DMTs. Five-fold cross validation was used to tune and evaluate traditional and regularized logistic regression, XGBoost, support vector machine, random forest and feed-forward neural network models. The best model was selected using the area under the ROC curve (AUC) and accuracy, recall, precision, F1-score and specificity were assessed. ***Results:*** Inpatient relapse was observed for 984 (5.2%) patients of 18,820 patients (mean age=44.2 years; females=75.8%). The XGBoost model had the best AUC (AUC=79.3%; accuracy=74.3%; recall=69.7%; precision=13.1%, F1=0.22, specificity=74.5%). Predictors of inpatient relapse included MS related HRU measures (previous IP or ER visit with MS diagnosis, number of MS related encounters, utilization of home care services and durable medical equipment), epilepsy/convulsions, paralysis, urinary tract infections, potential medication side effects (nausea and vomiting), use of muscle relaxants, anticonvulsants and antidepressants. Factors protective of relapse were increased PDC, older age, DMTs administered as infusion, Caucasian race and being female. ***Conclusions:*** Our study identified demographic and clinical predictors of inpatient MS relapse with high predictive accuracy. Our findings can potentially be utilized to better manage patients at high risk of relapse.

Economic Evaluation in Oncology Studies

EC1
A COST-EFFECTIVENESS ANALYSIS OF NIVOLUMAB PLUS IPILIMUMAB PLUS TWO CYCLES OF PLATINUM DOUBLET CHEMOTHERAPY VERSUS PLATINUM DOUBLET CHEMOTHERAPY IN THE FIRST-LINE TREATMENT OF STAGE IV OR RECURRENT NON-SMALL CELL LUNG CANCER IN THE UNITED STATES

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Objectives: To evaluate the cost-effectiveness of nivolumab plus ipilimumab plus two cycles of platinum doublet chemotherapy (NIVO+IPI+PDC) versus four cycles of PDC in the first-line (1L) treatment of stage IV or recurrent non-small cell lung cancer (NSCLC) from a health insurance perspective in the United States (US). ***Methods:*** A partitioned survival model with three health states (progression-free, progressed disease and death) was developed. Efficacy, safety and quality of life data were derived from the Phase-III CheckMate 9LA trial (CM9LA), with a minimum follow-up (FU) of 12.7 months for overall survival (OS)). Data from a more mature trial involving NIVO+IPI in 1L NSCLC, CM227 (37.7 months minimum FU for OS), were used to inform long-term OS over the 25-year (lifetime) horizon to capture the long-term survival effect observed from dual Immune-Oncology therapy. OS and progression-free survival was estimated based on CM9LA Kaplan Meier (KM) data up to 13 months then extrapolated using the conditional survival estimates from CM227. The CM9LA duration of treatment KM curves were used to estimate treatment costs. Resource use and direct medical costs (2020 USD) were included. EQ-5D based treatment-specific utility weights (US tariffs) were used. Annual discount rates of 3.5% for costs and outcomes were applied. Probabilistic sensitivity analyses (PSA) were conducted. ***Results:*** The incremental cost per quality-adjusted life-year (QALY) gained was $132,960. NIVO+IPI+PDC vs. PDC resulted in increased life-years (3.71 vs. 1.89), QALYs (2.86 vs. 1.37), and costs ($317,497 vs. 119,932). Drug acquisition cost for NIVO+IPI+PDC was the key driver of the difference in total costs. PSA results were consistent with the base case. ***Conclusions:*** NIVO+IPI+PDC offers a new cost-effective treatment option for patients in 1L NSCLC. Estimated incremental cost-effectiveness ratio is within the range of what is considered acceptable value for money within the metastatic cancer setting in the US.

EC2
MODELING APPROACHES TO ESTIMATE REALIZED REAL OPTION VALUE OF IPILIMUMAB IN METASTATIC MELANOMA

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Objectives: Real option value (ROV) is created when a drug enables a patient to live long enough to benefit from a future innovation, but few if any studies have quantified ROV observed in the real world. We aimed to estimate the realized ROV using real-world data (RWD) using ipilimumab in melanoma as a case study. ***Methods:*** We developed a framework for calculating ROV using RWD that accounted for the health gain in the standard therapy arm as well as the actual uptake of future innovative drugs. We developed a Markov model to estimate the quality-adjusted life-years (QALYs) gained with ipilimumab compared to chemotherapy for patients with or without subsequent cancer immunotherapy (CIT). The realized ROV of ipilimumab and chemotherapy was the additional health gain due to the CIT. To inform the model parameters, we used the nationwide Flatiron Health electronic health record-derived de-identified database to estimate real-world progression-free survival (PFS) and overall survival (OS) curves for patients stratified by the first- and subsequent-lines of therapy. Patients diagnosed with metastatic or advanced unresectable melanoma and started treatment between 1/1/2011 and date of 1st CIT approval (9/4/2014) were included. ***Results:*** The incremental QALYs gained for ipilimumab vs. chemotherapy without subsequent CIT were 1.74. With subsequent CIT, the incremental QALYs increased by 0.92, 0.60, 0.33, 0.18, 0.10, and 0.02 when CIT became available 0, 3, 6, 9, 12, and 24 months after the initiation of first-line ipilimumab, respectively. The results were sensitive to the survival benefit of ipilimumab, the survival benefit of subsequent CIT, and the uptake of CIT. ***Conclusions:*** This is the first study to demonstrate the realized ROV using RWD. The realized ROV was between 1%–54% of conventional value for patients diagnosed within 2 years before CIT availability. Further studies are needed to understand ROV in other diseases, particularly those with longer survival times.

EC3
ECONOMIC BURDEN OF CARDIOVASCULAR EVENTS IN PATIENTS WITH CHRONIC LYMPHOCYTIC LEUKEMIA TREATED WITH NOVEL AGENTS

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Objectives: Novel agent treatments (NATs) have improved survival in chronic lymphocytic leukemia (CLL), but can be associated with increased cardiovascular (CV) events. This analysis examined real-world healthcare costs associated with CV events in CLL patients treated with NATs. ***Methods:*** Using US-commercial administrative claims data (IBM MarketScan), we compared unadjusted healthcare costs among CLL patients taking NATs with and without a CV event during treatment (CV vs. noCV). Inclusion criteria were adult CLL patients, evidence of NATs (acalabrutinib, duvelisib, ibrutinib, idelalisib, venetoclax) between November 2013-November 2019 (index date=earliest fill date), continuous enrollment for 6-months pre-index (baseline), and no evidence of NATs or trial participation during baseline. Annual all-cause and CV-related healthcare costs (adjusted to 2019 US dollars) were measured in a fixed 12-month follow-up period while per-patient-per-month (PPPM) costs were compared in variable-length pre/post-CV event periods. ***Results:*** Of 1,886 CLL patients with NATs, 27.7% experienced a CV event during treatment, occurring a mean(SD) 103.0(93.9) days following NAT initiation. Almost half (47.1%) of CV patients had a CV event pre-index, the majority of which were hypertension. CV patients were older (71.7 vs. 65.8, $p<0.001$) and had a higher baseline NCI score (1.2 vs. 0.8, $p<0.001$) than noCV patients. Annual all-cause total healthcare costs were higher in the CV vs. noCV cohort ($203,349 vs. $165,144, $p<0.001$). Higher annual medical costs ($82,949 vs. $45,293, $p<0.001$) compensated for numerically lower NAT costs in CV vs. noCV cohort ($110,925 vs. $115,026, p=0.262). Pre-CV event, outpatient pharmacy PPPM costs contributed most to total healthcare costs; post-CV event, PPPM medical costs contributed more: outpatient pharmacy 74.8% vs. 38.8%, hospitalization 7.6% vs. 38.8%, and outpatient services 17.7% vs. 22.4%. ***Conclusions:*** In CLL patients with a CV event, higher medical costs compensate for decreased novel agent costs, suggesting increased medical management in addition to NAT discontinuation.

EC4
REAL-WORLD HEALTHCARE COSTS IN PATIENTS WITH CLASSICAL HODGKIN LYMPHOMA TREATED WITH PEMBROLIZUMAB AND NIVOLUMAB IN THE UNITED STATES

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Objectives: Patients with classical Hodgkin lymphoma (cHL) relapsed or refractory (R/R) disease incur substantial healthcare resource utilization and costs. The PD-1 inhibitors nivolumab and pembrolizumab were approved by the FDA (May 2016 and March 2017, respectively) as treatments for R/R cHL patients; however, literature on the healthcare costs of patients treated with these two medications is sparse. This retrospective study evaluated the medical costs of patients with cHL initiated on pembrolizumab compared to nivolumab in the US. ***Methods:*** Healthcare insurance claims from Symphony Health's Patient Integrated Dataverse® (07/2014-06/2018) were used to identify adult patients with cHL initiated on pembrolizumab or nivolumab (index date). Inverse probability of treatment weighting was used to adjust for differences in baseline patient characteristics between cohorts (evaluated in the 12 months prior to the index date). All-cause and cHL-related hospitalization and outpatient visit costs (based on provider charges) were reported per-patient-per-

year during the observation (post-index) period. Costs were compared between cohorts using cost ratios (CR), and confidence intervals (CI) and p-values were generated using non-parametric bootstrap procedures. ***Results:*** In total 92 and 218 patients were included in the pembrolizumab and nivolumab cohorts, respectively. After weighting, mean age was 55 years in both cohorts, while the proportion of females was lower in the pembrolizumab (35.3%) compared to the nivolumab cohort (44.1%). Mean Quan-Charlson comorbidity index score was well balanced (pembrolizumab: 4.2; nivolumab: 4.3). During the observation period (pembrolizumab: 295 days; nivolumab: 274 days), pembrolizumab initiators had significantly lower all-cause hospitalization costs (CR [95% CI]: 0.29 [0.06-0.76], p=0.016) and cHL-related hospitalization costs (CR [95% CI]: 0.09 [0.00-0.31], p<0.001) than nivolumab initiators. All-cause and cHL-related outpatient visit costs were not statistically different between cohorts. ***Conclusions:*** In this real-world study, adult cHL patients initiated on pembrolizumab had significantly lower all-cause and cHL-related hospitalization costs compared to patients initiated on nivolumab.

Economic Evaluation Applications: Burden and Value of Therapies

ED1
ANTIMICROBIAL RESISTANCE IN US HOSPITALS: BURDEN AND VALUE OF INVESTMENT IN DEVELOPING NEW TREATMENTS

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Objectives: This research aims to quantify the burden of antimicrobial resistance (AMR) from the perspective of hospital stakeholders and the value of continued investment in developing new treatments. ***Methods:*** A dataset representative of the US population demographics and health characteristics was constructed by merging the American Community Survey, Behavioral Risk Factor Surveillance System and data on nursing home residents. Prediction equations linking patient demographics and health characteristics to likelihood of hospitalization within hospital service lines were generated using the Medical Expenditure Panel Survey and applied to the population file. Data from the National Healthcare Safety Network were used to calculate state-specific rates of AMR in hospitalized patients experiencing an infection. Peer-reviewed published research provided estimates for AMR-attributable outcomes, including mortality, inpatient days, and direct & indirect costs. Results were calculated under a base case scenario reflecting current rates of infection continuing into the future, and alternative scenarios reflecting changes in future rates of infection and resistance. ***Results:*** Base case results suggested approximately 4,100 AMR-attributable deaths would occur in the base modeling year, resulting in over $700 million in direct costs, increasing to 5,300 deaths and $907 million in direct costs by 2035. Under a scenario in which rates of resistance increase to 100%, reflecting a hypothetical scenario where alternative antimicrobial treatments are no longer effective, projected 2035 AMR-attributable deaths increase to 30,700 (480% increase from base case) and direct costs of $8.4 billion (826% increase from base case). Infections are projected be highest in general surgery and thoracic surgery service lines, where high infection risk could potentially make surgeries too risky to perform. ***Conclusions:*** Though its current burden is substantial, AMR's potential future burden is significantly more concerning. Investing in AMR prevention strategies will be necessary to reverse course with respect to increasing resistance.

ED2
ELEMENTS OF VALUE FOR GENE THERAPY: A SYSTEMATIC REVIEW

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Objectives: ISPOR recommends that value assessments include elements beyond traditional quality-adjusted life years (QALYs) and costs. We aimed to identify non-traditional value elements relevant to gene therapies as it is unclear to what extent they have been included in gene therapy value assessments. ***Methods:*** We searched PubMed and Embase for full-text articles discussing non-traditional value elements defined by the 2018 ISPOR framework in the context of gene therapy that were published in English between 2015-2020. Health technology assessment (HTA) reports published by the Institute of Clinical and Economic Review and National Institute for Health and Care Excellence were collected. Articles and reports were included if they proposed methods for incorporation or accounted for specified value elements in economic evaluations or real-world decision making. ***Results:*** Twenty-four of 644 articles identified met inclusion criteria; 17 were peer-reviewed journal articles and 8 HTA reports. Disease areas for which specific gene therapies were discussed included cancer, beta thalassemia, inherited eye disease, hemophilia, spinal muscular atrophy, and severe immunodeficiency. The most common non-traditional value elements were productivity (n=12), severity of disease (n=10), equity (n=4), and scientific spillover (n=4). Productivity was captured as an indirect cost in cost-effectiveness analyses (CEAs). Although severity of disease, equity, and scientific spillover were not explicitly quantified, they were incorporated into HTA body decisions: severity through conditional market access, QALY weighting, higher CEA thresholds, and lower discount rates; equity through higher CEA thresholds and QALY weighting; and scientific spillover through accelerated market access. Multi-criteria decision analysis was also proposed. ***Conclusions:*** Use of novel value elements for gene therapies appears to be sparse in health economic studies to date. Methods of QALY weighting, varying CEA thresholds, discount rates, and specialized access pathways accounted for novel elements in value assessments. Future research on the feasibility, quantification, and incorporation of novel value elements for gene therapies is warranted.

ED3
SOCIETAL BURDEN OF DEMENTIA-RELATED PSYCHOSIS IN THE US: A COST OF ILLNESS ANALYSIS

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Background: Dementia-related psychosis (DRP), characterized by hallucinations and delusions, may accelerate the cognitive/functional decline among patients with dementia. Such declines have debilitating consequences on patients, caregivers, and society. While previous research has estimated total annual-direct DRP costs, analysis of both direct and indirect costs is important in understanding the overall societal burden of DRP. ***Objectives:*** To estimate the societal burden and associated costs of DRP in the US population. ***Methods:*** A Markov model was developed to assess the societal cost burden of DRP. The five DRP health states in the model were: mild, moderate, severe, end-of-life-care, and death as an absorbent health state. Cycle length was 30-days. Societal costs were calculated as a sum of total annual direct and indirect costs. Total indirect costs included both formal (paid by Medicare, Medicaid, or LTC insurance) and informal (caregiver time and patient out-of-pocket costs) caregiver costs, respectively. Prevalence, disease-severity, transition probabilities, and costs were derived from the literature. One-way sensitivity analysis was conducted to test the model's robustness by varying inputs and assumptions. ***Results:*** The estimated total annual-societal cost of DRP is $263B, and approximately $122B (46%) and $141B (54%) were indirect and direct costs, respectively. Of the total indirect costs, formal and informal caregiver costs including end-of-life-care costs were approximately $44.75B and $77.25B, respectively. End-of-life-care contributed $10B and $22B of the total formal and informal caregiver costs, respectively. ***Conclusions:*** Results of this analysis demonstrate that indirect costs contribute to approximately half of the total annual societal DRP costs; with caregiver costs contributing nearly 30% of the total. Given the aging US population, in addition to direct costs, indirect costs related to the caregiver and out-of-pocket costs may impose an enormous burden on the healthcare system. Given this public health concern, better management strategies and improved therapeutic options for DRP are needed.

ED4
ECONOMIC BURDEN OF ATTENTION-DEFICIT/HYPERACTIVITY DISORDER (ADHD) AMONG CHILDREN AND ADOLESCENTS IN THE UNITED STATES (US): A SOCIETAL PERSPECTIVE

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Objectives: To comprehensively assess the economic burden associated with ADHD among children and adolescents in the US in 2018. ***Methods:*** Excess costs (in 2018 US dollars) incurred by children and adolescents with ADHD were evaluated from a societal perspective. Direct healthcare costs were estimated using data from the Truven Health Analytics MarketScan® database (01/01/2013-12/31/2018). Direct healthcare costs, non-direct healthcare costs (i.e., research and training, education, substance use [adolescent only], and road traffic accidents [adolescents only]), and indirect costs (i.e., caregiving, unemployment [adolescent only], productivity loss [adolescent only], and premature mortality [adolescent only]) were assessed using academic and governmental publications. ***Results:*** Based on an estimated ADHD prevalence of 10.0% among children (N=2.9 million) and 6.5% among adolescents (N=1.7 million), total excess costs incurred by children and adolescents with ADHD were estimated at $19.4 billion ($6,799 per individual) and $13.8 billion ($8,349 per individual), respectively. Among children,