Methods: This is a population-based study based on Danish national cohort of 131 949 patients with type 2 diabetes who initiated pharmacotherapy with a GLD between 2005 and 2012. We estimated rates and adjusted hazard ratios (HRs) of community-based antibiotic use and hospital-treated infection according to choice of first GLD. We performed intention-to-treat analysis using Cox regression method.

Results: The rate of community-based antibiotic use was 362 per 1000 patient-years at risk [PYAR] and that for hospital-treated infection was 51/1000 PYAR. Compared to metformin, the risk of hospital-treated infection was slightly higher in sulfonylurea initiators (HR 1.12, 95% confidence interval [CI] 1.08 to 1.16) and substantially higher in insulin initiators (HR 1.63, 95% CI 1.54 to 1.72) initiators after adjustment for comorbid conditions, comedications, and other confounding factors. In contrast, virtually no difference was observed for overall community-based antibiotic use (HR 1.02, 95% CI 1.01 to 1.04, for sulfonylurea initiators; and 1.04, 95% CI 1.01 to 1.07, for insulin initiators). Compared with metformin initiators, sulfonylurea and insulin initiators experienced higher hospitalisation rates for viral and fungal infections, intra-abdominal infections, pneumonia, septicaemia, and urinary tract infections, and had higher rates of redeeming broad-spectrum antibiotics such as quinolones and cephalosporins.

Conclusions: Rates of community antibiotic treatment and infection hospitalization are high in first-treated patients with type 2 diabetes. Pharmacotherapy initiation with metformin was associated with lower infection risk compared with sulfonylurea or insulin initiation.

937. Treatment Discontinuation And Rates Of Hypoglycemia In Type 2 Diabetes Patients Treated With Dipeptidyl Peptidase-4 (DDP-4) Inhibitors or NPH Insulin As Third-Line Therapy

Cristiano S. Moura, Sasha Bernatsky, Michal Abrahamowicz, Hassan Behlouli and Louise Pilote

Department of Epidemiology, Biostatistics and Occupational Health, McGill University, Montreal, QC, Canada

Background: Clinical studies suggest that DPP-4 inhibitors are effective as third-line therapy for type 2 diabetes (T2D) patients. However, a direct comparison of DPP-4 inhibitors with NPH insulin in the general population is lacking.

Objectives: To compare therapy discontinuation and hypoglycemia hospitalization rates among T2DM patients initiating either DPP-4 inhibitors or NPH insulin.

Methods: Retrospective cohort study using the MarketScan database (2011-2014). We selected T2DM individuals who were newly dispensed either DPP-4 inhibitors or insulin NPH (basal insulin or mixtures containing NPH insulin) as third-line therapy, after metformin and sulphonylurea in combination. Cohort entry was defined by date of first prescription of the agent, and a 6-month pre-period was used to exclude prior users. Time to therapy discontinuation (prescription gap >90 days) and to first hospitalization for hypoglycemia were compared using Cox regression models. Patients were censored at time of death, transfer out of the health plan, or end of study period. Models were adjusted for baseline variables: age, sex, year of cohort entry, comorbidities, hypertension, and prior history of hypoglycemia or diabetic ketoacidosis.

Results: We studied 54,318 individuals, most (92.7%) were DPP-4 initiators. The NPH group included more women (47.2% versus 40.5% on DPP-4), and more had prior history of hypoglycemia at baseline (21.0% versus 4.1%). In multivariable analysis, treatment discontinuation during follow-up was higher for patients initiating NPH insulin compared with DDP-4 inhibitors (hazard ratio, HR = 1.48; 95%CI = 1.42-1.54). Risk of hypoglycemia was also higher in NPH insulin initiators (HR = 2.82; 95%CI = 2.57-3.10).

Conclusions: Our study suggests that T2D patients initiating third-line therapy with NPH insulin had higher risk of discontinuation and hypoglycemia when compared to DPP-4 inhibitors initiators. This real-world analysis suggests poorer control with NPH insulin versus DPP-4 inhibitors in T2DM patients in need of a third line agent although residual confounding may partially explain results.

938. Risk of Hypoglycaemia in Users of Sulphonylureas with Renal Impairment: A Population-Based Cohort Study

Judith van Dalem[1,2,3], Martijn Brouwers[4], Coen Stehouwer[4], André Krings[2], Hubert Leufkens[5], Johanna Driessen[1,3,5], Frank de Vries[1,5] and Andrea Burden[1,3,5]

DOI: 10.1002/pds

[1]*Department of Clinical Pharmacy, Maastricht University Medical Centre+, Maastricht, Netherlands;* [2] *Department of Clinical Pharmacy, Zuyderland MC, Heerlen, Netherlands;* [3]*Care and Public Health Research Institute (CAPHRI), Maastricht, Netherlands;* [4]*Department of Internal Medicine, Cardiovascular Research Institute Maastricht (CARIM), Maastricht University Medical Centre+, Maastricht, Netherlands;* [5]*Division of Pharmacoepidemiology and Clinical Pharmacology, Utrecht Institute of Pharmaceutical Sciences, Utrecht, Netherlands*

Background: Sulphonylureas (SUs) are a primary treatment option for patients with type 2 diabetes mellitus. Hypoglycaemia is a well-known severe side-effect that occurs more often in patients with renal impairment. However, data about the incidence of hypoglycaemia in patients with renal function is conflicting.

Objectives: To determine whether treatment with SUs only in patients with renal impairment is associated with a higher risk of hypoglycaemia compared to metformin-only users.

Methods: We conducted a retrospective cohort study using data from the Clinical Practice Research Datalink (CPRD) database (2004–2012). New users (N = 120,803) with at least one prescription for a non-insulin antidiabetic agent (NIAA) and aged 18+ were included. The first NIAA prescription defined start of follow-up. Patients were followed until the end of data collection or a record for hypoglycaemia or a blood glucose serum level < 3.0 mmol/l. The associations between the SU dose, renal impairment, different SUs used, and the risk of hypoglycaemia were determined using Cox proportional hazard models. Adjustments were made for age, sex, life style, comorbidity and drug use.

Results: The risk of hypoglycaemia in current SU-only users was significantly increased compared with current metformin-only users (adjusted Hazard Ratio [HR] 2.50 [95% Confidence Interval [CI] 2.23–2.82]). The higher risk in current SU-only users was further increased in patients with an eGFR < 30 mL/min/1.73 m2 (adjusted HR 4.96 [95% CI 3.76–6.55]). The risk of hypoglycaemia was also significant higher in patients with a high SU dose (adjusted HR 3.12 [95% CI 2.68–3.62]) and with current glibenclamide use (adjusted HR 7.48 [95% CI 4.89–11.44]). Results for gliclazide, the currently recommend SU of first choice, showed a similar risk of hypoglycaemia compared to other SUs.

Conclusions: SU-treatment in patients with a renal function below 30 mL/min/1.73 m2 should be considered with caution, especially the use of glibenclamide. In contrast with several guidelines, gliclazide does not seem to be superior compared to glimepiride, glipizide and tolbutamide.

939. Adjusting for the Effect of Switching Basal Insulin Treatment on the Risk of First Severe Hypoglycaemia

Houssem Khanfir[1], Pasi Korhonen[1], Sari Mäkimattila[2] and Fabian Hoti[1]

[1]*EPID Research, Espoo, Finland;* [2]*Novo Nordisk Farma, Espoo, Finland*

Background: Long-acting basal insulin analogues have shown a positive effect on the balance between glycaemic control and hypoglycaemia risk compared to insulin NPH (Neutral Protamine Hagedorn). Hazard ratio (HR) estimates of the risk of severe hypoglycaemia (SH) using standard methods may be biased in the presence of insulin switching.

Objectives: The objective of this study is to estimate and compare the incidence of first SH among type 2 diabetes mellitus (T2DM) patients treated with insulin detemir, glargine and NPH, accounting for insulin switching with the use of Marginal Structural Models (MSM).

Methods: T2DM patients aged >40 who initiated use of detemir, glargine or NPH during 2006-2009 were identified from the Finnish health care registers. The patients were followed until discontinuation of insulin treatment, death, end of 2009 or first SH event. In the MSM the causal effect of insulin use on the risk of first SH was estimated by applying the inverse of the probability to switch as weights in the Cox's Proportional Hazard (Cox PH) model. The probability to switch (from NPH to detemir or glargine) was estimated using logistic regression adjusting for both fixed and time dependent covariates on several time grids.

Results: Out of the total population of 27 267 patients, 5 292 (19.4%) initiated detemir, 11 980 (43.9%) initiated glargine and 9 995 (36.7%) initiated NPH. The mean follow-up time was 0.9 years and mean time to first switch was 1.0 years. From NPH initiators, 593

DOI: 10.1002/pds