tant to identify patients who are most likely to benefit. Doing so using clinical trials is prohibitively expensive; thus a mathematical modeling approach is required. **METHODS:** We developed a framework for stratified cost-effectiveness analysis using individual-based discrete-event simulations, consisting of a natural history component that captures mutation distribution, correlations between mutation and other risk factors (e.g. family history), and cancer incidence, progression and mortality, and a health care process component that captures interactions between the patients and the health care system, through genetic testing, screening, diagnosis and treatment, and their costs. The genetic screening strategy consists of 3 steps: a benefit- risk assessment step, in which patients are assessed for risk of carrying mutations and potential benefits from genetic testing, a genetic testing step, in which qualified patients within an optimal risk bracket are given the appropriate tests and an intervention step, in which patients are given care based on the results from the genetic tests. **RESULTS:** We use the following approach to explore and identify optimal strategies for 3 genetic screening applications: Dinh et al. demonstrated that primary screening for Lynch syndrome in patients at least 25 years old and with a risk of at least 5% was cost effective. Folse et al. showed that single-nucleotide polymorphism (SNP) screening for breast cancer risk for recommending patients to MRI screening was most cost-effective in women age 40 with a lifetime risk of 16 to 28%. Green et al showed that the same genetic test for recommending patients to chemoprevention was most cost-effective for women age 50-59 with a 5-year risk of 1.2-1.66%. **CONCLUSIONS:** As more genetic tests becomes available, this method can be used to identify screening strategies that maximize cost-effectiveness.

PRM124
DISCRETE EVENT SIMULATION FOR THE COST-EFFECTIVENESS EVALUATION OF PET-CT SCANS IN THE DIAGNOSIS OF CONN'S DISEASE IN HYPERTENSIVE PATIENTS

Maruszczak M[1], Stewart G[1], Kusel J[1], Brown MJ[2]
[1]Costello Medical Consulting Ltd., Cambridge, UK, [2]University of Cambridge, Cambridge, UK

OBJECTIVES: To develop a flexible and computationally efficient discrete event simulation (DES) model which could be employed in a cost-effectiveness analysis comparing the use of PET-CT scans versus current diagnostic procedures for Conn's disease in hypertensive patients. **METHODS:** Visual Basic was used for the model simulation with Microsoft Excel constituting the front-end software. In order to ensure a high level of flexibility, individual patients could be assigned a number of personal traits and the clinical, cost and utility inputs were easily adjustable. Individual diagnostic procedures were programmed in separate modules with the aim of simplifying potential modifications to the diagnostic pathway. **RESULTS:** A DES was constructed to evaluate the cost-effectiveness of new treatments based on the experience of patients assigned to intervention and comparator arms. Patients were considered individually in each arm, using the same background mortality. Time, gender and event dependent risk equations enabled efficient modelling of endogenous heterogeneity of the population. Continuous time accounting allowed for the modelling of competing adverse events and provided a realistic representation of patients' experience. Preliminary results indicate that the use of PET-CT scans for the screening of Conn's syndrome could be cost-effective. **CONCLUSIONS:** The newly developed model is the first formal attempt to evaluate the cost-effectiveness of this alternative screening technique for hypertensive patients who are suspected of suffering from Conn's disease. The model will be further developed to include probabilistic sensitivity analysis and bootstrapping in order to evaluate the robustness of the potential results. Evolutionary algorithms will be incorporated to define the most optimal solution from the continuous spectrum of potential screening strategies. As the model will utilise actual patient level data, it could be used by the decision maker to determine the most cost-effective diagnostic strategy.

PRM125
MODELLING LONG-TERM CHANGES IN OPIOID INDUCED CONSTIPATION (OIC)

Altincatal A[1], Lawson R[2], King F[3], Marsh K[4]
[1]Evidera, Lexington, MA, USA, [2]AstraZeneca, R&D | Global Medicines Development|Payer and Real World Evidence, Cheshire, UK, [3]AstraZeneca, Global Pricing and Reimbursement, Gaithersburg, MD, USA, [4]Evidera, London, UK

OBJECTIVES: Patients' experience of OIC may be unstable, with periods of constipation and non-constipation, an observation supported by physician reports. There is, however, a lack of quantitative evidence of this experience. Such evidence would be valuable to inform development of economic models for OIC treatments. The objective of this abstract is to fill this gap utilizing data from two pivotal Naloxegol studies, KODIAC 4 and 5, which demonstrated significant improvements in SBM frequency response compared to placebo over 12 weeks. **METHODS:** 892 non-cancer pain patients with OIC were randomized to Naloxegol 25 mg or placebo in two pivotal studies. A 4-week rolling determination of OIC and non-OIC status at weeks 4 through 12 was used in time-to-event analyses. Patients were considered OIC if they reported <3 SBMs for >=2 out of the 4 weeks and non-OIC if reported >=3 SBMs for >=3 out of 4 weeks. Those with non-OIC status at week 4 were selected as the baseline and first observed OIC status was considered an event. Parametric analyses with Exponential, Weibull, Gompertz, Log-normal, Log-logistic, and Generalized Gamma distributions were conducted. **RESULTS:** Based on the parametric time-to-event analysis results, the Log-normal distribution was selected as the best fit and provided plausible long term projections. Naloxegol had a noticeable separation for extending the time to first OIC event when compared to placebo over the projected long-term follow-up. **CONCLUSIONS:** This research demonstrates that the natural fluctuation between OIC and non-OIC is substantial and requires integration into an economic model. Even in the absence of treatment, a substantial proportion of patients become non-OIC, and a significant proportion of these remain in non-OIC subsequently. Nevertheless, a treatment effect for Naloxegol was observed over and above this 'background' placebo variation in the experience of OIC.

PRM126
COMPANION DIAGNOSTICS-TARGETED THERAPIES PAIRINGS MODEL-BASED ECONOMIC EVALUATION: REFLECTION ON A GENERAL MODELING FRAMEWORK AND KEY METHODOLOGICAL POINTS

Marty R[1], Roze S[1], Tisseau A[2], Borget I[3], Chouaid C[4]
[1]HEVA HEOR, Lyon, France, [2]Merck Serono, on belhalf of the LEEM Biomarker Working group, Lyon, Paris, France, [3]Institut Gustave Roussy, Villejuif, France, [4]Santé publique au cabinet, Creteil, France

BACKGROUND: Companion diagnostics (CD) testing aims to stratify the patient population. It conditions the choice of best available therapeutic options, limiting targeted therapy (TT) to subgroups most likely to benefit and triggers potential cost savings. **OBJECTIVES:** To provide a general framework and a list of key methodological points to be addressed while conducting a model-based economic evaluation of CD-TT pairings, especially in oncology. **METHODS:** Based on a health economic literature review and a clinical expert panel with examples drawn from cases of CD testing selection biomarker predictive of the response level towards an anti-cancer TT. **RESULTS:** As CD and TT have embedded values, it is important to assess them concomitantly within a shared modeling framework. We propose a decision tree to model the patient population stratification and to incorporate impacts of analytical and clinical validity. The former refers here to the inability of the CD to accurately and reliably inform the biomarker resulting in true (false) positive/negative cases, whereas the latter relates to the penetrance, i.e. the strength of association between the biomarker and clinical phenotypes (treatment effect). Such parameters are crucial especially in cases multiple distinct lab-tests (commercial vs. home-brew, technics, amount of informations provided regarding the biomarker). Each patient sub-group outcomes are required to be modeled (costs and health effects). A Markov state-transition model either based on treatment pathway and/or disease staging represents both adequate approaches to simulate the clinical outcomes, incorporating specific efficacy parameters per sub group depending on their biomarker expression levels. In instances, time spent until the CD result delivery exceeds a clinical significant threshold, testing delay shall be modelled such as all parameters driving loss of opporunity. **CONCLUSIONS:** Beyond reasonable simple binary-type of selection biomarker, more complex types of biomarkers and CD technologies (full sequences) has risen additional complexity and poses new methodological challenges.

PRM127
PATIENT PREFERENCES AND HIV DRUGS: WHAT ABOUT UNCERTAINTY?

Broekhuizen H[1], IJzerman MJ[2], Hauber AB[3], Groothuis-Oudshoorn CGM[1]
[1]University of Twente, Enschede, The Netherlands, [2]University of Twente and MIRA institute for Biomedical Technology & Technical Medicine, Enschede, The Netherlands, [3]RTI Health Solutions, Research Triangle Park, NC, USA

OBJECTIVES: Quantitative patient preferences are increasingly considered for health care policy decisions. The objective of this study is to develop a methodology to combine patient preferences with clinical evidence in a multi-criteria framework that takes into account uncertainty in both preferences and clinical evidence. The methodology will be illustrated with a case on antiretroviral treatments. **METHODS:** Treatments under consideration are eight highly active antiretroviral therapies (HAART) recommended for treatment-naïve patients by the National Institute of Health. The treatments are compared on the probabilities of virologic failure, hypersensitivity reaction, bone damage, and kidney damage; and on the treatability of bone/kidney damage. Preferences from 147 patients were elicited with a discrete choice method in an earlier study. Preferences were assumed to be distributed with a multivariate normal distribution. Treatment performances as identified from clinical trials were assumed to be distributed with beta distributions. The probability distributions around preferences and clinical performances were combined with a Monte Carlo simulation method to estimate the joint probability distribution around each treatment's patient-weighted utility. **RESULTS:** The three treatments with the highest mean patient-weighted utility were dolutegravir+abacavir/lamivudine (-0.4, 95% CI: -1.3 to 0.5), raltegravir+tenofovir/emtricitabine (-0.5, 95% CI: -1.6 to 0.7) and darunavir/ritonavir+tenofovir/emtricitabine (-0.6, 95% CI: -2.0 to 0.8). There was considerable overlap between the probability distributions of patient-weighed utilities (probability of first rank reversal: 49%; probability of any rank reversal: >99%). When ignoring uncertainty around patient preferences, the probability of a first rank reversal dropped to 12%, and that of any rank reversal dropped to 88%. **CONCLUSIONS:** A probabilistic multi-criteria methodology was developed that explicitly combines patient preferences and clinical evidence. The individual or joint impact of uncertainty in these on the treatments' patient-weighted utilities is assessed. Although limited by the small number of attributes, the illustrative case suggests the choice of HAART is highly sensitive to patient preferences.

PRM128
MODELLING HEALTH-RELATED QUALITY OF LIFE (HRQOL) LONGITUDINALLY. A BAYESIAN MIXED BETA REGRESSION APPROACH

Gheorghe M, Brouwer W, van Baal P
Erasmus University, Rotterdam, The Netherlands

OBJECTIVES: Cross-sectional studies showed that, for modelling health-related quality of life (HRQoL), beta regression is superior in terms of fit and predictive accuracy to other commonly used methods based on normality distribution assumption. Although, longitudinal HRQoL measurements are widely used in clinical trials, not much is known about beta regression suitability in this context. This is mainly due to software unavailability with classical estimation methods. This study proposes to model the longitudinal HRQoL outcome using a mixed beta regression estimated by Bayesian Markov chain Monte Carlo (MCMC) methods implemented in WinBUGS. Compared to the classical approach, not only the Bayesian estimation is considerably easier to implement but has other advantages; for example, the possibility of including informative priors, enabling analysts to incorporate multiple sources of evidence in a single model. **METHODS:** We used a 16-year longitudinal follow-up for modelling the relationship between SF-6D HRQoL and variables age, gender and mortality risk by means of a mixed beta regression. Besides modelling the mean