[6]Yamaguchi University Hospital, Ube, Yamaguchi, Japan, [7]CRECON Research & Consulting Inc, Tokyo, Japan, [8]Niigata University of Health and Welfare, Niigata, Japan, [9]Meijo University, Nagoya, Japan, [10]Okayama University, Okayama, Japan, [11]Ritsumeikan University, Kusatsu, Japan, [12]Osaka University, Osaka, Japan, [13]National Institute of Public Health, Wako, Japan

OBJECTIVES: Use of economic evaluation of health care technologies is intensively discussed in the government in Japan. In order to make evaluation results comparable, standardized method of evaluation is required. We proposed an economic evaluation guideline in Japan. **METHODS:** We organized a research team for developing guideline. After reviewing guidelines in HTA agencies in the world and current debate on issues, we investigated HTA reports and methodology of economic evaluation studies in several drugs, devices and procedures. Based on the review of these information, the research group discussed and proposed economic evaluation guideline suitable for Japan. **RESULTS:** Proposed guideline consist of 13 items: 1) Objective; 2) Perspective of analysis; 3) Comparators; 4) Method of analysis; 5) Time horizon; 6)Choice of outcomes; 7) Source of clinical data; 8) Costs; 9) Productivity loss; 10) Discounting; 11) Modeling; 12) Uncertainty; and 13) Budget impact analysis. Guideline sentences are classified into 3 levels, principal, recommended, and optional. **CONCLUSION:** This guideline is a proposal by a research team. However, it will be needed in the near future for using economic evaluation of health care technologies. Proposed guideline should be tested by adopting individual studies.

PRM219

DEALING WITH ZERO CELLS IN SPARSE NETWORKS IN BAYESIAN NETWORK META-ANALYSIS

Ivanescu C[1], Skaltsa K[2], Heemstra L[1], Van Engen A[1]
[1]Quintiles, Hoofddorp, The Netherlands, [2]Quintiles, Barcelona, Spain

OBJECTIVES: Bayesian Network Meta-Analysis (NMA) models for binary data are well established and special precautions do not usually need to be taken in the case of zero cell counts. Furthermore, trials with zero cells in both arms are usually excluded from the analysis. However, in sparse networks with only one trial per comparison and zero cells in unique link studies, their inclusion may be mandatory. Zero frequencies may result in numerical instability and/or large variances. The objective of this study was to investigate the effect of different methods dealing with zero cells in sparse networks in Bayesian NMA. **METHODS:** A review was conducted to identify methods dealing with zero cells for binary outcomes in sparse networks in a Bayesian setting. The identified methods were applied to a sparse network with six treatments and one study per comparison. The outcome was grade 3+ Adverse Events and measured by Odds Ratio. A fixed effects model was fitted with binomial likelihood. The performance of the methods was assessed by the residual deviance and the Credible Intervals' (CrI) width was compared. **RESULTS:** We identified three methods: apply a continuity correction (a constant factor of 0.5 or the reciprocal of the opposite treatment size), use of informative priors on treatment effects and placing a distribution on the baseline model. We applied all methods and combinations of them. The model fit was adequate for all methods (residual deviance [10;12.3] for 12 datapoints). The use of different informative priors improved the variability estimates. CrI widths were reduced up to 15 times with respect to the original model with vague priors. **CONCLUSIONS:** Although the debate on the inclusion of studies with zero events in NMA is still open, our research shows that methods are available to address this issue. However, no clear recommendations can be provided.

PRM220

QUALITY ASSESSMENT OF OBSERVATIONAL STUDIES FOR SYSTEMATIC REVIEWS

Kiss N, Tongbram V, Fortier KJ
Oxford Outcomes, Morristown, NJ, USA

Observational studies are frequently included in systematic reviews, especially in those disease areas where RCTs are limited. While there are very specific tools for and guidance on assessing the quality of RCTs, the assessment of observational studies is less standardized. OBJECTIVE: To understand and assess the different tools used to review the quality of observational studies and to make recommendations based on our evaluation. **METHODS:** First, a systematic review of literature from 2005-present was conducted in Embase and Medline to determine the frequency of use of quality assessment for observational studies and the type of tools used to conduct the assessment. Second, we reviewed documentation from NHS guidance on quality assessment of non-randomized studies. Finally, we reviewed two years of approved HTA submissions to see what methods of assessment have been used for submissions. **RESULTS:** A total of 1429 articles were screened. Compared to a similar study on older literature, our review found an increase in the use of quality assessment for observational studies. However, we found that many studies continue to devise their own tool or adapt existing tools rather than use a tool in its entirety. Downs and Black, MOOSE, and STROBE were the most referenced tools, although STROBE was not originally intended for such use. Guidelines centered on "non-randomized" studies were mixed and were not always found to be applicable to observational studies, but instead mostly to single-armed clinical trials. **CONCLUSIONS:** There is still a need for guidance and standardization for observational studies assessment for use in systematic literature reviews. Although quality assessment of observational studies is still not standardized, there are a few methods becoming more frequent in the literature but are difficult to compare across systematic literature reviews because they have often been adapted by each author.

PRM221

AN APPROACH FOR QUANTIFICATION OF PATIENT ADVOCACY GROUP INPUT IN THE HTA PROCESS

Hicks N[1], Toumi M[2]
[1]Commutateur, Paris, France, [2]University Claude Bernard Lyon 1, Lyon, France

Patient input in HTA pathways by the appropriate disease Patient Advocacy Group (PAG) uses principally humanistic and social studies as an evidence base followed by critical evaluation against traditional CEA (Cost Effective Analysis) via a scientific process. Patient and Public Involvement (PPI) in HTA is associated with a low evidence base potentially limiting its value. Research presented at ISPOR 2012 by the same authors concluded a need to improve and standardize PAG input integration in HTA decision making. To investigate the way different forms of knowledge / experience are used by PAGs in NICE HTA for guideline development and new technology review. We will look at: 1) Influence of PAG structure, resource capability, internal process and the impact of PAG advisory board physician representatives on scientific validation of patient input in HTA participation, and 2) Part I results will inform further research into selection and ranking criteria of social derived data compared with CEA. An iterative PPI best practice approach will be followed. Selection criteria: Five UK PAG groups (Neurological, Autoimmune, Rare disease, Cardiovascular and Oncology) will be invited to participate. The NICE PPI Unit will nominate groups when needed. Inclusion criteria: 1) willingness to participate, 2) prior involvement in guideline / new technology assessments; and 3) presence of medical advisory board. Research elements: Application of GRIPP criteria (Guidance Reporting Involvement Patient Public) to ensure a strong evidence base will guide development of an on-line survey and subsequent focus groups and interviews. The survey, designed for SAP review, will study: size of PAG, internal process for HTA involvement, previous HTA involvement, data submitted, PAG knowledge gaps and involvement of medical advisory board. Follow up by focus groups and interviews with PAG and advisory board members to identify insights/themes.

PRM222

JUGGLING JURISDICTIONS: METHODS FOR CONDUCTING MODULAR SYSTEMATIC REVIEWS?

Thompson J, Hawkins N
Oxford Outcomes Ltd., Oxford, UK

A crucial component of a systematic review is a clear description of the disposition of studies throughout the various steps of the review process (de-duplication, abstract review, full paper review and final inclusion). This is commonly achieved using a PRISMA diagram that shows the number of inclusions and exclusions at each stage of the review. This may be supplemented with details of the reasons for exclusion. To create the PRISMA diagram it is necessary to keep an on-going count of exclusions and inclusions throughout the review process. However, this can pose a challenge where the scope of a systematic review changes from the original specification. This may happen where the set of licensed treatments or HTA requirements vary between jurisdictions or over time. In these cases, it may be time consuming to recreate the on-going counts of exclusions that correspond to the modified scope. We present a methodology for conducting a modular systematic review in which PRISMA diagrams and other descriptions of study disposition can be generated corresponding to any subsequent changes of scope. This is achieved by splitting the review into a set of 'component-reviews' defined by mutually exclusive treatment search terms that comprise the full set of possible intersections between the individual treatments. Throughout the systematic review process separate counts of abstracts, papers and studies are maintained for each of these component-reviews. The results from the component-reviews can then be combined to reflect any final review scope (based on individual treatments). We will illustrate the methodology with an example review of the comparative efficacy of licenced thiazolidinedione's (TZDs) versus placebo in patients with type 2 diabetes mellitus (T2DM) where there are two TZDs licensed in the USA (pioglitazone and rosiglitazone) but only one in Europe (pioglitazone).

PRM223

SOCIAL NETWORK ANALYSIS OF AUTHORSHIP NETWORKS AND THE IDENTIFICATION OF EXPERT ADVISORS

Stoddart SDR[1], Siddiqui MK[2]
[1]HERON Evidence Development Ltd., London, UK, [2]Heron Health Private Ltd., Chandigarh, India

OBJECTIVES: Systematic reviews are often supplemented with the use of external experts to provide guidance on the nuances of the area. This can help add context if a review is used to support trial design or health economic model development. The ideal expert would have a deep understanding of the area and be well connected to those individuals conducting trials. The aim of the current research was to assess whether social network analysis of coauthor networks could be used to rapidly and objectively identify individuals with the qualities desired in an external expert. **METHODS:** Publication lists from a recent systematic review of rheumatoid arthritis were used to produce a list of links between authors and publications. This was then imported into the Gephi program for social network analysis. Within Gephi, matrix multiplication was used to transform this network into a coauthorship network. Eigenvector centrality was then used to infer the amount of access individual authors have to the research community as a whole. The use of eigenvector centrality as a measure of influence within the author network was then validated by correlating the centrality scores of a random sample of authors against independent ratings of desirability of those individuals' expertise. **RESULTS:** The coauthor network for rheumatoid arthritis, while not completely connected, showed a high degree of connectivity (mean degree: 26, network diameter: 5). Eigenvector centrality allowed the identification of key experts, with the highest scoring experts each providing direct access to approximately half of the whole network. Eigenvector centrality measures were a reliable predictor of mean desirability scores from ten raters ($F(1,9)=20.35$, $p=0.0015$, R-squared=0.69). **CONCLUSIONS:** Social network analysis of coauthor networks provides an efficient and robust method for the identification of expertise, and can be used as part of the systematic review process.

PRM224

SYSTEMATIC REVIEW APPROACHES FOR HTA: HORSES FOR COURSES?

Kenworthy J, Langham J, Chetty M
PHMR Associates, London, UK