ket access as well as potentially leading to significant price reductions. What do these changes mean for the industry? What are the main challenges and opportunities for companies and how can they best adapt? Many questions remain to be determined. Yet AMNOG sets the scene for a new Market access process in Germany, for which challenges can be foreseen. The industry will need to acquire new skills to interact with national Market access stakeholders, develop internal efficient processes to compile Benefit Dossiers, adapt the European launch sequence as well as investigate new Market access strategies, for example targeting subtarget population groups to demonstrate higher additional benefit or leveraging Phase IV data. **CONCLUSIONS:** Industry needs to prepare itself for developing their launch and commercial strategies in Germany as Germany is a key market from revenue, price referencing and credibility perspective.

PR4

ANALYSIS OF PRICE LEVELS OF PRESCRIPTION DRUGS AND DETERMINANTS OF INTERNATIONAL PRICE DIFFERENCES BETWEEN THE UNITED STATES AND SELECTED EUROPEAN COUNTRIES

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OBJECTIVES: Spending on prescription drugs in key OECD countries has increased by 50% or more in the last ten years, raising questions about overall system sustainability. The study analyses possible reasons for differences in prices and volumes consumed across key OECD countries, taking into account national differences in pharmaceutical policy and regulatory mechanisms. **METHODS:** Panel data modelling is used to investigate the effect of pharmaceutical pricing and reimbursement regulations, drug promotion, drug use, and competition on price levels. Data are from IMS Health and the US Federal Supply Schedule and include top-50 selling on patent and generic prescription drugs used in the study countries. Regulatory variables are included as dummy variables in the model. **RESULTS:** Preliminary results suggest that: a) cross-country price comparisons are only meaningful if the right prices are compared in each case. Here, we demonstrate how significant price differences are when ex-factory prices are compared and how these differences narrow down significantly when *public* prices are compared across countries; b) It seems that price differences of originator brands between the US and Europe have been exaggerated; generic prices are very often significantly lower in the US than in other countries; c) Cross-country public price differences and cross-country *ex-factory* price differences are not the same across the study countries; d) Off-patent originator brands account for a significant proportion of the price variation between US and the other study countries; e) Pricing regulation accounts for a considerable proportion of the variation in prices across the study countries; and f) Distribution and taxation can contribute significantly to the total cost of prescription medicines that health insurers pay. **CONCLUSIONS:** Price differences are significant when *ex-factory* prices are compared but are significantly reduced when *public* prices are compared across countries. Regulation, distribution, and taxes are key contributors to the total cost of medicines paid by insurers.

PODIUM SESSION II: MIXED TREATMENT COMPARISONS MATURE, IN ABSENCE OF SUFFICIENT HEAD-TO-HEAD COMPARISONS

MT1

IMPACT OF THE CHOICE OF PRIOR DISTRIBUTION ON RELATIVE EFFECT SIZES USING BAYESIAN NETWORK META-ANALYSIS

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OBJECTIVES: Bayesian network meta-analyses incorporate prior distributions ("priors") that are updated with new evidence to generate posterior distributions. The use of uninformative (vague) priors minimizes potential biases and promotes transparency. Guideline developers have recommended values for uninformative priors for binary outcomes. For continuous outcomes, the choice of priors is scale-dependent. In networks with heterogeneity and few studies, a more informed prior for estimation of between-studies standard deviation (σ) is justifiable, yet may impose subjectivity. Using a network meta-analysis of seven studies estimating the efficacy of three renal transplant immunosuppressants (tacrolimus, cyclosporine and belatacept), we estimated the impact of varying priors for σ to the relative effect sizes. **METHODS:** We established a clinically-plausible range for an uninformative prior distribution of σ. We then derived estimates for the indirect comparison of belatacept and tacrolimus expressed as true mean difference (TMD) in renal function, expressed as glomerular filtration rate (GFR; mL/min/1.73m^2); 95% credible intervals (CrI); and model fit (residual deviance and deviance information criterion). We conducted sensitivity analyses using more informed priors: half the uninformative range; a data-driven approach; half the data-driven range; and, as an extreme, a fixed-effect model ($\sigma = 0$). **RESULTS:** Using the uninformative uniform prior, U(0,20), the estimated TMD in GFR was 9.84 higher for belatacept than tacrolimus. This had the best model fit and the widest 95% CrI (−1.97, 20.51). As the upper bound of the prior distribution was restricted, the 95% CrIs narrowed yet the model fit degraded. The point estimate was stable. The narrowest informed prior was U(0,3) (TMD 9.84; 95% CrI 4.89, 15.90). **CONCLUSIONS:** In this analysis, the point estimates for TMD in GFR consistently favored belatacept, yet the CrIs and model fit were affected by the choice of prior for σ. Given the subjectivity in selecting priors for continuous outcomes, transparent reporting is essential.

MT2

THE USE OF CONTINUOUS DATA VERSUS CATEGORICAL DATA IN MTC: THE CASE OF HAQ MULTIPLIER IN RHEUMATOID ARTHRITIS

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OBJECTIVES: Each of the tumour necrosis factor alpha antagonists (anti-TNF-α) available to treat rheumatoid arthritis have demonstrated considerable efficacy in placebo controlled trials, but few head-to-head comparisons exist to date. This work estimates the relative efficacy among licensed anti-TNFs and highlights the advantages of continuous outcome measures in mixed treatment comparison models. **METHODS:** Relative efficacy was estimated using Bayesian mixed treatment comparison (MTC) models. Three different outcome measures were used; Risk ratios of achieving an ACR20 and ACR50 response (binomial outcomes) and the percentage improvement in HAQ score (continuous outcome). Five anti-TNF-α antagonists were included in the analysis; adalimumab, infliximab, etanercept, golimumab and certolizumab. **RESULTS:** All anti-TNF agents show a significant improvement over placebo across all outcome measures. The HAQ model outcomes provide evidence that all anti-TNF agents show improvement over infliximab. This effect is not found with the ACR outcomes for adalimumab and golimumab. Furthermore, the HAQ model indicates a superiority of etanercept over adalimumab. The evidence of certolizumab pegol providing improvement over golimumab, which can be found in the ACR outcomes, is not apparent in the HAQ outcomes. **CONCLUSIONS:** Continuous outcome measures make better use of the complete data than binomial measures and are therefore more sensitive to change. The results suggest that it may be the case, in mixed treatment comparison models, where the essence lies in detecting differences, a continuous outcome measure is more appropriate. Its enhanced sensitivity to change increases the power of the model to detect differences among treatments. The HAQ multiplier provides one such measure, but others exist.

MT3

A BAYESIAN APPROACH TO MODEL SELECTION PROCEDURES WITHIN MIXED TREATMENT COMPARISON FRAMEWORK

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OBJECTIVES: Model fit in Bayesian mixed treatment comparisons (MTC) is often assessed by the deviance information criterion (DIC). In some cases DIC is not conclusive. Our aim was to compare DIC with an alternative approach: formal Bayesian model comparison by estimating the posterior distribution over the model space. **METHODS:** DIC is a criterion which combines posterior mean of the deviance and deviance of posterior means. Models with lower DIC should be preferred, however if the difference in DICs is small the decision should not be based solely on DIC. Marginal data density (MDD) expresses probability of observing given dataset. Decision rule based on Bayesian model comparison is that the model with highest *a posteriori* probability should be chosen. Data from few systematic reviews indexed in Pubmed were extracted in order to find MTC datasets for which DICs for fixed (FEM) and random effects models (REM) are very similar. Two continuous variables datasets were chosen. Posterior distributions and DICs were estimated in WinBugs. The Newton-Raftery estimator of MDD was implemented in Java, together with the Gibbs sampler. In both cases, in which DIC was not conclusive, two *a priori* structures over the model space were assumed: an uniform distribution and one penalizing the models for the excessive number of parameters. **RESULTS:** In the first dataset difference in DICs was 1.3 (in favor REM), in the second dataset this difference was 2,0 (in favor FEM). In both cases REM turned out to have a higher value of MDD. Although a priori odds ratio was around 100:1 for FEM, the posterior distribution was in every case close to have probability of one (~0.9999) for the REM. **CONCLUSIONS:** Decision about model selection should include tools of formal model comparison, as conclusions coming from it are always interpretable and coherent within Bayesian inference.

MT4

MIXED TREATMENT COMPARISONS USING AGGREGATE- AND INDIVIDUAL-PARTICIPANT LEVEL DATA: AN EFFICIENT USE OF EVIDENCE FOR COST-EFFECTIVENESS MODELLING

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OBJECTIVES: Cost-effectiveness analysis must use all relevant sources of evidence to inform reimbursement decisions. Mixed treatment comparisons (MTC) extends the traditional pair-wise meta-analytic framework to facilitate the synthesis of information on more than two interventions. While most MTCs use aggregate data (AD), a proportion of the evidence base might be available at the individual level (IPD). This paper develops novel statistical models aimed to fully exploit the existing data, regardless of the format (i.e. AD or IPD). **METHODS:** We develop a series of novel Bayesian statistical MTC models to allow for the simultaneous synthesis of IPD and AD, while considering study and individual level covariates, and use these to inform a decision model. **RESULTS:** The effectiveness of home safety education and the provision of functioning smoke alarms (binary outcome – Yes/No) for the prevention of childhood injuries in the household was used as a motivating example. Case study included 20 trials (11 AD, 9 IPD), summing up to 11,500 participants. Seven strategies were defined and a network of evidence was constructed. Irrespective of the evidence format used, all models which did not consider information on covariate(s) showed equivalent results, i.e. more intensive interventions (providing education, equipment (with fitting) and home inspection) were more effective (OR vs usual care of 4.5 (95%