correction. A simple Markov model was built to illustrate the impact of the half-cycle correction. Half-cycle corrections appear to be used routinely in Markov models. In nearly all cases, the so-called "correction" is applied without due consideration of the implications. Two major flaws were identified with the approach. The first, mathematical, flaw is that the half-cycle correction approach assumes that all events occur at the mid-point of each cycle. It can be demonstrated that, for one-directional events (such as death), events will be more likely to occur in the first half of the cycle since more patients will be exposed to the event at the start of the cycle, and the number of patients 'at risk' falls throughout the cycle. The second flaw is that, for many events, the implications of the event will not actually become apparent until the next cycle. For instance, in oncology, the cycle correction approach may not become apparent until the next cycle. This study has produced two key recommendations to generate more accurate outcomes and to avoid biases in decision analytic models. ORMs


OBJECTIVES: To define the extent to which using the EQ-5D versus disease-specific instruments is critical in overall cost-effectiveness assessments, specifically regarding cost-utility. METHODS: Five ISPOR therapeutic areas (TAs) were randomly selected, and literature research found on PubMed for the UK, as well as other European publications, to retrieve publicly available data on health state utility scores in the respective TAs. Data were extracted into a database and various model structures reconstructed in order to determine the impact of different HRQOL instruments and cost-effectiveness. Standard Monte Carlo simulations were applied to generate simulations, informing both the expected cost-effective-ness and its associated uncertainty. Cost-utility as well as net monetary / health gain were calculated in order to determine the impact of different HRQOL instruments and cost-effectiveness in modelling. This study has produced two key recommendations to generate more accurate outcomes and to avoid biases in decision analytic models.

PM50 RANDOM NUMBER GENERATORS IN MONTE CARLO SIMULATION Mcwan P1, Foos V2, Christie M1, Lloyd A1, Palmer J1, Lamotte M1, Grant D1

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OBJECTIVES: Monte Carlo simulations are driven by the generation of pseudo random numbers (PRN) used in simulation. Random number generators are random processes that take any systematic pattern or bias has implications for simulation run time and accuracy. The objective of this study was to compare two commonly used PRN in an applied setting to illustrate potential limitations of low performance. METHODS: The IMS Core Diabetes Model (CDM) was used to explore their precision in detecting the onset of end stage renal disease (ESRD) using the MS-Visual C++ 2008 PRN generator (MSG) and Mersenne Twister generator (MTG). One-year probabilities of ESRD for a 65 year old female smoker were generated with a systolic blood pressure (SBP) of 135 mmHg (p = 0.000363) and 140 mmHg (p = 0.000444). The expected one-year incidence was compared to probabilistic observations in the CDM for both PRN generators. RESULTS: The expected yearly incidence of ESRD was 0.0363% (SBP 135 mmHg) and 0.0444% (SBP 140mmHg). Monte Carlo estimates were compared, and a scatter-plot was generated using the MSG and MTG for both SBP values. RESULTS: The MSG overestimated expected rates by 4.41% and 7.4%, the MTG underestimated the probability of ESRD by 34.16% and 46.17% SBP for 135mmHg and 140mmHg, respectively. The deterministic relative increase in incidence of ESRD (23.7%) associated with a 5mmHg increment in SBP was similar to the MSG (25.28%), using the MTG resulted in a 0% increase in the probability of ESRD. Analysis of the frequency distribution of the MTG displayed areas sparsely populated with random variables. CONCLUSIONS: The two PRN generators tested in this analysis produced substantially different results. The differences between the two PRN algorithms were most apparent when predicting relatively rare events, such as ESRD. When assessing the internal validity of Monte Carlo simulations the efficiency and robustness of PRN generators should not be assumed.

PM52 MINIMUM RUN-TIME REQUIREMENTS TO REDUCE MONTE CARLO ERROR IN STOCHASTIC SIMULATIONS Foos V1, Mcwan P1, Lloyd A2, Palmer J1, Lamotte M1, Grant D1

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OBJECTIVES: In health economic modeling the role of probabilistic sensitivity analysis (PSA) is to assess the uncertainty of model predictions with respect to the underlying parameter uncertainty. However, in Monte Carlo simulation parameter uncertainty can be distinguished from random noise due to Monte Carlo error (MCE). The objective of this study was to quantify the minimum run time requirements to reduce MCE to acceptable levels. METHODS: An established and validated model, the IMS CORE diabetes model (CDM), was used to compare computational efficiency of bootstrap simulations with 1000 replications and increasing number of patients ranging from 500 to 10000. Model projections were defined to evaluate the cost effectiveness of two hypothetical interventions with differences in clinical effectiveness of 0.5% HbA1c and a 2kg weight change in favor of the treatment vs. control arm. Each simulation was performed in three ways; 1st where no parameter sampling was applied, 2nd and 3rd where parameters were sampled around 5% (SE based PSA) and 25% (SD based PSA) of their mean values, respectively. The degree of MCE was determined according to the ratio of the confidence ranges (ICER per QALY) of the non sampling analyses versus PSA. RESULTS: The proportion of Monte Carlo error contained in overall ICER variability for simulations with increasing number of patients (2500, 5000, 10000, 25000, 50000 and 100000) was found at 110%, 107%, 73%, 54%, 45% and 32% for SE based PSA and 80%, 80%, 37%, 13%, 9%, and 6% for SD based PSA. CONCLUSIONS: Run time requirements to reduce MCE are lower whenever the uncertainty of included parameters is increased. Hypothesizing that not more than 40% of overall outcome variability should be attributable to MCE, the minimum run time requirement was found at 10000 and 10000 patients for SE and SD based PSA, respectively.

PM53 CAN THE DISUTILITY OF ALLERGIC RHINITIS AND CONJUCTIVITIS BE CALCULATED FROM THE AGGREGATED TOTAL SYMPTOMS SCORE? Langkilde LK1, Volk J2, Nørgaard Andraeensen J3

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OBJECTIVES: The use of rhinitis total symptom scores (RTSS) is the recommended method for documenting clinical effect of interventions in allergic rhinitis and conjunctivitis. For cost utility analysis a patient preference measure (health state utility scores) is needed. We explore whether the disutility of allergic rhinitis can be estimated from RTSS. METHODS: We explored the properties of the RTSS and compared these to the properties of the Rhinitis Symptom Severity Index (RSUI) - a multi-attribute utility function of rhinitis health states. Furthermore, we simulated the effects of a 2 week period of allergic rhinitis in a RSUI. The disutility in RSUI associated with each RTSS score to minimal important difference (MID) for utility. RESULTS: RTSS is a linear mapping of daily reported rhinitis symptoms with respect to frequency, type, and severity of symptoms. RSUI is multiplicative mapping of frequency, type and severity. This makes the RSUI a non-monotone mapping of RTSS which rules out direct one-to-one mapping from RTSS score to RSUI utility score. The simulation showed that a specific RTSS score can result in very different RSUI values; e.g. a RTSS score of 2.21 (fairly low symptom load) can be associated with a RSUI in the range of 0.376 to 0.784. Since the span of possible RSUI scores is large and each RTSS score is larger than the MID for utility by any standards, no approximated mapping is not possible without making further assumption on type of symptoms. CONCLUSIONS: The RTSS is a standard, recommended measure of clinical effect in rhinitis and conjunctivitis intervention studies. We need further research in order to be able to use RTSS to account for patient health state preferences and utility gains from interventions can be estimated from RTSS. These findings emphasize the importance of using validated methods/tools when estimating and comparing utility gains from separate interventions.

PM54 CORRELATING COST EFFECTIVENESS OUTPUT WITH PATIENT LEVEL DATA INPUT VIA THE IMS CORE DIABETES MODEL (CDM) Mcwan P1, Foos V2, Lloyd A1, Palmer J1, Lamotte M1, Grant D1

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OBJECTIVES: The use of patient level data (PLD) within cost-effectiveness models allows the potential to analyse the relationship between individual input profiles and model output. The objective of this study was to determine if PLD input profiles were predictive of cost effectiveness sub-groups in Type 2 diabetes mellitus (T2DM) subjects. METHODS: This study used the IMS Core Diabetes Model (CDM), a validated and established diabetes model to evaluate the cost effectiveness of a second line oral therapy (Treatment) compared to the baseline monotherapy (Control). Delta effects (favouring Treatment) were a 0.5% HbA1c reduction, 2kg weight change and a difference in symptomatic hypoglycaemia of 0.9/100 patient years. Annual diabetes specific therapy cost was £455 (Treatment) versus £20,000. HbA1c was linearly and negatively correlated with incremental cost utility (ICU) £569 per 1% increase (p < 0.000363) and 140 mmHg (p = 0.000444). The expected one-year incidence was compared to probabilistic observations in the CDM for both PRN generators. RESULTS: The expected yearly incidence of ESRD was 0.0363% (SBP 135 mmHg) and 0.0444% (SBP 140mmHg). Monte Carlo estimates were compared, and a scatter-plot was generated using the MSG and MTG for both SBP values. RESULTS: The MSG overestimated expected rates by 4.41% and 7.4%, the MTG underestimated the probability of ESRD by 34.16% and 46.17% SBP for 135mmHg and 140mmHg, respectively. The deterministic relative increase in incidence of ESRD (23.7%) associated with a 5mmHg increment in SBP was similar to the MSG (25.28%), using the MTG resulted in a 0% increase in the probability of ESRD. Analysis of the frequency distribution of the MTG displayed areas sparsely populated with random variables. CONCLUSIONS: The two PRN generators tested in this analysis produced substantially different results. The differences between the two PRN algorithms were most apparent when predicting relatively rare events, such as ESRD. When assessing the internal validity of Monte Carlo simulations the efficiency and robustness of PRN generators should not be assumed.