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OBJECTIVES: Economic evaluations in oncology require estimating survival benefits which is used to obtain quality adjusted life years (QALYs) and incremental cost-effectiveness ratios (ICERs). However, few guidelines exist on how survival data should be analyzed and extrapolated to obtain full survival benefit for economic evaluation. A recent NICE Decision Support Unit document details an algorithm for selecting survival models for economic evaluations alongside clinical trials. We use this algorithm and other published literature to demonstrate how different models lead to varying survival estimates and how survival data can be systematically assessed in a patient registry using patient-level data. **METHODS:** Data from the National Cancer Institute's Surveillance Epidemiology and End Results (SEER) were used. Surgical treatment for prostate cancer was used to illustrate the methods, but the approach is transferrable to other cancers and treatment strategies. Patients diagnosed with prostate cancer (PC) between 1991 and 2001 were included, the sample was limited to stage IV PC patients. Survival between surgery and non-surgery group was estimated via Kaplan Meier, parametric and semi-parametric methods. Several model fit criteria's such as visual inspection, log-cumulative hazard plots, Cox-Snell residuals, Akaike Information Criterion (AIC), Bayesian Information Criterion (BIC) along with proportionality assumption tests were used to select appropriate method and distribution. Observed and extrapolated mean estimates were calculated and compared. **RESULTS:** Analysis indicated that survival time and benefit differed based on the model selected. Our case example demonstrated the best fit was with Weibull and exponential distributions – however, consideration must also be given to the tail in any extrapolation of the parametric distributions selected. **CONCLUSIONS:** Systematic analysis of survival data is an important evaluation criterion by health technology assessments. Selection of survival models must be justified using appropriate steps as different models can yield varying estimates, and improper selection can translate to incorrect estimation of QALYs and the resulting ICERs.

CL3

CALIBRATING BAYESIAN MULTIPLE TREATMENT COMPARISON META-ANALYSIS WITH MULTIPLE COST-EFFECTIVENESS ACCEPTABILITY CURVES

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OBJECTIVES: To investigate the merits and challenges with calibrating Bayesian multiple treatment comparison meta-analysis (MTC) with cost-effectiveness (CE) analysis, in particular, construction of multiple cost-effectiveness acceptability curves and cost-effectiveness frontiers. **METHODS:** We calibrated a Bayesian MTC of pharmacotherapies for chronic obstructive pulmonary disease with a Bayesian CE markov model. We simulated 10000 observations and derived multiple cost-effectiveness acceptability curves for each of the treatments as well as the cost-effectiveness frontier. We separately repeated the analyses based on pair-wise meta-analysis estimates of treatment effectiveness. We compared the two approaches with respect to precision and inferred reasonable CE thresholds. **RESULTS:** The MTC approach generally yielded higher precision, and thus, had higher certainty surrounding the inferred CE thresholds. This was especially the case for comparisons with treatments in the extended dominance region, but close to the cost-effective treatments. **CONCLUSIONS:** Calibration of Bayesian multiple treatment comparison meta-analysis and Bayesian multiple cost-effectiveness acceptability curves appears to improve precision compared with the conventional approach.

CL4

MARGINAL STRUCTURAL MODELS USED IN ESTIMATING COST-EFFECTIVENESS OF TIME-VARYING DRUG THERAPY USING ADIMISTRATIVE DATABASES. THE CASE OF STATIN IN SECONDARY PREVENTION

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OBJECTIVES: Cost-effectiveness assessment using real-life data is important to improve health care management. We applied marginal structural models (MSMs) to evaluate cost-effectiveness of statin therapy and medication adherence in the secondary prevention of acute myocardial infarction (AMI), using health care administrative databases (HADs). **METHODS:** This is an observational longitudinal study based on HADs of the national health care system in Lombardy, a region in Northern Italy with about 9 millions of inhabitants. Patients hospitalized in 2003 for their first episode of AMI were followed until December 31, 2008, collecting data on health care services and vital status. Persistence and adherence to statin were measured as time-dependent variables. We adopted a net-benefit regression approach with related acceptability curves, using direct medical costs and gained life-years as outcomes. MSMs accounted for the dynamic interactive effects between treatment and the time-varying confounders, i.e. non-fatal cardiovascular (CV) events and others CV therapies. **RESULTS:** A total of 11,706 individuals (65% men) with a mean age of 70 years, were hospitalized for their first AMI during 2003. 26% of patients died during a median follow-up time of 5 years. The mean annul total cost per patient was €4,348 (95%CI: 4,264-4,408), 59% of which was attributable to CV diagnosis. Statin reduced the risk of death and medication adherence affected risk reduction. The incremental net-benefit of statin therapy was positive for values of willingness to pay (WTP) equal or greater than €0. The probability that statin therapy was cost-effective was 50% for WTP equal to €0 and about 75% for values equal or greater than €250. Medication adherence influenced cost-effectiveness. **CONCLUSIONS:** MSMs can be used in economic health care evaluations to account for time-varying confounding, trying to minimize the potential biases of longitudinal observational studies. This study confirms cost-effectiveness of statin therapy for secondary prevention in real-life settings and suggests further investigations on adherence effects.

PODIUM SESSION III: DRUG USE RESEARCH TO INFORM POLICY DECISION MAKING

DU1

A TIME SERIES ANALYSIS OF THE EFFECT OF THE CO-PAYMENT ON PHARMACEUTICAL CONSUMPTION IN TWO ITALIAN REGIONS

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OBJECTIVES: Since 2001 in Italy several regions have introduced a fixed co-payment with some differences in the amount and exemptions. The aim of the study was to assess, through a time-series analysis, the effect of the introduction of the co-payment on pharmaceutical consumption, using, as case study, two Italian regions: Piemonte and Puglia. **METHODS:** Monthly data between January 2000 and December 2010 related to both public and private outpatient consumption were used in the analysis. Public consumption data were obtained from AIFA's Medicines Utilisation Monitoring Centre (OsMeD); conversely, data on private consumption were obtained as difference between the total consumption (private and public) provided by IMS Health and public consumption. The data were expressed in Defined Daily Doses (DDD) per 1000 inhabitants. A segmented regression analysis was performed, controlling for the autocorrelation. **RESULTS:** In Piemonte Region the introduction of co-payment had an immediate significant effect on public consumption with a reduction of 74 DDD per 1000 inhabitants (*p-value* 0.007). The private consumption showed a significant increase of 119 DDD per 1000 inhabitants (*p-value* 0.03) after the introduction of the co-payment. In Puglia Region the co-payment didn't have the expected outcome; in fact both public and private consumption increased after the intervention. In the long term the public consumption steadily grew and there was a significant reduction in private consumption. **CONCLUSIONS:** The introduction of co-payment didn't have the expected effect in reducing the over consumption. In Piemonte Region the reduction of public consumption was balanced by the increase in private consumption (*substitution effect*). In Puglia Region the co-payment resulted in a lowering of private consumption, probably due to fewer available economic resources (*income effect*), and didn't have any effect on public consumption.

DU2

CONTRIBUTION OF PROLONGED-RELEASE MELATONIN AND ANTI-BENZODIAZEPINE CAMPAIGNS TO THE REDUCTION OF BENZODIAZEPINE AND Z-DRUG CONSUMPTION IN NINE EUROPEAN COUNTRIES

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OBJECTIVES: Insomnia is mostly treated by benzodiazepine (BZD) or Z-drugs that are efficacious but are also associated with safety issues like dependence and rebound insomnia. These safety concerns may present a major public health issue, particularly for the elderly. Prolonged-release (PR) melatonin is a non-sedative hypnotic that has demonstrated clinically relevant efficacy on quality of sleep and morning alertness, with a good safety profile. Several clinical trials demonstrated that the PR-melatonin could help reduce BZD/Z-drugs consumption. The objective is to analyze the impact of anti-BZD/Z-drug campaigns and the availability of PR-melatonin on the consumption of BZD/Z-drugs. **METHODS:** Nine European countries were studied. For each one, we studied the evolution of BZD/Z-drug sales volumes related to: the launch strategy of PR-melatonin, anti-BZD/Z drug campaigns, the market uptake of PR-melatonin and its reimbursement status. The sales differences from 2005 were interpreted graphically for BZD, Z-drugs and PR-melatonin. **RESULTS:** Three types of countries were identified: -Countries where the sales of BZD/Z-drugs decreased since 2007: Greece, Finland and Denmark. - Countries where the sales of BZD decreased while Z-drugs increased: Norway, the Netherlands and the UK. The anti-BZD campaigns seem effective for BZDs, but essentially resulted in the shift in prescription patterns towards Z-drugs. - Countries where the sales of BZD were stable and Z-drugs increased resulting in an overall increase in BZD/Z-drug sales despite anti-BZD/Z campaigns: France, Sweden and Spain. Campaigns aiming to reduce the use of BZD/Z-drugs failed when they were not associated with the availability and market uptake of PR-melatonin. The reimbursement of PR-melatonin supports better penetration rates and a higher reduction in sales for BZD/Z-drugs. The disreimbursement of BZD/Z-drugs did not have any effect on Z-drug prescriptions, with an increase noted during 2011. **CONCLUSIONS:** Policy makers wishing to change drug utilization patterns should consider the availability of pharmacological alternatives.

DU3

MARKET ACCESS DELAYS FOR CNS DRUGS IN EUROPE

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OBJECTIVES: A recent study[1] by the Tufts Center for the Study of Drug Development indicated that Central Nervous System (CNS) drugs take 35% longer to develop and are less likely to gain approval compared to other new prescription medicines. Once approved in Europe, Transparency Directive 89/105/EEC requires countries to determine pricing and reimbursement (P&R) within 180 days but this target is not always met. This study evaluated the time required to achieve P&R and to launch CNS products in Europe to quantify how such delays impact patients and