DALYs, 14.6%). For the age group 65 and over, after adjusting for population, the burden increases 7 fold. The 3 conditions, overall, represent 2,03 DALYs per 1000 Colombians in that age range. **CONCLUSIONS:** Despite the lower incidence of pneumococcal disease in adults, as compared with children, its burden is still significant, comparable, for example, to that of schizophrenia or epilepsy in Colombia. This study may provide a benchmark for future preventive interventions and for efficient resource allocation.

PIN65

THE CHANGING NATURE OF HIV IN THE PAST 5 YEARS: IMPLICATIONS FOR ECONOMIC MODELING

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OBJECTIVES: To review the changes in HIV in terms of course of the disease over the past five years and its consequences, to assess whether existing economic models in HIV would need to be updated to account for these changes in case these were used for the economic evaluation of new treatments in HIV. **METHODS:** A systematic literature review was carried out in PubMed, using both MeSH and key words, focusing on the following areas: opportunistic infections (OIs), health consequences, costs, quality of life, adherence and compliance and efficacy of treatments. In addition, current guidelines were identified and reviewed. For treatments we focussed on maraviroc, etravirine and raltegravir. **RESULTS:** At total of 1787 hits were obtained from the above-mentioned strategy. Finally data on 341 articles extracted. For treatments, data from six trials on efficacy and adverse event data were extracted and used in a meta-analysis (not reported here). In terms of OIs it was clear that fewer patients suffer from these infections compared to the early 2000s. Data on costs indicated that new costs were available by CD4 cell count. There are substantial new data available on quality of life in HIV, however, with several publications providing data by CD4-cell strata. Data on health consequences showed that patients increasingly live long enough to suffer from LT health consequences such as cardiovascular disease and cancer. Guidelines indicated that treatment algorithms had changed markedly in the last five years and that comparison to OBT is no longer an acceptable comparator strategy in economic modelling. **CONCLUSIONS:** The management of HIV has changed substantially since 2006. Patients live longer, are healthier and suffer from "common" health consequences such a cardiovascular disease and cancer. Any health economic model in this disease area should take these aspects into consideration.

PIN66

CONSTANT VS TIME-DEPENDENT: TWO DIFFERENT APPROACHES TO DETERMINE TRANSITION PROBABILITIES BETWEEN HEALTH STATES IN MODELING THE COURSE OF DISEASE – THE CASE OF HEPATITIS C

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OBJECTIVES: When modeling the course of disease it is crucial to make proper assumptions concerning transition probabilities between health states. Two different approaches may be adopted: constant or time-dependent probabilities (i.e. survival curves). Most of published economic analyses of hepatitis C treatment are based on models with constant probabilities. Using survival curves is more time-consuming and complex but may result in more accurate estimates. Our aim was to compare the impact of both methods on results of chronic hepatitis C modeling. **METHODS:** A Markov model was developed to describe hepatitis C patients flow. Time horizon of 50 years was chosen, cycle length was 1 year. Health states distinguished in the model were: fibrosis, compensated cirrhosis (CC), decompensated cirrhosis (DC), hepatocellular carcinoma (HCC), liver transplant (LT) and death. The possible transitions were: fibrosis->CC, CC->DC, CC->HCC, DC->HCC, DC->LT and from each state to death. Transition probabilities between health states were estimated based on clinical trials evaluating the natural course of chronic hepatitis C progression: either by calculating constant yearly rates or by using Weibull curves estimated from reported Kaplan-Meier curves (the same data source for each transition). Time spent in each of health states was compared between those two approaches. **RESULTS:** The average time spent by a CC patient in states CC, DC, HCC and LT was 18.3, 1.6, 0.3 and 1.3 years for constant probabilities, and 14.2, 3.2, 1.1 and 1.6 years for survival curves. Average survival was 21.5 and 20.2 years, respectively. **CONCLUSIONS:** Method of calculation of transition probabilities may have a significant impact on results of modeling, which may further influence incremental cost-effectiveness ratios in economic analyses. The decision on the method should be made on the base of nature of events that are being modeled – for some it may be more accurate to apply the survival curves approach.

PIN67

EXTENDED COX MODEL ANALYSIS WITH NON-PROPORTIONAL HAZARDS APPLIED IN REAL-WORLD OBSERVATIONAL DATA

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OBJECTIVES: To illustrate the application of an extended Cox regression model with time-dependent treatment effects to real-world observational data. **METHODS:** A retrospective US hospital database analysis was conducted among adult invasive aspergillosis (IA) patients receiving their first antifungal therapy during ICU stay. To assess the initial antifungal treatment effect on survival/LOS, a survival analysis was conducted with event defined as "discharged alive", censored being "expired in hospital", and time variable being treatment-initiation-to-discharge (DITD). Key demographic, clinical and treatment variables were included. Regimen A was the reference group and compared to regimen B (inactive against IA, possibly indicating a treatment delay). Proportional hazard assumptions for the treatment variable were assessed by the Schoenfeld residuals significance test. When significant, treatment-by-time interaction together with its main effects were included within an extended Cox model to account for the proportional hazard violation. Multiple functional forms for time were considered in treatment-by-time interactions. Due to the lack of direct SAS output for specific time points, time-specific hazard ratios (HR) between treatments were manually calculated incorporating both main effects and time covariates. **RESULTS:** A continuous linear treatment-by-time interaction was constructed for Drug B since the null hypothesis of Schoenfeld test was rejected. Consistent with an increasing time-interaction effect (HR=1.032, p<0.0001), HR of drug B increased over time: Drug B patients were 57% less likely (HR=0.43, p=.0001) to be discharged alive compared to Drug A at mean switch time to other IA-active drugs (9 days), and 27% less likely (HR=0.73, p=0.0297) to be discharged alive at mean DITD (25 days). Hazards would be equivalent (HR=1) at day 35, although by then most patients on regimen A (81%) had switched/been discharged. **CONCLUSIONS:** The extended Cox model can be implemented as an adjustment for the proportional hazard violation in observational data analysis to obtain unbiased survival results.

PIN68

IMPACT OF AT-RISK WINDOW ASSIGNMENT ON RETROSPECTIVELY-ESTIMATED INCIDENCE AND COSTS OF SAFETY AND TOLERABILITY AMONG MEDICAID HIV PATIENTS INITIATING PROTEASE INHIBITOR-BASED COMBINATION ANTIRETROVIRAL THERAPY IN THE UNITED STATES

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OBJECTIVES: In retrospective claims-based studies of drug exposures and resultant safety/tolerability issues (TIs), researchers must define an a-priori "at-risk window" – the time period in which observed TIs are classified as resulting from drug exposure. In HIV, interruption of combination antiretroviral therapy (cART) may cause detrimental clinical outcomes; thus, if a TI necessitates a switch in cART, the claims-based evidence of healthcare utilization for TIs may persist even after switching. This study quantified the impact of at-risk window assignment on retrospectively-estimated incidence and costs of TIs. **METHODS:** Data were Medicaid claims from 15 states. Subjects were HIV patients 18–64 years old initiating atazanavir, darunavir, fosamprenavir, or lopinavir-based cART regimens from January 1, 2003 to July 1, 2010. Outcomes: incidence and costs of new-onset medically-attended (ICD-9-CM-coded or treated) TIs (gastrointestinal, lipid abnormalities, diabetes/hyperglycemia, rash, jaundice) during a period of up-to 6 months post-cART-initiation or censoring at switch. **RESULTS:** Sample included 20,024 patients; mean age 42 years, 34% female, 48% black. When extending the at-risk window for 7 days post-switch, differences in incidence rates of TIs per 1,000 patient-months were: gastrointestinal (76.1 with extension vs. 73.7 without); lipid abnormalities (23.5 vs. 22.3); diabetes/hyperglycemia (9.0 vs. 8.8); rash (98.5 vs. 96.0); jaundice (0.59 vs. 0.57). When extending the cost-accrual window to include costs of TIs that persist after switching, differences in the estimated per-patient per-month (PPPM) costs of TIs were: gastrointestinal ($72 with extension vs. $75 without); lipid abnormalities ($27 vs. $22); diabetes/hyperglycemia ($71 vs. $67); rash ($7 vs. $8); jaundice ($0.4 vs. $2). **CONCLUSIONS:** Extension of at-risk windows increased estimated incidence rates of TIs, decreased estimated PPPM costs of acute TIs (i.e., gastrointestinal, rash, jaundice) and increased the estimated PPPM cost of chronic TIs (i.e., lipid abnormalities, diabetes/hyperglycemia). These novel results may inform future retrospective studies of TIs in cART.

SENSORY SYSTEMS DISORDERS – Clinical Outcomes Studies

PSS1

RELIEVING THE PRURITUS OF ATOPIC DERMATITIS: A META-ANALYSIS

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OBJECTIVES: Atopic dermatitis is a chronically relapsing inflammatory skin condition accompanied by pruritus which, when severe, can negatively impact a patient's quality of life. The objective of this study was to perform a meta-analysis of randomized controlled trials (RCTs) of topical therapies compared against their vehicles, and systemic therapies compared against their placebos, and to record how these therapies changed the magnitude of pruritus associated with atopic dermatitis. **METHODS:** Data for this meta-analysis were extracted from Medline, Embase, and the Cochrane Controlled Clinical Trials Register, as well as follow-up references in retrieved articles from years 1977 to 2011. Initial search of systemic therapies in relieving the pruritus of atopic dermatitis yielded 205 studies. Out of the 205 studies, 52 studies met the inclusion criteria, with 41 and 11 studies involving topical and systemic treatment of pruritus of atopic dermatitis, respectively. Standard inverse variance fixed-effects meta-analysis was used to calculate the pooled estimates for RCTs falling under each type of treatment. **RESULTS:** The 52 studies were analyzed using STATA SE version 10. Meta-analysis results showed that overall, compared to systemic medication of atopic dermatitis, the topical medications significantly reduced atopic pruritus by 35.3% (RR, 0.647; 95% CI, 0.619-0.677). Among the topical medications, compared to the use of vehicle, the use of anti-histamines, calcineurin inhibitors and topical corticosteroids as therapeutic agents significantly reduced the pruritus of atopic dermatitis by 27%, 36% and 34% in patients, respectively. **CONCLUSIONS:** The topical treatments were more successful at reducing atopic pruritus compared to the systemic treatments. Overall, calcineurin inhibitors were the most effective antipruritic agents. Verifiable pruri-