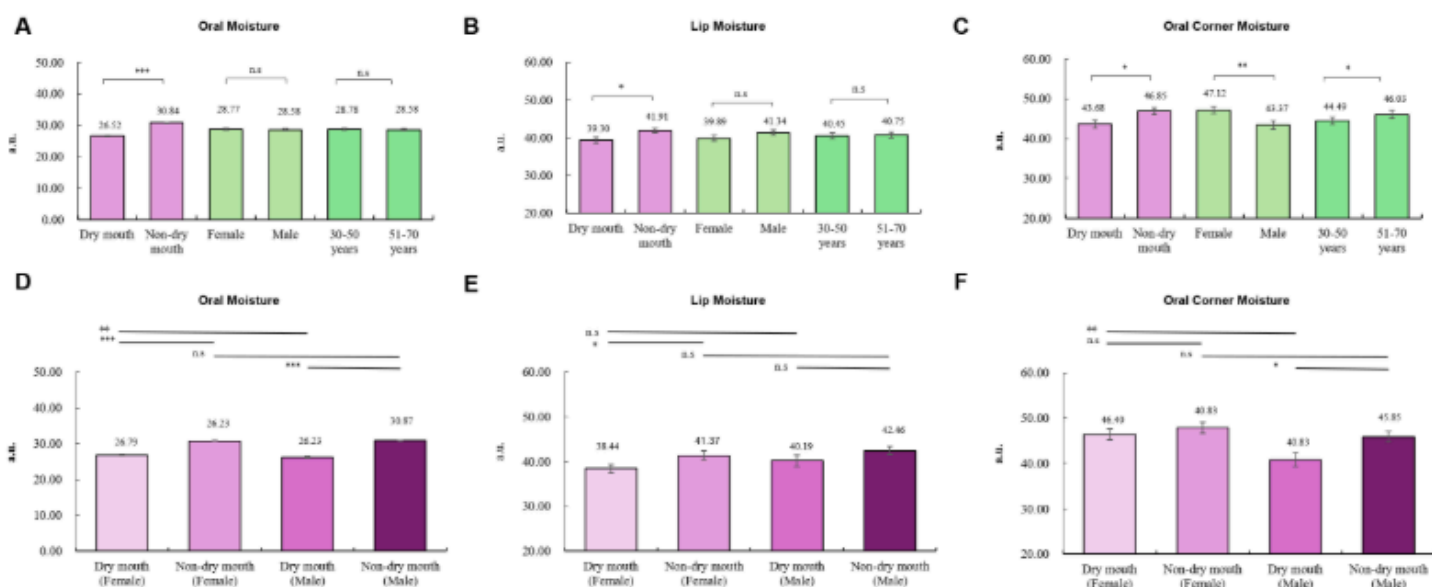


Figure 2

Moisture levels of the oral, lips, and oral corners in relation to dry mouth status, sex and age. (A–C) Overall comparisons of moisture levels in the oral (A), lips (B), and oral corners (C). (D–F) Sex-stratified subgroup analyses. Data are presented as mean ± SD. n.s. (not significant, $P > 0.05$), * $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$.

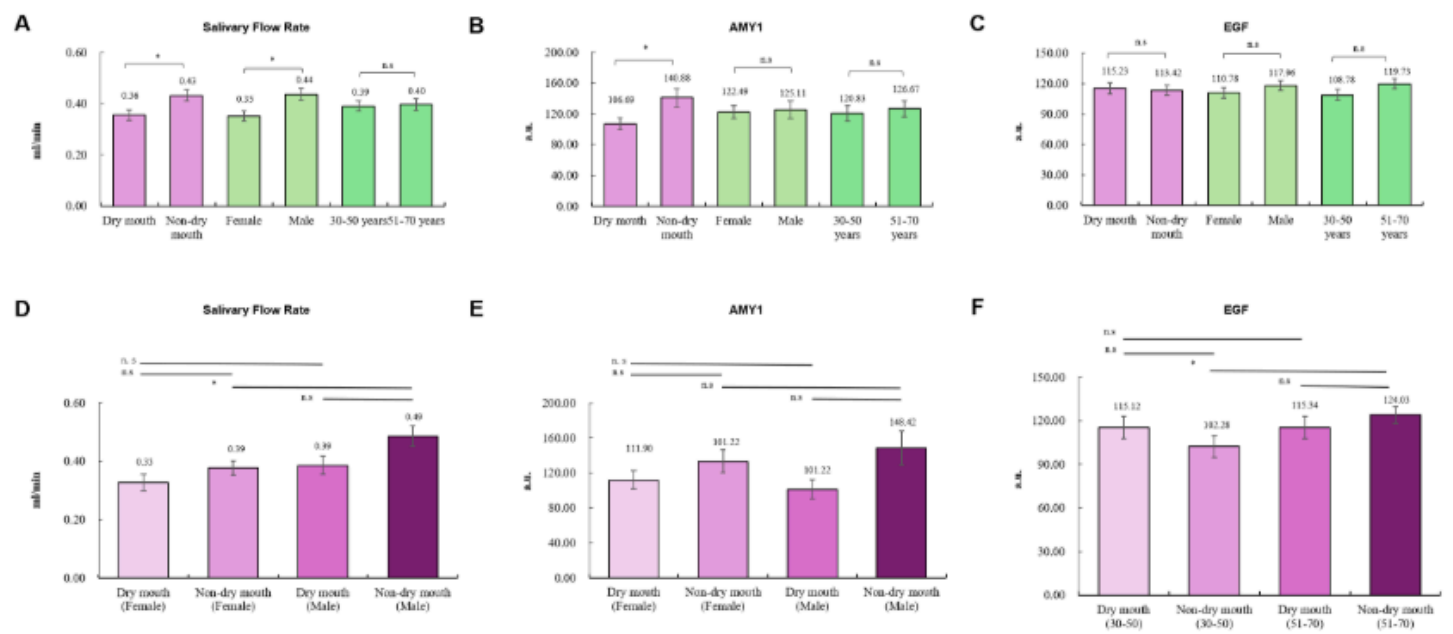


Figure 3

Evaluation of USFR and biochemical markers (AMY1 and EGF) according to dry mouth status, sex and age. (A–C) Overall comparisons of USFR (A), AMY1 (B), and EGF (C). (D–E) Sex-stratified subgroup analyses for USFR (D) and AMY1 (E). (F) Age-stratified subgroup analysis for EGF. Data are presented as mean ± SD. n.s. (not significant, $P > 0.05$), * $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$.

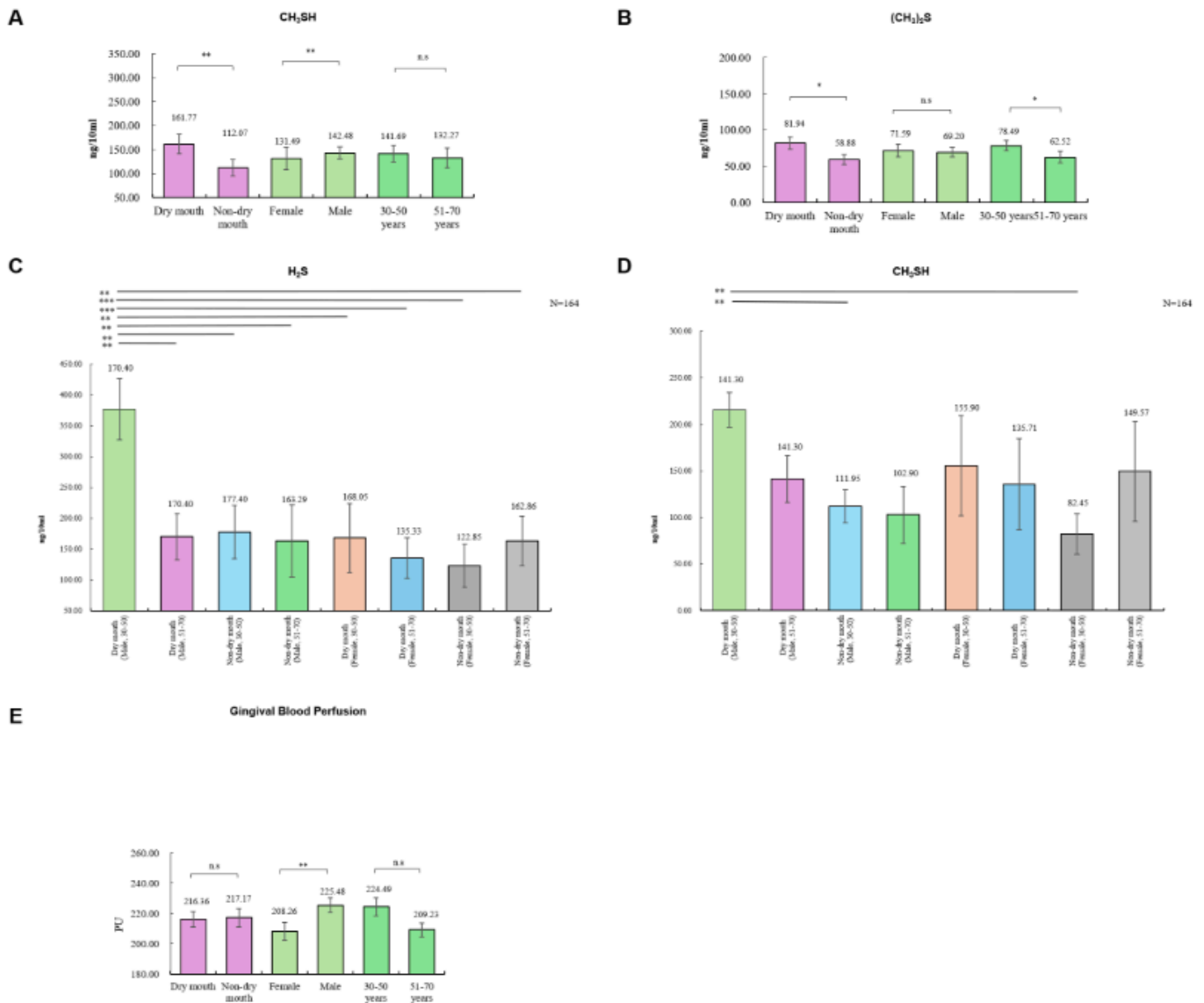


Figure 4

Assessments of VSCs and oral microcirculation according to dry mouth status, sex, and age. (A–B) Overall comparisons of CH₃SH (A) and (CH₃)₂S (B) concentrations. (C–D) Cross-stratified subgroup analyses for H₂S (C) and CH₃SH (D). (E) Overall comparisons of gingival blood perfusion. Data are presented as mean ± SD. n.s. (not significant, $P > 0.05$), * $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$.

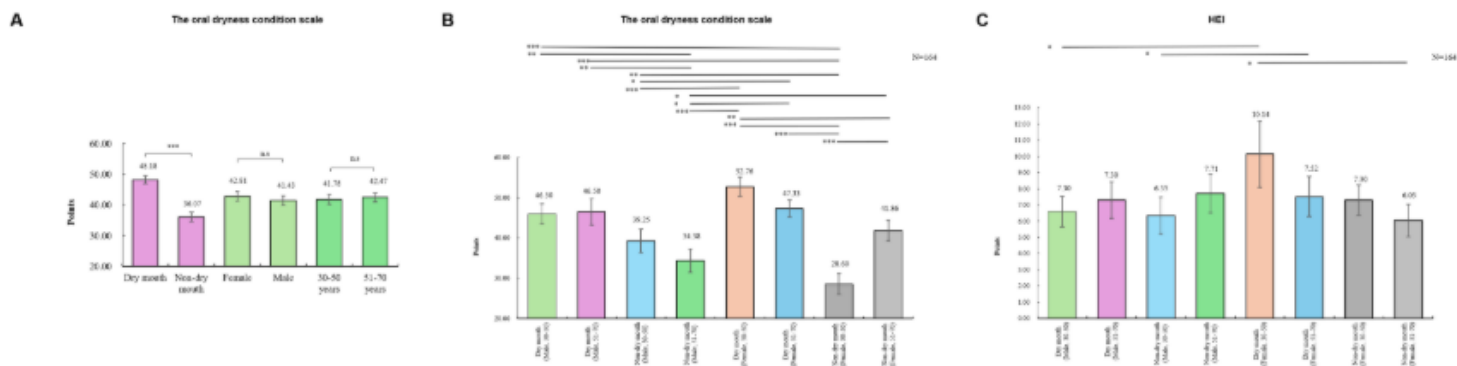


Figure 5

Assessments of patient-reported oral dryness and emotional distress according to dry mouth status, sex, and age. (A) Overall comparisons of the oral dryness condition scale. (B–C) Cross-stratified subgroup analyses for the oral dryness condition scale (B) and the Huaxi Emotional Index (HEI) (C). Data are presented as mean $\pm$ SD. * $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$; n.s., not significant.

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