COST-UTILITY ANALYSIS OF ONCE-WEEKLY SEMAGLUTIDE AND DULAGLUTIDE FOR PATIENTS WITH TYPE 2 DIABETES IN SAUDI ARABIA

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ISPOR acceptance code: EE23

Abstract

Aims and hypothesis: The prevalence of type 2 diabetes (T2D) in Saudi Arabia is one of the top ten prevalences globally, which imposes a substantial economic burden on the healthcare system. Glucagon-like peptide-1 agonists (GLP-1) are one of the novel treatments for diabetes. The research aims to determine whether Semaglutide 1.0 mg is cost-effective compared with Dulaglutide 1.5 mg from a Saudi public payer perspective.

Methods: A literature review was conducted to acquire the input parameters based on the available literature that could populate the cost-utility model to inform the Saudi decision-makers better. A literature review was developed to inform the cost-utility analysis (CUA) with the structure of the Markov model in terms of health states that could describe the patient journey, baseline risks that could simulate the patients' movements among the different health states, and clinical outcomes for the comparators, health utilities, and cost data. The second phase was developing the CUA based on the available literature, including only direct medical costs for a ten-year time horizon. The Incremental Net Monetary Benefit (INMB) was estimated based on the Saudi cost-effectiveness threshold (CET) of 50,000 SAR – 75,000 SAR. Structural and parameter uncertainties were explored by developing sensitivity and scenario analyses.

Results: Semaglutide 1.0 mg was dominant in the base case analysis with incremental 0.11 QALY, - 3,175 SAR. INMB ranged from 8,671 SAR to 11,419 SAR on the lower and upper bounds of the CET range, respectively. Semaglutide 1.0 mg sustained the results in all scenarios. One-way sensitivity analysis illustrated that the key drivers of the cost-effectiveness findings are treatment acquisition cost, the proportion of patients achieving HbA1C%, and hazard ratios of developing cardiovascular complications.

Conclusion: At the current prices, Semaglutide 1.0 mg is cost-effective compared with Dulaglutide 1.5 mg when the model considered macrovascular complications and chronic kidney disease (CKD).

Introduction

Healthcare expenditures per capita (international dollar) in Saudi Arabia increased from 1,610.8 $ in 2000, which accounted for 4.2% of the country's GDP to 2,696.3 $ in 2018 which accounted for 5.54% out of the country's GDP. Therefore, the country is witnessing a significant healthcare system transformation as part of the country's vision for 2030 in order to develop a value-based healthcare system. One of the main goals of the transition process is facilitating access to healthcare services with higher quality, ensuring financial sustainability and economic stability.[1]

Saudi has one of the highest prevalences of diabetes worldwide. In 2021, Saudi Arabia was estimated to have more than 4.27 million adults (20-79 years) suffering from diabetes, with a prevalence of 18.7% in adults and expected to reach an even higher 20.4% by 2030 which is an alarming increase.[2] Therefore, policymakers in Saudi Arabia aim to reduce the economic burden of diabetes and related complications.[3]
Glucagon-like peptide-1 agonists (GLP-1) provide a substantial value for T2D patients with cardiovascular complications. Cardiovascular diseases are considered the leading cause of mortality in T2D patients.[4] Semaglutide 1 mg and Dulaglutide 1.5 mg established their cardiovascular protection through SUSTAIN and REWIND cardiovascular outcomes trials (CVOT), respectively.[5,6] It would be helpful for the Saudi payers to evaluate the value for money for the different GLP-1 options.

Literature review

Methodology:
An electronic literature review was conducted using Embase, MEDLINE, and Web of Science (the 200 first relevant references). The literature review was developed to identify the available input parameters, e.g., cost data, intervention-related clinical outcomes, epidemiological data, or health utilities, that have been used to populate the model and to assess the critical challenges in obtaining the needed data for the model to explore the cost-effectiveness of Semaglutide 1.0 mg, which could inform decision-makers about the cost-effective option. The literature review was utilized to inform the structure of the CUA's Markov model, comparative effectiveness data for both comparators, baseline risks, health utilities, and the costing data.

Results:
Fig. 1 demonstrates a PRISMA flow chart for the search process. The literature review informed the Markov model by including cardiovascular and renal complications health states. Moreover, the literature review identified the majority of the costing data that reflect the proper payer perspective. The search could not identify Saudi relevant comparative effectiveness data, baseline risks, or health utilities, therefore, input parameters from different health jurisdictions have been utilized in the model.

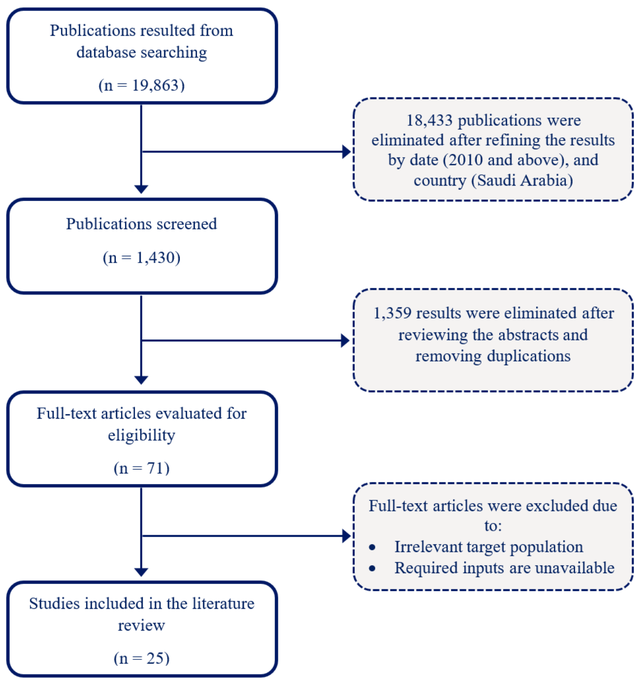


Figure: 1 Flow diagram of literature search.

Publication	Study design	Learnings
Yang et al., 2023 [7]	CEA	Markov model reflecting CV complications (MI, stroke, heart failure, and death) Comparators: GLP-1 receptor agonists versus long-acting insulins
Ekhlasi, et al., 2022 [8]	CEA	Markov model includes retinopathy and nephropathy Comparators: Dulaglutide Versus Liraglutide
Zupa, et al., 2021 [9]	CEA	Markov model includes nephropathy, MI, stroke, and heart failure Comparators: Empagliflozin versus once-weekly semaglutide
Guzauskas, et al., 2021 [10]	CEA	Markov model includes CHF, IHD, MI strokes, blindness, foot ulcers, amputations, renal disease, and mortality Comparators: Oral semaglutide versus sitagliptin, empagliflozin, and liraglutide
Deerochanawong, et al., 2023 [11]	CEA	Markov model included MI, stroke, and renal complication Comparators: Liraglutide Plus SoC Versus SoC
Abramson, et al., 2019 [12]	CEA	The model included drug administration and discontinuation health states Comparators: Oral Semaglutide versus daily injection and weekly injection of Semaglutide
Risebrough, et al., 2021 [13]	CEA	The model included fatal and nonfatal macrovascular (IHD or angina, CHF, MI, revascularization surgery, and stroke) and microvascular (amputation, blindness, and renal failure) complications, adverse events (AEs), and hypoglycemia events. Comparators: Oral Semaglutide Versus Dulaglutide and Liraglutide
Basu, (Global Health & Population Project on Access to Care for Cardiometabolic Diseases (HPACC)*), 2021 [14]	CEA	The model included cardiovascular events, heart failure, end-stage renal disease, vision loss, pressure sensation loss, hypoglycemia requiring medical attention, and drug-specific side-effects Comparators: GLP-1 & SGLT-2 I & DPP-4 i
Torre, et al., 2020 [15]	CEA	The model includes ischemic heart disease (IHD), stroke, and heart failure Comparators: Dulaglutide versus traditional therapies
Reifsnider, et al., 2021 [16]	CEA	The model included macrovascular, microvascular complications, and renal complications Comparators: Second line empagliflozin versus liraglutide
Morton, et al., 2023 [17]	CEA	The model included MI, stroke, HF and ESKD Comparators: SGLT-2 I & GLP-1
Al-Rubeaan, et al., 2016 [18]	Epidemiological cohort retrospective study	Adjusted HR for all-cause mortality: • Diabetes duration P10 years: 2.81 (2.23–3.55) • Insulin use: 1.12 (0.97–1.29)
Mokdad, et al., 2015 [19]	COI	Diabetes cost by categories of service, KSA 2014. Normal progression: 6,200 SAR and acute complication: 43,901 SAR
Alhowaish, A., 2013 [20]	COI	Diabetes-related expenditures stratified by age, sex, and nationality
Al-Jedai, et al., 2022 [3]	COI	HCRU and costs associated with cardiovascular and renal complications in T2D (but from a private payer perspective)
Al-Rubeaan, et al., 2013 [21]	COI	Cost of insulin therapy for T2D 1406 SAR
Almutairi, and Alkharfy, 2013 [22]	COI	HCRU & direct medical costs for T2D based on HbA1C%
Hnoosh, et al., 2012 [23]	COI	Costs of cardiovascular complications: Stroke (US$5973) and CHF (US$4992)
Alkhatib, et al., 2022 [24]	Cost of control	Cost of MACE management per patient: SAR 48,464 and prices of Semaglutide and Dulaglutide
Almalki, et al., 2020 [25]	CEA	Cost of severe complications: MI: 16,720 USD, Stroke: 29,576 USD, HF: 34,263 USD, Acute kidney injury: 5,570 USD
Osman, et al., 2011 [26]	COI	Direct medical cost and HCRU for Non-ST elevated MI & ST elevated MI
Altowaijri, et al., 2020 [27]	COI	Cost of STEMI, NSTEMI and IS
Alghamdi, et al., 2022 [28]	CEA	Cost of Nonfatal MI, Nonfatal IS, and post-event costs
Al-Jedai, et al., b, 2022 [29]	Identifying CET for KSA	Saudi cost-effectiveness threshold ranges from SAR 50,000 to 75,000 per QALY
Al-Omar, et al, 2022 [30]	COI	Annual cost of HF 7,713 SAR (public sector) CKD: 4785 SAR

Table: 1 Results of the literature review.

Cost utility analysis

Methodology:

A Microsoft Excel-based cost-utility analysis has been developed using a multistate Markov model that reflected the disease progression through T2D cardiovascular and renal complications (as described in Fig. 2). The model was developed based on a hypothetical cohort of adults with T2D with inadequate HbA1C%. Baseline demographics and characteristics were derived from SUSTAIN 7.[31] The analysis was conducted from a Saudi public healthcare payer perspective, including only direct medical costs. In the base case analysis, costs and health outcomes were discounted at 3.5% annually as the most commonly used discount rate for CEAs in Saudi Arabia.[32]

The model was conducted to evaluate the incremental cost-utility ratio for a ten-year time horizon using a one-year life cycle as the base case. In order to gauge the consistency of the results, the model simulated the results for a 40-year time horizon to explore the value for money for semaglutide in a lifetime.

As T2D is a progressive disease, the base case analysis assumed that patients would administer the two comparators under consideration for three years. Comparative efficacy data were derived from the SUSTAIN 7 trial and indirect treatment comparison that compared the CV outcomes for both comparators.[31,33]

The model was populated using transition probabilities derived from available literature conducted in healthcare jurisdictions other than the Saudi healthcare system. A meta-analysis was utilized to populate the utilities attributed to the different health states.[34] For the first three years, utilities were adjusted to accommodate the different weight loss impacts attributed to the different comparators.[35] Saudi national cost-effectiveness ratio was utilized SAR 50,000 – 75,000 per QALY gained. [29]

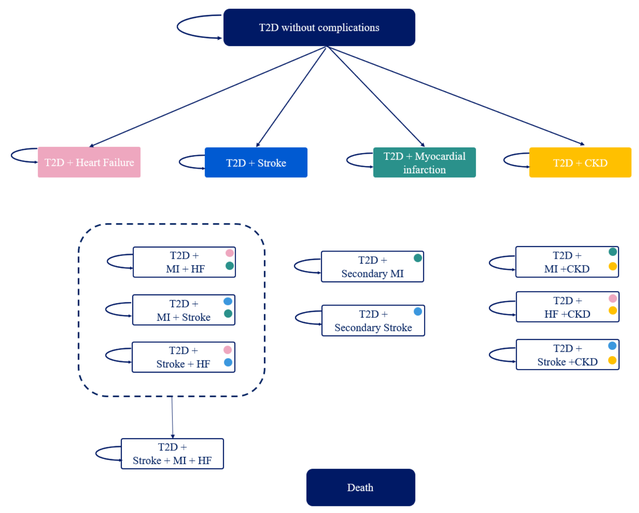
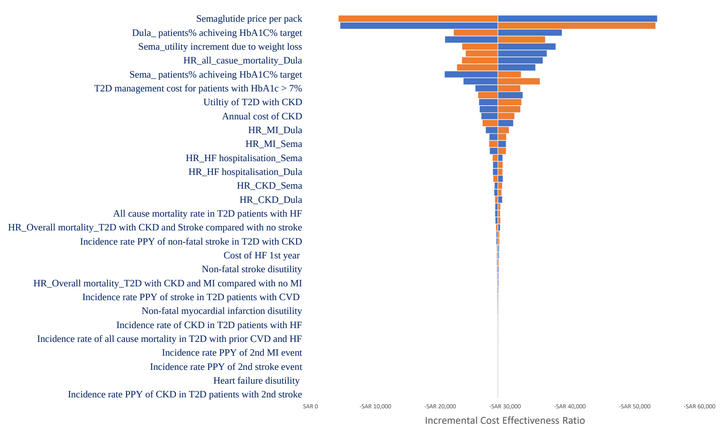


Figure: 2 Markov model structure and health states

Results:

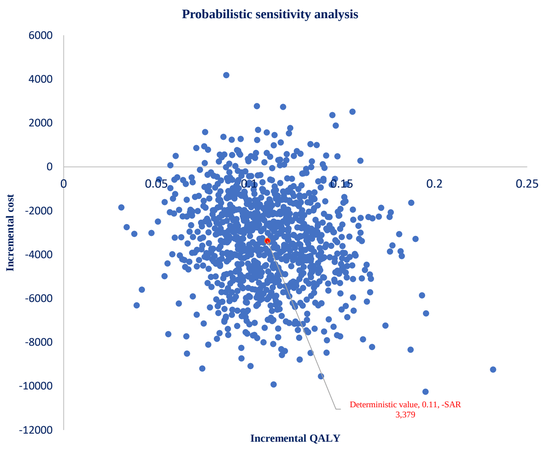
Setting	Semaglutide	Dulaglutide	ICUR	INMB
Base case analysis (10 years time horizon)	7.09 QALYs Total cost: 91,182 SAR	6.98 QALYs Total Cost: 94,357 SAR	Dominant	Lower bound: 8,671 SAR Higher bound: 11,419 SAR
40 years time horizon	13.2 QALYs Total cost: 207,667 SAR	12.97 QALYs Total Cost: 209,313 SAR	Dominant	Lower bound: 13,281 SAR Higher bound: 19,099 SAR

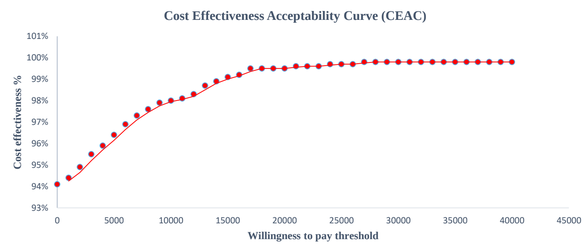
Deterministic sensitivity analysis (DSA)
DSA demonstrated that acquisition costs, followed by the proportion of patients achieving HbA1C% target, and HR for developing non-fatal stroke are the data inputs that most impacted the results.



Deterministic sensitivity analysis

Probabilistic sensitivity analysis (PSA)
PSA demonstrated that semaglutide 1 mg dominated dulaglutide 1.5 mg in 91% of the sensitivity analysis iterations. Furthermore, cost effectiveness acceptability curve demonstrated that semaglutide is 100% cost effective at willingness to pay 26,000 SAR per QALY.





Discussion

Semaglutide 1 mg demonstrated better HbA1C% reduction, weight loss, and better CV protection compared with dulaglutide 1.5 mg. The CUA model illustrated the value for money associated with semaglutide in the Saudi context. Deterministic and probabilistic sensitivity analyses demonstrated the robustness of the results, especially semaglutide maintained its cost-effectiveness dominance in different scenarios. Therefore, semaglutide adoption in the Saudi public sector may be associated with better overall population health.

This research included several strengths; the literature review was conducted and was helpful in designing the Markov model as most of the included CEA/CUA included major cardiovascular and renal complications. The literature review identified primary and secondary research that included unit costs and acquisition prices for both comparators. Moreover, all the utilized costs were calculated based on the public perspective in Saudi and reflected the adopted payer's perspective.

Data insufficiency has been reported to be a common challenge in most economic evaluations conducted in Saudi Arabia.[8] Therefore, there is an urgent need to improve the status of the data infrastructure and there is a huge data gap to address like to develop better utility value sets, that would reflect the Saudi preference for the different health states and epidemiological evidence that evaluate the baseline risks associated with the complications associated with T2D.

Including only data from Saudi Arabia in the literature review and excluding other data from the Middle Eastern and Arabian Gulf countries might be a limitation of the search strategy of the literature review. Regional literature would have been relevant to the research context.

The model lacks local expert validation, which would have helped with the other limitations of missing data and validates the international references used to inform the model and address the data gaps in the local literature. It would be beneficial to improve the face and internal validity of future CUAs conducted in Saudi Arabia to enrich the model with local expert validation.

Conclusion

The literature review informed the CUA of the model structure, and costs, but couldn't retrieve comparative efficacy data, baseline risks, and utilities that may reflect the Saudi context.

After, running the model based on the available data, semaglutide 1 mg dominated dulaglutide 1.5 mg with incremental 0.11 QALYs and incremental costs (3,175 SAR). In the scenario analysis, semaglutide maintained its dominance which endorsed the robustness of the model outcomes.

References

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