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Review

Associations between diseases of the mouth and mental disorders: A scoping review of longitudinal studies

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ABSTRACT

Background: Mental disorders and oral health conditions frequently co-occur. We mapped and critically reviewed the literature on longitudinal associations between oral health conditions and mental disorders.
Method: MEDLINE, Embase and PsycInfo were searched for longitudinal studies published during the last 25 years. Two reviewers independently screened, reviewed full-text and extracted data before synthesizing the evidence. Associations between oral and mental disorders were illustrated as Sankey diagrams. The review protocol was pre-registered (https://osf.io/vrpu9).
Findings: From 165 included studies, we identified 118 studies investigating 35 independent associations between 16 oral exposures and 12 mental disorder outcomes. Another 42 studies investigated 32 associations between 17 mental disorder exposures and 14 oral outcomes. Five studies reported bidirectional associations. Most reports linked tooth loss to Alzheimer's disease/other dementias (18 studies) and cognitive impairment (15 studies), with periodontitis linked to Alzheimer's disease/other dementias (16 studies). Conversely, depression (10 studies), dementia (6 studies) and sleep disorder (5 studies) were attributed to temporomandibular disorders (TMD; 10 studies), periodontitis (8 studies) and caries (7 studies) outcomes. Depressive and anxiety disorders were linked bidirectionally with TMD and eating disorders.
Interpretation: Prevention and early management of oral and mental disorders may mitigate their reciprocal risk, thereby lowering the overall disease burden.

1. Introduction

Mental disorders affect a significant portion of the population, with an estimated prevalence of up to 20%, and conditions such as depression, anxiety, and schizophrenia are among the most common. (Steel et al., 2014; Global Burden of Disease Study 2013 Collaborators, 2022) These disorders are among the leading contributors to disease burden, impacting functionality and quality of life for millions of people worldwide. Similarly, oral diseases affect approximately 45% of the global population, and contribute to chronic pain, tooth loss, and functional disability, thereby significantly impacting overall well-being. (Cormac and Jenkins, 1999; Kassebaum et al., 2017) The relationship between these two domains has gained increasing attention in recent years, revealing complex interactions between diseases of the oral cavity and mental disorders that extend beyond the basic psychosocial determinants of the comorbidity.

Individuals with psychiatric conditions frequently exhibit poorer oral health. This connection has long been understood in terms of psychosocial and biological mechanisms such as through reduced self-care, dental phobia and changes in dietary habits among individuals with mental health challenges, along with external factors such as limited access to healthcare services. (Cormac and Jenkins, 1999; Kisely et al., 2015) Furthermore, dry mouth is a common side effect of antidepressants, antipsychotics and mood stabilizers, while anxiolytics are known to reduce motivation leading to neglect of oral hygiene, and stimulants may cause reduced appetite and dietary alterations. (Bardow et al.,

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2001; Cockburn et al., 2017) Dry mouth, unhealthy dietary habits, altered oral microbiota and decreased oral hygiene practices directly increase the risk of oral diseases. Conversely, oral health conditions themselves may exacerbate mental health issues through systemic mechanisms or genetic vulnerability. Inflammatory mediators originating from inflamed periodontal tissues have been suggested to contribute to neuroinflammatory pathways implicated in mood disorders and cognitive decline. (Dantzer, 2017; Neupane et al., 2022) Thus, it is now increasingly accepted that oral health is crucial for mental well-being, just as mental health is essential for maintaining oral health. (Kisely, 2016)

Although many publications have addressed this interrelationship, most studies to date are cross-sectional, limiting the ability to establish the direction of these relationships and to capture dynamic interactions over time. These inherent limitations raise key questions: do mental disorders predispose individuals to poorer oral health, or, conversely, do oral diseases influence the development of psychiatric disorders through discernible biological, psychological or social factors? Alternatively, could the observed association be a result of spurious statistical correlations or residual confounding? Investigating this relationship in clinical and epidemiological settings is essential to determine if true bidirectional causal pathways exist. Such understanding has implications for the design of preventive and therapeutic interventions, as well as for assessing aggregated population health. With this scoping review, we aimed to map and analyze the longitudinal literature on the associations between mental disorders and oral cavity diseases, identifying the directions of association, types of studies conducted, geographic context, and key knowledge gaps in this field.

2. Methods

2.1. Protocol registration

The current review was conducted in accordance to JBI scoping review methodology (Peters et al., 2020) and the aligns with the checklist of the PRISMA extension for scoping reviews (PRISMA-ScR). (Tricco et al., 2018) The review protocol was registered with the Open Science Framework and is available at https://doi.org/10.17605/OSF.IO/VRPU9. This protocol also includes a subsequent meta-analysis of selected pairs of oral diseases and mental disorders, identified in the present scoping review.

2.2. Search strategy and selection criteria

2.2.1. Search strategy

A comprehensive list of search terms was created using the category C of the medical subject heading MeSH tree data available at National Library of Medicine website. We included all terms in the MeSH hierarchy under tree numbers F03 (mental disorders including neurocognitive disorders [F03.615]) and C07 (stomatognathic diseases) (National Library of Medicine, 2023). Stomatognathic diseases include general or unspecified diseases comprising the mouth, teeth, jaws, and pharynx. An academic librarian performed and renewed the systematic search using identical search strategy across the databases Medline (Ovid), Embase (Ovid) and APA PsycInfo from database inception to 11 February 2025. We did not consider non-research sources of evidence, as we did not anticipate finding relevant information published as grey literature that would meet the specific inclusion criteria within the broad research theme of this review. Full details of the search strings and included disorders or conditions are available in the *Supplementary material (eAppendix 1 and eAppendix 2)*. After deduplication, 13,990 unique reports were included in a blinded screening and analysed by four independent authors. For each report, title and abstract were reviewed by at least two authors using Rayyan- a web-based screening solution. (Ouzzani et al., 2016) Full text reviews were conducted on Covidence (Covidence, 2024) using the pre-determined eligibility criteria *(eAppendix 3)*.

Two independent reviewers evaluated the title and abstract of each record to screen for relevant papers based on the set eligibility criteria and a list of conditions to be included *(enlisted in the eAppendix 2)*. In case of discrepant decision between the two reviewers, a third reviewer stepped in and resolved the conflict. The records selected through screening were then subjected to full text review in duplicate. We did not contact primary authors in case of missing information from a report. We excluded 231 reports due to violation of inclusion criteria, the reasons for which are summarized in the PRISMA flow diagram (Fig. 1) and detailed in supplementary material *(eAppendix 4)*.

2.2.2. Selection criteria

Inclusion criteria

1. Participants and settings: Studies involving human subjects of all ages were included without restrictions related to geographic location, social or cultural factors, sex, or specific types of samples, whether clinical, experimental, community-based, or sourced from any type of database.
2. Thematic area: Studies that presented on at least one disease of the mouth and one mental disorder were considered.
3. Disease definition: Studies were considered if they followed standardized definition or classification of disease of the mouth and mental disorder, either as an exposure or an outcome. Any version of Diagnostic and Statistical Manual of Mental Disorders (DSM) or International Classification of Diseases (ICD) as well as any other classification systems were eligible. Substance use disorder or substance abuse or substance dependence are included. Studies without these diagnostic categories for any substance are excluded. Tobacco use or smoking was excluded, whereas, oral cancer/neoplasm was included. Dental phobia or dental anxiety was included only if a standard instrument was used to diagnose an anxiety disorder.
4. Study design: Longitudinal study with a clear study duration were considered; whereas, systematic reviews/meta-analysis were retained for secondary sources of literature.
5. Data type: The association between disease of the mouth and mental disorder had to be presented quantitatively.
6. Timeframe: Studies published from 1st January 2000 until 11 February 2025 were included.

Exclusion criteria:

1. Studies published before 1. Jan 2000 were excluded since we did not anticipate high-quality longitudinal studies on this area ante 2000.
2. Exclusively qualitative studies.
3. Studies published in languages other than English, Norwegian, Danish, Swedish, Spanish or Portuguese.
4. Studies without empirical data: Conference abstracts, protocols, case-reports, editorials, opinion pieces, correspondences or commentaries.

2.3. Data extraction and analysis

Data were independently extracted by all authors in groups of two and verified by the second reviewer performing the respective extraction. A standardized template was created in Covidence to extract the following data: study characteristics (authors, publication year, study design and setting, country or territory, design, sampling), population (sample size, study population, age and gender distribution), measures (direction of association, exposure and outcome diagnosis and criteria, follow up duration, and main findings). Any discrepant or dubious extraction was resolved through discussion among the authors. A cross-validation of the extraction process was done in a pilot extraction of the first 5 articles.

We synthesized the findings only descriptively. Our framework for

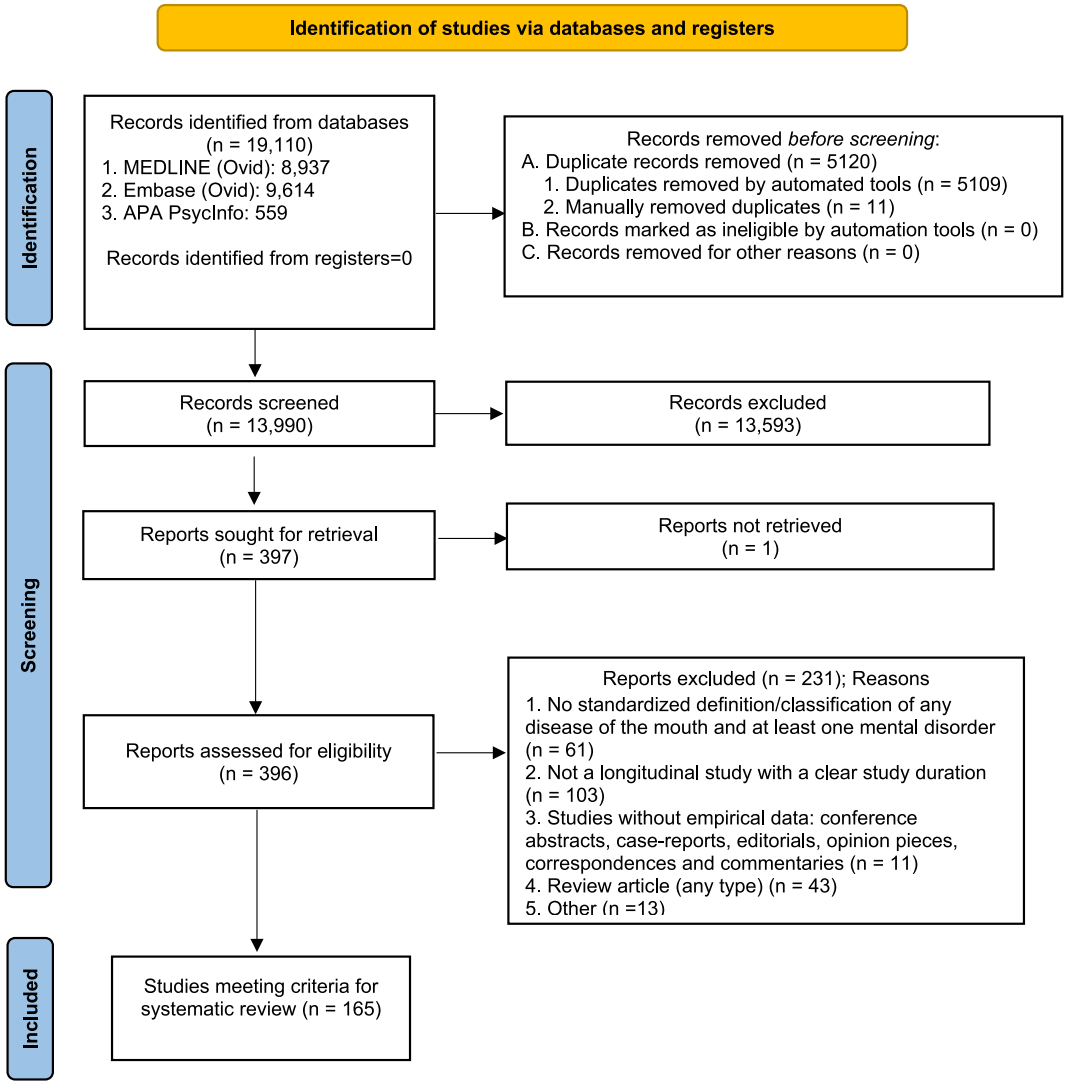

Fig. 1. PRISMA flow diagram for the current study.

synthesizing the data included mental and oral disease pairs, direction of association and number of publications for each association. Regarding the study outcomes, our analytical approach was limited to summarizing the association between exposure and the main outcome in plain language. Whenever the studies presented more nuanced finding, such as age or sex differences in the main findings, those were also enlisted. We then summarized frequency of studies with a shared finding, while also presenting a nuanced findings that deviates from the association trend. Sankey diagrams were created for each set of diseases for the associations examined, regardless of whether a positive, negative or null finding was reported. Sankey diagrams were created using SankeyMATIC, which builds on the open-source tool D3.js and code available as open source at github.com/nowthis/sankeymatic. We tabulated main prospective finding for the reported association in plain language without quantitative data, given the scope of the review. The outcome was categorized as a mixed or multiple (oral or mental) disorder when primary studies did not report a single discrete diagnostic entity. This included registry-based outcomes labeled broadly as "psychiatric disorders," combined outcomes such as depression/anxiety, or symptom-based outcomes assessed using validated scales capturing clinically relevant symptomatology without formal DSM or ICD diagnostic assignment. This categorization was applied to preserve fidelity to the original outcome definitions and to avoid post hoc diagnostic reclassification.

2.4. Quality assessment

We relied fully upon the included studies for the diagnostic criteria and case definition. Scoping reviews generally follow a systematic review process, however, a formal assessment of methodological quality is generally not performed. (Peters et al., 2020) Accordingly, although we applied stringent eligibility criteria we did not perform quality appraisal of the included studies. The primary aim was to map the breadth, direction, and characteristics of the longitudinal evidence rather than to quantify pooled effects or adjudicate study validity. The present scoping review was explicitly designed to inform a subsequent preregistered meta-analysis (https://doi.org/10.17605/OSF.IO/RCTB4). In that meta-analysis, issues related to risk of bias, confounding, and study quality will be formally addressed through structured risk-of-bias assessment, subgroup analyses based on study design and degree of covariate adjustment, and sensitivity analyses restricted to higher-quality studies.

3. Results

The database search resulted in 13,990 unique articles. Of those, 396 articles were selected for full text review that led to exclusion of 231 articles for different reasons (Fig. 1). The remaining 165 studies were included in this review (references provided in the *eAppendix 5*). The

majority of studies (N = 118) reported unidirectional associations arising from oral disorders and leading to mental health conditions. Forty-two studies examined associations originating from mental health conditions leading to oral disorders, while five studies reported on the bidirectional associations between oral and mental health disorders. The current review comprised of studies that investigated the associations of 35 independent oral-to-mental disorder sets and 32 mental-to-oral disease sets.

3.1. General study characteristics

As shown in Fig. 2, number of studies reporting on the longitudinal associations between oral conditions and mental disorders showed a tendency of steady increase during the period 2001–2024. Studies were conducted across 23 countries or territories, with 119 (72%) studies concentrated in six locations: Taiwan (42), USA (22), Japan (19), South Korea (14), Sweden (12), and mainland China (10) (Figs. 3A and 3B). Additionally, four studies utilized multinational datasets. Most studies (N = 89; 54%) had a prospective cohort design. Included studies had a large variation in sample size, age, gender distribution, study setting and follow-up duration. Sample sizes ranged from small clinical samples (Smith et al., 2014) followed for three months (Kumar et al., 2018) to nationwide samples followed-up for as long as 3 to 5 decades, e.g., (He et al., 2023; Tillman et al., 2018; Christensen and Mortensen, 2002)

3.2. Oral conditions as risk factors for mental disorders3

Studies showing oral conditions as risk factors of mental disorders are presented in Table 1. Of the 118 studies investigating 12 mental disorders as outcomes, 16 oral conditions were examined as possible exposure. The most frequent oral conditions were tooth loss (41 studies), periodontitis (30 studies), cleft lip and/or palate (8 studies), oral cancer (7 studies) and Sjogren's syndrome (6 studies). Twelve different mental disorders were examined as possible outcomes, including eight outcomes classified as mixed or multiple psychiatric disorders. The most frequent mental disorder outcome categories were Alzheimer's disease and other dementias (42 studies), depression (30 studies), cognitive decline or impairment (25 studies) and mixed or multiple psychiatric disorders (8 studies). Depression was examined as the most common outcome associated with 11 different oral conditions. Most frequent associations were reported for tooth loss as a risk for Alzheimer's disease and other dementias (18 studies) followed by periodontitis as a risk for Alzheimer's disease or other dementias (16 studies), and tooth loss as a risk for cognitive impairment or decline (15 studies). All but 10 studies of oral conditions as risk exposure of mental disorder found a positive association. Fig. 4 shows a Sankey diagram of these associations across the reviewed articles.

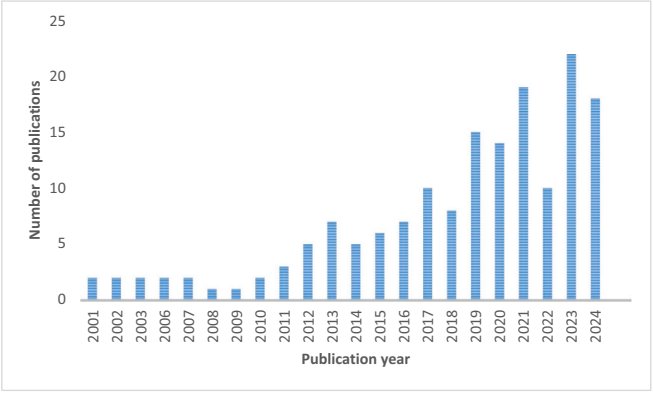

Fig. 2. Number of annual publications included in the current review showing the publication trend in longitudinal associations between mental and oral disorders during 2001–2024.

Several studies documented positive mental health effects of preventing or treating adverse oral conditions. Sustained natural dentition was associated with better cognitive function (Matsuyama, 2023) and denture use was associated with slower rate of cognitive decline. (Qi et al., 2024; Nakazawa et al., 2024) While periodontal emergencies increased the odds of dementia, periodontitis treatment was associated with reduced risk. (Chen et al., 2023; Lin et al., 2020) Trigeminal neuralgia and facial paralysis treatment were associated with reduced risk of depression, (Fan et al., 2021) anxiety and hopelessness. (Arslan et al., 2018) Several studies reported a dose-response relationship between tooth loss and rate of cognitive decline or incident dementia or depression severity. (He et al., 2023; Cho and Shin, 2022; Dintica et al., 2018; Xu et al., 2021; Bof de Andrade et al., 2021) Finally, exposure to oral conditions (eg., Temporomandibular disorder and periodontitis) were found to worsen mental outcomes including depression, anxiety and Alzheimer's disease. (Ide et al., 2016; Asquini et al., 2021)

Nonetheless, some studies have reported no association, a loss of statistical significance after adjusting for confounders, or more nuanced relationships, such as those that are specific to gender. An unexpected result of reduced 10-year dementia risk for patients with herpes labialis was reported, (Zilli et al., 2021) raising speculation of potentially preventative effects of antiviral treatment. Unlike other studies of associations between tooth loss and dementia, Hansson et al. (2014) upon 20-year follow-up did not find such an association in either sex. (Hansson et al., 2014) Similarly, Holmer et al. (2022) reported no association between periodontitis and incident dementia. (Holmer et al., 2022) Finally, the Taiwan national health insurance research database found among individuals with cleft lip/palate a higher risk of autism spectrum disorder, attention deficit hyperactivity disorder and schizophrenia without significant risk for bipolar disorder or major depression. (Huang et al., 2024)

3.3. Mental disorders as risk factors for oral conditions

Studies showing mental disorders as risk factors for oral conditions are presented in Table 2. Of the 42 studies examining associations of 17 mental disorders leading to 14 different oral conditions, the most frequent mental disorders were depression (10 studies), dementia (6 studies), sleep disorder (5 studies) and ADHD (3 studies). The most common outcomes evaluated were Temporomandibular disorders (10 studies), periodontitis (8 studies), caries (7 studies) and tooth loss (4 studies). The most frequent association was reported for depression as a risk for temporomandibular disorders (5 studies). All but 4 studies of mental disorder as risk factor for oral conditions found a positive association. Fig. 5 shows a Sankey diagram of these associations across the reviewed articles.

Few studies that reported the lack of associations involved the examined relationship between dental anxiety and dental caries in adolescence (Wong et al., 2020), depression/sleeping difficulties and TMD in adolescents, (Liljestrom et al., 2008) and dementia and tooth loss in older adults. (Chen et al., 2010) Finally, (Lee et al., 2023) found that depression and anxiety, but not bipolar disorder were separately associated with burning mouth syndrome events.

3.4. Bidirectional associations between oral conditions and mental disorders

Five studies have examined the bidirectional longitudinal associations between oral conditions and mental disorders (Table 3). These studies examined associations between tooth loss, Bell's palsy and TMD, and mental disorders including depression, anxiety, or eating disorder and cognitive impairment. Studies showed reciprocal relationships between oral health parameters and cognitive function. Depressive and anxiety disorders were linked bidirectionally with temporomandibular disorders and eating disorders. Additionally, a history of Bell's palsy increased the risk of depression and anxiety, with anxiety also increasing

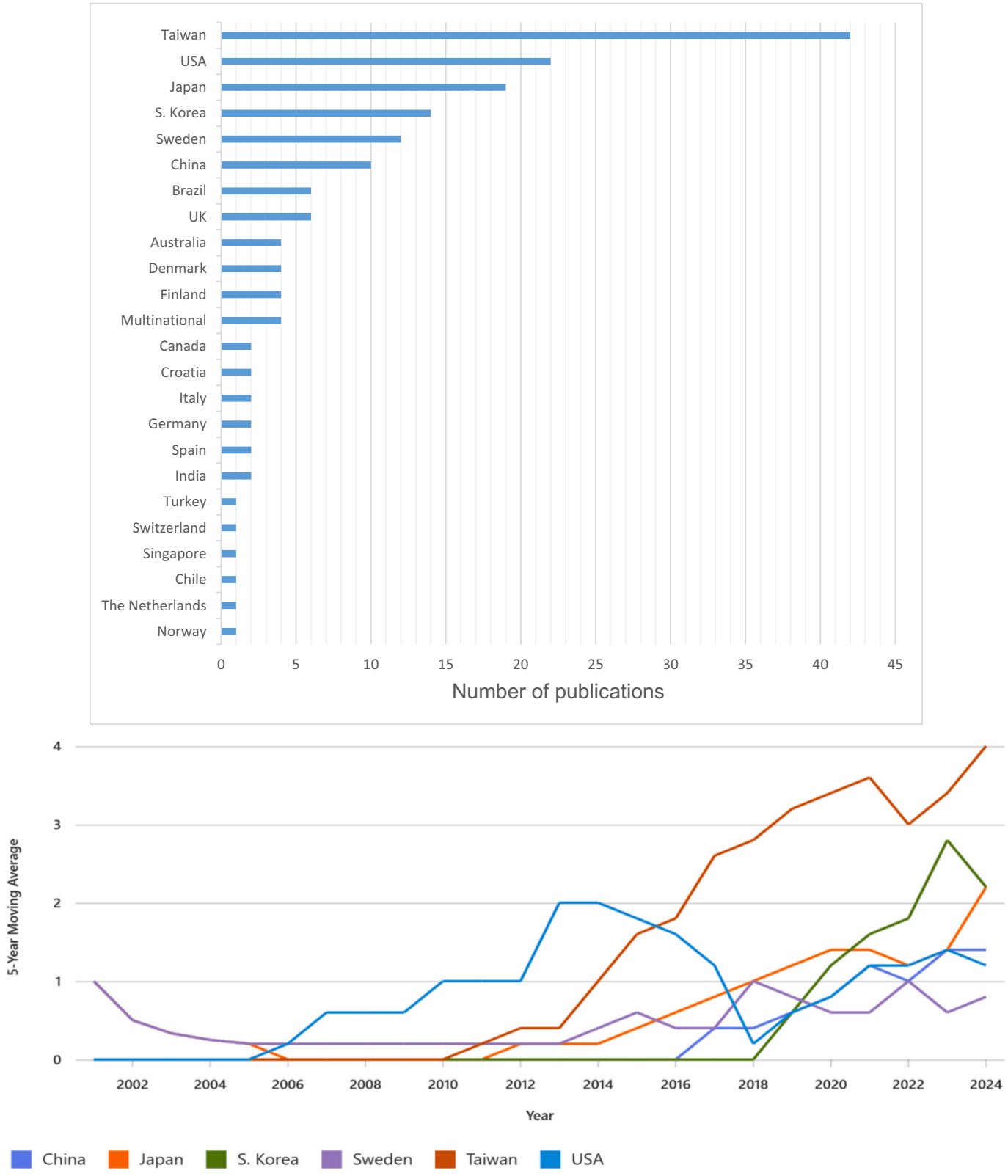

Fig. 3. A. Number of publications per country or territory included in the current review.
B. Five-year moving average number of publications for the most productive countries showing publication trend over the period 2001–2024.

Table 1
Study characteristics and prospective findings in longitudinal studies of oral conditions as predictors of mental disorders.

Study	Country/ territory	Study design	Sampling/setting	Sample size (Total) [a]; Women %	Sample age at baseline mean (SD)	Oral condition (exposure)	Mental disorder (Outcome)	Follow-up duration; mean (SD)	Main prospective finding in plain language
Jeong 2023	S. Korea	Retrospective cohort	Korea National Insurance Claims dataset	Bell's palsy cohort: 1210; 46.9% Ramsay Hunt cohort: 326; 44.3%	Bell's palsy: majority aged 30–59 years (56.5%). Ramsay Hunt majority aged 30–59 years (61.9%).	Bell's palsy	Depression	Up to 10 years	Both conditions significantly increased the risk of depression and anxiety compared to matched controls.
Lansing 2024	Sweden	Prospective cohort	Hospital Cohort	62; 100%	Cases: 30.5 yr (4.1); Controls: 30.4 yrs. (4.1)	Bell's palsy	Depression (postnatal)	12 months	No group differences in depression score across timepoint
Kim 2020	S. Korea	Retrospective cohort	Nationwide cohort	1086; 61.8%	45y: 701 (39.9%); 45–64y: 667 (37.9%); >64y: 390 (22.2%)	Burning mouth syndrome	Depression	1 to 12 years.	BMS associated with higher depression and anxiety; no association with dementia or Parkinson's.
Bertoldi 2018	Italy	Prospective cohort	Private dental office	40; 72,5%	35.4 years (13.6)	gingivitis or moderate periodontitis	Personality traits and the level of anxiety and depression	18 months	Periodontal disease doesn't causes depression or anxiety, but rather the opposite psychopathology worsens periodontal outcomes.
Gatchel 2006	USA	Prospective cohort	Hospital Cohort	63 (79.4%)	37 years	Temporomandibular disorder (acute TMD pain)	Depression	12 months	There is a high comorbidity between TMD and depression, with about half of the acute TMD patients meeting criteria for current or lifetime depression. However, baseline depression did not significantly affect the 12-month course of TMD pain or masticatory function.
Velly 2011	USA	Prospective cohort	TMJD patients recruited via media ads	570; 88%	35.9 years (12.5)	Temporomandibular muscle and joint disorders	Depression	18 months	Depression and catastrophizing were both associated with higher pain intensity and disability. Depression predicted disability at follow-up, but its effect ononset/ progression of clinically significant TMJD pain disappeared after adjustment for catastrophizing. Catastrophizing remained a strong independent predictor of onset and progression of chronic TMJD pain
Nascimento 2024	Singapore	Prospective cohort	National cohort of community-dwelling older adults (Singapore)	973; 52.1%	69.3 years (6.5)	chewing disorder	Somatoform/ conversion disorders (F44, F45)	Stress/adjustment disorders (F43)	Chewing disability associated with higher risk of cognitive impairment; part mediated by depression

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Table 1 (*continued*)

Study	Country/ territory	Study design	Sampling/setting	Sample size (Total) [a]; Women %	Sample age at baseline mean (SD)	Oral condition (exposure)	Mental disorder (Outcome)	Follow-up duration; mean (SD)	Main prospective finding in plain language
Paganini-Hill 2012	USA	Prospective cohort	Older adults in retirement community	5468; 68.3%	Age 52–105 years, median 81 years	chewing disorder	Substance abuse disorders (F10–F19)	Somatoform/ conversion disorders (F44, F45)	Inadequate natural masticatory function without dentures linked to higher dementia risk in men, not in women
Smith 2014	Australia and Canada	Prospective cohort	Multidisciplinary clinic	33; 54%	2.7 ± 2.1 months	Cleft lip and/or palate (CL/P) with sleep-disordered breathing (SDB)	Abnormal neurocognition	~3 years (36.7 ± 1.4 months)	Infants with CL/P and early SDB had overall normal neurocognition, growth, and QoL at age 3, but scored lower than controls in receptive/expressive language. Higher REM% in infancy predicted better cognition; more obstructive events predicted worse behavior; higher AHI predicted lower weight
Malic 2023	Canada	Retrospective cohort	Ontario province-wide administrative data	2515 (NR)	30 days (at OFC diagnosis)	Cleft Lip and/or Palate	Mixed or multiple psychiatric disorders	Follow-up ≥3y (max 20y)	Children with OFC had higher risk of psychiatric disorders and IDD than controls; cleft palate group highest risk
Christensen 2002	Denmark	Retrospective cohort	Danish Facial Cleft Database & Danish Psychiatric Central Registry	6462; 39.4%	NR	Cleft Lip and/or Palate	Mixed or multiple psychiatric disorders	Follow-up up to 57y; registry data	Facial cleft patients had higher risk of psychiatric hospitalization; strongest for isolated cleft palate; exceptions in neurosis and autism
Pedersen 2016	Denmark	Prospective cohort	Psychiatric hospitals	37,032; 39.3%	Age range 1–76 years	Cleft Lip and/or Palate	Mixed or multiple psychiatric disorders	43 years	Oral cleft patients had higher risk of psychiatric diagnosis than controls
Pedersen 2017	Denmark	Nationwide population-based cohort	Population-based	90,909; 39.4%	Birth cohorts 1936–2009; age at start of follow-up ≥1 year	Cleft Lip and/or Palate	Multiple psychiatric disorders	16 years	Oral cleft patients had higher risk of psychotropic use and psychiatrist visits than controls
Berg 2016	Norway	Prospective cohort	Population-based	1,416,156; 48.5%	0 (birth)	Cleft Lip and/or Palate	Intellectual disability	Follow-up until age 18; oldest 43y (end 2010)	Cleft lip + palate: higher risk of intellectual disability and cerebral palsy. Isolated cleft palate: higher risk of intellectual disability, anxiety, autism, learning disabilities, cerebral palsy, and epilepsy.
Tillman 2018	Sweden	Restrospective Cohort	Population-based	Sample size (Total): 95,888; OFC: 7842; Siblings: 9637; Controls: 78,409; Women %: NR	Age 0–5y (OFC diagnosed at birth or ≤ 5y)	Cleft Lip and/or Palate	Multiple psychiatric disorders	39 y (1973–2012)	Children with OFC had higher risk of psychiatric, intellectual, language, ASD, psychotic, ADHD, behavioral, and personality disorders. CL: higher risk of psychiatric, intellectual, and language disorders. CLP: higher risk of ASD. CPO:

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Table 1 (*continued*)

Study	Country/ territory	Study design	Sampling/setting	Sample size (Total) [a]; Women %	Sample age at baseline mean (SD)	Oral condition (exposure)	Mental disorder (Outcome)	Follow-up duration; mean (SD)	Main prospective finding in plain language
									higher risk for psychotic, ADHD, and behavioral disorder. No increased risk for suicide, affective, anxiety, eating, or substance use disorders.
Huang 2024	Taiwan	Retrospective cohort	Epidemiological; Taiwan National Health Insurance data	12,738; 48.4%	10.5 years (5.2)	Cleft Lip and/or Palate	Multiple psychiatric disorders	Follow-up from diagnosis (2001−2010) to 2011 or death (~1–10 years)	Higher risk of ASD, ADHD, and schizophrenia; no significant risk for bipolar or major depression
Li 2023	China	Prospective cohort	Participants from China Health and Retirement Longitudinal Study	16,501; 51.2%	58.8 years (9.5)	Edentulism	Cognitive impairment/ decline	6 years	Edentulism associated with greater cognitive decline
Matsuyama 2023	Japan	Retrospective cohort	Longitudinal panel study conducted via the Health and Retirement Study (HRS)	10,953, 59.7%	63.4 years (8.1)	Edentulism	Cognitive impairment/ decline	12 years	Maintaining natural teeth for 6y linked to better cognitive function and lower cognitive impairment
Jones 2023	USA	Retrospective cohort	Community-based	22,728; 58.2%	63.4 years (10.1)	Edentulism	Cognitive impairment/ decline	10 years	Edentulism associated with increased cognitive decline, independent of demographics, health, and socioeconomic factors
Luo 2021	USA	Retrospective cohort	Population-based	7805, 58,5%	Age groups: 65–74y (64–78%); 75–84y (19–30%); ≥85y (3–6%)	Edentulism	Cognitive impairment/ decline	6 and 12 years	Older adults with both DM and tooth loss had lowest cognitive scores; effects stronger than DM or tooth loss alone; similar by sex, except DM alone not significant in males
Arslan 2018	Turkey	Prospective cohort	Otolaryngology–Head and Neck Surgery inpatient unit	46	38.2 years (18–60)	Facial paralysis	Depression	1 month	Significant reduction in depression, anxiety, and hopelessness after facial paralysis treatment
Saadi 2019	USA	Retrospective cohort	Data from inpatients and outpatients	NR	Age < 18y and ≥ 18y; no further details provided	Facial paralysis	Depression	Follow-up: 2y after FP diagnosis	New depression within 2y of FP: 6.4% children; 9.7% adults (without prior depression)
Cirkel 2021	United Kingdom	Retrospective cohort	Outpatients	Case: 3223 (49.2%) Controls: 3223 (49.2%)	40.3 years (19.1)	Gingivitis	Depression	10 years	There was a positive and significant association between chronic gingivitis and depression
Kim 2023	S. Korea	Retrospective cohort	National Health Insurance Service database	135,530; 65.4%	~55.6 years (~12.6) in both groups	Hemifacial spasms (HFS)	Sleep disorder	90d before and after index case	The patients with HFS had a significantly higher risk for mental illnesses than control patients.
Kumar 2018	India	Prospective cohort	University hospital	75, 13%	≥18 years	Oral cancer	Depression	3 months	Depression increased from diagnosis to 3 m post-op; anxiety remain stable
Yamato 2023	Japan	Retrospective cohort	Hospital-based administrative claims (inpatients)	76,868; 41.5%	Median age: men 79 years (IQR 72–84); women 81 years (IQR 74–87)	Oral cancer	Delirium	Up to 1 year	Older age increased delirium risk in men and women; oropharyngeal cancer patients had higher

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Table 1 (*continued*)

Study	Country/ territory	Study design	Sampling/setting	Sample size (Total) [a]; Women %	Sample age at baseline mean (SD)	Oral condition (exposure)	Mental disorder (Outcome)	Follow-up duration; mean (SD)	Main prospective finding in plain language
									delirium risk than gastric cancer
Chang 2014	Taiwan	Prospective cohort	Population-based databases	2178, NR	Age ≥ 50 years	Oral cancer	Depression	5 years	Depression within 5y: 3.6% oral cavity cancer vs 1.5% controls; significantly higher risk; no gender difference
Kung 2021	Taiwan	Retrospective cohort	Population-based	21,217 (Oral cancer: 3031; Other cancer: 9093; Non-cancer: 9093); 12.04% in all 3 groups	~53.6 years (~13) in both groups	Oral cancer	Depression	13 years	Depression within 13y: 2.3% oral cancer vs 1.7% controls; significantly higher risk (oral cancer, especially tongue cancer).
Penn 2021	Taiwan	Retrospective matched-cohort	Population-based study	2970; 28.79% in both groups	~59.9 years (~5.8); in cses and controls	Oral cancer	Dementia	15 years	NPC patients had significantly higher risk of developing dementia vs controls
Speksnijder 2021	The Netherlands	Prospective cohort	Multi-centre cohort	141, 44.6%	65.6 years (12.8)	Oral cancer	Depression	5 years	Emotion-oriented coping style was strongest risk factor for depression at 5y; same association seen in controls
Humphris 2003	United Kingdom	Prospective cohort (Sample 1) + cross-sectional with follow-up (Sample 2)	Orofacial cancer out-patients	Sample 1: 87, 29%; Sample 2: 100, 32%	Mean ~ 58.3 years (SD 11.3)	Orofacial cancer (post-treatment)	Anxiety and depression	Sample 1: 7 months; Sample 2: ~2 years after baseline (mean 2.05 years, SD 1.99)	>80% reported fear of recurrence at 3 months, decreasing slightly to 72% at 7 months. At 2-year follow-up, ~64% remained concerned. Anxiety "caseness" was 37% at 3 months and 31% at 7 months; depression "caseness" was 28% and 23%. Fear of recurrence was consistently associated with anxiety but less strongly with depression.
Zilli 2021	USA	Prospective cohort	Community-based	6468; 55.7%	61–68 years (6–9 years)	Oral herpes	Dementia	10 years; up to 35 years	No association between infection serologies and dementia, brain volume, or WMH. Herpes labialis linked to lower 10 years dementia risk; *H. pylori* antibodies linked to worse cognition
Costa 2020	Brazil	Prospective cohort	Private dental clinic	124; 51.6%	Age ≤ 50 years: 51 (41.1%); >50 years: 73 (58.9%)	Periodontitis	Depression	6 years	Periodontitis recurrence was significantly higher in depresive group
Ehrenthal 2016	Germany	Prospective cohort	University Hospital	310; 62%	61.2 years (10.5)	Periodontitis	Depression	13 years	In periodontitis patients, fewer teeth predicted higher depression 13y later; significant in men only, independent of covariates
Bumb 2021	India	Prospective cohort	Dental outpatients attending routine checkups	140; 69.3%	72.5 years (4.3)	Periodontitis	Cognitive impairment/ decline	5 year	Poor oral hygiene and severe periodontal disease associated with higher risk

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Table 1 (*continued*)

Study	Country/ territory	Study design	Sampling/setting	Sample size (Total) [a]; Women %	Sample age at baseline mean (SD)	Oral condition (exposure)	Mental disorder (Outcome)	Follow-up duration; mean (SD)	Main prospective finding in plain language
									of cognitive impairment; associations remained after adjustment for multiple confounders
Iwasaki 2016	Japan	Prospective cohort	Community sample	55	79,3 years (3.7)	Periodontitis	Cognitive impairment/ decline	3 years	Severe periodontitis significantly associated with higher risk of cognitive decline and greater MMSE score decrease
Iwasaki 2019	Japan	Prospective cohort	5y longitudinal study supplemented with TLAS data	179, 65%	80.1 years (SD 4.4)	Periodontitis	Cognitive impairment/ decline	5 years	Severe periodontitis was significantly associated with MCI; periodontal inflammation also linked to higher MCI risk
Mameno 2024	Japan	Prospective cohort	Multisite (urban/rural) commnity dwelling adults ≥70 years	293 (52.9%)	Median = 70 years	Periodontitis	Cognitive impairment/ decline	9 years	Number of teeth was negatively associated with cognitive function.
Yoo 2023	S. Korea	Retrospective cohort	Health Insurance claims dataset	2,555,618; 35.5%	55.7 years (10.9)	Periodontitis	Dementia	9.2 years	Periodontal disease, caries, and tooth loss associated with higher risk of all-cause dementia
Kulkarni 2023	Multi-national (30+ countries)	Case-control	Outpatient	Normal oral health: 16,675,337 (53.1%); Poor oral health: 671,281 (54.5%)	72–74 years	Mixed or multiple oral conditions	Alzheimer's disease	5 years	Poor oral health linked to 2-fold higher AD risk; tooth-loss–related diseases strongest risk factor
Kim 2022	S. Korea	Retrospective cohort	National Health Insurance Service database	17,248 (65.9%)	70.9 years (4.8)	Periodontitis	Dementia	6.6 years (median)	Severe vs mild periodontitis linked to higher dementia risk, especially in men >70y
Choi 2019	S. Korea	Retrospective cohort	National Health Insurance Service-Health Screening Cohort	46,344 (43.2%)	Cases: 60.2 (SD = 7.3)	Periodontitis	Alzheimer's disease	11 years	Chronic periodontitis patients had elevated risk for overall dementia and Alzheimer's disease, and tendency toward increased vascular dementia risk.
Kim 2020	S. Korea	Retrospective cohort	Clinical epidemiological	20,230 (28.5%)	Range:40–79 years	Periodontitis	Alzheimer's disease	14 years	The risks of AD were significantly higher in patients with severe periodontitis with 1–9 remaining teeth.
Carballo 2023	Spain	Prospective cohort	Primary care centres; ≥60 years with periodontitis history	101 (NR)	71.6 years (mean)	Periodontitis	Cognitive impairment/ decline	2 years	Periodontitis was associated with poor cognitive performance and quicker progression of cognitive impairment.
Holmer 2022	Sweden	Retrospective cohort	Epidemiological linkage og dental and dementia registries	37,174 (43,8)	median 61 (52–68)	Periodontitis	Dementia	7.6 years (SD1.1)	No association between deep probing pocket depths (as a proxy for periodontitis and the incidence of dementia.

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Table 1 (*continued*)

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Nilsson 2018	Sweden	Retrospective cohort	Epidemiological; Swedish National Study on Ageing and Care	704 (56.4%)	range: 60–96 years	Periodontitis	Cognitive impairment/ decline	6 years	There was an association between prevalence of periodontitis and cognitive decline after adjustments of confounding factors of importance.
Chen 2017	Taiwan	Retrospective cohort	National Health Insurance Research Database. ≥ 50 years	27,963 (46.9%)	54.1 years (SD = 10.5)	Periodontitis	Alzheimer's disease	12 ± 2.6 yrs	Patients with 10-year chronic periodontitis exposure exhibit an increased risk of developing Alzheimer's disease.
Chen 2023	Taiwan	Case-control	Taiwan National Health Insurance Research Database	9889 (52.2%) cases and equal controls	range: 40–90+ years	Periodontitis	Dementia	3 years	Regular dental treatment for periodontitis was associated with a lower risk of dementia.
Hsu 2015	Taiwan	Retrospective cohort	Database; Patients with newly diagnosed periodontitis	Periodontitis: 12708 (48.5%) Control: 50,832 (48.5%)	Periodontitis: 43.91 (13.65) Control: 43.84 (13.89)	Periodontitis	Depression	6 to 11 years	Periodontitis was an independent risk factor for depression.
Huang 2020	Taiwan	Prospective cohort	Database	Chronic periodontitis: 32,528 (52.8) Control: 65,343 (53%)	44.8 years (14.7) (both groups)	Periodontitis	Bipolar disorder	Chronic periodontitis: 7.45 years Control: 7.36 years	Chronic periodontitis associated with increased risk of bipolar disorder after adjusting for sex, age, monthly income, urbanization, and co-morbidities.
Keller 2012	Taiwan	Case-control	Clinical epidemiological	197,136 (32,856 ED patients and 164,280 controls; (0%)	cases: 49.3 (SD 12.5) years Controls: 49.2 years (mean only)	Periodontitis	Erectile dysfunction	Prior history; duration not defined.	Higher odds of erectile dysfunction in patients with chronic periodontitis.
Lee 2017	Taiwan	Prospective cohort	National Health Insurance Research Database in Taiwan	Control: 3028 (45.8%) Periodontitis: 3028 (45.8%)	Control: 72.4 years Periodontitis: 72.4 years	Periodontitis	Dementia	Up to 13 years	After adjustment for sociodemographic characteristics and comorbidities, there was a modest increase in the risk of dementia in participants with periodontitis.
Lee 2017	Taiwan	Retrospective cohort	Taiwan National Health Insurance Research Database	182,747 (50.5%)	45–64: 139,416 65–74: 32,069 ≥ 75: 11,262	Periodontitis	Dementia	10 years	Subjects who had teeth extracted (proxy for periodontitis) and those who underwent no treatment had a significantly higher risk of dementia than those who received dental prophylaxis.
Lee 2020	Taiwan	Retrospective cohort	National registry	Control: 56,018 (51.6%) Periodontitis: 56,018 (51.6%)	≥50 years (mean NR)	Periodontitis	Dementia	8 years (average)	Periodontitis was associated with increased dementia risk
Tzeng 2016	Taiwan	Case-control	National Health Insurance Research Database; newly diagnosed periodontitis cases	8828 (38.6%)	20 years and above. 20–29 years = 1208 (13.68%), 30–39 years = 2128 (24.11%), 40–49	Periodontitis	Dementia	10 years	Patients with chronic periodontitis and gingivitis have a higher risk of developing dementia after

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					years = 2344 (26.55%), 50–59 years = 1728 (19.57%), 60–69 years = 784 (8.88%), ≥70 years = 636 (7.20%).				adjusting for potential confounders.
Chang 2020	Taiwan	Retrospective cohort	Ambulatory and inpatient claims datasets, newly diagnosed periodontitis	61,685 (48.7%)	20 yrs. or above; mean age for periodontitis group 44.0 ± 13.7 years, non-periodontitis group 43.9 ± 13.9	Periodontitis	Bipolar disorder	8.8 years (average)	Bipolar disorder risk was elevated in the periodontitis group than in the non-periodontitis group after adjustment for sex, age, and comorbidities.
Ide 2016	UK	Prospective cohort	Community-dwelling participants	59 (49.2%)	77.7 (8.6) years	Periodontitis	Alzheimer's disease	6 month	Exposure of periodontitis resulted in more severe dementia after 6 months.
Wang 2024	UK	Prospective cohort	General population	264,706 (52.45%)	55.35 (SD = 8.04) years range: 37–73 years	Periodontitis	Depression	median follow-up of 9.03 years	Periodontal disease was found to be consistently associated with an increased risk of depression, anxiety and their comorbidity
Demmer 2020	USA	Prospective cohort	General Population	8275 (55%)	63 (SD = 6) years	Periodontitis	Dementia	18.4 years (median)	In adjusted model, the risk of incident dementia was elevated on patients with severe periodontitis or edentulism.
Beydoun 2020	USA	Retrospective cohort	Nationally representative population aged 45 or above	4465 (range 51.5–58.6 years)	≥ 45 years	Periodontitis	Alzheimer's disease	up to 26 years	Alzheimer's disease incidence was associated with probing pocket depth (PPD), with evidence for an association between periodontal pathogens and AD, particularly for older adults.
Stein 2012	USA	Prospective cohort	Biologically Resilient Adults in NeurologicalStudies research program	158 (58,4% for control; 47.5%) for MCI; 74.3% for AD)	70.0 (6.5) for control, 72.1 (6.1) for MCI	Periodontitis	Alzheimer's disease	12,5 years	Antibody levels to periodontal bacteria associated with increased AD risk.
Lin 2020	Taiwan	Retrospective cohort	Register data (general population)	1,04,5570; dementia (55,6%); controls 465,480 (55,6%)	dementia =77.2 years (SD = 8.2), controls = 76.9 years (SD = 8.2%)	Periodontitis	Alzheimer's disease	10 years	Having two or more root canal treatment, or extraction reduced the odds of dementia; but two or more periodontal emergencies increased the odds of dementia.
Chen 2019	Taiwan	Retrospective cohort	Population-based registries	Cases: 4063 (73.4%) Control: 4063 (74.6%)	Cases: 63.7 years (9.4) Control: 63.6 years (9.3)	Sjogren's syndrome	Dementia	12 years	After adjustment for comorbidities, including Parkinson's disease, insomnia, and hypertension, there was a positive association between SS and dementia.

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Study	Country/ territory	Study design	Sampling/setting	Sample size (Total) [a]; Women %	Sample age at baseline mean (SD)	Oral condition (exposure)	Mental disorder (Outcome)	Follow-up duration; mean (SD)	Main prospective finding in plain language
Hou 2019	Taiwan	Retrospective cohort	National Database	Cases:17,072 (89.74%) Controls: 68,270 (89.56%)	Cases 54.20 (14.25) years Control: 54.02 (14.02) years	Sjogren's syndrome	Dementia	cases: 1897 days (1456 days) Control: 1855 days (1408 days)	When adjusted for age groups, gender, and comorbidities, the risk of developing dementia was higher in the cases than the controls.
Hsieh 2019	Taiwan	Retrospective cohort	Population-based Database	pSS cohort: 688 (88.7) non-pSS cohort: 3440 (88.7)	cases: 53 (13.6) years controls: 53.2 (13.6) years	Sjogren's syndrome	Depression	4 years	Patients (females but not males) with primary Sjogren's syndrome (pSS) showed a significantly higher risk of developing depressive disorder compared with the non-pSS comparison cohort. In males, pSS associated with anxiety disorders.
Ju 2019	Taiwan	Retrospective cohort	Epidemiological; Taiwan National Health Insurance data	63,200 (89.1%)	cases: 53.4 (SD 14.2) years; controls: 53.8 (SD 13.9) years	Sjogren's syndrome	Parkinson's disease	5.2 years (3.2) up to 11 years	Increased incidence of Parkinson's disease in patients with Sjogren's syndrome.
Liliang 2018	Taiwan	Retrospective cohort	Population-based data from health insurance database	86.5% for primary SS cohort, and 86.5% for non-SS cohort	SS: <36 years = 403 (9.03%), 36–50 years = 1402 (31.4%), 51–65 years = 1599 (35.8%), and > 65 years = 1059 (23.7%). non-SS cohort: <36 years =2015 (9.03%), 36–50 years = 7010 (31.4%), 51–65 years = 7995 (35.8%), and > 65 years = 5295 (23.7%).	Sjogren's syndrome	Alzheimer's disease	10 years follow-up	After adjusting for covariates, the risk of AD was higher in participants with primary SS
Shen 2015	Taiwan	Retrospective cohort	Population-based study	cases: 2686; (71.7%); controls: 10,744 (71.7%)	The median age of the patients with pSS was 45.31 years [interquartile range (IQR) 32.99–57.98]; for controls: 45.26 (32.93–57.99)	Sjogren's syndrome	Depression	up to 10 years, with median follow-up period of 4.70 years (IQR 2.93–7.17).	Patients with pSS had a higher risk for subsequent depressive disorder, anxiety disorder, and sleep disorder compared with controls.
Asquini 2021	Italy	Prospective cohort	Clinical; dental hospital	40; acute/ subacute TMD (88%females) and chronic TMD (94% females).	acute/subacute (median = 29 years); chronic TMD (median = 28 years)	TMD	Mixed or multiple psychiatric disorders		Chronic TMD was associated with worsened depression and anxiety.
Chang 2024	USA	Retrospective cohort	Epidemiological; Chronic tonsillitis patients undergoing tonisllectomy	29,748 (67.3%)	24.0 years (SD = 10.8)	Tonsillitis	Depression	5 year	Tonsillectomy was associated with increased depression risk versus matched controls.
Batty 2013	20 countries from Australasia, Asia, Europe	Prospective cohort	Clinical; diabetic outpatients	11,140 (42.5%)	66 years (SD 6–7; range 55–88) years	Tooth loss	Dementia	5 years	Relative to the group with the greatest number of teeth (≥ 22), having no teeth was associated with the highest

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	and North America								risk of both dementia and cognitive decline. Number of days of bleeding gums was unrelated to dementia or cognitive decline.
Bof de Andrade 2021	Brazil	Prospective cohort	Epidemiological; representative sample of individuals aged ≥60 years	1265 (62.3%)	≥ 60 years	Tooth loss	Cognitive impairment/ decline	Up to 10 years	Participants with 1–19 teeth and no teeth had lower MMSE scores than those with≥20 teeth. Denture wearers had greater MMSE score than non-denture wearers.
Cademartori 2021	Brazil	Prospective cohort	Community dwelling pregnant women	2470 (100%)	up to 46 years	Tooth loss	Depression	≥4 weeks	Positive association between dental caries and depression
Kunrath 2021	Brazil	Prospective cohort	General population; age ≥ 60 years	163 (73.8%) at follow-up	60–69 years: 57.3%, 70–79 years: 31.7%, ≥80 years or older: 11.0%	Tooth loss	Depression	6 years	Older adults who experienced tooth loss between and those with a sensation of dry mouth were at a higher risk of having depressive symptoms.
Ortuno 2023	Chile	Prospective cohort	Epidemiological; rural agricultural region of Maule, Chile	3335 (2 years follow up);2461 (4 years follow up); female % NR	53.5 years (SD 9.8) range: 38 to 74 years	Tooth loss	Depression	up to 4 years	Individuals with fewer than 20 teeth had higher odds of incident depression at both 2- and 4-year follow-ups. Specifically, edentulous individuals had significantly higher odds of depression, with greater severity noted in women.
He 2023	China	Prospective cohort	General population	Dementia: 1464 (59.4%) Control: 12,975 (48.9%)	≥30 years (mean NR)	Tooth loss	Dementia	40 years	There is a dose-response relationship between tooth loss and dementia risk, with hazard ratios increasing as the number of lost teeth rises. No significant associations were found between dental plaque status or oral mucosal lesions and the risk of dementia
Li 2017	China	Prospective cohort	General population ≥ 60 years	8153 (52.7%)	Older adults aged 60 years and above. Mean age = 83.5 years, SD = 0.1 (unweighted), and mean age = 74.4 years, SD = 0.1 (weighted)	Tooth loss	Cognitive impairment/ decline	13 years follow-up	Fewer teeth were associated with poorer cognitive function regardless of time.
Qi 2024	China	Prospective	Community dwelling adults ≥65 years	27,708 (56.6%)	86.0 (SD = 12.0)	Tooth loss	Cognitive impairment/ decline	mean 4.7 yrs. (range 0–10 yrs)	Compared to non-denture users, dentate participants who used dentures had better baseline cognitive function and a slower annual decline in cognitive function. For

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									edentulous participants, denture use was associated with higher baseline cognitive function but not with the rate of cognitive decline. Consistent across subgroups of dentate participants with various degrees of missing teeth.
Xu 2021	China	Prospective cohort	General population based cohort	11,862 (49%)	81.41 years (10.5)	Tooth loss	Cognitive impairment/ decline	median follow-up time of 5.93 (interquartile range:3.67–9.62) years)	Higher tooth loss rate was associated with an increased risk of cognitive impairment in elderly participants.
Yang 2022	China	Prospective cohort	Community sample aged ≥65 years	17,079 (52.7%)	Median age 83 years, interquartile range 74–90 year	Tooth loss	Cognitive impairment/ decline	The median follow-up time was 9.1 years and up to 17 years in total (interquartile range 3.8–13.3 years; 88,627 person-years)	compared with participants with 20+ teeth, those with 10–19, 1–9, and 0 teeth had increased risks of incident cognitive impairment (p-trend <0.001). Participants without dentures also had a higher risk of incident cognitive impairment, compared with those who wore dentures.
Jelavic 2022	Croatia	Prospective cohort	Clinical; Psychiatric Hospital units	43 (79%)	Median 50 years (41–56)	Periodontitis	Depression	3 months after treamtment with SSRI	Baseline periodontal status had a nonlinear significant and clinically relevant association with the MDD treatment outcome. In patients with good baseline periodontal status the severity of MDD symptoms was significantly improved.
Asher 2023	Finland	Prospective cohort	Epidemiological; aged ≥30 years	3426 (55.2%)	48.38 years (11.43)	Tooth loss	Dementia	11 year	Tooth loss (<20) was associated with lower baseline overall cognition, 11-year cognitive decline and higher 15-year dementia risk after adjusting for multiple confounders. After adjustment for dentures, associations became non-significant, except for 10–19 teeth remaining and dementia.
Asher 2025	Finland	Other: Prospective Cohort	Clinical; mulit-site dental treatment units; aged ≥30 years	4073 (NR)	NR	Tooth loss	Dementia	15 year	Posterior tooth loss was associated with increased risk of dementia.
Kiuchi 2022	Japan	Prospective cohort	General population	35,744 (54%)	73.1 (SD = 5.5)	Tooth loss	Dementia	6 years	There was a significant effect of the number of teeth on the onset of dementia.

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Komiyama 2020	Japan	Prospective cohort	Community-sample aged ≥70 years	838 (≥20 teeth: 50.6% 0–19 teeth: 51.9%)	≥20 teeth: 74. 2 years (3.6) 0–19 teeth: 74.3 years (3.3)	Tooth loss	Disability (functional)	8.2 years (mean); up to 13 years.	Participants with 0–19 teeth were more likely to develop functional disability than those with 20 or more teeth.
Kusama 2021	Japan	Prospective cohort	Epidemiological; Community-dwelling older adults aged ≥65 years	8875 (52.0%)	72.7 years (5.5)	Tooth loss	Depression	3 years	Fewer remaining teeth (≤19) was positively associated with depressive symptoms.
Kusama 2024	Japan	Prospective cohort	Epidemiological; Japan Gerontological Evaluation Study; adults aged ≥65 year	37,556 (53.2%)	72.8 years (5.5)	Tooth loss	Dementia	9 years	Having ≤19 remaining teeth, edentulism, chewing difficulty, and xerostomia were significantly associated with an increased risk of dementia onset, when adjusted for potential confounders.
Miyano 2024	Japan	Retrospective	Epidemiological; Community-dwelling adults aged ≥65 years	22,687 (59.9%)	73.6 years (5.9)	Tooth loss	Alzheimer's disease	12.2 months (mean)	Reduced occlusal contact and tooth loss were associated a higher frequency of developing AD in older Japanese people.
Nakazawa 2024	Japan	Prospective	Epidemiological; functionally independent older adults aged ≥65 years	50,169 (50.3%)	72.8 years (5.4)	Tooth loss	Depression	up to 3.25 years	Compared to those who had ≥20 teeth, the risk of depressive symptom onset was highest among those who had 0–9 teeth without dental prostheses, adjusting for confounders. However, this risk was lower in those with 0–9 teeth and dental prostheses.
Okamoto 2015	Japan	Prospective cohort	Epidemiological; Community-dwelling older adults aged ≥65 yr	2335 (female sample ranges from 45.1% to 51.8% for age categories	71.0 years (median)	Tooth loss	Mild memory impairment	5 years	There was an association between per 1 tooth loss at baseline, and the development of MMI during follow-up.
Saito 2018	Japan	Prospective cohort	Epidemiological; Community-dwelling older adults aged ≥65 years	140 (69.3%)	70.9 years (4.3 years)	Tooth loss	Cognitive impairment/ decline	4 years	Participants with fewer teeth (0–9 teeth) had a higher likelihood of developing cognitive impairment than those with more teeth (≥10 teeth).
Shimazaki 2001	Japan	Prospective cohort	Clinical epidemiological; Institutionalised older adults	719 (76.5%)	79.7 (7.5) years, range: 59–107	Tooth loss	Cognitive impairment/ decline	6 years	Mental impairment was associated with edentulism, not using dentures and having fewer teeth without dentures compared with those with 20 or more teeth was but they were not statistically significant.
Takeuchi 2017	Japan	Prospective cohort	Epidemiological; Community-dwelling adults ≥60 years	1566 (55.9%)	≥60 years	Tooth loss	Dementia	median follow-up 5.3 years	The multivariable-adjusted hazard of all-cause dementia was higher in subjects with

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									fewer or no teeth than in those with 20 teeth or more.
Yamamoto 2012	Japan	Prospective cohort	General Population; Community-dwelling individuals ≥65 years	4425 (51.2%)	N: 65–69: 1576 70–74: 1314 75–79: 950 80–84: 394 more than 85: 191	Tooth loss	Dementia	16,656 person-years. Up to 4 yrs	Dementia onset was associated with fewer teeth and not using dentures and chewing difficuilty.
Yamamoto 2017	Japan	Prospective cohort	Community-dwelling individuals aged ≥65 yr	7656 (50.6%)	≥65 years	Tooth loss	Depression	up to 4 years	Having no teeth, fewer teeth or other oral health problems predict an increase in risk of depressive symptoms after adjusting for possible confounders.
Woo 2020	S. Korea	Prospective cohort	General population; nationwide population-based cohort	153,165 (35.7%)	52.8 years (8.3)	Tooth loss	Parkinson's disease	median duration of 10.4 (interquartile range 9.5–11.7) yrs	The number of tooth loss (≥15) was positively related to new-onset Parkinson's disease development after adjusting variables.
Yoo 2019	S. Korea	Retrospective cohort	General population	209,806 (66.5%)	67.5 years	Tooth loss	Dementia	10 years	Individuals with tooth loss had a higher risk for dementia than those without tooth loss.
Cho 2022	S. Korea	Retrospective cohort	National Health Insurance Service users; individuals over 60 years of age	16,518 (68.9%)	∿78 years (SD 6)	Tooth loss	Cognitive impairment/ decline	unclear, calculated effect sizes are per year.	A unit increase in tooth loss was associated with approximately 1.7 point decrease in cognitive function per year. The association was independent of confounders.
Dintica 2018	Sweden	Prospective cohort	Epidemiological; random sample aged 60 years living at home or in institutions	2715 (62.8%)	range: 70.9–84.3 years	Tooth loss	Cognitive impairment/ decline	9 years	Tooth loss was significantly associated with a steeper cognitive decline and remained significant after adjusting for or stratifying by potential confounders.
Gatz 2006	Sweden	Nationwide twin cohort (case–control and co-twin control)	Swedish Twin Registry	Case-control: 310 dementia cases, 3063 controls; Co-twin: 106 discordant MZ pairs. ~72% women in case-control sample	35 years (cohort 1) and 15–47 years (cohort 2)	Tooth loss	Dementia	Cohort 1: 35y follow-up; Cohort 2: 25y	Case-control findings: Tooth loss <35y and low education are significant Alzheimer's disease risk factors; short height also linked to total dementia. Co-twin: Only tooth loss <35y remained Alzheimer's disease risk factor; low education linked to total dementia; lack of exercise to non-AD dementias.
Hansson 2014	Sweden	Retrospective cohort	Population-based	2075; 55.8%	71.2 years (8.2)	Tooth loss	Dementia	20 years	No significant association between dental status (natural teeth/dentures) and outcomes; same for men and women

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Table 1 (*continued*)

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He 2023	Sweden	Prospective cohort	Population-based	59.4% (dementia); 48.9% (no dementia)	Age ≥ 15y	Tooth loss	Dementia	FUP up to 40y (1973–2012)	Greater tooth loss linked to higher dementia risk, with evidence of dose–response; association stronger for dementia onset before 80y
Stewart 2015	Sweden	Prospective cohort	Population-based study of women	Women only; 1417 with tooth count data (1968–69); follow-up 2000–2005: 158 dementia, 539 non-dementia	Age ≥ 70y	Tooth loss	Dementia	37 years	<9 teeth linked to higher dementia risk in 1968 and 1980 cohorts; after adjustment, association remained significant only in 1980
Chen 2024	Taiwan	Prospective Cohort	University Hospital	516; 53.3%	72.6 years (5.3)	Tooth loss	Dementia	6 years	Dental caries and incomplete dentition (<28 teeth) associated with poorer memory, attention, and verbal fluency, especially with high IL-6. Tooth wear associated with better memory and executive function, more evident with low IL-6.
Chen 2025	Taiwan	Retrospective cohort	Population-based	1265 (56.3%)	Among ≥20 teeth, denture wearers mean age ~ 71.9y; non-wearers ~73.0y	Tooth loss	Dementia	up to 8 years	≥65 years: those with <20 teeth and no dentures had significantly higher dementia risk compared to peers with ≥20 teeth and dentures (lowest risk group). Having <20 teeth, with or without dentures, was linked to higher dementia incidence overall.
Chou 2024	Taiwan	Prospective cohort	Population-based (aged ≥65 years)	64,520 (48.1%)	72.9 years (6.3).	Tooth loss	Cognitive impairment/ decline	Follow-up: mean 4.6y, up to 7y	Older adults with 10–19, 1–9, and 0 teeth, including natural teeth and dentures, had higher risks of developing cognitive impairment than those with ≥20 teeth. Among those with 10–19 teeth at baseline, an increase of more than 1 level in tooth number during follow-up was associated with a lower risk of developing cognitive impairment compared with those with a stable tooth number.
Kaye 2010	USA	Prospective cohort	Community-dwelling men from the Veterans Affairs Dental Longitudinal Study (US)	597, 0%	Median 45.5 years	Tooth loss	Cognitive impairment/ decline	up to 32 years	Each tooth lost per decade increased risk of low MMSE and spatial copying; risks higher with bone loss,

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Table 1 (*continued*)

Study	Country/ territory	Study design	Sampling/setting	Sample size (Total) [a]; Women %	Sample age at baseline mean (SD)	Oral condition (exposure)	Mental disorder (Outcome)	Follow-up duration; mean (SD)	Main prospective finding in plain language
									pocket depth, and caries; strongest in men >45y
Naorungroj 2015	USA	Prospective cohort	ARIC participants aged 52–75 at Visit 4 (1996–1998), followed to 2004–2006	911; (61,5%)	64,7 years (4,3)	Tooth loss, number of teeth, periodontal disease (BGI index)	Cognitive impairment/ decline	Mean 7.6 years (1.0), median 8 years	Among 911 participants, 13.8% edentulous and 13% with severe periodontitis. Edentulous had lower cognitive scores, but poor oral health not linked to greater cognitive decline over time
Reyes-Ortiz 2013	USA	Prospective cohort	Population-based	3050; 51.8–63.2%	Age ≥ 65y; mean age 71.7–75.2y (SD 6.0–7.2)	Tooth loss	Cognitive impairment/ decline	5 years	Fewer teeth (0−12) associated with greater MMSE decline over 5y vs more teeth (13−32)
Stein 2007	USA	Retrospective cohort	Dental outpatients	144; 100%	84 years	Tooth loss	Dementia	Subset of 101 women followed 12	Having 0–9 teeth increased dementia risk during follow-up and at first cognitive exam compared to those with more teeth
Stewart 2013	USA	Prospective cohort	TheHealth ABC Study	1053; 50.2%	73.5 (2.8)	Tooth loss	Cognitive impairment/ decline	5 years	Worse oral health at Year 2 linked to cognitive impairment at Year 1–3; gingival index and plaque score remained significant after adjustment. Higher gingival index at Year 2 independently predicted cognitive decline at Year 3–5.
Zhang 2023	UK	Prospective cohort	UK Biobank study	425,183, 53.3%	57.0 (8.0)	toothaches, loose teeth, dentures	Dementia	9 years (2.93)	Oral problems such as painful gums, toothaches, and dentures were linked to higher dementia risk. Dentures were also related to faster cognitive decline and smaller brain surface areas, partly explained by brain changes and health behaviors.
Chang 2019	China	Retrospective cohort	General Hospital	61, 55.7% 45, 55.6%	Controls 62.1 (15.4) Trigeminal Neuralgia cases 65.7 (12.2)	Trigeminal Neuralgia	Depression	NR	Depression and anxiety positively associated with TN in adjusted models
Cheng 2017	China	Prospective cohort	General Hospital	128; 54%	47.5 (11.2)	Trigeminal Neuralgia	Depression	3 to 6 month	High prevalence of depression (64.8%) and anxiety (18.8%) in TN vs general population. Female gender, high pain intensity, and ineffective treatment were risk factors for depression/anxiety. MVD associated with significant improvement in depression

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Table 1 (*continued*)

Study	Country/ territory	Study design	Sampling/setting	Sample size (Total) [a]; Women %	Sample age at baseline mean (SD)	Oral condition (exposure)	Mental disorder (Outcome)	Follow-up duration; mean (SD)	Main prospective finding in plain language
									and anxiety symptoms at 6 months.
Fan 2021	China	Retrospective cohort	Hospital of Zhengzhou University	121, 59.5%	62.9 years (10.26)	Trigeminal Neuralgia	Depression	12 months	Post-op BNI-P, HADS, and PSQI scores significantly decreased over time (T1–T5 vs T0)
Cheng 2022	Taiwan	Retrospective cohort	Population-based	Cases: 480. 62.99% Controls: 1920, 62.99%	Cases: 64.0 (9.4) Controls: 64.7 (10.5)	Trigeminal Neuralgia	Dementia	15 year	Dementia incidence higher in TN (11.0%) vs non-TN (6.4%); TN patients had significantly higher dementia risk after adjustment
Wu 2015	Taiwan	Retrospective cohort	National insurance database	16,365; 38.3%	Median (IQR): 45.6 (33.9–54)	Trigeminal Neuralgia	Depression	3.08 years	TN associated with higher risk of depression, anxiety, and sleep disorders; no increased risk for schizophrenia or bipolar disorder
Kiuchi 2024	Japan	Prospective cohort	National epidemiological cohort (JAGES)	44,083; 53.2%	73.7 years (6.0)	Tooth loss	Dementia	Up to 10 years	Fewer teeth (0–19) associated with higher dementia risk vs ≥20 teeth

Notes: a = The sample size and women% apply for follow-up, whenever reported. In order to limit overestimations/inflation, we reported a single outcome measure whenever more than one concrete exposure was reported. It was termed mixed or multiple psychiatric disorders whenever more than one outcomes were reported. All corresponding authors of the articles included in this manuscript have identified their affiliated institutions or organizations, along with the corresponding country or geographic region. The authors of this manuscript remain neutral with regard to any jurisdictional claims.

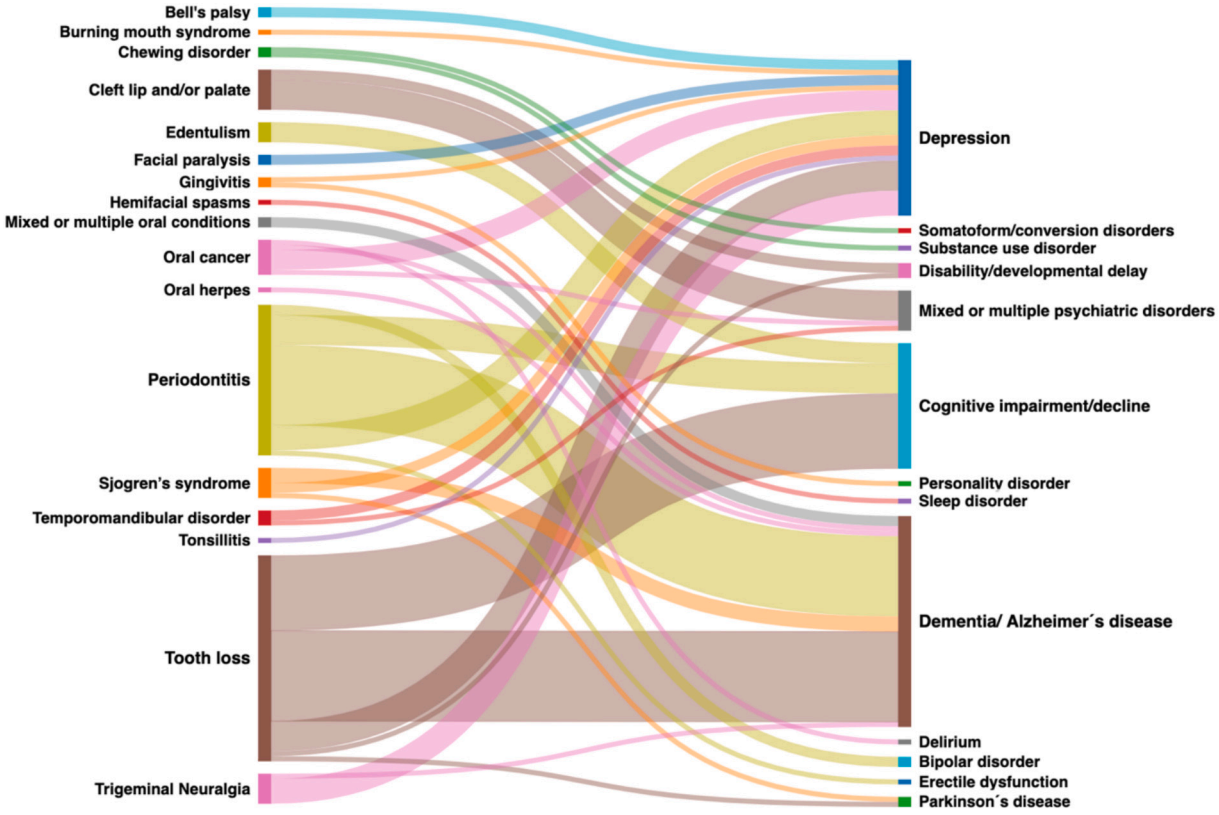

Fig. 4. Sankey diagram illustrating the relative frequency of studies reporting associations between various oral conditions and their potential roles as risk factors for mental disorders. The narrowest lines (for example, Burning mouth syndrome → Depression) represent one study for the association. The illustration reflects investigated associations, but not necessarily associations that are present.

the risk of Bell's palsy. On the contrary, depression did not increase the risk of Bell's palsy. (Lee et al., 2019)

4. Discussion

The present scoping review provides the first comprehensive mapping of the longitudinal associations between disorders of oral and mental health, including cognitive function. We systematically examined the temporal associations across all conditions formally categorized as oral diseases and mental disorders. The identified 165 longitudinal studies demonstrate a rapidly expanding field that also reflects a broader shift toward viewing oral and mental health as intertwined domains rather than separate systems. (Joury et al., 2023) The review included 118 studies reporting mental disorders as possible outcomes of oral conditions (35 independent oral-to-mental disorder sets), 42 studies exploring the reverse direction (32 mental-to-oral disease sets), and only five studies that addressed bidirectional relationships. By systematically mapping both directions, the current review highlights this conceptual gap and emphasizes the urgent need for a new generation of longitudinal and mechanistic studies that can elucidate the reciprocal causality between disorders of oral and mental health.

Expansion of longitudinal studies of oral-mental health associations has been geographically narrow: more than 70% of studies originated from only six countries or regions, and a consistent upward trend in publication activity observed in Taiwan, Japan and South Korea alone. The research productivity was driven by solid nationally representative registries available in these countries. On the contrary, research originating from Africa and most of Latin America remains absent. This geographic imbalance not only limits the generalizability of findings but also highlights an urgent need for studies in diverse sociocultural and healthcare contexts. (Loewenson et al., 2021)

Most of the longitudinal literature points in a single direction—oral health as most likely predictors of mental health outcomes. This is by far the largest and most internally consistent body of evidence. Except for a handful of studies, studies overwhelmingly reported that oral pathology precedes or increases the risk of psychiatric or cognitive outcomes. Such convergence suggests that oral diseases may act as upstream determinants of mental and cognitive health through potential pathways such as psychological, social and other systemic biological mechanisms. (Nakamura et al., 2021) Importantly, our synthesis is the first to quantify this pattern across the full spectrum of oral condition. This review also presented a more nuanced picture, such as lack of association between periodontitis or tooth loss and dementia in several cohorts, (Hansson et al., 2014; Holmer et al., 2022) and apparently preventive effects of antiviral therapy against herpes labialis on dementia risk. (Zilli et al., 2021)

Tooth loss and periodontitis consistently emerged as the most replicated predictors of cognitive decline and dementia, reported in more than thirty independent cohorts. The presence of dose–response relationships identified in several studies where risk rises with greater tooth loss or periodontitis severity - further strengthens causal plausibility. (Xu et al., 2021) Several longitudinal studies also point to reversibility: maintaining natural teeth, (Matsuyama, 2023) receiving regular periodontal treatment, (Chen et al., 2023) and using dental prosthesis (Qi et al., 2024; Nakazawa et al., 2024) were each associated with slower cognitive decline and lower dementia incidence. Together, these findings position oral pathology not merely as a correlate of neurodegeneration but also as a potentially modifiable risk factor and an overlooked entry point for dementia prevention strategies.

The reverse pathway—mental disorders predicting oral disease—has been explored far less but reveals a remarkably consistent pattern. Apart from four exceptions, 42 longitudinal studies showed that psychiatric morbidity was associated with poorer oral health trajectories, most frequently linking depression with temporomandibular disorders, facial

Table 2
Study characteristics and prospective findings in longitudinal studies of mental disorders as predictors of oral conditions.

Study	Country/ territory	Study design	Sampling/setting	Sample size (Total) a; Women %	Sample age at baseline mean (SD)	Mental disorder (exposure)	Oral condition (Outcome)	Follow-up; mean (SD)	Main prospective finding in plain language
Chalmers 2002	Australia	Prospective cohort	Clinical epidemiological	232; 43.1%	78.4% sample were below 79 yrs.	Dementia	Caries	1 year	Dementia positively related to coronal and root caries incidence.
Chalmers 2003	Australia	Prospective cohort	Community sample; Alzheimer's Association caregiver database	216; 43.1%	78.4% sample were below 79 yrs.	Dementia	Mixed or multiple oral conditions	1 to 2 years	Dementia positively associated with oral diseases and conditions (denture- related oral mucosal lesions; plaque accumulation; coronal and root caries; decayed retained tooth roots).
Kisely 2021	Australia	Retrospective cohort	Population-based record-linkage analysisof all contacts with emergency department	1,381,428; 52.4%	43.1 years (21.9)	Substance use disorder (SUD)	Caries	up to 2 years	SUD positively associated with toothache, dental abscesses and caries but not stomatitis or gum disease.
Kisely 2022	Australia	Prospective cohort	General population; birth cohort	2456; 59.8%	0 year	Depression	Dental decay	30 years	Dental extraction was associated with depression and other psychiatric disorders.
Kinalski 2019	Brazil	Prospective cohort	Birth cohort of randomly sampled children	537; 49.4%	22 years	Mixed or multiple psychiatric disorders	Bruxism	9 years	Common mental disorders associated with higher rates of bruxism.
Nascimento 2019	Brazil	Prospective cohort	General population; birth cohort	539; 49.4%	31 years	Depression	Periodontitis	31 years	Depressive symptoms associated with higher risk and more severe periodontitis.
Galera 2023	Canada	Prospective cohort	General population; birth cohort	2120; 49%	1.5 years	ADHD	Caries	$\geq$ 1 year	ADHD during middle childhood associated with dental caries during adolescence.
Caratan 2019	Croatia	Prospective cohort	Psychiatric hospital discharged patients	67; 44.8%	median 47 years (IQR 41 to 53)	Schizophrenia	Periodontitis	up to 6 months	Younger patients with worse periodontal status were at higher risk for poorer schizophrenia treatment outcomes and faster worsening of remission.
Ellefsen 2009	Denmark	Prospective cohort	Patients from hospital memory clinics	77; 63.6%	81.9 years	Dementia	Caries	one year	Higher rates of caries and filling increments for participants with Alzheimer's and other dementia.
Sipila 2013	Finland	case-control	Register based study (Northern Finland Birth Cohort)	5696; 81.3% (cases); 68.6% (controls)	31 years	Depression	Facial pain	3 years	Baseline depression associated positively with chronic facial pain.
Kindler 2012	Germany	Prospective cohort	Sample selected via population registries	3006; 50.4%	49.2 years (15.1); range: 20 to 79	Depression	Temporomandibular disorders	5 years	Depression and anxiety symptoms associated with TMJ symptoms.
Wong 2020	Hong Kong, China	Prospective cohort	School sample	279; 57%	12 years	Anxiety (dental)	Caries	up to 6 years	Dental anxiety at age 12 and 15 was not associated with dental caries three years later.
Ohara 2020	Japan	Prospective cohort	Community cohort	220; 63.6%	range 65–86 years (median = 72)	Eating disorder	Hyposalivation	6 years	Anorexia positively predicted hyposalivation.
Lee 2023	S. Korea	Retrospective cohort	Korea National Insurance Claims dataset.	11,316; 66.4%	Depression group: less than 45 years = 40.1%; 45–64 yrs.: 39.8%; over 64 yrs.: 20.1%	Depression	Burning Mouth Syndrome	10 years	Depression and anxiety but not bipolar disorder were separately associated with

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Table 2 (*continued*)

Study	Country/ territory	Study design	Sampling/setting	Sample size (Total) a; Women %	Sample age at baseline mean (SD)	Mental disorder (exposure)	Oral condition (Outcome)	Follow-up; mean (SD)	Main prospective finding in plain language
									Burning mouth syndrome events.
Heym 2023	Multinational (11 countries)	Retrospective cohort	Clinical medical records from the TriNetX network	309,278; 59.7%	43.4 years (24.5)	Somatoform disorder	Oral cancer	at least 5 years	Patients with somatoform disorders had a higher risk of developing OSCC compared to the control group.
Kim 2023	S. Korea	Prospective cohort	Community	502; groups range: 53.9% - 54.5%	mean 68 to 70 years (range 64 to 75)	Cognitive impairment/ decline	Tooth loss	5+ years	The mild cognitive impairment/dementia group had a fewer remaining teeth and higher rate of complete mandibular denture use
Kim 2021	S. Korea	Retrospective cohort	National Health Insurance Service- (NHIS-HEALS) database	468,882; 58.4%	61.0 years	Sleep disorder	Temporomandibular disorders	8 years	Primary sleep disorder patients had a higher risk for TMD compared with non-sleep disorder.
Tohidinik 2022	Spain	Prospective cohort	Community (58 secondary schools)	9617; 53%	16.2 years (1.46)	Sleep disorder	Stomatitis	29.9 weeks (19.7); up to 1 year	High levels of insomnia, hypersomnia, and sleep-related phenomena were moderately associated with an increased risk of recurrent aphthous ulcers (RAS).
Blomqvist 2011	Sweden	Prospective cohort	Community (School)	87; 24.1%	11 years (approx.)	ADHD	Caries	~6 years	Adolescents with ADHD have higher caries and gingivitis.
Fredricson 2022	Sweden	Case-control	Population based register	366,437; 27.1%	49.15 years (SD = 18.43) for control: Ranges from 39.31 years (SD = 15.96) to 49.96 years (SD) = 18.39 in cases	Mixed or multiple psychiatric disorders	Temporomandibular disorders	up to 53 years	Mental and behavioral disorders (mood, neurotic, stress-related, somatoform, personality disorder, psychological developmental disorder) associated positively with TMD.
Gabre 2001	Sweden	Prospective cohort	Dental clinical sample with intellectually	124; 43.5%	39.26 years (5.39)	Disability (intellectual)	Tooth loss	8.5 years	Persons with mild intellectual disability experienced more caries than other subjects and Down syndrome was associated with higher bone loss compared with other types of intellectual disability.
Jockusch 2021	Switzerland	Retrospective cohort	Nursing home residents	7922; 72.7% (dementia) - 75.0% (no dementia)	subgroups with and without dementia: 80.8 (8.9) - 83.7 (8.6)	Dementia	Edentulism	2 years	Group with severe dementia had larger increase in edentulism, chewing problems and oral complaints over time compared to group with no dementia or moderate dementia.
Chang 2021	Taiwan	Retrospective cohort	Epidemiological; Based on the National Health Insurance Research Database	5034; 50%	Cases: 35.6 years (16.6) Control: 36.1 years (17.0)	Obsessive-Compulsive Disorder	Sjögren's Syndrome	Cases:13,077 person-years Controls: 25,856 person-years	The risk for developing Sjögren's Syndrome is three-fold among patients with obsessive-compulsive disorder after adjusting for age, sex, and comorbidities.
Fann 2024	Taiwan	Retrospective cohort	Epidemiological; Taiwan National Health Insurance data	44,198; 49.13% (no depression);	cases 48.3 years (17.3); control group 45.1 years (16.7)	Depression	Bell's palsy	5 years	Depression associated with higher risk of Bell's palsy.

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Table 2 (*continued*)

Study	Country/ territory	Study design	Sampling/setting	Sample size (Total) a; Women %	Sample age at baseline mean (SD)	Mental disorder (exposure)	Oral condition (Outcome)	Follow-up; mean (SD)	Main prospective finding in plain language
				61.86% (depression)					
Hsu 2024	Taiwan	Prospective	Epidemiological; Taiwan National Health Insurance data	178,321; 19.1%	13.8 years	ADHD	Periodontitis	up to 11 years (2001−2011)	Adolescents with ADHD were more likely to develop periodontitis later in life than controls.
Hsu 2024	Taiwan	Retrospective	National population-level data	26,365; 75.2%	34.08 years (15.16)	PTSD	Sjögren's Syndrome	up to 10 years (2002−2011)	PTSD was associated with a significantly increased risk of Sjögren's syndrome, in a dose (PTSD severity)- dependent manner.
Hu 2019	Taiwan	Retrospective cohort	Epidemiological; Taiwan National Health Insurance data	3610; 47.6%	34.7 years (14.3)	Schizophrenia	Periodontitis	up to 1 year	Newly diagnosed schizophrenia patients had unusually high 1-year incidence of treated periodontal disease.
Lee 2014	Taiwan	Retrospective cohort	Epidemiological; Taiwan National Health Insurance data	127,569; 63.8%	52 years (17.0)	Sleep disorder	Periodontitis	Up to 14 years	Sleep disorder associated positively with severe periodontal disease incidence.
Lee 2014	Taiwan	Retrospective cohort	Epidemiological; Taiwan National Health Insurance data	125,648; sleep disorder (SD): 38%; Non-apnea SD: 64%; Control: 63%"	sleep apnea: 47.6 years(14.2) Non-apnea sleep disorder: 49.8 years (15.6) Control: 50.6 years (15.8)	Sleep disorder	Burning Mouth Syndrome	12 years	Compared with the non-SD cohort, the apnea SD and non-apnea SD were associated with a higher risk of burning mouth syndrome.
Liao 2011	Taiwan	Retrospective cohort	Epidemiological; Taiwan National Health Insurance data.	37,682; "Control: 48.1%; Depression: 60.6%"	<20 years: 30.5% depression; 4.9%controls. 20–39: 35.0% depression; 30.8% controls. 40–59: 35.7 depression; 23.2% controls. 60 or more: 28.6% depression; 11.3% controls.	Depression	Temporomandibular disorders	7–9 years	The risk of TMD was more than double in the depression cohort than in the non-depression cohort after controlling for confounders.
Liljeström 2008	Finland	Prospective cohort	Population-based; 13y-olds	198 (55%)	13 years	Depression	Temporomandibular disorders	3 years	Depressive symptoms and sleeping difficulties did not predict TMD signs.
Lin 2016	Taiwan	Retrospective cohort	Epidemiological; Taiwan National Health Insurance data	927,564; 50%	Propensity1 group: 26.2 (SD 13) no depression; 30.5 (SD 10.5) for depression group. Propensity2 group: 52.9 (SD 14.3) for no depression; 50.5 (SD 15.1) for depression group	Dysthymia	Temporomandibular disorders	8.7 years (2.2); up to 10 years	Dysthymia increased the risk of TMD in elderly and female-predominant patients who use more psychiatric health resources.
Lin 2017	Taiwan	Other: retrospective case-control	Epidemiological; Taiwan National Health Insurance data	2158 (1:1); "28.7%"	Control: 38.9 years Case: 39.5 years	Depression	Temporomandibular disorders	4.71 years (2.85)	TMD risk was significantly greater in dysthymia but not other depressive diagnosis.
Ma 2022	Taiwan	Retrospective cohort	Epidemiological; Taiwan National Health Insurance data	17,280; dementia: 51.68%; control: 51.32%	control/dementia ≤ 60 = 22.14%/ 23.90% 61 to 70 = 18.41%/18.85% 71 to 80 = 34.93%/ 33.91% ≥ 81 = 24.51%/23.33%	Dementia	Periodontitis	10 years	Dementia and AD were associated with a higher risk of PD dependent of age and independent of systemic confounding factors.

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Table 2 (*continued*)

Study	Country/ territory	Study design	Sampling/setting	Sample size (Total) a; Women %	Sample age at baseline mean (SD)	Mental disorder (exposure)	Oral condition (Outcome)	Follow-up; mean (SD)	Main prospective finding in plain language
Tsai 2023	Taiwan	Retrospective cohort	Epidemiological; Taiwan National Health Insurance data	38,203; 17.8%	14.7 years (2.1); range 12–19 years	Autism spectrum disorder	Periodontitis	up to 11 years	Autism spectrum disorder associated with increased risk of developing periodontitis as well as risk of earlier onset than individuals without autism.
Wu 2024	Taiwan	Retrospective	Epidemiological; Taiwan National Health Insurance data	21,255; 48.9%	16.91 years (2.09)	Bipolar disorder	Periodontitis	up to 11 years (2001–2011)	Bipolar disease associated with a higher risk of periodontitis than controls.
Chen 2010	USA	Retrospective cohort	Clinical; community-based geriatric dental clinic	491; Cases: 74.8%; Controls: 70.4%	without dementia: 73.8 years (10.7); range 44–103; With dementia: 81.5 years (9.2); range 49–102 years	Dementia	Tooth loss	Cases: 37.5 years (21.2) Control: 39.2 years (21.5)	Dementia was not associated with tooth loss.
Fillingim 2013	USA	Prospective cohort	Community volunteers	2737; 59.6%	27.1 years (7.8)	Mixed or multiple psychiatric disorders	Temporomandibular disorders	up to 5.2 years (mean 2.8 years)	Measures of poor psychological functioning, associated with psychiatric disorders, can predict first-onsetof TMD.
Frank 2019	USA	Retrospective cohort	Private pediatric dentistry clinic in an urban center	150; Not reported	Children 6–71 months. ASD: 3.3 ± 1.5; CP: 2.9 ± 1.0; CHD: 3.3 ± 1.6 DS: 3.2 ± 1.3; non-CSHCN: 2.4 ± 0.9. >71 months. ASD: 8.8 ± 2.2; CP: 8.6 ± 2.0; CHD: 8.3 ± 3.1 DS: 11.2 ± 5.4; non-CSHCN: 7.6 ± 1.1	Disability (developmental)	Caries	5.3 years (median)	Congenital heart disease and autism spectrum disorders associated with higher risk of dental caries.
Naorungroj 2013	USA	Other: Prospective cohort	Register data based on Atherosclerosis Risk in Communities (ARIC) study. Two waves, 1990–1992 and 1996–1998	10,050; 55.5%	56.8 years (5.7)	Cognitive impairment/ decline	Tooth loss	6 years	Greater decline in all cognitive function was associated with increased odds of complete tooth loss.
Sanders 2013	USA	Other: prospective and case-control	multisites; the OPPERA cohort and case-control studies	4320; 59.4%	range: 18 to 44 years	Sleep disorder	Temporomandibular disorders	up to 6 years (median 2.8)	Obstructive sleep apnea was associated with an elevated risk of first-onset as well as chronic TMD.
Slade 2007	USA	Prospective cohort	General popuation	194; 100%	53% sample aged 18–22; 47% sample 23–34 years	Depression	Temporomandibular disorders	up to 3 years	Depression, perceived stress, and mood were associated with pain sensitivity and were predictive of 2- to 3-fold increases in risk of TMD.

Notes: a = The sample size and women% apply for follow-up, whenever reported. All corresponding authors of the articles included in this manuscript have identified their affiliated institutions or organizations, along with the corresponding country or geographic region. The authors of this manuscript remain neutral with regard to any jurisdictional claims.

Fig. 5. Sankey diagram illustrating the relative frequency of studies reporting associations between various mental disorders and their potential role as risk factors for oral conditions. The narrowest lines (for example, ADHD → Periodontitis) represent one study for the association. The illustration reflects investigated associations, but not necessarily associations that are present.

pain/ paralysis, periodontitis, and dental decay. Cognitive decline, dementia and sleep disorders were also recurrently connected to oral deterioration, while several studies reported that ADHD increases the risk of caries and periodontitis. Collectively, these findings suggest that mental illness may act as a systemic vulnerability state predisposing individuals to progressive oral pathology through putative mechanisms such as behavioral neglect, medication side effects, and inflammatory dysregulation. (Neupane et al., 2022; Kisely et al., 2016; Choi et al., 2021) Mechanistically, these findings reinforce the view that psychiatric illness can create biological and behavioral vulnerability to oral disease. Depressive and anxiety disorders often lead to reduced motivation for oral hygiene, dietary changes, and irregular dental attendance; psychotropic medications contribute additional risk through xerostomia and metabolic side-effects. (Joury et al., 2023) Specific mechanisms may underlie certain sets of associations. For example, the association between depression and an increased risk of temporomandibular disorder (TMD) may reflect heightened pain sensitivity in individuals with depression. (Liao et al., 2011; Hermesdorf et al., 2016) Indeed the relatively smaller focus in oral conditions among patients with mental disorders are concentrated on severe mental disorders, where affected individuals face challenges in self-care. (Jerjes, 2024)

Generally, dementia and tooth loss were reported to be temporally associated in multiple studies. However, several studies have also reported a lack of association in either direction. In a retrospective study of older adults, dementia was not found to predict tooth loss after 3 decades. (Chen et al., 2010) Another study reported that neither natural teeth nor denture use was temporally associated with dementia two decades later in either sex. (Hansson et al., 2014) These results remind us that not all psychiatric conditions uniformly worsen oral outcomes across populations, and that moderator such as age, sex, treatment exposure, or socioeconomic status likely shape risk.

The literature investigating bidirectional associations between oral and mental disorders were limited to five positive reports for tooth loss or edentulism and cognitive impairment/decline; TMD and depression/anxiety/eating disorder; and Bell's palsy and anxiety. Lee and colleagues reported a more nuanced picture: a history of Bell's palsy increased the risk of depression, but the reverse risk was not evident. (Lee et al., 2020) Overall, we encourage systematic reporting of null findings as well as more nuanced results on disaggregated data for identifying intervention targets. We also emphasize the importance of limiting exaggerated causal claims when methodological rigor is lacking. These gaps highlight the need for better designed longitudinal studies encompassing standardized definitions, consistent confounder adjustment, representative sampling, and transparent reporting of all outcomes. Only then can the field move from suggestive correlations to robust causal inference.

Importantly, the literature displays a strong preponderance of positive results, suggesting possible publication bias. Nonetheless, the recurrence of similar effect patterns specific disease sets across independent cohorts supports the idea that at least part of these associations reflects genuine biological relationships rather than artefactual findings. A small number of studies—less than 10% across comparisons—reported null or mixed associations. Examples include the lack of predictive value of dental anxiety for caries (Wong et al., 2020) and the absence of a link between depressive symptoms and temporomandibular signs. (Liljestrom et al., 2008) Some evidence also points to sex-specific vulnerability profiles: for instance, in primary Sjögren's syndrome, women showed higher risk of subsequent depression whereas men were more prone to anxiety disorders, underscoring the need for stratified analyses. (Hsieh et al., 2019) Thus, our review also highlights heterogeneity in the evidence base and the need for nuanced understanding of the observed associations. Since a scoping review does not allow detailed synthesis, this should be addressed through targeted umbrella reviews of literature on specific pairs of oral and mental disorders.

Across the longitudinal literature, a clear hierarchy of replicated associations emerges. The most consistently reported dyads involve oral pathology as a predictor of neurocognitive outcomes, with most reports linking tooth loss to Alzheimer's disease and other dementias, as well as to cognitive impairment or decline, and periodontitis repeatedly associated with Alzheimer's disease and related dementias. Beyond replication, several of these associations point to potentially modifiable risk factors: periodontal disease severity, reduced tooth retention, and the

Table 3
Study characteristics and prospective findings in longitudinal studies of bidirectional associations between oral conditions and mental disorders.

Study	Country/territory	Study design	Sample size (Women%)	Sample age at baseline mean (SD)	Oral condition	Mental disorder	Follow-up duration	Main prospective finding in plain language
Kang 2020	UK	Prospective cohort	5477 (56.4%)	63.1 years (8.9)	Tooth loss/edentulism	Cognitive impairment/decline	10 years	There is a reciprocal relationship between oral health and cognitive function. Similar magnitude and direction of the reciprocal association was evident between cognition and oral health related quality of life.
Lee 2019	S. Korea	Retrospective cohort	17,360 (52%, Bell's palsy); 305,340 (66%, depression)	≥20 years	Bell's palsy	Depression	4.8–6.3 years (SD 3.3–3.6)	A history of Bell's palsy increased the risk of depression. On the contrary, depression did not increase the risk of Bell's palsy.
Liou 2023	Taiwan	Retrospective cohort	23,175 (range 56.0% to 66.5%)	Range: 34.10 (15.49) to 43.38 (17.05) years	TMD	Depression/anxiety	up to 16 years	Temporomandibular disorders were associated with higher risk of developing subsequent major depressive disorder and vice versa.
Tseng 2017	Taiwan	case-control	40,350 (60.2% with/without anxiety); 24,900 (46.7% with/without Bell's Palsy	Median 42 (IQR: 33–53 with/without anxiety); Median 47 (IQR:35–60 with/without Bell's Palsy)	Bell's palsy	Anxiety	5–9 years	Anxiety disorders were associated with higher risk of Bell's palsy and vice versa.
Tseng 2024	Taiwan	Retrospective	165,649 (67.5% with/without TMJD); 13,409 (91.4% with/without ED)	37.51 (SD = 16.94) years for TMJD and 27.98 (SD = 9.98) for ED	TMD	Eating disorder	up to 16 years	Temporomandibular disorders were associated with increased risk of eating disorder development and vice versa.

Notes: TMD: Temporomandibular disorders. All studies except Kang (2020) were based on data from the Korean National Health Insurance Service- National Sample cohort. All corresponding authors of the articles included in this manuscript have identified their affiliated institutions or organizations, along with the corresponding country or geographic region. The authors of this manuscript remain neutral with regard to any jurisdictional claims.

need for prosthetic rehabilitation. These exposures when subjected to prevention or treatment tended to follow more favorable cognitive trajectories, supporting their plausibility as actionable targets rather than fixed correlates. In contrast, evidence for bidirectionality remains comparatively limited, with only a small number of studies formally addressing reciprocal temporal relationships, and proposed biological and behavioral mechanisms largely inferred rather than directly tested. An important and often underappreciated consideration in the mental-to-oral direction of association is the potential confounding role of psychiatric treatment and care-related factors. Several psychotropic medications commonly used to treat depressive, anxiety, psychotic, and neurocognitive disorders are associated with xerostomia, altered salivary composition, metabolic changes, and increased inflammatory burden, all of which may predispose to periodontal disease, dental caries, and tooth loss. In parallel, mental disorders may indirectly affect oral health through reduced motivation for self-care, dietary changes, irregular dental attendance, and structural barriers to accessing dental services, particularly among individuals with severe or chronic psychiatric conditions. These treatment- and care-related mechanisms provide a unifying psychiatric framework for interpreting the relatively consistent longitudinal associations linking mental disorders to subsequent oral pathology, while underscoring that such findings should not be interpreted as evidence of direct causality.

4.1. Outstanding questions

We noted a paucity of studies with bold hypotheses. For example, we identified literature investigating the more apparent risk of periodontitis in schizophrenia, (Caratan et al., 2019; Hu et al., 2019) while we did not identify schizophrenia investigated as a possible outcome of oral pathology. Of note, schizophrenia and related psychotic disorders are arguably the mental disorders with most extensive evidence for biological and systemic risk indicators. (Arango et al., 2021; Pillinger et al., 2019)

A striking feature of the evidence is its uneven quality and coverage. While the sheer number of studies suggests a maturing field, closer inspection reveals significant methodological gaps. Diagnostic criteria for both oral and mental disorders varied widely, with some studies relying on administrative codes, others on self-report, and only a minority on standardized clinical assessments. Follow-up times ranged from months to decades, often without sensitivity analyses for duration effects. Importantly, only a subset of studies applied rigorous adjustment for confounding factors such as socioeconomic status, comorbidities, or health behaviors, raising concerns about residual bias. Thus, important nuances in the examined associations may be provided by methodologically sound studies that contain better variable definition, applied statistical or methodological adjustment for relevant confounders along with longer follow-up in larger samples. (Stang, 2010) Several of these issues will be addressed in a subsequent meta-analysis (https://doi.org/10.17605/OSF.IO/RCTB4) through structured risk-of-bias assessment, subgroup analyses based on study design and degree of covariate adjustment, and sensitivity analyses restricted to higher-quality studies. Understanding how oral interventions, such as the treatment of periodontitis, can influence the occurrence and progression of mental health pathologies—particularly those that typically take a long time to develop, such as cognitive impairment and Alzheimer's disease—is extremely valuable for population health.

5. Conclusion

The accumulated longitudinal evidence suggests deep interconnections between oral and mental health. The compelling longitudinal associations do not necessarily imply causality, but the observed links are potentially mediated through a complex interplay between biological, psychological, behavioral and social mechanisms. An example is the emerging role of oxidative stress pathways linking

periodontal inflammation and neurodegeneration in Alzheimer's disease. (Papadakis et al., 2025) The publication landscape in this field appears skewed toward positive results. While most research has focused on unidirectional risks, the reviewed literature points to dynamic, potentially bidirectional relationships that warrant mechanistic exploration through involvement of transdisciplinary teams. (Joury et al., 2023) Routine oral screening in psychiatric care and mental health assessment in dental settings could enable earlier detection and prevention of the second disorder while enhancing treatment outcomes of both domains. Furthermore, the knowledge is directly useful for informing clinical and care guidelines, such as guidelines for the care of elderly with dementia.

CRediT authorship contribution statement

Sudan Prasad Neupane: Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision, Software, Resources, Project administration, Methodology, Investigation, Funding acquisition, Formal analysis, Data curation, Conceptualization. **Ifeoma N. Onyeka:** Writing – review & editing, Validation, Methodology, Formal analysis, Data curation. **Vibeke H. Bull:** Writing – review & editing, Validation, Resources, Formal analysis, Data curation, Conceptualization. **Federico M. Daray:** Writing – review & editing, Writing – original draft, Validation, Methodology, Formal analysis, Data curation, Conceptualization.

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Declaration of competing interest

No conflicts of interest.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.nbd.2026.107285.

Data availability

Data will be made available on request.

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