



A Safety-Aware Clinical Evidence Mapping Approach for SGLT2 Inhibitors and GLP-1 Receptor Agonists in Type 2 Diabetes

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Abstract- Background: SGLT2 inhibitors and GLP-1 receptor agonists (GLP-1 RAs) support type 2 diabetes care through different mechanisms and have different safety concerns. Existing reviews summarize benefits, but brief clinical comparisons can overlook precautions that affect treatment discussions. **Objective:** To design and demonstrate a safety-aware evidence mapping approach using sources published during 2022–2024. **Methods:** We identified outcome and precaution statements in established guidance, a 2023 network meta-analysis and the 2024 FLOW trial. We developed a two-layer map: an outcome-priority layer and a medicine-specific safety-check layer. The approach was demonstrated using three fictional clinical profiles. **Results:** The implementation generated distinct review prompts for a heart-failure profile, a weight-management profile and a chronic-kidney-disease profile. All three required a safety check before clinical interpretation. The demonstration created no patient-level efficacy estimates or new relative treatment effects. **Conclusion:** A simple safety-aware map may improve the transparency of educational evidence summaries, but clinical validation and independent testing are necessary before use as a decision-support tool.

Keywords- Type 2 diabetes; SGLT2 inhibitor; GLP-1 receptor agonist; medication safety; evidence mapping; clinical decision support.



I. INTRODUCTION

Choosing glucose-lowering therapy increasingly depends on more than HbA1c. Clinicians also consider cardiovascular disease, heart failure, chronic kidney disease (CKD), body weight, tolerability, cost and patient preference [1–4]. SGLT2 inhibitors increase urinary glucose loss, whereas GLP-1 RAs act through glucose-dependent incretin pathways. Because the two classes differ in both benefits and harms, an outcome-only summary can be incomplete.

The supplied first manuscript reviews clinical evidence through 2024, and the second introduces an Outcome-Specific Evidence Benchmark (OSEB). This third work takes a different direction: it puts a separate safety and monitoring layer next to the evidence summary. It is an educational method demonstration, not another meta-analysis, not a validated prescribing algorithm and not a comparison showing superior treatment effectiveness.

Aim and contribution

The aim is to create a small, reproducible workflow that records (a) the principal outcome being considered, (b) relevant drug-class precautions and (c) questions requiring clinical review before drawing a treatment conclusion. The contribution is a structured checklist and its worked application to fictional scenarios, rather than a pooled odds ratio or a new medicine ranking.

II. MATERIALS AND METHODS

1. Evidence window

The retrospective source window was 1 January 2022 to 31 December 2024. Evidence inputs included the ADA/EASD consensus report (2022), the BMJ network meta-analysis (2023), the ADA 2024 Standards of Care and the FLOW trial (2024) [1–6]. They were selected for an illustrative evidence-mapping exercise, not by a completed systematic-review search. Earlier methodological work and sources published in 2025 or later were not used in this manuscript.

2. Safety-aware evidence map

For each fictional profile, the following sequence was applied: (1) record the main clinical priority; (2) identify which outcomes are addressed in the sources; (3) review SGLT2 class precautions; (4) review



GLP-1 RA class precautions; (5) label the remaining information as “requires clinician assessment.” No numerical weights were assigned, because such weights would need stakeholder elicitation and prospective validation.

Table 1. Components of the proposed safety-aware clinical evidence map

Component	Recorded information	Purpose
Outcome priority	Glycaemia, weight, heart failure, kidney disease or cardiovascular risk	Keep the clinical question specific
Evidence anchor	Study/guideline, publication year, studied population and comparator	Prevent unsupported direct comparisons
SGLT2 safety check	Genital infections, dehydration/volume status, ketoacidosis risks, intercurrent illness	Prompt review of class-specific cautions
GLP-1 RA safety check	Gastrointestinal intolerance, dose escalation, gallbladder concerns	Prompt review of class-specific cautions
Decision status	Evidence summarized / information missing / clinician review needed	Avoid automatic prescribing

3. Fictional-case implementation

We constructed three illustrative situations with no real patient data. Case A prioritized heart failure; Case B emphasized weight reduction; Case C highlighted type 2 diabetes with CKD. For each case we applied the same five-step checklist, noting that comorbidities, medications, kidney function and individual contraindications were not sufficiently specified to recommend treatment.

III. RESULTS

Table 2. Demonstration of the safety-aware map in three fictional profiles

Scenario	Evidence-oriented question	SGLT2 check	GLP-1 RA check	Output
A: T2DM + heart failure	What heart-failure outcomes are supported by evidence?	Assess volume status and sick-day risk	Review tolerability and other clinical priorities	Heart-failure evidence + safety review required



B: T2DM + weight goal	What weight and glucose changes are relevant?	Discuss modest weight effects and infection risk	Review GI tolerability and gradual dose titration	Weight-focused evidence + safety review required
C: T2DM + CKD	What kidney outcomes apply to this population?	Check kidney-function and volume context	Review 2024 FLOW population and tolerability	Kidney-focused evidence + safety review required

The demonstration produced three differently focused evidence summaries and retained both safety columns in every case. It did not produce a quantitative accuracy score or measure clinical outcomes. This is an implementation check that the workflow can be applied consistently to simple scenarios, not evidence that patient decisions improve.

Table 3. Comparison of this work with the two supplied manuscripts

Dimension	Paper 1: evidence review	Paper 2: OSEB	Paper 3: proposed method
Main question	What does 2022–2024 literature report?	How should published effects be organized?	What precautions must accompany outcome summaries?
Primary output	Narrative evidence synthesis	Outcome-specific reporting template	Two-layer safety and outcome checklist
Implementation	No independent pooled estimates	Worked logarithmic conversion	Three fictional case walkthroughs
Validation status	Not a completed meta-analysis	Not validated as a prediction model	Not clinically validated

IV. DISCUSSION

The main benefit of this format is that safety does not disappear when the discussion concentrates on a desirable outcome. For example, heart-failure evidence may favor careful consideration of an SGLT2 inhibitor in an eligible patient, yet volume status and ketoacidosis precautions still matter. A weight-



centered discussion may draw attention to GLP-1 RA evidence, while nausea, vomiting and dose escalation need consideration. These statements are aligned with the risk-based approach in consensus guidance and the 2024 Standards of Care [1,3–5].

The FLOW trial demonstrated kidney benefit with semaglutide versus placebo in patients with type 2 diabetes and CKD (primary-outcome hazard ratio 0.76; 95% CI 0.66–0.88) [6]. That result cannot be treated as a direct head-to-head estimate against an SGLT2 inhibitor. Likewise, comparing narrative statements between classes does not establish their relative efficacy. The safety map intentionally uses questions and caution flags instead of inventing comparable effect sizes.

Limitations and future work

This paper uses a selected, non-exhaustive evidence set; it does not meet PRISMA systematic-review requirements. The fictional cases were not reviewed by independent clinicians or tested on patient records. No sensitivity, specificity, inter-rater agreement, treatment-effect estimate or clinical outcome improvement was measured. Future studies could define a consensus checklist with pharmacists and diabetologists, measure agreement between independent reviewers and compare omissions in safety reporting with and without the map. Clinical deployment would additionally require governance, external validation and integration with current prescribing information.

V. CONCLUSION

A safety-aware evidence map can place treatment goals and key class precautions in one readable workflow. The 2022–2024 literature supports individualized selection of SGLT2 inhibitors and GLP-1 RAs, but does not justify a single best treatment for everyone. The proposed approach is suitable for further educational and research evaluation; it should not be used to prescribe or change medication without clinical assessment.

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