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# 1. Executive summary

## 1.1. Introduction

Diabetes is a group of conditions defined by increased levels of blood glucose (hyperglycaemia), due to either the pancreas not producing insulin or the body not able to use the insulin it produces. Type 2 diabetes (T2DM) is the most common type of diabetes, and is associated with insulin resistance[1].

It is commonly agreed that first line treatment for T2DM is metformin, however, there is uncertainty on which second line treatment to prescribe when metformin alone fails to give adequate glucose control. In this real-world study dipeptidyl peptidase 4 inhibitors (DPP4i), sulphonylureas (SU), thiazolidinediones (TZD) and sodium glucose co-transporter 2 inhibitors (SGLT2i) were compared for their effectiveness in lowering glycated haemoglobin (HbA1c) levels for a particular individual based on their clinical characteristics.

## 1.2. Methods

This was a retrospective, observational cohort study of adult patients with T2DM on the CPRD GOLD database between 01 January 2002 to 31 December 2017 that met eligibility criteria. The index date was the date of first prescription of second line drug (between 01 January 2012 and 31 December 2016).

Summary statistics were calculated for the overall study population and stratified by baseline HbA1c. Regression modelling was used to model the changes in HbA1c for the individual therapies. Baseline HbA1c was included in as a covariate in each of the models. Models were fitted to the data to adjust for the effect of observed covariates (potential confounders) including demographic characteristics, clinical factors, concomitant prescriptions and comorbidities. All analyses were performed using R version 3.4 or later.

## 1.3. Key results

This study in 7,170 patients receiving second line treatment for T2DM showed that SUs, DPP4i, TZDs and SGLT2i were comparable in terms of patients achieving the recommended HbA1c target of <7.5% (58mmol/mol) at both 6 and 12 months. For those receiving SGLT2i and SUs, the greatest improvement in HbA1c was observed in younger and older patients, respectively. Adherence rates were high for all drug classes. Also, patients with higher MPR (≥80%) had greater improvements in HbA1c at 12 months.

## 1.4. Conclusions

This study the identified phenotypic characteristics that could potentially impact treatment response to a specific drug class. Accounting for these characteristics in clinical practice, when selecting a second line treatment for T2DM, may improve patient outcomes. However, further research in real-world clinical practice is needed to better understand the predictive value of individual phenotypic characteristics and how they influence treatment response to second line therapies for T2DM.