(mCRC) was not recommended in the UK (until June 2009), but accepted under a price volume agreement scheme with prior authorization in Italy, and without restriction in France and Germany. These products are funded on top of DRG costs in France, but not in other countries. We reviewed how such differences might affect usage of TRZ and CTX in France, Germany, Italy and UK. **METHODS:** Data on drug utilization from June 2006 to July 2009 were extracted from the Synovate Oncology Monitor, an ongoing database tracking prescribing of anti-cancer therapies. Sample sizes varied between countries and indications, from 1700 to 6200 patients. **RESULTS:** Proportions of patients receiving TRZ from July 08 to June 09 ranged from 9% (UK) to 16% (Italy) in early BC, 12% (Italy) to 19% (France) in first-line advanced BC and 10% (France) to 34% (Italy) in second-line (irrespective of HER2 screening). For CTX, utilization rates ranged from 0% (UK) to 13% (France) in first-line and 2% (UK) to 19% (Italy) in second-line. Utilization of TRZ increased over time in early stage BC. Utilization of CTX was stable in France, increased in Germany and decreased in Italy. Dosages and patient profiles were comparable across countries. **CONCLUSIONS:** Funding on top of DRG does not appear to increase drug uptake. Health technology assessment conclusions influence utilization strongly. When access is granted, administrative constraints may reduce first-line utilization to the benefit of second-line. This should be considered when decisions are made about access to innovative medicine.

HT3

MULTICRITERIA DECISION ANALYSIS (MCDA) FOR DRUG COVERAGE DECISION BY A PUBLIC HEALTH PLAN: CASE STUDY OF TRAMADOL FOR CHRONIC NON-CANCER PAIN (CNCP) IN CANADA

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OBJECTIVES: To field-test a decision support framework (EVIDEM) and explore its utility to a drug advisory committee using tramadol for chronic non-cancer pain (CNCP) as a case study. **METHODS:** The EVIDEM framework includes a multicriteria decision analyses matrix (MCDA) composed of 15 quantifiable components of decision including six domains (disease impact, context of intervention, intervention outcomes, type of benefit, economics and quality of evidence) and a qualitative tool including six components of decision regarding ethical considerations, system capacity and political/historical context. A synthesized health technology assessment (HTA) report tailored to investigate each component of decision was developed for tramadol for CNCP. MCDA weights and scores, and qualitative considerations were provided by each committee member to evaluate tramadol from a public health plan perspective. **RESULTS:** The committee estimated the value of tramadol for CNCP at 44% (min: 36%, max: 61%) of maximum value on the MCDA scale. Main contributors to the MCDA value estimate were size of population affected by disease (15% of total), disease severity (11%) and impact on adverse event expenditures (8%). Limited improvement in efficacy, safety and patient reported outcomes were not significant contributors to MCDA value. For a majority of committee members, ethical considerations on utility, efficiency and fairness had respectively a positive, neutral and negative impact on the value of tramadol. **CONCLUSIONS:** By systematizing consideration of all components of decision and underlying evidence, the framework allows consistent approach to evaluating health care interventions. Further testing and validation is needed to advance MCDA approaches in health care decisionmaking.

HT4

PRAGMATIC CLINICAL TRIALS FOR DRUG APPROVAL: IS IT REALISTIC?

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BACKGROUND: Patients, clinicians, payers and policymakers increasingly are interested in understanding comparative "real world" effectiveness of pharmaceutical products, often noting that traditional clinical trials performed for regulatory approval may not address important questions about the full range of benefits and harms of new drugs used in typical clinical settings. While more pragmatic designs are used for post-marketing studies, to date, no group formally has considered their utility and feasibility for regulatory approval trials. **METHODS:** In 2009, the Center for Medical Technology Policy convened an expert stakeholder working group to characterize recurring gaps in evidence that generally are not addressed in regulatory trials, explore the reasons for those shortcomings, and generate ideas for improving methods to make these trials more informative for patient and physician choices and reimbursement and coverage decisions. The working group included representatives from pharmaceutical companies, regulatory bodies, private and public payers, academics, consumers, and technology assessment organizations. Using discussions from this meeting and continued engagement of the working group over time, we developed a conceptual, methodological and policy framework to improve the design and implementation of pragmatic regulatory trials. **RESULTS:** There emerged greater than anticipated consensus among the regulators and payers participating in the working group that some pragmatic features are desirable and feasible to include in regulatory trials. The working group developed eight basic principles for making regulatory trials more pragmatic, covering the engagement of post-regulatory decision makers early in the design process to methods for designing more efficient trials. **CONCLUSIONS:** The optimal approach to pragmatic trials may not involve incorporating all possible pragmatic features, as are typically associated with large, simple trials. Some domains of pragmatism are more important to payers than others and any incremental movement toward more pragmatic designs may be not only highly valuable, but feasible.

PODIUM SESSION I: RESEARCH ON PRO METHODS (INCLUDING UTILITIES)

PR1

INCORPORATING TARIFF-LEVEL UNCERTAINTY AROUND ESTIMATES FROM THE CATALOGUE OF EQ-5D SCORES

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OBJECTIVES: Analysts typically take as "fixed" the underlying tariff scoring function of a given utility instrument when conducting probabilistic sensitivity analysis, ignoring an important source of uncertainty. An "off-the-shelf" catalogue of EQ-5D scores from a nationally representative U.S. population has recently been published. The current study aims to incorporate the uncertainty in the underlying U.S. EQ-5D tariff function by estimating confidence intervals around estimates from the catalogue. **METHODS:** The Medical Expenditure Panel Survey (MEPS), a general population survey in the U.S., was pooled (2000, 2001, 2002 and 2003) to create a sample of 79,524 adults with valid EQ-5D responses. Chronic conditions were classified by ICD-9 codes and Clinical Classification Category (CCC) codes. Censored least absolute deviations (CLAD) regression methods were used to estimate the marginal disutility of each condition controlling for age, comorbidity, gender, race, ethnicity, income and education. US tariffs for the EQ-5D (Shaw) were applied to questionnaire responses. However, instead of taking the US EQ-5D tariff as a "fixed" function of the questionnaire responses, 500 bootstraps were conducted drawing from a distribution of possible EQ-5D tariffs based on the standard errors from the original scoring estimation. **RESULTS:** A catalogue of marginal disutility (EQ-5D) scores for each chronic ICD-9 and CCC code were estimated 500 times based on the distribution of possible EQ-5D tariffs. The 95% range of these potential marginal disutilities is presented and compared. **CONCLUSIONS:** Scores and marginal disutilities for a wide variety of chronic ICD-9 and CCC codes can be used to estimate QALYs in cost-effectiveness analyses. This research provides a range of values around each marginal disutility in the catalogue of "off-the-shelf" EQ-5D scores. Uncertainty in the underlying US EQ-5D estimation tariff is incorporated in these ranges to encourage better understanding of the inherent uncertainty in EQ-5D estimates and to facilitate future probabilistic sensitivity analyses.

PR2

EVALUATING THE MEASUREMENT PROPERTIES OF AN AUGMENTED EQ-5D WITH THE INCLUSION OF TWO SINGLE QUALITY-OF-LIFE (QOL) INDICATORS USING THE MEDICAL EXPENDITURE PANEL SURVEY (MEPS)

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OBJECTIVES: To evaluate the measurement properties of the EQ-5D profile augmented with its 0–100 mm visual analogue scale (VAS) and a 5-point summary self-rating of health (SRH). **METHODS:** We used data from 4,001 adults from the 2003 MEPS who had ≥1 of 7 most prevalent chronic conditions and completed the EQ-5D, VAS, and SRH. The original 101 VAS categories were collapsed into a 9-category item with sufficient responses in each category. Five SRH categories included "excellent", "very good", "good", "fair" and "poor". The Rasch rating scale and partial credit models were used to calibrate the EQ-5D and the single items, respectively. Calibrations were conducted using 4 different combinations: EQ-5D alone; EQ-5D+SRH; EQ-5D+VAS, and EQ-5D+SRH+VAS. Model goodness-of-fit was assessed in each disease group using INFIT mean squares (≤1.40). Principal Component Analysis of Rasch Residuals was used to confirm dimensionality examining the proportion of total variance explained by Rasch scale, person measures and item measures, respectively. **RESULTS:** Respondents were predominantly white, female, middle aged and suffered most commonly from hypertension (32%), diabetes (17%) and depression (15%). EQ-5D item "anxiety/depression" consistently showed misfit to the model across 7 conditions when EQ-5D was evaluated alone. The inclusion of VAS and/or SRH not only improved model fit, but also increased overall variances explained, and improved overall distribution of persons and items along the latent health trait. Specifically, when both items were included, 4 groups showed good model fit (mean squares ≤1.40). Consistently across all groups, VAS captured more person measures while SRH captured more item measures. **CONCLUSIONS:** The EQ-5D's measurement qualities are enhanced by the inclusion of VAS/SRH, which captures integral aspect of self-valuations on health that are possibly overlooked by the EQ-5D. The EQ-5D+VAS+SRH may serve as a suitable measurement framework for deriving population preference-weights. Consequently, a new valuation algorithm is called for.

PR3

NATIONAL CULTURE AND EQ-5D VALUE SETS

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Background Despite the growing importance of the EQ-5D descriptive system as a basis for the valuation of QALYs in cost-utility analysis, for most countries there are no EQ-5D social value sets. Researchers and policy makers wishing to use the EQ-5D descriptive system in a country for which there is no value set are advised to use one from a nearby or 'similar' population. Factors other than geographic proximity can affect the relative values of EQ-5D states. **Objective** This study explores the links

between national culture and EQ-5D value sets. **Method** Rank correlation analysis is used to explore relationships between the relative values of a set of EQ-5D states and dimensions of national culture. The latter are taken from Hofstede's framework which operationalizes national culture in 5 dimensions. The analysis is carried out using data from the countries for which EQ-5D value sets and scores on Hofstede's dimensions of culture both exist: Argentina, Denmark, Germany, Japan, Korea, The Netherlands, Poland, Spain, UK, USA. **Results** Some relationships among the EQ-5D dimensions and culture are observed. Eg. the culture dimension: Power-Distance correlates strongly with the EQ-5D dimension: Anxiety-Depression (Spearman's Rho for Power-Distance indices and TTO valuations of EQ-5D states 11112 and 11113 are 0.523 and 0.815 respectively). Strong and moderate relationships are observed among other culture dimensions (Individualism, Masculinity, Uncertainty-Avoidance) and EQ-5D dimensions (Pain, Self-Care). **Discussion** Different cultures appear to value EQ-5D dimensions differently. The correlation patterns observed in this study are generally consistent with a priori expectations based on the nature of the dimensions of culture and the EQ-5D model. This analysis demonstrates the potential of national culture in providing insight into the drivers of the relative values of EQ-5D dimensions for different countries, and in informing decisions about which EQ-5D value sets to use in situations where one does not exist.

ARE HEALTH STATES "TIMELESS"? A TEST OF THE UTILITY INDEPENDENCE ASSUMPTION: COMPARING A REPEATED MEASURES DESIGN AND LATENT GROWTH MODELING

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OBJECTIVES Primary study objective was to test whether individuals' responses to standard gamble (SG) questions do not depend on the duration of time spent in the health scenario presented ("timelessness"). Secondary objective of the study was to test the "timelessness" of VAS responses. **METHODS** Face-to-face interviews were conducted in a convenience sample of healthy volunteers (n = 59) aged 20 to 63. Individuals rated their preferences for three health states of varying post chemotherapy nausea and vomiting (PCNV) severity and current health, assuming six different time horizons. Repeated measures analysis of variance (RM-ANOVA) was conducted (SX6X4X2) to determine the affect of time (6 levels:3 days, 3 months, 1-, 5- and 20- year(s) and rest of life), health state (4 levels: mild, moderate and severe PCNV and current health), and method (2 levels: SG and VAS) on preference. **RESULTS** Results were analyzed using RM-ANOVA and latent growth modeling (LGM). Both showed that preferences decreased over time for SG and VAS ($p < 0.05$). For the RM-ANOVA, all main effects and interaction terms were significant ($p < 0.05$). LGM showed acceptable fit and significant slope parameters for all PCNV. The slopes were decreasing over time. Significant latent variances for LGM showed that not all individuals change at the same rate over time ($p < 0.05$) **CONCLUSIONS** There is a clear advantage in the use of LGM over RM-ANOVA because LGM can evaluate group differences in addition to individual changes over time. For the majority of respondents the utility independence assumption for SG and VAS did not hold both at the group and the individual level. Similar to Bala et al (1999) and Franic et al (2003) the results of this study indicated preferences as measured by SG and VAS are not timeless. Regardless of the preference measure used: both SG and VAS yield higher preferences for shorter time horizons.

PODIUM SESSION I: RISK MANAGEMENT STUDIES

COMPARATIVE PERFORMANCE OF RISK ADJUSTMENT MEASURES IN A SAMPLE OF COMMERCIALLY-INSURED PATIENTS UNDER AGE 65— TWO SIMPLE MEASURES OUTPERFORM CURRENT STANDARDS

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OBJECTIVES: Numerous studies have compared risk adjustment measures (RAMs), yet none have done so across various outcomes in multiple acute and chronic conditions in a single database with uniform programmatic operationalization. This study compares the performance of 7 RAMs and highlights practical programming considerations for hands-on data analysts operationalizing RAMs. **METHODS:** Data were administrative claims from the 2006–2008 MarketScan® Commercial Database. Seven RAMs (2 Deyo-Charlson Comorbidity Index variations, Chronic Disease Score [CDS], 2 3-digit ICD-9-CM code count variations, number of unique National Drug Classification [NDC] codes, and number of unique drug molecules) measured over a 1-year baseline period were compared in 7 conditions (acute coronary syndrome, sample N = 14,951; rheumatoid arthritis [RA], N = 27,085; depression, N = 129,206; diabetes, N = 126,087; hypertension, N = 225,080; asthma, N = 56,172; fibromyalgia, N = 52,365) on the basis of 3 outcomes (total health care cost, emergency room [ER] visits, inpatient admissions) measured over a 1-year follow-up period. Goodness-of-fit statistics (chi-squared statistic for total health care costs and c-statistic for ER visits and inpatient admissions) were compared across age and sex-adjusted regression models for each individual RAM. **RESULTS:** A unique 3-digit ICD-9-CM code count that excluded 'rule-out' diagnoses consistently outperformed, i.e., had highest chi-squared and c-statistics, every other RAM in every condition and outcome with the exception of the number of unique NDC codes, which performed the best for all outcomes in depression and fibromyalgia patients. The number of unique NDC codes

was generally the second-best performing RAM across all outcomes. The CDS performed worst across every condition and outcome. **CONCLUSIONS:** Complex RAMs are subject to inconsistencies in their operationalization and application from a programming perspective. Across multiple acute and chronic conditions, the two simplest and programmatically-transparent RAMs were the most predictive measures of total health care cost, ER visits, and inpatient admissions.

IMPACT OF ADHERENCE WITH STATIN THERAPY ON HOSPITALIZATION RISK AND MORTALITY AMONG PATIENTS WITH DIABETES

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OBJECTIVES: The objective of this study was to evaluate the impact of adherence with statin therapy on diabetes-specific hospitalization and all-cause mortality among patients with diabetes enrolled in a state Medicaid program. **METHODS:** The authors conducted a retrospective cohort study of patients with diabetes who were continuously enrolled in a state Medicaid program from January 2002 to December 2004. The date of the first medication claim for statin during the first six months of 2002 was the index date. Adherence to statin was assessed within one year following the index date. Adherence was assessed using the proportion of days covered (PDC) and patients with a PDC of 0.8 or greater considered being adherent. The primary outcomes of interest were diabetes-specific hospitalization and all-cause mortality during the follow-up period (end of adherence measurement to December 31, 2004). Multivariate regression analyses were performed to assess the impact of adherence with statin therapy on outcome measures. **RESULTS:** A total 10,839 patients were included in the study. Mean age 60.3 ± 10.0 years, 23.8% male, 76.2 female; 31.7% white, 50.4% black. At 12 months after the index prescription, only 23.9% of patients were adherent with their prescribed statin therapy. During follow-up After controlling for age, gender, race, prior hospitalization, and Charlson comorbidity index, patients who were adherent to statin therapy were 48.7% (OR: 0.513; 95%CI: 0.421–0.624) less likely to have diabetes-specific hospital admissions in comparison to nonadherent patients. Adherence with statin therapy had no statistically significant impact on all-cause mortality (OR: 0.801; 95%CI: 0.454–1.412). **CONCLUSIONS:** Adherence with statin therapy was poor among patients with diabetes enrolled in a Medicaid program. Adherence with statin therapy was associated with significantly less risk for diabetes-specific hospitalization. Greater efforts are needed to facilitate diabetes self-management behaviors to improve patient outcomes.

RISK OF FALLS AND FRACTURES IN OLDER ADULTS USING ATIPSYCHOTIC AGENTS- A PROPENSITY-MATCHED RETROSPECTIVE COHORT STUDY

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OBJECTIVES: To examine the risk of falls/fractures associated with atypical antipsychotic use compared to typical antipsychotic use in community dwelling older adults. **METHODS:** The population based retrospective cohort analysis based on propensity score matching was conducted using IMS LifeLink™ Health Plan claims data. Patients were included in the cohort if they met following criteria: ≥ 50 years of age, new users of atypical or conventional antipsychotics who began taking antipsychotics between July 2000 and December 2007, and continuously enrolled for six months before and at least six months after initiation of antipsychotic treatment. Patients taking atypical antipsychotics were matched with those using typical antipsychotics using propensity score greedy matching technique. Kaplan-Meier survival curves and Cox proportional hazard model stratified on matched pair was employed to examine risk of hospitalization/emergency visit due to falls or femur fractures within one year. Duration of antipsychotic therapy and exposure to other psychotropic medications were controlled for in the final model. **RESULTS:** A total of 11,160 older adults (5,580 atypical and 5,580 typical users) were identified as new users of antipsychotics after matching. Within one year of follow up period, 456 patients (8.06 %) in atypical drug group had falls/femur fractures compared to 375 (6.72%) in typical antipsychotic group. No significant difference was found between atypical users compared to typical agents with respect to risk of falls/fractures [Hazard Ration (HR) 1.01, 95% CI 0.83–1.22]. However, duration of therapy more than 90 days was significantly (HR, 1.81, CI, 1.35–2.43) associated with increased risk of falls/fractures compared to less than 30 days. **CONCLUSIONS:** The study results show no significant difference in the risk of falls/fractures between atypical and typical antipsychotic use among older adults. However, there is a need to be cautious while prescribing atypical and typical antipsychotics in older adults for longer periods of time.

CONFOUNDING EFFECT OF AGE IN THE ASSOCIATION OF CARDIOVASCULAR RISK AND DIETARY SUPPLEMENT USE AMONG US ADULTS

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OBJECTIVES: Dietary supplement (DS) use has been found to be associated with cardiovascular disease (CVD) risk. This study assessed whether age moderates or confounds the association between CVD risk and DS use. **METHODS:** Data were taken from the 1999–2004 waves of the National Health and Nutrition Examination Survey. Inferences were restricted to US population members ≥20 years of age as