BACKGROUND: As age increases, prevalence of type 2 diabetes in the U.S. rises dramatically as the population approaches and enters Medicare eligibility (CDC). Although ensuring category access, CMS formulary guidelines for Medicare Part D (MPD) coverage do not take into account the effects of cost-sharing burden on patient compliance. Literature demonstrates that patient adherence is reduced with higher copayment costs and consequently, the beneficial clinical impacts may likely be unrealized for many patients. **OBJECTIVES:** To investigate access to diabetic medications for MPD patients compared to commercially covered lives. Exploring copay differentials amongst these populations, insight is gained on how MPD differs from commercial access to diabetes medications. **METHODS:** Analysis of the Walters Kluwer Pharma Solutions Source Longitudinal Patient Database, sampling of 26.7 million commercial lives and 5 million Medicare Part D lives in 2009. Low Income Subsidy covered lives were excluded. **RESULTS:** Average drug copayment for metformin and sulfonylurea for commercial and MPD patients is $15 and $19 respectively. Average drug copayment for insulin glargine in commercial is $17 and $27 for MPD patients, for branded pioglitazone $31 and $52, and exenatide $32 and $68. **CONCLUSIONS:** Copayment differentials across these populations are small for generic therapies and grow larger for branded, novel diabetic agents. This data would suggest a broader, more inclusive review is needed to assess how the financial burden felt by MPD diabetes patients affects patient compliance and outcomes. Further investigation is needed to study the potential value that CMS would benefit from re-evaluating the cost sharing burden for this patient population.

PHP107

BIOMARKERS: A CHANGING PARADIGM FOR DEVELOPMENT

Pardini AT, Saraf S, Sparrowhawk K
PriceSpective Ltd., London, UK

The general perception is that pharma companies generally incorporate biomarker (BM) development into their processes when a drug response is not optimal following the results of phase 3 studies. Usually this is when poorer than expected efficacy results are achieved. In this scenario, the BM development enables targeting of a niche population that is representative of the responders, thus effectively increasing the efficacy making the product more attractive to payers and healthcare professionals. This late stage approach to BM development also fits with the commonly held belief that BMs are linked to reduced market access (MA), lower market shares and decreased product revenues. In such a situation BMs are often only developed retrospectively to overcome access issues. Our objective is to demonstrate that investment into BMs in the early phase of drug development (DD) is more commercially attractive. **METHODS:** Three scenarios of drug development were defined: 1) the current/traditional model, 2) where biomarker development is incorporated from phase I of development and 3) where biomarker development involves a concurrent Phase III investigation or Phase IV retrospective analysis. These scenarios were analyzed to determine the relationship between risk and reward using assumed cash-flow curves and net-present value analysis based upon those curves. In each case, the implications of integration of BM development at various stages and how this affects risk-reward were assessed. **RESULTS AND CONCLUSIONS:** The scenario analysis demonstrates that by shifting investment to earlier in the DD process, costs associated with investment-heavy Phase III will be reduced. Early incorporation of BMs into DD will improve the commercial and healthcare benefits and the drug will have the potential to benefit from shortened approval time, early MA and higher price.

PHP108

THE CASE OF RARE DISEASE DRUGS BEFORE AND AFTER THE INTRODUCTION OF PRICING BODIES: LESSONS LEARNED FROM BRAZIL AND CANADA, IMPLICATIONS FOR THE UNITED STATES

Cost P, Snyder T, Zaidi Q
HERON Evidence Development LLC, Somerville, NJ, USA

OBJECTIVES: This poster examines the pharmaceutical price implication for rare disease products in two countries which recently developed technology assessment and pricing processes with a look toward the potential implications for the United States. **METHODS:** Case studies are built out of examining prices for the Multiple Sclerosis drugs interferon beta-1a and natalizumab in the context of Brazil, while the Gaucher's disease products imiglucerase and miglustat are studied in Canada. In each case, a brief overview of the health systems is given, with specific attention to the pricing bodies. The prices for drugs which came to market before and after the advent of a pricing body are compared relative to each other. These differences are then compared to the price differential in the US and UK to determine if the HTA body was instrumental in this pricing change. **RESULTS:** In Canada miglustat is 17.8% of the cost for imiglucerase while in the US it is 38%, with a similar trend in the price of MS drugs in Brazil. To some degree, the lower price is expected as the drug classes are different. However, the disparity between a 17.8% differential and a 38% differential suggests that the Canadian pricing body is used to apply downward pressure on the price of rare disease drugs. **CONCLUSIONS:** The price differential has distinct implications for the US market, in which payers may look towards developing a technology assessment process using cost effectiveness research to drive down costs due to the current environment. As one of the most important markets for pharmaceutical profits, this has considerable ramifications for industry in terms of income and innovation incentive.

PHP109

AN OUTCOMES PROFILE REGISTRY FOR ESTABLISHING A BASELINE MATRIX IN COMPARATIVE EFFECTIVENESS STUDIES IN PREDICTIVE PHARMACOLOGY

Wheeler C
NTELX, Inc, Vienna, VA, USA

We propose a novel applied decision analytics solution in clinical outcomes analysis for deriving outcomes to be used as benchmarks in designing appropriate therapies in personalized medicine and predictive pharmacology. The efficacy of comparative effectiveness research in clinical medicine and pharmacology is limited by the lack of a defined solution to derive clinical outcomes across diverse patient populations and a variety of disparate data sources that collectively define a clinical profile at particular point in time. An outcome at time T_1 is driven not only by static factors such as race, ethnicity and occupation, that are generally time-independent, but also by the condition profile and resultant outcome of the patient's condition at T_0. Our solution is an ensemble analytical framework that leverages a temporal rule induction algorithm to create derived outcomes profiles across the time continuum. It performs analysis on structured and unstructured data from EMR/EHR, clinical, biological, biomarker, behavioral and demographic data sources that are integrated into a composite data warehouse via our propriety semantic resolution and natural language processing algorithms. The outcomes profiles reflect an index or aggregate score for the amalgamation of all available data for a particular patient at a particular time. Outcomes profiles from thousands of samples are catalogued and normalized in a registry and are used to establish a baseline matrix for application in higher level statistical and predictive analyses for comparative effectiveness studies in pharmacology. Using this approach, it is possible to determine based on available data both the appropriate treatment to affect a desired outcome and the predicted outcome based on a given treatment at a given time.

PHP110

BIOSIMILARS LITERATURE REVIEW: THE CURRENT LANDSCAPE AND IMPLICATIONS OF RECENT HEALTH CARE LEGISLATION FOR THE UNITED STATES MARKET

Maiese BA, Lee EH, Toscani MT
Jefferson School of Population Health, Philadelphia, PA, USA

Biosimilars represent an emerging area of interest for the pharmaceutical industry. Biosimilars are essentially 'generic' versions of 'branded' biologics, but are not considered identical to the innovator biologic. In 2009, half of the top ten selling drugs were biologics; this proportion is expected to reach 80% by 2015. Biosimilars are seen as a cost-saving alternative to payers, and as generic drugs take over the market, manufacturers are depending on biologics to drive growth. However, they will need to consider the inherent challenges in this market. This literature review was undertaken to provide a summary of the current state of affairs with biosimilars, including a review of the recent healthcare legislation and policies in countries that already have formal guidance regarding biosimilars approval. Significant resources are required to participate in the biosimilars market, including regulatory expertise, manufacturing capabilities, and global market reach. One concern to potential market players is the uncertainty regarding the approval process for biosimilars in the United States (U.S.). The Patient Protection and Affordable Care Act (PPACA 2009) authorized the FDA to develop an abbreviated regulatory pathway for biosimilar approval but guidance has not yet been issued. It is important for the U.S. to learn from other countries. This review includes a summary of other countries' approaches to biosimilars approval. For example, since 2006, the European Medicines Agency has had extensive requirements for pre-clinical and clinical data to demonstrate quality, safety, and efficacy of the product seeking approval. Questions remain including: How will the competitive landscape look as biosimilars enter the market? What will be the comfort level with substitutability of biosimilars? Will there be patent protection for the manufacturing process? And, what will the FDA require in terms of clinical trials and other supportive data to recognize biosimilars? The literature review will address these questions and more.

PHP111

OVER INFLATION OF THE GENETIC CONTRIBUTION TO SCHIZOPHRENIA: IMPLICATIONS FOR NOVEL THERAPEUTICS

Fleming M, Martin CR
University of the West of Scotland, Ayr, UK

The biological model of schizophrenia remains the dominant model within mental health services and has a powerful and enduring influence on the prevailing format of mental health care delivery to patients with the diagnosis. There exists almost universal acceptance of a genetic cause for schizophrenia though in many instances this conflicts both philosophically and clinically with a person-centred recovery orientated approach. A review of the underpinning research that supports the genetic argument was conducted. Appraisal of family, twin and adoption studies uncovers serious flaws in the methodologies and statistical analyses used in studies. These flaws tend to artificially inflate the perceived genetic contribution to schizophrenia and moreover may also invalidate many of the reported study findings. There exists an absence of a replicable and consistent finding indicating a clear genetic pathway to schizophrenia. Novel therapeutic approaches aimed at neurotransmitter receptor site abnormalities should not therefore be discouraged by any fundamental refocus on gene therapy approaches.

PHP112

DEFINITIONAL CRITERIA FOR CHRONIC FATIGUE SYNDROME: A CRITICAL REVIEW

Christley Y, Duffy T, Martin CR
University of the West of Scotland, Ayr, UK

Chronic Fatigue Syndrome (CFS) is an enigmatic and misunderstood clinical entity. A broad range of etiological mechanisms have been suggested including endocrine, immune, infectious, muscular and neurological abnormalities. However, the cause remains elusive thus impacting on developing models of evidenced based thera-

peutic intervention and trial monitoring and outcome evaluation. Complicating this situation is inconsistencies in CFS case definition. The main objective is to provide a critical review of the similarities and differences between the varying approaches to CFS case definition. The conflicts and controversies that have emerged as a result of the differing definitional criterion for CFS are highlighted and the potential impact on future research is identified. A critical review of the most frequently used case definitions in CFS was conducted. There are currently five case definitions of CFS; however, the most prominent is the 1994 Centre for Disease Control and Prevention Case Definitions. However, prima face comparative advantages of this definition are elusive and indeed, it has been widely criticized for its lack of specificity. Counterintuitively, there is little compelling evidence to support the efficacy of any of the case definitions have produced evidence to demonstrate their accuracy or precision at defining cases of CFS. A summary description of the symptom profile for each of the case definitions is provided. The inconsistencies that have emerged in CFS research as a consequence of differing approaches to case definition are contrasted and discussed. Clinical and research implications are highlighted.

PHP113

IQWIG AND HIQA, WHAT ARE THEY GOOD FOR? THE EVOLUTION OF THE HTA AGENCY: TIME FROM CREATION TO FIRST ASSESSMENT AND IMPACTFUL APPRAISAL

Green MJ
HERON Evidence Development LLC, Somerville, NJ, USA

OBJECTIVES: To evaluate the time spent from the creation or charter of an HTA agency to endpoints indicating their effectiveness, such as publication of assessments and evidence of the incorporation of assessment into meaningful appraisal influencing patient access to health technologies. **METHODS:** This study looks at the creation of HTA agencies (e.g. AHRQ, HIQA, IQWiG, PBAC, CADTH and NICE) and their evolution in terms of roles in assessment (advisory, coordinating, decision-making) and the relationship they have with appraisal. **RESULTS:** It has been demonstrated that the time it takes for an agency to generate assessments impacting patient access varies widely. For example, in Ireland, HIQA was chartered in May 2007, and entrusted with performing HTA assessments. In 2008 and 2009, HIQA has published one health technology assessment per year, both of which were received and in turn implemented by the Minister for Health and Children. In comparison, NICE in the UK was founded in 1999, but its appraisals were not supported by mandate until 2005. Meanwhile, HTAs driven by DAHTA@DIMDI in Germany are known to rarely play a role in pricing and reimbursement. **CONCLUSIONS:** The evolution of HTA bodies has varied from country to country. However, evolution in scope and impact may provide useful lessons for countries where HTA is receiving renewed emphasis or where appraisal is under consideration for implementation, especially as new agencies are created and existing agencies evolve.

PHP114

OPTIMIZING THE ORGANIZATION; MIGRATING HEALTH SERVICES RESEARCH OPERATIONS INTO THE COLLABORATIVE SCIENCE CENTER OF EXCELLENCE

Benson J, Enterline L
Bristol-Myers Squibb, Plainsboro, NJ, USA

The execution and management of Health Services Research projects can be an onerous task. Often there is no centralized body of knowledge within an organization around process and requirements. This leads to long execution timelines, difficulties with vendors and ultimately reduced productivity. The Collaborative Science Center of Excellence (CSCoE) was established in 2008 at Bristol-Myers Squibb (BMS). This group manages the global operations of a wide variety of programs, a portion of which includes worldwide investigator sponsored research, non-clinical research, expanded access, and risk evaluation and mitigation programs. Beginning June 2009, operational management of the entire US Health Economics and Outcomes Research (HEOR) book of work was moved from the OR Scientists into the CSCoE. This included administration, contract execution, master service agreement negotiation, financial management, protocol writing, AMCP dossier updates, and invoice tracking and payment. Within the first year over 90 projects were migrated into the CSCoE. Benefits the Health Services Research group realized included: 1. A consolidated 2010 and planned 2011 book of work; 2. A reportable repository of project information; 3. HEOR protocol and AMCP dossier improvement through standardization of in-house scientific writing; 4. Expedited contract execution; 5. Innovative cost-sharing; 6. Tiered and batched review of contracts reduced corporate legal hours; 7. Rapid response to organizational queries. Centralized process management unlocked latent value by allowing OR Scientists to focus on value-added activities, increased organizational transparency and agility, and moved operations to a lower cost environment.

POSTER SESSION I: DISEASE-SPECIFIC STUDIES

Cardiovascular Disorders – Clinical Outcomes Studies

PCV1

DOES ROUTE OF ADMINISTRATION FOR ESTROGEN HORMONE THERAPY IMPACT RISK OF VENOUS THROMBOEMBOLISM: ESTRADIOL TRANSDERMAL SYSTEM VERSUS ORAL ESTROGEN-ONLY HORMONE THERAPY

Laliberté F[1], Dea K[1], Duh MS[2], Kahler KH[3], Rolli M[3], Lefebvre P[1]
[1]*Groupe d'analyse, Ltée, Montreal, QC, Canada,* [2]*Analysis Group, Inc., Boston, MA, USA,* [3]*Novartis Pharmaceuticals Corporation, East Hanover, NJ, USA*

OBJECTIVES: To evaluate the risk of developing venous thromboembolism (VTE) events associated with the use of estradiol transdermal system (ETS; Vivelle-Dot®) relative to oral estrogen-only hormone therapy (HT) agents. **METHODS:** A health insurance claims analysis was conducted using the Thomson Reuters MarketScan database from January 2002 through October 2009. Patients ≥35 years old newly initiated on an ETS or oral estrogen-only HT with ≥2 dispensings were analyzed. VTE was defined as ≥1 diagnosis code for deep vein thrombosis or pulmonary embolism. As a secondary outcome we assessed incident VTE resulting in hospitalization. Cohorts of ETS and oral estrogen-only HT were matched 1:1 based on both exact factor and propensity score matching. Incidence rate ratio (IRR) was used to compare the rates of VTE between the matched cohorts. Remaining baseline imbalances from matching were included as covariates in multivariate adjustments. **RESULTS:** Among the matched ETS and oral estrogen-only HT users (27,018 subjects in each group), the mean (SD) ages of the cohorts were 48.9 (7.1) years; in each cohort 6,044 (22.4%) and 1,788 (6.6%) patients had a hysterectomy and an oophorectomy at baseline, respectively. The mean (median) drug exposure for the ETS and oral estrogen-only HT cohorts was 391 (264) and 401 (272) days, respectively. A total of 115 ETS users developed VTE compared to 164 subjects in the estrogen-only HT cohort (unadjusted IRR: 0.72; 95% CI: 0.57-0.91, $P=0.006$). After adjustments, ETS remained statistically significantly associated with a lower incidence (33% reduction; $P=0.0134$) of VTE. The incidence rate reduction for hospitalization-related VTE events among the ETS users was even more pronounced with the adjusted incidence being 62% lower for ETS users relative to oral estrogen-only HT users. **CONCLUSIONS:** Results of this large population-based study showed that patients receiving ETS had a significantly lower incidence of VTE compared to patients receiving oral estrogen-only HT.

PCV2

THE RISK OF CARDIOVASCULAR EVENTS ASSOCIATED WITH DIETARY CALCIUM AND VITAMIN D SUPPLEMENTS IN PATIENTS WITH OSTEOPOROSIS

Chang JY[1], Nichol MB[2]
[1]*University of Southern California, Alhambra, CA, USA,* [2]*University of Southern California, Los Angeles, CA, USA*

OBJECTIVES: Calcium and vitamin D supplements have been widely used and recommended for women to prevent or delay the onset of osteoporosis and the risk of bone fractures. Other benefits include the improvement of blood pressure and lipid levels and a lowering of body weight. In theory, the beneficial effects of calcium and vitamin D suggest improvements in cardiovascular health. Recent publications suggest the contrary and allude to increase serum calcium as a risk factor for adverse cardiovascular events. This study examines whether the exposure to these supplements are associated with cardiovascular events. **METHODS:** The study was based on California Medicaid (Medi-Cal) fee-for-service administrative claims data from January 1995 to December 2002. The study population consist of patients >50 years with recorded diagnoses of osteoporosis followed from diagnoses date to the end of eligibility. Patients were excluded for prior use of the supplements or diagnosis of cardiovascular events or drug induced osteoporosis. Propensity score matching based on age, gender, elixhauser comorbidities and eligibility data created case (n= 1594) and control groups (n=4782). Chi-square analysis was conducted for comparison of the cardiovascular events defined as ICD9 codes for myocardial infarction and searchable terms of "cerebral infarction, hemorrhage, ischemia" for stroke. **RESULTS:** No statistically significant relationship was found between the study groups for stroke ($p=0.56$) and myocardial infarction ($p=0.54$). Components of stroke included cerebral artery occlusion ($p=0.94$), precerebral artery occlusion ($p=0.27$), intracerebral hemorrhage ($p=0.23$), and subarachnoid hemorrhage ($p=0.05$). The clinical benefits of the supplements were evident with subarachnoid hemorrhage with 0 recorded diagnoses in the case group compared to 12 recorded diagnosis in the control group; however statistical significance was not established. **CONCLUSIONS:** The use of calcium and vitamin D supplementation yielded no relationship to the risk of adverse cardiovascular events. Moreover, no broad cardio-protective effects can be concluded from the study.

PCV3

RISK OF HOSPITALIZATIONS FOR VENOUS THROMBOEMBOLISM IN ATYPICAL VERSUS TYPICAL ANTIPSYCHOTIC USERS IN A NATIONAL SAMPLE OF MEDICARE BENEFICIARIES: A CLAIMS DATA ANALYSIS

Dharmarajan SH, Yang Y, Athavale AS, Bentley JP, Null KD, Banahan BF
University of Mississippi, University, MS, USA

OBJECTIVES: To examine the difference between typical and atypical antipsychotic drug use in the risk of hospitalization for venous thromboembolism (VTE) in an elderly Medicare population. **METHODS:** This is a retrospective cohort study using 5% national sample of 2006-2007 Medicare claims data. Medicare beneficiaries with continuous Part A, B, and D enrollment in 2006-2007 and who initiated atypical or typical antipsychotic drug therapy in July 2006-June 2007 were included. All study subjects were followed for a period of 180 days from the date of index prescription. Atypical and typical users were matched on propensity score, calculated using pre-index demographics, clinical comorbidities, and medication use. A conditional logistic regression model stratified on the propensity score-matched pair using the Greedy matching algorithm was used to compare the risk of hospitalization for VTE in new users of atypical and typical antipsychotic drugs. Sensitivity analysis in the unmatched cohort was performed using propensity score as a continuous, linear term in logistic regression. **RESULTS:** A total of 15,637 new users of atypical and 2,337 new users of typical antipsychotic drugs were identified. There were 472 (2.6%) individuals with a hospitalization for VTE during follow-up. 417 were atypical and 55 were typical antipsychotic users. A 1:1 propensity score match yielded 2,333 matched pairs (4,666 individuals). In the matched cohort, 55 typical and 64 atypical drug users were hospitalized for VTE in the follow up period. Compared to typical antipsychotic users, users of atypical antipsychotics were less likely to have