
APPENDICES

Appendix 1: Initial Cohort Definition

The following criteria were applied to all patients:

- 14,639,234 patients were acceptable in October 2016
- 14,638,819 patients were either male or female
- 9,966,480 patients were registered at a GP practice between 01/01/2004-31/12/2015
- 9,135,950 patients had at least 6 months of up-to-standard (UTSt) follow-up at their practice

A total of 23 new user groups were identified from the 9,135,950 study patients, where the treatment of interest was acarbose, alogliptin, canagliflozin hemihydrate, dapagliflozin, dulaglutide, empagliflozin, exenatide, glibenclamide, gliclazide glimepiride, glipizide, linagliptin, liraglutide, lixisenatide, metformin hydrochloride, nateglinide, pioglitazone hydrochloride, repaglinide, rosiglitazone maleate, saxagliptin hydrochloride, sitagliptin phosphate, tolbutamide and vildagliptin. Patients also had to fulfill the following criteria:

1. Patients received their first ever prescription for a noninsulin antihyperglycemic drug in their therapy file on or after 01/07/2004 and before 31/12/2015 as specified in a code list that included 373 products code and was validated by endocrinologist (Dr. Smith). The cohort entry date will be set as the date of this first ever prescription.
2. Patients had at least 6 months continuous follow up (baseline period) prior to the cohort entry date. This was implemented so that there is enough baseline information to compare patients receiving different drugs.
3. Patients had a diagnosis of type 2 diabetes mellitus any time prior to the cohort entry date.
4. Patients had no prescription for a treatment in the same class as the initiating drug during the 6-month baseline period.
5. Patients had at least 1 prescription for a noninsulin antihyperglycemic drug.

6. Patients were eligible for linkage to Inpatient Hospital Episode Statistics (HES), UK Office for National Statistics (ONS) Mortality and Deprivation data.

This resulted in 182,852 unique patients fulfilled the criteria for the cohort. For the linked analysis, from the case cohort of which 109,616 unique patients were eligible for linkage to Inpatient HES, ONS Mortality and Deprivation data.

We further removed patients who did not use metformin as first-line therapy, resulting in 103,690 patients.