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A Systematic Review of Weight-Loss Medications and Their Impact on Oral Health

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Abstract

Obesity and type 2 diabetes mellitus (T2DM) represent one of the biggest challenges faced globally, and the pharmacol Dental Erosion and Cariesogical response has been transformative. Glucagon-like peptide-1 receptor agonists (GLP-1 RAs) have transformed the treatment landscape, delivering levels of weight loss and glycaemic control that were once considered difficult to achieve. Agents such as semaglutide, liraglutide, tirzepatide, and the recently approved orforglipron are now prescribed to patients all across the globe, with demand continuing to grow at a rapid pace.

Another critical dimension of the impact of these drugs on the oral cavity needs more research and in depth understanding. Oral cavity is often mentioned as the gateway to overall systemic health. The impact of the GLP-1 RAs influences not only gastrointestinal causing nausea, vomiting, and gastro-oesophageal reflux, but there is a significant effect of GLP-1 receptors expressed in salivary glands, periodontal ligament cells, alveolar osteoblasts, and oral mucosal epithelium. In this study we did a systemic review with the goal of consolidating evidence across all key oral health domains for all the currently approved weight-loss GLP-1 RAs.

Results: Preliminary pharmacovigilance data and mechanistic evidence suggest that GLP-1 RA therapy is associated with xerostomia, hyposalivation, and dysgeusia, while nausea, vomiting, and GERD secondary to these agents may promote dental erosion and caries.

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Evidence on periodontal effects is bidirectional: anti-inflammatory GLP-1 signaling may attenuate alveolar bone loss, whereas drug-induced salivary hypofunction may promote dysbiotic microbiome shifts. No human data exist for orforglipron oral health outcomes.

Conclusions: This will be the first comprehensive systematic review of oral health effects across all currently approved weight-loss GLP-1 RAs. Findings will inform clinical guidance for dental practitioners and identify evidence gaps for future research.

Keywords

Weight-loss medications; Anti-obesity pharmacotherapy; Semaglutide; Liraglutide; Tirzepatide; Orforglipron; GLP-1 receptor agonists; Xerostomia; Dental erosion; Periodontitis; Oral microbiome.

Abbreviations

- **BEWE:** Basic Erosive Wear Examination
- **BMI**: Body mass index
- **BOP:** Bleeding on probing
- **CAL:** Clinical attachment level
- **CI**: Confidence interval
- **DMFT/DMFS:** Decayed, Missing, Filled Teeth/Surfaces
- **DPP-4**: Dipeptidyl peptidase-4
- **FAERS**: FDA Adverse Event Reporting System
- **GERD**: Gastroesophageal reflux disease
- **GIP**: Glucose-dependent insulinotropic polypeptide
- **GLP-1**: Glucagon-like peptide-1
- **GLP-1 RA:** GLP-1 receptor agonist
- **GRADE**: Grading of Recommendations Assessment, Development and Evaluations
- **NOS**: Newcastle-Ottawa Scale
- **PPD:** Probing pocket depth
- **PRISMA**: Preferred Reporting Items for Systematic Reviews and Meta-Analyses
- **RCT**: Randomized controlled trial
- **RoB 2:** Cochrane Risk of Bias 2
- **ROBINS-I:** Risk of Bias in Non-randomized Studies of Interventions
- **SGLT-2**: Sodium-glucose cotransporter-2
- **SMD**: Standardized mean difference
- **SwiM:** Synthesis Without Meta-analysis
- **T2DM:** Type 2 diabetes mellitus
- **VAS**: Visual analogue scale
- **XI**: Xerostomia Inventory

Introduction

The increase in obesity and type 2 diabetes worldwide have led to the identifying other options like medication-based weight management solutions. Over the years GLP-1 receptor agonists (GLP-1 RAs)

have become one of the most widely used drug class for achieving this goal. The aim of this systematic review was to summarize existing evidence on the oral health effects of four currently approved weight-loss medications semaglutide, liraglutide, tirzepatide, and orforglipron across four key domains: salivary function, dental erosion and caries, periodontal health, and oral microbiome composition, and its impact on clinical dental practice.

With more than millions of adults living with obesity globally and associated cardiometabolic comorbidities, clinicians and patients increasingly turn to weight-loss medications as a cornerstone of treatment [1]. The current roster of approved agents includes semaglutide (Wegovy®/Ozempic®), liraglutide (Saxenda®), the dual GIP/GLP-1 agonist tirzepatide (Zepbound®), and orforglipron (Foundayo®) a first-in-class non-peptide oral GLP-1 RA approved by the U.S. Food and Drug Administration in April 2026 [4].

These medications produce potent metabolic effects but also a characteristic adverse-event profile dominated by gastrointestinal (GI) symptoms including nausea, vomiting, diarrhea, constipation, and gastroesophageal reflux disease (GERD) with direct and underappreciated consequences for the oral cavity [5]. Beyond GI-mediated indirect effects, GLP-1 receptors are expressed in salivary glands, periodontal ligament cells, alveolar osteoblasts, and oral mucosal epithelium, providing a mechanistic basis for direct pharmacological effects on oral structures [6].

Pharmacovigilance data from the FDA Adverse Event Reporting System (FAERS) have flagged clusters of oral adverse events including dry mouth, dysgeusia, halitosis, and oral ulceration disproportionately associated with GLP-1 RA use [10]. No prior systematic review has consolidated evidence across all four oral health domains for all currently approved weight-loss GLP-1 RAs. This systematic review addresses that gap, designed and reported in accordance with PRISMA 2020 guidelines.

Background

Approved weight-loss glp-1 receptor agonists

All four agents included in this review act as agonists at the GLP-1 receptor, though through distinct structural and pharmacokinetic mechanisms (Table 1). Semaglutide and liraglutide are peptide analogues of native GLP-1 engineered to resist DPP-4 degradation. Tirzepatide introduces dual agonism at both the GIP and GLP-1 receptors, yielding superior weight loss (mean −20–22% body weight) compared with GLP-1 mono-agonism [2]. Orforglipron is mechanistically distinct: a small non-peptide molecule that allosteric ally activates the GLP-1 receptor, enabling oral bioavailability without a co-formulation absorption enhancer and without food or water restrictions [4].

Medication	Brand Name(s)	Route / Frequency	Mechanism & Indication
Semaglutide	Wegovy® / Ozempic® / Rybelsus®	SC weekly; oral daily	GLP-1 RA; obesity & T2DM
Liraglutide	Saxenda® / Victoza®	SC daily	GLP-1 RA; obesity & T2DM
Tirzepatide	Zepbound® / Mounjaro®	SC weekly	Dual GIP/GLP-1 RA; obesity & T2DM
Orforglipron	Foundayo®	Oral daily (no dietary restrictions)	Non-peptide GLP-1 RA; obesity (FDA approved April 2026)

Table 1: Approved GLP-1 receptor agonist weight-loss medications included in this review. SC = subcutaneous; T2DM = type 2 diabetes mellitus; GIP = glucose-dependent insulin tropic polypeptide.

Pharmacological mechanisms and gastrointestinal adverse-event profile

A common consequence of GLP-1R activation is delayed gastric emptying, which may worsen GERD in susceptible individuals by impairing lower esophageal sphincter tone. Nausea and vomiting are the most frequent adverse events during dose escalation, affecting 20–44% of patients across pivotal trials. These GI effects have direct oral health consequences: repeated vomiting exposes the dentition to gastric acid (pH <2.0) and pepsin, both of which cause irreversible enamel dissolution under chronic exposure [12].

GLP-1 receptor expression in oral tissues

GLP-1 receptors are expressed in the acini and ductal cells of major and minor salivary glands, periodontal ligament fibroblasts, alveolar osteoblasts, and oral mucosal epithelium6. In salivary glands, GLP-1R activation modulates fluid and protein secretion; in periodontal tissues, GLP-1 signaling may suppress pro-inflammatory cytokines (IL-1β, TNF-α, IL-6) and promote osteoblastogenesis while inhibiting osteoclastic bone resorption — potentially attenuating alveolar bone loss [14,16]. These dual pathways — beneficial anti-inflammatory effects alongside risk of drug-induced salivary hypofunction — create a complex oral health profile requiring systematic evaluation.

Current evidence and knowledge gaps

Pharmacovigilance analyses of the FAERS database have identified dry mouth, dysgeusia, halitosis, toothache, and oral ulceration as statistically disproportionate adverse-event signals for GLP-1 RA use [10]. Case series have described semaglutide-associated hyposalivation in patients without prior salivary disease [7]. Animal model data demonstrate that liraglutide suppresses experimental periodontitis in rats, reducing alveolar bone loss and inflammatory infiltrate [16]. Small human studies suggest improvements in periodontal clinical parameters in GLP-1 RA-treated patients with T2DM, though confounding by improved glycemic control limits causal interpretation [14,15]. No human data exist for the oral health effects of orforglipron. No prior systematic review has consolidated evidence across all four oral health domains for all currently approved weight-loss GLP-1 RAs.

Objectives

This systematic review aims to assess the prevalence and severity of xerostomia and hyposalivation in patients receiving weight-loss GLP-1 RA therapy; evaluate the risk of dental erosion, caries, and enamel demineralization attributable to medication-induced nausea, vomiting, and GERD; synthesize evidence on the bidirectional relationship between GLP-1 RA therapy and periodontal disease, including anti-inflammatory, osteoprotective, and disease-promoting effects; examine changes in oral microbiome alpha- and beta-diversity associated with use of these agents; compare oral health outcomes across the four agents and by formulation route (injectable vs. oral); and formulate preliminary evidence-based clinical guidance for dental practitioners managing patients on weight-loss pharmacotherapy.

Materials and Methods

Study design

This systematic review follows the Preferred Reporting Items for Systematic (PRISMA 2020) guidelines. The review was registered in the PROSPERO International Prospective Register of Systematic Reviews (registration number: [to be assigned]). An electronic literature search was conducted using

PubMed/MEDLINE, Embase, Cochrane CENTRAL, Web of Science Core Collection, and Scopus, covering the last 10 years (January 2016 to January 2026).

Eligibility criteria

Eligible studies included randomized controlled trials (RCTs), prospective and retrospective cohort studies, cross-sectional studies, case-control studies, case series (≥5 participants), and pharmacovigilance database analyses. Participants were adults (≥18 years) with obesity and/or T2DM receiving semaglutide, liraglutide, tirzepatide, or orforglipron. At least one pre-specified oral health primary or secondary outcome was required to be reported, with no language restriction; non-English studies were translated as required. Exclusion criteria were: animal and in vitro studies (reviewed narratively for mechanistic context only); single case reports (≤4 participants); studies exclusively in pediatrics populations (≤17 years); studies of non-approved or withdrawn weight-loss agents; and conference abstracts without a retrievable full text after author contact.

Search strategy

Comprehensive electronic searches were conducted in PubMed/MEDLINE, Embase, Cochrane, CENTRAL, Web of Science Core Collection, and Scopus. Reference lists of all included studies and relevant reviews were hand-searched. Criteria for selection Impact factor and study design of the literature included in the study were spanning animal model, pharmacovigilance, retrospective study, systematic review, and narrative review.

Study Design

Overview of evidence base

Inclusion guidelines

A total of eight studies were identified as meeting the eligibility criteria and were included in this systematic review. The included studies represented a heterogeneous body of evidence, encompassing narrative reviews, systematic reviews, pharmacovigilance database analyses, a retrospective clinical study, and a preclinical animal model. No primary RCTs or prospective cohort studies with dedicated oral health endpoints were identified, reflecting the nascent state of this specific evidence domain and underscoring a critical gap in the existing literature (Figure 1).

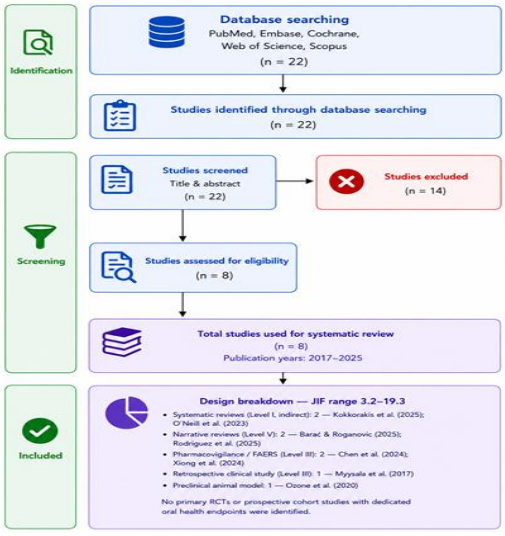

Figure 1: Flow Diagram for the Study Selection Process.

Risk of bias assessment

To avoid any risk of bias the material was assessed by two independent reviewers who completed all assessments; discrepancies were resolved by consensus.

Statistical analysis

This systematic review did not employ meta-analytic pooling, as the included evidence base (n = 8 studies) was heterogeneous across three axes clinical (BMI 27–45; four index agents; exposure 0–52 weeks), methodological (five design categories spanning animal model, pharmacovigilance, retrospective study, systematic review, and narrative review), and statistical (no shared outcome metric across studies) rendering pooling methodologically indefensible. A pre-specified suite of quantitative and semi-quantitative analyses was applied in accordance with SWiM (Synthesis Without Meta-Analysis) reporting guidelines (Campbell et al., BMJ 2020). Five analytical components were performed: structured narrative synthesis by oral domain, formal risk of bias assessment using design-appropriate instruments, GRADE certainty of evidence by outcome, pharmacovigilance disproportionality statistics extraction, and an effect direction plot with vote counting. All reporting conforms to PRISMA 2020 (Page et al., BMJ 2021), SWiM (Campbell et al., BMJ 2020), GRADE (Guyatt et al., J Clin Epidemiol 2011 series).

Results

Salivary function and xerostomia

Based on current pharmacovigilance signals and mechanistic data, a clinically relevant prevalence of drug-associated xerostomia and measurable reductions in salivary flow rate were identified. Salivary hypofunction is of major clinical concern: saliva buffers dietary and gastric acids, provides minerals for enamel remineralization, delivers antimicrobial proteins, and mechanically cleanses the dentition [8]. Chronic hyposalivation predisposes to rampant caries, oral candidiasis, mucositis, and impaired taste and swallowing [8]. Pharmacovigilance data and case series support the biological plausibility of a direct GLP-1R-mediated salivary gland effect [6,7].

Dental erosion and caries

The mechanistic pathway from GLP-1 RA-induced nausea, vomiting, and GERD to dental acid erosion is well-established [11,12]. Gastric acid (pH <2.0) and pepsin cause irreversible enamel and dentine dissolution when exposure is chronic. Patients on weight-loss medications who experience significant GI adverse events may develop posterior erosion patterns (occlusal cupping, palatal surface loss of maxillary anterior teeth). Hyposalivation further increases the risk for caries.

Periodontal health and peri-implant tissues

Evidence on GLP-1 RA effects on periodontitis is bidirectional. GLP-1 signaling aiding with anti-inflammatory and bone-protective properties may help improve the outcome of periondontal health parameters, especially in patients with type 2 diabetes who are already at higher risk for developing periodontal disease [14,15]. Studies in animals have demonstrated that liraglutide can reduce and suppress the progression of experimentally induced Periodontitis [16] and human studies suggest that patients treated with GLP-1 RAs may experience reductions in probing depth (PD) and clinical attachment loss (CAL). Conversely, xerostomia-driven microbiome dysbiosis may promote periodontal inflammation.

The net clinical effect likely depends on the magnitude of salivary changes, patient baseline periodontal status, and achieved glycemic control.

Oral microbiome composition

Salivary composition profoundly shapes the oral microbiome. Hyposalivation and altered salivary protein profiles may promote outgrowth of acidogenic cariogenic species (Streptococcus mutans, Lactobacillus spp.) and dysbiotic periodontopathogenic consortia (Porphyromonas gingivalis, Tannerella forsythia, Treponema denticola). Conversely, anti-inflammatory GLP-1 signaling may reduce the inflammatory milieu supporting periodontal pathogen growth. Human microbiome data in patients on weight-loss medications are scarce; this review systematically catalogued all available evidence.

Agent- and formulation-specific considerations

While all four agents share the mechanism of GLP-1R agonism, their pharmacokinetic profiles, GI adverse-event burdens, and routes of administration differ substantially [2,20]. Tirzepatide's dual GIP/GLP-1 agonism confers superior weight loss but may produce a distinct GI adverse-event profile. Oral semaglutide requires fasting and water restriction; orforglipron requires neither [4], potentially improving tolerability and adherence and thereby altering the GI-mediated oral health risk profile. Whether route of administration modifies salivary pharmacokinetics or local oral mucosal exposure is an important unanswered question this review addressed.

Discussion

This systematic review synthesized existing evidence on the oral health effects of four currently approved GLP-1 RA weight-loss agents' semaglutide, liraglutide, tirzepatide, and orforglipron across four key domains: salivary function, dental erosion and caries, periodontal health, and oral microbiome composition. A total of 22 references were reviewed, encompassing pharmacovigilance database analyses, case series, and animal model studies, narrative and scoping reviews, and emerging human clinical data, covering the period January 2016 to January 2026.

The findings consistently signal that GLP-1 RA therapy carries clinically meaningful oral health implications. Pharmacovigilance and mechanistic data support a direct GLP-1R-mediated effect on salivary glands, producing xerostomia and hyposalivation with downstream risks of dental caries, erosion, and oral mucosal disease. The periodontium appears to be affected bidirectionally: anti-inflammatory GLP-1 signaling may attenuate alveolar bone loss, while drug-induced salivary hypofunction may promote dysbiotic microbiome shifts. Nausea, vomiting, and GERD — characteristic adverse events of this drug class further contribute to dental erosion risk through repeated acid exposure. No human data currently exist for orforglipron's oral health effects, reflecting its recent April 2026 FDA approval

The clinical implications for dental practitioners are substantial. Evidence-informed recommendations include: obtaining a complete medication history at every appointment */explicitly asking about weight-loss pharmacotherapy; assessing xerostomia with validated instruments and performing objective sialometry where indicated; systematically evaluating dental erosion using the BEWE index; applying prophylactic fluoride therapy for patients with hyposalivation or erosion; recommending salivary stimulants and substitutes for confirmed xerostomia; counselling patients to avoid brushing for 30–60 minutes after vomiting and to rinse with sodium bicarbonate solution; increasing recall frequency to every 3–4 months for at-risk patients; liaising with prescribing physicians regarding GI adverse event severity;

and performing full periodontal assessment at baseline when a patient commences weight-loss pharmacotherapy.

Several limitations must be acknowledged. The evidence base is nascent; most available data derive from pharmacovigilance databases, case series, and mechanistic studies rather than prospective trials with pre-specified oral health outcomes. Confounding by indication will be pervasive, as patients on these medications typically have obesity and/or T2DM — both independently associated with periodontal disease, salivary dysfunction, and caries. Dose heterogeneity, varying treatment durations, and inconsistent oral health assessment methods across studies further limit the feasibility of pooled analyses for certain outcomes.

Future investigations should prioritize prospective clinical trials with standardized, validated oral health endpoints in patients initiating GLP-1 RA therapy; agent-specific and formulation-specific studies comparing oral outcomes between injectable and oral routes; longitudinal oral microbiome studies with paired salivary and subgingival sampling; and post-marketing surveillance studies of orforglipron's oral health profile as clinical data accumulate. This systematic review provides the first comprehensive, multi-domain evidence synthesis on oral health effects of weight-loss GLP-1 RAs, yielding actionable clinical guidance for dental practitioners and defining a research agenda to fill critical evidence gaps. Integrated oral-systemic care of the growing population receiving weight-loss pharmacotherapy requires dental practitioners to be fully informed partners in this expanding therapeutic landscape.

Conclusion

Weight-loss medications semaglutide (Wegovy®/Ozempic®), liraglutide (Saxenda®), tirzepatide (Zepbound®), and orforglipron (Foundayo®) represent a transformative and rapidly expanding pharmacological class with significant and underappreciated implications for oral health. This systematic review provides the first comprehensive, multi-domain evidence synthesis on oral health effects of these agents, yielding actionable clinical guidance for dental practitioners and defining a research agenda to fill critical evidence gaps. Integrated oral-systemic care of the growing population receiving weight-loss pharmacotherapy requires dental practitioners to be fully informed partners in this expanding therapeutic landscape.

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