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 or broadening the scope of patients evaluated. We found also suitable tools, which can be used both during the design and evaluation of reliability of PRCTs: PRECIS, PRE-tool, Pragmascope tool or CONSORT. METHODS: Properly assessing the relation between information about the efficacy from RCTs and PRCTs 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
El Kehir S1, Gauchoux R2, Nichols SE3

OBJECTIVES: Collecting patient data in longitudinal studies is often a concern in terms of data accuracy and patient follow-up. Physician assessment alone might not be 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 international 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 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 well 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 retrieved through patient 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 physicians and the regulatory bodies, a clear overview of the procedures and responsibilities in every 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
Nndihardi E1, Wasmuth T1
Nowmore GmbH, Nürnberg, Germany.

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 pharmacological interventions. 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 assessment of the development 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 benefits and harms in an aspect cannot 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
Durackinsky M1, Taron C1, Matei M1, Chassany O2
Assistance Publique-Hopitaux de Paris, Paris, France

OBJECTIVES: In investigator-based clinical trials, the use of placebo is often justified as it increases the probability from the peers’ expectations to gain a public grant. The following study aimed to assess the following: METHODS: A systematic review of 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 a placebo. In 31% of the study was a document and the price is a major concern for 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 sponsor-shi, the institution of the study while taking the responsibility of funding the placebo or to be 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
O’Day K1, Bramley T2
1Gland, Palm Harbor, FL, USA, 2Xcenda, LLC, Palm Harbor, FL, USA

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. METHODS: 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 example, for a given percentage change in a model input, the resulting change in a 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
Hawryluk EA, Malhotra M, Chawla V, Doyle J
Quintiles Global Consulting, Hawthorne, NY, USA

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 paid. 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-
ILE AND ADAPTABLE FRAMEWORK CAN BE APPLIED TO ANY THERAPEUTIC AREA AND USED TO EVALUATE ANY NUMBER OF VARYING PRODUCT PROFILES. IT INVOLVES UNDERSTANDING HOW STAKEHOLDERS VALUE ASSET ATTRIBUTES AND HOW THEIR WILLINGNESS-TO-PAY HELPS QUANTIFY EACH INDIVIDUAL ATTRIBUTES’ CONTRIBUTION TO A PRICE.

PRM161 A PARADIGM SHIFT IN HEALTH ECONOMIC EVALUATIONS FOR DEVELOPING COUNTRIES - OPTIMIZATION MODELLING FOR ASSESSING WHICH MIX OF MALARIA PREVENTION STRATEGIES ACHIEVES A DEFINED PUBLIC HEALTH TARGET AT THE LOWEST BUDGET
Van Vlaenderen I1, Saabouni C2, Van Rellingeren LA1, Standaert B2
1CHESS, Terrasa, Belgium, 2GlasswingMedicine Vaccines, Waacre, Benin, Belgium
Malaria remains one of the leading causes of ill health with the majority of cases and deaths occurring in young children in Sub-Saharan Africa. Key interventions currently recommended for preventing childhood malaria include Insecticide Treated Nets, Indoor Residual Spraying, Intermittent Preventive Treatment in infancy of infusion (IPTi) and IPTp. The optimal combination of interventions in cost-effectiveness and budget impact analyses fail to examine the health and economic impact of multiple interventions implemented simultaneously, and are therefore unable to evaluate the optimal integration of available malaria preventive interventions and partially efficacious vaccines currently in development. Moreover, an incremental cost-effectiveness ratio with recommended willingness-to-pay threshold provides limited guidance in developing countries. OBJECTIVE: Defining an approach to identify the optimal sequence of introducing different preventive interventions, achieving progressively increasing public health targets for malaria control in children <5 years old at the lowest budget. METHODS: Our suggested optimization approach integrates two distinguished models to assess combinations of interventions. A vector model simulates the impact of varying coverages of vector control interventions on vector infectiousness capacity and associated reduction in Entomological Inoculation Rate (EIR) for children. A human host model applies this reduced EIR to simulate disease incidence at varying coverages of interventions directly acting within humans. These connected models provide all potential intervention combinations achieving a pre-defined public health target (e.g. reducing childhood mortality by ≈50%). Considering malaria policy evolutions at increasing public health targets, a lower bound is set on intervention coverages at each optimization step. The remaining options are ranked according to their budget impact considering cost of interventions and disease management in a health system perspective. CONCLUSION: Using the optimization process with progressively increasing public health targets provides an indication on the optimal sequence of introducing interventions at the lowest budget. Therefore, this approach can support decision-making in prioritization of malaria preventive interventions.

PRM162 APPROPRIATE COMPARATIVE TREATMENTS FOR EARLY BENEFIT ASSESSMENT (EBA) IN GERMANY. COMPARING THE SUGGESTIONS BY THE JOINT FEDERAL COMMITTEE (GBA) AND THE PHARMACEUTICAL COMPANIES
Brod F1, Scherer J2, Schäulenbarg II2
1EcoStat Consulting Ltd., Great Yarmouth, Norfolk, UK, 2EcoStat Consulting Ltd., Sidestrand, Norfolk, UK
OBJECTIVES: The expected value of perfect information (EVPI) assesses, at a given willingness-to-pay threshold, the expected gain in net benefit from further research for which further research is believed to be most valuable can be assessed by calculating the expected value of perfect information (EVPi) from a HTA perspective. Objective of this analysis was to assess the use of EVPI in economic evaluations and health technology assessment (HTA) from the perspective of the NHS in the UK. METHODS: An unrestricted search was performed in MEDLINE for literature that contains references to EVPI and cost-effectiveness analysis (CEA) within HTA. The literature obtained was assessed to establish the extent to which EVPI is used in economic evaluation and HTA. Guidelines from the National Institute for Health and Clinical Excellence (NICE) were also checked for references to EVPI. RESULTS: The literature search indicated that out of 73,795 results for HTA or cost-effectiveness analysis, only 35 (≈0.05%) of these also reported EVPI. There were 21 examples of calculating the EVPI in an economic evaluation from a UK perspective, the earliest was published in 2004. The NICE guide to the methods of technology appraisal (2008 update) states that value-of-information methods can be used within a probabilistic sensitivity analysis (PSA) to assess the contribution of each parameter to the overall decision uncertainty. However, the specification for manufacturer/sponsor submission of evidence does not explicitly request the EVPI to be calculated as part of the PSA. CONCLUSION: The EVPI is a measure which can aid decision-makers in prioritizing the value of further research in an area, but it is not widely reported in published economic evaluations.

PRM164 ENSURING THE VALUE OF A MEDICAL DEVICE INNOVATION PRIOR TO MARKET LAUNCH
Hvidefall P
EVI Eppf School of Technology, Huddinge, Sweden
In order to ensure that new products entering health care markets are cost-effective over existing products Health Technology Assessment programs are implemented in health care systems. Whereas HTA agencies can screen out underperforming products it is equally important that they design and implement procedures to ensure that no underperforming products are developed and brought to market in the first place. By analogy, there are standards that companies need to comply with to ensure that their products are safe, similar standards or methods to ensure that new products are cost-effective could be developed. Based on 20 years experience of medical device innovation in industry, academia and consulting a conceptual model to ensure cost-effective innovation is proposed. The method divides the value assurance process into 3 Stages: concept generation, concept validation and market entry strategy. During the concept generation phase solving a critical problem with an unmet clinical need and a related disease burden are generated and evaluated with the core group of clinicians and multiple stakeholders according to costs, risks and benefits. The most promising concepts are iteratively tested and validated according to freedom to operate, safety, efficacy, ease-of-use, invasiveness, procedure success rate and head-to-head comparative cost-effectiveness until a candidate product can be addressed to a target patient group and practitioners at a profitable price. Finally, markets with the best clinician community support, largest size, highest attainable prices and lowest barriers to entry are addressed. This may sound as commonsense, but there are some important evolutionary principles hidden: 1) downstream market selection criteria are translated into early upstream tests; 2) multiple concepts are generated to handle early uncertainty; and 3) iterative tests are performed until a satisfying concept is selected. This model should ensure a product will pass HTA cost-effectiveness evaluation if eventually exposed to it.

PRM165 VALIDATING HEALTH ECONOMIC MODELS: DEVELOPING A METHODOLOGICAL APPROACH
Hart WM1, Chandler F2
1EcoStat Consulting Ltd, Sidestrand, Norfolk, UK, 2GlasswingMedicine Vaccines, Waacre, Benin, Benin
OBJECTIVES: The expected value of perfect information (EVPI) assesses, at a given willingness-to-pay threshold, the expected gain in net benefit from further research for which further research is believed to be most valuable can be assessed by calculating the expected value of perfect information (EVPi) from a HTA perspective. The objective of this research is to define an approach to identify the optimal sequence of introducing different preventive interventions, achieving progressively increasing public health targets for malaria control in children <5 years old at the lowest budget. METHODS: Our suggested optimization approach integrates two distinguished models to assess combinations of interventions. A vector model simulates the impact of varying coverages of vector control interventions on vector infectiousness capacity and associated reduction in Entomological Inoculation Rate (EIR) for children. A human host model applies this reduced EIR to simulate disease incidence at varying coverages of interventions directly acting within humans. These connected models provide all potential intervention combinations achieving a pre-defined public health target (e.g. reducing childhood mortality by ≈50%). Considering malaria policy evolutions at increasing public health targets, a lower bound is set on intervention coverages at each optimization step. The remaining options are ranked according to their budget impact considering cost of interventions and disease management in a health system perspective. CONCLUSION: Using the optimization process with progressively increasing public health targets provides an indication on the optimal sequence of introducing interventions at the lowest budget. Therefore, this approach can support decision-making in prioritization of malaria preventive interventions.

PRM163 THE USE OF EXPECTED VALUE OF PERFECT INFORMATION ANALYSIS WITHIN ECONOMIC EVALUATIONS AND HEALTH TECHNOLOGY ASSESSMENTS IN THE UK
Almond C1, Brereton NJ2
1Bristol Health Solutions, Sheffield, South Yorkshire, UK, 2Bristol, Sheffield, UK
OBJECTIVES: The expected value of perfect information (EVPI) assesses, at a given willingness-to-pay threshold, the expected gain in net benefit from further research for which further research is believed to be most valuable can be assessed by calculating the expected value of perfect information (EVPi) from a HTA perspective. The objective of this analysis was to assess the use of EVPI in economic evaluations and health technology assessment (HTA) from the perspective of the NHS in the UK. METHODS: An unrestricted search was performed in MEDLINE for literature that contains references to EVPI and cost-effectiveness analysis (CEA) within HTA. The literature obtained was assessed to establish the extent to which EVPI is used in economic evaluation and HTA. Guidelines from the National Institute for Health and Clinical Excellence (NICE) were also checked for references to EVPI. RESULTS: The literature search indicated that out of 73,795 results for HTA or cost-effectiveness analysis, only 35 (≈0.05%) of these also reported EVPI. There were 21 examples of calculating the EVPI in an economic evaluation from a UK perspective, the earliest was published in 2004. The NICE guide to the methods of technology appraisal (2008 update) states that value-of-information methods can be used within a probabilistic sensitivity analysis (PSA) to assess the contribution of each parameter to the overall decision uncertainty. However, the specification for manufacturer/sponsor submission of evidence does not explicitly request the EVPI to be calculated as part of the PSA. CONCLUSION: The EVPI is a measure which can aid decision-makers in prioritizing the value of further research in an area, but it is not widely reported in published economic evaluations.