Proceedings Paper:
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essential to ensure credibility of the results. The objective was to assess the impact of most common calibration methods on cost-effectiveness analysis (CEA): manual, Nelder-Mead algorithm and controlled random search (CRS). **METHODS:** We used a previously published and validated model from Spain. Data targets were age-specific HPV prevalence and CC incidence. Model outcomes included lifetime risk of cancer, quality-adjusted life years (QALYs), and lifetime costs (€). We compared the mean percentage deviation of model-predicted endpoints from available data for the three calibration methods and incremental cost-effectiveness ratios (ICERs) of different CC prevention strategies currently under discussion in Europe. **RESULTS:** Results showed that with a non-calibrated random matrix, the deviation was 79%. For the manually calibrated matrix, the deviation was 2%, although it required 40 days of analyst work. Regarding automatically calibrated matrices, the deviation was about 7% and 5% with computation times of 25 hours and 100 hours for Nelder-Mead and CRS respectively. Although the most cost-effective strategy remained invariable based in a CEA threshold of 20,000€/QALY, the magnitude of ICERs changed substantially (7,655€/QALY-14,745€/QALY). **CONCLUSIONS:** Important differences in both goodness of fit and CEA are found depending on the calibration approach. As was expected, the non-calibrated matrices produced HPV prevalence and CC incidence curves very far away from the target values and the largest differences on the cost-effectiveness results.

MO2

HOW IRELAND'S COLORECTAL SCREENING PROGRAMME COULD SAVE MORE LIVES, SAVE MONEY AND STAY WITHIN EXISTING COLONOSCOPY CAPACITY LIMITS: EVIDENCE FROM THE MISCAN MICROSIMULATION MODEL

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OBJECTIVES: To demonstrate why microsimulation modelling of colorectal cancer screening indicates that there are likely gains to be made by reconfiguring BowelScreen, Ireland's national colon cancer prevention programme. This analysis aims to show how the omission of relevant alternative screening strategies in a prior cost-effectiveness analysis of colon cancer screening in Ireland has likely led to a sub-optimal policy and that better outcomes at lower cost can be achieved by using a lower quantitative cut-off in the faecal immunochemical testing (FIT) employed. **METHODS:** We used the MISCAN microsimulation model of colorectal cancer screening to simulate the costs, effects and follow-up colonoscopy capacity requirements of 144 alternative screening strategies. These varied in their start and stop ages, screening intervals and FIT quantitative cut-off levels. Included in the simulations are Ireland's current programme of biennial screening of 60-69 year-olds using a FIT cut-off of 225ng/ml of haemoglobin. We simulate strategies with FIT cut-offs as low as 50ng/ml. The resulting estimates are plotted in the cost-effectiveness plane, checked for dominance and incremental cost-effectiveness ratios are calculated. **RESULTS:** We find that a combination of a reduction in the FIT cut-off to 50ng/ml, an extended screening interval of 3 years and a reduced screening start age of 55 saves 20% more QALYs, reduces costs by 7%, and yields a 17% reduction in colonoscopy requirements. In general, employing a lower FIT cut-off dominates strategies with higher cut-offs, such as those currently employed in BowelScreen. While extending the screening programme to a larger population would be possible and more cost-effective, it requires a lengthening of the screening interval from two to three years. **CONCLUSIONS:** Very simple changes to BowelScreen could save many more lives annually, reduce costs and relieve pressure on already constrained colonoscopy capacity. This simulation evidence suggests that BowelScreen should be re-examined.

MO3

MODELING COVARIATE-ADJUSTED SURVIVAL FOR ECONOMIC EVALUATIONS IN ONCOLOGY

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OBJECTIVES: Survival data from randomized controlled trials (RCT) is routinely extrapolated for economic evaluations in oncology. Imbalances in prognostic and/or predictive factors across treatment arms should be adjusted to generate unbiased estimates. To date no formal guidance has been developed regarding how such adjustments should be made. We compared various covariate-adjusted survival modeling approaches, based on parametric regression and propensity score matching, applied to the ENDEAVOR RCT in multiple myeloma that assessed carfilzomib-dexamethasone (Cd) versus bortezomib-dexamethasone (Vd). **METHODS:** Overall survival (OS) data and baseline characteristics were used for a subgroup (bortezomib-naïve/one prior therapy) reflecting the population where Cd is recommended in England and Wales. The following adjusted survival modeling approaches were compared: multiple Weibull regression model including prognostic/predictive covariates jointly fitted to the two arms to predict survival i) using the mean value of each covariate and ii) using the average of patient-specific survival predictions; iii) applying an adjusted hazard ratio derived from a Cox proportional hazard model to the baseline risk estimated for Vd with a Weibull model; iv) propensity score matching followed by fitting a Weibull model to the two arms of the balanced data including treatment group as the only covariate (matched data approach). **RESULTS:** The difference in mean OS estimated by the matched data approach was 2.06 years (0.02-5.01) with the smallest variance among the estimates. Despite other approaches estimated similar differences, the mean OS appeared biased (using the mean value of each covariate yielded skewed survival estimates), had limited external validity (implausible long-term OS predictions), and required assumptions not statistically appropriate, e.g. proportional hazards were not satisfied for all covariates. **CONCLUSIONS:** Adjusted survival modeling based on matched data approaches provides a flexible and robust method to correct for covariate imbalances in economic evaluations. The conclusions of our study may be generalizable to other settings.

MO4

DIFFERENT METHODS FOR MODELLING SEVERE HYPOGLYCAEMIC EVENTS: IMPLICATIONS FOR EFFECTIVENESS AND COST-EFFECTIVENESS ANALYSES

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OBJECTIVES: Published clinical trials report severe hypoglycaemic events in different ways. Some report number of patients who suffered at least one event out of total number randomised and others report number of events for a given total exposure. The different data types can be modelled in different ways; therefore, three models have been used in published Bayesian Network Meta Analyses (NMAs) of hypoglycaemic events; models with a binomial likelihood reporting odds ratios (using a logit link) or hazard ratios (using the complementary log log link) and models with a Poisson likelihood reporting hazard ratios. The objective of this paper is to establish the impact of using different models on effectiveness estimates and the outputs from cost-effectiveness models. **METHODS:** We analysed a dataset used in a recent NMA conducted to inform NICE guideline recommendations regarding insulin choice for patients with type 1 diabetes using the three previously used models, plus a shared parameter model combining different types of data. **RESULTS:** The relative treatment effects are similar regardless of which model or scale is used. Differences were seen when the probability of having an event on the baseline treatment was calculated using the different models with the logit model giving a baseline probability of 0.07, the clog-log 0.17 and the Poisson 0.29. These translate into differences of up to £110 in the cost of a hypoglycaemic event and 0.004 in associated disutility when calculating the absolute probabilities of an event to use in an economic model. **CONCLUSIONS:** While choice of outcome measure may not have a significant impact on relative effects for this outcome, care should be taken to ensure that the baseline probabilities used in an economic model are realistic and accurate to avoid over or underestimating costs and effects.

BREAKOUT SESSION XIII

P13: METHODOLOGICAL STUDIES IN CANCER

CN5

PROGRESSION-FREE SURVIVAL AS A SURROGATE ENDPOINT FOR OVERALL SURVIVAL IN PATIENTS WITH RELAPSED OR REFRACTORY MULTIPLE MYELOMA

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OBJECTIVES: In a previous study, the quantitative relationship between progression-free survival (PFS) and overall survival (OS) in multiple myeloma (MM) was assessed. However, that analysis combined studies of newly-diagnosed MM and relapsed/refractory MM (rrMM) and, since that analysis, there have been several randomized controlled trials (RCTs) of novel treatments for rrMM. The aim of this study is to provide an update of that analysis using randomized controlled trials (RCTs) only conducted in rrMM. **METHODS:** Two bibliographic databases (PubMed and Embase) were systematically searched for RCTs published between 1970 to 2017. Firstly, the association between median PFS and median OS was assessed using the non-parametric Spearman's rank correlation coefficient. Secondly, the quantitative relationship between PFS and OS was assessed using the Two Stage Least Square (2SLS) estimator. This approach was justified by relevant statistical tests in favor of the instrumental variable approach. **RESULTS:** 22 RCTs (42 treatment arms, 7,884 rrMM patients) were included. The average median PFS and median OS were 8.26 months (SD= 4.85), and 24.34 months (SD= 9.80), respectively. The correlation coefficient of median PFS and median OS was 0.712 ($P < 0.00001$). After adjustment for median age, sex and publication year, a 3.10 month (95%CI: 2.20 to 4.00) increase in median OS is estimated for each additional month increase in median PFS. **CONCLUSIONS:** Based on newer evidence from RCTs, PFS can be used to predict OS in rrMM and this analysis suggests that novel treatments may be providing additional months of OS gained for each month of PFS.

CN6

CAN BAYESIAN METHODOLOGY PREDICT LONG-TERM EFFECTIVENESS RATHER THAN EFFICACY? AN APPLICATION WITH OVERALL SURVIVAL IN TWO ONCOLOGY INDICATIONS

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OBJECTIVES: We assessed the impact of combining real-world evidence (RWE) with randomized controlled trials (RCTs) data for overall survival (OS) extrapolations. **METHODS:** Two RCTs in non-small cell lung cancer (NSCLC) and renal cell carcinoma (RCC) were selected. Based on the RCT control arms, similar NSCLC and RCC populations were identified from a German claims dataset. In WinBUGS, parametric survival models were fitted on both RCTs', and two parametric models were fitted over the RWE. We performed two analyses. First, the active treatment coefficients from the RCTs' parametric survival curves were combined with the corresponding RWE parameters. Second, the RWE shape parameters were used to inform the RCTs' shape parameters. Several priors were tested. **RESULTS:** The Weibull curve fitted best on both RWE datasets. In RWE, predicted mean OS was 15.5 (95%CI:13.0-18.8) and 31.4 (95%CI:24.9-42.5) months in NSCLC and RCC, respectively. In trials, predicted mean OS was 24.7 (95%CI:18.5-36.2) vs 40.7 (95%CI:28.1-61.2) months in NSCLC and 23.9 (95%CI:20.2-28.9) vs 27.9 (95%CI:23.0-35.2) months in