

Will empagliflozin reduce mortality in the real world?



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Background

The EMPA-REG OUTCOME trial¹ was designed as a non-inferiority randomised placebo-controlled trial to investigate cardiovascular outcomes and mortality with empagliflozin in a type 2 diabetes cohort who were at high risk of cardiovascular disease. However, the trial demonstrates a significant reduction in all-cause mortality in the treatment group. Despite an inclusive approach to patient selection, extrapolation of results to clinical practice should be undertaken cautiously.

Aim

The sodium glucose co-transporter 2 (SGLT2) inhibitors are relatively new class of oral diabetes. We analyse the current use this drug class in the real world and compare the characteristics of real world patients to those of the EMPA-REG trial.

We begin to answer the questions:

- Will we see the benefits shown by the EMPA-REG trial translated into real world benefits?
- How well does the EMP-REG patient cohort represent real world patients treated with SGLT2 inhibitors?

Methods

A large cohort of people with type 2 diabetes (N=34,278) was identified from the Royal College of General Practitioners Research and Surveillance Centre (RCGP RSC) database, using routinely collected primary care data. Prescription data was extracted from primary care records on the use of SGLT2 inhibitors in the diabetes cohort.

We report the proportion of people prescribed SGLT2 inhibitors who have the same cardiovascular risk factors as those included in the EMPA-REG trial. We also compare the characteristics of the trial population with those of real world SGLT2 users with high cardiovascular risk

Results

A small proportion of the cohort (2.2%; n=752) had been initiated on SGLT2 inhibitors since their introduction although prescribing rates are increasing rapidly; rates in our sample (prescriptions per 10,000 people with type 2 diabetes) increased from 34 in April 2014 to 133 in April 2015 (Figure 1).

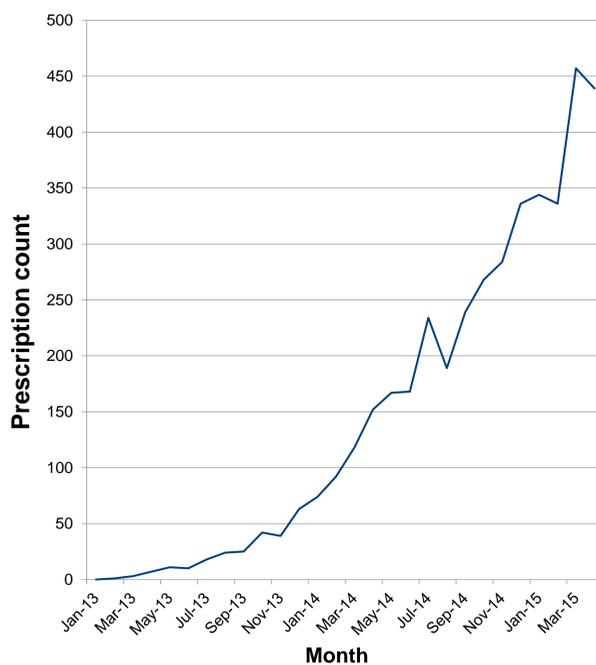


Figure 1. Number of prescriptions for SGLT2 inhibitors dispensed per month in a population of 34,278 people with T2DM. Prescriptions for dapagliflozin, empagliflozin, and canagliflozin are included.

Only 120 (16.0%) of the real world cohort had the same cardiovascular risk factors as the population of the EMPA-REG trial. The clinical characteristics of these people were similar to those included in the EMPA-REG trial (Table 1). The proportion of women in both the trial and the real world population was low in both the real world and trial cohorts. Mean ages were also similar. However, the real world cohort had a higher initial BMI and initial HbA1c.

Discussion

Only a small proportion of real world users of SGLT2 inhibitors have similar cardiovascular risk to people included in the EMPA-REG OUTCOME trial and have a higher baseline BMI and HbA1c. However, it has previously been shown that those with the highest BMI and baseline HbA1c derive the largest improvements in clinical practice.²

Whilst the trial results should encourage confidence in the use of empagliflozin in people with high cardiovascular risk, real world monitoring is required to ensure the described benefits translate into clinical practice.

Key findings

- SGLT2 inhibitors prescribing rates are increasing rapidly.
- Only 16% of people prescribed SGLT2 inhibitors in clinical practice had the same cardiovascular risk as people included in the EMPA-REG trial.
- Real world, high cardiovascular risk, patients treated with SGLT2 inhibitors have higher HbA1c and higher BMI than people in the EMPA-REG trial.

References

1. Zinman B, Wanner C, Lachin JM, Fitchett D, Bluhmki E, Hantel S, et al. Empagliflozin, Cardiovascular Outcomes, and Mortality in Type 2 Diabetes. *New England Journal of Medicine* (373):2117-28.
2. McGovern AP, Dutta N, Munro N, Watters K, Feher M. Dapagliflozin: Clinical practice compared with pre-registration trial data. *Br J Diabetes Vasc Dis*. (2014). 14:138-143.



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Table 1. Characteristics of participants of the EMPA-REG trial compared with those using SGLT2s in the real world. *Only people with similar cardiovascular risk factors to those in the EMPA-REG trial are included.

	Clinical trial population n (%) or mean (SD)	Real world population* n (%) or mean (SD)	P value
Total population	7,121 (100.0)	120 (100.0)	
Female	1,351 (28.8)	32 (26.7)	P=0.606
Age (years)	63.1 (8.6)	62.1 (7.8)	P=0.208
BMI (kgm ⁻²)	30.6 (5.3)	34.2 (6.6)	P>0.0001
HbA1c (%)	8.1	8.9	P>0.0001

