dation. **RESULTS:** Forty-two assessments were published. Of these, sofosbuvir was the focus of 29% of assessments, followed by simeprevir (26%), daclatasvir (12%) and ledipasvir + sofosbuvir (12%). These 33 HTAs met the criteria for further analysis. Eleven recommendations were positive without restriction (33%); 20 were positive with restrictions (60%) and two were negative (6%). Ledipasvir + sofosbuvir received the lowest proportion of positive recommendations without restriction (20%). Simeprevir and daclatasvir had the highest proportions, with 41% and 41%, respectively. Sofosbuvir, the first marketed and highest priced, was the only drug to receive negative recommendations. Clinical benefit was recognised as being an important criteria in 19 (58%) of the 33 reports. The main negative critique (reported in 11/33 cases) was lack of direct comparative evidence and the resulting uncertainty around cost-effectiveness. In three cases, positive recommendations were based on price negotiations with the manufacturer. The 20 positive recommendations were restricted to subpopulations where the cost-effectiveness was highest (progressed patients, with fibrosis and facing transplantation). **CONCLUSIONS:** Recently, 4 effective, but costly HCV drugs were launched. No clear trend was observed regarding order of market entry and HTA recommendation. However, in most cases, agencies restricted access to subpopulations. Cost seemed to be a key decision driver: simeprevir and daclatasvir most often received a positive recommendation.

RESEARCH ON METHODS STUDIES – I

RM1

ADJUSTING FOR TREATMENT SWITCHING IN RCTS – IDENTIFYING, ANALYSING AND JUSTIFYING APPROPRIATE METHODS: A CASE STUDY IN METASTATIC MELANOMA

Bell H[1], Latimer N[1], Amonkar M[2], Swann S[2]
[1]*University of Sheffield, Sheffield, UK,* [2]*Novartis Pharmaceuticals Corporation, Wayne, PA, USA*

OBJECTIVES: Participants in oncology randomised controlled trials (RCT) are often permitted to switch from their randomised treatments onto alternative treatments. Intention-to-treat (ITT) assessments are prone to bias in the presence of switching and consequently the overall survival (OS) benefit and cost-effectiveness of the novel treatment may be underestimated. Regardless, decision-makers frequently reject statistical analyses which adjust for treatment switching in health technology assessment, often due to poor justification of methodological assumptions. This study applies adjustment methods to an RCT comparing dabrafenib to dacarbazine in patients with BRAF V600E/K mutation-positive metastatic melanoma, and investigates which adjustment method best fits this specific case study. **METHODS:** The adjustment methods applied included the Rank Preserving Structural Failure Time Model (RPSFTM), Inverse Probability of Censoring Weights (IPCW), and two-stage adjustment. The suitability of each method was assessed by investigating their assumptions and trial characteristics. **RESULTS:** 37/63 (58.7%) dacarbazine patients switched to dabrafenib (direct switching). Also, 16 (25.4%) dacarbazine patients and 27 (14.4%) of 187 dabrafenib patients received other small molecule targeted treatments post-study (indirect switching). The ITT hazard ratio (HR) for OS was 0.81 (95% confidence intervals (CI) 0.56 - 1.16,) favouring dabrafenib. An RPSFTM analysis to adjust for direct switching, combined with a two-stage analysis to adjust for indirect switching, appeared most appropriate, producing an adjusted HR of 0.68 (95% CI 0.33 - 1.63). It was not possible to robustly adjust for direct and indirect switching simultaneously using standalone IPCW or two-stage methods due to small patient and event numbers. Whilst it is not possible to perfectly test the common treatment effect assumption required by the RPSFTM, our investigations did not find strong evidence against this. **CONCLUSIONS:** Adjusting for switching showed an increased OS effect for dabrafenib. Methodological assumptions must be rigorously investigated to demonstrate whether and which adjustment methods are justified.

RM2

AVOIDING OVERESTIMATION IN ANNUALIZATION OF EVENT RISK FROM RISK FUNCTIONS FOR USE IN ECONOMIC MODELING

Lothgren M[1], Danese M[2], Taylor B[3], Villa G[1]
[1]*Amgen (Europe) GmbH, Zug, Switzerland,* [2]*Outcomes Insights - Epidemiology & Health Economics, Westlake Village, CA, USA,* [3]*Amgen Inc, Thousand Oaks, CA, USA*

OBJECTIVES: The standard approach to derive transition probabilities for use in state-transition cost-effectiveness models based on available risk functions with different time horizon than the model cycle length is to use an exponential distribution (constant event rate assumption) to derive model cycle risk. However this does not remove any age effect on risk, resulting in potential overestimation of cycle-specific risks in the case age is included as a risk factor. We present an approach for annualization of event risk predictions that ensures the correct risk is predicted. **METHODS:** The proposed approach ensures that the starting age-specific event rate multiplied by the cumulative effect of increasing age during the time horizon of the risk function equals the original risk prediction. To illustrate and compare the standard and the proposed approach, 10-year risk is modelled and compared to the initial 10-year predicted risk using the latest Framingham risk function for primary cardiovascular (CVD) event risk (D'Agostino et al. 2008). Scenarios are investigated using different starting age and different initial predicted risk level. **RESULTS:** The standard risk annualization approach consistently overestimates the modelled risk over a 10-year horizon compared with the initial risk prediction for the same period. To illustrate, for a 50-year old male with initial 10-year CVD risk of 20%, 30% or 40% the corresponding modelled risk is 25%, 37% and 49%, respectively. The proposed method for risk annualization provides the exact 10-year initial risk. **CONCLUSIONS:** Careful application of approach for time period adjustment of existing risk functions for use in state-transition models is needed when age is included as a risk factor and the model cycle length differs from the time horizon of the risk function. The standard risk annualization approach will lead to an overestimation of modelled risk and a more favorable estimate of cost-effectiveness.

RM3

PARTITIONED SURVIVAL VERSUS STATE TRANSITION MODELING IN ONCOLOGY: A CASE STUDY WITH NIVOLUMAB IN ADVANCED MELANOMA

Briggs A[1], Baker TM[2], Gilloteau I[3], Orsini L[3], Wagner S[4], Paly V[2]
[1]*Institute of Health and Wellbeing, University of Glasgow, Glasgow, UK,* [2]*ICON Plc, Morristown, NJ, USA,* [3]*Bristol-Myers Squibb, Princeton, NJ, USA,* [4]*Bristol-Myers Squibb, Washington Crossing, PA, USA*

OBJECTIVES: This analysis aimed to investigate potential differences in estimated survival outcomes between partitioned survival models and state transition (Markov) models in the common three-state model of pre-progression, post-progression, and death by using nivolumab trial data in advanced melanoma. **METHODS:** Each approach was applied separately to patient-level data from a phase 1b trial of nivolumab in 304 patients with previously treated advanced solid tumors (107 melanoma patients). All patients were included in parametric survival analyses (with a parameter identifying melanoma patients) to model overall survival (OS), progression free survival (PFS), and post-progression survival (PPS) to extrapolate (10 years) beyond maximum trial follow-up for melanoma patients specifically. Alternative fits to the data were compared on the basis of Akaike Information Criterion (AIC) and the plausibility of the long-term extrapolation. **RESULTS:** The Weibull parametric model was judged to be the most conservative in terms of extrapolation and forms the basis of these results. Log-normal and log-logistic generally had better fit in terms of AIC, but fatter tails were less suitable for extrapolation. The area under the curve (AUC) for extrapolated PFS and OS was 23.5 and 41.5 months, respectively, suggesting 18 months of PPS using the partitioned survival approach. The AUC for PPS was 12.5 months, which gives an estimated OS of 36 months under the Markovian assumption. Relaxing this assumption to allow time dependency for transitioning between states with a Weibull model for PPS gives an estimated PPS of 17.1 months and an OS of 40.6 months. **CONCLUSIONS:** Partitioned survival modeling and Markov modeling make intrinsically different assumptions; nevertheless, by relaxing the Markovian assumption and allowing time dependency, the two modeling forms are shown to be functionally equivalent. The selection of approach should be driven by what best represents the disease, treatment effect, and available clinical data.

RM4

PROPENSITY SCORE MATCHING DOES NOT ALWAYS REMOVE CONFOUNDING WITHIN AN ECONOMIC EVALUATION BASED ON A NON-RANDOMIZED STUDY

Guertin JR[1], Bowen JM[1], O'Reilly D[2], Tarride J[2]
[1]*St. Joseph's Healthcare Hamilton, Hamilton, ON, Canada,* [2]*McMaster University, Hamilton, ON, Canada*

OBJECTIVES: To compare the economic results of a non-randomized study using propensity score (PS) methodology to adjust for confounding versus a restriction approach based on clinical opinion. **METHODS:** We used data from a published non-randomized study, which enrolled 195 patients (58.2%) to receive open surgical repair (OSR) and 140 patients (41.8%) to receive endovascular aneurysm repair (EVAR) for the treatment of abdominal aortic aneurysm. OSR patients were classified as being at low risk (LR) or high risk (HR) for post-surgical complications based on clinical opinion and scoring algorithms while all EVAR patients were classified as HR. The database included baseline characteristics, patient level 1-year cost and survival data. One-to-one PS matching was used within the full population to select a more balanced patient sub-population. Incremental cost-effectiveness ratios (ICERs) were assessed within the HR sub-population and the PS-matched sub-population. **RESULTS:** The HR sub-population was composed of all 140 EVAR patients (100.0%) and 50 OSR patients (25.6%). EVAR was identified as the dominant treatment option within the HR sub-population. The PS-matched sub-population was composed of 77 HR EVAR patients (55.0%) and 77 OSR patients (39.5%), of which 48 (62.3%) were OSR-LR patients and 29 (37.7%) were OSR-HR patients. Unlike results obtained within the HR sub-population, the ICER of EVAR was estimated at $93,608 per life-year gained within the PS-matched sub-population. Differences in the results may be explained by confounding; although balance was improved within the PS-matched sub-population, unbalance remained on several patient characteristics. **CONCLUSIONS:** Results of this study highlight the fact that PS matching may not always fully adjust for confounding. Clinical opinion may be influenced by unmeasured confounders which may not be adjusted for by PS matching. Balance within patient subsets following PS matching must be evaluated when conducting economic evaluation based on non-randomized studies, especially in studies with small sample sizes.

VACCINE STUDIES

VA1

PUBLIC HEALTH IMPACT AND COST-EFFECTIVENESS OF MALARIA ROUTINE VACCINATION IN INFANTS

Sauboin C[1], Sicuri E[2], Van Bellinghen L[3], Van de Velde N[1], Van Vlaenderen I[3]
[1]*GSK Vaccines, Wavre, Belgium,* [2]*ISGlobal, Barcelona, Spain,* [3]*CHESS in Health, Ternat, Belgium*

OBJECTIVES: Final phase III trial results of the first malaria vaccine candidate RTS,S have been published. Based on these results, our study aims at estimating the public health impact and cost-effectiveness of RTS,S implementation in infants in 42 sub-Saharan countries. **METHODS:** We developed a stochastic individual-based Markov model, calibrated against data from the control and vaccine arms of the RTS,S vaccine trial, published age distribution data and case-fatality rate. The simulated 2017 birth cohort was vaccinated at 6, 10, 14 weeks without and with a 4th dose at 21 months of age and followed-up over 15 years. Impact of sequelae and mortality was accounted over lifetime. Country-specific inputs were demographics, parasite prevalence, access to care, and diphtheria-tetanus-pertussis third dose vaccination coverage (DTP-coverage), with RTS,S 4th dose coverage assumed at 80% DTP-coverage. Costs for malaria outpatient visits and hospitalizations were taken from a study in 3 sub-Saharan countries. RTS,S price and cost of administration per dose