CONCLUSIONS: This exploratory analysis suggests that use of a broader range of metrics to assess and benchmark value across tumor types may be needed to appropriately inform decision-makers looking to maximize clinical benefit to patients while managing constrained resources.

PRM61

SAMPLE SIZE ESTIMATION FOR PROSPECTIVE OBSERVATIONAL STUDIES

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OBJECTIVES: Unlike randomized clinical trials (RCTs), prospective observational studies typically address objectives rather than test specific hypotheses. Nevertheless, a minimum sample size is required to allow for adequate exploration of the objectives, and estimation of sample size is an important part of the planning process for these studies. Sample size estimation for observational studies is more complex than sample size calculation for RCTs; subgroup analyses and modeling are to be expected in observational studies, and these analysis methods may require more assumptions and larger sample sizes. At the same time, sample sizes must not be so large as to raise concern that the study includes an unnecessarily high number of sites and patients. This is particularly true for product registries where a specific product is being observed. **METHODS:** This poster will provide examples/case studies of sample size estimations performed for a variety of prospective observational studies and objectives. These case studies will focus on the following **METHODS:** 1) Incorporation of planned propensity score matching to support comparisons of cohorts or subgroups; 2) Investigation of factors that influence outcomes within subgroups; 3) Estimation expressed as number of person-years rather than persons; and 4) Re-estimation of sample size based on interim results. RESULTS AND **CONCLUSIONS:** These methods illustrate the difference between sample size estimation in prospective observational studies and sample size calculation in randomized clinical trials.

PRM62

THE IMPACT OF CENTRE SELECTION ON THE GENERALISABILITY OF ECONOMIC EVALUATION RESULTS FROM MULTI-CENTRE RANDOMISED CONTROLLED TRIALS

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OBJECTIVES: Economic evaluation (EE) estimates for individual centres in multi-centre randomized controlled trials (RCTs) can differ significantly from the trial-wide result. The existing methods addressing the generalisability of EE results from RCTs (e.g. bivariate hierarchical modelling) assume that the recruiting centres are representative for their jurisdictions, but this assumption has not been generally verified. No explicit method of selecting centres and their recommended sample sizes has been described, despite having been suggested in the literature. **METHODS:** The working hypothesis is that transparent centre selection is a crucial step in assessing the generalisability of EE results from RCTs. Two questions arise: 1) What criteria underpin the current practice of selecting centres for RCT-based EEs? and 2) Can a valid quantitative algorithm be formulated to assist the centre selection process at the trial design stage? **RESULTS:** First, the use of modelling-based methods addressing generalisability has to be supported by evidence that centres are representative for the jurisdiction under scrutiny. There is, thus, a need to assess the current practice of selecting centres for RCT-based EEs. Second, a quantitative methodology for purposively selecting centres for RCTs coupled with EEs has to be devised in order to underpin an objective centre selection process. The proposed operational measure is a generalisability index (GIx) which aggregates relevant generic and intervention-specific covariates and can be formulated at both jurisdiction and centre-level. The GIx can be validated against centre-level cost-effectiveness estimates. **CONCLUSIONS:** A successfully validated GIx will provide evidence towards the legitimate use of existing generalisability techniques. The GIx will allow an objective generalisability assessment for centres that did not participate in the RCT. Describing the rationale for centre selection must become a standalone item in reporting checklists for RCTs and EEs. Furthermore, such a methodology will bridge policy and research by correlating jurisdictional interests with RCT design.

PRM63

MULTIPLE CHOICES - HOW TO MAKE RATIONAL DECISIONS ACROSS SEVERAL INTERVENTIONS WHEN FACED WITH DIFFERENT OUTCOMES AND PERSPECTIVES?

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OBJECTIVES: In any assessment to facilitate decision making to allocate limited funding across multiple innovations, the relative value of clinical outcomes or cost containment depends upon preferences. In the case of allocating funds across a portfolio of interventions, one could maximise cases-, hospitalizations-, or deaths-avoided; and/or minimize costs from a health care payer or societal perspective. The optimal mix of innovations to reach the preferred target can be investigated by applying operational research modelling. However, a composite outcome is required in order to maximise multiple endpoints consecutively depending upon preferences for different endpoints. **METHODS:** An optimization model was developed in Microsoft Excel® using the solver function to evaluate the optimal mix of vaccines to implement within a portfolio, in order to avoid specific clinical outcomes (GP-visits, hospitalisations, deaths) or maximise QALYs gained within specific constraints including budget. A composite endpoint was developed to take into account different endpoints, clinical and cost, weighted according to preferences defined by the assessor. The composite endpoint was used as the objective function. **RESULTS:** Depending upon the preference weights defined when determining the composite endpoint, the allocation of resources across a portfolio of several vaccines resulted in different recommendations. If deaths-avoided was weighted highest then the model would optimize on elderly influenza vaccination, adolescent HPV and infant pneumococcal vaccines. If cases-avoided was the highest preference then varicella, rotavirus and pertussis vaccines were recommended. If cost-offsets from a payer perspective were maximised then the recommendation would be to first implement adolescent HPV, elderly influenza and rotavirus vaccination. The combination of preferences to avoid mortality and/or morbidity and/or maximize cost offsets resulted in the recommendation to implement different vaccines from the portfolio. **CONCLUSIONS:** The use of a composite measure and operational research modelling provides a tool to facilitate resource allocation across a portfolio of interventions depending upon decision-maker preferences.

PRM64

THE ROLE OF THE INSTRUMENT DEVELOPER IN THE TRANSLATION OF PATIENT REPORTED OUTCOME MEASURES

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OBJECTIVES: Developers of patient reported outcome (PRO) measures are often involved in the translation of their measures into other languages, and they provide valuable guidance by reviewing concept elaboration and back translation review documents and participating in harmonisation meetings. **METHODS:** However, many of the translation problems that they help resolve are due to difficulties in translating concepts in the measure that are either culturally bound or idiomatic to the source language, and these are features that might be addressed more effectively at an earlier stage. **RESULTS:** The developer can have a positive impact on future translations right from the onset by considering the 'translatability' of concepts when they are developing their conceptual model and generating their item pool, thereby aiming to create a measure which can be translated more accurately. **CONCLUSIONS:** We will examine common linguistic and cultural features which may make measures difficult to translate, and how developers can avoid these to help create global PRO measures that can be applied to all cultures and be administered in global clinical trials and health research.

PRM65

SHOULD WE AGGREGATE COST-EFFECTIVENESS OVER AN INTERVENTION'S ENTIRE IMPLEMENTATION LIFETIME?

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OBJECTIVES: Recent work has suggested that interventions' cost-effectiveness should be assessed over their entire lifetime of implementation, not just over the period of use for a single cohort as typically modelled (Hoyle and Anderson, Medical Decision Making, 2010; Hoyle, PharmacoEconomics, 2011). Such lifetime modelling can capture changes in costs and effects over time. These changes in costs and effects can result from price changes, disease dynamics or the application of differential discounting of costs and health effects. **METHODS:** Suggesting cost-effectiveness be assessed over an intervention's complete lifetime carries assumptions regarding the nature of the decision problem in healthcare resource allocation. In particular, it suggests resources be allocated on the basis of the total cost-effectiveness over all periods in which it is implemented. This lifetime perspective can conflict with the alternative perspective that resources be allocated on the basis of relative cost-effectiveness within each given period. We discuss a number of simple theoretical examples in which the rank ordering of cost-effectiveness of two interventions is different under the two perspectives. The examples include when the prices of interventions trend and have different expected lifetimes, when differential discounting is applied in certain circumstances, or simply when the price of only one intervention falls following patent expiry. **RESULTS:** These examples prompt us to consider which perspective is more appropriate. We argue that as health care resource allocation is an ongoing, repeated resource allocation problem, not one over a finite horizon, that the lifetime perspective is not appropriate. CONCLUSION: Advances in decision analytic modelling need to carefully reflect the actual nature of policy choices. The per-period perspective appears more appropriate to healthcare resource allocation problems than the total implementation lifetime perspective. However, the actual resource allocation process is likely to more complex than either perspective alone might suggest.

PRM66

COMPARISON OF RECONCILIATION AND REVIEW METHODOLOGIES FOR THE TRANSLATION OF PATIENT REPORTED OUTCOME (PRO) MEASURES

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METHODS: The first is the reconciliation of two independent translations by an in-country investigator (a lead translator). The second is the back translation review - the reconciled translation is translated back into English and the project manager reviews the English translation(s) against the source text, then the translation is refined through discussion between the project manager and the investigator. Both stages are conducted via email, and the back translation review report is usually reviewed by the instrument developer once all issues have been addressed. We will present an alternative methodology whereby the reconciliation and back translation review are conducted through live conversations (in teleconferences or otherwise) involving forward translators and the instrument developer. **RESULTS:** We will compare these two processes in terms of the types of discussion