

offers similar or reduced HbA1c reduction, had comparable significant weight loss to other SGLT-2s and GLP-1s, and appeared to have a superior weight loss profile compared with DPP-4s and TZDs. No increased risk of adverse events were observed for empagliflozin compared with placebo and other ADs.

PDB6

COMPARATIVE EFFICACY AND SAFETY OF EMPAGLIFLOZIN WITH OTHER ANTIDIABETIC DRUGS FOR THE THIRD LINE TREATMENT OF TYPE 2 DIABETES MELLITUS

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OBJECTIVES: The aim of the present network meta-analysis is to compare the efficacy and safety of empagliflozin versus other antidiabetic drugs used in third line for the treatment of patients with type 2 diabetes mellitus (T2DM). **METHODS:** We conducted a systematic review randomized controlled trials (RCTs) and Bayesian network meta-analysis to establish the comparative efficacy and safety of SGLT-2s, DPP-4s, GLP-1s, and TZDs. RCTs enrolling subjects with T2DM inadequately controlled on metformin plus sulfonylurea were included. The principal outcome of this analysis was the effect of these drugs on HbA1c, weight, systolic blood pressure (SBP), incidence of hypoglycaemia and urinary tract infections (UTIs) at 24 weeks. **RESULTS:** From 6969 abstracts, 13 were included in the analysis. No RCTs involving TZDs were identified. Compared with placebo, mean changes in HbA1c were -0.65% [95% confidence interval (CI) -1.59 to -0.08%] and -0.60% [95%CI -1.14 to -0.14%] for empagliflozin 10mg and 25mg. No significant differences were detected between interventions. Mean changes in weight with empagliflozin 10mg and 25mg were -1.77 [95%CI -2.19 to -1.35] and -2.00 [95%CI -2.44 to -1.57], respectively. Mean weight losses were fairly similar across SGLT-2s and GLP-1s ranging between -1.26 to -2.12. All DPP-4s were associated weight gains, ranging from 0.33 to 0.98, of which most were statistically significant. SBP data were only available for SGLT-2s and DPP-4s. Empagliflozin 10mg and 25mg compared with placebo had statistically significant reductions of -2.70 and -2.09. All interventions (except exenatide) yielded relative risk of hypoglycaemia greater than 1.00. For UTIs, no differences were found between SGLT-2s or DPP-4s and placebo. **CONCLUSIONS:** Compared with other SGLT-2s, DPP-4s, and GLP-1s, empagliflozin generally offers similar HbA1c control at week 24, an advantageous profile in weight loss and reduction of SBP, as well as similar safety profile.

PDB7

COMPARATIVE EFFICACY AND SAFETY OF EMPAGLIFLOZIN WITH OTHER ORAL ANTIDIABETIC DRUGS FOR THE SECOND LINE TREATMENT OF TYPE 2 DIABETES MELLITUS

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OBJECTIVES: To compare the efficacy and safety of empagliflozin versus other second-line treatment for patients with type 2 diabetes mellitus (T2DM). **METHODS:** A systematic review and Bayesian network meta-analysis were performed to identify randomized controlled trials (RCTs) assessing the efficacy and safety of SGLT-2s, DPP-4s, GLP-1s, TZDs, and SUs in patients with T2DM. RCTs enrolling subjects with T2DM inadequately controlled with metformin monotherapy were included. The principal outcomes were HbA1c, weight, systolic blood pressure (SBP), hypoglycaemia, and urinary tract infections (UTIs) at 24 weeks. **RESULTS:** Forty-eight RCTs were included. The mean differences (MD) in HbA1c were -0.56% [95% confidence interval (CI) -1.06% to -0.08%] and -0.64% [95%CI -1.14 to -0.14%] for Empagliflozin 10mg and 25mg vs placebo. All other interventions yielded similar reductions and no significant differences were detected between interventions. Empagliflozin 10mg and 25mg significantly changed patients' weight by -1.63kg (95%CI -2.66 to -0.64) and -2.01kg (95%CI -3.02 to -1.02), versus placebo. Other SGLT-2s had similar MDs, all DPP-4s had no change, and GLP-1s fell in between. All SUs and TZDs were associated with significant weight gain versus placebo. For SBP, the MDs for Empagliflozin 10mg and 25mg versus placebo were -4.09mmHg (95%CI -6.97 to -1.18) and -4.81mmHg (95%CI -7.69 to -2.00). No significant differences between Empagliflozin and other interventions were detected. Incidence of hypoglycaemia for empagliflozin 10 and 25 mg relative to placebo was 2.71 [95%CI 0.46 to 11.44] and 1.97 [95%CI 0.23 to 9.57], respectively. No significant differences were detected between empagliflozin and other interventions. For UTIs, all yielded relative risks close to 1.00 when compared with placebo. **CONCLUSIONS:** Compared with other SGLT-2s, DPP-4s, GLP-1s, TZDs, and SUs, empagliflozin offers similar HbA1c control at 24 weeks, a marked reduction in weight compared with DPP-4s, TZDs, and SUs, and a similar safety profile as other interventions.

PDB8

LONG-TERM MODELING OF USING MANUALLY CODED AND AUTOCODED BLOOD GLUCOSE METERS IN DIABETES TREATMENT

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OBJECTIVES: To obtain long-term clinical outcomes of using manually coded and autocoded blood glucose meters in diabetes treatment in the Russian Federation. **METHODS:** The model used in this study analyzed the influence of errors in blood glucose measurements (due to using manually or autocoded glucose meters) on the treatment of patients with Type 1 and Type 2 diabetes during the 26 years period (the life-time period). Life years gained (LYG) was chosen as an outcome measure in assessment of health intervention. Calculation of LYG was based on prior clinical studies that evaluated glucose meters' errors in glucose level measurements and risk of complications associated with blood glucose level. Data for patients with diabetes was obtained from prior epidemiological studies that had been provided in Russian Federation. **RESULTS:** Use of manually coded blood glucose meters in the analyzed population with median age of 53 years during

26 years period was associated with 18,59 LYG. At the same time use of autocoded blood glucose meters was associated with 18,92 LYG. In case of using autocoded meters instead of using manually coding meters patients obtained 0,33 LYG more (120 days). **CONCLUSIONS:** Obtained results showed that difference in glucose measurement errors between manually coded and autocoded blood glucose meters can lead to the difference in long-term outcomes in diabetes treatment.

PDB9

ASSESSING THE RELATIONSHIP BETWEEN IMPROVED LIFE EXPECTANCY DUE TO BETTER CARDIOVASCULAR RISK FACTOR MANAGEMENT AND THE LIKELIHOOD OF MICROVASCULAR COMPLICATIONS IN TYPE 2 DIABETES MELLITUS

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OBJECTIVES: Type 2 diabetes mellitus (T2DM) is a chronic disease associated with increased risk of cardiovascular (CV) and microvascular complications. Improvements in blood pressure and cholesterol control have resulted in a reduction in CV event rates in clinical practice. The objective of this study was to assess the relationship between increased life expectancy, due to reduction in CV event rates, and the risk of microvascular disease for a range of glycemic control levels. **METHODS:** A lifetime analysis was conducted using the CORE diabetes model (CDM). Newly diagnosed T2DM simulated patients aged 52 years at baseline with HbA1c 7.1%, SBP 135.1 mmHg, total cholesterol: HDL 5.2 mmol/l were modelled. The impact of HbA1c on microvascular complications was assessed by running the CDM with baseline HbA1c $\pm 1\%$ for scenario 1: 100% of patient receiving CV risk factor management; and scenario 2: no CV risk factor management. **RESULTS:** Improved CV risk factor management reduced the predicted cumulative incidence of fatal myocardial infarction (MI) from 27% to 18%, increasing life expectancy by an average of 2 years. For scenario 1, baseline HbA1c +1% versus -1% was associated with a 20%, 11% and 4% increase in microalbuminuria (MA), gross proteinuria (GRP) and end stage renal disease (ESRD), respectively; for scenario 2, the increase was 15.5% for MA, 7.6% for GRP and 2.5% for ESRD. Cumulative incidence of neuropathy ranged from 68.4% (baseline HbA1c +1%) to 42.1% (baseline HbA1c -1%) for scenario 1 and from 65.2% (baseline HbA1c +1%) to 39.7% (baseline HbA1c -1%) for scenario 2. Cumulative retinopathy rates were similar across both scenarios: 56.7% versus 56.0% for scenarios 1 and 2, respectively. **CONCLUSIONS:** This modeling study suggests that improvements in blood pressure and cholesterol management may result in increased rates of microvascular complications, in particular renal disease, over the long term as patient survival increases.

PDB11

A SYSTEMATIC REVIEW AND NETWORK META-ANALYSIS ASSESSING THE EFFECTIVENESS AND TOLERABILITY OF GLIPTINS AND SULFONYLUREAS AS MONOTHERAPY IN PATIENTS WITH TYPE 2 DIABETES MELLITUS IF METFORMIN IS NOT CONSIDERED APPROPRIATE

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OBJECTIVES: A significant proportion of patients with type-2-diabetes mellitus (T2DM) are unable to take Metformin as recommended first-line therapy due to gastrointestinal intolerance or contraindications such as chronic kidney disease. In contrast to combination therapy no network meta-analysis (NMA) has been undertaken for oral anti-diabetic drugs (OAD) as monotherapy in this population - particularly with respect to gliptins and sulfonylureas as second-line options. The purpose of this study is to assess the comparative effectiveness and tolerability of gliptins versus sulfonylureas in terms of glycated hemoglobin (HbA1c), body weight and hypoglycemia. **METHODS:** A systematic review was conducted searching bibliographic databases, reports of regulatory authorities and clinical trial registries through July 2012 to identify randomized controlled trials in adult T2DM patients receiving at least 12 weeks of OAD monotherapy or placebo. A Bayesian NMA was performed to yield mixed treatment comparisons. Consistency was examined by the node split method. **RESULTS:** A total of 62 studies enrolling 21,302 patients informed the entire network. Due to their improved model fit estimates from random effect models are reported to account for heterogeneity across the set of studies. After a mean follow-up of 32 weeks, the difference in mean HbA1c was 0.26, 0.95 credible interval (CrI_{0.95}): [0.1; 0.42], in favour of sulfonylureas. However, gliptins induced weight loss (difference in means: -1.21 kg; CrI_{0.95}: [-1.57; -0.84]) and were associated with a considerably lower incidence of any hypoglycemia compared to sulfonylureas (odds ratio: 0.22; CrI_{0.95}: [0.15; 0.31]). All effect estimates were statistically significant and consistent in terms of combining direct and indirect evidence. **CONCLUSIONS:** This is the first network assessing OAD monotherapy that can readily be extended to emerging therapies. With regard to glycemic control gliptins were slightly inferior to sulfonylureas, whereas they positively affected body weight and risk of hypoglycemia, confirming their role in second-line monotherapy.

PDB12

GLYCEMIC, LIPID, AND BLOOD PRESSURE CONTROL AMONG INDIVIDUALS WITH TYPE 2 DIABETES MELLITUS IN SAUDI ARABIA

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OBJECTIVES: Inadequate glycemic, blood pressure (BP), and low-density lipoprotein (LDL) control among persons with type 2 diabetes mellitus (T2DM) increases the risk of T2DM-related complications, which require more intensive and costly therapy. Extending on a recently-conducted study in Dubai, UAE, we assessed levels of glycemic, LDL, and BP control, and estimated the proportion of those meeting

guideline targets, among a cohort of individuals treated for T2DM in Riyadh, Saudi Arabia. **METHODS:** Charts from 455 adults with T2DM who visited the King Fahad National Guard Hospital from October 2009 to March 2010 (enrolment period) were systematically sampled until the target ($n=250$) was reached. Haemoglobin A1c (HbA1c), LDL, and BP test results from enrolment to September 2011 were abstracted. The most recent test values were compared to guideline targets. The proportion of well-controlled (target met on all tests) and never-controlled (target not met on any test) subjects over the study period was calculated. Analyses were stratified by T2DM duration. **RESULTS:** Forty-four percent of the cohort was male; at enrolment, mean (SD) age was 61 (13) years and mean T2DM duration was 11 (8) years. At the most recent assessment, 36 subjects (14%) had HbA1c $<7\%$, 91 (36%) had HbA1c $\geq 9\%$, and 177 (72%) had LDL $<100\text{mg/dL}$. Although 109 subjects (44%) met BP targets ($<130/80\text{mmHg}$), 30% had BP $\geq 140/90\text{mmHg}$. HbA1c, LDL and BP were well-controlled in 5.2%, 45.9%, and 8.4% of subjects, respectively, while 71.2%, 13.4% and 22.9% were never-controlled, respectively. The proportion of the cohort that was never-controlled for HbA1c increased with T2DM duration. **CONCLUSIONS:** While rates of HbA1c control were low among subjects with T2DM, nearly half met BP targets and nearly three quarters met LDL targets. Given the increased risk of complications associated with poor control, achieving higher rates of control could reduce the burden of T2DM in Saudi Arabia.

PDB13

BUDGET IMPACT ANALYSIS

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OBJECTIVES: To quantify the number and costs of relapses avoided over 2 years in the first-line treatment of RRMS based on the findings of the Cochrane report. **METHODS:** An Excel-based financial model estimated the relapses and costs incurred by a hypothetical cohort of 1000 RRMS patients treated with first-line disease-modifying drugs (DMDs). The modelled cohort evaluated the consequences of treatment with subcutaneous (SC) interferon beta-1a versus intramuscular (IM) interferon beta-1a, as this was the only comparison whose data quality was assessed as 'high' by the Cochrane Review (Filippini et al., 2013). Risk of relapse was based on the 2-year data from the Cochrane Review network meta-analysis. The analysis was performed from a US payer perspective. The cost of a relapse was sourced from Panitch et al., 2005, and adjusted to 2012 US dollars. Net annual cost of therapy was based on wholesale acquisition cost. Given the model's short time horizon, disability-related costs were not included as these tend to be an important economic driver only over the long-term progression of the disease. In order to test how variability in the model's inputs might impact the analysis' results, two-way sensitivity analyses were performed based on the reported 95% risk of relapse credible intervals for SC interferon beta-1a and IM interferon beta-1a. **RESULTS:** In a hypothetical cohort of 1000 RRMS patients, treatment with SC interferon beta-1a is expected to result in the avoidance of 173 (sensitivity analysis range: -20 to 399) relapses versus IM interferon beta-1a over 2 years. Assuming a direct cost of relapse of \$5141, this represents a savings of \$890,212 (sensitivity analysis range: -\$102,138 to \$2,052,934) versus IM interferon beta-1a. **CONCLUSIONS:** Subcutaneous interferon beta-1a is likely to result in fewer relapses and lower direct costs of relapse versus IM interferon beta-1a over a 2-year period treatment.

PDB14

A DECISION-FOCUSED MIXED TREATMENT COMPARISON (MTC) OF ALTERNATIVE DPP-4 INHIBITORS (DPP-4i'S) USED IN COMBINATION WITH METFORMIN OR A SULFONYLUREA FOR THE TREATMENT OF TYPE 2 DIABETES MELLITUS (T2DM)

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OBJECTIVES: To conduct decision-focused mixed treatment comparisons (MTCs) of the relative efficacy and safety of a new DPP-4 inhibitor (DPP-4i), alogliptin 25mg daily compared to current DPP-4i's used in UK clinical practice (sitagliptin, saxagliptin, linagliptin, vildagliptin) in dual therapy for the treatment of type 2 diabetes mellitus (T2DM) in combination with metformin or sulfonylurea (SU). **METHODS:** A decision-focused systematic review was conducted to identify RCTs comparing the DPP-4i's in combination with metformin or SU compared to metformin or SU alone or against each other in the target patient population. Separate Bayesian MTCs were conducted for each DPP-4i combination. Outcomes of interest were change in HbA_{1c} from baseline (primary), weight change, proportion of patients HbA_{1c} $<7\%$, and proportion of patients ≥ 1 hypoglycaemic episode. Fixed and random effects models were run with sensitivity analysis conducted to account for confounding factors (study length, baseline HbA_{1c}), study heterogeneity and inconsistency. **RESULTS:** Twenty-five RCTs met inclusion criteria for the MTCs. For the primary outcome, fixed effects models suffered from heterogeneity problems whilst random effect models struggled to estimate between trial heterogeneity. However, the base case and all sensitivity analyses showed the same results - alogliptin in combination with metformin or SU had a high probability of non-inferiority to comparator DPP-4i's in HbA_{1c} change (61%-100% at a 0.3% HbA_{1c} margin). Deletion of trial outliers via leverage plots vastly improved model fit within fixed effects models whilst not changing underlying results. For all other outcomes alogliptin was shown to be comparable to alternative DPP-4i's. **CONCLUSIONS:** Alogliptin 25mg has comparable efficacy and safety as other DPP-4i's at their recommended doses in UK clinical practice. This is in line with expectations based on prior meta-analyses of DPP-4i's. The use of a decision-focused approach to the MTC enables a focus on the data of direct interest for clinical and HTA based decision making.

PDB15

IDENTIFYING CONSISTENT INCONSISTENCY IN NETWORK META-ANALYSES - AN ILLUSTRATION IN TYPE 2 DIABETES

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OBJECTIVES: Network meta-analyses (NMA) provide estimates of comparative efficacy for multiple treatments based on an analysis of connected networks of trial comparisons. A key concern is the comparability of treatment effect estimates from different trials. Where there is both indirect and direct evidence for one or more comparisons ('loops' in the network) it is possible to evaluate empirically the 'consistency' of the network. **METHODS:** A variety of methods have been proposed to examine inconsistency including: (i) node-splitting where the direct and indirect estimates are compared across the network (ii) comparison to an 'inconsistency' model where estimates for each treatment comparison are allowed to be independent, (iii) inclusion of treatment by design interaction terms, (iv) investigation of residual deviance estimates for individual trial arms, and (v) investigation of mixed predictive p-values. We compare the implementation and, most importantly, the interpretation of these methods using a previously published NMA in type 2 diabetes. In this analysis HbA1c was compared across six treatments in a network of 22 studies with multiple 'loops'. **RESULTS:** The methods agreed in showing the presence of inconsistency with the network. For example, the inconsistency model showed an improved fit (DIC -62.35) compared to the consistency model (DIC -60.25). The node splitting method identified statistically significant inconsistency in two treatment arcs (liraglutide 1.8mg vs placebo and liraglutide 1.8mg vs exenatide QW). **CONCLUSIONS:** The alternative methods vary in their ability to provide an omnibus 'test' of inconsistency across the network and their ability to identify which parts of the network contain inconsistencies. We highlight that none of the methods alone can identify individual studies as being the cause of inconsistencies and argue that we need to consider the whole structure of the network and the characteristics of the studies (in terms of treatments, subjects and design) within the network.

PDB17

THE EFFICACY AND EFFECTIVENESS IN HBA1C-LOWERING IS DEPENDENT ON BASELINE BODY MASS INDEX (BMI) FOR SITAGLIPTIN BUT NOT CANAGLIFLOZIN IN THE TREATMENT OF TYPE 2 DIABETES MELLITUS (T2DM)

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OBJECTIVES: To investigate HbA1c-reduction by baseline BMI in patients treated with canagliflozin or sitagliptin, using clinical trial and electronic medical record (EMR) data. **METHODS:** Patient-level data from two randomised controlled trials (RCTs) were used to explore HbA1c-reduction from baseline after 52 weeks treatment with canagliflozin (100/300mg) or sitagliptin (100mg) by baseline BMI. Ordinary least squares (OLS) regression was performed with HbA1c, BMI, eGFR and demographics as covariates, in patients with metformin (MET) or metformin+glimepiride (MET+SU) background therapy. EMR-data (UK General Practitioner data from CPRD) on HbA1c over time in patients treated with sitagliptin were analysed by background therapy using repeated measures analysis, with baseline BMI, HbA1c and demographics as covariates. **RESULTS:** In both RCTs sitagliptin showed a decreasing HbA1c-reduction by increasing baseline BMI, while efficacy of canagliflozin was independent of BMI. The estimated HbA1c-reduction (%) from baseline for sitagliptin in patients with baseline BMI of 25 vs. 40 varied between -0.87 to -0.58 (MET; $\Delta=0.29$, $p=0.01$) and -0.87 to -0.54 (MET+SU; $\Delta=0.33$, $p=0.0014$), while a non-significant increase in HbA1c-reduction was observed in high BMI-patients in all canagliflozin-arms (Δ between -0.04 and -0.07). EMR-data showed similar decreasing effectiveness of sitagliptin in obese patients. Estimated HbA1c-reduction (month 10; baseline HbA1c 9%) was significantly less (MET: $\Delta=0.30$, MET+SU: $\Delta=0.35$, $p<0.0001$) in patients with BMI 40 vs. 25. No data for canagliflozin were yet available. Lower efficacy of sitagliptin in obese patients has been previously reported in the literature. **CONCLUSIONS:** RCT and EMR-data consistently show that the relative efficacy of anti-diabetic treatments may depend on baseline BMI. Reduced efficacy of sitagliptin and DPP-4 inhibitors in general in obese patients may be explained by a higher degree of insulin-resistance. Efficacy of canagliflozin is independent of BMI, due to its insulin-independent mechanism of action. Patients' BMI should be taken into account to select effective therapeutic options for patients with T2DM.

PDB18

TREATMENT MAINTENANCE DURATION OF DUAL THERAPY WITH METFORMIN AND SITAGLIPTIN IN TYPE 2 DIABETES - REAL-WORLD DATA FROM ODYSSEE STUDY

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OBJECTIVES: Comparative effectiveness of new oral anti-diabetic drugs in primary care practice remains poorly characterized. This presentation focus on the relevant statistical methods used to handle common potential bias related to real-world observational designs. **METHODS:** Multicenter, longitudinal, observational study, conducted in primary care in France. Participating physicians were to include adult type 2 diabetes patients initiating a treatment with metformin and sitagliptin dual therapy (M-Sit group) or metformin and sulfonylurea dual therapy (M-SU group). Planned follow-up period was three years. The primary endpoint was the treatment maintenance duration, from initiation of dual therapy to a strict change, defined as the addition, replacement or withdrawal of an agent used for initial dual therapy. Survival Kaplan-Meier analysis, multivariate Cox model adjusted on the propensity score in order to limit bias due to baseline imbalance between the two groups and sensitivity analyses including multiple imputations to deal with missing data have been performed. **RESULTS:** A total of 3 453 patients have been analyzed: 1 874 in the M-Sit group and 733 in the M-SU group. In the principal analysis, the median treatment maintenance duration was 20.2 months in the M-SU group and 43.2 months in the M-Sit group ($p<0.0001$).