

Trends in Acidosis Incidence Among New Users of SGLT2 Inhibitors Following Expanded Indications, 2020-2023



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BACKGROUND

- SGLT2 inhibitors (SGLT2i) were initially approved for glycemic control in type 2 diabetes (T2D), but indications have since expanded to include heart failure (HF) and chronic kidney disease (CKD)
 - New mix of patients with higher comorbidity burden and different risk profiles
- Diabetic ketoacidosis (DKA) and related events are serious complications of SGLT2i use and can occur even in patients without diabetes
- As SGLT2i's increase in popularity, there may be an increased population-level acidosis risk profile that differs from previously known
- Post-marketing, real world evidence is critical to monitor how acidosis incidence evolves alongside shifting prescribing patterns and an increasingly complex patient population

OBJECTIVE

To quantify the acidosis incidence among new SGLT2i users and evaluate trends in exposure, indications, and risk using recent U.S. claims data

METHODS

- Retrospective cohort study
- Commercial claims data (Jan 2020 - Jun 2024) via National Drug Codes (NDC)

- Inclusion Criteria**
- Adults with no SGLT2i fills in the 12 months prior to first qualifying fill
 - ≥12 months of continuous medical and pharmacy enrollment prior to index date

- Data Collected and Outcomes**
- Baseline characteristics, indications of SGLT2i use, acidotic events
 - Follow-up until 12 months post-index, censored at first acidosis event
 - Acidosis identified using broad ICD-10 codes to improve capture of events
 - Only acidosis events occurring ≥7 days post-index
 - SGLT2i exposure at acidosis
 - Primary outcome was acidosis incidence rate per 1,000 person years (PY), calculated as (total acidosis events / total follow-up years) x 1,000
 - Patients were categorized as having diabetes, HF, CKD, multiple indications (≥2 of 3), or other based on diagnosis codes from baseline

Scheme 1. Study Cohort Selection and Attrition Flowchart

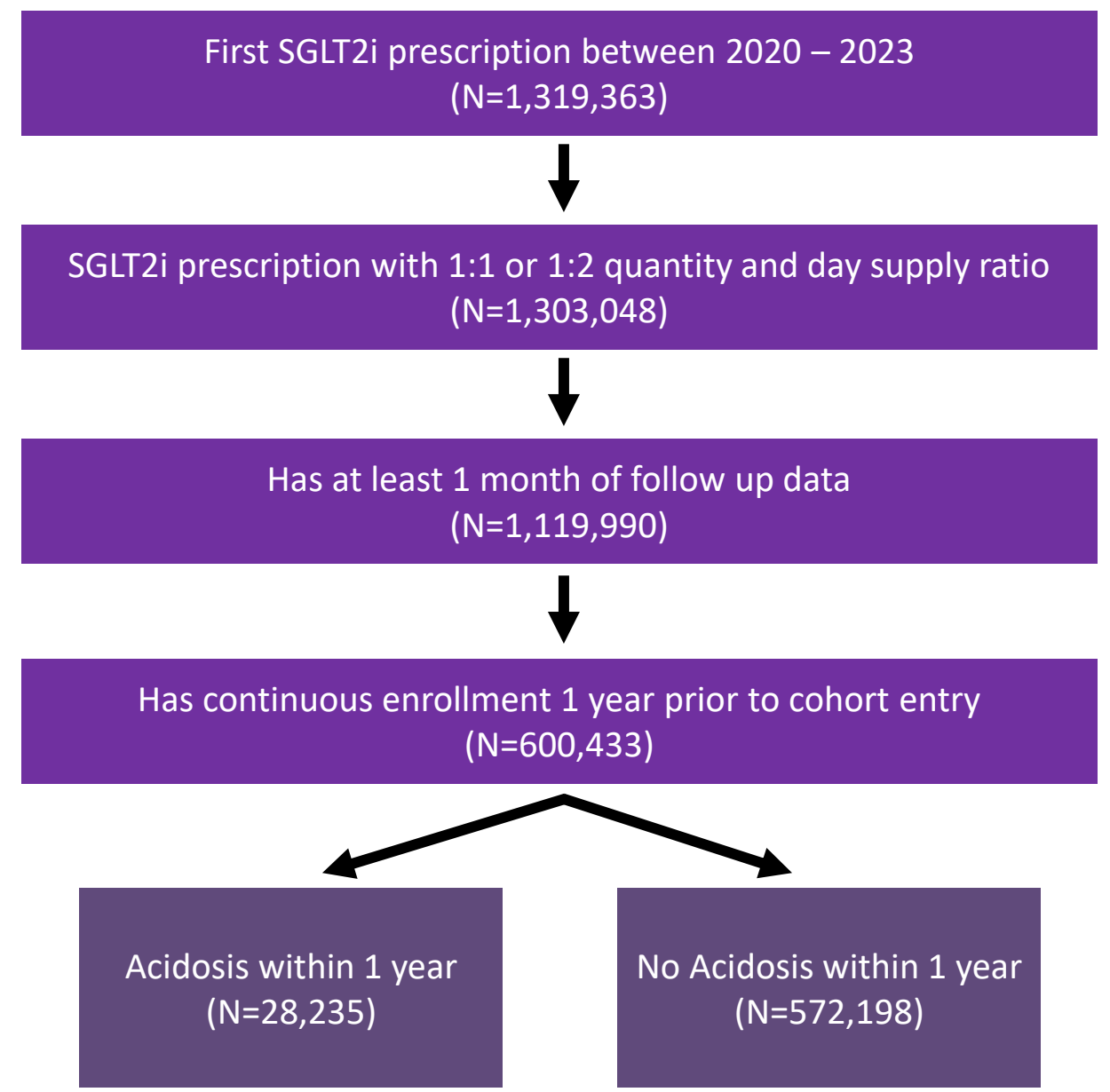


Figure 1. Monthly New SGLT2i Users and Acidosis Counts

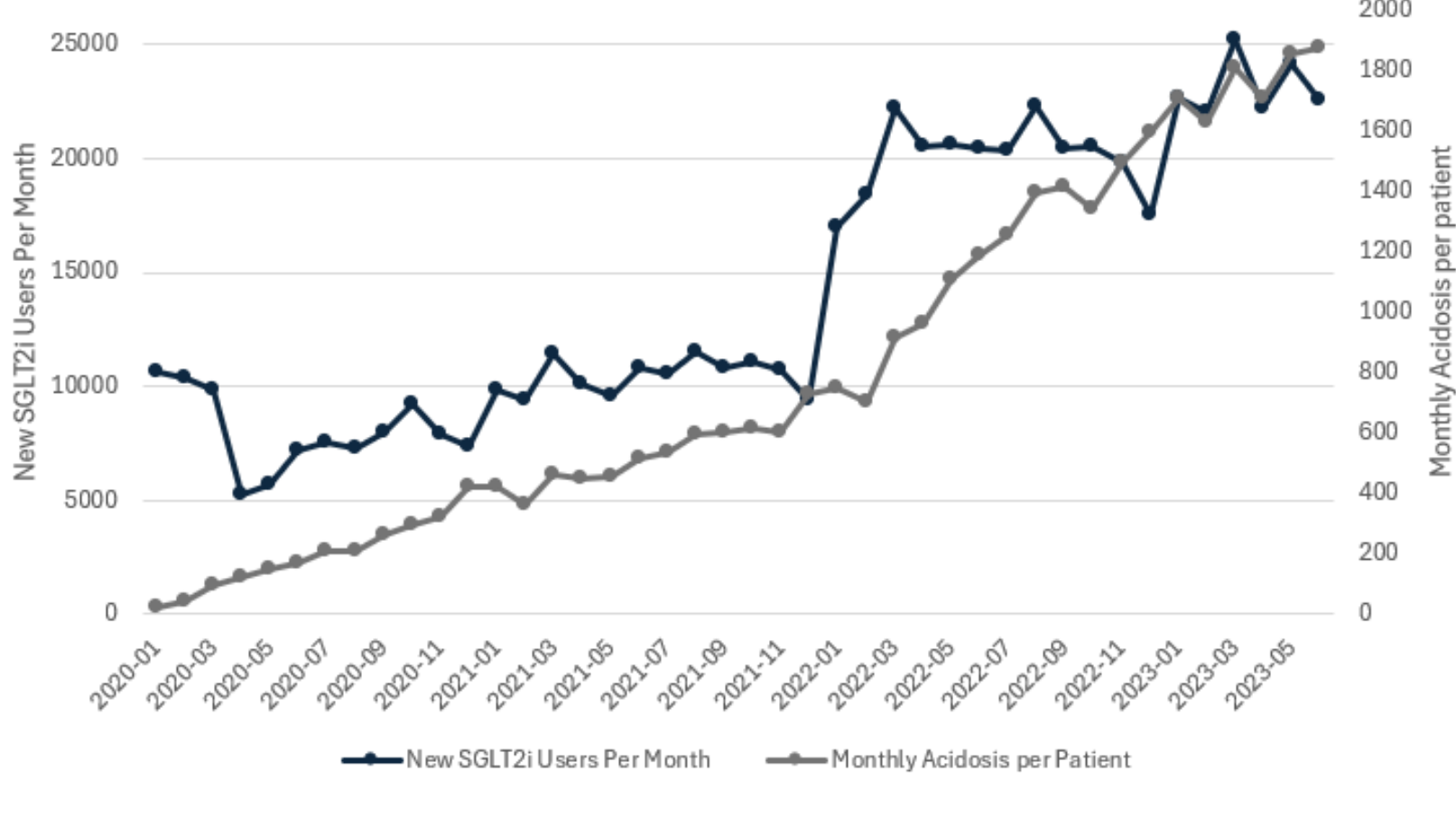


Table 1. Annual and Average Monthly New SGLT2i Users by Index Year

Year	Count of New Users Per Year	Average New User per Month
2020	96,384	8,032
2021	125,144	10,429
2022	240,064	20,005
2023	138,841	23,140

RESULTS

Figure 2. Monthly New SGLT2i Users by Indication Over Time

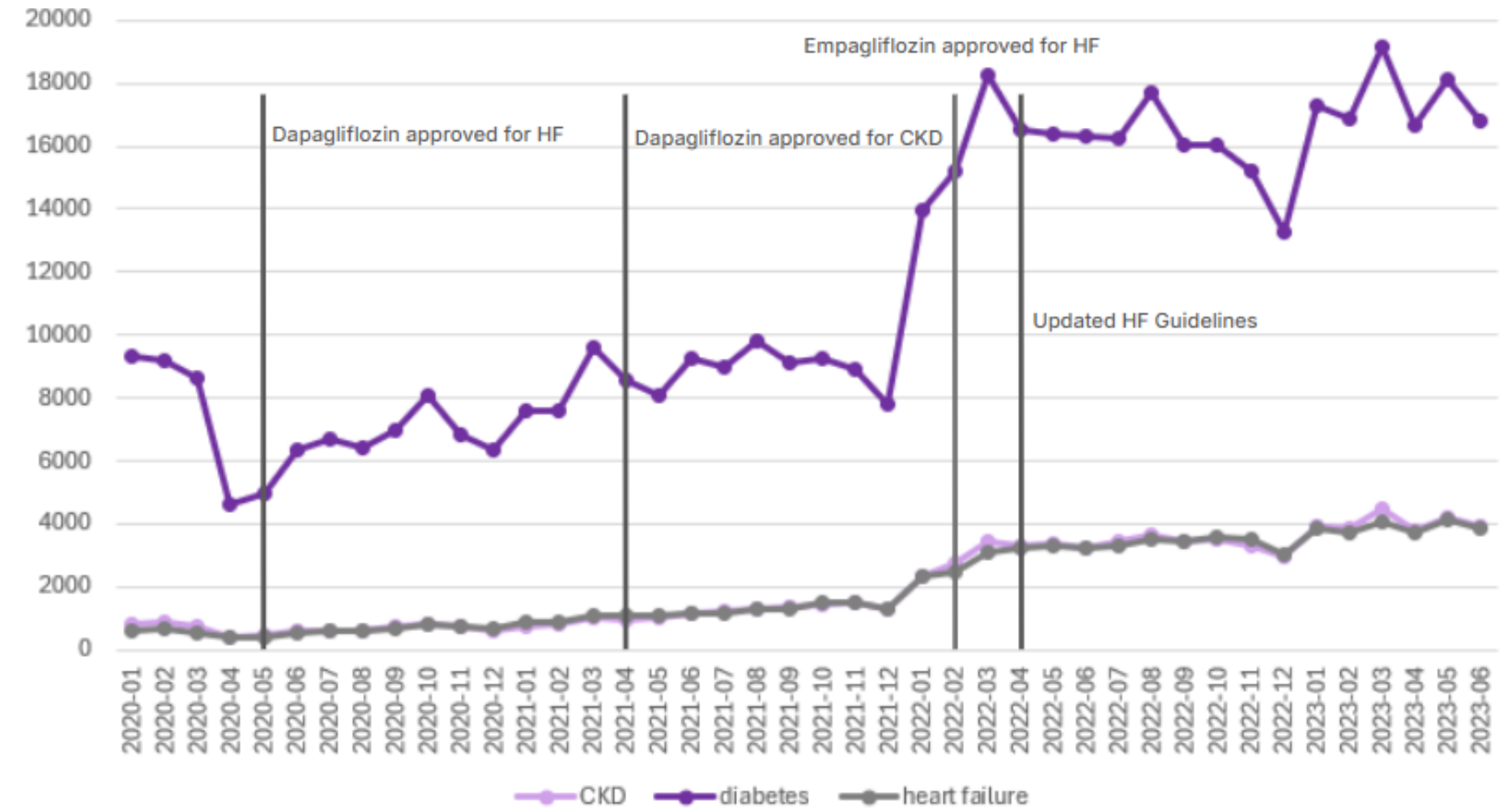


Table 2. Distribution of SGLT2i Indications Among New Users (N=600,433)

Indication	Count of New SGLT2i Users
Multiple Indications	111,083 (19%)
Diabetes	379,629 (63%)
Heart Failure	22,882 (4%)
Chronic Kidney Disease	6,875 (1%)
Other Indication	79,964 (13%)

Table 3. Acidosis Events and Clinical Outcomes Among New SGLT2i Users (N=600,433)

Outcome	Count of New SGLT2i Users
Acidosis during Follow Up	46,744 (8%)
Acidosis within 90 days	9,848 (2%)
Acidosis within 6 months	16,937 (3%)
Acidosis within 1 year	28,235 (5%)
SGLT2i exposure during acidosis	23,067
Inpatient Hospitalization	22,096

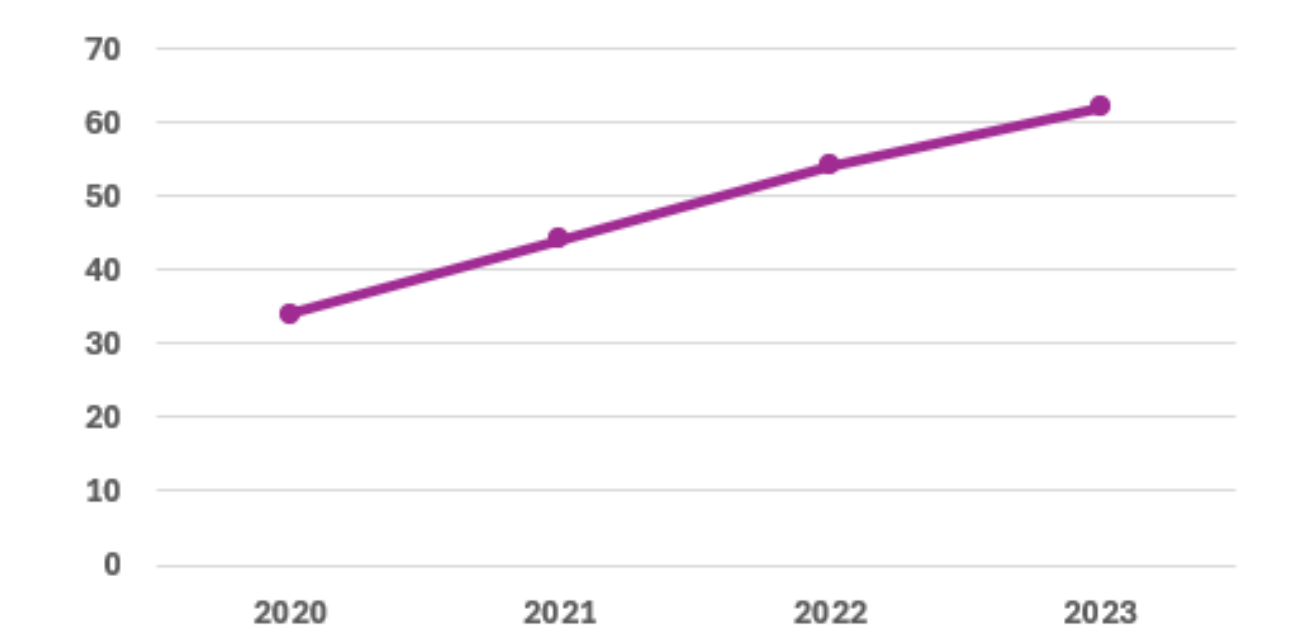
Table 4. Distribution of Indications Among Patients with Acidosis Within One Year (N=28,235)

Indication	Count of Patients with Acidosis
Multiple Indications	12,076 (43%)
Diabetes	11,718 (42%)
Heart Failure	1,657 (6%)
Chronic Kidney Disease	607 (2%)
Other Indication	2,177 (8%)

Table 6. Primary Outcome of Annual Acidosis Incidence Rate

Year	Incidence Rate per 1000 PY
2020	34
2021	44
2022	54
2023 (up to June)	62

Figure 3. Trend in Acidosis Incidence Rate per 1,000 Person-Years



CONCLUSIONS

- SGLT2i new user volume grew 188% from 2020 to 2023, and acidosis incidence rates rose concordantly
- 72% of acidosis events occurred during active SGLT2i exposure, suggesting a class level safety signal
 - Highlights the importance of patient education and prescriber vigilance at the time of initiation
- 43% of acidosis cases occurred in patients with multiple indications for SGLT2i use
 - Reflects the growing complexity of real world SGLT2i users and the need for individualized risk-benefit assessment

These findings support the need for ongoing post-marketing surveillance, updated clinical guidelines, and risk mitigation strategies as SGLT2i indications continue to expand beyond T2D and evoke a larger risk of acidotic events

DISCLOSURES

No external financial support was provided for this project.

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