caused by the bounded scale. Various analytical approaches have recently been proposed for short-form 36 items, however, less attention is paid to longitudinal designs. We examined the use of different regression models to analyze HRQL data over time using two empirical examples. METHODS: The HRQL measures employed in our empirical examples were the generic SF-6D and the disease-specific Stroke Impact Scale (SIS). Data came from the German KoRA cohort study and from a clinical setting, respectively. We fitted mixed and marginal beta models and explain the conceptual difference between these two model classes, namely the population-averaged and the subject-specific perspective. We compared overall fit and predictive accuracy of the models to the commonly used linear mixed model (LMM) and SF-6D data were highly skewed to the left and the beta distribution exhibited a pronounced ceiling effect. In both examples, the beta distribution fitted the data better than the normal distribution. Beta regression accounted for the fact that predicted values must fall into the bounded support of the scales and overall fit was evaluated with deviance residuals for both LMM and beta regression. Among improved patients were 1.20 and 1.05 for physical and total score, respectively, indicating large changes, and 0.59 for emotional domain, indicating moderate changes.

RESULTS: The beta regression specifications accounted for the specific characteristics such data typically have. However, our results show that, in practice, estimates may only differ slightly from those of commonly used methods.

PRM135
VALIDITY, RELIABILITY AND RESPONSIVENESS OF THE SPANISH MINNESOTA LIVING WITH HEART FAILURE QUESTIONNAIRE
Bilbao A1, Escobar A1, Fernandez-Soto ML2, Gonzalez-Saenz de Tejada M2, Lafuente I1
1Basurto University Hospital (Laaskidetz), Bilbao, Bizkaia, Spain, 2Donostia University Hospital (Chuautzeda), Donostia, Guipuzcoa, Spain, 3Galdakao-Usansolo University Hospital (Chuautzeda) - CIBER Epidemiologia y Salud Publica (CIBERESP), Bilbao, Bizkaia, Spain, 4Galdakao-Usanoso Hospital (Chuautzeda), Galdakao, Bizkaia, Spain

OBJECTIVES: The Minnesota Living with Heart Failure Questionnaire (MLHFQ) is one of the specific instruments measuring quality of life in patients with heart failure. It comprises 21 items conforming a total score, as well as two domains: the physical and the emotional. The aim of this study was to evaluate the reliability, validity, and responsiveness of the Spanish MLHFQ. METHODS: Patients completed the MLHFQ and the SF-12 during their hospitalization for heart failure (n = 1175), and 6 months after discharge (n = 473). Reliability was assessed by Cronbach’s alpha coefficient. Convergent factor analysis (CFA) for categorical variables was used to study construct validity. Convergent validity was assessed by correlation of the SF-12 and the SF-36. To study known groups validity, MLHFQ at 6 months were compared according to readmission. Responsiveness was evaluated by effect sizes and according to patients classified as improved, equal, or worsened than at baseline. RESULTS: Cronbach’s alpha was >0.80 for the three domains. CFA confirmed the two factor model, with factor loadings ranging from 0.56 to 0.87. Both Tucker-Lewis and Comparative Fit indexes were >0.90, but the root mean squared error of approximation was >0.08. The highest correlations were obtained between MLHFQ and SF-12 physical domains (r = 0.55), and between the emotional MLHFQ and mental SF-12 domain (r = 0.53), supporting the convergent validity. The correlation between MLHFQ and SF-12 physical domains was >0.50, and was >0.40 between scores with patient were with readmission (P < 0.0001). Responsiveness parameters among improved patients were 1.20 and 1.05 for physical and total score, respectively, indicating large changes, and 0.59 for emotional domain, indicating moderate changes. CONCLUSIONS: The Spanish MLHFQ is valid, reliable and responsive 6 months after discharge for patients hospitalized with heart failure. Because of its simplicity and ease of application, it may be useful in routine practice and clinical research. Further, its cross-cultural characteristics make it very useful for comparisons among countries.

PRM136
A UTILITY SINGLE SCORE DERIVED FROM SHORT FORM-36 AND HEALTH ASSESSMENT QUESTIONNAIRE IN PATIENTS WITH ANTIPHOSPHOLIPID ANTIBODY SYNDROME: A METHODOLOGICAL PROPOSAL
Abreu MM1, Domingues V1, Sigorelli P1, Eannes S1, Levy KA1
1Universidade Federal de São Carlos, São Carlos, São Paulo, Brazil, 2New York Presbyterian Hospital/Weill Cornell Medical College, new york, NY, USA, 3Hospital Universitário Pedro Ernesto, Rio de Janeiro, São Carlos, Brazil, 4Fernandes Figueira Institute, Rio de Janeiro, Brazil, 5Erasmus University Rotterdam, Rotterdam, The Netherlands

OBJECTIVES: To propose a single score for quality of life (Qol) derived from the SF-36 and the HAQ in patients with APS in a tertiary care center. METHODS: It is a cohort study. Sample was stratified in two groups according to the numbers of changes in the worst 12 months over a period of two groups: Group 1 (12 changes in 12 months) and Group 2 (> 6 changes in 12 months). This change was due to INR oscillation. To assess quality of life, SF-36 and HAQ instruments at baseline and after 12 months of follow-up were used. To derive the single score, a descriptive analysis was performed. Principal component analysis (PCA) was done to reveal the internal data structure that explains the data variance. APS score was calculated by the sum of the values obtained by weighting the factor scores for each component by the proportion of variability explained by the respective component. To measure APS score consistency to patient class, we performed a bootstrap analysis (1000 replicates) to assess whether APS score revealed a consistent and meaningful expected value. RESULTS: Group 1 had a worse quality of life. To test it, we evaluated APS score into the two time points. To corroborate these results, we applied repeated measures ANOVA technique. For all statistical tests, the significance level used was < 5%. RESULTS: Group 1 had a worse quality of life. To test it, we evaluated APS score into the two time points. To corroborate these results, we applied repeated measures ANOVA technique. For all statistical tests, the significance level used was < 5%.

PRM137
REMINDERS HELP IMPROVING COMPLETION RATE OF HOME-ADMINISTERED LIFESTYLE QUESTIONNAIRES
Wiederkher B1, Streu M2, Faure C1, Fournie X2
1Registre-Mapi, LYON, France

OBJECTIVES: To administer a questionnaire to 14,000 women in order to measure various aspects of women’s lifestyle, including sensitive habits, and health. METHODS: A first population-based mailing was sent to around 31,000 women, inviting them to complete a questionnaire on a dedicated website or on paper. Women who did not initially respond were reminded to complete the questionnaire first through an additional mailing and then, for the ones who still did not respond, through telephone calls. Participants were offered the possibility to complete the questionnaire over the telephone. Each reminder was performed after a 3-week waiting period. RESULTS: Among the 30,917 women contacted, 26.0% completed initially the questionnaire. After the first reminder, the questionnaire was completed by 18.6% of the women who did not respond to the first mailing and, after the second reminder, by 24.2% of the women who did not respond after the first reminder. The first mailing followed by the two reminders resulted in a 52.4% completion rate of the questionnaires. Questionnaires received after the first mailing, then after the first and second reminder accounted for respectively 49.6%, 26.9% and 23.4% of the total amount of completed questionnaires. When offered the possibility to complete the questionnaire on paper or on a dedicated website, only 18.8% of the women choose the on-line method. During the telephone call of the second reminder, when offered the possibility to send the questionnaire over the telephone (53.7%). CONCLUSIONS: The methodology employed resulted in an overall good completion rate (52.4%). The objective of 14,000 completed questionnaires would have not been achieved without proactive and direct to subject contacts using reminders, including telephone contacts, allowing finally a two-fold increase of the initial responders rate.

RESEARCH ON METHODS - Statistical Methods

PRM138
A PROPENSITY TO GET IT RIGHT: A MONTE CARLO SIMULATION STUDY COMPARING STATISTICAL METHODS TO OBTAIN CORRECT COST-EFFECTIVENESS ESTIMATES IN OBSERVATIONAL STUDIES
van Gils CWM1, Goossens LMA2, Redekop WK3
1Erasmus University, Rotterdam - ClausSmithKline, Zeist, The Netherlands, 2Erasmus University Rotterdam, Rotterdam, The Netherlands

OBJECTIVES: Estimates of real-world cost-effectiveness are mostly based on observational data. While in randomized clinical trials the assignment of treatment to patients is randomized, observational studies are subject to non-random selection based on a variety of factors. These factors can lead to selection bias, which may cause the results of observational studies to differ from those of randomized controlled trials. METHODS: We performed a Monte Carlo simulation study comparing different methods to estimate real world cost-effectiveness. PS, IPTW, and IPD methods were compared in a situation where the PS was known. Simulations were performed to study the performance of the methods. The outcome we were interested in measuring was the difference in cost per quality-adjusted life-year (QALY) between two treatments. RESULTS: The simulations showed that the selection bias was reduced by these methods, but PS had the worst bias. In accordance with these results, a simulation study on the performance of these methods for estimating the average treatment effect in the treated (ATT) found that the ATT was underestimated when not accounting for selection bias; however, ATT was underestimated when accounting for selection bias. CONCLUSIONS: PS, IPTW, and IPD methods are useful and can improve the performance of observational studies. These methods can help to reduce selection bias and thus improve the performance of observational studies.

PRM139
INCLUDING PATIENTS IN MULTIPLE GROUPS AND MULTIPLE TIMES IN THE SAME GROUP IN LONGITUDINAL OBSERVATIONAL RESEARCH: A CYSTIC FIBROSIS EXAMPLE
Nadal A485
4ICON Late Phase & Outcomes Research, San Francisco, CA, USA

OBJECTIVES: In longitudinal observational studies, patients can meet eligibility criteria for more than one group and can be eligible multiple times for the same group. We used Epidemiologic Study of Cystic Fibrosis data to explore different inclusion decisions when evaluating dornase alfa treatment. METHODS: The dornase alfa group included patients enrolled ≥2 years before starting consistent dor-
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 who did not report 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 subselect into the index impaired lung function 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 ± 0.11 (P = 0.005). Subsetting comparators to 4985 cases from 2836 patients not also in the dornase alfa group gave 0.61 ± 0.12 (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 ± 0.14 (P = 0.35). Patient-level variance component ratios were sensitive to the selected studies and the methodology applied. Ensuring that proper techniques are used is critical to estimate an unbiased outcome. RESULTS: 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-analysis technique applied. When a random-effect model was applied to estimate vaccination effectiveness against tuberculosis, the log odds ratio was −0.436 (confidence interval: [−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.

PM141
AN APPLIED COMPARISON OF META-ANALYSIS TECHNIQUES USING BACILLE CALMETTE GUERIN VACCINE STUDIES
Lewis-Beck C1, Baser B2, Baser O3
1STATMed Research/The University of Michigan, Ann Arbor, MI, USA
2STATMed Research/Pharmerit, Ann Arbor, MI, USA
3Pharmerit International, York, UK
Numerous assumptions and techniques are necessary to perform meta-analysis. Some overall structural guidelines and best practices on meta-analysis exist. However, various papers comparing 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-analysis technique applied. When a random-effect model was applied to estimate vaccination effectiveness against tuberculosis, the log odds ratio was −0.436 (confidence interval: [−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.

PM142
SUCCESS OF BODY SURFACE AREA AS A DETERMINANT OF DOSE IN CANCER STUDIES
Trappe R1, Cooke C2, Healey R1, Johnson R1, Wiener C2
1Universitätsklinikum Schleswig-Holstein, Kiel, Germany, 2Complete Clarity, Macksville, New South Wales, UK
OBJECTIVES: With the lack of alternative strategies for calculating the dose of cytotoxic chemotherapy regimens, body surface area (BSA), despite well-documented limitations, remains the most frequently used measure for dosing guidelines. OBJECTIVES: To determine the suitability of dose calculation based on the assumption that physiological variables related to body function and metabolism, and 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 recognized this is probably not the most accurate method of calculating chemotherapy doses, since the formula was derived from a small number of subjects. The practice of calculating chemotherapy dose adjusted to BSA has drawn attention due to its lack of 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 1.72m² vs males 1.86m²), between different tumour types (range 1.74m² to 1.93m²). Furthermore, it was shown that the BSA of 1.8m² approximated the population mean and identified the dispersion to be 1.72-1.87m² and was therefore a valid approximation for the majority of cancer patients in Europe. CONCLUSIONS: Considering 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.

PM143
CLUSTER ANALYSIS AND PRINCIPAL COMPONENT ANALYSIS TO ASSESS THE VARIABILITY OF DATA IN COST EVALUATIONS: METHODS AND APPLICATIONS IN ONCOLOGY
1PharmiMed International, York, UK, 2PharmiMed International, York, UK, 3Clínica Sant Joan de Déu, Barcelona, Spain, 4Institut Jules Bordet, Brussels, Belgium
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 effects 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 CONNeCTiveTis- sueNetwork (CONNeCTANET). 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 Italy. Sarcoma patients, transferability is then limited for chemotherapy during the initial treatment in France and the follow-up 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.

PM144
CARDIOLOGISTS’ KNOWLEDGE AND AWARENESS OF GUIDELINES FOR MEDICAL DEVICE SAFETY AND PRODUCT RISK MANAGEMENT
Rożkurt E1, Yıldırım B2
1Turkish Quality Security Institute, Ankara, Turkey, 2ED University, Ankara, Turkey
OBJECTIVES: To investigate the knowledge, awareness and attitudes of cardiologists about the risk and benefits associated with medicines and medical devices, 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