# Differences in persistence by class of oral therapy for the treatment of type 2 diabetes

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## Background

**Higher rates of adherence and persistence to anti-hyperglycaemic medications among patients with type 2 diabetes (T2DM) have been shown to be associated with improved glycaemic control[1], reduced cardiovascular events and mortality[2-4], and reduced costs[5].**

**Sub-optimal adherence is a significant problem for those managing and living with T2DM, with rates reported as ranging between 60-80% depending on the medication class, patient population, and environment.[6,7] While adherence is acknowledged as a multi-factorial predicament, medication factors are an important dimension.**

## Aim

We compare medication persistence across all commonly used non-insulin medication classes used for treatment of type 2 diabetes adjusting for confounders of adherence.

## Methods

We performed a **retrospective cohort analysis** using a primary care based population (Royal College of General Practitioners Research and Surveillance Centre cohort).

We identified prescriptions for all medication classes utilised by people with T2DM between 1st January 2004 and 31st July 2015. We compared crude median, primary persistence (persistence from first ever prescription) across each class with non-persistence defined as prescription gap of ≥90 days. We also compared non-persistence between classes, adjusted for known confounders of adherence, using Cox regression. Confounders included: age, gender, ethnicity, socioeconomic status, alcohol use, smoking status, glycaemic control, duration of diabetes, diabetes complications, comorbidities, number of previous and concurrent diabetes medications. The analysis was performed using R version 3.2.3.

## Results

From 58,717 people with T2DM and a median duration follow up since diagnosis of T2DM of 6.75 (IQR 7.58) years, we identified 76,734 prescriptions for new medications. Metformin and sulphonylureas were the most commonly prescribed (Table 1).

Crude median persistence rates varied by drug (Figure 1). In regression models shorter persistence was associated with younger age, non-white ethnicity, extremes of HbA1c (<42 and ≥70 mmol/mol), peripheral neuropathy, renal disease, dementia, depression, heart failure, and a higher number previous diabetes medications. Longer persistence was associated with hypertension, and a higher number of concurrent diabetes medications.

After adjusting for these confounders, non-persistence was higher with all medications compared to metformin (other than SGLT2 inhibitors) (Table 1).

The largest intra-class variation in persistence was within DPP-4 inhibitors (Figure 2).

| Medication class | n | % | HR (95% CI) | p value |
|---|---|---|---|---|
| Biguanides (metformin) | 37,956 | 49.5% | 1.00 [reference] | |
| Alpha-glucosidase inh. | 241 | 0.3% | 1.83 (1.60-2.10) | <0.001 |
| Fixed dose combinations | 1,545 | 2.0% | 1.70 (1.61-1.80) | <0.001 |
| DPP-4 inhibitors | 9,038 | 11.8% | 1.50 (1.45-1.55) | <0.001 |
| GLP-1 analogues | 2,958 | 3.9% | 1.78 (1.70-1.87) | <0.001 |
| Meglitinides | 497 | 0.6% | 1.93 (1.75-2.13) | <0.001 |
| SGLT2 inhibitors | 1,217 | 1.6% | 1.06 (0.93-1.20) | 0.372 |
| Sulfonylureas | 19,173 | 25.0% | 1.23 (1.20-1.25) | <0.001 |
| Thiazolidinediones | 4,109 | 5.4% | 1.61 (1.55-1.67) | <0.001 |

**Table 1. Adjusted hazards ratios for primary non-persistence with 76,734 new diabetes prescriptions.** Adjusted for were age, gender, ethnicity, alcohol intake, smoking status, baseline glycaemic control, duration of diabetes, presence of complications, and comorbidities.

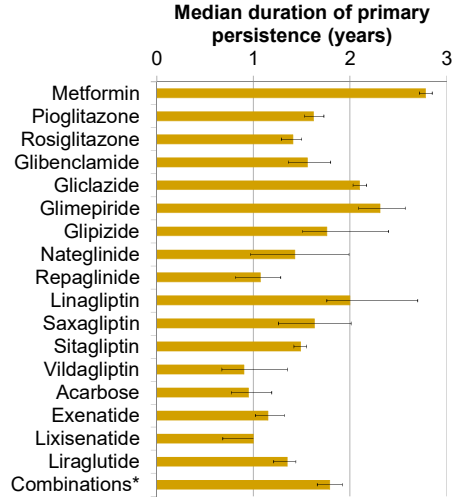


**Figure 1. A comparison of the median duration of primary persistence for all commonly used non-insulin therapies in the UK.** 95% confidence intervals are shown. SGLT2 inhibitors have not yet reached median persistence. *combinations include only metformin containing fixed dose combinations.

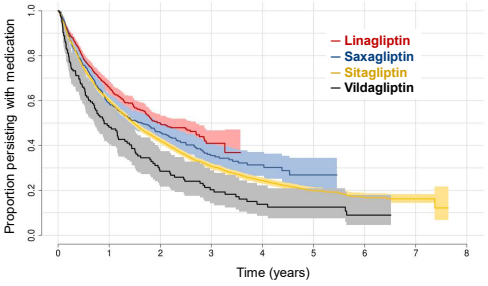


**Figure 2. Kaplan Meier survival plot of proportion of people remaining persistent with different DPP-4 inhibitors over time.** Linagliptin (n=1429), Saxagliptin (n=666), Sitagliptin (n=6,475), Vildagliptin (n=144). 95% confidence intervals are shown by the shaded areas.

## Conclusion

There is considerable variability in persistence between medication classes after adjusting for important confounders. These data may help facilitate proficient medication selection from the vast array of therapies currently available. We plan further work to understand the factors underlying these differences including a qualitative analysis of behavioural and attitudinal factors not available from electronic records.

## Key findings

- There is considerable variation in medication persistence between classes of therapy used in type 2 diabetes
- Metformin had the longest persistence and lowest hazard ratio for non-persistence.
- SGLT2 inhibitors show good early persistence.

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