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HDL AS A HANDLE LEVELS OF EVIDENCE IN HEALTH ECONOMIC MODELLING

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OBJECTIVES: To address the practical and methodological issues associated with using low-evidence quality evidence in health economic modelling. METHODS: A cost-effectiveness model for disease-modifying drugs (DMDs) in multiple sclerosis (MS) in The Netherlands was used to assess how to deal with low-evidence quality evidence in health economic modelling. The model adopted a 10-year time horizon and a societal perspective. A Markov model was constructed based on EDS5 staging in MS, including relapse. The central focus was on disease progression — instead of relapse — which appeared to be the driver of the cost-effectiveness outcomes. The main data source was a recent Cochrane review estimating relative efficacy and acceptability of DMDs in relapse-remitting MS. Other data sources included additional published literature, clinical trials, and official guidelines. The analysis was based on the Cochrane review data showed that interferon beta-1a-RA (Rebif) is cost-effective over interferon beta-1a-A (Avonex) (dominant) and interferon beta-1b (E27.654/QALY), but that interferon beta-1a is not cost-effective over glatiramer acetate. However, for disease progression, the level of evidence is considered very low (level 1) for all drugs, except interferon beta-1a-R (moderate - level 3), implying a gold standard is lacking for handling levels of clinical evidence in health economic models. One alternative, presented here, would be to assume placebo efficacy in such cases.

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BEST PRACTICES FOR NETWORK META-ANALYSIS METHODOLOGY: COMPARATIVE EFFECTIVENESS OF INTERFERON-BETA THERAPIES IN RELAPSING-REMITTING MULTIPLE SCLEROSIS

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OBJECTIVES: To evaluate different statistical methodologies in a network meta-analysis (NMA) comparing the effectiveness of interferon-beta (IFN) therapies across all IFN DMDs in relapsing-remitting multiple sclerosis (RRMS) to determine potential best practices. METHODS: A systematic literature review (1996-2014) was conducted to identify randomised, controlled trials of FDA- and EMA-approved IFN DMDs in RRMS, including subcutaneous (SC) IFN-β1a (44µg or 22µg 3x/wk), SC IFN-β1b (125µg every 2wks), intramuscular (IM) IFN-β1a (30µg 1x/wk), and SC IFN-β1b (250µg EOD). Data were extracted for patients relapse-free, patients without disability progression, and patients without new MRI activity at study end. Results were reported in two aspects: effects Bayesian network meta-analysis, and sensitivity analyses investigated results using different analysis frameworks or effects distributions. RESULTS: 644 articles were retrieved; 41 met inclusion criteria and included evaluable data in evidence network. Ten comparisons in the network were based on at least five trials. The network includes 33 direct comparisons across all MS trials. Significant results were found in the overall comparison of IFN therapies. CONCLUSIONS: Future studies should include all IFNs, and also generalizability of the various results obtained by using these models and poses problems to all stakeholders involved in HTAs.

PM79

INVESTIGATING THE IMPACT OF STRUCTURAL CHANGES IN A NICE SINGLE TECHNOLOGY APPRAISAL COST-EFFECTIVENESS MODEL

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OBJECTIVES: One of the major critiques with submitted manufacturer’s cost-effectiveness model for disease-modifying drugs (DMDs) in multiple sclerosis is surrounding the structural uncertainty. The methods dealing with structural uncertainties are not well-developed, even though these might have a significant impact on model results. This study investigates the impact of structural variations of the NICE single technology appraisal cost-effectiveness model of Erlotinib versus Best Supportive Care as a maintenance therapy for patients with non-small cell lung cancer. The model submission was critical in identifying a “Markov” model not governed by transition probabilities. It considered an independent projection survival functions for progression-free survival and overall survival, which allowed a negative post-progression survival (FPS) estimate to appear in the model cycle. Our study restructured alternative models to this study adopted three approaches, covering both fixed- and time-varying, to estimate state transition transition probabilities that are used in a restructured Markov model. RESULTS: Unlike for placebo, the parametric approach estimates post-progression probabilities and probabilities of death for Erlotinib differently than fixed-time- transition approaches. The best fitting curves are achieved for both FPS and probability of death across the time for which data were available, but the current model structure is complex. The parametric Markov model which extrapolates the curves forward in time suggests that this difference between a time-varying and fixed-transition becomes even greater. The alternative models produce an Incremental Cost-Effectiveness Ratio (ICER) of £54k -£6k per quality adjusted life year (QALY) gain, which is comparable to an ICER presented in the MS (£55k/QALY gain). CONCLUSIONS: The results from restructured alternative models do not suggest different cost-effectiveness results to those reported in the manufacturer submission; however, in terms of magnitude they vary. This variation in cost-effectiveness results produced by restructured models might be crucial for interventions falling near a threshold value.

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COMPARING THE EVALUATION OF PATIENT LEVEL DATA TO INFERENCE OF ADPKD PROGRESSION GENERATED WITHIN THE ADPKD OUTCOMES MODEL

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OBJECTIVES: Autosomal dominant polycystic kidney disease (ADPKD) is a genetic disorder characterised by enlarged kidneys and declining renal function. ADPKD progression rates are heterogeneous, influenced by age, gender, renal size and genotype. Disease models often utilise progression rates derived from published studies. This study aimed to compare ADPKD progression, in terms of changes in total kidney volume (TKV) and renal function, modelled from summary versus patient-level data (PLD), and assess the consistency of predictions with trial observations. METHODS: Regression equations were derived from the TEMPO 3.4 trial placebo arm (natural history) to predict annual changes in TKV and estimated glomerular filtration rate (eGFR). Candidate covariates included age, gender, ethnicity, region/country, TKV and eGFR. Predictions were compared using the PLD regression equations or linear interpolation of summary rates of change in four patient populations. RESULTS: Finally, the predictions were compared with a sample of patient-level data representing early and late disease from the HALT-PKD trials, and predicted progression compared to trial observations. RESULTS: For patients initiated with the average TEMPO 3.4 placebo profile, predicted eGFR trajectories based on PLD or cohort data were similar (p-value < 0.05). However, for patients initiated with a high TKV profile, predicted eGFR trajectories were different to the PLD stochastically (p-value < 0.05). However, in terms of magnitude they vary. This variation in cost-effectiveness results produced by restructured models might be crucial for interventions falling near a threshold value.