ments and supports the feasibility of this approach. CONCLUSIONS: This novel design seeks to address the bias inherent in observational research through the imposition of randomization. By separating data collection into a preliminary phase collecting only variables needed for treatment identification and randomization and a separate full review of only these randomly-selected patient records, chart abstraction burden is minimized. Furthermore, the use of propensity score matching to create two matched cohorts for comparison allows greater control of potential confounding in analyses of treatment effect.

SB4 A METHODOLOGY FOR ASSESSING TREATMENT EFFECT IN THE PRESENCE OF DISEASE SEVERITY AND COMORBIDITY IN RETROSPECTIVE OBSERVATIONAL STUDIES

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OBJECTIVES: There are many examples in health outcomes research where inadequate control for comorbidity influence has resulted in effect estimates confounded by disease severity. Selection bias is a common feature of data from routine healthcare setting where the decision to give a particular drug to a patient with a given disease is generally based on patient characteristics, including disease condition. Thus, failure to properly control for the bias could result in false associations. Propensity scores methodology is commonly used despite its limitations because of its potential for minimizing the association between exposure and confounding factors. We describe a methodology for assessing drug effect in longitudinal data that minimizes confounding by disease severity generally associated with observational studies. METHODS: For a particular outcome of interest, we obtain the profiles of rates ratios from two sets of matched cohorts. In set A, patients with disease X are compared with others free of X in the period prior to and post diagnosis of X. In set B which involves only patients with disease X, those exposed to treatment Y are compared with those unexposed to the drug in the periods prior to and post exposure. The two sets of profiles are then assessed using simple logistic regression on respective periods. In effect, we attempt to disentangle the disease and treatment effects. Data from the UK GPRD are used to assess possible association between a particular outcome and treatment in COPD RESULTS: We found evidence of association between the outcome and COPD but none of the drug. CONCLUSIONS: The profile approach utilizes the data collected over the disease natural history and exposure history to assess the relationships between the outcome and both the disease and treatment. This is a key strength often ignored when results are reported as point estimates. By design, it also minimizes the effect of selection bias.

POD IUM SESSION II RESEARCH ON METHODS: COST-EFFECTIVENESS ANALYSIS

CE1 COST-EFFECTIVENESS SENSITIVITY ANALYSIS: A METROLOGY OF ONE-WAY SENSITIVITY, ANALYSIS OF COVARIANCE, AND EXPECTED VALUE OF PARTIAL PERFECT INFORMATION

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OBJECTIVES: Advanced sensitivity methods including varying value of information were developed to quantify overall decision uncertainty and to assess the cost-effectiveness of additional analysis that would reduce that uncertainty. Our objective was to compare the information gained by utilizing three alternative sensitivity methods with increasing complexity: a simple one-way sensitivity analysis, probabilistic analysis of covariance (ANCOVA), and expected value of partial perfect information (EVPPF) of input parameters. METHODS: We replicated and expanded a published HIV/AIDS cost-effectiveness Markov model (zidovudine vs. zidovudine plus lamivudine in the UK) using TreeAge®. Health states included three HIV/AIDS states and death. Our outcome of interest was the incremental net monetary benefit (INMB) assuming a willingness-to-pay of £20,000/QALY. We generated one-way and probabilistic sensitivity analyses of the INMB using published input parameter uncertainties. One-way sensitivity analysis identified the top 10 most influential parameters. A total of 10,000 Monte Carlo draws were used to estimate the ANCOVA results from the same ten parameters. EVPPF for each of the same ten parameters was estimated specifying 1000 inner and 1000 outer Monte Carlo draws. We ranked the parameters by their influence on variance for each sensitivity method and compared them using Spearman’s rank correlation. RESULTS: Mean INMB was £9914 in favor of combination therapy. The two most influential inputs were the same across all methods, contributed 78% of variation in outcome (ANCOVA), and were the only inputs with non-zero EVPPF values. The rank order for the top ten inputs from all methods was very similar (correlation: 0.99 for one-way vs. ANCOVA, 0.70 for one-way vs. EVPPF and 0.70 for ANCOVA vs. EVPPF, all p-values < 0.05). CONCLUSIONS: The correlation was significant between one-way and more advanced sensitivity analyses. Although each method provides unique information, the additional resources needed to generate advanced analyses should be weighed especially when the outcome decision uncertainty and therefore value of information is low.

CE2 A NOVEL WAY OF ESTIMATING COST-EFFECTIVENESS RATIOS FROM CLINICAL TRIALS WITH MISSING DATA: A SIMULATION STUDY

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OBJECTIVES: In a simulated dataset, evaluate incremental cost-effectiveness ratios (ICERs) adjusted for covariates and missing data using three different regression models. The regression parameter of interest is the incremental net monetary benefit (INMB). Models are ANCOVA, mixed effects (ME), and joint mixed effects and log time-to-dropout (joint ME), a selection model. METHODS: Traditional cost-effectiveness analysis (CEA) uses the incremental cost-effectiveness ratio (ICER), a measure of the additional cost and additional effectiveness associated with the introduction of a new therapy. CEA can estimate incremental net monetary benefit (INMB) and avoid these statistical issues while adjusting for covariates as well as missing data. The cost-effectiveness acceptability curve (CEAC) generated from a family of these regressions allows the ICER adjusted for the factors included in the INMB (HIV/AIDS) regression is the point on the CEAC where the probability of being cost-effective is 50%. Data were simulated to include missing at random (MAR) and missing not at random (MNAR). Simulated treatment effect provided a “true” INMB for model evaluations that included bias (absolute difference from “true”), precision (ratio of variances), and CEACs with willingness-to-pay (A) values from $0 to $100K. RESULTS: The ANCOVA and ME models produced the least biased estimates. At A = 50K, bias was $1.3K, $1.4K, and 2.3K, and precision was 1.27, 0.90, and 1.24 for ME, ANCOVA, and joint ME, respectively. The joint ME model performed best when missingness was high. CONCLUSIONS: One of the CEACs had been generated, deriving ICERS adjusted for covariates and missing data from those CEACs based upon INMB regressions proved easy and feasible. The models used in this simulation analysis performed differently under alternative missingness conditions and were sensitive to nonresponse mechanisms. All estimates were poor when missingness was high, suggesting prevention of missing data should be a goal of research.

CE3 COST-EFFECTIVENESS ANALYSIS AND BUDGET IMPACT ASSESSMENT: A GRAPHICAL WAY TO COMBINE THE TWO FOR THE AID OF DECISION-MAKERS

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OBJECTIVE: Cost-effectiveness analysis (CEA) has traditionally been seen as a means of satisfying a specific and explicit social objective subject to a fixed budget constraint. As a result, existing CEA methods largely ignore budget impact considerations in health systems where budgets are not fixed. In particular, none of the traditional methods of presenting results (such as the cost-effectiveness plane, ICER tables and CEAC graphs) can be used to summarize the results of a CEA and budget impact assessment simultaneously. Our objective was to develop such a method in a manner which is meaningful to decision makers. METHODS: We present a novel way of combining cost-effectiveness and budget impact considerations into a single graph. To do this, we disaggregate the incremental costs of the new technology into those which fall on the health budget and displace other technologies (resulting in forgone health) and those which lead to an expansion of the health budget (resulting in a net budget impact). The incremental health benefit of the technology and any forgone health are combined to give the net health benefit of the technology, which is plotted against the net budget impact. RESULTS: Our method clearly reveals the trade-off between the cost-effectiveness and budget impact of the technology in question. This trade-off is simultaneously revealed across a range of plausible values of the cost-effectiveness threshold. CONCLUSIONS: Decision makers who are concerned with both the cost-effectiveness and budget impact of new technologies have tended to consider each of these separately, with the inherent trade-off between the two blurred in the process. Our proposed method makes this trade-off explicit and does so across a range of threshold values, enabling analysis to provide meaningful information to decision makers while respecting decision makers’ authority in determining the appropriate threshold to use.

CE4 USING DYNAMIC TRANSMISSION MODELS TO ESTIMATE THE COST-EFFECTIVENESS OF VACCINES: FOUR DIFFERENT METHODS AND THEIR RELIABILITY FOR DECISION-MAKERS

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OBJECTIVES: To compare the differences in the methods used to estimate the cost-effectiveness of vaccination programs using the clinical outcomes from dynamic transmission models. METHODS: A targeted electronic literature search of title words in the PubMed databases was performed to identify studies published since 2000 that included a description of the methods and presentation of results of cost-effectiveness analysis of vaccination programs based on data from dynamic transmission models for any infectious disease. Further studies were identified in the bibliographies of the initial set of papers. RESULTS: Information was abstracted from 29 papers presenting cost-effectiveness analyses of vaccination programs for influenza, HPV, varicella virus, pertussis, meningocecal meningitis, rotavirus, H. pylori, and hepatitis A. Both cohort and population-based estimates of cost-effectiveness were presented. The population-based estimates had variable time horizons (mean time horizon for influenza or pertussis (the steady state year) up to 100 years for HPV, varicella, and meningococcal vaccination). All cohort analyses used a lifetime time horizon. Four method types for the estimation and presentation of a cost-effectiveness ratio were identified: 1) average population values (costs and benefits) over a long time horizon assuming a continuing vaccination program (20 papers) 2) average population values over a long time horizon estimated duration vaccination program (1 paper) 3) population values for the steady-state year only (1 paper) and 4) cohort values with a lifetime horizon (7 papers). CONCLUSIONS: The variability of the estimation framework (population or cohort) and time horizon used as well as the variability in other input parameters observed