nase alfa therapy. A lung function test ("index") separated a 2-year pre-index period from a 2-year post-index period for which intercepts and slopes were independently estimated. The comparator group included patients not yet reported to have received dornase alfa; their index lung function test was associated with their eighth or subsequent even-numbered birthday. Comparator patients could contribute more than one set of pre- and post-index periods and could also subsequently be included in the dornase alfa group. To account for the repeated use of patients, variance components were estimated at the patient level as well as the case level. Different subsets of the comparator cases were analyzed. **RESULTS:** There were 2230 dornase alfa patients; the comparator group included 5970 cases from 3517 patients. The estimated difference in change in slope was 0.73±.31 (P=0.020). Subsetting comparators to 4985 cases from 2836 patients not also in the dornase alfa group gave 0.61±0.32 (P=0.058); including each of those patients only the last time eligible gave 0.68±0.36 (P=0.059). Subsetting to 3662 cases from 2030 patients never on dornase alfa gave 0.32±0.34 (P=0.35). Patient-level variance components corresponding to difference in slope and difference in intercept were near zero and so were dropped. **CONCLUSIONS:** In longitudinal observational studies, patients should be included in each group for which they meet eligibility criteria, possibly multiple times (with appropriate covariance structures). This avoids bias from using future information to decide whether to include a patient and loss of power from limiting cases unnecessarily.

PRM140

AN APPLIED COMPARISON OF META-ANALYSIS TECHNIQUES USING BACILLE CALMETTE GUERIN VACCINE STUDIES

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Numerous assumptions and techniques are necessary to perform meta-analysis. Some overall structural guidelines and best practices on meta-analysis exist. However, few papers compare meta-analysis techniques in application. **OBJECTIVES:** To review primary meta-analysis methods and their assumptions. After methodology review, we applied various meta-analysis techniques to the data of various Bacille Calmette Guerin (BCG) vaccine studies and compared the results. **METHODS:** Of the currently available meta-analysis techniques, the most basic technique was applied first. Fixed effect models assume treatment effect homogeneity across studies. Then, random effect models and meta-regression were explored. Each technique explicitly models treatment heterogeneity. Lastly, the possibility of publication bias was tested through the use of a funnel plot. **RESULTS:** Treatment effect estimates differed depending on the meta-technique applied. When a fixed effect model was applied to estimate vaccination effectiveness against tuberculosis, the log odds ratio was −0.436 (confidence interval [CI]: −0.528, −0.344). After testing for heterogeneity and fitting a random effects model, the estimate was reduced to −0.741 (CI: −1.120, −0.352), and the CI became wider. When covariates were added to the model to explain the heterogeneity, the effect of treatment was reduced even further. **CONCLUSIONS:** Meta-analysis results are sensitive to the selected studies and the methodology applied. Ensuring that proper techniques are used is critical to estimate an unbiased outcome.

PRM141

COMBINING AN ORDERED LOGIT MODEL WITH INDIVIDUAL PATIENT-LEVEL DATA TO ROBUSTLY ESTIMATE WITHIN-CATEGORY VISUAL ACUITY STARTING DISTRIBUTIONS: AN INNOVATIVE MODELING APPROACH IN THE CASE OF VITREOMACULAR TRACTION

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OBJECTIVES: The ISPOR Task force (TF) on Good Research Practices for RCT-CEA aims to foster improvements in the conduct of trial-based economic analysis. The TF recognizes the sample size of randomized clinical trials (RCT) as one of the challenges for trial-based economic analysis, as it is typically based on the primary clinical outcomes only. In the case of vitreomacular traction (VMT), using RCT individual patient-level data (IPD) to establish model starting distributions within visual acuity (VA) health-states magnifies this challenge due to the small patient numbers within each relevant VA health-state. Our objective was to develop an innovative approach to robustly estimate patient within-category VA health-state starting distributions. **METHODS:** A baseline VA-adjusted ordered logit model used RCT IPD to predict a patient's VA starting distribution as a function of treatment allocation, macular hole, vitreomacular adhesion and previous vitrectomy status. The observed ordinal variable consisted of 6 response categories i.e. VA state as a function of an unmeasured, continuous, latent variable Y whose values determine the patient's VA-state dependent specific VA thresholds. **RESULTS:** Treatment allocation was not a significant predictor for within-category VA health-state starting distributions (at the 5% significance level), while MH, VMA and previous vitrectomy status were significant and retained in the final model. The proportional odds assumption was tested using a likelihood ratio test and confirmed that the relationship between each pair of VA health-states was the same (chi2 = 0.0906). **CONCLUSIONS:** In eye-disorders like VMT, estimating within-category VA health-state starting distributions requires a different approach due to the small number of IPD in each VA health-state. Using an ordered logit model allows a more accurate and robust estimation of within-category VA health-state starting distributions. Macular hole, VMA and previous vitrectomy status were significant predictors of a patient's within-category VA health-state starting distribution, while treatment allocation was not.

PRM142

USE OF BODY SURFACE AREA AS A DETERMINANT OF DOSE IN CANCER STUDIES

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OBJECTIVES: With the lack of alternative strategies for calculating the dose of cytotoxic drugs in chemotherapy regimens, body surface area (BSA), despite well-documented limitations, remains the most frequently used measure for dosing guidelines. This is based on the assumption that physiological variables related to drug metabolism and elimination, such as basal metabolic rate, renal and hepatic function, vary between individuals according to BSA. BSA has traditionally been calculated using a formula derived from Du Bois and Du Bois and published in 1916. It is recognised this is probably not the most accurate method of calculating chemotherapy doses, since the formula was derived from metabolic studies using a small number of subjects. The practice of calculating chemotherapy dose adjusted to BSA has drawn attention due to its lack of clear scientific basis, and lack of applicability to different genders, disease states, and culture. **METHODS:** A systematic literature review was conducted using CRD methodology to establish the average BSA in cancer patients in Europe and the variability between genders, tumour types, and cultures. **RESULTS:** Meta-analysis of the findings showed significant differences between genders overall (females 1.72m^2 vs males 1.88m^2), between different tumour types (range 1.68m^2 to 1.93m^2) and between different European countries (range 1.74m^2 to 1.83m^2). However, statistical modelling showed that a BSA of 1.80m^2 approximated the population mean and identified the dispersion to be 1.72-1.87m^2 and was therefore a valid approximation for the majority of cancer patients in Europe. **CONCLUSIONS:** Establishing a patient's BSA is important in determining the appropriate dosage regimen, but the population norm serves as a useful basis for drugs administered in a fixed dose formulation.

PRM143

CLUSTER ANALYSIS AND PRINCIPAL COMPONENT ANALYSIS TO ASSESS THE VARIABILITY OF DATA IN COST EVALUATIONS: METHODS AND APPLICATIONS IN ONCOLOGY

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OBJECTIVES: In the context of today's highly globalized environment, the interest in the transferability of data of cost evaluation in health care has strongly intensified. A methodology is proposed to explore similarity versus dissimilarity of cost evaluation data in adult sarcoma and hence their transferability across locations (France and Italy). **METHODS:** Main steps are (i) definition of the objects (e.g. countries), identification of potential variability factors, selection of final variability factors, and construction of variability areas (e.g. unit cost of personnel); (ii) measure of distances between the objects, determination of clusters and construction of a hierarchical tree using the cluster analysis (CA); (iii) projection of the objects into factorial planes and linkage between objects and areas of variability using principal component analysis (PCA). Suggested methods are applied to an international cost evaluation performed within the European network of excellence CONnectiveTIssuesCAncersNETwork (CONTICANET). **RESULTS:** Twelve objects and 16 areas of variability were defined. CA shows four clusters meaning that data belonging to different clusters are dissimilar (i) chemotherapy in France, (ii) follow-up with relapse in Italy, (iii) diagnosis, surgery, chemotherapy, radiotherapy, and follow-up without relapse in Italy, (iv) diagnosis, surgery, radiotherapy, follow-up without relapse, and follow-up with relapse in France. PCA opposes (i) follow-up with relapse in Italy to diagnosis, radiotherapy, and follow-up with relapse in France; (ii) chemotherapy in France to follow-up without relapse in France. In sarcoma patients, transferability is then limited for chemotherapy during the initial treatment in France and the follow-up with relapse in Italy. Diagnosis cannot be transferred either between France and Italy regarding the quantities and unit costs of the biopsies. **CONCLUSIONS:** Using CA and PCA enables health care professionals to rapidly emphasize the variability of data and therefore to determine the transferability of cost evaluations across locations.

PRM144

CARDIOLOGISTS' KNOWLEDGE AND AWARENESS OF GUIDELINES FOR MEDICAL DEVICE SAFETY AND PRODUCT RISK MANAGEMENT

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OBJECTIVES: To investigate the knowledge, awareness and attitudes of cardiologists about the risk and benefits associated with medicines and medical devices and equipment, and of how well they are regulated and communicated in Turkey. **METHODS:** An on –line questionnaire has been developed which include questions about the level of education and experience; perceptions of the risks and benefits associated with medicines and medical devices; experiences of medicines and medical devices; perceptions of and attitudes towards the regulation of medicines and medical devices; attitudes towards the communication of information about the risks and benefits associated with medicines and medical devices; usage of and trust in communication of information about the risks and benefits associated with medicines and medical devices. **RESULTS:** A total of 250 members of the Turkish

Society of Cardiology responded to the on – line questionnaire. The majority of respondents agree that medical devices and equipment are not adequately regulated at the moment in Turkey. Moreover they believe that manufacturing companies have too much influence on how medical devices and equipment are regulated. The majority of the cardiologists value recommendations from colleagues. When making risk/benefit decisions, surgeons rely on sharing information about the merits and drawbacks of particular devices within their local peer groups, especially Turkish Society of Cardiology, rather than using more formal avenues. Cardiologists would be most likely to turn to the risk assessment unit at the hospital they work for. Then they woul like to report the adverse events to the Ministry of Health of Turkey General Directorate of Pharmaceuticals and Pharmacy, which is the main regulating institution in Turkey. **CONCLUSIONS:** The qualitative analysis results indicate that efforts should be directed to inform cardiologists about the functioning of General Directorate of Pharmaceuticals and Pharmacy and the guidelines of medical device regulations.

PRM145

A MAXIMUM LIKELIHOOD SIMULATION TECHNIQUE FOR ESTIMATING ADVERSE EVENT RATES FROM PUBLISHED TRIALS

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OBJECTIVES: Clinical trial publications commonly report only adverse event (AE) rates occurring above an arbitrary threshold. Our objective was to devise a meta-analysis technique that allowed trials to be included even when AE rates fell below thresholds. **METHODS:** A maximum likelihood simulation (MLS) was devised that assumed all AE trial results lay in the same binomial distribution truncated by reporting thresholds. AE data from osteoarthritis trials were retrieved. The MLS was executed using the random number generator and binomial distribution function of CafeSim, a Java modeling toolkit. Ten million iterations, needed for convergence, were run for each tenth of a percent up to the highest rate reported. For each iteration the values generated from the binomial function were compared to the published AE rates and/or thresholds. The rate with the most matches was designated the point estimate (PE). The range from the 2.5 to 97.5 percentiles of matches was the 95% confidence interval (CI). Verification was conducted for 2 AEs of 2 compounds. Results for 2 AEs reported in all etoricoxib trials were compared to Comprehensive Meta-Analysis (CMA) results. Results for 2 AEs below reporting thresholds of one or more diclofenac trials were compared to results from equivalent SAS code using RANBIN and PROC FREQ. **RESULTS:** The MLS estimated PEs and CIs for the etoricoxib AEs within 0.001 of CMA (hypertension PE = 0.058 (0.059 for MLS), CI [0.051, 0.065]). The MLS executed in CafeSim estimated PEs and CIs for the diclofenac AEs within 0.002 of those estimated in SAS, identical for hypertension, (PE = 0.027, CI [0.022, 0.032]). When trials reported widely differing rates the MLS converged slowly. The MLS estimated 0.000 when no trials reported the AE rate. **CONCLUSIONS:** An MLS technique assuming a common binomial distribution may provide a useful estimate of AE rates when they occasionally fall below reporting thresholds.

PRM146

AN EXCEL CALCULATOR TOOL TO PERFORM META-ANALYSIS

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INTRODUCTION: An Excel calculator tool was created to perform meta-analysis in a rapid manner. The tool performs both direct and indirect treatment comparisons. A recent meta-analysis study examining rheumatoid arthritis (RA) was replicated using the calculator. **OBJECTIVES:** To quickly perform meta-analyses, both direct and indirect treatment comparisons, using Microsoft Excel. **METHODS:** We used a random effects DerSimonian and Laird model by inputting the number of studies and binary outcomes variables to report the Relative Risk (RR) for each study and a pooled overall RR. The Q-statistic and the I-squared statistic were used to examine heterogeneities across studies. Indirect treatment comparisons between specific studies were performed *post hoc*. Indirect pair-wise comparisons were also performed between studies. **RESULTS:** Three studies (Lipsky, Keystone, and Klareskog) were examined, comparing a combination of tumor necrosis factor (TNF) inhibitors plus methotrexate (MTX) to MTX monotherapy. Each study was evaluated using the number of patients achieving American College of Rheumatology (ACR) scores 20, 50, and 70. To test the Excel calculator, the number of patients obtaining ACR20 scores was used in the replication. The overall RR was 1.89 (95% CI: 0.89, 4.00), which was not statistically significant (p-value=0.10). There were significant heterogeneities across treatments and the I-squared statistic was 96.2% (p-value<0.000). The Lipsky and Keystone studies had statistically significant treatment effects relative to the Klareskog trial: Lipsky vs. Klareskog: RR 2.23 (95% CI: 1.37, 3.64, p-value=0.001); Keystone vs. Klareskog: RR 2.17 (95% CI: 1.63, 2.89, p-value<0.001). **CONCLUSIONS:** The meta-analysis Excel calculator is a simple and quick way to run random effect models with binary data. The replication output matched the results of the original paper.

PRM147

COMPARISON OF INDIRECT AND MIXED TREATMENT COMPARISON (MTC) META-ANALYSIS TECHNIQUES USED IN THE EVALUATION OF NEW PROTEASE INHIBITORS FOR THE TREATMENT OF CHRONIC HEPATITIS C

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OBJECTIVES: To compare indirect and MTC meta-analysis techniques used in the evaluation of the protease inhibitors, boceprevir and telaprevir, in combination with peginterferon alfa and ribavirin for the treatment of patients with genotype 1 chronic Hepatitis C. **METHODS:** A systematic search of the literature was conducted in EMBASE and MEDLINE (January 2008 to May 2012) to identify studies that utilised either indirect or MTC meta-analysis techniques to derive the relative treatment effect between boceprevir and telaprevir. A qualitative comparison was made between the methodologies and results of the identified studies. **RESULTS:** Two publications were identified: a conference poster (Diels *et al.*) and a full publication (Cooper *et al.*). The main difference between the methodologies is that Cooper *et al.* used an adjusted indirect comparison and a random-effects MTC model whereas Diels *et al.* used a fixed-effects MTC model. Diels *et al.* included three further studies that compare peginterferon alfa-2a and alfa-2b without active therapies. Cooper *et al.* conducted a random-effects adjusted indirect comparison that included two additional telaprevir trials that were excluded from Diels *et al.* The primary outcome in both studies was the proportion of patients achieving sustained virologic response. Diels *et al.* reported no significant difference in treatment naive patients and a significant effect in favour of telaprevir for treatment experienced patients. When Diels *et al.* applied a random-effects model the effect of telaprevir being superior in treatment experienced patients was non-significant. The results reported by Cooper *et al.* showed no significant difference between boceprevir and telaprevir, and did not vary in sensitivity analyses. **CONCLUSIONS:** Comparison of these two studies highlights considerable methodological differences between the two approaches, which result in differing conclusions. While MTC methods are growing in popularity and importance, certain nuances of approaches can result in important differences in interpretation.

PRM148

SAMPLE SIZE AND POWER CONSIDERATIONS IN NETWORK META-ANALYSIS

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OBJECTIVES: To extend well-established methods for sample size in power calculations in pair wise meta-analysis to the scenario where multiple treatments are being analyzed in a network meta-analysis **METHODS:** We derive methods of approximating the 'effective number of patients' in indirect comparison meta-analysis where no head-to-head evidence is available. We calibrate these approaches with conventional approaches for estimating the required sample size and power in pair wise meta-analysis. **RESULTS:** The calibration of the above two methods allow for a simple assessment of the power and strength of evidence for each treatment comparison in a network of treatments. The resulting measures are 1) the statistical power associated with each treatment comparison made in a network meta-analysis; 2) the effective number of patients for each comparison contrasted, which can be contrasted with the required sample size for the particular comparison to gauge the strength of evidence. We provide an illustrative example using data from a network meta-analysis of interventions for smoking cessation. **CONCLUSIONS:** The proposed measured follow the format of well-known sample size and power measures. They are easy to calculate and will resonate with a statistically non-sophisticated audience.

PRM149

A RANDOM UTLITY MODEL USING A TRANSACTION COST POLITICS APPROACH TO ADJUST HEALTH SYSTEMS TO ECONOMIC TRANSITION

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OBJECTIVES: This research uses a comparative analysis framework between national health care systems and continues the theoretical development of the 3P theory. It demonstrates that sets of cost reduction strategies and by physicians, Pharmacists and Patients as well as different meanings of cost (cost the system, cost to the physician, and cost to the patient) choices per group of physicians lead to very different decision points in each system and variations in sets of clinical choices for similar patients. A random utility model is proposed. **METHODS:** Data are extracted from the endep/biomed database for 600 physicians, transcripts from qualitative focus groups and estimates from the centralized database of 6 patients' surveys on cost of medicines (www.endeplux.org). The thinking about cost is classified in Cost S (cost to the System), Cost Ph (cost to the Physician) Cost Pa (cost to the Patient).The conceptual framework has been mainly developed from pair of country comparisons, especially from the French, German and Italian physicians analysis (Huttin, Andral; 2003; Atella et als; 2003; Brenner et als, 2002). **RESULTS:** A comparative intercountry framework is used to weight differently combinations of (Cost S, Cost Ph, Cost Pa) in the system. A generalization will be proposed with a list of different possible combinations aCostS+bCostPh+CostPa for each physician ij among N physicians in J Health financing systems. **CONCLUSIONS:** This research step aims to propose a link between a research line on transaction cost politics and several statistical developments for a stated revealed preference disease econometric model. It will help to identify the type of random utility models that would clearly model how variations of preferences from Physicians, Pharmacist, Patients that could help to manage variations between different national health care financing systems.

PRM150

LATENT TRANSITION ANALYSIS AS A TOOL FOR ANALYSING CLINICAL DATA

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OBJECTIVES: To uses Latent Transition Analysis (LTA) to assess the difference in the change in severity of a Neurological disorder between patients in two treatment groups. The patients in the study were assigned to one of two treatment groups Active or Placebo over a period of 6 months and the results to a question-