gain. Microsimulation and Markov cohort models use simpler models with average annual HAQ progression rates that can differ between treatments. A few of the Markov cohort models treat disease progression as separate states of the DAS28 and estimate transition probabilities between such states over time. Disease progression of a radiographic score was modelled in one study, assuming a decreased deterioration of the radiographic score while being on treatment. No study modeled the impact of disease progression models on ACR response criteria. Finally, the two reviews did not include any cost-effectiveness analysis using decision trees that contained a disease progression model. **CONCLUSIONS:** Health economic decision models in RA include disease progression predominantly through the HAQ score. The impact of disease progression on discrete outcomes such as ACR20/50/70 is rarely considered in health economic models in RA.

PRM127
THE FUTILITY OF COST-EFFICACY ANALYSIS
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OBJECTIVES: Cost-efficacy analysis (CEA) (e.g., cost per cure or short-term response) is increasingly being used as an alternative or a supplement to cost-utility analyses (CUA) employing the incremental cost per quality-adjusted life-year (QALY) gained. The objective of this study was to investigate whether conclusions drawn from such CEAs were consistent with those of the gold standard CUA. **METHODS:** We developed a model comparing standard of care (SOC) with a new drug. At the end of therapy, patients incurred short-term costs and either achieved a response or not. Non-responders incurred additional long-term costs and lost additional QALYs compared with responders. We evaluated two scenarios. In Scenario A: the short-term cost was $40,000 and efficacy was 65% with SOC. Drug cost and efficacy were $50,000 and 90%, respectively. For responders, the long-term cost offsets were $10,000 and additional QALYs were 0.5. Scenario B differed from Scenario A in only two aspects: the drug was more costly ($60,000), and the additional QALYs were higher (2.0 QALYs). We computed average cost-efficacy ratio (ACER), incremental cost-efficacy ratio (ICER), and incremental cost-utility ratio (ICUR). The assumed threshold for cost-effectiveness was $50,000/QALY. **RESULTS:** We found that a lower ACER than SOC was neither necessary (Scenario A: $66,667 vs $61,539/responder and ICUR=$35,000/QALY) nor sufficient (Scenario B: $55,556 vs $61,539/responder and ICUR=$60,000/QALY) for a more efficacious drug to be considered cost effective. Although the drug had a higher ICER in Scenario A ($80,000 per additional responder) than Scenario B ($40,000/responder), the drug was cost-effective in Scenario A, and not so in Scenario B. We derived a formula that related ICER to ICUR. **CONCLUSIONS:** A lower average or incremental cost-efficacy ratio from a CEA was neither a necessary nor a sufficient condition for a new drug to be considered cost effective compared with SOC based on a CUA.

PRM128
THE LIMITATIONS OF ICERS IN SCREENING INTERVENTIONS AND THE RELATIVE NET BENEFIT ALTERNATIVE
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OBJECTIVES: To demonstrate the limitations of the incremental cost-effectiveness ratio (ICER) as a measure of improved cost-effectiveness in the context of periodic screening and to propose a new measure based on net benefit that quantifies the proportional gain in cost-effectiveness relative to the status quo. **METHODS:** We use published cost-effectiveness estimates of cervical cancer screening to show why the ICER is not an appropriate measure of improvement in cost-effectiveness when screening performance improves, either through enhanced test characteristics or better risk stratification. We then propose a new metric based on the net health benefit measure previously devised by Stinnett and Mullahy. **RESULTS:** It is shown how an improvement in screening may enhance cost-effectiveness, represented by an outward shift of the efficient frontier in the cost-effectiveness plane, but that this improvement is not necessarily reflected in the ICER. This is because the whole efficient frontier may shift when all strategies are affected by a common technological change, and so ICERs on the frontier can be insensitive to this improvement. It is also shown that the ratio of costs to effects of a given strategy before and after a technological improvement also does not provide a useful measure of improved cost-effectiveness. The alternative measure of the proportional increase in net health benefit following the adoption of a new technology is then demonstrated. This metric quantifies the increase in net health benefit resulting from the new technology over a range of threshold values. **CONCLUSIONS:** ICERs will remain important for the identification of optimal intervention strategies. However, they are not suited for all circumstances. The net benefit alternative proposed here is a simple quantification of improved cost-effectiveness. The results presented here most readily apply to screening interventions, but also have application in other cases in which a technological development enhances multiple strategies simultaneously.

PRM129
COST-EFFECTIVENESS ANALYSIS OF CEREBROLYSIN IN THE TREATMENT OF PATIENTS WITH ACUTE ISCHEMIC STROKE MODERATE AND SEVERE DEGREES OF SEVERITY IN THE RUSSIAN FEDERATION
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OBJECTIVES: To estimate the cost-effectiveness of neurotrophic and neuroprotective drug cerebrolysin as treatment for patients with ischemic stroke of moderate and severe degrees of severity for one year. **METHODS:** Information retrieval was conducted in the public domain. We used the pharmacoeconomic analysis method – cost-effectiveness analysis and analysis of the direct and indirect costs. For reference, we accepted the exchange rate was 1 EUR = 60,64 RUB. **RESULTS:** In this study the life-years gained (LYG) was used as a criterion of the efficiency. During the cost-effectiveness analysis we have found that the cost of one LYG less for the therapy of ischemic stroke moderate and severe degrees of severity using a drug cerebrolysin compared with standard therapy, cost-effectiveness ratios (CER) were obtained 419656 RUB (6920 EUR) and 563183 RUB (9287 EUR), respectively. **CONCLUSIONS:** The standard therapy in combination with drug cerebrolysin has a lower CER compared with standard therapy, therefore, it is a dominant technology from the perspective of the cost-effectiveness analysis.

PRM130
USING MACHINE LEARNING TO DETECT PATIENTS WITH UNDIAGNOSED RARE DISEASES: AN APPLICATION OF SUPPORT VECTOR MACHINES TO A RARE ONCOLOGY DISEASE
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OBJECTIVES: Diagnostic algorithms to detect undiagnosed patients with rare diseases have the potential to improve patient health and reduce costs associated with misdiagnosis. Accurate algorithms are difficult to develop, typically having to overcome Challenges including the tendency for models to I) over-fit, arising from low degrees of freedom / high-dimensionality and II) under-predict the rare disease, arising from the low ratio of confirmed to unconfirmed cases (skewed outcome class distribution). Support Vector Machines (SVMs) are a highly successful class of machine learning algorithms with well-established methods for handling high-dimensionality and skewed outcome class distribution. SVMs therefore represent a promising method to detect patients with undiagnosed rare diseases. This study estimated risk scores for a rare oncology disease using SVMs. The performance of the models was compared to classical methods based on logistic regressions. **METHODS:** Risk scores for confirmed diagnosis were estimated with logistic regressions (standard, weighted and Firth) and SVMs (regularization, weights and kernel parameters were optimized using internal cross-validation). Patients with high risk scores and without a confirmed diagnosis have a higher probability of being undiagnosed cases. Model development, validation and testing were carried out on separate random samples from linked primary and secondary care data in the UK (Clinical Practice Research Datalink and Hospital Episode Statistics). The key performance metric was maximizing Sensitivity at a Positive Predicted Value (PPV) of 10% based on test data. **RESULTS:** 334 confirmed cases were identified from approximately 1 million total cases. For a PPV of 10%, the Sensitivity for the best performing logistic regression (standard with no weights) and SVM (RBF kernel) was 44% and 58% respectively on test data. **CONCLUSIONS:** SVMs represent a promising method for detecting undiagnosed patients with rare diseases, out-performing more conventional approaches based on logistic regressions. Greater adoption of these methods for this purpose is encouraged.

PRM131
HEALTH ECONOMIC PROGRAMMING USING ROYSTON-PARMAR "HAZARD RATE" MODELS: PROVIDING FLEXIBILITY AND SPEED FOR EVENT MODELLING IN COHORT AND DES MODELS
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OBJECTIVES: Many diseases (e.g. oncology) display changing hazard rates over time that conventional parametric methods cannot replicate accurately. Various "flexible parametric" methods exist with increased number of parameters to alleviate this problem (Generalised Gamma and Generalised F distributions being examples). Royston-Parmar Hazard Rate Models (RPHRM) differ in one crucial regard – all key survival statistics (survival probability, cumulative hazard and hazard rate) can be calculated in closed form. This makes them ideal for HE models where speed of calculation is essential. It is relatively straight-forward to program such models in R to represent competing risks, non-proportional hazard ratios, adding RCT obtained hazard ratios to observational study standard of care baseline hazard estimates, and extrapolation under various scenarios. All of this is possible under both Semi-Markov Cohort and Patient Level Discrete Event Simulation, DES, modelling. We display theory and R example code that illustrates these features. **METHODS:** Publicly available example datasets were analysed using RPHRM within Stata (ado stpm2) under a maximum likelihood framework (Bayesian MCMC methods could be programmed). Parameters obtained were entered into various R functions. Key functions were those that derived the restricted cubic spline basis (and its derivative) associated with log time and its interaction with covariates deemed to have time varying effects. For DES modelling a Newton-Raphson algorithm was simple to program to generate event times. Competing risks were modelled by numeric integration (trapezium rule) to generate cumulative incidence functions from cause-specific hazards using established formula. **RESULTS:** Models were able to replicate the real features of the inputted data. Output was validated against published results. PSA was conducted successfully and quickly. Required R functions were relatively short. **CONCLUSIONS:** RPHRM is the most suitable of "flexible parametric" survival models for HE modelling. It can represent any baseline hazard and hazard ratio time path without requiring time-consuming calculations.

PRM132
CONDITIONAL COPULA MODELS WITH APPLICATIONS TO BIOMARKERS IN RHEUMATOID ARTHRITIS
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OBJECTIVES: Rheumatoid arthritis (RA) is a chronic autoimmune disease that causes pain, stiffness and limited motion and function of joints. There are several biomarkers (HAQ,VAS,DAS28) known for measuring disease activity from different point of views. The main objective is to investigate the association among them based on advanced statistical methods. **METHODS:** Different biomarkers of 489 RA patients were collected in one of the largest Arthritis Center in Hungary from 5th Jun 1998 to 27th Feb 2015. Copula models are simple yet powerful tools for modeling joint distribution of multivariate variables. There are several parametric