cluded from the review. The studies included were categorised based on criteria such as type of study, statistical methods for the learning effect, mathematical framework for the economic analysis, year of publication, country and intervention. **RESULTS:** The database search produced 930 articles. Only 2% of the studies obtained were included given the above criteria. Of the excluded studies, 70% were excluded as they were not economic evaluations and 23% were excluded as they did not present the learning effect. The remaining studies were excluded based on other reasons: duplicates, non-English, non-human. The majority of the studies are published after 2000. Of the included studies, the majority presented a learning effect related to health care costs. Two percent of the included studies referred to utilities. Only one study synthesized cost and utilities.

**CONCLUSIONS:** Although the learning effect can have a notable impact on the effectiveness of health care interventions, the economic evaluation literature on the subject is very limited.

**PM12 AN APPLICATION OF A PROPOSED FRAMEWORK FOR FORMULARY LISTING IN LOW-INCOME COUNTRIES: CASE OF CÔTE D’IVOIRE**

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**OBJECTIVES:** The Mutuelle Générale des Fonctionnaires et Agents de l’Etat de Côte d’Ivoire (MUGEFCI) is a health mutual providing coverage services for its enrollees (medical consultations, lab tests, medication expenses). This organization aims at improving cost-reimbursement process because of budgetary constraints. This study, therefore, aims at evaluating the feasibility of developing a new formulary for the MUGEFCI in Côte d’Ivoire, by implementing a formulary listing framework specifically designed for under researched settings. **METHODS:** The application of this framework, based on Multi-criteria Decision Analysis (MCDA) was carried out in 4 steps. First of all, we identified and weighted relevant formulary listing criteria with their levels of variation. Then, we determined a set of priority diagnostic/treatments to be assessed. Furthermore, scores were assigned to these treatments according to their performance on the formulary listing criteria levels. Last, we constructed a composite league table to rank the set of treatments by priority order of reimbursement. A budget impact analysis was also conducted to appraise the economic implications of the new composite drugs league table. **RESULTS:** Policymakers in Côte d’Ivoire consider targeting cost-effectiveness and severity of diseases as the most significant criteria for priority reimbursement of drugs. This translates into a general preference for antimalarial, treatments for asthma and antibiotics for urinary infection. Moreover, the results of the BIA suggested that the new priority list of reimbursable drugs will be affordable when the real cost of the highest priced drug is under 66 USD. Over this threshold, the MUGEFCI will have to select the reimbursable drugs according to their rank in the priority list along with their respective budget impact per patient (cost per patient). **CONCLUSIONS:** It is feasible to use MCDA to establish a formulary for low-income countries. The application of this method is a step forward to transparency in policymaking.

**PM13 ASSESSING THE METHODS FOR SYSTEMATIC REVIEWS OF ECONOMIC EVALUATIONS**

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**OBJECTIVES:** Robust and explicit methods to conduct systematic reviews of economic evaluations are required to guarantee quality of reviews and their findings. This is especially needed when assessing high resource-consuming topics such as those related to the introduction of new imaging technologies. Our aim is to analyse the methods for systematic reviews of economic evaluations of health technologies. **METHODS:** We carried out a systematic review of methods for systematic reviews of economic evaluations by reading relevant parts of HTA methodological manuals (“manuals”) and HTA reports from UK (“reports”) in English and Italian at September 2010. **RESULTS:** We identified 27 manuals and 53 potential reports. Among them, 6 and 40 contained relevant information respectively. None of the 6 manuals described the criteria used for the identification or formulation of the methods, or gave guidance on which method to follow. Among the 40 reports included, 38/40 (95%) reports described search strategy and data bases used to identify studies and inclusion criteria were presented in 21/40 (53%) reports. The reports indicated use of quality assessment instrument were 9/40 (22.5%) while 20 different instruments were identified in the remaining reports. No report carried out a quantitative synthesis of the data from the systematic review and 9/40 reports (22.5%) clearly stated this. The reports that appear to include the data selectively in their economic evaluation were 13/40 (32.5%). **CONCLUSIONS:** The absence of clear methodological guidance in manuals is reflected in the reports. These show unclear rationale, methods and use of data from systematic reviews of economic evaluations.

**Research On Methods – Database & Management Methods**

**PM14 MONDRIAN: A DUTCH ‘POPULATION’ LABORATORY**

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**OBJECTIVES:** Many excellent health care databases are available in The Netherlands for (pharmaco-)epidemiologic research. However, in isolation these data remain scattered and have limitations with regard to sample sizes and/or detail of the registered information. The objective of Mondriaan is to optimize access to en linkage of routine health care databases in The Netherlands for (pharmaco-)epidemiologic research. **METHODS:** We have built an ICT infrastructure for data collection and linkage of healthcare/research data in The Netherlands. To protect privacy, pseudonymisation and linkage is performed by a trusted third party (TTP). A data catalogue on subject level has been developed to allow queries within the connected databases to support designing (pharmaco-) epidemiologic studies (including sample size calculations, assessment of completeness of data). **RESULTS:** We are able to routinely link all pharmacy records from the National Foundation of Pharmaceutical Statistics (SFG) (n=14,000,000) on a patient base to several routine health care databases such as the Almere Health Care database (n=200,000), the Julius GP Network (n=200,000), and the AGIS claims database (n=1,200,000). Currently we are integrating several other databases in The Netherlands. **CONCLUSIONS:** The project will deliver a large-scale, high-quality data platform for innovative (pharmaco-)epidemiologic research.

**PM15 THE OUTCOME OF ISPOR EUROPEAN AND INTERNATIONAL CONGRESSES BETWEEN 2005-2009**

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**OBJECTIVES:** Many of the former socialist countries of Central and Eastern Europe (CCEE) joined to the European Union in 2004. The aim of this study is to analyse to outcome of ISPOR European and international congresses between 2005-2009 with a special respect to the activity of CCEE. **METHODS:** We analysed the abstracts presented to the ISPOR European and International congresses and published in the Value in Health journal between 2005-2009. We performed a database analysis of value in Health journal on the Web of Science (Thomson Reuters) electronic database of scientific publications. Three indicators were selected: author’s country, institution (university) and name: **RESULTS:** The top-10 most active countries were (number of abstracts): Switzerland (483), Wales (310), Sweden (262), Denmark (253), Belgium (25-0), The Netherlands (23-0), England (19-3), Canada (18-3), Scotland (16-0) and Hungary (14-7). Furthermore Slovakia (8-2) was ranked 16th, Czech Republic (5-0) 24th, Poland (4-1) 26th and Serbia (3-3) 29th. The top-10 most active universities were (number of abstracts): Univ So Cali (140), Univ Toronto (107), Univ Washington (100), Ohio State Univ (98), Erasmus Univ & MC (94), Univ Maryland (93), Univ Pécs Hungary (93), Univ York (89), Harvard Univ (89) and McMaster Univ (76). Three more CCEE university were ranked: Med Univ Warsaw from Poland (38), Conrins Univ Budapest from Hungary (30) and Comenius Univ from Slovakia (27). The most active 10 authors were (number of abstracts): Boncz, I (Hungary, 96), Taixe, C (France, 83), Balkrishnan, R (USA, 87), Sebestyen, A (Hungary, 71), Valentine, WJ (Switzerland, 65), Mantovani, LG (Italy, 50), Caro, J (USA, MA, 57), Annemans, L, (Belgium, 54), Krizsaberce, I (Hungary, 52), Rejas, J (Spain, 50). **CONCLUSIONS:** Former socialist countries of Central and Eastern Europe (CCEE) showed a significant activity at ISPOR European and International congresses.

**Research On Methods – Modeling Methods**

**PM16 COVARIANCE STRUCTURES FOR MODELING LONGITUDINAL DATA**

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**OBJECTIVES:** The objective of this analysis is to compare several covariance structures that are used in longitudinal modeling of longitudinal data. **METHODS:** A PUBMED search reveals a steady increase in prospective observational studies over the past five years. Repeated measures models are frequently used to analyze longitudinal data. For the purpose of these comparisons, a series of longitudinal datasets are generated. In order to facilitate comparisons with applications to longitudinal datasets involving utilities, the dependent variable in the simulation datasets is a continuous variable restricted to the support interval [0, 1]. The predictor variables include a set of categorical and continuous variables, including a time varying covariate. Datasets with four different types of time dependence were compared (no time trend, log time trend, linear trend, exponential trend). Models with the following covariance structures were evaluated: compound symmetry, unstructured, autoregressive, heterogeneous autoregressive, variance components and Toeplitz. Model comparisons were based upon Akaike information criteria (AIC) and the Bayesian information criteria (BIC). **RESULTS:** The preferred covariance structures for the dataset without a time trend were heterogeneous autoregressive (AIC) and unstructured (BIC). The preferred covariance structure for the log trend dataset was unstructured (AIC and BIC). The preferred covariance structures for the linear trend dataset were variance components (AIC) and heterogeneous autoregressive (BIC). The preferred covariance structure for the exponential trend dataset was variance components (AIC and BIC). **CONCLUSIONS:** The unstructured covariance matrix is often the default choice for the covariance matrix for longitudinal models. This model has the least number of assumptions and allows for the modeling of each patient individually. However, the unstructured covariance structure requires the most degrees of freedom and in some cases the estimated covariance matrix does not converge. In these cases, covariance structures such as variance components and heterogeneous autoregressive may present attractive options.

**PM17 SUITABILITY OF CLAD-CQR MODELS FOR OBTAINING QALYS**

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The EQ-5D was interview-administered in the 2006 Catalan Health Interview Survey, a cross-sectional study of a representative sample of the non-institutionalised general population (n=15,926). As well as CLAD-CQR, Tobit model was adjusted to assess utility losses associated with 15 chronic conditions. Goodness of fit was assessed by cross-validation (Mean Square Error - MSE, Mean Absolute Deviations - MAD). RESULTS: As ceiling effect was over 50%, CQR models on the 30 percentile had to be applied instead of CLAD models on the median. CQR showed a slightly worse fit to data (MSE=0.084, MAD=0.246) than Tobit (MSE=0.068, MAD=0.218). The impact of the different chronic conditions measured in QALYs obtained from the CQR was on average around 70% larger than the ones of the Tobit model. CONCLUSIONS: Tobit and CLAD-CQR model latent quality of life, not anchored in 0–1 perfect health. While Tobit allows estimation of observed utilities and marginal effects, interpretable as QALYs, CQR do not in the case of right-censoring. This leads to overestimation of effects and makes CLAD-CQR models inappropriate for obtaining QALYs, just as the untransformed Tobit’s latent variable. Moreover, the suitability of modelling percentiles differing from the median should be discussed.

PRM18 SENSITIVITY ANALYSIS IN MULTI-CRITERIA DECISION (MCDA) MODELS FOR BENEFIT-RISK ASSESSMENT

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OBJECTIVES: Regulators of medical technologies are facing increasing pressure to make their deliberations concerning the benefits and risk more transparent. Both benefits and risks are often measured via multiple competing outcomes. Hence, MCDA models like the Analytic Hierarchy/Network Process are valuable tools in quantifying decision trade-offs. The objective of this paper is to demonstrate how the use of MCDA models for benefit-risk assessment and the use of sensitivity analysis to assess the impact of uncertainty and parameter confidence can be used in practice. METHODS: An existing data set about anti-depressants we construct a decision model for use with AHP weights, including clinical endpoints, adverse events and quality of life. AHP priorities for the main criteria (benefits and risks) were obtained from the general public (n=15) using face-to-face interview. After base-case analysis of decision trade-offs, three forms of sensitivity analysis for MCDA models were employed. RESULTS: We applied three forms of sensitivity analysis, including 1) manual adjustment of criteria weights using a slider, 2) probabilistic sensitivity analysis (PSA) of the criteria weights; and 3) PSA of the expected drug performance on each of the criteria. The values will be graphically presented and discussed. CONCLUSIONS: One of the advantages of AHP/ANP is its ease of use. However, in order to make judgments about benefits and risks decision makers, may wish to generalize to a wider population and as well as to quantify decision trade-offs in subgroups of patients. The methods can be combined, and if preferred, the decision model can be extended by using these two techniques; and provides feedback on ease of use and clarity of concepts of the different techniques. RESULTS: Results based on the first 30 responses show that EVIDEM is easy to understand and takes little time to complete, three minutes on average. Criteria weights derived using the EVIDEM technique and best/worst scaling were consistent. Comparing the rank order of criteria. There is more resemblance in rank order of criteria calculated with the EVIDEM technique. Compared to AHP/ranking/point-allocation, EVIDEM takes less time to complete but is only preferred by 33% of decision-makers. AHP/ranking/point-allocation was used primarily in settings where there is a need to model the respondents’ opinion. CONCLUSIONS: The simple technique is proposed as a starting point for users who are about to implement the EVIDEM framework in the own context. Other techniques may be preferred and their impact on the MCDA value estimate generated by applying the framework is being explored. This project is part of a larger collaborative work that includes developing and validating this framework to facilitate sound and efficient MCDA applications.

PRM19 MODELLING THE IMPACT OF MULTIPLE INDICATION DRUG LAUNCH ON TOTAL REVENUE

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OBJECTIVES: It is becoming increasingly common that early stage drug candidates have potential applications in several therapy areas. This is especially prevalent where several diseases share a similar aetiology. Areas such as immunology, oncology and metabolic disorders can have ailments that are characterised by different physiological involvement but share a similar underlying cause. The objective of this study was to model the impact of a multiple indication launch on drug revenue over time, as well as develop a tool to enable launch strategy scenario testing. METHODS: Patients were stratified into seven acute and three chronic disease groups. The NPV of each therapy area was assessed using a combination of qualitative and quantitative methods. Therapy areas are scored and ranked by defined metrics allowing the optimum therapy area to be selected as the first launch indication. The assessment is repeated for the remaining therapy areas to account for changes in the initial launch indication, to generate the next most attractive therapy area and so on. NPV for the drug is then calculated based on a trade-off between patient population size and pricing dynamics across indications. RESULTS: In general, the larger patient populations translate into lower drug costs to meet with budget impacts. The decision-making tools are therefore vital for manufacturers to understand the optimal trade-off between price and population size across indications in order to maximise the overall commercial potential of a drug. When different indications have significantly different sized patient populations, drug pricing becomes an issue. The research concluded that if the correct strategy is employed, a drug launch strategy can be optimised to generate the maximum possible revenue over the greatest number of indications. CONCLUSIONS: Modeling changes in price and population size during multiple-indication launches can be a vital tool in understanding total revenue potential of a new product, and optimal launch sequencing.

PRM20 COMPARISON OF THREE METHODS FOR MEASURING MULTIMORBIDITY ACCORDING TO THE USE OF HEALTH RESOURCES IN PRIMARY HEALTH CARE

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OBJECTIVES: To compare three methods of measuring multimorbidity according to the use of health resources (costs of care) in primary health care (PHC). METHODS: Design: retrospective study using computerized medical records. Setting: thirteen PHC teams in Catalonia (Spain). Participants: assigned patients requiring care in 2009. Main measurements: the socio-demographic variables, co-morbidity and costs. Methods of comparison were: a) Combined Comorbidity Index (CCI); b) Charlson Index (CHI); and c) Adjusted Clinical Groups case-mix: resource use bands (RUB). The cost model was constructed by differentiating between fixed (operational) and variable costs. Statistical analysis: developed 3 multiple linear regression models to assess the explanatory power of each measure of co-morbidity were compared to the of the determination coefficient (R2). RESULTS: A total of 227,235 patients were included. Woman: 55.6%, average age was 44.1 years, means years of episodes: 4.5, average visits/patient/year: 8.1, the mean unit cost of was 1654, average explained a R2=0.49, the CHI was R2=0.38, and the RUB=0.7% of the variability of the cost. The ICC is acceptable behaviour, albeit with low scores (1 to 3 points), showed no conclusive results. CONCLUSIONS: The CCI may be a simple method of predicting PHC costs in routine clinical practice. If confirmed, these results will allow improvements in the comparison of the case-mix.

PRM21 VALIDATING A MULTI-CRITERIA DECISION ANALYSIS (MCDA) FRAMEWORK FOR HEALTH CARE DECISION MAKING

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OBJECTIVES: When evaluating healthcare interventions, decision-makers are increasingly asked to consider multiple criteria to support their decision. The MCDA-based EVIDEM framework was developed to support this process. It includes a simple weight elicitation technique, designed to be easily applicable by a broad range of users. The objective of this study was to compare the EVIDEM technique with more traditional techniques. METHODS: An online questionnaire was developed containing the EVIDEM technique with four alternative techniques including AHP, best/worst scaling, ranking and point-allocation. A convenience sample of 60 Dutch and Canadian students were asked to fill out the questionnaires as if they were sitting in an advisory committee for reimbursement/prioritization of health-care interventions. They were asked to provide weights for 14 criteria using two techniques, and to provide feedback on ease of use and clarity of concepts of the different techniques. RESULTS: Results based on the first 30 responses show that EVIDEM is easy to understand and takes little time to complete, three minutes on average. Criteria weights derived using the EVIDEM technique and best/worst scaling were consistent. Comparing the rank order of criteria weighted using the two techniques; there is more resemblance in rank order of criteria calculated with the EVIDEM technique. Compared to AHP/ranking/point-allocation, EVIDEM takes less time to complete but is only preferred by 33% of decision-makers. AHP/ranking/point-allocation was used primarily in settings where there is a need to model the respondents’ opinion. CONCLUSIONS: The simple technique is proposed as a starting point for users who are about to implement the EVIDEM framework to the own context. Other techniques may be preferred and their impact on the MCDA value estimate generated by applying the framework is being explored. This project is part of a larger collaborative work that includes developing and validating this framework to facilitate sound and efficient MCDA applications.