Methods: This study used the Behavior Risk Factor Surveillance System, a nationally representative health-related telephone survey, to compare cancer screening rates using surveys of 2012, 2014, 2016 and 2018 based on Medicaid expansion status. A difference-in-difference-in-difference (DDD) model was used to compare the trends. Several sample populations were included in this study for different types of cancer screening. All states were analyzed in this study. States expanded Medicaid during the study period were regarded as the treatment group, otherwise, as a control group. Robustness checks were conducted after main analysis. Statistical analysis was conducted in Stata/SE 15.1 (StataCorp LLC, College Station, TX). ***Results:*** Medicaid expansion slightly improved screening rate by 2%, 0.3% and 2% respectively for breast cancer, cervical cancer and prostate cancer for respondents whose income were below or at 138 % federal poverty line (FPL) in expansion states comparing respondents whose income were over 138 % in non-expansion states. The screening rate for prostate cancer had a marginally significant improvement, increased by 4% comparing respondents with household income below or at 138 % FPL in expansion states with respondents with household income over 400 % FPL in non-expansion states. And these effects have disparities in different racial groups. ***Conclusions:*** The effect of Medicaid expansion on cancer screening was not significant for most cancer screening in this study and only marginally significant for prostate cancer when comparing respondents with household income below 138 % FPL in expansion states with respondents with household income over 400 % FPL in non-expansion states.

MC3
DISPARITIES IN HEALTH INSURANCE STATUS AMONG YOUNG ADULT CANCER PATIENTS IN STATES WITH AND WITHOUT MEDICAID EXPANSION: ANALYSES OF THE SURVEILLANCE, EPIDEMIOLOGY AND END RESULTS REGISTRIES, 2007 - 2016

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Objectives: Health insurance coverage is an important determinant of outcomes among cancer patients, particularly for young adults in the U.S. who have the highest rates of being uninsured. Our objective was to measure the impact of the Affordable Care Act provision of Medicaid expansion on uninsured rates among young adult cancer patients. ***Methods:*** We conducted a retrospective cohort study of adults ages 20-39 years diagnosed with cancer between 2007 and 2016 in the Surveillance, Epidemiology, and End Results Program registries. We collected information on sociodemographics, clinical characteristics, insurance status at diagnosis and Medicaid expansion status. Covariate-adjusted difference-in-differences (DID) analyses were performed to determine changes in rates of uninsured young adult cancer patients over time. ***Results:*** From an overall cohort of 9,103 young adult cancer patients identified in 18 population-based registries, 7,196 (79%) resided in states with Medicaid expansion occurring by 2014. Expansion states experienced a reduction in the proportion of uninsured young adult cancer patients in 2014–2016 compared to 2007–2009 (11.3% to 9.1%, diff -2.2%), whereas non-expansion states did not (16.2% to 20.3%, diff 4.1%; DID -6.4%, P<0.01). Reductions in uninsured rates were most consistent among patients ages 20-29 years (DID -11.1%, P=0.047) and non-Hispanic white patients (DID -8.7%, P<0.01). No statistically significant reductions in uninsured rates attributable to Medicaid expansion were observed among among adults ages 30-39 years (DID -5.0%, P=0.07) and non-Hispanic black (DID -5.2%, P=0.37), Hispanic (DID -4.5%, P=0.66) and non-Hispanic Asian/Pacific Islander patients (DID -7.7%, P=0.32). ***Conclusions:*** Between 2007 and 2016, rates of uninsured young adult cancer patients in Medicaid expansion states decreased, whereas there was a relative increase in rates of uninsured young adults with cancer in non-expansion states. Future research and policies to expand health coverage for young adults should consider the unequal gains observed across age and racial/ethnic minority groups.

MC4
IMPROVEMENT IN MEDICATION ADHERENCE FOR MEMBERS ENROLLED IN A ZERO DOLLAR COPAY PROGRAM IS SENSITIVE TO SOCIOECONOMIC STATUS: A BLUE CROSS BLUE SHIELD OF LOUISIANA PERSPECTIVE

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Objectives: Blue Cross Blue Shield of Louisiana (Blue Cross)'s Zero Dollar Copay (ZDC) program removes the copay for a large set of medications related to certain chronic diseases. We aimed to evaluate the effects of the ZDC program on medication adherence by drug class and socioeconomic status. ***Methods:*** We analyzed Blue Cross members aged 18 years and above who were continuously enrolled in a chronic disease management (DM) program (asthma, chronic obstructive pulmonary disease, coronary heart disease, hypertension, diabetes, or chronic kidney disease) from March 2017 to March 2019. The ZDC treatment cohort was comprised of fully-insured members who had Blue Cross pharmacy benefit that included copays. Members without a copay or who were covered by employers contracting for administrative services only were included in the control group. All study participants were taking ZDC program-related drugs during the study period with at least 1 month of claims following ZDC enrollment. Propensity score weighting was performed to control for several baseline factors, and difference-in-difference (DID) regression models were used to measure program effects. ***Results:*** Adherence rates in the ZDC cohort increased for most drug classes compared to the control group, and the largest DIDs were observed for diuretics (8.4%), anti-diabetics (6.2%), and calcium channel blockers (6.1%). Across all income levels, average medication adherence increased for members in the ZDC group relative to controls. Members in the lowest income bracket (income between $0 and $39,000) showed the greatest improvement in medication adherence compared to other income groups, with average rates increasing by 1.2% in the ZDC group and decreasing by 2.4% in the control group. ***Conclusions:*** The ZDC program increased medication adherence rates relative to controls, an effect that was primarily driven by members with lower socioeconomic status.

Missing Data Studies

MD2
COMPARISON OF COVARIATE BALANCE AMONG PROPENSITY SCORE MATCHING VERSUS PROPENSITY SCORE WEIGHTING AND STRATIFICATION IN OBSERVATIONAL MEDICAL DEVICE RESEARCH

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Objective: Propensity score matching (PSM) is a popular statistical technique to mitigate confounding by measured variables in observational studies. The generalizability of PSM results may be threatened by loss of treated observations as a result of matching with a caliper. Propensity score weighting (PSW) and stratification (PSS) are alternative methods to achieving balance while retaining all treated cases. We compare these three techniques in a real-world study that evaluates the safety of a target medical device to similar devices. ***Methods:*** The Premier Healthcare Database, which comprises hospital billing records from over 970 hospitals in the US, was queried for all patients who had disposable electrodes used in surgery from January 2000 to December 2018. Patients were classified into target device group (treated) or comparison device group (control). Propensity scores were calculated with a logistic regression model that had 13 covariates, including but not limited to: age, gender, teaching status, and Charlson comorbidity score. For each covariate, standardized mean differences (SMD) were calculated before and after implementing PSM, PSW, and PSS. Covariate balance was assessed by the number of covariates with SMD < 0.1. ***Results:*** There were 298,505 patients in the treated group and 329,664 patients in the control group. Prior to balancing, 9 out of 13 covariates were unbalanced. After 1:1 PSM (caliper = 0.2), 230,707 (77.3%) patients were retained in the treated group and 12 covariates were balanced. PSW resulted in all treated patients retained and all 13 covariates balanced. PSS (strata=10) also had all treated patients retained, but 8 covariates remained unbalanced. ***Conclusion:*** PSW achieved balance on all covariates while retaining all treated cases, but PSM resulted in a substantial loss of treated cases and PSS led to residual imbalance in some covariates. Further analysis is warranted to compare the estimates of safety outcomes after the implementation of three covariate balance techniques.

MD3
RISK ESTIMATION BY BOOSTED DOUBLY ROBUST METHOD

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Objectives: The choice of a covariate adjustment method may affect risk estimates in observational studies. We developed a method, the boosted doubly robust (BDR), that can effectively handle numerous correlated covariates and reduce bias and variance in the effect estimates. The method may be applied to many outcome analyses including costs. ***Methods:*** BDR combines the merits of boosted propensity scoring (BPS) and doubly robust (DR) estimation. BDR first uses BPS to match the joint distribution of the pre-treatment covariates. Secondly, BDR uses an outcome model to handle residual confounding. Statistical arguments suggest that BPS reduces the bias in the risk estimates and that DR reduces bias and variance still further. As an example, we examined the established association between diazepam, a long-acting benzodiazepine, and alprazolam, a short-acting benzodiazepine, and risk of injury using BDR and conventional adjustment methods including no adjustment, Poisson regression, propensity scoring using logistic regression (LPS), and high dimensional propensity scoring (HDPS). ***Results:*** The study included 78,829 and 118,579 patients with a prescription for diazepam or alprazolam respectively in the IBM MarketScan Database. We compared risk of treatment in the 1-15 days following the initial prescription (post-treatment) with the risk in the 1-365 days prior to treatment (pre-treatment) and computed the post- to pre-treatment rate ratio (RR) in each treatment cohort. We computed the ratio of the RRs

(RRR) and 95 percent confidence limits in the treatment and comparison cohorts using all methods. The confidence limits for BDR were narrowest consistent with statistical arguments that BDR reduces variance. The RRRs were 2.85 (0.82, 9.90) for no adjustment, 2.86 (0.89, 9.15) for Poisson regression, 3.27 (1.66, 6.44) for LPS, 3.28 (1.67, 6.46) for HDPS and 2.27 (1.17, 4.39) for BDR. ***Conclusions:*** BDR improves balance in the pre-treatment covariates, reduces bias and reduces variance and deserves consideration in outcomes research studies.

MD4
ERROR PROPAGATION FOR SIMULATED TREATMENT COMPARISONS

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Objectives: In comparative effectiveness research Simulated Treatment Comparisons (STCs) are becoming increasingly common in the absence of head-to-head trials. STCs use estimates from limited IPD to adjust for covariate imbalance between trials, however the uncertainty from these estimates is generally ignored when estimating relative treatment effects. This study demonstrates the need to account for this uncertainty when conducting STCs. We introduce an STC method that accounts for the uncertainty due to covariate adjustment, and demonstrate its effectiveness via simulation. ***Methods:*** We simulated two single arm studies (N=300 for both), each containing age and overall survival. We assume study 1 has individual patient data available, and study 2 only has aggregate age data and a digitized Kaplan-Meier curve. We compute a covariate adjustment term based on the mean age difference between the studies and the age coefficients from fitting a parametric survival model to the observed study 1 IPD. We then estimate the variance of this adjustment term via bootstrapping and incorporate this uncertainty into a Bayesian STC model which estimates the relative treatment effect for the two study datasets converted to a digitized Kaplan-Meier format. ***Results:*** The proportion of 95% CrI's that captured the true treatment effect was 86.8% without error propagation, whereas 92.0% of CrI's captured the true treatment with error propagation. 94.9% of CrI's contained the true treatment effect when using survival regression with the complete IPD. ***Conclusions:*** Failing to account for uncertainty from covariate adjustment when conducting simulated treatment comparisons generally leads to underestimating the uncertainty of relative treatment effects. This method better captures the uncertainty introduced when conducting an STC.

Modeling & Simulation Studies

MS1
VALIDATION OF MODELED 5-YEAR SURVIVAL OUTCOMES AMONG PATIENTS WITH CYSTIC FIBROSIS (CF) TREATED WITH THE CF TRANSMEMBRANE CONDUCTANCE REGULATOR MODULATOR (CFTRM) IVACAFTOR USING US CF FOUNDATION PATIENT REGISTRY (USCFFPR) DATA

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Objectives: CF is a rare genetic disease characterized by life-shortening lung function decline. Ivacaftor, a highly effective CFTRm, was introduced in 2012. A model was developed to project the impact of ivacaftor on survival based on known relationships between CF patient characteristics and mortality. This study validates the model methodology and survival projections using data from a recent real-world, postapproval, long-term safety study (LTSS) (Volkova 2019) that followed ivacaftor patients and matched comparators for 5 years (2012-2016). ***Methods:*** The patient-level simulation model assesses the impact of initiating ivacaftor at age ≥6 years vs best supportive care (BSC) on outcomes in US CF patients with CFTR gating mutations. Lifetime survival was estimated using parametric equations fitted to historical USCFFPR survival data to estimate age-specific baseline mortality risk for each patient. Mortality hazards were estimated as the age-specific hazard adjusted for fixed and time-varying patient-level characteristics corresponding to published risk factors (Liou 2001). BSC disease progression was derived from published studies using the USCFFPR, and the expected impact of ivacaftor on ppFEV$_1$, pulmonary exacerbations, and weight-for-age derived from clinical trials. LTSS patient characteristics were entered into the model at baseline and outcomes simulated; 5-year model-projected mortality with bootstrapped credible intervals (CrI) was compared to LTSS mortality. ***Results:*** Modeled 5-year mortality projections closely approximate real-world data in both the BSC (6.4% [95% CrI: 5.3%-7.6%] modeled vs 6.0% observed) and ivacaftor-treated (3.5% [2.8%-4.5%] vs 3.1%) populations. The model also predicts that ivacaftor-treated patients have a 5-year relative risk of mortality of 0.54 ([0.48-0.61] modeled, 0.51 observed) vs untreated patients. ***Conclusions:*** Modeled 5-year survival projections for CF patients initiating ivacaftor vs BSC track closely to observed registry data. Findings support the validity of modeling CF using the approach described herein to predict long-term survival and estimate clinical and economic outcomes of CFTRm. Sponsor: Vertex Pharmaceuticals.

MS2
TREATMENT SWITCHING ANALYSES ON PATIENT-LEVEL DATA TO INFORM TRANSFERABILITY OF A TRIAL-BASED HEALTH ECONOMIC ANALYSIS IN METASTATIC COLORECTAL CANCER: A CASE STUDY USING PATIENT-LEVEL DATA FROM THE FIRE-3 TRIAL

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Objectives: Geographic transferability of health economic analyses (HEA) may be facilitated by addressing differences in treatment and patient characteristics of an original trial population vs the population of interest. For a health technology assessment–driven HEA, applicability of the FIRE-3 trial comparing cetuximab to bevacizumab added to FOLFIRI (CET+F; BEV+F) as first-line treatment of *RAS* wild-type metastatic colorectal cancer was explored. In FIRE-3, a proportion of patients received panitumumab (PAN) as a subsequent treatment. Treatment-switching analyses were used to adjust overall survival (OS) for later-line treatment effects in jurisdictions where PAN is unavailable. ***Methods:*** The two-stage method (TSM) was applied to adjust trial outcomes. In scenario analyses, excluding (EXC) or censoring (CEN) PAN-receiving patients from FIRE-3 OS was explored. TSM adjusts patients' survival times (ST) by multiplying ST beyond start of second-line treatment with an acceleration factor (AF), which represents relative effectiveness of PAN vs other subsequent treatments (first step). AFs were derived from the FIRE-3 trial (internal [INT]) and external (EXT) published data. Resulting counterfactual ST estimates were calculated for each patient according to the first-line treatment received (second step). Recensoring was applied to correct for imbalances resulting from AF <1. Counterfactual ST were compared, and hazard ratios (HRs) were calculated for each method. Bootstrap analyses were performed to estimate uncertainty over the outcomes. ***Results:*** The FIRE-3 trial HR (95% CI) for CET+F vs BEV+F was 0.697 (0.539-0.903). HRs adjusted for subsequent PAN use were 0.682 (0.526-0.885; TSM INT), 0.696 (0.530-0.914; TSM EXT), 0.702 (0.531-0.929; EXC), and 0.714 (0.540-0.944; CEN). P-values for all HRs were ≤0.05. ***Conclusions:*** Adjusted HRs showed OS improvement favouring CET+F. Bootstrap analyses confirmed deterministic results. Consequently, data from the FIRE-3 trial can be applied in HEA in a range of jurisdictions to calculate robust ICERs for CET+F vs BEV+F.

MS3
PREDICTING OPTIMAL TREATMENT REGIMENS FOR HR+/HER2- BREAST CANCER BASED ON ELECTRONIC HEALTH RECORDS USING RANDOM FOREST

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Objectives: This exploratory study uses random forest (RF) to predict optimal treatment resulting in longest overall survival (OS) for patients initiating first or second line of therapy (LOT) for HR+/HER2- metastatic breast cancer (mBC) to build understanding of how machine learning may help inform clinical decision-making. ***Methods:*** Flatiron Health electronic health records (EHR) were used. Eligible patients were adult females diagnosed with mBC who received ≥1 LOT for mBC between 15Feb2015 and 31Jan2019. Individual regimens were grouped into hierarchy regimen classes with top three included in this analysis (CDK4/6 inhibitor-based therapy, endocrine therapy and chemotherapy). Study cohort was randomly partitioned 1000 times into 80% training and 20% validation subsets. RF survival models were used to predict optimal regimen in each LOT separately based on baseline demographics and clinical characteristics. The gains in OS from patients who received an estimated optimal regimen vs those who did not were examined using Kaplan-Meier method, parametric survival modeling, and Cox proportional hazards regression, adjusted for baseline characteristics imbalance by inverse probability weighting. ***Results:*** The study cohort included 3965 and 2455 patients with first and second LOT, respectively. Less than 50% of patients in the study cohort received optimal regimen classes. RF models suggested greater use of CDK4/6 therapies to maximize OS: increasing from observed 42.2% to estimated optimal 73.9% in first LOT and from observed 40.5% to estimated optimal 66.5% in second LOT. The OS gain, in terms of restricted mean survival time over a 10-year horizon, was 0.63 and 1.09 years, with hazard ratio (95% confidence interval) 0.81 (0.64, 1.04) and 0.62 (0.46, 0.85), in first and second LOT, respectively. ***Conclusions:*** RF was feasible using oncology EHR data, building the evidence to inform how machine learning may