PRM166
THE CHALLENGE OF ASSESSING HEALTH TECHNOLOGIES EARLY IN THE DEVELOPMENT. SYSTEMATIC LITERATURE REVIEW OF METHODS IN USE
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2Medical devices are being developed continuously and their developers are under pressure to provide better evaluations of their products. Early assessment gathers the preliminary evidence to estimate clinical, financial, organizational, and social/ethical consequences of a particular technology. It seems a useful tool in predicting the potential of new devices at the stage in which it can be adapted to fit the environment or the environment can be prepared for the technology. If the potential is low, further development can also be stopped. Although early assessment is recognized as an important part of medical device development process, there are many uncertainties about its nature and regarding the methods that are being used for its purpose. OBJECTIVE: To review different methods and their use in the early assessment of medical technologies. METHODS: An extensive systematic literature review of different early assessment methods. The authors systematically searched: computerised databases, published bibliographies of related topics, citations in articles reviewed, and references provided by colleagues. RESULTS: We identified 40 studies that met the inclusion criteria. 18 papers were either systematic literature reviews (5) or theoretical papers (13). 10 papers were addressing specific applications of early assessment methodologies, and 12 papers were addressing theoretical concepts combined with examples. Those 22 articles were analysed and categorised with regard to the stage of development of the technology, innovation type, perspective and aims of the analysis. Aims, outcome and uncertainties with regard to the outcome of the analysis were assessed. CONCLUSIONS: The need to clarify the aims and value of early assessment methods of medical devices to developers and policy makers, if early assessment methods are to become an integrated part of early activities in the development process.

PRM167
THE VALUE OF CHOICE IN A COLLECTIVELY FUNDED HEALTH SYSTEM: AN EXTENDED ANALYTICAL APPROACH TO EXAMINE THE CONFLICT BETWEEN DECISIONS AT INDIVIDUAL AND SOCIETAL LEVEL
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Cost-effectiveness analysis is a well recognized tool to support decisions about resource allocation in health care, particularly in the context of collectively funded health systems. When a new technology is restricted based on cost-effectiveness (because it is deemed too expensive relative to its expected benefits) a potential conflict can arise between the social interests (i.e. maximization of the population health subject to fixed budget constraint) and individuals who want to maximize their own health or utility. It has been previously argued that decisions that consider heterogeneity add value to the health care system. On the one hand, if a centralized decision process is implemented (e.g. NICE in the UK), subgroup analysis is appropriate. On the other hand, if a decentralized process is to be implemented, the effect of unrestricted choices on the social interests must be assessed. We have recently presented an analytical approach to estimate the expected health forgone (or gained) as a consequence of implementing a decentralized decision process. In the simplest case it was assumed that social planners and patients focus on the same metric of health, i.e. patients maximise health (for example, QALYs) and social decision makers maximise net health (net QALYs). This piece of work assumes the case where patients choose according to a different maximand. The analysis shows that if a single and different argument of the patient’s maximization function can be identified, the expected net health benefits forgone (or gained) from implementing unrestricted choices can be estimated as an extension of the “lost” of the reduction in utility of a robust expected joint distribution of potential outcomes, discussing gaps that require further research. The contribution of this analysis for policy decisions about individualized care is illustrated with a stylized numerical example.

PRM168
AN INTEGRATED FORMAL FRAMEWORK FOR REIMBURSEMENT, RESEARCH AND DECISION MAKING IN HEALTH TECHNOLOGY ASSESSMENT
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Reimbursement and research decisions about the utilisation of health care interventions can be formally characterised using methods for economic evaluation. Reimbursement decisions are informed by establishing the expected cost-effectiveness of the intervention. Research decisions are informed by estimating the expected value of additional information (the cost of uncertainty). Price negotiation can be used to alter conclusions about the benefits of reimbursement and the need for further research. In practice each of these elements may be considered separately and their combination to form a single evaluation. Previous research has shown (i) the impact of future changes on the payoff from reimbursement in the presence of irrecoverable costs and uncertainty that will be resolved over time, and; (ii) how the reimbursement and research decisions interact in terms of the ability to arbitrage additional delay on the payoffs and the size of the population that can benefit. The objective of this paper is to bring together established methods, using a consistent set of notation, to describe a general algebraic framework. The aim is to show systematically how irrecoverable costs, uncertainty that can be resolved by means of research and uncertainty that will be resolved over time can be formally incorporated in an integrated framework to estimate both cost-effectiveness and the value of further research that reflects the interaction between the reimbursement and research decisions. Furthermore we show how effective price negotiation would affect the payoff and ranking of the alternative policy options. A simple numerical example is used to demonstrate the application of this general algebraic framework and how the results might be presented to decision makers. The advantage of a single integrated framework is that reimbursement, research and pricing decisions can be informed simultaneously, transparently and consistently.

PRM169
INTERNAL AND EXTERNAL VALIDITY IN ECONOMIC MODELING: CONSIDERATIONS BASED ON A PUBLISHED EXAMPLE
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OBJECTIVE: Economic modeling is an established tool used for allocation of health care resources. Modeling was designed to demonstrate the influence of variables on defined outcomes (e.g. cost-effectiveness) in complex systems. Valid information for health care decisions can be obtained if five types of bias can be avoided: selection-, performance-, attrition-, detection-, and sampling-bias. In this study the validity of results derived from economic modeling is investigated addressing these five types of possible biases. METHODS: A published economic model of costs and benefits of drug treatment in mild-to-moderate Alzheimer’s disease (Guo et al., J Med Econ 2010;13:641-654) was used for this analysis. Nine questions were asked to confirm the validity of the obtained results. Internal validity was tested by checking the first four of the above types of bias, external validity by checking for a possible sampling bias. RESULTS: The presented model is flawed by absence of an explicit study question. Selection bias cannot be excluded as the patient data were obtained from pooled clinical trials and other sources. Performance bias is likely as the outcomes in patients extracted from pooled clinical trials differed considerably to the outcomes of patients treated outside of trials. A diagnosis bias is likely as observed data were compared with extrapolated data. Also the external validity of the study is likely to be impaired as the patients profiles were not derived from real world conditions but from patients enrolled in two clinical trials. CONCLUSIONS: This appraisal shows that phrasing a study question is essential for selection of the appropriate study method. Economic modeling is useful to discuss models and their assumptions but it always implies a high risk of bias. Therefore, results from modeling should only be accepted when internal as well as external validity of the used method has been confirmed.

PRM170
OPTIMIZING PUBLIC HEALTH DECISION OVER TIME: A DYNAMIC BUDGET OPTIMIZATION MODEL WITH MULTI-CRITERIA DECISION MAKING
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To guide health care decision, modeling efforts have mainly focused on cost-effectiveness appraisals (CEAs) between two mutually exclusive interventions. As CEAs do not document the impact of interventions on health care budget, they are generally complemented with budget impact analysis (BIs). BIs provide financial projections not only and do not necessarily reflect the health benefit effect an intervention may have on the population targeted. Additionally, decision makers may have different and several competing preferences and priorities on what constitutes the population health value of an intervention. A typical example is the public health impact of large childhood vaccination campaigns. Reduction of incidence, prevalence, hospitalizations, deaths, costs, etc. are the many criteria assessed by decision makers beyond the QALY’s gained when they contemplate vaccination campaigns. In this research, we design a transparent dynamic budget optimization model based on an analytical framework. The model of a general multi birth cohort model with yearly cycle and adaptable time horizon (from 3 years onwards). Optimization is realized yearly based on the population outcomes achieved the year before, the annual budget constraints and through different combinatorics and weightings of decision preferences. Decision maker preferences can be weighted on number of cases avoided, GP visits avoided, hospitalizations avoided, length of in-hospital stay reduction, number of in-hospital beds avoided, number of death avoided, Life-Years gain and QALYs gain. The model is intended to address specific questions that usually emanate from decision makers confronted with the introduction of mass vaccination campaigns: What is the yearly budget needed to achieve specific public health goals? What are the yearly and overall expected outcomes at the population level (i.e. the public health impact or in others words, the return-on-investment in terms of public health benefits)? Which intervention should be given additional (less) resources to maximize (minimize) impact if the available budget is increased (decreased)?

PRM171
OPTIMAL SHOPPING: AN EVOLUTION OF DECISION RULES IN COST-EFFECTIVENESS ANALYSIS
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Standard decision rules in CEAs are founded on a single objective to maximize health subject to a single and exogenous budget constraint. In essence, this is a well-specified additional constrained optimisation problem. The difficulty of using mathematical programming (MP) solutions to inform the allocation problem is that the informational demands are not feasible. However, it does provide an opportunity to evaluate the performance of simple ex-ante decision rules that have been proposed, some of which are being used to make decisions about health care technologies. Different decision rules are evaluated which compare: 1) the health gained and forgone for a new technology based on an estimate of the cost-effectiveness
threshold, and 2) the health effects of the new technology with the health effects of those technologies which must be displaced to accommodate its additional costs. The performance of each is evaluated through a simulation exercise, which uses shopping at the supermarket as an analogy to the health care system. An initial basket of goods represents the initial allocation and specifies the budget constraint. The task is to improve the contents of the basket by examining other things on the shelves. We discover that the decision rules are able to improve the performance of each test close each can get to the optimal basket (a MP solution), and 2) how quickly each improves the initial basket. We explore when each decision rule performs at its best and when one is likely to outperform the other. This includes: indivisibility of techniques and programmes, size of the budget relative to programme costs, the efficiency of exiting technologies, the type of information available to decision makers and whether they are able to learn from examining more products. This helps to identify where additional information (e.g., a better estimate of the threshold-old) might be most valuable.

PRM172

THE VALUE OF PERSONALIZED MEDICINE: IT IS MORE ABOUT UNVEILING THE PERFORMANCE OF THE COMPANION DIAGNOSTIC

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Personalized medicine (PM) is notably typified by the development of companion diagnostic tests to guide optimal treatment selection. PM has thus the potential to dramatically improve patients' outcomes and optimise allocation of resources. However, very few attempts exist that transparently include diagnostic test performance such as Sensitivity (Se) and Specificity (Sp) into cost-effectiveness and budget impact models. This research proposes an analytical framework to unveil diagnostic added-value according to different diagnostic performance scenario. The framework is based on a decision tree and compares two hypothetical treatment strategies: C (the current standard of care not associated with any test) versus T (a test with the performance of the test that is the fundamental determinant of the potential value of a PM strategy. An extension of the model to the case of 2 competing PM strategies (and thus 2 competing tests) is shown. We conclude that cost-effectiveness and test performance is key to achieve the promises of PM. This analytical framework allows payers, HTA bodies and manufacturers to gauge the potential value and financial impact of a PM strategy at all stage of its development.

PRM173

ON THE PROBABILITY OF INTERRUPTIONAL INDIFFERENCE

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Issues on discounting health effects have spurred debates on appropriate decision rules. Consensus is that empirically observed rates of time preference be incorporated in the model, however, is known to suffer from cognitive limitations. The human nervous system perceives how long sensory events last and the latter impact on perceptual decision making which is the act of choosing from a set of alternatives on the basis of available sensory evidence, in our case the indifference balance between present and future consumption. Statistical tools for such purposes are non-parametric and normality assumptions often fail to hold. Therefore, we derive a stochastic distribution by maximum entropy principle (MaxEnt). A MaxEnt distribution is one which best represents the current state of knowledge. Furthermore, MaxEnt distributions minimize the amount of prior information built into the distribution. Such distributions are usually sought by maximization of entropy constrained on what is known. In our case, we assume that the expected indifference amount at time t compared to an amount, y, now given by E(T(t))=y/w(t) where w(t) is a general time-inhomogeneous discount weight. With that constraint and the usual probability constraints, we derive a maximum entropy distribution for such a future amount. That is, we provide a closed-form distribution of the probability that an individual is indifferent between some quantity Y(t) at time t and a quantity Y(0)=y, now given E(T(t))=y/w(t)

PRM174

THE NEED TO CONDUCT FUTURE RESEARCH ON THE BENEFIT OF THE PROSTATE SPECIFIC ANTIGEN SCREENING TEST USING THE VALUE OF INFORMATION FRAMEWORK

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OBJECTIVE: Personalized medicine (PM) is the second most common cancer in men worldwide and the second leading cause of cancer deaths in men in the United States. Recently, the prostate specific antigen (PSA) test used to screen and diagnosis PC has been questioned due to concerns regarding clinical utility and its inability to help abnormality treat men with PC. This research aims to estimate the Value of Information (VOI) of the PSA screening research and to determine whether future PSA screening research should be focused on specific populations. METHODS: This research uses the Minimal Modeling Approach (MMA) in order to determine the expected value of information for PSA research. The population expected value of information (pEVI) for racial (African Americans and non-African Americans) and age (65-75 years, 76-85 years, >85 years) subgroups will be determined. Investigators will model survival based on published randomized controlled trials of PSA screening and will use data from the Surveillance Epidemiology and End Results (SEER) Medicare dataset for both survival and costs. Investigators will structure analyses by modeling the net benefit of men who received a prostate specific antigen screening exam between 2000 and 2007. RESULTS: VOI is required for answering the questions about the health benefits and costs of the intervention possible. In order for the pooling of data from international clinical trials to be possible, it is important that translations of a VOI measure mean the same to all respondents, not just in terms of the phrasing, but also in terms of the intensity and nuance of the phrases used. It is often the case that terms used frequently in VOI measures will have a direct and literal translation into the target language. However, problems can occur when terms used in the source text are culturally bound i.e., when the direct translation of a term has a different meaning than that of the source text, in terms of intensity or connotations, or is used in a different way. For example, the term ‘frustrated’ has a direct translation in most languages; however, this word is not used in some countries and can refer to a mental health issue. Issues can also arise when there is no equivalent of the source term in the target language. We will discuss common terms, expressions and nuances that are frequently used in VOI measures and how their meaning can be different across varying languages and cultural backgrounds. We will examine how to prevent these issues and how to avoid the mistranslation of culturally bound terms, by discussing the importance of detailed concept elaboration documents, input from the instrument developer, and in-depth pilot testing and cognitive debriefing. By using these methods it is possible to accurately anticipate these potential issues and explore alternative ways of conveying the intended meaning.

PRM176

THE VALUE OF FURTHER RESEARCH: THE ADDDED VALUE OF INDIVIDUAL-LEVEL DATA

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OBJECTIVE: Judgements based on average cost effectiveness estimates may disguise sources of heterogeneity that should be reflected in decision making. Making decisions considering patient heterogeneity has been proved consistent with an efficient use of limited resources. Although individual level data (IPD) is often not available to inform decision models, these provide unbiased and more precise estimates, particularly in the presence of heterogeneity. This paper seeks to assess the added value of having access to IPD, compared to using aggregate data (AD) in a relatively poorly understood subgroup of information analysis. METHODS: This paper develops a framework that informs the understanding of the implications of considering IPD when assessing the value of additional research in the search for the exclusion of mutually exclusive population subgroups. RESULTS: The developed framework explores the capabilities of the available evidence (i.e. IPD and AD) in guiding and in quantifying the value of further research in the absence and presence of subgroups. Issues around the optimal number of subgroups and for which population subsets should further research be undertaken are discussed. These exercises are supported by a motivating example on the cost effectiveness of child accident prevention programmes. CONCLUSION: The use of IPD rather than AD estimates may influence not only the extent to which an appropriate understanding of existing heterogeneity is achieved, but, more importantly, it may shape approval decisions for particular population subgroups and judgements of further research.

PRM177

WHAT IS THE ROLE OF EARLY HEALTH TECHNOLOGY ASSESSMENT OF BIOMARKERS IN THE PRE-CLINICAL DEVELOPMENT PHASE? A REFLECTION ON LESSONS LEARNED WITH MULTIPLE MYELOMA

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OBJECTIVES: Biomarkers associated with treatment efficacy and safety can be used to develop pharmacogenomic tests. However, translation of the evidence into clinical practice is difficult due to barriers to development and the difficulty to demonstrate clinical and economic utility. Health technology assessment (HTA) methodology may be used to inform decisions at many points during the product lifecycle. In this paper, we present a case study of pharmacogenomic tests in multiple myeloma. METHODS: Early Stage hta was conducted separately for two clinical applications of biomarkers: 1) a safety-based companion diagnostic, and 2) a prognostic test. We reviewed the methods that were useful in answering the questions about the health benefits and costs of the intervention and comparison and strategies comparators in each scenario were reviewed. RESULTS: An evidence-based approach was applied for both scenarios. Using literature reviews and