simulation model of type 2 diabetes, based on the UKPDS 68 outcomes equations, was executed with and without the application of antithetic variates. The impact of the technique was evaluated through comparison of total cost and benefit estimates, predicted over a long-term horizon of 40 years. **RESULTS:** An approximate four-fold reduction was observed in the Monte Carlo Error (MCE) associated with estimated mean incremental costs and benefits, when antithetic variates were applied over 1,000 simulations of 1,000 individuals. For a fixed number of runs (1,000), the number of replicated individuals required to achieve 99% accuracy (MCE/mean<1%) in incremental cost and benefit estimates fell from approximately 500 and 550 respectively, to fewer than 50 with antithetic variates. Similarly, for a fixed cohort size (1,000) the same level of precision was produced with fewer than 10% of the simulation runs required otherwise. **CONCLUSIONS:** The use of antithetic variates can improve the precision of modelling output; reducing the number of simulation runs and thus computation time required to perform analyses. The use of such variance reduction techniques should be pursued in the simulation of chronic conditions, as a means of achieving manageable run times and facilitating the extensive scenario and sensitivity analyses required as part of economic evaluations.

PRM63
MODELLING THE ADENOMA AND SERRATED PATHWAY TO COLORECTAL CANCER (ASCCA)

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OBJECTIVES: Most models developed for colorectal cancer (CRC) screening evaluations are based on the adenoma-carcinoma pathway only. Currently, there is increasing evidence that serrated lesions can also develop into CRC. This study aimed to develop a model that reflects both the adenoma-carcinoma pathway and the serrated pathway to CRC and that includes characteristics of polyps. **METHODS:** The Adenoma and Serrated pathway to Colorectal CAncer (ASCCA) model was built using the scientific literature, expert opinion, data from the Dutch COCOS trial and Dutch cancer registry data. A flexible model structure was chosen to examine the impact of two alternative natural history assumptions: (i) all CRCs arise from adenomas and (ii) 15% of CRCs arise from serrated lesions. The two model versions were calibrated manually using a systematic, step-by-step approach. **RESULTS:** Calibration resulted in 19 parameter sets for the adenoma-carcinoma pathway and 13 for the serrated pathway, matching the age- and sex-specific adenoma and serrated lesion prevalence in the COCOS trial and several other intermediate model outcomes. For the first natural history assumption, progression rates from advanced adenoma to CRC between 1.6% and 2.7% were found to produce model-based age-standardized incidence rates within the 95% confidence interval of the Dutch incidence in 2009. For the second assumption, these progression rates were between 1.3% and 2.2%. Mean duration from adenoma to CRC was 24 years. **CONCLUSIONS:** The ASCCA model will be used to evaluate the (cost-)effectiveness of different screening and surveillance strategies for CRC. Future analyses will evaluate the upcoming Dutch screening program using the two calibrated model versions. The implication of different test accuracies for different types of polyps with their characteristics can be taken into account in a straightforward manner. Furthermore, the impact of structural as well as parametric assumptions concerning the serrated pathway can be addressed.

PRM64
MICROSIMULATION OR COHORT MODELLING? A CASE STUDY IN CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD)

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OBJECTIVES: Markov models are commonly used to study time dependent disease progression. While most models are cohort based, due to their limitation of dealing with heterogeneities, continuous variables, and dynamic strategies, individual-based microsimulation is being increasingly used. The objective was to compare microsimulation to cohort approach in modeling COPD, while validating the two approaches against findings from TORCH trial. **METHODS:** We developed both models to study COPD progression in a cohort defined by the characteristics of TORCH patients. The microsimulation randomly generated a large number of patients and tracked each patient's the lung function (FEV1), exacerbations, and mortality, based on individual's characteristics and disease history. The cohort model included four COPD stages and death; it modeled exacerbations as events, assuming no impact on transitions or future exacerbations. Both models were populated by published data and results were compared against TORCH findings. **RESULTS:** The mean decline in FEV1 over 3-year was 126 ml in microsimulation, 49 ml in cohort model, compared to 117 ml in TORCH. The annual rates of moderate and severe exacerbations were 0.94 and 0.18 in microsimulation, 1.12 and 0.18 in cohort model, compared to 1.13 and 0.19 in TORCH. The 3-year mortality was 17.4% in microsimulation, 12.2% in cohort model, and 15.2% in TORCH. Microsimulation required simulating at least 3500 patients to obtain stable estimates, which took 4 minutes to run each scenario. It would take 300 hours to run 5000 scenarios for sensitivity analysis, while the cohort model took less than 1 minute. **CONCLUSIONS:** In COPD, patient heterogeneity and disease history can be conveniently captured in microsimulation, while parameter uncertainties are easily assessed using cohort approach. The cohort approach is simple to develop, but its inherent Markovian property cannot fully represent COPD pathology. Microsimulation is flexible in mimicking COPD progression, but it is computational expensive.

PRM65
SIMULATING PATIENT POPULATIONS – DIFFICULTIES IN CONTROLLING THE ROLL OF THE DICE

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OBJECTIVES: In developing probabilistic models to analyse cost-effectiveness, it is possible to control many model parameters using random seeds so that output differences should be due to the interventions being modelled rather than due to chance differences in the model parameters. However, at the point of intervention, the simulated patient effectively enters a parallel universe where outcomes may legitimately be better or worse irrespective of the intervention. The purpose of this study was to present an example of reduced health outcomes contrary to expectation. **METHODS:** Using a model developed to evaluate the impact of different MRI-based breast cancer surveillance strategies, the total benefits measured for individual simulated patients were compared between surveillance and no surveillance. Random seeds were used to ensure model parameters were matched between different model runs. Model structure ensured that later detection of cancer could not be associated with a better outcome. For breast cancer occurrence, random seeds were matched until the first incidence. Individuals could have multiple cancers. **RESULTS:** Across 7 surveillance strategies, compared to a situation of no surveillance, life expectancy was unchanged for between 97.7% and 99.0% of individuals. Depending on the surveillance strategy, between 0.98% and 2.2% of individuals had increased life expectancy, and between 0.04% and 0.1% of simulated individuals experienced a reduced life expectancy. A larger number of individuals had reduced life expectancy due to surveillance, but this is attributable to the detection of DCIS which does not always develop into invasive cancer. **CONCLUSIONS:** When comparing interventions using probabilistic models, chance variation can result in poorer outcomes despite the intervention. Although these anomalies are not apparent in summary figures as there may be an "on average" benefit, their occurrence is legitimate and should not be artificially prevented.

PRM66
ADHERENCE TO DISEASE-SPECIFIC RECOMMENDATIONS FOR PHARMACOECONOMIC STUDIES IN RHEUMATOID ARTHRITIS

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OBJECTIVES: Previous research has demonstrated wide varieties in modelling methods of pharmacoeconomic (PE) studies focussing on biological drugs for the treatment of rheumatoid arthritis (RA). To eradicate this variety, disease specific guidelines were presented in 2002 by OMERACT-ILAC. The objective of this study is to assess whether recently published PE studies adhered to these recommendations. **METHODS:** A literature review was conducted for PE studies evaluating TNF-α inhibitors use in RA. Four different databases (e.g. Embase, NIHR-EED) were searched for PE studies published that focus on Adalimumab between October 2003 and May 2013. Methodological quality of included studies was checked against the CHEC-checklist. Data extraction forms were used to retrieve information such as study outcomes (QALY's, costs, ICER) and modelling methods and parameters (e.g. time horizon, sources for costs and effectiveness data). Finally, information retrieved from all studies was compared to recommendations proposed by the OMERACT-ILAR guideline to assess adherence to these recommendations. **RESULTS:** Nine studies were identified that met all inclusion criteria and were included in our analysis. All studies met at least 12 of the 19 items of the CHEC checklist for quality and 3 studies met all 19 items. Study outcomes varied considerably in QALY's calculated, costs and ICER's. Patient subtypes, modelling methods, sources for cost and effectiveness data also varied significantly. Only 2 of the 12 recommendations published in the OMERACT-ILAR guideline were unanimously implemented in all 9 studies of our review. Only 1 study was found to contain all elements of guideline recommendations, albeit with some limitations **CONCLUSIONS:** We demonstrate that modelling methods still widely differ and adherence to disease-specific guidelines for the conduct of PE studies in RA is very low. Development of strict disease-specific guidelines in RA and subsequent adoption by re-imbursement agencies is vital to ensure comparability,validity and credibility of future PE studies.

PRM67
MODELING A SWITCH FROM TRIVALENT TO QUADRIVALENT INFLUENZA VACCINE IN CANADA AND THE UNITED KINGDOM

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OBJECTIVES: Current trivalent influenza vaccines (TIVs) contain only one of the two currently circulating influenza B lineages (Victoria and Yamagata). Worldwide, in about half of all influenza seasons since co-circulation of the two B lineages commenced, the dominant B lineage did not match the one chosen for inclusion in the TIV. Quadrivalent influenza vaccines (QIVs) would help address this problem by including both B lineages each season. We modeled the impact of a country-wide switch from TIV to QIV on the yearly population-wide rates of influenza cases and influenza-associated events, in both Canada and the UK. **METHODS:** We calculated projections using a dynamic transmission model which incorporates four interacting influenza strains, transmission-rate seasonality and age-specific mixing within the population, run over a 40-year time horizon. Influenza vaccine coverage rates in Canada and the UK were taken from public sources, TIV efficacy was obtained from a meta-analysis (Tricco et al., in press), and QIV efficacy was assumed to be similar to TIV without B lineage mismatch. **RESULTS:** Across Canada, the model estimates that a switch from TIV to QIV would, in an average influenza season, avert 9% (relative) of influenza cases (=237,000 cases), 9% (=86,000) of general practitioner (GP) visits, 9% (=12,000) of emergency room (ER) visits, 8% (=2,500) of hospitalizations, and 7% (=330) of deaths. Across the UK, the model estimates that 0.7% (=70,000) of influenza cases, 0.8% (=19,000) of GP visits, 0.8% (=600) of ER visits, 0.8% (=800) of hospitalizations, and 3% (=270) of deaths would be averted. **CONCLUSIONS:** In both Canada and the UK, a country-wide TIV-QIV switch is predicted to bring about a clear reduction in the burden of influenza. The relatively greater impact of the switch in Canada is due principally to that country's higher vaccine uptake among people younger than 65 years.