BACKGROUND

- The incidence of Type 2 diabetes mellitus is increasing and there are expected to be five million people with diabetes in the UK, with type 2 diabetes mellitus (T2DM) accounting for approximately 90% of cases [1].

- The management of T2DM aims to prevent or delay the development of long-term diabetes-related complications by control of blood glucose and other cardiovascular risk factors [2].

- Lifestyle advice (diet and exercise) is initially offered and metformin monotherapy is recommended first if blood glucose control remains or becomes inadequate, with further anti-hyperglycaemic agents and/or insulin added when needed. Sulphonylureas are recommended as a second-line option, but are associated with hypoglycaemia[3]. Pioglitazone or a dipeptidyl peptidase-4 (DPP-4) inhibitors (vildagliptin or sitagliptin) are recommended if there is a significant risk of hypoglycaemia or SU is contraindicated or not tolerated [2].

- Secondary care activities (inpatient, outpatient care & ambulance services) have been estimated to account for 38.5% of total NHS diabetes spend [4].

- The aim of this study was to compare secondary healthcare resources used by patients prescribed an SU as the initial add-on to metformin monotherapy (Met+SU) compared with patients prescribed other oral anti-hyperglycaemic therapies as the initial add-on to metformin (Met+OHA).

OBJECTIVES

- The primary objective was to assess the impact of using ‘metformin plus sulphonylurea’ (Met+SU) in comparison with ‘metformin plus other oral anti-hyperglycaemic agents’ (Met+OHA) in patients with T2DM on diabetes-associated secondary healthcare utilisation in the UK.

- The secondary objective was to assess elements of the composite primary outcome stratified by hospital admissions versus outpatient visits, cause of hospitalisation, route of hospital admission (accident & emergency [A&E] and non-A&E), length of hospital stay (short vs. long stay) and outpatient specialty.

- Exploratory outcomes included average annual cost and medication possession ratios (MPR) (ratio of actual days supply vs. days observed).

METHODS

- A retrospective observational cohort study of patients with a record of T2DM, using data from the Clinical Practice Research Datalink (CPRD) linked to Hospital Episodes Statistics (HES) was conducted.

- Eligible patients were defined using Medical Read codes for type 2 and unspecified diabetes, records of metformin prescribing and age at diagnosis (≥40).

- Patients initiated on dual therapy with Met+SU or Met+OHA following metformin monotherapy were identified during the period April 2003–March 2012 and comprised the two study cohorts. Other OHAs included sitagliptin, vildagliptin, linagliptin, pioglitazone and saxagliptin.

- Propensity scores were used to address the risk of channelling bias. Scores were estimated and Met+SU patients caliper matched to Met+OHA patients to balance the covariates (including HBA1c, age and duration of diabetes at baseline).

- Diabetes-associated secondary healthcare utilisation (inpatient admissions and outpatient visits) were measured from 6 month post-initiation of dual therapy until treatment change or end of follow-up.

- Outcomes for the primary and secondary objectives were calculated as rate ratios, adjusted for over dispersion using negative binomial regression and propensity score for covariates.

RESULTS

- A total of 128,079 CPRD GOLD patients were identified with an incident or prevalent record of T2DM and eligibility for HES linkage. Of these, 11,453 had an incident dual therapy prescription MET+SU following MET monotherapy and 2,992 for MET-OHA.

- From each cohort, 2,681 patients were successfully matched, 1,704 of whom had at least 6 months exposure to the dual therapy regime of interest.

- The mean age at cot death entry was 61.7 years (SD 9.9) in the Met+SU cohort and 61.4 years (SD 9.8) in the Met+OHA cohort. Baseline characteristics of both cohorts were well balanced (Table 1). The mean duration of exposure was 1.5 years (SD 0.9) in both cohorts. The mean duration of diabetes at baseline was 4.3 years in both cohorts.

- After adjustment, the use of Met+SU compared with Met+OHA was directionally associated with a 25% increase in the rate of hospitalisations (adjusted rate ratio 1.25, 95% CI 0.97–1.62). The adjusted rate ratio was higher for admitted patient care admissions 1.38 (95% CI 0.95–2.00) than outpatient visits 1.00 (95% CI 0.85–1.28).

- Diabetes-associated outpatient visits were associated with an average annual cost of 122.8 GBP (95% CI 98.4–169.4) in the Met+SU cohort compared with 100.3 GBP (95% CI 83.4–127.4) in the Met+OHA cohort. Visits to cardiology accounted for 25.4 GBP (95% CI 20.8) in the Met+SU cohort and 12.4 GBP (95% CI 7.7) in the Met+OHA cohort. There were less noticeable differences for the other specialties.

CONCLUSIONS

- To our knowledge, this is the first study that has evaluated the impact of alternative dual combination therapy regimens on secondary healthcare utilisation in patients with T2DM using T2DM data from the real world setting in the UK.

- Glucose-lowering combination therapy with metformin plus sulphonylurea is associated with a directionally higher rate of secondary healthcare utilisation than metformin plus other oral anti-hyperglycaemic agents.

- The higher rate of macrovascular complications with Met+SU compared with the Met+OHA cohort is in line with previous evidence [5–11], but warrants further research.

This study adds to the evidence that long-term clinical and health economic outcomes should be considered in treatment decisions for T2DM.