methods have been developed for synthesis of diverse sources of evidence: multiple outcomes, potentially dependent, may be considered endpoints or other 

external evidence. These methods were applied to an example in rheumatoid arthritis where outcomes such as the Health Assessment Questionnaire (HAQ), the Disease Activity Score (DAS-28) and the American College of Rheumatology (ACR20) are synthesized. External information about correlations between the outcomes was included in the form of informative prior distributions. Estimates of HAQ were then mapped onto EQ-SD. Also in an alternative approach, the multivariate framework was applied to jointly the utility estimates and the clinical effect of other outcomes. RESULTS: The use of multivariate meta-analysis led to reduced uncertainty around the effectiveness and utility estimates. Combining the HAQ with DAS-28 gave a 19% reduction in the uncertainty around the estimate of HAQ and also 16% around the estimate of EQ-SD. CONCLUSIONS: By allowing all clinical and external evidence to be incorporated in economic evaluations of new health technologies, this multivariate approach to meta-analysis can lead to reduced uncertainty and hence more efficient decision-making in health care.

PRIM19 NETWORK META-ANALYSIS OF MULTIPLE OUTCOMES: A SIMULATION STUDY AND APPLICATION

Achana F, Dequen P, Gray L, Cooper NJ, Abrams KR, Owen RE
University of Leicester, Leicester, UK

The usefulness of a multivariate approach to compare treatments in the context of pairwise meta-analysis has been widely demonstrated in the literature. However, this approach has not yet been considered for multiple comparisons. We believe that extending such methodology to network meta-analysis (NMA) will allow the precision of relative treatment effectiveness and relative treatment impact of outcomes to be examined. OBJECTIVES: To extend standard NMA to incorporate multiple outcomes of interest and evaluate the use of multivariate NMA models through simulated and real datasets. RESULTS: We have developed a multivariate model to account for the correlation between multiple outcomes. The potential benefits of this method were demonstrated in a simulated example comparing univariate and bivariate NMA models for continuous outcomes. We further explored the application of a common multivariate NMA model for a case study model of obesity pharmacological interventions for weight circumference, weight change and BMI change from baseline. RESULTS: The simulation study showed that through the use of multivariate NMA the precision in relative treatment effectiveness was increased when compared to standard univariate NMA. This held true under multiple scenarios testing model parameters including both within- and between-outcome correlations. Similar findings were obtained from the application to the example data set in obesity. CONCLUSIONS: This method proves particularly useful in reducing uncertainty around relative effectiveness estimates when the outcomes included for analysis are highly correlated. However, the advantages of the multivariate NMA are limited where there is little correlation between outcome measures. Further work will expose the applicability of multivariate NMA methods to different types of outcomes such as binary outcome measures.

PRIM192 HANDLING VARIABILITY IN TIME ENDPOINTS IN MULTI-CENTRE TIME AND MOTION (T&M) STUDIES: A CASE STUDY OF ERTHYPROFEOSEIS-STIMULATING AGENTS FOR ANTI-TUBERCULOSIS MANAGEMENT IN PATIENTS IN ITALY

Kritikos P1, De Cock E1, Prokoskovsky I1, Payne KA2, Tomczak R2
1Evidera, London, UK, 2Evidera, Barcelona, Spain

OBJECTIVES: In multi-centre Time and Motion (T&M) studies, time endpoints can be highly variable due to differences in centres practice. Our aim was to assess the impact of the type of analysis employed on the results of a T&M study. METHODS: Data from 133 patients were analysed in relation to each of the following: drug preparation, distribution, and injection, using three methods. Base case methodology included a random intercept generalised linear mixed model assumption gamma distribution with log link function to account for potential cluster centre clustering effect and non-normality of the outcome measure. The two alternative methods were: standard linear regression (assuming time data are normally distributed) and gamma regression with log link function (assuming time data are positively skewed), both of which do not account for centre clustering effect. Sample means and variability as measured by 95% confidence interval (CI) were also compared. RESULTS: For the base case, mean time was 0.53 min (95% CI: 0.39-0.68) for "preparation", 0.30 min (95% CI: 0.22-0.40) for "distribution", and 0.07 min (95% CI: 0.04-0.13) for "injection". Mean time resulting from the standard linear regression was markedly higher for "preparation": 0.66 (95% CI: 0.59-0.73), and similar for "distribution" and "injection": 0.34 (95% CI: 0.30-0.37) and 0.94 minutes (95% CI: 0.79-0.88), respectively. Using the gamma regression yielded slightly less results to standard linear regression: 0.65 (95% CI: 0.59-0.71), 0.31 (95% CI: 0.29-0.34), and 0.83 minutes (95% CI: 0.79-0.88), respectively. The base case scenario detected a "centre-clustering" effect, hence producing substantial variability included to both standard and gamma regressions. The mean variability in the data. CONCLUSIONS: Although mean task times remained relatively stable across the various methods, 95% CIs were substantially wider for random intercept model. If centre-clustering is detected, random effects regression models may be employed to produce valid confidence intervals around point estimates.

PRIM193 BAYESIAN NETWORK META-ANALYSIS TO ASSESS RELATIVE EFFICACY AND SAFETY OF CANFILGLOFIN IN PATIENTS WITH TYPE 2 DIABETES MELLITUS (T2DM) INADEQUATELY CONTROLLED WITH METFORMIN

Perozzi M1, Tauri V1, Abdou K2, di Paola J1, rivoli S1, Ciarm M1, Schroeder M2, Kaur V3, Nielsen AT1, Nihoahso S1, Neisalan C1, Hemels M1
1Amaris, London, UK, 2The Institute of Cancer Research, Sutton, UK, 3Janssen Pharmaceutica, Beerse, Belgium, 4Janssen Cilag, Birkerød, Denmark, 5Janssen UK, High Wycombe, UK, 6Consultant, Mumbai, India, 7Janssen Global Services LLC, Baranji, NY, USA

OBJECTIVES: To assess the relative efficacy and safety of canfilglofin (CANA), a sodium-glucose co-transporter 2 (SGLT2) inhibitor, and other oral antihyperglycaemic therapies to metformin suggests that CANA 300mg is associated with increased HbA1c reduction versus DPP-4 and dapagliflozin while CANA 100mg provides at least similar effects. Additionally, results suggest increasing relative efficacy of CANA over time versus dapagliflozin and CANA reached at least as large HbA1c reductions as liraglutide at 104w. Weight reduction was comparable to GLP-1s and substantially higher than all other classes. All classes showed significantly less risk of hypoglycaemia compared to SU.

PRIM194 ESTIMATING CHRONIC DISEASE PREVALENCE FROM CLAIMS DATA: REDUCING BIAS ACCOUNTING FOR DISEASED INDIVIDUALS WHO DO NOT GENERATE CLAIMS

Simpkinson J1, De G2, Drabo E3, Guerin A4
1Analysis Group, Inc., Boston, MA, USA, 2Analysis Group, Inc., New York, NY, USA, 3University of Southern California, Los Angeles, CA, USA, 4Analysis Group, Inc., Montreal, QC, Canada

OBJECTIVES: Claims data are often used to estimate the prevalence of chronic diseases, typically by dividing the number of patients with disease-related claims (e.g., ≥1 or ≥2 claims) by the total number of patients in the study sample. Such estimates will have a downward bias because not all diseased patients will generate disease-related claims within their enrollment period. This downward bias can be substantial for underserved diseases that lack effective treatments. We explored whether the empirical Bayes approaches, which are frequently used to estimate numbers of unobserved cases in ecological studies, were used to estimate the number of diseased individuals without claims, and provide which adjusted prevalence estimates. RESULTS: Out of 65 chronic conditions that can be identified within 1 year of claims, 2-206 had disease-related claims, comprised of n=1,422 with one claim, n=317 with two claims, n=134 with 3 claims, etc. The traditional method for estimating prevalence identified 4.9 cases per 10,000 persons. After applying the empirical Bayes approaches, the estimated prevalence increased to 7.9 cases per 10,000 persons, and became closer to published prevalence estimates based on non-claims data sources. CONCLUSIONS: In this example application, prevalence estimates based on data from claims with 60% or more by using empirical Bayes approaches to account for large numbers of diseased individuals who did not generate claims. The increased prevalence estimates were more consistent with the published literature.

PRIM195 APPLICATION OF COPULAS IN ECONOMIC EVALUATION

Gonzalo C1, Monleon A1, Diaz W2, Rodriguez C1, Broma M3, Ross M3
1University of Barcelona, Barcelona, Spain, 2Southern California, Los Angeles, CA, USA, 3Analysis Group, Ltee., Montreal, QC, Canada

OBJECTIVES: To apply the copulas distribution in economic evaluation from an example. This study analyses data from an observational prospective study of patients with allergic rhinitis in Spain (n=498). Main data were direct cost (€/2012) and Health Related Quality of Life (SF-12). We have calculated the goodness of fit for copulas (Gumbel copula, Clayton copula, Frank copula, Normal copula, Plackett copula (and T copula) based on the empirical process comparing the empirical copula with a parametric estimate of the copula derived under the null hypothesis. We have used inversion of Kendall’s tau method to fit copulas. A multivariate independence approach was generated by comparing copula with Spearman’s correlation coefficient. Such estimates were then replicated for a 100 times to obtain p-values by bootstrap method. RESULTS: Marginal distribution of direct cost was a 3-parameter Gamma distribution (shape=1.856, scale=0.55, location=10.952). Kendall’s tau correlation of the utility of Health Related Quality of Life was associated to a 1-gamma (shape=2.9253 and scale=0.1601). P-value range were 0.093 to 0.144 for independent distribution, 0.004 to 0.031 for Gumbel copula, 0.246 to 0.522 for Clayton copula, 0.545 to 0.814 for Frank copula, 0.403 to 0.716 for Normal copula, 0.373 to 0.628 for T copula and 0.30 to 0.478 for Plackett copula. Frank copula and Plackett copula had the best goodness of fit. Kendall’s Tau for Frank copula had a correlation of 0.4212. CONCLUSIONS: Copula distribution allows us to adjust the better the non-linear relationship between cost and effectiveness. Furthermore, this kind of approach could improve probabilistic sensitivity analyses.