and the true treatment effects were used to compare the scenarios. For the two largest networks, meta-regressions were also conducted to adjust partially on the heterogeneity. ***Results:*** From scenarios 1 to 3, including additional studies in the networks while increasing the heterogeneity level reduced the MRDs when conducting standard NMAs (respectively 48.2%, 21.3% and 18.6%). However, a higher MRD was obtained for the largest network (scenario 4: 24.4%) compared to scenarios 2 and 3. Conducting meta-regressions markedly reduced the MRDs for the scenario 3 (7.2% with meta-regression vs. 18.6%) and scenario 4 (9.1% with meta-regression vs. 24.4%). ***Conclusions:*** This simulation study shows that including additional studies in case of a small network in a NMA context can be relevant, especially if it allows for a meta-regression to be conducted.

Oncology Studies

CN1
PATTERNS OF UTILIZATION AND IMPLEMENTATION EXPERIENCES OF ONCOLOGY MONOCLONAL ANTIBODIES (MABS) BIOSIMILARS IN THE U.S.: FROM BOTH PAYERS AND HEALTHCARE PROFESSIONALS (HCPS) PERSPECTIVES

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Objectives: Biosimilars are highly similar to an originator biologic, with no clinically meaningful differences in safety or efficacy. The adoption of biosimilars might provide an opportunity to lower costs and increase patient access to biologics. The current study sought to understand real-world implementation experiences associated with oncology MAbs biosimilars (trastuzumab, rituximab, and bevacizumab) from both payer and healthcare professional (HCP) perspectives. ***Methods:*** In-depth qualitative telephone interviews with 20 each of US HCPs (including 3 practice managers) and payers were conducted. The HCPs were either affiliated with a healthcare network or were community-based. They specialized in hematology/oncology and had experience prescribing oncology biosimilars. Participating payers included Managed Care Organizations (MCOs), Integrated Delivery Networks (IDNs) and Pharmacy Benefit Managers (PBMs). Audio transcripts of the interviews were coded using MaxQDA software. ***Results:*** Over 80% of HCPs interviewed perceived biosimilars to be highly comparable to originators in efficacy and safety. About 70% of HCPs reported using biosimilars in $\geq$50% of their treatment-naïve patients and were comfortable with use of biosimilars in all approved indications. To encourage utilization, approximately 75% of MCO/PBM payers preferred biosimilars over originators in treatment-naïve patients, which was implemented through step therapy. HCP involvement in choosing a biosimilar for their patients was minimal, and biosimilars were often automatically ordered by pharmacists or administrators based on practice protocols or patients' cost due to insurance preferences. The major factor that influenced both payers' coverage decisions and HCP adoption of biosimilars was potential cost savings. Moreover, payers considered HCPs' clinical confidence with biosimilars as a factor influencing their biosimilar coverage decisions. ***Conclusions:*** Both HCPs and payers in the US have favorable views of oncology MAbs biosimilars, particularly among treatment-naïve patients. A framework for biosimilars integration into oncology practice is developing, which is primarily driven by insurance coverage policy, contracting, and cost benefits.

CN2
ELICITING UNREPORTED SUBGROUP-SPECIFIC SURVIVAL FROM AGGREGATE RANDOMIZED CONTROLLED TRIAL DATA

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Objectives: Subgroup analyses are vital components of health technology assessments but randomized controlled trials (RCTs) do not commonly report survival distributions for subgroups. This study developed an analytical framework to elicit unreported subgroup-specific survival information from aggregate RCT data. ***Methods:*** Assuming exponentially-distributed subgroup survival times, we developed an optimization model which aimed to approximate the restricted mean survival time (RMST) for the overall population via weighted average of the RMSTs of two mutually exclusive and exhaustive subgroups in each arm. Reported hazard ratios from the forest plots between the arms were used to enforce the relationship among subgroups' hazard rates in the model. The performance of the model was tested in a case study consisting of 8 RCTs in advanced stage gastrointestinal tumors (3 in hepatocellular carcinoma, 3 in gastric/gastroesophageal junction/esophageal cancer and 2 in colorectal cancer) which also reported Kaplan-Meier (KM) curves for overall survival (OS) for 40 subgroups in total. For each subgroup, predicted median survival, OS rates and the RMSTs were compared against the actual OS rates, median survival and the RMSTs as well as their 95% confidence intervals (CIs). ***Results:*** - Predicted median survivals and RMSTs were within the 95% CIs of the reported values in 32 and 35 out of 40 subgroups, respectively. In 8 of the subgroups, the gap between the estimated RMSTs from the predicted and the reported survival curves was less than 5%. In 6 of the subgroups, predicted survival curves laid within the 95% CIs of reported KM-curves in at least 90% of the time. Across all subgroups, on average, predicted survival curves laid within the 95% CIs of reported KM-curves in 71% of the time. ***Conclusions:*** Our study offers a useful and reliable approach for extracting subgroup-specific survival from aggregate RCT data to better inform economic and comparative effectiveness analyses for subgroups.

CN3
IT'S ALL IN THE FAMILY: MICROSIMULATION MODELLING OF GENETIC TESTING

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Objectives: Around 20-25% of ovarian cancers and 5-10% of breast cancers are due to an inherited predisposition. The primary clinical and economic benefit of hereditary breast and ovarian cancer (HBOC) testing is from preventing cancers in unaffected relatives who present for predictive/cascade testing for a known pathogenic variant in the family. Population-based genetic testing (GT) as an alternative to current practice has been gaining momentum, as it enables identification of high-risk women before they develop cancer. Existing evaluations of population-based GT mostly rely on heavily simplified comparators, and are based on selected point estimates for probabilities of identifying relatives and cascade testing uptake. This likely overestimates the benefit of population-based testing. ***Methods:*** We developed a microsimulation model for evaluating HBOC testing that includes individuals linked within family structures (thus a more sophisticated cascade testing component). Family structures are modelled using an analysis of 11,143 pedigrees from an Australian genetics clinic. The genetic component includes Mendelian inheritance of pathogenic variants for eight high- and moderate-risk genes. HBOC risk associated with single nucleotide polymorphisms was incorporated through polygenic risk scores. Life histories for individuals are generated, considering their gender, age, and genetic risk. ***Results:*** This microsimulation model, called NEEMO, more accurately reflects current practice using a simulated family-based approach. It has been validated for gene-specific cancer incidence, mortality, pathology, and uptake of cancer risk management. It has also been validated for genetic testing referral rates, and uptake of predictive GT in relatives. ***Conclusions:*** Modelling GT presents challenges due to the nature of inheritance and interaction between individuals. Clinical genetics is complex and highly specialised, with a commonly cited barrier to GT being a lack of awareness or understanding in non-genetics specialists around eligibility and management. The NEEMO model will be useful for evaluating changes in risk assessment, target GT populations, and modifying cancer prevention strategies.

CN4
PATIENT-REPORTED OUTCOMES FROM THE PHASE 3, RANDOMIZED STUDY OF ACALABRUTINIB WITH OR WITHOUT OBINUTUZUMAB VERSUS CHLORAMBUCIL PLUS OBINUTUZUMAB FOR TREATMENT-NAÏVE CHRONIC LYMPHOCYTIC LEUKEMIA (ELEVATE-TN)

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Objectives: Report patient-reported outcomes of fatigue and health-related quality of life (HRQoL) from the randomized, phase 3, ELEVATE-TN study (NCT02475681) in patients with treatment-naïve chronic lymphocytic leukemia (CLL). ***Methods:*** Patients received acalabrutinib alone (A), A plus obinutuzumab (AO), or chlorambucil plus obinutuzumab (CO). Assessments included the FACIT-Fatigue Global Fatigue Score (GFS) (scale: 0–52; lower score=worse outcome [clinically meaningful improvement: $\geq$+3]) and the EORTC QLQ-C30

Global Health Status (GHS) score (scale: 0–100; lower score=worse HRQoL [clinically meaningful improvement: >+8]) in all patients (excluding those who progressed) and those with severe fatigue at baseline (GFS ≤34), analyzed using mixed-model repeated measures methodology. A post-hoc analysis assessed time to clinically meaningful deterioration (TTD; change ≤−3) in GFS. ***Results:*** Among 535 randomized patients, 449 completed the GFS (A, n=156; AO, n=152; CO, n=141) and 450 completed the GHS (A, n=157; AO, n=151; CO, n=142) at baseline. Overall, 151 randomized patients had severe fatigue (A, n=56; AO, n=53; CO, n=42); all completed both questionnaires at baseline. In all arms, GFS and GHS improvements were observed by week 4 (mean changes: 2.76 and 5.35 for A [n=136, n=137], 2.33 and 2.17 for AO [n=138, n=138], 1.26 and 2.53 for CO [n=121, n=122]) and maintained at 96 weeks (4.94 and 7.01 for A [n=81, n=82], 3.91 and 5.25 for AO [n=92, n=92], 3.86 and 2.41 for CO [n=38, n=38]); this benefit was larger in patients with severe fatigue. Median TTD in fatigue was longer in acalabrutinib-containing arms (A: 16.9 mo; AO: 16.7 mo) versus CO (5.7 mo [*P*=0.0376 vs A; *P*=0.1596 vs AO]). ***Conclusions:*** In ELEVATE-TN, all treatments improved fatigue scores; TTD of fatigue was significantly longer with acalabrutinib-containing treatment. The previously reported statistically significant progression-free survival increases with A/AO versus CO (*Lancet*. 2020;395:1278-91) were accompanied by clinically meaningful HRQoL benefits.

Clinical Outcome Assessment Studies

CO1
THE NATURAL HISTORY, CLINICAL OUTCOMES AND UNMET NEEDS OF PATIENTS WITH ARGINASE 1 DEFICIENCY (ARG1-D): A SYSTEMATIC REVIEW OF CASE REPORTS

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Objectives: ARG1-D is a debilitating, progressive, inherited, metabolic disease characterized by hyperargininemia leading to significant morbidity and early mortality. The objective of this study was to systematically review the literature to assess the natural history, clinical outcomes, and unmet needs of patients with ARG1-D. ***Methods:*** We searched MEDLINE, EMBASE, and other databases for case reports describing patients with ARG1-D. Eligible studies reported natural history (patient demographics, diagnosis methods, clinical manifestations), treatments, and/or clinical outcomes (cognitive, motor, growth, death). Two individuals independently screened records, extracted data, and assessed study quality using the Joanna Briggs Institute Critical Appraisal Tool. ***Results:*** We included 90 studies that described 157 unique patients with ARG1-D. The most frequently reported and observed clinical manifestations were motor deficits (126/133; 95%), including lower limb spasticity (102/114; 89%); intellectual disability or cognitive impairment (87/112; 78%); and seizures (78/101; 77%). Most clinical manifestations were documented by 3 years of age; mean age of diagnosis was 6.4 years (median 5; range 0-27). Physician-prescribed dietary restriction was the most commonly reported intervention (62%), followed by use of nitrogen scavengers (45%), essential amino acids (21%), dialysis (5%), and liver transplantation (3%). Few studies reported clinical outcomes: 23 reported motor function (11 patients improved, 12 did not), 19 reported cognitive function (15 patients improved, 4 did not), and 10 reported growth (6 patients improved, 4 did not). Sixteen patients died, all but one before 25 years and six before age 2. ***Conclusions:*** This review describes the natural history of ARG1-D in terms of clinical presentation and diagnosis. It illustrates that the current standard of care is ineffective at managing the disease and does not improve clinical outcomes. The large sample of included cases highlights a significant disease burden, risk of mortality, and a clear unmet need for clinically effective treatment options for patients with ARG1-D.

CO2
HEALTHCARE UTILIZATION, COST, AND QUALITY AMONG HIGH-NEED, HIGH-COST MEDICARE BENEFICIARIES IN MEDICARE FEE-FOR-SERVICE VERSUS MEDICARE ADVANTAGE

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Objectives: More than one-third of Medicare beneficiaries are enrolled in a managed Medicare Advantage (MA) plan, yet there is little data comparing outcomes among MA Beneficiaries (MAB) compared to traditional Medicare Fee-for-Service Beneficiaries (FFSB). The objective of this study was to identify high-need, high-cost cohorts of MAB and FFSB and compare their healthcare resource utilization, costs, and quality outcomes. ***Methods:*** This retrospective study used data from a national sample of MA encounter data and 100% Medicare Parts A, B, and D claims data from 2015-2017. A validated algorithm was applied to identify distinct clinical cohorts of high-need, high-cost beneficiaries in FFS and MA, including disabled under age 65, frail elderly, and major complex chronic patients. Propensity score matching was used to assure the populations had similar demographic and clinical characteristics; matching resulted in a study sample of 1,262,180 patients in both cohorts. We compared performance on a discrete set of health outcomes selected as relevant indicators of the impact of care management practices. ***Results:*** Overall, MA performed better than FFS on 17 of 22 quality measures, including preventive care (e.g., 50% more likely to receive pneumonia vaccine; 18-27% more likely to be screened/treated for depression). MAB had 10% fewer inpatient stays, but higher use of outpatient and physician office visits. MAB were about 50% less likely to be hospitalized for potentially preventable complications. Total medical and pharmacy spend was 15% lower in MA. ***Conclusions:*** This study found significant differences in health outcomes of high-cost high-need MAB compared to similar FFSB. Enrollment in MA continues to rapidly expand, projected to reach 47% of Medicare by 2029. This study indicates the incentives in MA to better coordinate care and provide flexible medical/non-medical benefits are associated with better care at lower cost, which is the goal of value-based purchasing.

CO3
COMPARISON OF GOAL ATTAINMENT AND MEASURES OF FUNCTION IN TWO DEMENTIA CLINICAL TRIALS.

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Objectives: Questionnaire-style outcome measures are often used in clinical trials. It is unclear whether this type of outcome measurement can capture change that is personally meaningful to individuals. In contrast, Goal Attainment Scaling (GAS) is an outcome measure where patients and clinicians develop and track an individualized set of treatment-related goals that are important to the patient. Here, we compared attainment of daily function goals to questionnaire-style measures of function in two mild-moderate dementia clinical trials. ***Methods:*** Data were from the Atlantic Canadian Alzheimer Disease Investigation of Expectations (ACADIE) and the Video Imaging Synthesis of Treating Alzheimer disease (VISTA) trials. Both used GAS as a primary outcome. ACADIE used the Functional Assessment Questionnaire, Lawton-Brody Physical Self-Maintenance Scale, and Lawton-Brody Instrumental Activities of Daily Living which we normalized to a 100-point scale. The VISTA trial used the 100-point Disability Assessment for Dementia to assess function. ***Results:*** Subjects were demographically comparable between ACADIE and VISTA (75.9±7.8, 76.3±7.6 years of age; 73%, 64% women; and baseline Mini-Mental State Examination scores 19.7±5.2, 20.8±3.3), respectively. Baseline function scores were near-normal in ACADIE (mean=46.8±15.2, median=44) and negatively skewed in VISTA (mean=76.3±19.7, median=83). Patient-rated daily function goal attainment correlated with change in questionnaire-based measures of function (ACADIE: r=0.25, p=0.022; VISTA: r=0.37, p=0.044) but clinician-rated daily function GAS was not correlated in VISTA (ACADIE: r=0.60, p<0.001; VISTA: r=0.07, p=0.7). There was no change in daily function GAS (ACADIE: mean=50.6±9.4, p=0.6; VISTA: mean= 51.5±14.2, p=0.5), but questionnaire-based measures of function declined (ACADIE: mean change=-3.6±10.0, p<0.001; VISTA: -5.2±11.8, p=0.003). ***Conclusions:*** Questionnaire-style outcome measures were correlated with patient-rated daily function GAS goals. However, GAS clearly showed that patients maintained important aspects of daily living when questionnaire-based measures showed net decline. Individualized outcome measures like GAS can detect meaningful change that could be missed by standard outcome assessments.

CO4
PREDICTORS OF INPATIENT RELAPSE IN MULTIPLE SCLEROSIS PATIENTS USING FIRST-LINE DISEASE MODIFYING THERAPIES: A MACHINE LEARNING STUDY OF REAL WORLD DATA

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Objectives: Relapse among multiple sclerosis (MS) patients is associated with disability progression and worsening outcomes. This study aims to identify characteristics of inpatient MS relapse using claims data and machine learning techniques. ***Methods:*** MS patients with a new prescription or administration of a disease modifying therapy (DMT) were identified based on ICD-9/10 diagnosis codes in de-identified Optum® Clinformatics® Data Mart from 2000-2019. The first DMT date was the index date with >=2 MS diagnoses required in the preceding 6 months (baseline). Inpatient relapse was defined as an inpatient visit with a primary MS diagnosis code during the 12 months following the index date. Features included demographics, comorbidities, concomitant medications, healthcare resource utilization (HRU), DMT route of administration and proportion of days covered (PDC) for