-ORIGINAL ARTICLE

Oral Candidiasis and Dry Mouth with SGLT2 Inhibitors in FAERS, 2013 Q1–2025 Q2: A Disproportionality Analysis

Rachmat Hidayat[1*], **Firman Hadi**[2]

[1]Department of Medical Biology, Faculty of Medicine, Universitas Sriwijaya, Palembang, Indonesia

[2]Department of Dentistry, Lumajang Private Family Clinic, Lumajang, Indonesia

ARTICLE INFO

ARTICLE TYPE
Original Article

ARTICLE HISTORY
Received: October 30, 2025
Accepted: November 25, 2025
Published: December 30, 2025

KEYWORDS
FAERS; oral candidiasis; pharmacovigilance; SGLT2 inhibitors; xerostomia

CORRESPONDING AUTHOR
Rachmat Hidayat
E-mail:
dr.rachmat.hidayat@gmail.com
ORCID: 0000-0001-5770-1201

DOI
https://doi.org/10.59345/crown.v3i2.327

ABSTRACT

Background: Oral adverse-event reporting with sodium-glucose cotransporter 2 (SGLT2) inhibitors remains poorly characterized.

Objective: To evaluate disproportionate reporting of oral candidiasis, dry mouth, and periodontal disease with pure SGLT2 inhibitors in FAERS from 2013 Q1 through 2025 Q2.

Methods: A retrospective case–non-case analysis used source-reported aggregates from 54 quarterly FAERS extracts. Latest-version handling, deletion-file exclusion, curated drug mapping, exact MedDRA Preferred Terms, reporting odds ratios (RORs) with 95% confidence intervals (CIs), and Benjamini–Hochberg-adjusted q values were applied. A signal required at least three co-reports, a lower CI bound greater than 1, and $q < 0.05$; role-scope and diabetes-indication comparator analyses assessed directional consistency.

Results: Among 17,415,743 retained reports, 174,627 contained a mapped pure SGLT2 inhibitor. Primary-suspect analysis identified oral candidiasis (103 co-reports; ROR 1.71, 95% CI 1.41–2.07; $q = 8.89 \times 10-8$) and dry mouth (578 co-reports; ROR 1.54, 95% CI 1.42–1.67; $q = 1.99 \times 10-24$). Both estimates remained above 1 across broader role-scope and active-comparator analyses; periodontal disease was non-conclusive.

Conclusion: Oral candidiasis and dry mouth showed hypothesis-generating disproportional reporting. The findings support targeted case review and external validation but do not estimate incidence, comparative risk, or causality.

1. Introduction

Sodium-glucose cotransporter 2 (SGLT2) inhibitors have become central therapies across type 2 diabetes, heart failure, and chronic kidney disease. Large contemporary randomized trials showed clinically important benefits of empagliflozin or dapagliflozin in heart failure with preserved or mildly reduced ejection fraction, chronic kidney disease, and patients hospitalized for acute heart failure.[1–4] A 2022 systematic review and meta-analysis integrating cardiovascular outcome trials likewise found broad cardiorenal benefit while emphasizing the need to evaluate adverse effects alongside efficacy.[5] As treatment expands across indications and specialties, events recognized in dental or oral-medicine settings may become more visible and clinically relevant.

The adverse-event literature for SGLT2 inhibitors is dominated by metabolic, renal, and genitourinary outcomes. A large FAERS study covering 2013-2021 characterized class and ingredient safety signals,[6] while a 2025 meta-analysis with FAERS disproportionality analysis confirmed increased genitourinary infection reporting and trial risk.[7] Recent cohort and spontaneous-report studies have further shown that genital-infection patterns may vary by sex and patient characteristics and that the apparent safety profile changes with drug combinations and reporting scope.[8–10] These findings establish a pharmacovigilance rationale for examining other mucosal sites, but urinary glycosuria is anatomically remote from the oral cavity and cannot by itself establish an oral drug effect.

Diabetes already affects the oral environment. A 2022 systematic review and meta-analysis found altered salivary parameters in adults with diabetes,[11] and comparative cross-sectional studies reported more xerostomia, lower salivary flow, or salivary dysfunction among patients with diabetes than among controls.[12,13] A 2025 meta-analysis estimated a substantial prevalence of xerostomia in type 2 diabetes, although the contributing studies were heterogeneous,[14] and another meta-analysis linked diabetes with salivary alterations relevant to dental caries.[15] Glycemic control, autonomic dysfunction, renal disease, age, hydration, and concomitant medicines may therefore influence a Dry mouth report independently of an SGLT2 inhibitor.

Diabetes is also associated with oral Candida carriage, but carriage is not equivalent to clinical infection. Recent microbiological studies from Iran and Mexico identified diverse Candida species and genotypes in oral samples from patients with diabetes,[16–18] while contemporary reviews describe the transition from colonization to oral candidosis as dependent on fungal virulence, epithelial integrity, host immunity, saliva, prostheses, antibiotics, corticosteroids, and local oral conditions.[19,20] These determinants are not captured reliably in spontaneous reports, creating substantial potential for confounding and outcome misclassification.

Salivary dysfunction may connect oral dryness with candidal disease. A 2022 systematic review and meta-analysis associated xerostomia or hyposalivation with oral Candida growth and clinical oral candidiasis.[21] Direct SGLT2-specific oral evidence remains sparse: a 2024 case report described burning mouth syndrome after empagliflozin,[22] while a separate case series of semaglutide-associated hyposalivation illustrates that oral dryness can also be reported with a non-SGLT2 glucose-lowering therapy.[23] Neither type of case evidence can establish incidence, comparative risk, or a class mechanism.

Periodontal disease requires separate consideration because it is chronic, multifactorial, and often documented outside medication-safety encounters. Recent systematic

reviews support a bidirectional association between diabetes and periodontal disease and evaluate periodontal treatment as part of glycemic management.[24–26] A sparse periodontal signal in FAERS would therefore be difficult to interpret as evidence for or against the established diabetes-periodontitis relationship.

Spontaneous-report systems are useful for detecting unusual drug-event co-reporting across large populations. FAERS/AEMS contains voluntary and mandatory individual case safety reports made available through quarterly FDA extracts.[27] It has no treated-population denominator and is affected by under-reporting, stimulated reporting, missing data, duplicates, indication channeling, event competition, and reporter attribution. Disproportionality consequently measures relative reporting within a database reference set; it does not estimate incidence and does not establish causality.

The documented literature assessment found no class-level oral-outcome study that combined exact Oral candidiasis, Dry mouth, and Periodontal disease terms with nested drug-role scopes, diabetes-indication active comparators, selected strata, and ingredient-era outputs. This combination is clinically relevant because oral symptoms can be recognized by dentists, prescribers, or patients and may be coded differently across reporting channels. This study therefore aimed to evaluate whether these oral outcomes were reported disproportionately with pure SGLT2 inhibitors in source-reported FAERS aggregate results from 2013 Q1 through 2025 Q2. Secondary objectives were to assess directional consistency across drug-role and comparator definitions and to describe selected stratum and era outputs without interpreting them as subgroup effects or causal comparisons.

2. Methods

Study design and reporting framework

We conducted a retrospective case-non-case disproportionality study using publicly available FAERS/AEMS individual case safety report extracts. The analytic interval extended from 2013 Q1 through 2025 Q2, and the unit of analysis was the deduplicated case report. No dated protocol, registration record, or executable analysis plan was available for this manuscript revision. Outcomes, role scopes, comparator analyses, strata, era analyses, and signal criteria are therefore described as specified in the supplied aggregate analytical report rather than as prospectively prespecified. Reporting was structured using the READUS-PV statement and explanation-and-elaboration document.[28,29]

Data source and extraction period

The FDA distributes quarterly FAERS/AEMS ASCII files containing demographic and administrative information, drug records, reaction terms, indications, outcomes, therapy dates, and source information.[27] FAERS combines voluntary and mandatory reports. A report may contain multiple drugs and reactions, and follow-up versions may update the same CASEID. The database contains no population exposure denominator and cannot provide incidence, prevalence, or person-time. The supplied analysis covered 54 quarterly archives from 2013 Q1 through 2025 Q2; the official FDA page was used to verify archive availability.

Archive integrity and database ingestion

The supplied analytical summary stated that archives were checked using expected file size, SHA-256 information when available, ZIP integrity, and cyclic redundancy checks, then imported into DuckDB with quarterly row-count reconciliation. It reported zero source-to-ingest row-count mismatches. The underlying ingest logs, code, archive digests, and DuckDB version were not supplied, so these quality-control results are reproduced as source-reported rather than independently verified.

Case-version deduplication and deletion handling

The supplied rule retained the most recent FDA_DT for each CASEID, followed by the highest CASEVERSION and then PRIMARYID for ties. CASEIDs appearing in FDA deletion files were excluded before analytical tables were constructed. The aggregate source reported 20,297,836 raw demographic rows, 17,415,743 retained latest non-deleted reports, 2,882,093 rows excluded before the retained set, and 95,602 deletion-file identifiers. Because the raw-to-final difference equals 2,882,093, the relationship between superseded rows and deletion-file identifiers is not separately recoverable from the supplied counts. These values are therefore not presented as additive sequential exclusions. Residual duplicates submitted under different CASEIDs may remain.[30,31]

Drug-name normalization and exposure classification

The source described curated normalization of generic, brand, and active-ingredient strings with RxNorm audit. The documented pure-SGLT2 ingredient-era outputs included canagliflozin, dapagliflozin, empagliflozin, and ertugliflozin; sotagliflozin was treated separately as a dual SGLT1/2 inhibitor. The full drug dictionary, fixed-dose-combination rules, salt and spelling rules, and complete ingredient lists for DPP-4 inhibitors, GLP-1 receptor agonists, and the broader active non-SGLT2 group were not supplied. Fifty -gliflozin drug rows remained unmatched, but their unique-report and oral-event impact was unavailable. Exposure and comparator mapping therefore could not be independently audited.

Drug-role scopes

The primary analysis used reports in which the SGLT2 inhibitor was designated primary suspect (PS). Suspect-only included PS and secondary suspect, whereas all-role additionally included concomitant and interacting records. Reporter-assigned role is not a formal causality assessment. The supplied estimates were compared across these nested scopes to assess directional consistency; role-specific contingency cells and denominators were unavailable.

Oral outcome definitions

The exact MedDRA Preferred Terms Oral candidiasis, Dry mouth, and Periodontal disease were the principal outcomes. The MedDRA version and cross-version handling procedure were not recorded in the supplied documentation. Dry mouth was treated as a reaction label and not equated with validated xerostomia or measured hyposalivation. The source also reported an oral candidiasis spectrum composite, but its component Preferred Terms were unavailable. Prioritizing the exact term and demoting the composite to non-auditable supplementary information was a retrospective reporting safeguard applied during manuscript revision.

Primary reference set and contingency tables

For each outcome, reports containing an SGLT2 inhibitor within the applicable role scope formed the exposed series and other eligible reports formed the reference series. Conceptually, the 2x2 table contained a, reports with exposure and event; b, exposed reports without the event; c, reference reports with the event; and d, reference reports without the event.[30–32] A report could

contribute to more than one outcome because reactions were not mutually exclusive. The complete a/b/c/d cells were not supplied, so the central estimates could not be independently reconstructed.

Active-comparator analyses

The supplied sensitivity outputs restricted analyses to reports with a recorded diabetes indication and compared pure SGLT2 reports with DPP-4 inhibitor, GLP-1 receptor agonist, and broader active non-SGLT2 groups, excluding pairwise overlap. The indication-recognition algorithm, full class lists, role rules, multi-class handling, and comparator denominators were unavailable. These outputs address one aspect of confounding by indication but do not establish exchangeability or comparative risk; market age, channeling, co-medication, disease severity, and reporting patterns may differ.[30]

Bias framework

Interpretation considered confounding by diabetes and its complications, indication channeling, co-medication, differential recognition, notoriety and stimulated reporting, masking or competition, exposure and outcome misclassification, and residual duplication.[29–31] Role-scope and active-comparator results were treated as source-reported sensitivity outputs. None can identify a causal effect. Because FAERS has no source population denominator, a conventional power calculation was not applicable; co-report counts and CIs were used to describe precision.

Selected stratum and launch-era outputs

The supplied report provided only the stratum with the largest co-report count for calendar year, country, age group, sex, reporter type, seriousness, and diabetes-indication dimensions. These data-selected cells were summarized descriptively in Supplementary Table S4 and were not used to infer effect modification or cross-stratum robustness. Ingredient-era outputs contrasted a reported first-two-year period with later years, but exact launch dates, quarterly intervals, denominators, and multiplicity families were unavailable. Era results were therefore treated as exploratory source-reported summaries in Supplementary Table S5.

Statistical analysis and signal criteria

The source reported ROR=(a × d)/(b × c), log-scale 95% CIs and two-sided Wald tests for non-sparse tables, and two-sided Fisher exact tests for sparse tables.[32] Benjamini-Hochberg adjustment was reported, but the hypothesis-family definitions, test counts, and mapping of tests to q values were not documented.[33] A source-defined signal required at least three co-reports, lower 95% CI greater than 1, and $q<0.05$. Finite periodontal estimates were generated using an unspecified zero-cell correction and are reproduced only as non-verifiable source outputs; the zero-event result is interpreted as non-conclusive.

Analytical estimand and report contribution

The estimand was relative reporting within the database reference set, expressed as the odds that a selected oral-event label appeared rather than other reaction labels among reports meeting the exposure definition, compared with the corresponding odds in reference reports. It was not a patient-level odds ratio for developing disease. A deduplicated report, rather than a unique person verified across submissions, was the analytical unit. Each report could contain several drugs and reactions and could contribute to more than one outcome-specific 2x2 table. Within any one drug-event analysis, contribution was binary at report level. The aggregate documentation did not describe how multiple products from the same class, duplicate reaction rows within a report, or drug-role conflicts were collapsed; these implementation details could not be reconstructed.

Evidence hierarchy for manuscript interpretation

The exact Oral candidiasis and Dry mouth primary-suspect outputs formed the highest interpretive tier because their labels, co-report counts, estimates, and uncertainty were explicitly available. Role-scope and active-comparator estimates were treated as directional sensitivity outputs. Data-selected stratum cells and ingredient-era estimates were exploratory descriptive outputs. The candidiasis-spectrum composite and finite periodontal zero-cell estimates were retained only as qualified source-reported secondary information because their term composition or correction method was unavailable. This hierarchy was established during manuscript revision to align the strength of interpretation with reproducibility of the supplied documentation; it was not represented as an original prospective protocol hierarchy.

Aggregate-output reconciliation

Verification was limited to internal reconciliation of the supplied manuscript. We compared every available retained-report count, exposed-report count, co-report count, ROR, CI, and q value across the source narrative, six source tables, source figure, revised abstract, main text, and main displays. Reference numbering and claim support were audited bidirectionally. This process can detect transcription conflicts and internally inconsistent presentation, but it cannot validate the original database query, mapping decisions, statistical computation, or clinical content of individual reports. No source value was recalculated from invented or back-calculated denominators.

Reporting and presentation conventions

Counts were reported as whole deduplicated reports or drug rows according to their source label. RORs and 95% CIs were retained to two decimal places, while q values were reformatted from machine-style notation to multiplication notation without changing precision. Terms such as signal, elevated reporting, and directional consistency refer only to disproportionality within the specified database comparison. We avoided patient-risk language, did not convert RORs to percentages or absolute risks, and did not compare point estimates as though their reference populations were exchangeable. Main-text displays prioritize the exact outcomes and principal role/comparator results; complete supplied aggregate values remain in the supplement. Unavailable methods are identified at the location where they affect interpretation rather than being reconstructed from the reported estimates.

Analytical alternatives considered

Adjusted multivariable modeling was considered but rejected because no case-level covariates, reference-category denominators, missing-data codes, or temporal variables were available. A true multivariate model was not appropriate because the outcomes were not jointly modeled and patient-level co-occurrence was unknown. Alternative disproportionality measures, Bayesian shrinkage, time-to-onset analysis, interaction tests, and influence diagnostics likewise required data not supplied. The analysis therefore reports the existing unadjusted aggregate ROR outputs with sensitivity descriptions and explicit residual-bias limitations rather than adding unsupported models to obtain apparent completeness or significance.

Data completeness and analytic feasibility

The aggregate source reported missing sex, age, and country rates among retained reports, but missing-value codes were unavailable; no imputation was performed in the available outputs. Public quarterly FAERS files can be obtained from the FDA. The study-specific case-level dataset, ingest and analysis code, drug and outcome dictionaries, complete contingency cells, full stratum output, software versions, and detailed logs were not supplied. Consequently, we reconciled source-reported aggregates across manuscript components but could not independently rerun case handling, reconstruct RORs, fit adjusted models, reproduce sparse-cell corrections, or perform influence and diagnostic analyses.

Ethics and research governance

Ethical approval was granted by the CMHC Ethics Committee Indonesia (No. 003/CMHC/Ethics/08/2025). The study used publicly available de-identified safety reports and involved no recruitment, intervention, direct participant contact, or access to identifiable clinical records. Individual informed consent was not applicable to this secondary database analysis. The manuscript reports only aggregate counts and estimates and reproduces no case narrative that could enable re-identification. Public availability of FAERS does not guarantee clinical accuracy or authorize inference about an identifiable person; reporter statements, missing fields, and administrative classifications were therefore treated as unverified database content. The ethics approval is separate from protocol registration and data-sharing permission for study-specific derived files. No registration record was supplied.

3. Results

Report processing and data quality

The supplied pipeline covered all 54 quarterly extracts and reported 20,297,836 raw demographic rows, 17,415,743 retained latest non-deleted reports, and 174,627 reports containing at least one mapped pure SGLT2 inhibitor (approximately 1.00% of the retained set). The source separately reported 2,882,093 rows excluded before the retained set and 95,602 deletion-file identifiers; these figures cannot be interpreted as additive sequential exclusions because their overlap was not documented. Zero quarterly ingest row-count discrepancies were reported. Missing sex and age rates were 13.43% and 42.72%, respectively, while the source reported 0.00% missing country; coding definitions were unavailable. Fifty -gliflozin drug rows remained unmatched, as detailed in Table 1.

Table 1. Source-reported data processing and quality metrics.

METRIC	VALUE	INTERPRETATION
Raw demographic rows	20,297,836	source-reported count
Rows excluded before retained set	2,882,093	derived raw-minus-final; components unavailable
Deletion-file identifiers	95,602	source-reported; not additive
Latest non-deleted reports	17,415,743	source-reported count
Pure SGLT2-exposed reports	174,627	source-reported count
Unmatched -gliflozin drug rows	50	source-reported drug rows
Missing sex	13.43	% (coding unavailable)
Missing age	42.72	% (coding unavailable)
Missing country	0.00	% (coding unavailable)

Note: Counts are reproduced from the supplied aggregate report. Rows excluded before the retained set and deletion -file identifiers must not be added because their relationship was not documented. SGLT2, sodium-glucose cotransporter 2.

Primary-suspect outcome analysis

In the source-reported primary-suspect analysis, Oral candidiasis had 103 co-reports and met the compound signal rule (ROR 1.71, 95% CI 1.41-2.07; $q=8.89 \times 10^{-8}$). Dry mouth had 578 co-reports and also met the rule (ROR 1.54, 95% CI 1.42-1.67; $q=1.99 \times 10^{-24}$). Periodontal disease had zero co-reports and was non-conclusive. Its finite source-reported estimate depended on an undocumented zero-cell correction and was excluded from the primary figure. The two exact signals and their confidence intervals are shown in Figure 1.

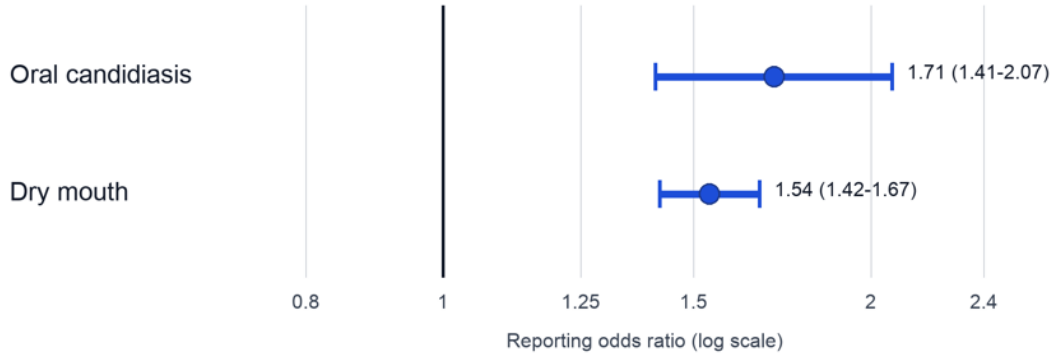

Figure 1. Source-reported reporting odds ratios and 95% confidence intervals for the two exact outcomes meeting the study signal rule in the primary-suspect SGLT2 analysis. The vertical line indicates ROR=1. The non-auditable candidiasis composite and the undocumented zero-cell periodontal estimate are excluded.

Interpretive hierarchy of oral outcomes

The two exact outcomes with at least three co-reports, lower confidence bounds above 1, and q values below 0.05 were retained as the main findings. The candidiasis-spectrum composite had 145 primary-suspect co-reports and a source-reported ROR of 1.91, but it was not used to strengthen the principal conclusion because its component Preferred Terms were unavailable. The periodontal result was treated differently from a conventional negative association: zero primary-suspect co-reports meant that the count and interval conditions failed, while the finite point estimate and q value depended on a correction that could not be reproduced. Thus, the available outputs supported two reporting signals and one non-conclusive sparse outcome, not three comparable effect estimates.

Drug-role sensitivity outputs

Oral candidiasis and dry mouth estimates remained above 1 across the supplied all-role, suspect-only, and primary-suspect analyses. Oral-candidiasis point estimates ranged from 1.66 to 1.71 as co-reports declined from 169 in all roles to 103 in the primary-suspect scope. Dry-mouth estimates ranged from 1.49 to 1.54, with corresponding co-report counts from 942 to 578. The lower confidence bound remained above 1 for both outcomes in all three source-reported scopes. Periodontal disease remained sparse, with one all-role co-report and no suspect-only or primary-suspect co-reports; its finite corrected estimates were not independently verifiable. Because scope-specific totals and contingency cells were unavailable, the narrow point-estimate ranges demonstrate directional consistency within the supplied output, not independent replication or proof that role assignment had no influence, as detailed in Table 2.

Table 2. Source-reported oral outcome disproportionality by drug-role scope.

OUTCOME	ROLE SCOPE	CO-REPORTS	ROR (95% CI)	BH Q
Oral candidiasis	All roles	169	1.66 (1.42-1.93)	1.00×10^{-10}
Oral candidiasis	Suspect only	114	1.67 (1.39-2.01)	6.56×10^{-08}
Oral candidiasis	Primary suspect	103	1.71 (1.41-2.07)	8.89×10^{-08}
Dry mouth	All roles	942	1.49 (1.39-1.58)	1.18×10^{-32}
Dry mouth	Suspect only	638	1.51 (1.39-1.63)	4.76×10^{-24}
Dry mouth	Primary suspect	578	1.54 (1.42-1.67)	1.99×10^{-24}
Periodontal disease	All roles	1	0.12 (0.02-0.84)*	0.005
Periodontal disease	Suspect only	0	0.09 (0.01-1.42)*	0.009
Periodontal disease	Primary suspect	0	0.10 (0.01-1.61)*	0.012

*Note: BH, Benjamini-Hochberg; CI, confidence interval; ROR, reporting odds ratio. A signal required at least 3 co-reports, lower 95% CI >1, and q<0.05. *Finite sparse/zero-cell estimate reproduced from the source; correction constant and exact reconstruction were unavailable.*

Active-comparator sensitivity outputs

Within the source-defined diabetes-indication restriction, oral candidiasis and dry mouth estimates remained above 1 against DPP-4 inhibitors, GLP-1 receptor agonists, and the broader active non-SGLT2 group. Magnitudes varied substantially by comparator, especially for oral candidiasis, whose reported ROR ranged from 2.95 to 12.95. Periodontal comparisons contained zero SGLT2 events and were non-conclusive. The principal event counts and estimates are detailed in Table 3; missing group definitions and denominators preclude interpretation as head-to-head risk.

Table 3. Source-reported active-comparator analyses within diabetes-indication reports.

COMPARATOR	OUTCOME	EVENTS SGLT2/REFERENCE	ROR (95% CI)	BH Q
DPP-4 inhibitors	Oral candidiasis	69/12	2.95 (1.60-5.44)	7.41×10^{-04}
DPP-4 inhibitors	Dry mouth	313/102	1.57 (1.26-1.97)	2.89×10^{-04}
GLP-1 receptor agonists	Oral candidiasis	72/14	12.95 (7.31-22.96)	3.67×10^{-18}
GLP-1 receptor agonists	Dry mouth	319/431	1.87 (1.61-2.16)	4.57×10^{-17}
Active non-SGLT2	Oral candidiasis	65/32	11.47 (7.51-17.51)	1.87×10^{-29}
Active non-SGLT2	Dry mouth	288/638	2.56 (2.22-2.94)	4.46×10^{-39}

Note: BH, Benjamini-Hochberg; CI, confidence interval; DPP-4, dipeptidyl peptidase-4; GLP-1, glucagon-like peptide-1; ROR, reporting odds ratio; SGLT2, sodium-glucose cotransporter 2. Group definitions and denominators were unavailable; values must not be interpreted as comparative risk.

Comparator-dependent magnitude

The dry-mouth comparator RORs occupied a narrower range, from 1.57 against DPP-4 inhibitors to 2.56 against the broader active non-SGLT2 group, whereas the oral-candidiasis estimates varied more than fourfold across comparator definitions. Directional agreement therefore coexisted with substantial reference-set dependence. The available data did not show whether this variation arose from exposure prevalence, event prevalence, class composition, overlap exclusions, channeling, market age, or competition from other reported reactions. Comparator outputs were consequently used to qualify, rather than rank, the two main signals.

Numerical traceability

All co-report counts, RORs, CIs, and q values shown in the main manuscript and supplement matched the supplied aggregate tables. No complete role-specific or comparator-specific 2x2 table was available, and the 174,627 overall exposed-report count could not substitute for those missing denominators. Internal transcription consistency therefore passed, while independent statistical reconstruction remained unavailable. Scientific notation was reformatted for readability without changing the underlying values.

Selected stratum outputs

Each dimension contributed one oral-candidiasis cell and one dry-mouth cell. Event counts ranged from 18 to 80 for the selected oral-candidiasis cells and from 95 to 399 for the selected dry-mouth cells. These are not complete stratum distributions: cells with smaller counts, estimates below 1, or wider intervals were not available for comparison. The isolated values were therefore not used to assess subgroup consistency, effect modification, or differential reporting across levels. Representative high-volume cells are summarized in Table 4.

Exploratory launch-era outputs

Early cells contained zero to 28 events, whereas several later cells were more populated. The table shows pronounced imprecision for sparse ingredients and outcomes, including zero to three events in all ertugliflozin cells. Exact launch dates, calendar boundaries, exposed/reference totals, and multiplicity definitions were unavailable. These outputs are presented descriptively and do not test temporal change, stimulated reporting, or ingredient-level risk differences. Selected ingredient-era estimates are shown with the representative strata in Table 4.

Table 4. Selected source-reported stratum and ingredient-era results.

STRATUM OR ERA	OUTCOME	NO. EVENTS	ROR (95% CI)	BH Q
Country: US	Oral candidiasis	80	2.75 (2.21-3.43)	4.54×10^{-18}
Sex: Female	Oral candidiasis	52	1.89 (1.44-2.48)	1.49×10^{-05}
Diabetes indication	Oral candidiasis	72	4.25 (3.25-5.57)	1.54×10^{-25}
Country: US	Dry mouth	399	1.59 (1.44-1.76)	3.68×10^{-19}
Age: 45-64 years	Dry mouth	142	1.34 (1.13-1.58)	0.001
Diabetes indication	Dry mouth	319	1.98 (1.75-2.23)	6.84×10^{-29}
Canagliflozin: later	Oral candidiasis	29	2.12 (1.48-3.06)	2.05×10^{-04}
Empagliflozin: later	Oral candidiasis	38	1.74 (1.27-2.40)	0.001
Dapagliflozin: first 2 y	Dry mouth	28	2.09 (1.44-3.03)	4.26×10^{-04}
Empagliflozin: first 2 y	Dry mouth	16	3.50 (2.14-5.74)	2.66×10^{-06}

Note: BH, Benjamini-Hochberg; CI, confidence interval; ROR, reporting odds ratio. These representative source-reported cells are descriptive. Complete stratum and ingredient-era outputs are provided in Supplementary Tables S4 and S5.

4. Discussion

The supplied FAERS aggregate output showed two directionally consistent reporting patterns. Oral candidiasis and dry mouth met the source-defined compound signal rule in the primary-suspect analysis, and their estimates remained above 1 across the reported broader role scopes and diabetes-indication comparator groups. These directions do not constitute independent replication because the underlying contingency cells, dictionaries, and code were unavailable. Periodontal disease had zero primary-suspect co-reports and remained non-conclusive; neither a protective interpretation nor absence of association is supported.

The oral candidiasis signal should be interpreted against two overlapping but distinct bodies of evidence. First, SGLT2 inhibitors have a well-characterized association with genital mycotic infection. Randomized and observational studies attribute that association partly to pharmacologically induced glycosuria, while identifying female sex and prior infection as important risk markers.[6-10] Second, people receiving SGLT2 inhibitors often have diabetes, a condition already associated with oral mucosal and salivary abnormalities.[11-23] The present signal could therefore reflect a drug contribution, the underlying metabolic disease, the characteristics of patients selected for an SGLT2 inhibitor, or a combination of these mechanisms. FAERS cannot separate these explanations because it lacks standardized information on glycemic control, diabetes duration, oral hygiene, denture use, smoking, nutrition, antimicrobial exposure, inhaled corticosteroids, immune status, and salivary measurements.

A direct oral extension of the genitourinary mycotic mechanism is biologically uncertain. SGLT2 inhibition increases glucose in urine, not necessarily in saliva. Diabetes and poor glycemic control, however, can alter salivary quantity and composition, and several studies have related salivary glucose or impaired salivary function to Candida carriage.[11-18,21] Candida colonization alone is also not synonymous with clinical oral candidiasis. Transition to symptomatic infection depends on fungal biofilm behavior, epithelial interaction, local immunity, salivary defense, prosthetic surfaces, and other host factors.[19,20] The exact MedDRA term used here likely improves specificity relative to an unrestricted fungal-event search but cannot confirm whether a reporter documented pseudomembranous candidiasis, erythematous candidiasis, angular cheilitis, denture stomatitis, culture results, cytology, or empiric antifungal treatment. Thus, the ROR indicates unusual co-reporting of the label Oral candidiasis, not a validated clinical phenotype.

The secondary oral candidiasis spectrum composite produced slightly larger estimates than the exact term, including a primary-suspect ROR of 1.91 compared with 1.71. That difference could indicate capture of related clinical coding, but it could also reflect inclusion of nonspecific or differently ascertained terms. Because the component Preferred Terms were not supplied, readers cannot judge its sensitivity, specificity, overlap, or susceptibility to coding drift. Restricting the main conclusion to exact Oral candidiasis therefore represents a

deliberate reporting safeguard. Future work should publish complete MedDRA term lists and, ideally, evaluate narrow and broad definitions side by side with case-level validation.

The dry-mouth finding was numerically the largest by report count and highly precise in the primary analysis. Its direction was similar across the supplied role and comparator outputs, but missing denominators and group definitions prevent determining whether attribution or comparator construction explains the pattern. Nevertheless, Dry mouth in FAERS is a subjective reaction term. It may represent xerostomia, thirst, dehydration, oral burning, medication-related dryness, or a symptom entered without objective salivary assessment. This distinction is clinically important: xerostomia can occur with apparently normal salivary flow, and hyposalivation can be present without a prominent dryness complaint.[11–15,23] Diabetes, older age, polypharmacy, autonomic dysfunction, kidney disease, depression, and many commonly used medicines can all influence oral dryness. Osmotic diuresis or volume depletion from SGLT2 therapy provides one possible pathway, but the available reports do not permit mediation analysis or confirmation of temporal sequence.

The coexistence of dry-mouth and candidiasis signals warrants particular attention because salivary dysfunction can reduce mechanical clearance, buffering, lubrication, and antimicrobial activity. Meta-analytic evidence has associated xerostomia or hyposalivation with Candida growth and clinical oral candidiasis.[21] However, the present data do not show that the same patients had both events, that dryness preceded candidiasis, or that an SGLT2 inhibitor caused either event. A shared reporting environment could also generate both signals: patients with diabetes who seek care for oral discomfort may be examined more closely, producing additional fungal diagnoses, while clinicians aware of dehydration or infection risks may be more likely to attribute the event to the drug. Patient-level co-occurrence, time-to-onset, and sequential mediation analyses would be needed to test a linked pathway.

Periodontal disease provides a useful contrast. Diabetes is an established modifier of periodontitis and medical-dental consensus recommends integrated risk assessment and care.[24–26] Yet the FAERS primary-suspect analysis contained no periodontal co-report. This discrepancy does not weaken the established diabetes-periodontitis literature; instead, it illustrates the limits of spontaneous reporting for chronic, multifactorial oral disease. Periodontitis develops over time, may be diagnosed outside the encounter in which a drug is prescribed, and is unlikely to be considered an acute adverse drug reaction. Coding may also be distributed across gingivitis, tooth loss, periodontal infection, dental abscess, or procedure terms rather than a single Periodontal disease Preferred Term. The absence of a signal therefore reflects reporting and case-definition properties at least as much as biology.

The source-reported drug-role sensitivity results add directional context but require restraint. The oral candidiasis ROR ranged only from 1.66 to 1.71 and the dry-mouth ROR from 1.49 to 1.54 across all-role, suspect-only, and primary-suspect analyses. This limited variation suggests that broader inclusion of concomitant roles increased event counts without reversing or materially diluting the associations. However, roles are assigned by reporters or manufacturers and can be influenced by knowledge of labeled adverse events, timing, incomplete medication lists, or regulatory follow-up. Consistency across role scopes reduces dependence on a single definition; it does not transform a spontaneous report into a causal observation.

The broader SGLT2 pharmacovigilance literature provides context for interpreting an oral signal without treating database recurrence as causal confirmation. Recent spontaneous-report studies have examined pancreatitis, acute kidney injury, ketoacidosis, renal cancer, ertugliflozin-specific profiles, pancreatitis across newer diabetes medicines, statin-associated myotoxicity reporting, and creatinine-clearance patterns.[34–41] Collectively, these studies show that the apparent signal landscape changes with the event definition, ingredient, co-medication, comparator, database period, reporting threshold, and analytic specification. They also demonstrate why a statistically precise ROR cannot substitute for clinical adjudication or an exposure denominator. For the present analysis, this literature supports the choice of multiple role and comparator views, but it does not independently validate the oral-event estimates because the studies addressed different phenotypes and analytical populations. The oral findings should therefore enter the same staged evidence pathway used for other potential safety signals: verify coding and report quality, examine timing and alternative causes, reproduce the analysis with complete definitions, test transportability in another reporting system, and then estimate clinical occurrence in controlled observational or prospective data. This staged interpretation is particularly important for oral candidiasis and dry mouth because both can arise from diabetes, polypharmacy, hydration status, local oral conditions, and care-seeking behavior. A coherent signal across several FAERS specifications is a reason to investigate; it is not evidence that the medicine caused every reported event.

The source-reported active-comparator results addressed one aspect of confounding by indication by restricting analyses to reports with a diabetes indication. Directional consistency was observed, but the magnitude for oral candidiasis varied from an ROR of 2.95 against DPP-4 inhibitors to approximately 13 against GLP-1 receptor agonists. Such a spread is unlikely to be explained solely by a stable biological effect. Comparator classes differ in route of administration, duration on the market, treatment position, patient phenotype, kidney function, weight, gastrointestinal adverse effects, media attention, and reporting propensity. Some non-case events may also be highly represented in one comparator group, producing masking or competition bias.[29–31] Accordingly, the source-reported analyses show directional agreement within the supplied output but do not rank oral safety among glucose-lowering therapies and should not be interpreted as comparative incidence.

Magnitude deserves particular caution even in the primary analysis. An ROR of 1.71 for oral candidiasis means that the odds of the event label relative to other reported events were higher among the selected SGLT2 reports than in the reference reports under the specified case-non-case construction. It does not mean that patients were 71% more likely to develop candidiasis, nor can it be converted into an absolute risk. The dry-mouth ROR of 1.54 has the same constraint. In a database shaped by reporting decisions, a modest, precise ROR may reflect a common but weak reporting imbalance, whereas a large sparse ROR may reflect few cases, a narrow comparator, or stimulated reporting. Clinical priority therefore depends on case quality, seriousness, reversibility, plausibility, exposure extent, and corroboration from other designs, not on point-estimate rank alone.[27,29–32]

The selected stratum cells are descriptive only. The source supplied the densest cell for each dimension and outcome rather than all levels, so the estimates cannot establish subgroup robustness or effect modification. Apparent differences between female oral-candidiasis cells and male dry-mouth cells, or between reporter and seriousness categories, may reflect data-dependent selection, report composition, exposure patterns, or competing reactions. Complete stratum tables with denominators and appropriately justified heterogeneity tests would be needed for subgroup inference.

The exploratory ingredient-era outputs were heterogeneous and often sparse. However, the exact launch dates, quarterly boundaries, denominators, and multiplicity families were unavailable, so early-versus-later estimates cannot test temporal change, stimulated reporting, or accumulated exposure. Their defensible role is to show that ingredient-specific source outputs vary in precision and should not be generalized uniformly across the class.

For clinical practice, these findings support careful documentation when a suspected oral event is encountered, not a validated screening program or routine discontinuation. Relevant details include symptom onset relative to treatment, oral examination, salivary symptoms, dentures, antibiotics or corticosteroids, glycemic control, kidney function, hydration, co-medications, treatment response, and any drug interruption or rechallenge. The established cardiovascular, heart-failure, and kidney benefits of SGLT2 inhibitors remain central to individualized decisions.[1–5] A spontaneous-reporting signal alone is insufficient to withdraw effective therapy.

The findings also have implications for collaboration between pharmacovigilance and oral health. Oral adverse events may be fragmented across dental records, primary care, endocrinology, nephrology, and patient self-reports. A standardized oral-event module for suspected medicine-related cases could distinguish xerostomia from measured hyposalivation, Candida carriage from clinical candidiasis, and chronic periodontitis from acute periodontal infection. Incorporating denture status, oral hygiene, HbA1c, salivary flow, antibiotic or corticosteroid exposure, and photographs or laboratory confirmation where appropriate would markedly improve report utility. Such detail would help reviewers determine whether oral candidiasis and dry mouth are independent outcomes, sequential events, or manifestations of another process such as dehydration or uncontrolled diabetes.

Strengths of the supplied analysis include broad quarterly coverage, a stated deterministic within-CASEID latest-version rule, deletion-file handling, exact primary outcome terms, nested drug-role scopes, active-comparator outputs, and a compound signal criterion that does not treat a small q value alone as a positive finding. This manuscript further separates exact terms from an undocumented composite and applies READUS-PV to expose missing analytical details rather than mark them as complete.[28,29] These strengths concern the structure and reporting of the supplied aggregate output; they do not overcome the absence of study-specific data, dictionaries, code, and complete contingency tables.

Generalizability is bounded by both the database and the treatment population. FAERS accepts reports from the United States and other countries, but reporting laws, access to dental care, diagnostic terminology, and awareness of adverse reactions differ across settings. Country was complete in the supplied summary, yet completeness of a country field does not imply comparable surveillance intensity. SGLT2 prescribing also changed during the study period as indications expanded from glycemic control to heart failure and chronic kidney disease. Later users may be older, have different comorbidity patterns, or receive the medicine from different specialties than early users. The class-level analysis consequently represents a changing mixture of ingredients, indications, reporters, and health systems. It is appropriate for hypothesis generation across the observed database but should not be generalized directly to a particular drug, dose, country, dental population, or patient with or without diabetes. Ingredient-specific and indication-specific estimates with exposure denominators are necessary for those questions.

The limitations are substantial. FAERS has unknown and changing reporting probabilities, no exposed-population denominator, and cannot estimate prevalence, incidence, risk difference, or number needed to harm.[27,30,31] Residual duplicates may remain across CASEIDs, while indication, dose, duration, comorbidity, co-medication, oral status, chronology, and clinical confirmation are often missing. The aggregate report-flow counts could not be decomposed into separately additive superseded and deletion exclusions. Full exposure/comparator dictionaries, MedDRA version handling, composite terms, contingency cells, hypothesis families, zero-cell correction, complete strata, launch intervals, software versions, and code were unavailable. Consequently, the reproduced RORs and q values could not be independently recalculated, and adjusted models, diagnostics, alternative definitions, and influence analyses were not feasible. Active-comparator, selected-stratum, and era outputs do not remove confounding, channeling, masking, competition, notoriety, or selection bias.[29–31] External replication was not performed.

The report-flow ambiguity illustrates why aggregate provenance matters even when headline counts appear internally plausible. The raw-to-final difference exactly equals the value labeled as removed versions, yet deletion-file identifiers are also reported as an exclusion. Possible explanations include overlap, a combined exclusion label, or counts taken at different processing stages, but the supplied files cannot distinguish them. We therefore retain each source value, prevent readers from adding the exclusions as sequential losses, and avoid a false flow diagram. Resolving this ambiguity and enabling independent verification require the exact archive list and quarter-level audit log, explicit intermediate counts, ingestion and transformation code, deletion handling, drug and indication dictionaries, the MedDRA version and term sets, report-level collapsing rules, role-specific reference definitions, complete contingency cells, multiplicity families, software versions, and generated outputs. Publishing these materials would permit reconstruction of the current estimates and testing of alternative specifications. Until they are available, the defensible contribution is a transparent, clinically situated account of supplied aggregate signals and their evidential boundaries, not a reusable analysis package.

Oral-health validation should also improve phenotype quality. A prospective or record-linked study could separate the subjective Dry mouth label from standardized xerostomia instruments and measured unstimulated or stimulated salivary flow. Oral candidiasis should be confirmed by examination, with mycology when clinically indicated, and distinguished from colonization, denture stomatitis, angular cheilitis, burning symptoms, and empiric antifungal treatment. Periodontal outcomes require longitudinal dental assessment rather than

reliance on a single spontaneous-report term. Recording dentures, oral hygiene, caries burden, smoking, antibiotics, inhaled corticosteroids, immune status, HbA1c, renal function, hydration, and co-medications would address major alternative explanations. Predefined diagnostic criteria, blinded outcome adjudication, and protocolized collection timing would reduce differential misclassification and clarify whether symptoms preceded antifungal or supportive treatment. These measurements would determine whether the two reporting signals represent independent events, a dryness-to-candidiasis pathway, characteristics of treated populations, or reporting behavior.

The most informative next study would combine three evidence layers. A case-level FAERS review should adjudicate diagnosis, timing, dechallenge, rechallenge, competing causes, and co-occurrence of dryness and candidiasis. A second spontaneous-report database could test transportability using identical exposure and event definitions. Most importantly, an active-comparator cohort using claims or electronic health records should estimate incidence and adjusted relative risk, while a nested dental study measures salivary flow, oral Candida, glycemic control, hydration, and prosthesis use. Such triangulation could determine whether the present signals reflect causal drug effects, characteristics of SGLT2-treated populations, reporting behavior, or several mechanisms acting together.

5. Conclusion

In the supplied FAERS aggregate output for 2013 Q1 through 2026 Q2, Oral candidiasis and Dry mouth met the source-defined disproportionality signal rule for pure SGLT2 inhibitors and remained directionally above 1 across reported role-scope and active-comparator analyses. Periodontal disease was non-conclusive because of zero or near-zero co-reporting and an undocumented sparse-cell correction. These source-reported findings justify targeted case review and independent replication using complete drug and outcome definitions, contingency cells, and controlled clinical data. Before magnitude is interpreted externally, the report-flow ambiguity and missing analytical specifications should be resolved. Publication of transformation code, dictionaries, denominators, and complete contingency tables would make the signal estimates independently assessable. The findings do not estimate incidence, compare treatment risks, or establish causality.

Declarations

Ethics approval: Ethical approval was granted by the CMHC Ethics Committee Indonesia (No. 003/CMHC/Ethics/08/2025).

Consent to participate: Not applicable to this secondary analysis of publicly available de-identified safety reports.

Funding: This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Conflicts of interest: The authors declare that they have no competing financial or non-financial interests relevant to this work.

Author contributions: Both authors contributed to the conception and design of the study, interpretation of the findings, and critical revision of the manuscript; approved the final version; and agree to be accountable for all aspects of the work.

Data availability: FAERS/AEMS quarterly extracts are publicly available from the US Food and Drug Administration. Aggregate results used in this article are reported in the manuscript. The study-specific case-level analytic dataset, drug and outcome dictionaries, and executable code were unavailable for independent audit.

Use of artificial intelligence: The authors declare that no generative artificial intelligence tools were used in the conceptualization, analysis, writing, editing, or preparation of this manuscript.

References

1. Anker SD, Butler J, Filippatos G, et al. Empagliflozin in heart failure with a preserved ejection fraction. N Engl J Med. 2021;385(16):1451-1461. doi: 10.1056/NEJMoa2107038.
2. Solomon SD, McMurray JJV, Claggett B, et al. Dapagliflozin in heart failure with mildly reduced or preserved ejection fraction. N Engl J Med. 2022;387(12):1089-1098. doi: 10.1056/NEJMoa2206286.
3. EMPA-KIDNEY Collaborative Group, Herrington WG, Staplin N, et al. Empagliflozin in patients with chronic kidney disease. N Engl J Med. 2023;388(2):117-127. doi: 10.1056/NEJMoa2204233.
4. Voors AA, Angermann CE, Teerlink JR, et al. The SGLT2 inhibitor empagliflozin in patients hospitalized for acute heart failure: a multinational randomized trial. Nat Med. 2022;28(3):568-574. doi: 10.1038/s41591-021-01659-1.
5. Marilly E, Cottin J, Cabrera N, et al. SGLT2 inhibitors in type 2 diabetes: a systematic review and meta-analysis of cardiovascular outcome trials balancing their risks and benefits. Diabetologia. 2022;65(12):2000-2010. doi: 10.1007/s00125-022-05773-8.
6. Zhou X, Ye X, Guo X, et al. Safety of SGLT2 inhibitors: a pharmacovigilance study from 2013 to 2021 based on FAERS. Front Pharmacol. 2021;12:766125. doi: 10.3389/fphar.2021.766125.
7. Yoosuf BT, Kt MF, D P S, et al. Risk of genitourinary tract infections with SGLT-2 inhibitors in type 2 diabetes mellitus: a meta-analysis of randomised controlled trials and disproportionality analysis using FAERS. Endocrine. 2025;90(2):439-452. doi: 10.1007/s12020-025-04393-7.
8. Kajiwara-Morita A, Kugimoto S, Oniki K, et al. Sex-specific risk factors for genital infections associated with SGLT2 inhibitors in type 2 diabetes: a retrospective cohort study and disproportionality analysis using JADER. Ther Adv Drug Saf. 2026;17:20420986261462669. doi: 10.1177/20420986261462669.
9. Tian C, Yang Z, Zhao S, et al. Adverse event reporting of combining SGLT2 inhibitor and GLP1 receptor agonist: a real-world study from FAERS. Nutr Metab Cardiovasc Dis. 2025;35(1):103758. doi: 10.1016/j.numecd.2024.09.028.
10. Ahsan M. Serious adverse events reported with sodium-glucose cotransporter-2 inhibitors in the FAERS database (2013-2024): a pharmacovigilance study. Naunyn Schmiedebergs Arch Pharmacol. 2026;399(5):6939-6958. doi: 10.1007/s00210-025-04841-1.
11. Marques RCR, da Silva JR, Vieira Lima CP, et al. Salivary parameters of adults with diabetes mellitus: a systematic review and meta-analysis. Oral Surg Oral Med Oral Pathol Oral Radiol. 2022;134(2):176-189. doi: 10.1016/j.oooo.2022.03.001.
12. Al-Maweri SA, Altayyar MO, AlQahtani KW, et al. Xerostomia, salivary flow, and oral health status among Saudi diabetic patients: a comparative cross-sectional study. Clin Cosmet Investig Dent. 2021;13:451-458. doi: 10.2147/CCIDE.S337581.
13. Sánchez Garrido I, Ramírez L, Muñoz Corcuera M, et al. Xerostomia and salivary dysfunction in patients with diabetes mellitus: a cross-sectional study. J Oral Pathol Med. 2024;53(10):622-636. doi: 10.1111/jop.13583.
14. Huang S, Zeng X, Deng S, et al. Prevalence of xerostomia in patients with type 2 diabetes mellitus: a systematic review and meta-analysis. BMC Oral Health. 2025;25(1):662. doi: 10.1186/s12903-025-05992-6.
15. Zhou G, Shu X, Long Y, et al. Dental caries and salivary alterations in patients with type 2 diabetes: a systematic review and meta-analysis. J Dent. 2024;150:105321. doi: 10.1016/j.jdent.2024.105321.
16. Nouraei H, Jahromi MG, Jahromi LR, et al. Potential pathogenicity of Candida species isolated from oral cavity of patients with diabetes mellitus. Biomed Res Int. 2021;2021:9982744. doi: 10.1155/2021/9982744.
17. Zarei N, Roudbary M, Roudbar Mohammadi S, et al. Prevalence, molecular identification, and genotyping of Candida species recovered from oral cavity among patients with diabetes mellitus from Tehran, Iran. Adv Biomed Res. 2022;11(1):29. doi: 10.4103/abr.abr_26_21.
18. Pérez-Vielma NM, Gómez-López M, Martínez-Godínez MLÁ, et al. Candida variety in the oral cavity of Mexican subjects with type 2 diabetes mellitus and TLR2 gene expression. Clin Pract. 2024;14(2):417-425. doi: 10.3390/clinpract14020031.

19. Lu SY. Oral candidosis: pathophysiology and best practice for diagnosis, classification, and successful management. J Fungi (Basel). 2021;7(7):555. doi: 10.3390/jof7070555.
20. Patel M. Oral cavity and Candida albicans: colonisation to the development of infection. Pathogens. 2022;11(3):335. doi: 10.3390/pathogens11030335.
21. Molek M, Florenly F, Lister INE, et al. Xerostomia and hyposalivation in association with oral candidiasis: a systematic review and meta-analysis. Evid Based Dent. 2022. doi: 10.1038/s41432-021-0210-2.
22. Seixas R, Pessegueiro P. Management and diagnosis of empagliflozin-induced burning mouth syndrome: a case report. Cureus. 2024;16(10):e70701. doi: 10.7759/cureus.70701.
23. Mawardi HH, Almazrooa SA, Dakhil SA, et al. Semaglutide-associated hyposalivation: a report of case series. Medicine (Baltimore). 2023;102(52):e36730. doi: 10.1097/MD.0000000000036730.
24. Stöhr J, Barbaresko J, Neuenschwander M, et al. Bidirectional association between periodontal disease and diabetes mellitus: a systematic review and meta-analysis of cohort studies. Sci Rep. 2021;11(1):13686. doi: 10.1038/s41598-021-93062-6.
25. Simpson TC, Clarkson JE, Worthington HV, et al. Treatment of periodontitis for glycaemic control in people with diabetes mellitus. Cochrane Database Syst Rev. 2022;4(4):CD004714. doi: 10.1002/14651858.CD004714.pub4.
26. Alwithanani N. Periodontal diseases and diabetes mellitus: a systematic review. J Pharm Bioallied Sci. 2023;15(Suppl 1):S54-S63. doi: 10.4103/jpbs.jpbs_515_22.
27. US Food and Drug Administration. FDA Adverse Event Monitoring System (AEMS) quarterly data extract files. Available from: https://fis.fda.gov/extensions/FPD-QDE-FAERS/FPD-QDE-FAERS.html. Accessed August 4, 2026.
28. Fusaroli M, Salvo F, Begaud B, et al. The Reporting of a Disproportionality Analysis for Drug Safety Signal Detection Using Individual Case Safety Reports in PharmacoVigilance (READUS-PV): development and statement. Drug Saf. 2024;47(6):575-584. doi: 10.1007/s40264-024-01421-9.
29. Fusaroli M, Salvo F, Begaud B, et al. The REporting of A Disproportionality Analysis for DrUg Safety Signal Detection Using Individual Case Safety Reports in PharmacoVigilance (READUS-PV): explanation and elaboration. Drug Saf. 2024;47(6):585-599. doi: 10.1007/s40264-024-01423-7.
30. Gravel CA, Douros A. Considerations on the use of different comparators in pharmacovigilance: a methodological review. Br J Clin Pharmacol. 2023;89(9):2671-2676. doi: 10.1111/bcp.15802.
31. Fusaroli M, Sartori D, van Puijenbroek EP, et al. Charting and sidestepping the pitfalls of disproportionality analysis. Drug Saf. 2026;49(2):147-162. doi: 10.1007/s40264-025-01604-y.
32. Rothman KJ, Lanes S, Sacks ST. The reporting odds ratio and its advantages over the proportional reporting ratio. Pharmacoepidemiol Drug Saf. 2004;13(8):519-523. doi: 10.1002/pds.1001.
33. Benjamini Y, Hochberg Y. Controlling the false discovery rate: a practical and powerful approach to multiple testing. J R Stat Soc Series B Stat Methodol. 1995;57(1):289-300. doi: 10.1111/j.2517-6161.1995.tb02031.x.
34. Palapra H, Viswam SK, Kalaiselvan V, et al. SGLT2 inhibitors associated pancreatitis: signal identification through disproportionality analysis of spontaneous reports and review of case reports. Int J Clin Pharm. 2022;44(6):1425-1433. doi: 10.1007/s11096-022-01476-7.
35. Chen G, Li X, Cui Q, et al. Acute kidney injury following SGLT2 inhibitors among diabetic patients: a pharmacovigilance study. Int Urol Nephrol. 2022;54(11):2949-2957. doi: 10.1007/s11255-022-03211-7.
36. He Z, Lam K, Zhao W, et al. SGLT-2 inhibitors and euglycemic diabetic ketoacidosis/diabetic ketoacidosis in FAERS: a pharmacovigilance assessment. Acta Diabetol. 2023;60(3):401-411. doi: 10.1007/s00592-022-02015-6.
37. Xu B, Zhou J. Sodium-glucose cotransporter 2 inhibitors and renal cancer in the US FDA adverse event reporting system. Eur J Clin Pharmacol. 2024;80(12):1959-1966. doi: 10.1007/s00228-024-03759-6.
38. Dong H, Guo Q, Cai M, et al. Post-marketing safety profile of ertugliflozin: insights from a real-world pharmacovigilance analysis based on the FAERS database. Eur J Pharmacol. 2025;1005:178077. doi: 10.1016/j.ejphar.2025.178077.
39. Alenzi KA, Alsuhaibani D, Batarfi B, et al. Pancreatitis with use of new diabetic medications: a real-world data study using the post-marketing FDA Adverse Event Reporting System database. Front Pharmacol. 2024;15:1364110. doi: 10.3389/fphar.2024.1364110.
40. Gravel CA, Krewski D, Mattison DR, et al. Concomitant use of statins and sodium-glucose co-transporter 2 inhibitors and the risk of myotoxicity reporting: a disproportionality analysis. Br J Clin Pharmacol. 2023;89(8):2430-2445. doi: 10.1111/bcp.15711.
41. Uwai Y, Nabekura T. SGLT2 inhibitors may increase creatinine clearance: data mining utilizing the FDA Adverse Event Report System database and pharmacokinetic study with rats. Pharmacology. 2025;110(5):301-308. doi: 10.1159/000546838.