Estimating Population Health Impacts of New Indications: A Case Study of SGLT2 Inhibitors

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BACKGROUND

- Therapeutic classes often evolve through new indication expansions, extending population health benefits beyond the initial approved use
- In the context of ongoing drug pricing reforms, including the Inflation Reduction Act (IRA), there is increasing interest in how lifecycle innovation contributes to population health
- Sodium-glucose cotransporter-2 (SGLT2) inhibitors represent a prominent example, with indications spanning type 2 diabetes (T2D), heart failure (HF), and chronic kidney disease (CKD) (**Figure 1**)

OBJECTIVES

This study aimed to

(1) develop a transparent framework to quantify population health impacts attributable to new drug indications

(2) apply this framework to SGLT2 inhibitor indication expansions, and

(3) estimate potential health benefits foregone in the absence of these expansions

METHODS

Study Design

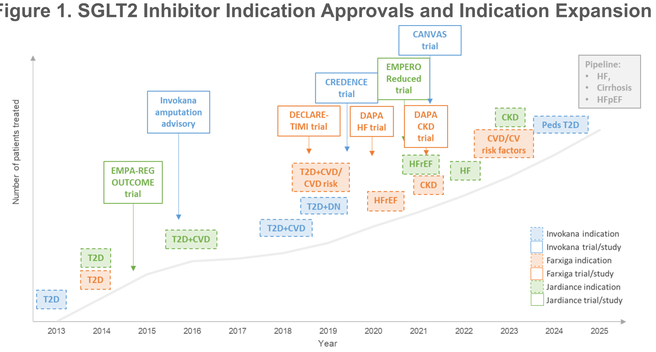
- Population health modeling study estimating U.S. impacts of SGLT2 inhibitor indication expansions
- Focus on canagliflozin, dapagliflozin, and empagliflozin
- Analysis conducted from 2013-2025 approvals

Population

U.S. populations eligible:

- Type 2 diabetes (T2D)
- Heart failure (HF, HFrEF)
- Chronic kidney disease (CKD)
- Pediatric T2D

Figure 1. SGLT2 Inhibitor Indication Approvals and Indication Expansion Timeline



Data Sources

- FDA regulatory documents
- Epidemiological studies (population size)
- Randomized clinical trials (treatment effects)
- Real-world evidence (uptake, effectiveness)
- Cost-effectiveness analyses (QALY estimates)

Model Approach

Prevalence-based model estimating (**Figure 2** and **Table 1**):

- Life-years (LYs) gained and quality-adjusted life-years (QALYs) gained
- Hospitalizations avoided and premature mortality averted

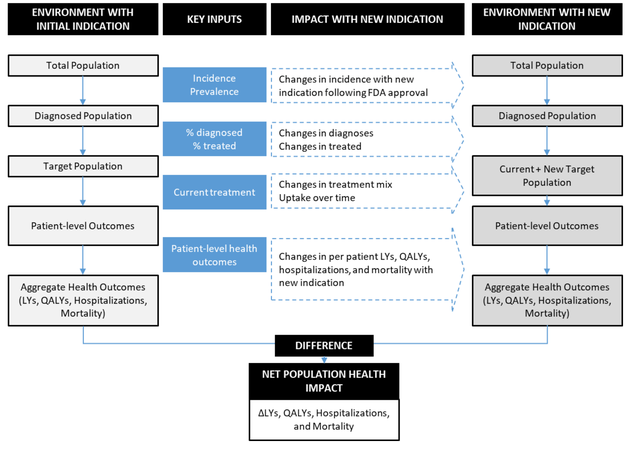
Outcomes calculated as:

- Per-patient effect × eligible population × treatment uptake

Comparator

- Standard of care (SoC) without SGLT2 inhibitors
- Results reflect incremental gains from indication expansion

Figure 2. Measuring the Population Health Impacts of New Indications



Time Horizon

- Lifetime horizon

Scenario Analyses

- Time horizon scenarios: 4-, 8-, and 12-year inclusion of indications

Counterfactual scenario:

- No new indications post-approval (inc. HF, HFrEF, CKD, pediatric T2D)

Table 1. Model Inputs and Assumptions for Estimating Population Health Impacts of SGLT2 Inhibitor Indication Expansions

FDA indication details:

- T2D: An adjunct to diet and exercise to improve glycemic control in adults with T2D.
- HFrEF: To reduce the risk of CV death and hospitalization for HF in adults with HFrEF (NYHA class II-IV).
- CKD: To reduce the risk of sustained eGFR decline, ESKD, CV death and hospitalization for HF in adults with CKD at risk of progression.
- HF: To reduce the risk of CV death plus hospitalization for HF in adults with HF.
- Pediatric T2D: As an adjunct to diet and exercise to improve glycemic control in adults and pediatric patients aged 10 years and older with T2D.

Notes:

1. Treatment uptake inputs were based on published real-world utilization estimates for each population. Uptake was extrapolated using a linear growth assumption. Baseline and latest uptake correspond to the earliest and most recent reported values, with 2025 projections derived from annualized growth rates. For indications without empirical data, estimates were based on analogous populations.

2. All incremental outcomes, including LYs and QALYs were estimated relative to placebo or standard of care.

Category	Parameter	Base-Case Value	Data Source
Total Eligible Population (estimate)	T2D	28,004,000	[1]
	HFrEF	1,199,300	[2,3]
	CKD	8,420,00	[4,5]
	HF	6,700,000	[2]
	Pediatric T2D	19,200	[6]
Treatment uptake[1]	T2D	17.2%	[7]
	HFrEF	40.2%	[8]
	CKD	14.8%	[9]
	HF	22.0%	[8]
	Pediatric T2D	5.0%	Estimate
Incremental LYs[2]	T2D	0.27	[10]
	HFrEF	0.51	[11,12]
	CKD	1.70	[13]
	HF	0.27	[14]
	Pediatric T2D	0.15	[10]
Incremental QALYs[2]	T2D	0.55	[10]
	HFrEF	0.53	[11,12]
	CKD	0.82	[13]
	HF	0.16	[14]
	Pediatric T2D	0.55	[10]

Abbreviations: CKD, Chronic Kidney Disease; HF, Heart Failure; HFrEF, Heart Failure with Reduced Ejection Fraction; LYs, Life-Years; QALYs, Quality-Adjusted Life-Years; T2D, Type 2 Diabetes.

RESULTS

Across SGLT2 inhibitor indication expansions (HFrEF, CKD, HF, pediatric T2D):

- 3.85M LYs
- 4.12M QALYs gained (**Table 2**)

Table 2. Population Health Impacts Including Approved Indications Over Time

Time horizon	Number of patients treated	LYs gained (millions)	QALYs gained (millions)
4 years	4,816,688	1.30	2.65
8 years	5,298,807	1.55	2.90
12 years	7,756,081	3.85	4.12

Abbreviations: LYs, Life-Years; QALYs, Quality-Adjusted Life-Years.

Counterfactual Scenario

- 2.55M LYs
- 1.47M QALYs foregone (**Table 3**)

Interpretation

- If no new indications post-approval: 66.2% of LYs and 35.7% of QALYs would be foregone

Table 3. Estimated Population Health Outcomes Foregone without Post-Approval Indication Expansions

Outcome	Total impact (millions)	Foregone impact (millions)	Foregone (% of total)
LYs	3.85	2.55	66.2%
QALYs	4.12	1.47	35.7%

Abbreviations: LYs, Life-Years; QALYs, Quality-Adjusted Life-Years.

Note: Indications aligned with FDA labels; population estimates illustrative; uptake from real-world data (linear projection); outcomes relative to standard of care.

LIMITATIONS

- LYs and QALYs were projected over a lifetime horizon and may not fully reflect future changes in survival, adherence, disease progression, or treatment patterns
- Estimates do not account for future competing therapies or changes in standard of care over time
- Inputs from trials, epidemiologic studies, and real-world data may limit generalizability, and some overlap across indication-specific may exist

CONCLUSIONS

- Following the initial SGLT2 inhibitor approval, subsequent indication expansions can generate substantial cumulative population health benefits
- Our findings suggest that lifecycle population health gains should be considered in policy discussions related to drug pricing reform, including potential unintended consequences of the IRA on incentives for indication expansion, particularly for small-molecule therapies

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