lematic. There is no single ICD-9 code to identify FN; therefore an algorithm must be created to identify FN patients. Previously published algorithms are generally comprised of 3 main codes: (1) neutropenia (primary designation (ICD-9 code 288.0)) (2) fever (ICD-9 780.6) (3) infection. However, the primary designation of neutropenia is only used if there is no clear source of infection. Additionally, infection in the neutropenic cancer patient can often be difficult to confirm due to the lack of neutrophils and typical clinical symptoms and signs; the febrile response may also be blunted. Therefore, the FN algorithm may use neutropenia alone, likely identifying patients with neutropenia alone in addition to those with FN. In a study utilizing claims data, FN was defined as primary or secondary diagnosis of neutropenia or infection during the first chemotherapy course; 41% of cancer patient newly initiating chemotherapy were classified as having FN. When the FN definition was narrowed to primary or secondary diagnosis with neutropenia and either 1) fever or 2) infection 4.5% were classified as having FN; when the definition was broadened to diagnosis with neutropenia or fever or infection or a procedure code for infection treatment 64.7% were classified as having FN. There is a strong need to validate the coding associated with submitting medical claims for the treatment of FN in cancer patients receiving chemotherapy in real-world practice in order to utilize claims data to investigate FN.

PCN158

A METHOD TO INCREASE SAMPLE SIZE BY REMOVING THE CONTINUOUS ENROLLMENT REQUIREMENT

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OBJECTIVES: We introduce a method whereby the continuous enrollment requirement can be removed to increase the sample size and correct for incomplete information with an advanced statistical technique. METHODS: The inverse probability weighted least squares model is used to estimate the outcomes from a sample that does not require continuous enrollment in the inclusion criteria. This method involves two steps: probabilities are estimated using a non-parametric approach, and standard errors of the outcomes regression are adjusted for the first step estimation. RESULTS: To demonstrate the technique, we used U.S. claims data. Patients with incidents of cases of lung cancer were used. A total of 236 patients were identified without the continuous enrollment requirement of one year after diagnosis. With the continuous enrolment requirement, our sample size would be 87. Incomplete cases were more likely to have surgery and higher rates of comorbidities. R-squared increased 25% with the inverse probability weighted technique. Standard errors decreased with 35% and therefore improved the precision of our estimators. CONCLUSIONS: The continuous enrollment requirement does not have to be applied for pharmacoeconomical studies. Results might be biased if there are substantial differences between complete and incomplete observations. Even though there are no differences, removing this requirement increases the sample size and provides efficient estimators, especially in rare events.

PCN159

HFS 14: A SPECIFIC QUALITY OF LIFE SCALE FOR PATIENTS WITH HAND-FOOT SYNDROME

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BACKGROUND: Hand-foot syndrome or Hand-Foot skin reaction is a common adverse effect of certain chemotherapy agents, such as capecitabine or pegylated doxorubicin, where it is estimated to occur in 50% of cases. **OBJECTIVES:** The aim of this study is to develop and validate a hand-foot syndrome-specific quality of life scale in order to be able to measure the impact of the condition on patients and secondly to be able to assess the value of certain specific treatments in this indication **METHODS:** The questionnaire was developed after conducting a series of structured interviews with patients with forms of hand-foot syndrome of varying severity, which yielded a detailed and rigorous collection of verbatim transcripts. The Pilot-Testing are realised. **RESULTS:** Thirty-one items were identified, and 14 items were selected as being relevant and non-overlapping after initial evaluation. The first question in the HFS14 addresses which member is affected (hand, foot or both). The second question addresses the pain with three possible responses (very, moderately or not painful). The 14 items can be organised in 2 modules: the first module more specifically assesses the handicap generated by involvement of the "feet" and the second assesses the handicap generated by involvement of the "hands". **CONCLUSIONS:** The hand-foot syndrome-specific HFS14 scale is easy to use and meets the requirements of a quality of life scale. This scale now needs to be tested in longitudinal studies (for example in clinical trials) to confirm its ability to measure a change in status.

PCN160

PATIENT-REPORTED OUTCOMES SUPPORTING ONCOLOGY PRODUCT LABELING CLAIMS: TRENDS AND CHALLENGES

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The FDA has advocated the PRO Draft Guidance released in 2006 as the main vehicle for evaluating PRO and HRQOL claims in oncology product approvals. Additionally, FDA-affiliated researchers have identified factors inhibiting acceptance of HRQOL-based claims for oncology product labels, including: trial design, missing data, multiplicity, and inconsistent findings of HRQOL data. The views of the FDA on PRO and HRQOL claims are extensive per its own guidance, which puts forth detailed, restrictive requirements on use. These matters clarify why the FDA has not yet allowed the utilization of PRO or HRQOL data as primary evidence to support an oncology product approval. In contrast, the EMEA since its establishment in 1995 has conducted authorizations without an explicitly defined approach for evaluating HRQOL and other PRO data. Further, a reflective paper released in 2005 offered only broad recommendations on HRQOL labeling claims. As a result, the importance of HRQOL or other PRO data in the review process is based more broadly on its relevance to a given drug and overall assessment of the study in the eyes of the reviewers. The varying approaches between the FDA and the EMEA partly stem from divergent underlying organizational characteristics. The FDA enforces laws regarding medical product quality. Alternatively, the EMEA serves as a coordinating body, leaving enforcement responsibility to member states. Consequently, the EMEA provides more generic advice, whereas the FDA insists on rigorous criteria for conceptual and study design issues surrounding PRO claims. Otherwise, the EMEA is more likely to accept use of well-established PRO and HRQOL measures, whereas the FDA is inclined to request new PRO measures that explicitly satisfy the agency's most recent evaluative standards. Finally, the FDA places greater focus on symptom-based endpoints reflecting the direct consequences of treatment, whereas the EMEA is more willing to accept global HRQOL claims.

DIABETES/ENDOCRINE DISORDERS – Clinical Outcomes Studies

PDB1

ASSOCIATION BETWEEN GLYCOSYLATED HEMOGLOBIN AND CARDIOVASCULAR OUTCOMES IN PATIENTS WITH TYPE 2 DIABETES MELLITUS: A NESTED CASE-CONTROL STUDY

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OBJECTIVES: To describe the association between the three-year average glycosylated hemoglobin (A1C) and cardiovascular outcomes in adults with type 2 diabetes mellitus (T2DM). **METHODS:** In this nested case-control study, 245,346 adults (≥18 years) with T2DM were identified among members of Kaiser Permanente Southern California. Type 2 diabetic patients had at least two ICD-9 diagnosis codes for T2DM (250.x0, 250.x2) and either A1C > 7.5% or prescriptions for hypoglycemic agents from 2002–2007. Using hospital records and death certificates, cases were defined as patients with a nonfatal MI, nonfatal stroke, or death due to cardiovascular (CV) causes (MI, stroke, heart failure, arrhythmia, sudden cardiac death) in the period 2005–2007. Four controls from the T2DM pool were matched to each case based on age, sex and index date (date of the case defining event). A conditional logistic regression model was used to estimate the odds-ratio (OR) of cardiovascular events comparing patients with an average A1C ≤ 6 % and those with average A1C > 8% to patients with average A1C between 6–8%, considered 'near A1C target'. A1C categories were assigned to each patient based on average A1C over the three years prior to the index date. **RESULTS:** A total of 44,628 controls were matched to 11,157 cases. After adjusting for CV related medications, comorbidities, and other confounders, patients with an average A1C ≤6% were 50% more likely to experience a CV event than the 'near A1C target' T2DM patients (OR = 1.50, 95% CI 1.33–1.69, $p < 0.0001$). Patients with an average A1C > 8% experienced a 14% increase in odds of a CV event (OR = 1.14, 95% CI 1.03–1.26, $p = 0.01$). **CONCLUSIONS:** Compared to those with mean A1C levels between 6–8%, patients with T2DM who achieved mean A1C levels of ≤6% or failed to decrease their A1C below 8% over a 3-year period are at increased risk for cardiovascular events.

PDB2

THE IMPACT OF ORAL ANTIDIABETICS ON WEIGHT IN THE ELDERLY WITH TYPE 2 DIABETES MELLITUS IN THE AMBULATORY SETTING

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OBJECTIVES: To assess the impact of oral antidiabetics agents on weight change in Type 2 Diabetes Mellitus (T2DM) patients age 65 years and older. **METHODS:** An electronic medical record, General Electric Centricity research database, containing the ambulatory health records of US patients was used to conduct a historical cohort study of the T2DM elderly patients identified by ICD-9 codes, OAD prescription or both. Six months of continuous OAD monotherapy activity was required, and study period included 395 days pre/210 days post from the index date. Two BMI/weight readings were mandated, at baseline, and follow up. Data were analyzed using ANOVA with Tukey test to correct for multiple comparisons. **RESULTS:** A total of 2720 patients with a primary diagnosis of T2DM were included in the study. The overall mean age was 72.7 years. Statistical significant differences between users of different OADs at baseline were found for diastolic blood pressure ($p = 0.0009$), and age ($p < 0.001$) The most prescribed OAD medications were metformin (58.9%), glipizide (14.52%) and glimepiride (7.76%).The overall mean change in A1C level was –0.92 ($p < 0.001$) units and statistically significant differences were found when compared Metformin/Glipizide (mean difference 0.51320, 95% CI 0.06411–0.96230). The overall mean baseline BMI among all of the OAD groups was 29.08 kg/m^2. Significant differences in BMI units change were found for meglitinide users, (-1.27), metformin users (-1.06), and the sulfonylureas (-0.14). An average of 3.97 lb weight loss for all of the OAD groups was found. Major weight loss was found in the Metformin group (-6.41lb), and the Sulfonylureas group reported the least weight loss (-0.89lb). **CONCLUSIONS:** An association was found between the OAD use and

change in weight measured by BMI and raw weight in elderly T2DM patients in a real-world setting. The likelihood of weight loss in OAD users was somewhat consistent with the literature.

PDB4

PREVALENCE OF RENAL INSUFFICIENCY IN A COMMERICALLY-INSURED POPULATION WITH TYPE 2 DIABETES MELLITUS ENROLLED IN A LARGE, US NATIONAL HEALTH PLAN

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OBJECTIVES: Renal insufficiency (RI), a common complication of type 2 diabetes mellitus (T2DM), is associated with increased morbidity, mortality and costs. Early and accurate detection of RI among patients with T2DM is essential in delaying or reducing these outcomes. Consensus guidelines advocate the use of estimated glomerular filtration rate (eGFR) to assess renal function. The objective of this retrospective database analysis was to evaluate the prevalence of RI in a commercially-insured population with T2DM using ICD-9-CM codes and laboratory data from a large, national US health plan. **METHODS:** The study sample consisted of commercially-insured health plan members ≥18 years of age with evidence of T2DM from 1/1/06–12/31/07 and continuous enrollment for 12 months before and after identification of T2DM. The prevalence of RI was determined by physician diagnosis using ICD-9-CM codes ("physician-diagnosed"), and eGFR calculation using serum creatinine (SCr), age and gender ("eGFR-diagnosed"). Approximately 26.8% of members had laboratory data (≥1 SCr value) after identification; physician-diagnosed and eGFR-diagnosed RI prevalences were identified in this subset. RI was identified using the National Kidney Foundation (NKF) 5-stage classification system and defined as ≥ stage 2, or an eGFR of £89 ml/min. Comparisons between cohorts were made using chi-squares. **RESULTS:** Among over 13.7 million commercially-insured members within the database, 664,619 (4.8%) had evidence of T2DM. The sample included 259,295 members after applying continuous enrollment and other study criteria, of which 20,914 (9.2%) had evidence of physician-diagnosed RI. Among the subset with laboratory data available (n = 69,439), 6,795 (9.8%) had physician-diagnosed RI while 17,981 (25.9%) had evidence of eGFR-diagnosed RI ($p < 0.001$). **CONCLUSIONS:** The prevalence of RI within a commercially-insured population with T2DM was significantly higher using eGFR, the recommended method of estimating RI, than physician diagnosis of RI. It is likely that RI in the commercially-insured is under-estimated using diagnosis codes in claims data.

PDB5

GLYCAEMIC CONTROL AND INSULIN UTILIZATION IN UK PATIENTS WITH TYPE 2 DIABETES INITIATED ON EITHER BIPHASIC INSULIN ASPART 30 OR BIPHASIC HUMAN INSULIN 30

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OBJECTIVES: The objective of this study was to compare glycaemic control and insulin utilisation in insulin naïve patients with type 2 diabetes (T2D) after initiation on biphasic insulin aspart 30 (BIAsp) or biphasic human insulin 30 (BHI) **METHODS:** A retrospective cohort study was conducted using the IMS Disease Analyzer a UK primary care database. Study inclusion required subjects to be insulin naïve with at least one prescription for an oral anti-diabetic agent (proxy for T2D diagnosis), 12 months history and follow up and treatment with either BIAsp or BHI. Patients with a diagnosis of type 1 diabetes were excluded. Glycemic control (HbA1c) was compared at baseline (-6 to 0 months) and at follow-up (+6 to 12 months). Average daily insulin dose (ADD) was compared at follow-up. Effect of age and sex as covariates on the difference in HbA1c and ADD between BIAsp and BHI was controlled for using ANOVA. **RESULTS:** Analyses were conducted on 630 BIAsp and 751 BHI patients on whom full data was available. The mean age for BIAsp patients was 61.6 years (59.7% men). For BHI, the mean age was 64.4 (51.9% men). From baseline to follow-up, the mean HbA1c for BIAsp dropped from 9.95% to 8.16% (change = 1.79%) and for BHI the HbA1c dropped from 10.34% to 8.62% (change = 1.72%). The HbA1c difference was borderline significant ($p = 0.07$). The ADD of BIAsp was 46.97 insulin units whereas the BHI ADD was 63.28 IU ($p < 0.01$). **CONCLUSIONS:** In this large retrospective analysis in insulin naïve patients initiated on pre-mixed insulin there was a trend towards better glycaemic control for users of BIAp compared to BHI. Moreover, BIAsp was associated with a clinically relevant and statistically significantly lower ADD compared to BHI ($p < 0.01$). This has important implications for patient management and control of UK NHS costs.

PDB6

RELATIVE EFFECTIVENESS MANAGEMENT OF TYPE II DIABETES IN EUROPE: CAN THE AGENCIES' DEMANDS BE MET?

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OBJECTIVES: As decision-makers and the citizens they serve demand stronger evidence to support coverage, prioritization, and pricing, the need for relative effectiveness research has come to the fore. Whilst it is well known and documented that differences in costing structures, practise patters and unit costs can lead to differences in cost effectiveness estimates for any given clinical effect, less is known about the heterogeneity of treatments and their utilization to demonstrate Relative Effectiveness (RE) among EU countries. This study investigated differences in treatment availability and utilization using recommendations from HTA agencies as a proxy. METHODS: HTA reports were searched using 7 European HTA agencies websites (i.e., NICE, SMC, IQWIG, HAS, CAHTA, CVZ, TLV with the following keywords: pioglitazone, rosiglitazone, sitagliptin, vildagliptin, exenatide, glargine, detemir, aspart, glulisine and lispro. Recommendation was classified in three categories: recommended, restricted recommended, and not recommended in relation to indication based on marketing authorisation. RESULTS: No HTA agency had similar recommendations for all treatments. IQWIG recommended none of the products assessed (8), while Sweden recommended 86% of the products assessed (7). NICE, SMC, HAS, CAHTA and CVZ assessed 18, 8, 18, 15, and 10 products, recommending 22%, 50%, 56%, 13% and 0%, restricting 78%, 50%, 22%, 47% and 50% respectively. CONCLUSIONS: Large differences in recommendation of products among EU countries exist. As diabetes is a well established disease area, one would expect a more uniform armamentarium of recommended treatments. In light of the RE management plans, this research questions whether it is possible and desirable to develop a unified approach. Future research should focus on standardization of methods and address questions about acceptable methodology and its limitations.

PDB7

GLYCAEMIC CONTROL AND INSULIN UTILISATION IN PATIENTS WITH TYPE 2 DIABETES INITIATED ON A LONG-ACTING INSULIN ANALOGUE IN A DUTCH REAL-LIFE SETTING

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OBJECTIVES: The objective of the study was to compare real-life glycaemic control, insulin utilisation and body weight in patients with type 2 diabetes initiated on insulin detemir (IDet) or insulin glargine (IGlar) and to discuss the results against treatment guidelines. METHODS: Patients with a history of oral anti-diabetic use starting treatment with IDet or IGlar from 2004 through 2006 were included in a retrospective cohort study using the Dutch PHARMO data network. Glycaemic control (HbA1c < 7%) and daily insulin dose during unchanged insulin treatment up to 1 year of follow-up were compared between IDet and IGlar users using multivariate regression analysis adjusted for age, gender, propensity scores, baseline HbA1c and basal-bolus therapy. The observed results are discussed in context of European diabetes guidelines. RESULTS: A similar ($p = 0.44$) drop in HbA1c (from 8.6% to 7.5%) was observed for both IDet (n = 199) and IGlar (n = 479). Few patients were at goal at baseline (15.6% with IDet and 12.1% with IGlar). A similar proportion were at goal at follow-up (38.7% with IDet and 33.4% with IGlar) (adjusted OR 1.06; 95% CI 0.74:1.53). The average daily dose was similar at 29 IU/day (adjusted mean difference 0.2; 95% CI -2.9:3.2). Median weight loss was 1 kg among IDet users and 0 kg among IGlar users, but this was not statistically tested due to low patient numbers. CONCLUSIONS: There was no significant difference between users of IDet and IGlar with respect to glycaemic control and insulin dose in a real-life setting in the The Netherlands. However, compared with treatment guidelines, the results showed few patients treated to target, which may indicate that basal insulin analogues are not titrated intensive enough or that rapid-acting insulin should be added to improve glycaemic control.

PDB8

FEWER TREATMENT CHANGES WITH PREMIXED INSULIN ANALOGUES COMPARED TO PREMIXED HUMAN INSULIN—A REAL-LIFE TREATMENT PATTERN ANALYSIS OF PATIENTS WITH TYPE 2 DIABETES IN THE NETHERLANDS

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OBJECTIVES: Studies suggest that premixed insulin analogues may improve the balance between glycaemic control and hypoglycaemia compared with human premixed insulin in type 2 diabetes (T2D) patients. This study aimed to observe prescription patterns of premixed insulin analogues compared to human premixed insulin among T2D patients. **METHODS:** Data for T2D patients starting premixed insulin in the period 2004–2006 were extracted from the Dutch PHARMO database. Patients were categorized into insulin naïve and prior insulin users. The proportion of patients changing treatment (discontinuing, adding fast-acting insulin or switching treatment) within one year was determined. Data was analyzed using Chi-Square tests for categorical data and t-tests for continuous data. **RESULTS:** The study included 3530 patients initiated on premixed insulin, of which 2324 (65.8%) were insulin naïve. Overall, 2134 (60.5%) started on analogues; the proportion of prescribed analogue insulin was greater among prior insulin users (812 of 1206 = 67.3%) vs. naïve users (1322 of 2324 = 56.9%). Patient characteristics did not differ between human insulin and analogue users, except from baseline HbA1c: in the group of prior users (1206 / 34.2%), a significant difference in baseline HbA1c was observed between those using human premixed insulin (8.5%) and premixed analogue (8.0%, $p < 0.001$). Within one year, 44.1% of human premixed users and 33.5% of premixed analogue users changed treatment. Among human premixed users 20.1% discontinued treatment (230 days), 6.5% added fast-acting insulin to their therapy (114 days), and 17.6% switched treatment (143 days); among premixed analogue users 14.9% discontinued treatment (245 days), 5.8% added fast-acting insulin (137 days), and 12.9% switched treatment