articles published in English and German between 2000-2015. The search strategy aimed to identify studies answering the question: what is an adequate discount rate for the evaluation of vaccines in Germany? Abstracts were screened independently by two reviewers. Studies included in the qualitative analysis were categorized according to publication type and analyzed by the nature of arguments. **RESULTS:** 459 records were identified and 16 studies included in the final analysis. 8 were categorized as reviews, 4 as empirical and another 4 as methodological papers. A variety of theoretical, empirical and normative arguments were identified. Due to the unclear economic outlook since the 2008 financial crisis, there is no clear evidence for an appropriate discount rate of costs. Furthermore, there is even less evidence for an appropriate discount rate of effects. However, there is a strong body of evidence for discounting costs and effects differently for vaccination programs or any other preventative medical program for which the benefit is accrued far over time. **CONCLUSIONS:** Although there is no consensus about what should be a right discount rate for vaccinations or medical prevention, using 3% for costs and effects similar to the German guidelines for therapeutics seems inappropriate if the benefit is largely displaced over time. The rates for cost and effect should be lower than 3% and different from each other.

PRM83

EMPIRICAL ASSESSMENT OF THE IMPACT OF MODEL CHOICE (MARKOV STATE TRANSITION VERSUS PARTITIONED SURVIVAL) IN MODELLING SMALL-CELL LUNG CANCER

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OBJECTIVES: Health technology assessments in small cell lung cancer (SCLC) are typically based on Markov models (MM) or partitioned survival models (PSM). There is a lack of empirical evidence quantifying the accuracy of predicted survival outcomes for these modelling approaches. The objective of this study was to generate empirical evidence to assess the consequences of using a MM or PSM to model SCLC. **METHODS:** Using Weiball survival curves, we simulated a cohort of 250 patients, producing mean survival times for treatment (control) arms of progression-free survival (PFS) 26.7 (23.8) weeks; post-progression survival (PPS) 13.7 (6.9) weeks; and overall survival (OS) 40.4 (30.7) weeks. PSM and MM lifetime models were constructed to assess the consistency between approaches in predicting PFS, PPS and OS. The MM model was assessed with time-independent (TI), time-dependent (TD) and time-and-treatment-dependent (TTD) transition rates. Goodness-of-fit was assessed using root mean square error (RMSE); analysis was undertaken using R version 3.2.1. **RESULTS:** The PSM approach consistently produced the most accurate results based on the difference between observed (simulated) minus predicted survival across treatment arms for PFS, PPS, and OS: range = –1.03 to –0.21 weeks. The MM using TI transitions provided the poorest fit to the data: range = –4.86 to 1.93 weeks; the MM with TTD transitions provided numerically inferior but comparable estimates to the PSM approach: range = –1.23 to 0.15 weeks. RMSE for the PSM was 0.59; RMSE for the MM employing TI, TD and TTD transition rates was 2.68, 2.65 and 0.78 respectively. **CONCLUSIONS:** A PSM is likely to produce the most accurate replication of observed survival outcomes; however, a MM populated with appropriately flexible survival equations would not be expected to produce significantly different results. Consequently, the choice of MM or PSM may be influenced by other factors, including modelling treatment discontinuation and therapy sequences.

PRM84

COMPARISON OF MARKOV MODELS USED FOR THE ECONOMIC EVALUATION OF COLORECTAL CANCER SCREENING: A SYSTEMATIC REVIEW

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OBJECTIVES: Economic evaluation of colorectal cancer screening is challenging because modeling requires accounting for several parameters that are not directly observable. The objective of this article is to describe the available Markov models and to critically analyze their main structural assumptions. **METHODS:** A systematic search was performed in eight relevant databases (Medline, Embase, Econlit, NHS EED, HEED, HTA, CEA, and EURONHEED), identifying 35 studies that met the inclusion criteria. A comparative analysis of model structure and parameterization was led using two checklists and guidelines for cost effectiveness screening models. **RESULTS:** Two modeling techniques were identified. One strategy utilized a Markov model to reproduce the natural history of disease and an overlaying model that reproduced the screening process, while the other used a single model to represent a screening program. The majority of studies included only adenoma-carcinoma sequences, while a few also included de novo cancer pathways. Parameterization of adenoma dwell time, sojourn time and surveillance differed between studies, with few of them including time dependent transition probabilities. There was a lack of validation and statistical calibration against local epidemiological data. Most of the studies analyzed failed to perform an adequate literature review and synthesis of diagnostic accuracy properties of the screening tests modeled. Structural uncertainty wasn't analized in any of these studies. **CONCLUSIONS:** Several strategies to model colorectal cancer screening have been developed, but many challenges remain to adequately represent the natural history of the disease and the screening process. Structural uncertainty analysis and estimation of intermediat outputs could be a useful strategy for understanding the impact of the assumptions of different models on cost effectiveness results.

PRM85

REPLACING INPUT PROBABILITY DISTRIBUTIONS WITH MEAN VALUES CAN BIAS SIMULATION OUTPUT: AN ILLUSTRATION USING THE CORE DIABETES MODEL

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OBJECTIVES: Monte Carlo simulation is widely used in diabetes models principally due to the ease with which conditional time-dependent logic and risk factor and health state interactions can be handled. Stochastic variability (1st order uncertainty) is minimised by increasing the size of the simulated cohort and the sampling of input parameters is typically restricted to conducting probability sensitivity analysis (PSA). The objective of this study was to illustrate why input parameters should be sampled regardless of whether PSA output is required. **METHODS:** We used the IMS-CORE Diabetes Model to illustrate the effect of replacing sampled input parameters with their means when estimating time to therapy escalation (TTE). The following published input parameters [means (standard deviation)] were used: HbA1c at diagnosis 7.8% (1.9%); baseline HbA1c 7.3% (1.2%); treatment effect 0.67% (0.14%). The UKPDS HbA1c progression equation was also used with/without sampled regression coefficients. Therapy escalation was assumed to occur at a threshold of 7.5%. **RESULTS:** Holding all input parameters at their mean TTE was 2 years. Sampling all input parameters resulting in mean TTE of 2.7 years (SD=3.4); minimum 0 years, maximum 29 years. The majority of observed variability in TTE was attributable to HbA1c at diagnosis which, when sampled in isolation, resulted in mean TTE of 2.8 years (SD=3.4); minimum 0 years, maximum 29 years. Sampling only the UKPDS HbA1c progression equation coefficients resulted in mean TTE of 2.7 years (SD=0.1); minimum 1 year, maximum 3 years; while sampling only the treatment effect resulted in mean TTE of 1.8 years (SD=1.2); minimum 0 years, maximum 5 years. **CONCLUSIONS:** Replacing input parameter probability distributions by their means can result in biased model output, particularly when their effects within the model are non-linear and used in conjunction with structural parameters; for example, therapy escalation thresholds.

PRM86

STRUCTURED REVIEW OF HEALTH ECONOMIC MODELS IN ASTHMA

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OBJECTIVES: Given the burden of asthma, it is important that robust cost-effectiveness analyses are undertaken to inform decision making. This research reports the results from a structured literature review of cost-effectiveness models in asthma to inform the development of a new cost-effectiveness model in asthma. **METHODS:** A structured review of published literature was conducted in Embase, Medline, EconLIT and Evidence-Based Medicine Reviews using the OVID search engine. Searches were limited to full-text English publications (January 2004–May 2016). Additional searches were conducted in the conference proceedings of the International Society for Pharmacoeconomics and Outcomes Research (ISPOR) and published Health Technology Assessment (HTA) submissions (January 2004–May 2016). **RESULTS:** A total of 31 publications reporting cost-effectiveness models for asthma were identified. Active comparators included: combination therapy of high-dose inhaled glucocorticosteroids and long-acting β2-agonists (n=17), add-on therapy with tiotropium (n=5) and the biologic omalizumab (n=9) in the treatment of asthma. The cost-effectiveness models identified in the review were largely Markov models (MMs) (n=26). Of these, three were country adaptations of the same model, and the design of the remaining five were unspecified. The majority utilised three health states; controlled, partially controlled and uncontrolled as defined by the Global Initiative for Asthma (GINA/GEMA) (n=8) or non-exacerbation, exacerbation or exacerbation with hospitalisation as defined by the British Thoracic Society and Scottish Intercollegiate Guidelines Network (BTS/SIGN) (n=3). The models were developed to inform decision making in: Italy, Spain, US, Columbia, Netherlands, UK, Canada, Japan, Republic of Belarus, Russia, Belgian, Mexico, Australia, Poland, Portugal, Greece and Brazil. None of the models reviewed appeared to capture the health and cost impact of inhaler handling errors. **CONCLUSIONS:** There are a number of cost-effectiveness models developed in the area of asthma. Despite some common features identified, there is no clear consensus on the best approach to fully capture the clinical and economic impact of asthma.

PRM87

THE IMPLICATIONS OF PARAMETER INDEPENDENCE IN PROBABILISTIC SENSITIVITY ANALYSIS

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OBJECTIVES: In probabilistic sensitivity analysis (PSA), it is typical to see distributions assigned to all (relevant) parameters in a model. However, attention is only usually paid to estimating covariance or interactions between a small number of parameters, if any at all. The study explores the impact of interaction and non-interaction assumptions on the outcomes of PSA. **METHODS:** A range of very simple models (additive, multiplicative and ratio-based) were developed, with corresponding input parameters. For each model, a range of alternative approaches were taken. These included adding 'sub-level' inputs to each parameter to add detail (for example, rather than a single input parameter for 'monthly cost of health state X', individual parameters were created for 'cost of physician visits', 'cost of tests', 'cost of drugs', 'cost of hospital visits', etc. These were all varied independently in the PSA. **RESULTS:** The implications of ignoring parameter interactions in PSA varied widely depending on the type of model. Models where QALYs and costs are likely to be positivity correlated (i.e. in survival-based models such as oncology) displayed the opposite effect to those where QALYs and costs are inversely related (i.e. for long-term chronic conditions such as diabetes). Furthermore, the analysis demonstrates that, if a specific input parameter is broken down into several components which are varied independently, then it is likely that the variation in each parameter will cancel out the effect of the changes in the other parameters. Indeed, the greater the 'granularity' of the input parameters, the greater the likelihood that the variations will offset each other, this suggesting a false level of certainty in the PSA's results. **CONCLUSIONS:** This analysis demonstrates the outcomes of a PSA can be influenced by the level of detail that the modellers choose to include