provide recommendations for physicians in choosing treatments that improve outcomes for patients with HR+/HER2- mBC.

MS4
A NOVEL ARTIFICIAL INTELLIGENCE ALGORITHM OF SYNTHETIC SAMPLING FOR BOOSTING ACCURATE MACHINE-LEARNING PREDICTION OF INFREQUENT HEALTH OUTCOMES

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Objectives: Real-world clinical health outcomes are usually not balanced or evenly distributed. For example, the incidence of severe adverse drug event is often less than 5%. Imbalanced classes of outcome create significant bias in developing machine-learning (ML) prediction models. We developed a novel artificial intelligence (AI) algorithm (SynSam) that generates synthetic samples to boost samples with infrequent health outcome occurrence. The algorithm can handle clinical health data with both continuous and categorical predictors. In this study, we compared a ML model prediction performance with the SynSam sampling to random over-sampling (bootstrap), and to no over-sampling (naïve). ***Methods:*** We simulated a virtual patient cohort (N=50,000) with a 1% adverse drug event occurrence. Using NHANES data we also assembled a cohort of adults who suffered from asthma (N=6177) for the prediction of emergency department visit due to asthma (rate = 9%). With split-validation design, we set aside 20% random sample of each cohorts as an independent validation dataset and used the rest of 80% for prediction model training with the Extreme Gradient Boosting algorithm. We applied the 5-fold cross validation for final model selection. We compared the performance of the final prediction model with respective over-sampling approaches for the validation datasets. ***Results:*** In the virtual patient cohort, the naïve model correctly predicted the events 55% of the time (sensitivity) while predicting all non-events (specificity). Application of bootstrap increased sensitivity to 70%. The SynSam approach increased the sensitivity to 90% while maintaining the specificity at 96%. In the NHANES cohort, the naïve model had a 19% sensitivity and 95% specificity. The bootstrap approach increased the sensitivity to 24%. The SynSam approach achieved the sensitivity of 51% with a specificity of 88%. ***Conclusions:*** The AI-based SynSam approach may be useful to boost ML prediction model performance for infrequent health outcomes.

Neurological Disorders Studies

ND1
ACCESS AND UNMET NEEDS OF ORPHAN DRUGS IN 194 COUNTRIES AND SIX AREAS: A GLOBAL POLICY REVIEW WITH CONTENT ANALYSIS

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Objectives: 300 million people living with rare diseases worldwide are disproportionately deprived of in-time diagnosis and treatment when compared to other patients. Policies that optimise development, licensing, pricing, and reimbursement of orphan drugs are instrumental in addressing this neglected but significant burden. An overview of global orphan drug policies is proposed to inform policy development. ***Methods:*** Pharmaceutical legislation and policies related to access and regulation of orphan drugs were examined from 194 World Health Organisation member countries and 6 areas. Orphan drug policies were identified through internet search, emails to national pharmacovigilance centres, and systematic academic literature search. Texts from selected publications were extracted for content analysis. ***Results:*** 171 drug regulation documents and 77 academic publications from 162 countries/areas were included. 92 of 200 countries/areas (46·0%) had documentation on orphan drug policy. 34 sub-themes from content analysis were categorised into six policy themes, namely, orphan drug designation, marketing authorisation, safety and efficacy requirements, price regulation, incentives that encourage market availability, and incentives that encourage research and development. Countries/areas with orphan drug policy were statistically wealthier (GNI per capita = $10875 vs. $3950, $p<0·001$). Country/area income was also positively correlated with the scope of the respective orphan drug policy (r_s=0.57, $p<0.001$). ***Conclusions:*** Globally, number of countries with orphan drug policy is rapidly growing since 2013. However, there are disparities in orphan drug policy establishment by geographical distribution and income levels. Furthermore, identified policy gaps in "price regulation", "incentives that encourage market availability", and "incentives that encourage research and development" should be addressed to improve access to available and affordable orphan drugs.

ND2
BURDEN OF HOSPITALIZATIONS IN HEREDITARY TRANSTHYRETIN AMYLOIDOSIS (HATTR) WITH AND WITHOUT HEMATOPOIETIC STEM CELL TRANSPLANT: A PROPENSITY SCORE MATCHED ANALYSIS OF IN-PATIENT CLAIMS DATABASE

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Objectives: To examine trends in hospital length of stay and total costs in hATTR patients with and without Hematopoietic Stem Cell Transplant (HSCT). ***Methods:*** The latest available 2016 National Inpatient Sample (NIS) data set from the Healthcare Cost and Utilization Project was utilized in order to determine the number of hospital admissions for patients with NHL. Propensity score matched analysis was conducted to compare hospital LOS and costs in hATTR patients with and without HSCT. Thirty comorbidities were assessed using Elixhauser scoring. Multivariate logistic regression was conducted to assess predictor variables for LOS and costs. ***Results:*** In 2016, there were an estimated 23,335 hospitalizations with a diagnosis of hATTR, of which 260 also had a procedure code for HSCT. The mean age was 60.6 (SD 8.4) and 70.3 (SD 13.8) in hATTR patients with and without HSCT, respectively. 46.1% and 43.3% were female in hATTR with and without HSCT, respectively. Most common comorbidities (more than 20%) were congestive heart failure (46.1%), cardiac arrhythmias (40.4%), uncomplicated hypertension (38.2%), complicated hypertension and renal failure (44.7%). The propensity score matched hospital LOS was 19.1 and 6.4, with a statistically significant difference of 12.6 days (SE 1.61, $P<0.05$), in hATTR patients with and without HSCT. The propensity score matched hospital charges were $255,968 and $69,640, with a statistically significant difference of $186,327 (SE $30668 $P<0.05$), in hATTR patients with and without HSCT. Predictor variables for hospital LOS and costs were HSCT, cardiac arrhythmias and coagulopathy. ***Conclusions:*** hATTR patients with HSCT incur significantly longer hospital length of stay and nearly 4 times the costs compared to patients without HSCT. There is a need for better treatment management for patients with hATTR undergoing HSCT.

ND3
ORPHAN DRUG MARKET ACCESS CHALLENGES IN EUROPEAN UNION FIVE.

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Objectives: To assess the challenges of orphan drug pricing and reimbursement in European Union Five (EU5) countries (France, Germany, Italy, Spain, and the United Kingdom). ***Methods:*** The focus was on four orphan drugs (plerixafor, eculizumab, ofatumumab, and nelarabine) in the area of hematology/oncology. The information was retrieved from different sources, including the websites of health technology assessment (HTA) agencies, Cochrane Library reviews, and specialist European orphan disease resources. We reviewed the evaluation of the orphan drugs made by different HTA agencies including National Institute for Health and Clinical Excellence (NICE), Scottish Medicines Consortium (SMC), Transparency Commission France (TC), L' Unità di Valutazione dell'Efficacia del Farmaco / Efficacy (UVEF), Italian Medicines Agency (AIFA), Institute of Health Carlos III-Spain (ISCIII), and the Federal Joint Committee (Gemeinsamer Bundesausschuss) (G-BA). ***Results:*** Uncertainties have been strongly associated with negative HTA feedback. These uncertainties include uncertainty around net therapeutic benefit, safety and adverse events offsetting therapeutic benefit, high cost relative to therapeutic benefit, high budget impact, and uncertainty around the incremental cost-effectiveness ratio (ICER). The clinical-effectiveness issues identified were related to the small numbers of patients that made efficacy assessment difficult. On the other hand, the economic evaluation issues include the study design, the health economics modeling techniques, in addition to the health-related quality of life and utility data that were not measured in the trials. ***Conclusions:*** Payers are asked to reimburse high priced orphan drugs with limited clinical data (i.e., true long-term therapeutic and safety profile are unknown). Huge unmet medical needs force the high demand for access to orphan drugs, but the healthcare budget is limited in many countries. To limit the impact of coverage decisions on healthcare budgets, HTA agencies in EU5 biggest markets have restricted conditions to reimburse costly new drugs, which affected patient access to orphan drugs.

ND4
DEVELOPMENT OF A STATISTICAL MODEL TO PREDICT EUROQOL FIVE DIMENSIONS (EQ-5D) UTILITIES IN PARKINSON'S DISEASE

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Objectives: To develop a statistical model to predict EQ-5D 3-level (EQ-5D-3L) utilities as a function of patient demographics and PD severity, as measured by the