Cost-Effectiveness of Metformin vs. SGLT2 Inhibitors as the First-Line Treatment in Type 2 Diabetes Management

Atalay Demiray, MD, MSc[1], Reza Yaesoubi, PhD[1]

[1]Department of Health Policy and Management, Yale School of Public Health, New Haven, CT, USA (atalay.demiray@yale.edu)

There are no conflicts of interest to disclose for this study.

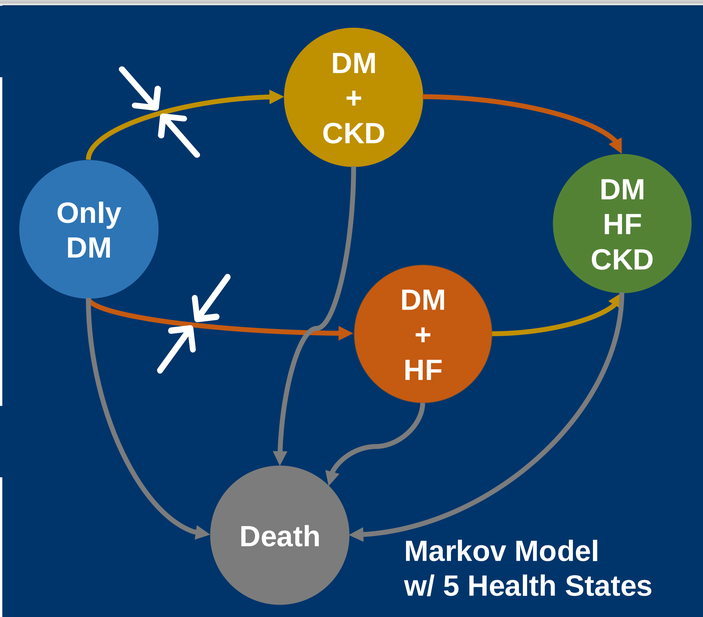
Research Question: Can SGLT2 inhibitors be a cost-effective first-line treatment for type 2 diabetes compared to metformin?

Introduction

The prevalence of type 2 diabetes is rising globally, leading to increased healthcare costs, particularly in combination with CKD and HF. SGLT2 inhibitors have emerged as promising medications due to their cardio-renal protective effects, which can help prevent the onset and progression of CKD and HF. Despite their significant health benefits, SGLT2 inhibitors are not recommended as a first-line therapy due to their substantially higher cost than metformin, the current standard treatment. This study aims to evaluate whether SGLT2 inhibitors can be cost-effective despite their higher costs, considering their long-term cardio-renal benefits.

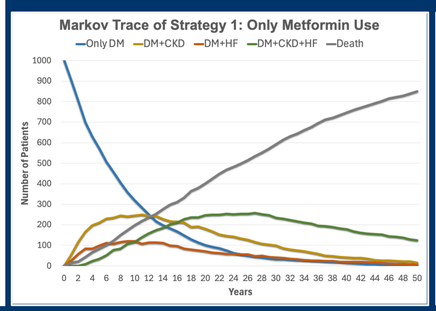
Methods

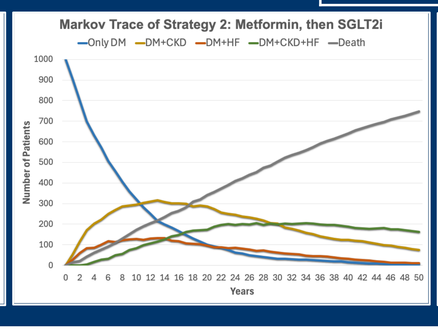
- A health state transition Markov model was used to evaluate the cost-effectiveness of SGLT2 inhibitors versus metformin for a cohort of 1000 treatment-naïve Type 2 DM patients. Transition probabilities and efficacy of medications were derived from the current literature.[4,5,6,7]
- The model was conducted over a lifetime horizon, from a healthcare perspective, with a 3.0% annual discount rate applied to costs and QALYs.
- Three treatment strategies are simulated as follows:
- **Strategy 1 (Metformin):** Patients only receive metformin.
- **Strategy 2 (Metformin, then SGLT2i):** Patients start with metformin, then SGLT2 inhibitors added only if HF or CKD develops. (Current recommendation)
- **Strategy 3 (SGLT2i):** Patients receive SGLT2 inhibitors as first-line.

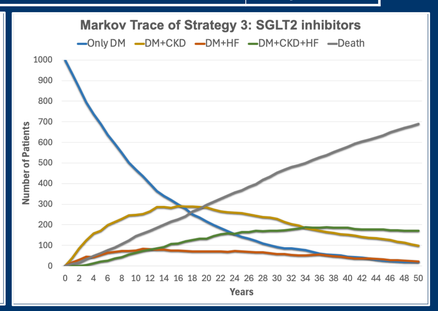


Abbreviations	
DM	Type 2 Diabetes Mellitus
CKD	Chronic Kidney Disease
HF	Heart Failure
SGLT2i	Sodium-glucose cotransporter-2 inhibitors
→←	Effect of SGLT2 inhibitors For Primary Prevention

Health States	Costs[1]	Utilities[2]
Only DM	$12,545	0.76
DM + CKD	$21,894	0.74
DM + HF	$29,570	0.719
DM + CKD + HF	$46,507	0.699
Death	0	0
Annual cost of metformin[3]		$ 17
Annual cost of SGLT2i[3]		$ 5,427

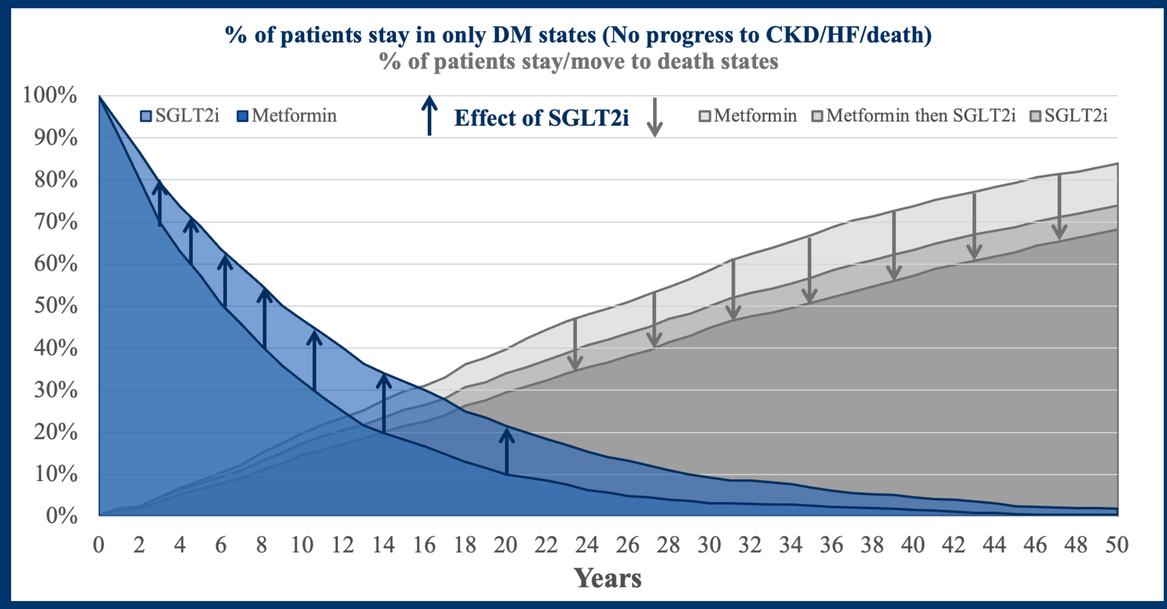






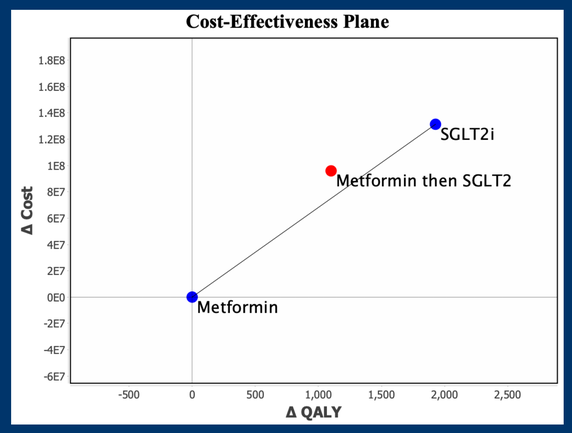
Results

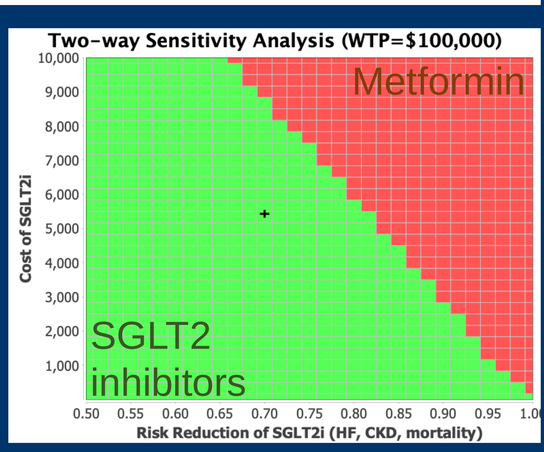
Treatment Strategy	Cost (95% Confidence Interval)	QALY (95% Confidence Interval)	ICER ($ / QALY)
Metformin	**$ 397,260** ($348092, $446427)	**11.89** (10.84, 12.94)	**Baseline**
Metformin then SGLT2i	**$ 469,438** ($413795, $525081)	**12.87** (11.78, 13.95)	**Weakly-dominated**
SGLT2i	**$ 493,358** ($442134, $544582)	**13.66** (12.59, 14.73)	**$ 54,221**



Conclusion

SGLT2 inhibitors can be a cost-effective first-line treatment for diabetes, with an ICER of $54,221 per QALY compared to metformin. Despite their higher cost, the long-term benefits of SGLT2 inhibitors in preventing CKD, HF, and death in diabetic patients are significant.





Limitations

- The model does not account for the impact of varying age groups or the duration of diabetes on outcomes.
- The model does not differentiate between CKD stages (excluding ESKD) or heart failure subtypes (HFrEF vs. HFpEF).
- Differences in efficacy and side effect profiles of individual SGLT2 inhibitors within the drug class were not considered.

References

1. United States Renal Data System. 2022 USRDS Annual Data Report: Epidemiology of kidney disease in the United States. National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases, Bethesda, MD, 2022.
2. Simon J. Neuwahl, Ping Zhang, Haiying Chen, Hui Shao, Michael Laxy, Andrea M. Anderson, Timothy E. Craven, Thomas J. Hoerger, the Look AHEAD Research Group; Patient Health Utility Equations for a Type 2 Diabetes Model. Diabetes Care 1 February 2021; 44 (2): 381–389. https://doi.org/10.2337/dc20-1207
3. Barber MJ, Gotham D, Bygrave H, Cepuch C. Estimated Sustainable Cost-Based Prices for Diabetes Medicines. JAMA Netw Open. 2024;7(3):e243474.
4. Alison K. Wright, Matthew J. Carr, Evangelos Kontopantelis, Lalantha Leelarathna, Hood Thabit, Richard Emsley, Iain Buchan, Mamas A. Mamas, Tjeerd P. van Staa, Naveed Sattar, Darren M. Ashcroft, Martin K. Rutter; Primary Prevention of Cardiovascular and Heart Failure Events With SGLT2 Inhibitors, GLP-1 Receptor Agonists, and Their Combination in Type 2 Diabetes. Diabetes Care 1 April 2022; 45 (4): 909–918. https://doi.org/10.2337/dc21-1113
5. Ofri Mosenzon, Itamar Raz, Stephen D. Wiviott, Meir Schechter, Erica L. Goodrich, Ilan Yanuv, Aliza Rozenberg, Sabina A. Murphy, Thomas A. Zelniker, Anna Maria Langkilde, Ingrid A.M. Gause-Nilsson, Martin Fredriksson, Peter A. Johansson, John P.H. Wilding, Darren K. McGuire, Deepak L. Bhatt, Lawrence A. Leiter, Avivit Cahn, Jamie P. Dwyer, Hiddo J.L. Heerspink, Marc S. Sabatine; Dapagliflozin and Prevention of Kidney Disease Among Patients With Type 2 Diabetes: Post Hoc Analyses From the DECLARE-TIMI 58 Trial. Diabetes Care 1 October 2022; 45 (10): 2350–2359. https://doi.org/10.2337/dc22-0382
6. Saeed, H., Abdullah, M. B. B. S., Naeem, I., Zafar, A., Ahmad, B., Islam, T. u., . . . Goyal, A. (2024). Demographic trends and disparities in mortality related to coexisting heart failure and diabetes mellitus among older adults in the united states between 1999 and 2020: A retrospective population-based cohort study from the CDC WONDER database. International Journal of Cardiology Cardiovascular Risk and Prevention, 23, 200326. doi:10.1016/j.ijcrp.2024.200326
7. Beatriz Fernández-Fernandez, Pantelis Sarafidis, Maria José Soler, Alberto Ortiz, EMPA-KIDNEY: expanding the range of kidney protection by SGLT2 inhibitors, Clinical Kidney Journal, Volume 16, Issue 8, August 2023, Pages 1187–1198, https://doi.org/10.1093/ckj/sfad082

Yale SCHOOL OF PUBLIC HEALTH