PODIUM SESSION II: INFECTIOUS DISEASE OUTCOMES RESEARCH STUDIES

IN1 INTERVIEWS WITH PATIENTS WITH CHRONIC HEPATITIS C (CHC) VIRUS INFECTION DOCUMENT UNMET NEEDS, CONTENT VALIDITY, AND COMPREHENSION OF PROS FOR CLINICAL TRIALS
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OBJECTIVES: Recent advances in treatment for chronic hepatitis C (CHC) virus infection have shortened duration of treatment and increased the likelihood of treatment success. To understand what unmet needs remain with available CHC treatments, patient interviews explored what it is like to live with CHC infection and undergo CHC treatment. A subset of interviews also evaluated the content validity and comprehension of patient-reported outcome (PRO) questionnaires for use in CHC clinical trials. METHODS: Sixty-five patients with clinician-confirmed diagnosis of CHC infection provided informed consent and completed interviews in Germany (n=15), France (n=15), the USA (n=16), and Canada (n=19). Targeted sampling enrolled a demographically and clinically diverse sample. Consenting patients (n=58) using in-depth, open-ended questioning encouraged spontaneous discussion of patients’ experience of CHC and its treatment. Patients in the USA and Canada also completed cognitive debriefing (CD) interviews using a ‘think aloud’ protocol to evaluate content validity and comprehension of the Fatigue Severity Scale (FSS, n=34), Work Productivity and Activity Impairment questionnaire for Hepatitis C (WPAI:HC, n=21) and the SKINDEX-16 (n=19). Verbatim transcripts were translated to English and analyzed using thematic analysis. RESULTS: Treatment-related symptoms cause a significant burden for patients during treatment with tiredness (60.0%), sleep problems (57.5%), fatigue (50.0%), depression (45.0%), and nausea (40.0%) among the most commonly reported symptoms mentioned in CE interviews. In the 40 patients with CHC treatment experience, treatment-related symptoms led to discontinuation or lack of adherence in 25% and 0%, respectively. CD interviews confirmed that the questionnaires were relevant, understandable and easy to complete. Patients suggested minor wording changes that may make these questionnaires easier to complete. CONCLUSIONS: Treatment-related symptoms cause a significant burden for CHC patients and affect their adherence to treatment. The FSS, WPAI:HC, and SKINDEX-16 are valid tools for PRO assessment in CHC clinical trials.

IN2 CLINICAL CHARACTERISTICS AND TREATMENT DURATION AMONG PATIENTS WITH CHRONIC HEPATITIS C VIRUS (HCV) INFECTION INITIATING DIRECT-ACTING ANTIVIRAL THERAPY IN A LARGE COMMERCIAL INSURANCE DATABASE IN THE UNITED STATES
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OBJECTIVES: To describe patient characteristics and treatment duration among patients initiating telaprevir (T) or boceprevir (B) combination treatments with pegylated interferon and ribavirin (T/PR, B/PR) using administrative claims data. METHODS: A retrospective cohort study was conducted using MIMIC (index date) was conducted (MarketScan Research Databases 2011-2012). Study criteria included 7 months of continuous enrollment pre-index, 6 months post-index, and first-line treatment of CHC and claims within 40 days of index. Pre-index comorbidities were ascertained using ICD-9-CM codes. Indicated T duration is 12 weeks (84 days); and minimum indicated B duration is 24 weeks (168 days; maximum 44 weeks). Medication Possession Ratios (MPR, adherence indices) were calculated for each patient and the prescribed duration of treatment for each drug respectively. RESULTS: A total of 3288 patients met the study criteria (T/PR, n=2582 [79%]; and B/PR, n=706 [21%]). Age (meansSD) and gender were similar between cohorts (T/PR=53.7±8.4 years, 35% female; B/PR=53.8±8.7 years, 39% female). Patients treated with T/PR were more likely to have a claim for liver cirrhosis in the pre-index period (T/PR=24%, B/PR=18%, p=0.002). Prevalence of other comorbidities was similar between cohorts (T/PR=14%, B/PR=13%, hypertension (T/PR=12%, B/PR=12%), and anxiety or depression (T/PR=11%, B/PR=11%). MPR (meansSD) was 0.91±0.2 for T/PR patients in the first 84 days post-index and 0.78±0.3 for B/PR in the first 168 days post-index. AUC (area under the curve) for 84 days, 82% (95% confidence interval [CI]: 80%-83%) of T/PR patients were on therapy compared with 84% (CI: 81%-87%) of B/PR patients. 54% (CI: 51%-58%) of B/PR patients were still on therapy at 168 days. CONCLUSIONS: Chronic HCV-infected patients initiating telaprevir or boceprevir combination treatment had similar demographic characteristics and no significant difference in other comorbidities. Cirrhosis was more prevalent among patients receiving telaprevir combination treatment. Data suggest adherence to indicated duration of treatment was higher among telaprevir patients than boceprevir patients.

IN3 THE BURDEN OF HCV TO INSURERS IN THE UNITED STATES: TRENDS IN HEALTH CARE RESOURCE UTILIZATION 2002-2012
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OBJECTIVES: Trends in health care utilization among CHC patients have demonstrated marked increases between 1994 and 2001, particularly among individuals aged 40 to 60 years. Furthermore, the proportion of treatment-seeking individuals who achieve disease cure remains relatively low. This has potentially resulted in a large economic burden, as HCV leads to costly liver disease and other morbidity. The objective of this study was to examine trends in HCV-related care utilization in the United States. METHODS: Years 2002-2010 of the National Inpatient Sample (NIS) data set of hospital admissions from the Healthcare Cost and Utilization Project (HCUP) were utilized in order to determine the number of adult hospital admissions occurring in HCV-infected individuals (identified by ICD-9-CM diagnosis code). The data included a total of 71.7 million hospital admissions from 1,051 US hospitals. The number of admissions occurring to HCV-infected patients was recorded for each year, as well as total charges. Trends over time were compared for three insurers: Medicare, Medicaid, and private. RESULTS: Of the 71 million admissions examined over the study period, 5,350,991 were admissions for HCV-infected adults. More HCV-related admissions were covered by Medicaid and Medicare as compared to private insurance. In 2002, total HCV-related charges were $693M for admissions covered by Medicare, $708M for Medicaid, and $579M for private insurance (costs adjusted to 2010 values). Between 2002 and 2010, total HCV-related charges increased most for private insurers (157%), followed by Medicare (127%) and Medicaid (86%). CONCLUSIONS: Use of inpatient care for HCV-infected patients has increased rapidly. Increases in the number of HCV patients who seek care, as well as possible increases in the intensity of care and/or escalation in hospital charges has resulted in nearly doubling HCV-related charges from 2002-2010.

IN4 DIRECT AND INDIRECT COST BURDEN OF CHRONIC HEPATITIS C INFECTION IN PRIVATELY-INSURED PATIENTS, STRATIFIED BY LIVER DISEASE SEVERITY
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OBJECTIVES: To assess the direct health care and indirect cost burden of chronic hepatitis C virus (HCV) infection and stratify the economic burden by disease severity. METHODS: Health insurance claims from 60 self-insured US companies and disability data for employees in 29 of these companies covering the period 01/2001-09/2011 were analyzed. Adult patients with 3 diagnoses of chronic HCV infection and no HIV diagnosis were selected. HCV patients were stratified into groups of non-cirrhotic, compensated cirrhotic, and decompensated cirrhosis, and liver disease severity for each treatment group (PT). RESULTS: Patients with non-cirrhotic liver disease were significantly less costly for all PT as compared to patients with cirrhosis, but higher than those with no liver disease. Subgroup cost burden was highest for patients with HCV-related cirrhosis and lowest for those without liver disease. Attendance of the largest increases in treatment costs for patients with HCV-related cirrhosis occurred in the PT of boceprevir ($2,466M), telaprevir ($1,967M), and pegylated interferon ($1,236M). CONCLUSIONS: Direct health care costs are increased most for cirrhotic CHC patients, and the magnitude of the cost burden increased with disease severity.

PODIUM SESSION II: MEDICATION ADHERENCE STUDIES

MA1 IMPACT OF A VALUE-BASED COPAYMENT WAIVER BENEFIT ON MEDICATION ADHERENCE AND SPENDING
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OBJECTIVES: Most copayment waiver (value-based benefit design) programs have been applied at the individual level. In this study we evaluate the impact of family and child copayment waiver at a large employer. METHODS: Employees with diabetes in eligible health and all of their family members (regardless of health status) were automatically enrolled in a copayment waiver ($0 copay) benefit beginning January 2011 for diabetes, cardiovascular, and lipid lowering medications, screenings, and related medical services. The study included 708 enrollees who were propensity score matched to a comparison group (total n=1377) of companies nine similar companies without these benefits. A difference-in-difference model was defined as percent of days covered by a medication class greater than or equal to 80%. A falsification test of adherence to asthma and migraine medications, where copayments did not change, was conducted. RESULTS: Price to program implementation, enrollees in the value-based program had a similar level of
adherence to diabetes medications than the comparison group (p<0.15). After the program, percent adherence grew 29.7% over baseline (p<0.01) net of trends in the comparison group. A smaller impact was observed for cardiovascular medications (p=0.11). 

CONCLUSIONS: The_cutdown intervention had a positive impact on medication adherence for patients with diabetes. Further research is needed to understand the mechanisms behind this improvement.

MA2

BEYOND AVERAGE ADHERENCE: TEMPORAL PATTERNS OF MEDICATION ADHERENCE PREDICT HOSPITALIZATION RISK MORE ACCURATELY THAN THE MEDICATION POSSESSION RATIO


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OBJECTIVES: A patient’s temporal pattern of medication adherence may contain signals for clinical risks that are not captured by aggregate measures such as the medication possession ratio (MPR). We used hierarchical clustering to identify natural adherence patterns to dornase alfa in patients with cystic fibrosis (CF), and assessed whether these patterns were associated with hospitalization risk.

METHODS: CF patients with a dornase alfa prescription followed by ≥1 year of health plan enrollment were included in a national claims database (2005-2011). Hierarchical clustering was used to identify common patterns of adherence over time based on prescription fills. To evaluate the clinical and economic relevance of the clusters, their association with CF-related hospitalization risk was assessed using Poisson regression with adjustment for MPR and other characteristics.

RESULTS: A total of 985 CF patients with ≥1 prescription for dornase alfa were included. Average MPR was 45%. Half of the patients were identified six adherence clusters based on temporal patterns of adherence: patterns 1) high; 2) low-high; 3) low; 4) low-low; 5) low-high-low; and 6) low-low-low. MPR distributions overlapped between clusters. In the Poisson regression, each 1% increase in MPR was significantly (p<0.05) associated with an approximate 1% reduction in hospitalization risk. Including effects of cluster membership into the model with MPR significantly improved fit (P<0.001). After adjusting for MPR, hospitalization risk varied significantly across clusters, and was increased by 97%, 115%, 52%, 286% and 57% in clusters 2-6, respectively. The predictive significance of the clusters was robust to further adjustment for quadratic effects of MPR.

CONCLUSIONS: In this study of CF patients, temporal patterns of medication adherence predicted hospitalization risk more accurately than MPR alone. Temporal adherence patterns beyond MPR may have clinical and economic utility across therapeutic areas and warrant further study.

MA3

REVISION AND VALIDATION OF THE MEDICATION ADHERENCE REASONS SCALE (MAR–SCALD)

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OBJECTIVES: Medication non-adherence is a complex phenomenon that requires tailored interventions to improve it. A new self-reported measure of medication non-adherence was developed based on the commonly reported reasons for non-adherence. The goal of the study was to test the psychometric properties of the scale with tailored interventions. The objectives of this study were to revise the original Medication Adherence Reasons Scale (MAR-SCALD) based on expert opinion through cognitive interviewing and establish the psychometric properties of the scale.

METHODS: A cross sectional design was used in collaboration with the Intermountain Medical Center Outpatient clinic for cholesterol lowering (CLM) and asthma maintenance medications (AMM). The study was conducted in two phases: Phase 1 - the original MAR-SCALD was revised based on expert opinion and cognitive interviewing, Phase 2 - the revised MAR-SCALD was tested for psychometric properties in a random sample of 350 subjects each on CLM and AMM.

RESULTS: Revisions were made based on expert opinion that included asking a global question about adherence in the past 7 days, simplifying the items and converting them into first person sentences, objective anchoring of the scale, and expanding the “forgetfulness” item. Cognitive interviewing added one new item to the scale. The MAR-SCALD estimates the response rate in the respondents and 65% of the AMM respondents as non-adherents. An exploratory factor analysis identified four domains in medication with Cronbach alpha ranging from 0.84 to 0.93 in CLM and 0.82 to 0.89 in AMM. For validity, the scale exhibited significant correlations (0.434 for CLM and 0.539 for AMM at p<0.01) with the well validated Morisky scale and also had significant negative correlation with self-efficacy (-0.226 for CLM and -0.329 for AMM at p < 0.01).

CONCLUSIONS: The revised MAR-SCALD that demonstrated better psychometric properties than the original scale.

MA4

USING LATENT CLASS PROBABILITY ESTIMATION AND RESIDUAL INCLUSION TO ADDRESS CONFOUNDING IN MEDICATION ADHERENCE MODELING

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OBJECTIVES: It is well-established that patients’ medication adherence is often suboptimal and variable in chronic disease settings, but less is known about the association between adherence and outcomes, in part due to potential confounding by unobserved disease severity when using claims data. Our objective was to estimate adherence unexplained by observed characteristics and use this estimate to proxy severity, which could motivate better adherence interventions. As an outcome of the methods, the Asymptomatic Carotid Surgery Trial (ACST). The Metropolis-Hastings Markov Chain Monte Carlo (MCMC) method was used to predict a posteriori the membership to better or worse adherer types. Using GLS regression adjusting for patient characteristics and the ‘healthy adherer effect’, the determinants of this probability were estimated. A residual inclusion approach was used in a Cox proportional hazards model to estimate the effect of adherence on cardiovascular events.

RESULTS: In a sample of new statin users, groups of low- and high-adherers existed. While year one adherence was not associated with cardiovascular events, year two mean adherence was (0.49 vs. 0.46, P<0.001). In the second year of statin use, the probability of being a high-adherer increased for males, those over 65 years and, relative to cluster 1, was increased by 97%, 115%, 52%, 286% and 57% in clusters 2-6, respectively. The Cox model adjusting for MPR, hospitalization risk varied significantly across clusters, and included residuals per se increased hazard by 28% (P=0.04), versus a 20% reduction when the residual was not included. The included residuals per se increased hazard by 28% (P<0.04), consistent with a disease severity effect.

CONCLUSIONS: MAR estimation reveals adherence ‘types’. Estimating the probability of the ‘type’ allows isolation of a measure to address unobserved characteristics, such as disease severity, when modeling outcomes.

PODIUM SESSION II: RESEARCH ON METHODS – MODELING STUDIES

MO1

MODELING FUTURE PREVALENCE OF NEUROLOGICAL CONDITIONS AND DEMAND FOR PHARMACEUTICALS IN THE UNITED STATES

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OBJECTIVES: Accurately forecasting future disease prevalence and resulting demand for pharmaceuticals requires modeling changes in demographics, economic considerations, health care policy, disease risk factors, and treatment options. This study forecasts future neurological condition prevalence and related use of prescribed medications.

METHODS: Using a microsimulation approach and model building, future prevalence of neurological conditions and pharmaceutical use for each person in a stratified random sample (n~3M) of the population in the United States. The population database uses statistical matching to combine (1) population distribution, (2) claims data, and (3) health data from National Nursing Home Survey. Sample weighting is derived from Census Bureau population projections. Logistic regression analysis with the Medical Expenditure Panel Survey estimates the propensity of people with neurological conditions to use prescribed medications to treat Alzheimer’s, attention deficit hyperactivity disorder, cerebral degeneration, epilepsy, extrapyramidal disease not otherwise classified, mental retardation, migraine, mono-neuropathy of limb, multiple sclerosis, Parkinson’s, and sleep disorders. Forecasts through 2030 consider household income and demographic trends, and improved medical coverage under health care reform. For each year from 2012, 26.6 million people (9% of US population) had a diagnosed neurological condition. Between 2012 and 2030, the population with neurological conditions will grow by 17% with the largest percentage growth occurring in Alzheimer’s and Fibromyalgia. Major conditions with the largest percentage growth in prevalence are cerebral degeneration (72% growth), Parkinson’s disease (60%) and Alzheimer’s disease (59%). Use of medications will grow 2-3% through expanded medical coverage under PPACA.

CONCLUSIONS: The results for diagnosed neurological conditions are expected to grow at similar rates over the next 20 years. Given the large increase in prevalence, the utilization of treatments (e.g., levo-dopa, MAOIs, cholinesterase inhibitors, and memantine) will rise accordingly.

MO2

ANALYZING CAROTID ARTERY STENOSIS TREATMENT CLINICAL TRIAL RESULTS FROM A BAYESIAN PERSPECTIVE

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Objective: Rationalizing the use of clinical trial results is based on the null hypothesis that no difference exists between the competing strategies. Bayesian statistics permits the calculation of the probability that a treatment is superior based on observed data and prior information. Output of Bayesian analysis allows the observation of how new information affects the output, especially if the information builds on the prior information.

OBJECTIVES: To further analyze using Bayesian methods clinical trial results for the treatment of asymptomatic carotid artery stenosis surgery vs. medical management whose results were previously reported using frequentist methods.

METHODS: The outcome of interest was the mean difference in the probability of stroke or perioperative death between carotid endarterectomy (CEA) and aggressive medical management (AMM). The Metropolis-Hastings Markov Chain Monte Carlo (MCMC) method was used to predict a posteriori the membership to better or worse adherer types. The Cox model adjusting for MPR, hospitalization risk varied significantly across clusters, and included residuals per se increased hazard by 28% (P=0.04), consistent with a disease severity effect.

CONCLUSIONS: 

The clinical trial results from the Asymptomatic Carotid Atherosclerosis Study (ACST). The likelihood distribution was sourced from the Asymptomatic Carotid Surgery Trial (ACST). The Metropolis-Hastings Markov Chain Monte Carlo (MCMC) method was used to predict a posteriori the membership to better or worse adherer types. A 4% mean difference was chosen as the threshold for clinical-economic significance. In sensitivity analysis, the prior distribution was replaced with results of The European Carotid Surgery Trialists’ Collaborative Group (ECST) study.

RESULTS: The likelihood distribution (ASCT results) had an 86.5%