Methods for developing new Clinical Outcome Assessments (COAs) are well-established and documented. While the COA development literature emphasizes the importance of linguistic and cultural equivalence, exact methods to achieve this are often not clearly presented. For multinational or multicultural studies, Simultaneous Item Development (SID) of a COA in all languages and cultural groups required for the research program is the most efficient approach to ensure valid COA data and interpretable results. This is because SID increases the likelihood the COA data collected in multiple languages or cultures will be conceptually equivalent and culturally relevant. This paper provides an overview of how to implement SID is limited, this presentation provides an overview of a purposeful and pragmatic (recognizing the practical challenges associated with COA development) SID approach that incorporates both qualitative and quantitative methodology. In our experience, SID is valuable at four stages of COA development: concept elicitation, item generation, cognitive testing, and content harmonization. Generally, SID is most efficient when a single reference or ‘core’ version is used throughout the four stages (typically the English language version for the UK or United States) while stage by stage, the data can be managed by researchers fluent in the language for the core version. Their primary objective is to ensure that the core COA version has a clear conceptual framework that evolves in a consistent manner across language/culture versions at each stage to find themes that can be generated processes serve and development of an entire scientific field, such as health economics, and not exhaust the use of a few tools on a few themes.

PM161

RESOURCE MODELLING: THE MISSING PIECE OF THE HTA JIGSAW?
Thokala P., Dixon S.
University of Sheffield, Sheffield, UK

OBJECTIVES: Resource modelling has been largely ignored in health technology assessment (HTA) and this paper argues the need for it to be considered as a separate set of analyses to deal with the issue of implementation and feasibility. METHODS: Economic evaluations including budget impact models, which are the two economic analyses that currently feed into HTA, are briefly described before highlighting their limitations in informing issues of feasibility and implementation. Resource modelling is defined as the quantitative assessment of technology diffusion courses, their related resource use and cost, and the economic impact of implementing new technologies in the field, under the creation of courses, masters and specialization, and the creation of research groups. CONCLUSIONS: Taking as a reference these studies it is possible to identify the areas that can be generated processes use and develop a conceptual framework of an entire scientific field, such as health economics, and not exhaust the use of a few tools on a few themes.

DISEASE-SPECIFIC STUDIES

MENTAL HEALTH – Clinical Outcomes Studies

PMH1
MIRTAZAPINE ANTIDEPRESSANT THERAPY IS ASSOCIATED WITH REDUCED Rhabdomyolysis Risk
Al Ak
Eli Lilly and Company, Indianapolis, IN, USA

OBJECTIVES: Among other factors, the breakdown of skeletal muscle fibers (rhabdomyolysis) is a leading cause of acute kidney failure. While rhabdomyolysis is multifactorial in etiology, there has been a concern about the link between therapy with mirtazapine and the condition. This paper characterizes rhabdomyolysis signals for mirtazapine and other antidepressants. METHODS: Adverse event reports submitted for antidepressants between 1997 and 2012 were retrieved from the FDA Adverse Event Reporting System (FAERS). Reporting Odds Ratios (RORs) were calculated for the disproportionality of rhabdomyolysis between individual antidepressants, including mirtazapine. The MedDRA preferred term and drug generic names were used for drug exposure. RESULTS: Twenty drug-event combinations with RORs ≥ 2.0 were identified as means that warrant further review. ROR results: RORs > 2.0 were identified for RORs > 2.0 were identified. Proportionality measures were found for rhabdomyolysis (2.0, 1.53-3.0), tricyclics (1.2, 1.1-1.3), and monosodium glutamate oxidases (1.7, 0.9-4.9). There was no evidence of between-dose or between-study heterogeneity in weight. RESULTS: Pooling was performed for only mirtazapine and other antidepressants. In light of inherent limitations of spontaneous reporting systems, such as FAERS, signal evaluation activities in real-world data are required to further characterize rhabdomyolysis risk in relation to mirtazapine and other antidepressants.

PMH2
META-ANALYSIS OF DRIVERS OF COST-EFFECTIVENESS FROM SHORT-TERM LURASIDONE CLINICAL TRIALS: EFFECT OF CHANGING DAILY DOSE ON PANSS TOTAL SCORE AND WEIGHT
Pikalov A1, Hsu J1, Loebel A1

OBJECTIVES: Estimates of efficacy and safety are required for economic models developed for health technology assessments and provide guidance to decision-makers regarding the benefit/risk profile of a drug. Studies synthesising clinical trial outcomes of antipsychotics in schizophrenia often demonstrate a degree of between-study heterogeneity. The objective of this analysis was to assess dose-related efficacy and weight changes after 6 weeks of treatment with lurasidone, an atypical antipsychotic indicated for treatment of schizophrenia at an effective dose range of 20 mg to 160 mg/day. METHODS: Random-effects meta-analysis was used to synthesize evidence from five, 6-week, randomized, double-blind, placebo-controlled studies of lurasidone in patients with acute schizophrenia. Outcome measures included PANSS total score and weight (kg). RESULTS: A total of 330 patients were included in this meta-analysis. The mean (SD) daily dose at week 6 was 86.3 (35.7) mg. Mean and 95% CI for the difference in PANSS total score at Week 6 versus baseline was 1.42 (1.37-1.47) mg. Mean and 95% CI for the difference in weight was 0.56 (0.29-0.75) kg. There was no evidence of between-dose or between-study heterogeneity in weight. CONCLUSIONS: Changes in PANSS total score from this meta-analysis suggest that lurasidone in the daily dose range of 40-120 mg had similar efficacy versus placebo. The 160 mg daily dose was associated with greater reduction in PANSS total score versus placebo; however, this finding was based on evidence from a single study. This analysis found evidence of no dose-related weight gain.

PMH3
ANTICHOLINERGIC MEDICATION USE AND RISK OF DEMENTIA AMONG ELDERLY NURSING HOME RESIDENTS WITH DEPRESSION
Aparasu R1, Chatterjee S2, Carnahan RM2, Chen H1, Johnson ML1

OBJECTIVES: Use of anticholinergic medications in the elderly can lead to adverse cognitive outcomes. This study examined the risk of dementia among elderly nursing home residents with depression using anticholinergic medications. METHODS: A nested case-control study was conducted using 2007-2010 Medicare data from all states. Patients who had continuous coverage for Medicare Part A, B and D and no HMO coverage during the study period or until death were included. The base cohort consisted of residents aged > 65 years, diagnosed with depression, and who did not have dementia in 2007 (Baseline Period). Cases were identified as patients who developed dementia following the baseline period. For each case, 4 age and sex-matched controls were selected using incidence density sampling. The primary outcome was diagnosis of dementia, between January 1, 2008 and December 31, 2010. Anticholinergic exposure was defined using the Anticholinergic Drug Scale (ADS). Prescription of level 2/3 anticholinergic medications 30 days preceding the event date formed the primary exposure. Conditional logistic regression model stratified on matched case-control sets was used to assess the dementia risk, after controlling for baseline demographic and variable dementia risk factors. RESULTS: The base cohort consisted of 291,504 elderly residents with depression and without dementia diagnosis. The study included 64,466 cases diagnosed with dementia during the follow-up period. After adjusting for other covariates, high-level anticholinergic use was associated with significant risk of dementia (Relative Risk, RR 1.12; 95% CI, 1.18-1.23) compared to non-use. The findings remained consistent across levels of anticholinergic potency (Level 2, RR 1.07, 1.04-1.11; Level 3, RR 1.07, 1.04-1.11). CONCLUSIONS: Use of anticholinergic medications was associated with a higher risk of dementia compared to no use among elderly residents with depression. With increasing evidence regarding cognitive effects of anticholinergics, there is a significant need to optimize anticholinergic use, especially for those who are at-risk for dementia.