interventions. Three out of the 172 letters were associated with a change in the cost-effectiveness conclusion. ***Conclusions:*** Between 2018 and 2019, stakeholders have leveraged ICER evaluations as an opportunity to promote dialogue about the evidence of the value of technologies. Although stakeholders' inputs had little influence on ICER assessment's cost-effectiveness analysis conclusions, actionable, evidence-based recommendations were often accepted.

HT2
EVALUATION OF TUCATINIB FOR HER2-POSITIVE BREAST CANCER PATIENTS WITH BRAIN METASTASES: A UNITED STATES-BASED COST-EFFECTIVENESS ANALYSIS

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Objectives: To evaluate the cost-effectiveness of tucatinib in human epidermal growth factor receptor 2 (HER2)-positive breast cancer (BC) patients with brain metastases (BMs) and the subgroup of active BMs from the United States (US) payer perspective. ***Methods:*** A three-state Markov model was developed to compare the cost-effectiveness of tucatinib, trastuzumab and capecitabine (TTC) with placebo, trastuzumab and capecitabine (PTC) in HER2-positive BC patients with BMs;subgroup analysis of active BMs was also performed.Pseudo-individual patient data were generated from digitized Kaplan-Meier curves.Costs were derived from official databases and the literature.Health state utility values were consistent with published literature and adjusted by adverse events.Lifetime costs,quality-adjusted life years (QALYs),incremental cost-effectiveness ratio (ICER) and incremental net health benefit (INHB) were estimated.The willingness-to-pay (WTP) threshold was $200,000/QALY.The robustness of the model was tested by sensitivity analysis and scenario analyses were also performed. ***Results:*** In patients with BMs,the PTC and TTC strategies cost $87,905.23 and $503,637.21,yielding 0.68 and 1.68 QALYs,respectively.While in the subgroup of active BMs,the two strategies cost $81,968.50 and $451,699.62 and the QALYs were 0.61 and 1.75,respectively.The ICERs yielded by TTC were $418,007.01/QALY and $324,465.03/QALY, and INHBs were -1.08 QALYs and -0.71 QALY, compared with PTC in these two groups,respectively.The results were most sensitive to the cost of tucatinib.Probabilistic sensitivity analysis suggested that the probability of TTC being cost-effective was low at the current WTP threshold in the patients with BMs and the subgroup of active BMs. ***Conclusions:*** The additional using tucatinib (TTC) is unlikely to be cost-effective in HER2-positive BC patients with BMs from the US payer perspective,-but shows a better economics in patients with active BMs.Therefore, selecting favorable population would be a good way to optimize the cost-effectiveness of tucatinib.To meet the economical demands of public health,it may be a preferable option to reduce the price of tucatinib or offer appropriate drug assistance policies.

HT3
WHAT IS VALUE? A SYSTEMATIC REVIEW OF VALUE ASSESSMENT FRAMEWORKS

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Objectives: To investigate how value is defined and measured in existing value assessment frameworks (VAFs) in health care. ***Methods:*** We searched PubMed, Embase, the Cochrane Library and Centre for Review and Dissemination from 2008 to 2019. We also performed backward citation chaining of included studies and previously published systematic reviews. Studies reporting the development of a VAF in health care were included. For each included framework, we extracted and compared the context, target users, intended use, methods used to identify value attributes (e.g., patient/public engagement), description of the attributes, and attribute scoring approaches. ***Results:*** Out of 8151 articles screened, 53 VAFs described in 56 articles were included. The value attributes included in 52 VAFs were grouped into nine categories, namely, health benefits (50/52, 96%), affordability (42/52, 81%), societal impact (39/52, 75%), the burden of disease (35/52, 67%), quality of evidence (31/52, 60%), cost-effectiveness (30/52, 58%), ethics and equity (25/52, 48%), unmet needs (22/52, 42%), and innovation (15/52, 29%). The remaining VAF uses three broad attributes for diagnostics: medical value, planning value and psychic value. Literature review has been used to identify value attributes in 34 VAFs. Patient/public was engaged in the development of only 11 VAFs. Weighting has been used to score 29 VAFs, among which 19 used the methods of multicriteria decision analysis (MCDA). ***Conclusions:*** Substantial efforts have been made to facilitate value assessment in health care. There are substantial variations in defining and measuring value. A particular concerning finding is that patient/public engagement was poor in this process.

HT4
PATIENT-RELEVANCE OF ENDPOINTS OTHER THAN OVERALL SURVIVAL (NON-OS ENDPOINTS) IN ONCOLOGY HEALTH TECHNOLOGY ASSESSMENTS BY THE FEDERAL JOINT COMMITTEE (G-BA) IN GERMANY

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Objectives: To investigate the G-BA's decisions regarding patient-relevance of non-OS endpoints across breast cancer (BC), chronic lymphocytic leukaemia, melanoma, non-small cell lung cancer, ovarian cancer, and prostate cancer (PC). ***Methods:*** All published G-BA appraisal reports (January 2011–October 2020) in the 6 selected indications were reviewed and relevant data were extracted for analysis. ***Results:*** Reviewed G-BA appraisals (n=101) yielded 307 individual decisions regarding patient-relevance of non-OS endpoints, employing 56 different outcome measures. Although in 74% of decisions (n=226/307) non-OS endpoints were deemed patient-relevant in general, in 79% (179/226) of these cases, no additional medical benefit was granted either due to lack of compliance with G-BA's methodological requirements, inadequate/missing data, or statistically insignificant results. The G-BA did not accept progression-free survival, metastasis-free survival, complete remission, and objective response rate measured per imaging or laboratory tests. Patient-relevance decisions for health status (n=59), quality of life (n=103), and pain (n=10) related endpoints were positive across all indications. Decisions regarding the patient-relevance of other non-OS endpoints were indication-specific and variable, e.g. relapses as proxy for the failure of therapy with curative intent were judged patient-relevant in both BC (neo-adjuvant and adjuvant settings) and melanoma (adjuvant setting), and symptomatic progression in the palliative setting in PC was judged patient-relevant. In comparison, time-to-first-subsequent-therapy and time-to-onset-of-cytotoxic-therapy were judged patient-relevant in principle, but not accepted due to methodological deficiencies, and/or lack of correlation with patient-relevant side-effects of subsequent treatment. ***Conclusions:*** Strict compliance with methodological requirements and specific relevance to disease context and treatment setting were key drivers of G-BA's acceptance of patient-relevance for non-OS endpoints. The impact of G-BA's stringent methodological requirements on establishing the holistic patient-relevance of non-OS endpoints requires further debate.

Impact of COVID-19 on Health Systems, Treatment, and Value

IN1
TREATMENT JOURNEY OF COVID-19 PATIENTS IN HOSPITAL SETTINGS

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Objectives: Severe cases of COVID-19 have overwhelmed hospital systems across the nation. To better understand patient's journey within hospital setting, this study described the treatment journey of COVID-19 patients from hospital admission to 30 days after discharge for inpatients and hospital-based outpatients. ***Methods:*** A retrospective cohort study was conducted using a large geographically diverse all-payer hospital administrative database (Premier Healthcare Database). Patients were identified by their first discharges between April 1 and July 31, 2020, with a principal or secondary discharge diagnosis of COVID-19 (ICD-10 diagnosis code, U07.1). ***Results:*** Of 369,894 patients, 39% were inpatients and 61% were outpatients. Inpatients were older (median age 64 vs. 44 years) and more likely to be male (52% vs. 44%) and have baseline comorbidity (60% vs. 19%) compared to outpatients. (All $p<0.05$). Among inpatients, 80% originated from home, 9% from another acute care facility, and 94% were admitted through emergency department (ED). Of these patients, 23% were admitted to intensive care unit, 16% (n=22,665) died during initial hospitalization, 48% were discharged home, 14% to skilled nursing facility, 11% to home health, 6% were transferred to another hospital, and 3% to hospice. Within 30 days, an additional 0.7% (n=1,009) died, 4% were readmitted to same hospital, and 2% visited ED due to COVID-19. Among outpatients, 66% were ED outpatient visits. During initial visit, 91% were sent home, 2% were transferred to an acute care hospital, and 0.3% (n=712) died. An additional 0.4% (n=802) died, 7% visited ED, and 4% were hospitalized due to COVID-19 during follow-up visits within 30 days. ***Conclusions:*** This study shows that COVID-19 is associated with high-level of ED utilization, ICU admission, and in-

hospital mortality. Over one-third of inpatients required post-hospital healthcare services. Such info may help healthcare providers better allocate resources to take care of COVID-19 patients during the pandemic.

IN2
CHARACTERISTICS OF PATIENTS DIAGNOSED WITH CORONAVIRUS DISEASE 2019 (COVID-19) ACROSS THE THREE WAVES IN THE US: A CLAIMS-BASED STUDY USING A LARGE NATIONAL SAMPLE

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Objectives: To assess how characteristics of patients diagnosed with COVID-19 have changed over the three waves in the US (April, July and November 2020) and evaluate the temporal relationship of disease severity. ***Methods:*** This retrospective database study used IQVIA's medical (Dx) and longitudinal prescription claims (LRx) databases. Patients with a new medical claim with a diagnosis code of COVID-19 (ICD-10-CM: U07.1) in April, July or November 2020 were identified (first diagnosis = index date). Demographics, comorbidities and prescriptions within 6-months pre-index and diagnoses (symptoms/complications) and healthcare resource utilization within 14-days pre- or post-index were descriptively assessed by index month. Logistic regression was used to evaluate adjusted odds of serious complication and hospitalization by index month. ***Results:*** The study sample comprised 1,401,309 patients diagnosed with COVID-19 (330,110 April/452,663 July/618,546 November). Half of April/July/November cohorts were female (53.5/56.0/53.7%) with mean age 57.4/47.3/50.1 years and mean CCI score 1.3/0.7/0.6. Region varied with 20.8/60.2/40.4% located in the South. The top 3 comorbidities were more common in April: hypertension (35.8/23.4/19.6%), T2DM (20.7/13.6/10.6%) and dyslipidemia (19.3/13.6/11.0%). Similarly, the top 3 symptoms were more common in April: cough (25.4/14.8/14.5%), fever (22.7/11.4/8.5%) and shortness of breath (19.8/11.3/9.9%). Pneumonia was the most common serious complication and highest in April (33.4/17.8/16.9%). Proportion with ER visit (42.1/36.1/32.4%) and hospitalization (32.5/17.3/14.7%) was highest in April; conversely, COVID-19 diagnostic testing (24.2/45.0/43.5%) was lowest in April. After adjusting for baseline characteristics, July/November cohorts were associated with 51.4/57.4% lower odds of pneumonia and 49.0/62.1% lower odds of hospitalization compared to the April cohort, respectively (all $p<0.0001$). ***Conclusions:*** This research confirms that the underlying population contracting COVID-19 has changed over time. While new cases have increased, the burden and severity of illness appeared to be highest in April. These changing trends likely reflect improvements in the knowledge, treatment and management of the disease, as well as increased testing.

IN3
ECONOMIC VALUE AND HEALTH SYSTEM IMPACT OF REMDESIVIR IN TREATING HOSPITALIZED COVID-19 PATIENTS IN THE UNITED STATES

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Objectives: In the ACTT-1 study in hospitalized adults with laboratory confirmed COVID-19, remdesivir was found to be superior to placebo in shortening time to recovery from COVID-19. However, the economic value and health system impact of remdesivir treatment is still unclear. This study evaluated remdesivir's long-term cost-effectiveness and impact on health system capacities versus standard of care (SoC) for hospitalized COVID-19 patients in the United States (US). ***Methods:*** A hybrid decision-tree and Markov model simulated health and economic outcomes for hospitalized adult COVID-19 patients (average age of 58.9 years) from a US health system perspective over a lifetime horizon. Clinical inputs (e.g., hospitalization duration, mortality) were extracted from the ACTT-1 trial and real-world data. Cost inputs were sourced from an internal analysis or from the literature. Remdesivir acquisition cost was $390/vial, and patients were assumed to receive 6.25 vials per treatment course. One-way and probabilistic sensitivity analyses were performed. A separate treatment capacity analysis was performed on a national scale, assuming a population of 328,200,000 and one monthly incident cohort of 201,000 patients eligible for treatment. ***Results:*** Relative to SoC, remdesivir was associated with a decrease in total costs (savings of $8,844.49 per patient), increased life years (+0.62), and quality-adjusted life years (+0.47). Remdesivir was therefore dominant versus SoC (less costly and more effective). Results were robust in one-way and probabilistic sensitivity analyses. In the treatment capacity analysis, remdesivir increased the available hospital capacity by 1.4%, available ICU capacity by 32.1%, and total ventilator capacity by 2.3%. ***Conclusions:*** Remdesivir is a cost-effective option for the treatment of patients hospitalized with mild, moderate, and severe COVID-19 versus SoC. In addition, due to its demonstrated ability to shorten time to recovery, remdesivir is projected to increase treatment capacity by increasing the percentage of available hospital bed-, ICU bed-, and total ventilator capacity.

IN4
NON-HEALTH CONSIDERATIONS IN ECONOMIC EVALUATIONS OF COVID-19 INTERVENTIONS: A SYSTEMIC REVIEW

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Objectives: To examine whether and how economic evaluations for COVID-19 interventions incorporate non-health impacts. ***Methods:*** Using pre-specified keywords, we searched the National Institute of Health's *iSearch* COVID-19 portfolio, containing both pre-prints and peer-reviewed articles, as our primary database to identify economic evaluations of COVID-19 interventions in December 2020. We retained studies that empirically evaluated economic as well as health consequences of COVID-19 interventions. We supplemented our search with additional sources, such as Google Scholar, COVID Scholar, EconLit, and NBER. Based on the Second Panel's "Impact Inventory," modified for COVID-19, we examined in the identified studies any consideration of non-health impacts, such as reduced productivity due to remote work, short-term job-related income loss, long-term unemployment, and other impacts on gross domestic product (GDP), and other sectors (e.g., related to environment or housing). ***Results:*** Of 274 articles screened, 61 met our inclusion criteria. The sample was comprised of 39 (64%) cost-effectiveness analyses (CEA), 17 (28%) cost-benefit analyses, and 5 (8%) other economic evaluations. The most commonly examined intervention was mobility restrictions, including stay-at-home orders and travel/gathering bans (n=25, 41%), followed by testing strategies (n=15, 25%) and therapeutics (n=15, 25%). Out of 22 CEAs that reported cost-per-quality-adjusted-life-years (QALY) outcomes, the median incremental cost-effectiveness ratio was lowest for therapeutics ($848/QALY, n=7, inter-quartile range [IQR]: $547-$10,306) and highest for testing strategies ($2,172,300/QALY, n=9, IQR: $993,550-31,376,150). Twenty-nine studies (47%) included some type of non-health impact, most commonly lost income (n=17, 28%), followed by GDP impacts (n=11, 18%) and productivity (n=6, 10%). ***Conclusions:*** Consideration of non-health impacts is lacking in evaluations of COVID-19 interventions. Omission of these impacts can skew the value of pharmaceutical and non-pharmaceutical interventions and could have consequences for policy determinations as the pandemic continues. Researchers should consider including societal impacts in their analyses to more closely reflect the true value of interventions.

Machine Learning Applications in Health

ML1
COMPARING MORTALITY IN CARDIAC PATIENT SURGICAL CLUSTERS WITH MACHINE LEARNING CLUSTERS IN THE NATIONAL INPATIENT SAMPLE

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Objectives: This study investigates mortality in cardiac patient clusters based on surgery type versus patient clusters created through unsupervised machine learning (ML). ***Methods:*** The 2017 National Inpatient Sample describes US patient discharges and is provided by the Healthcare Cost and Utilization Project (HCUP). Patients included in this study were ≥18 years old with a "Major Therapeutic" primary cardiac procedure per HCUP Procedure Classes and Clinical Classification Software, and with a complete discharge record. Clusters were created through two different methods: 1) based on the three most common cardiac procedures; 2) based on patient and hospital characteristics, independent of mortality, through the ML algorithm K-prototypes. ***Results:*** A total of 170,326 discharges met inclusion criteria. The three prevalent cardiac procedures were percutaneous transluminal coronary angioplasty (PTCA) – 40.2%, coronary artery bypass graft (CABG) – 16.1%, and heart valve procedures (HV) – 15.0%. The prevalent procedures within each ML cluster were: Cluster 1: PTCA – 31.2% and CABG–22.6%; 2: HV – 30.1% and CABG – 20.5%; 3: PTCA – 73.7% and CABG – 8.6%. The surgery clusters contained 121,423 discharges, while the ML clusters contained all 170,326 discharges. While the average Elixhauser Comorbidity Indices (ECI) based on the surgery clusters were different (PTCA: 2.1; CABG: 3.6; HV: 4.6; $p<0.0001$), the ML clusters revealed a clear difference in the average ECI (Cluster 1: 9.8; 2: 2.9; 3: 0.8; $p<0.0001$). While the mortality rate within each surgical group was different (PTCA: 1.6%; CABG: 1.7%; HV: 2.3%; $p<0.0001$), the ML clustering exposed a stark distinction in mortality between clusters (Cluster 1: 7.6%; 2: 0.8%; 3: 0.7%; $p<0.0001$).