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