

non-medical) favored watchful-waiting. When comparing two treatment options, the majority of criteria did not favor one option over another. System capacity (0.02 ± 0.02) and Non-medical costs and constraints (0.02 ± 0.03) tip the scale in favor of lanreotide and Cost of intervention in favor of octreotide (0.08 ± 0.12). Sub-criteria Impact on autonomy and Impact on dignity favored lanreotide. Wide SDs reflect variability of drivers of decision across participants. **CONCLUSIONS:** Exploration of scenarios identified drivers of decision for GEP-NET management and revealed the diversity of participants perspectives. Holistic MCDA embedded with evidence supports individual reflection and informed shared-decisionmaking.

PRM157

DEVELOPMENT AND CONTENT VALIDITY OF THE ADVANCED SYSTEMIC MASTOCYTOSIS SYMPTOM ASSESSMENT FORM (ADVSM-SAF)

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OBJECTIVES: Advanced forms of systemic mastocytosis (advSM) are rare diseases characterized by neoplastic mast cell infiltration of tissues, and shortened survival. AdvSM comprises three subtypes: aggressive SM (ASM), SM with an associated hematologic non-mast cell disease (SM-AHNMD), and mast cell leukemia (MCL). SM patients suffer from many disease-related symptoms; therefore, a content-valid patient-reported outcome (PRO) instrument is important for assessing the efficacy of novel treatments. The research goal was to develop a content-valid PRO questionnaire, the Advanced Systemic Mastocytosis Symptom Assessment Form (advSM-SAF), for use in clinical trials. **METHODS:** The most common and relevant symptoms to advSM patients were identified through a literature review, expert input, and patient concept elicitation interviews. These results informed the development of the preliminary advSM-SAF, which is being tested for comprehensibility and comprehensiveness through cognitive debriefing interviews (CDIs) with patients. **RESULTS:** Based on detailed clinical and pathologic review of medical reports, 12 advSM patients (SM-AHNMD=6, ASM=3, MCL=3) were included in the study. These patients reported 33 unique disease-related symptoms, the most frequent including vomiting ($n=9$, 75%), abdominal pain ($n=8$, 67%), spots on the skin ($n=8$, 67%), diarrhea ($n=7$, 58%), nausea ($n=7$, 58%), tiredness/fatigue ($n=7$, 58%), itching ($n=5$, 42%), and flushing ($n=4$, 33%). Patients most desired improvement in abdominal pain, tiredness/fatigue, and nausea. These results, along with the literature review and expert input, informed the development of the advSM-SAF, a ten-item electronic diary assessing abdominal pain, nausea, spots, itching, flushing, tiredness/fatigue, vomiting, and diarrhea using a 24-hour recall period and an 11-point (rated 0-10) numeric response scale. CDIs evaluating the tool to inform potential modifications are ongoing. **CONCLUSIONS:** The advSM-SAF is being developed in accordance with scientific practices and regulatory guidelines. Next steps involve finalization of the advSM-SAF based on the CDIs and its translation into additional languages for psychometric evaluation in multinational clinical trials.

PRM158

CONCEPTUAL MODEL AND CLINICAL OUTCOMES ASSESSMENTS FOR ANGELMAN'S SYNDROME: UTILIZING PRAGMATIC METHODS IN RARE DISEASES

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OBJECTIVES: Remaining patient-centered when developing a COA strategy in rare diseases can be challenging. Angelman Syndrome (AS) is a rare (1/15,000) neuro-genetic disorder characterized by happy demeanor and significant delay across developmental milestones. While there are currently no therapeutics to treat AS and no AS-specific COAs, recent research led to the discovery of potential therapies. This study used pragmatic methods to select relevant and valid measures for AS, without delaying a therapeutic trial. **METHODS:** Review of AS published research and caregiver blogs, and discussions with clinical experts, advocacy groups and parents of children with AS aided in the development of an AS conceptual model. Using this model, we performed a literature review searching for COAs that meet FDA COA guidelines. FDA/EMA websites, clinicaltrials.gov, Pubmed and Google were searched for relevant instruments used in AS or in diseases with similar neurodevelopmental profiles. Comparisons of instrument content validity and psychometrics were made. **RESULTS:** Key concepts identified included: developmental delay (including motor, cognition and speech), behavior and sleep and other physical problems (e.g. seizures), impact on patients and caregivers, and possible mediators. We evaluated 88 AS-specific and 149 related-neurodevelopmental disease articles and 56 instruments (18 Behavior, 12 motor, 7 cognition, 7 communication, 6 sleep and 6 caregiver impact). No instruments, other than one for sleep, were specifically developed for AS. We will present the comparison of instruments' content validity and psychometrics. **CONCLUSIONS:** Our research yielded an AS conceptual model and measures for potential use in clinical trials, though validation in AS is required. Pre-existing specific measures in rare diseases, such as AS, represent high unmet need. Methods need to be appropriately robust and pragmatic, to ensure that treatments are not delayed, or even dismissed, due to lack of measurement strategies for rare disease populations. When successfully implemented, all stakeholders benefit, and most importantly, the patients themselves.

PRM159

ANALYZING A GERMAN INDEX FOR THE EQ-5D-5L BASED ON EXPERIENCED HEALTH

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OBJECTIVES: Quality of life indices based on valuations of experienced health states provide average valuations for the population surveyed. For the EQ-5D-3L, such indices exist for Sweden, Germany, and China. For the EQ-5D-5L, this study is the

first to analyze a German index. Results may provide useful for researchers and decision makers relying on health experienced. **METHODS:** The index is derived from three yearly representative population surveys conducted in Germany 2012-2014, VAS (visual analogue scale) valuations of the own health state of participants, and a generalized linear model with binomial error distribution and constraint parameter estimation. Sensitivity of model specification is tested for three ways of integrating total problem level reported (no consideration/existence of any problem/maximum problem level). Employing a split-sample design and 1000 simulation runs, cross-validation compares estimated and observed values by mean absolute error (MAE) and sum of squared errors (SSE). The index is further compared to observed valuations, to a respective value set for the EQ-5D-3L, and to a traditional index based on preferences over hypothetical health states. **RESULTS:** With $N=6074$ respondents, 265 health states were observed, with problem levels summing up to 24 for the most restricted individual. For all 3125 health states, the index model considering existence of any problem performed best regarding MAE and SSE in cross-validation. These indicators were also smaller than those for the external validation of a previous 3L index. Graphical comparison by health states indicates close correlation of the index with mean observed values for states occurring at least three times but systematic differences to traditional utilities. **CONCLUSIONS:** For the EQ-5D-5L, a first German index based on experienced health states is found to be feasible and to display acceptable psychometric characteristics. Future testing in clinical populations is needed for respective use.

PRM160

THE IMPACT OF COUNTRY-SPECIFIC UTILITY TARIFFS ON THE OUTCOME OF COST-UTILITY ANALYSES; A CASE STUDY

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OBJECTIVES: Countries generally use their own utility tariff to convert EQ-5D-3L health states to utility scores. However, it is unclear what the impact of these country-specific tariffs on the outcome of a cost-utility analysis is. Therefore, the aim of the current study was to evaluate this issue. Because the EQ-5D-3L mainly focusses on physical aspects of HRQOL, we evaluated this using data from two studies; a randomized controlled trial in patients with a physical disorder (low back pain) and a randomized controlled trial in patients with a mental disorder (depression). **METHODS:** A literature search was done to identify EQ-5D-3L utility tariffs derived using the Time Trade Off method. Missing data was imputed using Multiple Imputation by Chained Equations (MICE). Incremental Cost-Utility Ratios (ICURs), cost-effectiveness planes and cost-effectiveness acceptability curves (CEA curves) were estimated. **RESULTS:** Thirteen utility tariffs were identified. In the low back pain study, the ICUR using the Dutch tariff was 11,600 €/QALY, and ranged from 8,278 €/QALY for the Taiwanese tariff to 18,355 €/QALY for the Polish tariff. The probability of cost-effectiveness at a ceiling ratio of 30,000 €/QALY was 0.77, and ranged from 0.61 for the Polish tariff to 0.83 for the UK tariff. In the depression study, the ICUR using the Dutch tariff was 50,574 €/QALY, and ranged from 36,124 €/QALY for the US tariff to 96,551 €/QALY for the Japanese tariff. The probability of cost-effectiveness at a ceiling ratio of 30,000 €/QALY was 0.39, and ranged from 0.30 for the Japanese tariff to 0.45 for the US tariff. **CONCLUSIONS:** The results show that depending on the utility tariff that is chosen, the intervention may be considered cost-effective in comparison with usual care in one country and not cost-effective in another country. This suggests that results from cost-utility analyses cannot be unthinkingly transferred from one country to another.

PRM161

USING ORTHOGONAL DESIGN IN SELECTING HEALTH STATES FOR THE CONSTRUCTION OF EQ-5D-3L VALUE SET

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OBJECTIVES: EQ-5D-3L is widely used to generate the utility part of QALY (Quality adjusted life years). When valuing health states of the EQ-5D, a subset of health states with empirically determined values is used to estimate the utility of all possible health state. Clear guidance is lacking on what subset of health states is most suitable for direction valuation. In literature on experimental design issues, different desirable properties have been identified which cannot all be satisfied at the same time and no design is universally the best. Hence, researchers take a leap of faith when estimating a value set in the sense that the suitability of their design is unknown. In this study, we explore the use of orthogonal design as guidance in selecting health states and make comparison with designs used in previous studies. **METHODS:** 126 students in Erasmus University Rotterdam valued all 243 EQ-5D-3L health states using VAS (Visual Analogue Scale). Next, we examined different orthogonal and non-orthogonal designs in predicting the values of health states. To make comparison with orthogonal design, we used the samples of the 42 MVH states, the 17 Dutch/Japanese states and 25 Paris states. Stability was tested by changing the orthogonal coding and by reducing the observations by half. **RESULTS:** Among all the designs, an orthogonal design with 54 health states gave the lowest MAEs. Tweaking the orthogonal design to include more common health states had no obvious effect. The main effect model outperformed the N3 model in all designs. The MVH, Dutch/Japanese and Paris samples are suboptimal, compare to orthogonal designs. The result of orthogonal design remains stable when change the orthogonal coding or reduce the observations by half. **CONCLUSIONS:** The orthogonal design appears to be a promising health-state selection method for EQ-5D-3L valuation studies. Future studies should test its performance in time trade-off values and for the EQ-5D-5L system.

PRM162

ELICITING STATED PREFERENCES REGARDING LIFE EXTENSIONS NEAR THE END OF LIFE: A PILOT STUDY FOR A REFINEMENT OF THE QALY