



Introduction: Real-World Evidence in Type 2 Diabetes

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The International Diabetes Federation estimates that 463 million people are affected by diabetes worldwide, 79% of whom live in middle- or low-income countries [1]. Moreover, the number of people living with diabetes is predicted to increase by 51% in the next 25 years and reach 700 million by 2045 [1]. The greatest increases will be seen in Africa, Southeast Asia, and Central or South America [1]. Many of the people with diabetes in the world do not have access to the latest treatments recommended by

guidelines for developed countries such as those from the American Association of Clinical Endocrinologists (AACE) [2], American Diabetes Association (ADA) and European Association for the Study of Diabetes (EASD) [3]. Nevertheless, these individuals in low- or middle-income countries deserve to receive effective and safe treatments, with proven benefits.

Randomised clinical trials are important to answer questions relating to drug efficacy and safety under controlled conditions that maximise statistical certainty ('can this product work?'). However, because of the strictly controlled conditions of a clinical trial, they need to be supplemented by data from real-world populations of patients to ensure that the findings are generalisable to a wider population of patients ('does it work?') [4, 5]. Together the evidence from controlled trials and real-world studies provides guidance on how treatments will work in clinical practice.

Sulfonylureas represent an important class of agents for the treatment of type 2 diabetes mellitus (T2DM) as second-line therapy in patients who do not achieve optimal glycaemic control on metformin alone. Clinical trial data and real-world clinical experience with these agents have been accumulating for many decades. Moreover, these agents are inexpensive with a per-dose cost that is much lower than that of the newer classes of agents such as the sodium-glucose cotransporter 2 inhibitors

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(SGLT2i) or glucagon-like peptide-1 receptor agonists (GLP-1RA) [6].

SGLT2i and GLP-1RA are recommended for T2DM patients with cardiovascular disease based on evidence from the large-scale cardiovascular outcomes trials [3, 7, 8], but the majority of patients with T2DM requiring second-line therapy do not have cardiovascular disease [9–11]. For patients without cardiovascular disease, international guidelines differ in their recommendations. Sulfonylureas are the agents of choice as add-on therapy to metformin in the World Health Organisation (WHO) guidelines for T2DM management in countries with limited resources [12]. They are also recommended as a preferred second-line therapy in guidelines from the International Diabetes Federation [13], UK National Institute for Health and Care Excellence [14] as well as professional bodies in Australia [15] and India [16]. AACE and ADA/EASD guidelines, however, recommend newer classes of agents ahead of sulfonylureas [2, 3], but these guidelines are consensus- rather than evidence-based and would score poorly on the Appraisal of Guidelines for Research and Evaluation (AGREE) scale for guideline quality [13]. Moreover, not all sulfonylureas are created equal, with gliclazide showing a more favourable effect on cardiovascular mortality than other sulfonylureas [17], and the lowest risk of hypoglycaemia [18].

The article in this supplement summarises the presentations at a symposium entitled “Real-world evidence and new perspectives with gliclazide MR” at the International Diabetes Federation Congress in Busan, South Korea, on 4 December 2019. These presentations described the place of sulfonylureas generally, and gliclazide MR specifically, in the treatment of T2DM and emerging real-world evidence to support this role, including in patients who are fasting during Ramadan. Finally, the article describes the role of sulfonylureas as first-line therapy in patients with a primary defect in insulin secretion—those with maturity onset diabetes of the young (MODY). The truly international focus of this symposium on the role of sulfonylureas provides insights into how these important agents can be used globally to

improve outcomes in a range of patients with diabetes.

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