EE433

Cost-effectiveness evidence overview for metformin and SGLT2is in type 2 diabetes patients with cardiorenal risk: a targeted literature review

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CONCLUSIONS

- **SGLT2i initiation for T2D without comorbidities lacks sufficient evidence**
- **Metformin is the rational economic choice in early T2D**
- **Metformin use in patients with CVD/CKD is supported by robust clinical evidence**
- **Overall, metformin remains reliable, effective, cost-effective and affordable across the T2D spectrum**

INTRODUCTION

- US (ADA) guidelines[1] shift T2D treatment away from the "glucocentric" approach towards a "complication-based" approach with focus on avoidance of key T2D complications
- Drivers are CV outcome trials in people with T2D with CVD, CKD and/or multiple risk factors; a decreasing proportion of the real-world overall T2D population due to improved surveillance and earlier diagnosis[2]
- Early, optimal glycaemic control has long been proven effective at reducing CVD and kidney disease events and all-cause mortality[2]
- Evidence generated for newer vs traditional T2D treatments is different: evidence for newer agents is centred on higher risk patients, whereas treatments such as metformin included a wider variety of patients and treatment settings[3]

OBJECTIVES

- Explore the economic evidence base supporting rational decision-making across the T2D continuum, i.e. from very early patients to those with established CVD/renal disease or multiple comorbidities
- Focused on two treatment classes:
  - SGLT2is: new therapy class recently recommended at first-line based on CV outcomes data[1]
  - Metformin: available for >60y and used daily by >200 million patients worldwide[4]

METHODS

- Literature was reviewed in order to identify clinical/economic evidence characterizing SGLT2is or metformin in adult patients with T2D
- Following pilot searches, time horizon selected was 2019–2024 in order to capture the most current literature while ensuring sufficient breadth; protocol-led screening was applied to search results in order to ensure consistency of inclusion/exclusion
- Analysis focused on economic studies, supported/interpreted according to findings from the other reviews

Economic studies
Systematic search in MEDLINE via PubMed

Clinical trials
With SGLT2i (dapagliflozin, empagliflozin or canagliflozin) as main intervention and registered with the US NLM[5]

Key clinical guidelines

Cochrane reviews[6]

RESULTS

- The study included four treatment guidelines from around the world[1,7-9], five Cochrane reviews, 95 clinical studies, and 70 economic analyses (**Figure 1**)
- While most literature examined the USA, a good spread of both clinical and economic studies was identified worldwide, including a range of both high- and low-income regions; economic studies accounted for a larger proportion of European & Latin American studies vs rest of world (**Figure 2**)

Figure 1. PRISMA flow (economic review)

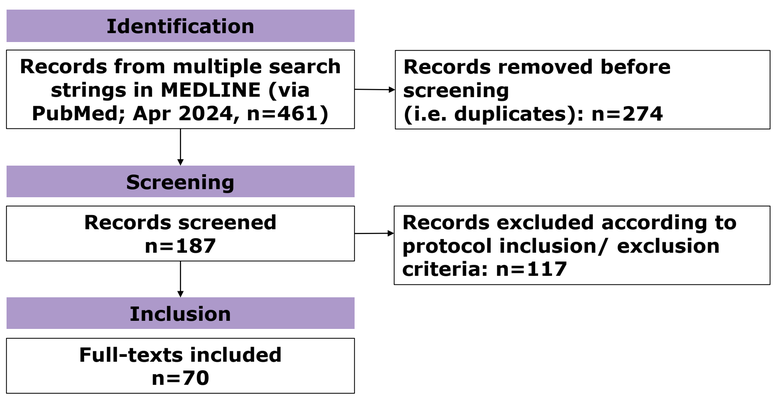


Figure 2. Geographical distribution of included clinical & economic studies

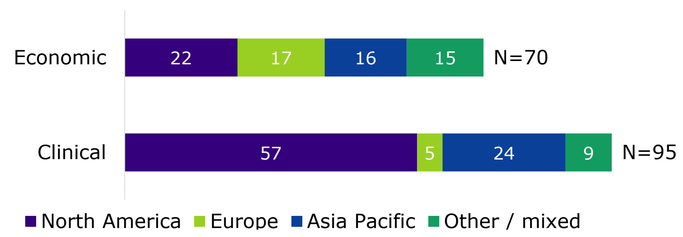
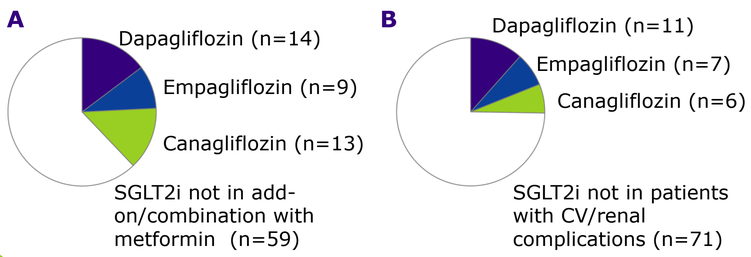


Figure 3. SGLT2i clinical studies investigating (A) add-on/combination with metformin & (B) patients with CV/renal complications



- Clinical & economic studies were identified investigating both SGLT2is and metformin across the spectrum of diabetes (from early/prediabetes to advanced/comorbid disease), and both as monotherapy or in combination
- The majority of economic studies (n=62) included SGLT2i; 24 included metformin
- SGLT2is were more often described as add-on therapy than metformin; e.g. 1 in 3 of the clinical studies examined SGLT2i + metformin. One in 4 SGLT2i studies investigated patients with high CV/renal risk (**Figure 3**)

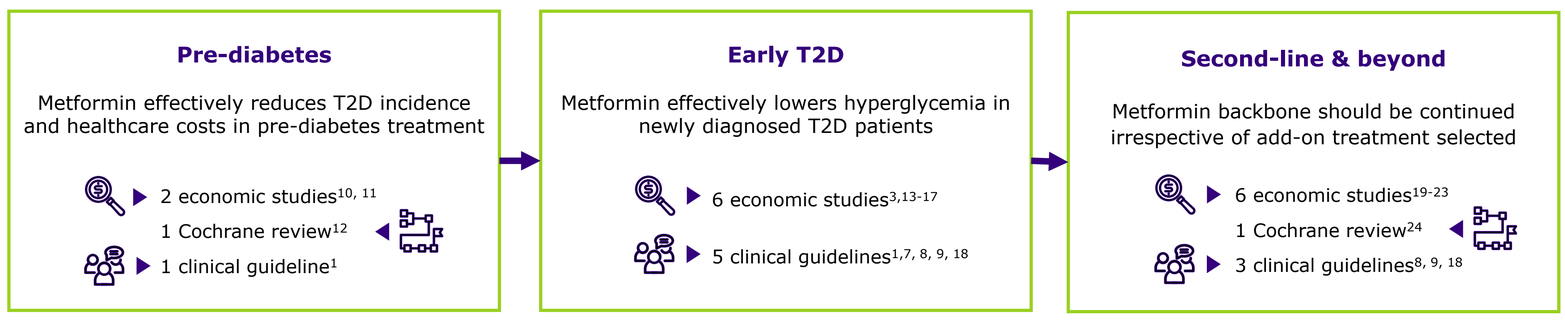
While 2024 US (ADA) guidelines[1] note SGLT2i as an option in early diabetes, the majority of clinical and economic data study SGLT2is in later line therapy and in particular added on to metformin:

- Of SGLT2i economic studies reporting relevant data by T2D stage, 68% (24 studies) examined SGLT2i in combination with metformin, 39% (12 studies) specified prior failure of metformin monotherapy and 5 studies examined SGLT2i in first-line, the latter highlighting that the significant costs may not be justified by the clinical outcomes achieved

Economic studies were identified characterizing metformin across the spectrum of T2D, from prediabetes to later-line – and in patients with cardiovascular/renal risks (**Figure 4**)

- Economic analyses highlighted metformin as an affordable and even cost-saving strategy vs other management approaches, including in T2D prevention in middle/low-income countries

Figure 4. Key evidence characterizing metformin costs & outcomes across the T2D spectrum



CV/renal risk

Metformin remains an important treatment option with positive impact on diabetes-related CV & renal risk reduction across the T2D continuum

7 economic/clinical studies[25-31] | 2 Cochrane reviews[32,33] | 1 clinical guideline[8]

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Abbreviations: CKD=chronic kidney disease; CV(D)=cardiovascular (disease); SGLT2i=sodium-glucose cotransporter-2 inhibitor; T2D=type 2 diabetes

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