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evaluation of the found publications demonstrated that the best reflection of the conditions of routine practice (generalizability) in PRCTs can be obtained mostly through the development of broader inclusion criteria, minimizing the exclusion criteria or broadening the scope of patients evaluation. We found also suitable tools, which can be used both during the design and evaluation of reliability of PRCTs: PRECIS, PR-tool, Pragmascope tool or CONSORT. **CONCLUSIONS:** Properly assessed PRCTs data in conjunction with information about the efficacy from RCTs will serve as a whole to facilitate business decisions in medical practice, as well as health organizations and rationalization of cost-reimbursement of used or new medical technologies.

PRM156

HOW TO INCREASE PATIENT RETENTION RATE DURING THEIR PARTICIPATION IN LONGITUDINAL STUDIES

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OBJECTIVES: Collecting patient data in longitudinal studies is often a concern in terms of data accuracy and patient follow-up. Physician assessment alone might be not sufficient or feasible. Multiple strategies can maximize patient retention. The methods to achieve these goals are intensive and made even more complex in global studies where regulatory requirements vary across individual countries. The objective of this research is to summarize the means used to improve patient retention. **METHODS:** The selected methods for patient retention have been used for three ongoing longitudinal safety registries requested by the European Medicines Agency and/or the Food and Drug Administration **RESULTS:** Three studies were conducted to assess safety follow-up over 20, 10 and 6 years, one of them was Pediatric and all were evaluating drugs in Inflammatory Bowel Disease area. A total of 8, 000 children and 13,250 adults have to be enrolled by Gastroenterologists in 27 countries. Maintaining long-term interest from investigators is essential. This is aided by careful site selection and training and provision of targeted study materials like patient profiles and newsletters as we as fair compensation. To mitigate patient attrition, these studies implemented direct-to-patient contact. This strategy minimizes loss-to-follow-up and enables data collection directly from the patients, increasing data quality. Data can be supplemented through additional contacts with relatives/legal guardians and/or other Health Care Providers. This methodology needs to be detailed in the protocol and study material to provide, to patients and the regulatory bodies, a clear overview of the procedures and responsibilities in each country. **CONCLUSIONS:** A correlation between good comprehension of the stakes and study procedures by the sites and patient retention is commonly established. However, specific actions which target maintaining patient interest and commitment is also important to successful retention. The means must be adapted to the design and the patient population.

PRM157

METHODOLOGICAL CHALLENGES OF IQWIG'S EFFICIENCY FRONTIER CONCEPT ELICITED BY MULTIPLE PATIENT-RELEVANT ENDPOINTS – WHY PRIORITIZATION OF ENDPOINTS CANNOT BE AVOIDED

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OBJECTIVES: The Institute for Quality and Efficiency in Health Care (IQWiG) in Germany evaluates benefits/harms and economic implications of medical interventions. For the purpose of cost-benefit analysis, IQWiG has developed the efficiency frontier concept to determine the maximum reimbursable price for pharmaceuticals. Within this concept benefits/harms are evaluated for each patient-relevant endpoint. If a compound shows additional/less benefit or less/more harm in several aspects of benefit, the creation of several efficiency frontiers would be required. The objective of this contribution was to assess whether the existence of multiple patient-relevant endpoints is a common feature within benefit assessments according to article 35a Social Code Book V which would entail multiple efficiency frontiers. **METHODS:** IQWiG's homepage was browsed for completed benefit assessments. Between January 2011 and May 2012, 21 benefit assessments were published by IQWiG. All assessments were screened in detail for information on patient-relevant endpoints and endpoint-specific benefit assessments. **RESULTS:** In 11 dossier assessments, benefit was endpoint-specifically assessed, whereas in 10 assessments, no endpoint-specific assessment was performed. Within the 11 dossier assessments, 19 subpopulations with endpoint-specific assessments were identified. For each subpopulation, between one and five endpoints were assessed by IQWiG. In total, 50 patient-relevant endpoints were detected. On average 2.63 patient-relevant endpoints per subpopulation were assessed. **CONCLUSIONS:** Since benefits/harms are evaluated for each patient-relevant endpoint the existence of multiple patient-relevant endpoints constitute a challenge for the compilation of the efficiency frontier and the subsequent determination of the maximum reimbursable price. Recommendations will likely be imprecise due to endpoint-specific benefits/harms. Prioritizing and weighting benefit and harm aspects can therefore not be avoided within IQWiG's proposed efficiency frontier concept if the decision maker requires precise recommendations for the maximum reimbursable price. Thus, an aggregation of benefit and harm parameters into one single efficiency frontier is needed.

PRM158

PLACEBO-CONTROLLED CLINICAL TRIALS: A DIFFICULT BALANCE "JUSTIFICATION VERSUS FEASIBILITY" FOR ACADEMIC SPONSORS

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OBJECTIVES: In investigator-based clinical trials, the use of placebo is often justified as it increases the probability from the peers' expertise of 1/ gaining a public grant; 2/ publishing results in higher-rank journals. **METHODS:** Among the 139 randomized clinical trials (RCT) evaluating drugs and currently managed by the Paris Hospitals, 68 are placebo-controlled. Aim is to analyze the hurdles in obtaining the placebo and its justification. **RESULTS:** Half of the studies had difficulties in obtaining the placebo. In rare cases, the study was unfeasible. When the placebo concerns a new drug, the company may accept to provide the drug and its placebo, at the eventual expense for the institutional sponsor to provide all the data without any further compensation. It may be considered as a disguised industrial sponsorship, the institutional sponsor while taking the responsibility of the study, being relegated to a role of a CRO. Obtaining a placebo of an old drug is trickier since the company may not sell anymore its product and generic companies are not able and/or interested to manufacture the placebo. The request of a manufacturer can be so expensive (up to 200.000€) that is exceeds by far the price of the verum, and of the grant. The rationale for using a placebo as comparator is to ensure a double-blind. However, when the drug administration is short (e.g. emergency setting), or when the endpoint is "hard" (i.e. mortality, imaging, biology), it is unlikely that any placebo effect from subjects and/or investigators may impact the endpoint assessment. In such situations, the comparator may be "no treatment" with whenever possible a blind assessment. **CONCLUSIONS:** Placebo-controlled RCT are challenging for institutional sponsors. Investigators and methodologists when writing a protocol and peers' expertise of a grant or a publication submission should consider the necessity and the feasibility of placebo.

RESEARCH ON METHODS - Conceptual Papers

PRM159

SENSITIVITY ANALYSIS VERSUS UNCERTAINTY ANALYSIS IN HEALTH ECONOMIC DECISION MAKING

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OBJECTIVE: To distinguish sensitivity analysis and uncertainty analysis, characterize their differential roles in health economic decision making, and to provide practical examples of their use and presentation in health economic analysis. **METHOD:** The role of one-way sensitivity analysis is to quantify the impact of varying a single parameter on the output of a model. However, this obscures an important distinction between parameter uncertainty and variability. Sensitivity analysis quantifies parameter variability in terms of the percentage change in a model output for a given percentage change in a model input. Sensitivity is therefore an objective property of the model. Uncertainty analysis, on the other hand, propagates a decision maker's subjective parameter uncertainty through a model to estimate the conditional uncertainty of the model output. Accordingly, the functional role of sensitivity analysis is to help a decision maker to understand and validate the internal model structure in order to gain trust in the model itself; whereas the functional role of uncertainty analysis is to assess the potential impact of a decision maker's subjective parameter uncertainty on confidence in a particular model-based decision. These distinctive roles are both critical in health economic analysis and decision making. We provide examples of sensitivity analysis versus uncertainty analysis, show how to report the results of sensitivity and uncertainty analyses, and discuss the implications of this distinction for conducting one-way and probabilistic analyses. **CONCLUSION:** Confidence in model-based decision making requires 1) confidence in the model itself, and 2) confidence in the model output given one's subjective parameter uncertainty. Sensitivity analysis and uncertainty analysis, respectively, serve these differential roles.

PRM160

A NEW VALUE-BASED PRICING FRAMEWORK FOR THE OPTIMAL PRICING OF PHARMACEUTICAL ASSETS

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Three common methods of estimating optimal prices for pharmaceutical assets are willingness-to-pay, health economic price appraisal, and reference price benchmarking. **PROBLEM:** Each method has significant drawbacks. Willingness-to-pay, assessed through primary research, can be limited by lack of knowledge of product list prices and the disconnect between respondent answers and real-life price acceptance. Health economic appraisals, utilizing cost-of-treatment models to estimate the price at which new products are cost-effective, are subject to error, interpretation, and are rarely accepted by stakeholders who drive price decisions. Reference price benchmarking, using market analogues to gauge price points for new products, does not take into account unique differences, perceived or real, of assets. None of these methods are able to quantify market intangibles such as unmet need and strength of competition. **SOLUTION:** To address these weaknesses, the authors have developed a mathematical framework using all three pricing methodologies to triangulate on a price range. The Value-Based Pricing Framework equation is a collection of activities that allows for the economic quantification of an asset's attributes, critical to determining an asset's overall value-based price. These activities include: 1) Willingness-to-pay Assessment: utilizes qualitative and quantitative feedback from decision makers to understand price expectations and thresholds vis-à-vis current competitors and comparators; 2) Reference Price Benchmarking: Assesses pricing structure of comparators to predict performance; and 3) Health Economic Analysis: Estimates product pricing as a function of health economic differentiation and determines cost-savings that can be offset in price. **CONCLUSION:** Value-Based Pricing is a structured way of estimating asset price based on its perceived value by various stakeholders. This flex-