OBJECTIVES: The effects of acute coronary syndrome (ACS) events on health-related quality of life (HRQoL) and the time dependency of these effects are unknown. The aim of this study is to characterise health utilities in ACS patients. This will help development of future economic models estimating the cost per quality adjusted life year impact of ACS events and potential treatments. **METHODS:** Multicentre, non-interventional, longitudinal evaluation of health utility in patients experiencing ACS or stroke events. EuroQol-5 dimension surveys were sent to patients (≥18 years) from three centres in the UK 1 month following hospital admission for myocardial infarction (MI), unstable angina (UA) or stroke. Patient demographics, lifestyle and baseline utility score were collected in the first survey. Follow-up surveys were sent at 6, 12, 18 and 24 months to prospectively capture utility and subsequent health events. A group of patients were also identified retrospectively and patient demographics, lifestyle, and time since previous ACS event were collected. General healthy population utility values were assumed for pre-event HRQoL. **RESULTS:** Between January 2011 and March 2014, 2103 prospectively/retrospectively identified patients (mean age 68.3 [range 24–97] years; 67.9% male) responded: 1176 (55.9%) MI; 898 (42.7%) UA; 29 (1.4%) stroke; 24% had type 2 diabetes. Utility values post-event were lower than general healthy population values, although significant differences in utility among subsequent 6, 18, 12 and 24-month timepoints were not detected. However, a significant difference in utility between 12 and 18 months for the retrospectively identified subgroup only was observed. Through multivariate regressions analyses, wheelchair use, current smoking and secondary mental and joint health events were associated with the greatest utility decrements (>0.250 decrease). **CONCLUSIONS:** This study indicates that health utility decreases following a CV event and, while some improvement occurs over the subsequent 24 months, general healthy population utility is not necessarily attained.

UT4
MAPPING QUALITY OF LIFE SCORES FROM FACT-G, FAACT AND FACIT-F ONTO PREFERENCE-BASED UTILITIES USING THE 5-LEVEL VERSION OF EQ-5D QUESTIONNAIRE

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OBJECTIVES: The aim of this study was to develop and validate mapping algorithms to predict EQ-5D-5L utilities from two questionnaires (Functional Assessment of Anorexia/Cachexia Treatment – FAACT and Functional Assessment of Chronic Illness Therapy-Fatigue – FACIT-F) and their common component (Functional Assessment of Cancer Therapy-General – FACT-G) in patients with non-small cell lung cancer - cachexia (NSCLC-C). **METHODS:** Data were collected at five occasions over a 12-week period in two multicenter, placebo-controlled trials (ROMANA 1 and ROMANA 2). The study sample was divided into development and validation datasets according to patient's country of origin. Generalized estimating equations (GEEs) were performed to predict EQ-5D utilities from FACT-G, FAACT and FACIT-F scores. Five different sets of independent variables were tested including overall, Trial Outcome Index (TOI) and individual subscales results. The best performing models were selected based on mean absolute error (MAE) and root-mean square error (RMSE). **RESULTS:** A subset of 96 patients completed both EQ-5D-5L and FAACT/FACIT-F questionnaires. Models using the individual domains separately yielded the lowest MAE/RMSE in most of study time points; however, even algorithms modeling the overall scores showed a high predictive performance. In FACT-G models, Physical Well-Being had the highest explanatory value (0.0094; p<0.001), while Emotional Well-Being did not significantly affect the EQ-5D score; Anorexia-Cachexia (0.0035; p=0.007) and Fatigue (0.0059; p<0.001) subscales were highly statistically significant in FAACT and FACIT-F models, respectively. The Eastern Cooperative Oncology Group status was the only covariate retained in the final models after backward selection. All the differences between mean observed and predicted EQ-5D utility were below the Minimal Important Difference (0.08) established in cancer for UK-index scores. **CONCLUSIONS:** The developed algorithms enable the estimation of Quality-Adjusted Life Years (QALYs) from three cancer-specific instruments in cost-effectiveness analyses where EQ-5D data are missing. Further research evaluating model performance in an independent sample of NSCLC-C patients is encouraged.

BREAKOUTS – SESSION III

CARDIOVASCULAR OUTCOMES RESEARCH STUDIES

CV1
COMPARISON OF ORAL ANTI-COAGULANTS FOR STROKE PREVENTION IN NON-VALVULAR ATRIAL FIBRILLATION: TWO MULTI-CRITERIA DECISION ANALYSES

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OBJECTIVES: To compare five oral anticoagulants (OACs) available in the UK for stroke prevention in patients suffering from non-valvular atrial fibrillation (NVAF), based on factors relevant for payers and prescribers. **METHODS:** Two multi-criteria decision analyses (MCDA) were developed to compare apixaban, dabigatran, edoxaban, rivaroxaban and a vitamin K antagonist (VKA; i.e., warfarin) from payer and prescriber perspectives. Final evaluation models included up to ten clinical and three non-clinical criteria. The clinical criteria were ranked based on either expected changes in event mortality rates from the worst to best

performing treatment, as demonstrated in clinical trials, or based on variation of health-related costs (both acute and follow-up for one year). These rankings were used to compute centroid weights. An additive model was used to combine treatment performance with centroid weights to estimate the overall value of each OAC. Probabilistic and structural sensitivity analyses were conducted. **RESULTS:** Dabigatran was the best treatment in centroid weight analyses with 7%/8% higher overall value than the second best performing treatment, apixaban. Dabigatran also had the highest first rank probability (72% / 70%) in probabilistic sensitivity analyses, with apixaban being second (22% / 24% first rank probability). Rivaroxaban performed worse than other non-VKA OACs, but better than VKA (both with 0% first rank probability). The results were largely insensitive to changes in model structure, although changing availability of reversal agent to be the least important criterion increased apixaban to have approximately the same overall value as dabigatran. **CONCLUSIONS:** Despite using only rank-based preference data, we were able to demonstrate dabigatran to be the most and warfarin the least preferred treatment with an MCDA incorporating all factors relevant for distinguishing OACs.

CV2
USING SUBPOPULATION TREATMENT EFFECT PATTERN PLOT TO IDENTIFY MORE EFFICIENT RESOURCE ALLOCATION POLICIES

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OBJECTIVES: When cost-effectiveness analyses are conducted alongside randomized controlled trials it is important to acknowledge patient heterogeneity as this may result in more efficient resource allocation policies. In this study, we sought to explore to what extent the use of Subpopulation Treatment Effect Pattern Plot (STEPP) may facilitate such subgroup analysis strategies. **METHODS:** The analysis was based on data from the COACH study, in which 1,023 patients with heart failure were randomly assigned to three treatments: care-as-usual, basic support, and intensive support. First, using predicted 18-month mortality risk as the stratification basis, a suitable strategy for assigning different treatments to different risk groups of patient was developed. To that end a graphical exploration of the difference in net monetary benefit (NMB) across treatment regimens and baseline risk was used. Next, the efficiency gains resulting from this proposed subgroup strategy were quantified by computing the difference in NMB between our stratified approach and the best performing population-wide strategy. **RESULTS:** The STEPP approach allowed distinguishing between subgroups, i.e., intensive support appeared optimal for low-risk patients (18-month mortality risk ≤ 0.16), while basic support appeared optimal for intermediate to high-risk patients (18-month mortality risk > 0.16). The average gain in NMB resulting from a stratified approach compared to basic support for all was €1,312 (95% CI: €390-€2,346). **CONCLUSIONS:** A risk-based analysis using STEPP seems promising to explore the impact of baseline risk for the relative cost-effectiveness in optimizing treatment trade-off and subsequently in the quest for more efficient reimbursement policies.

CV3
POLICY OBJECTIVE OF GENERIC MEDICINES FROM THE INVESTMENT PERSPECTIVE: THE CASE OF CLOPIDOGREL

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OBJECTIVES: The objective of generic drug policies in most countries is defined from a disinvestment perspective: reduction in expenditures without compromising health outcomes. However, in countries with restricted access of patients to original patented drugs, the objective of generic drug policies can also be defined from an investment perspective: health gain by improved patient access without need for additional health budget. The objective of this study was to assess whether generic clopidogrel entry reduced the role of affordability constraints and increased clopidogrel utilization in European countries. **METHODS:** We analyzed the determinants of clopidogrel utilization in Europe between 2004 and 2014 using hierarchical linear models on country-level longitudinal data. The first generic clopidogrel entry occurred in 2009 in the majority of countries. **RESULTS:** Clopidogrel utilization was strongly affected by affordability constraints (as proxied by GDP per capita) before entrance of generic medicines, but this effect decayed by 2014. Our estimated hierarchical linear models found a substantially larger trend increase of clopidogrel utilization in lower-income European countries than in the higher-income ones. Similarly, generic entry increased clopidogrel consumption in lower-income countries but did not have an effect in the highest-income ones. The models also suggest that an earlier generic entry was associated with a larger effect. **CONCLUSIONS:** The case of clopidogrel indicates that the entrance of generics may increase patient access to effective medicines, most notably in lower-income countries, thereby reducing inequalities between European patients. Policymakers should also consider this investment aspect of generic medicines when designing international and national pharmaceutical policies.

CV4
ARE COMPONENT ENDPOINTS EQUAL? A STUDY INTO THE PRACTICE OF COMPOSITE END POINTS IN CLINICAL TRIALS

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OBJECTIVES: Clinical trials comparing treatments for coronary revascularization generally use composite end points in order to increase statistical precision and

efficiency, resulting in trials becoming smaller and less costly. However, the use of composite end points is questioned because it assumes that all unfavourable outcomes of a treatment are equal. We aimed to examine patients' perspectives regarding the use of composite end points and the utility patients put on possible unfavourable outcomes of treatment. **METHODS:** In this single-centre, prospective, observational PRECORE study, 140 CAD-patients who underwent either a Percutaneous Coronary Intervention (PCI) or Coronary Artery Bypass Grafting (CABG) at the Thoraxcentrum Twente, Medisch Spectrum Twente (Enschede, The Netherlands) between May 2016 and June 2016, were invited to participate in this study. A total of 126 (90%) patients gave consent to participate in this study. A novel methodology, a survey-based BWS choice experiment, was conducted to determine the relative importance of each component end point to CAD-patients. **RESULTS:** Patients considered "repeat PCI within a year post-intervention" (OR=204.8 ± SD=47.7, p<0.001),"stroke where symptoms disappear within 24 hours"(OR=53.3 ± SD=11.7, p<0.001), "MI where symptoms disappear within three months" (OR=43.4 ± SD=9.3, p<0.001), "recurrent angina pectoris"(OR=26.6 ± SD=5.4, p<0.001), "repeat CABG within a year post-intervention" (OR=11.9 ± SD=2.3, p<0.001), and "MI causing permanent disability" (OR=2.9 ± SD=0.4, p<0.001), less severe than "death", but considered "stroke causing permanent disability" worse than "death" (OR=0.7 ± SD=0.1, p=0.05). Subgroup (revascularization procedure, prior-MI, and prior revascularization) differences can be found for the relative weights attributed to "death" versus "stroke causing permanent disability". **CONCLUSIONS:** CAD-patients do not consider the components of a composite end point equal. The fact that patients do weight the individual components differentially has significant implications for trial statistics, and the interpretations of trial data, since these can be misleading.

PRICING POLICY STUDIES

PR1
ASSOCIATION BETWEEN THE PRICES OF ORPHAN DRUGS IN ONCOLOGY AND THE PATIENT POPULATION SIZES
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OBJECTIVES: High prices of orphan drugs are often linked to the necessity to recover the development costs from sales to small patient populations. If this is true, drugs with smaller target population sizes should be more costly. We sought to compare the prices of orphan drugs in oncology with their respective patient population sizes. **METHODS:** A list of orphan drugs designated by the FDA between June 2011 and June 2016 was retrieved from the FDA website. We include: a) drugs approved by the FDA; b) treatments in oncology. We exclude: a) products not specifically indicated to treat cancer (e.g., imaging, palliative care or treatment of a cancer-associated condition). Diseases prevalence data was obtained from the FDA orphan drug approval reviews. Average Wholesale Prices per unit were obtained from the Micromedex database. Prices per year of treatment were calculated based on the drugs' dosage from the FDA labels. We used descriptive statistics to compare drug prices per year of treatment to the target populations of patients for each indication. **RESULTS:** Out of 187 orphan designated indications, 70 led to drug approvals by the FDA. 37 approvals were in oncology. Eight regimens had two approved indications and one had five indications. There were 25 unique regimens of which two were for drug combinations. There was no clear association between the drug prices and the sizes of their respective patient populations. **CONCLUSIONS:** The current orphan drug policies have encouraged the development of novel treatments, but have also led to extremely high prices of these drugs. Whereas drug prices may depend on factors other than population size alone, our findings suggest that there is no apparent link between the prices and target population sizes. This should help policy makers formulate future orphan drug policies that encourage innovation, but that are based on drivers other than potential market size alone.

PR2
PAY FOR PERFORMANCE: A PROPOSAL FOR AND SIMULATION OF REAL TIME OUTCOMES-BASED PHARMACEUTICAL PRICING USING ROUTINELY COLLECTED DATA
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OBJECTIVES: Electronic medical records (EMR) provide a rich source of routinely collected real-world data on health outcomes and resource use, which could be potentially used in economic models to adjust pharmaceutical pricing in real time to reflect the value a product delivers to the health care system. Our aim was to simulate how real time outcomes-based pricing could be operationalised using the example of visual acuity outcomes associated with treatment with ranibizumab for age-related macular degeneration (AMD) collected in a UK EMR database. **METHODS:** A 5-year patient-level simulation model was developed to synthesise cost and outcomes of patients treated with ranibizumab for AMD recorded in EMR and patients' natural history reported in the placebo arms of pivotal trials. The model was updated at daily intervals following the first treatment in 2008 until 2012 with the cumulative visual acuity outcomes recorded in EMR. The price of ranibizumab was adjusted each day to maintain a target incremental cost effectiveness ratio (ICER). **RESULTS:** The price of ranibizumab was reported at daily intervals over the course of the simulation. The first price of ranibizumab could be calculated after 3 months and reached GBP434.76 per vial at the end of the simulation when targeting an ICER of GBP30,000 per QALY. The simulation included data on 8,681 patients treated across 1,416 days. At the end

of the simulation, the mean number of QALYs accumulated by patients was 3.05 in the treatment arm compared to 2.56 in the natural history arm over the five year time horizon. **CONCLUSIONS:** Real world data may be used to monitor the cost-effectiveness of on-market drugs and to regularly refine their prices based on the value delivered in clinical practice. Performance-based pricing could be used to negotiate earlier market access for pharmaceuticals in advance of mature data on cost-effectiveness.

PR3
DIFFERENCES IN PRICING POLICIES FOR GENERIC AND BIOSIMILAR MEDICINES
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OBJECTIVES: In the view of their increasing importance biosimilar medicines might be subject to specific policies. The study aims to analyze possible differences between pricing policies for generics and for biosimilar medicines in European countries. **METHODS:** Policies for biosimilar and generic medicines were surveyed with competent authorities for pharmaceutical pricing and reimbursement. A questionnaire was launched in January 2016 to survey information valid as of the beginning of the year 2016. A draft compilation of findings was shared with the respondents for validation in April 2016. **RESULTS:** We received responses from 25 EU Member States (all but Ireland, Italy, and Luxembourg), and Albania, Belarus, Iceland, Norway, Serbia, Russia, Turkey, and Ukraine. While 23 of the 33 surveyed countries set the price of the generic in relation to the price of the originator, 13 countries reported to do so for biosimilar medicines. Usually, the price difference between the biosimilar and the originator medicine was set at a lower percentage rate than between the generic and originator (e.g. 30% – generics, 15% – biosimilars in Croatia; 50% – generics, 30% –biosimilars in Lithuania; 35% – generics, 20% – biosimilars in Romania). Only Austria, Latvia and Turkey apply the same price difference for generic and biosimilar medicines (the first follower – either generic or biosimilar medicine – has to be 48%, 30% and 40% below the price of the originator). The Netherlands have been tendering for generics in the out-patient sector during the last decade, but biosimilars were included in tenders only recently. **CONCLUSIONS:** In principle, European countries tend to apply similar pricing policies for generic and biosimilar medicines. However, while certain policies are established standard for generics, their implementation for biosimilar medicines appears not to have been decided yet. Overall, policy-makers tend to grant biosimilar medicines more favorable conditions compared to generics.

PR4
THE DETERMINANTS OF INNOVATIVE DRUGS PRICES: THE CASE OF ONCOLOGY DRUGS, COMPARATIVE ANALYSIS
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OBJECTIVES: The variation in health system regimes creates cross-country differences in prices for the same pharmaceutical product. Additionally, the price of an innovative drug (Pi) is generally dependent on the cost of the reference treatment (R), and the added value relative to the reference treatment. Pi = R+ D. Then the objective of this study is threefold: First to the assess trends in prices of anticancer drugs in different OECD countries. Second to examine the impact of the specifics regulations in the pricing. Third to examine the effect of the value added of the innovative anticancer drugs in the pricing. **METHODS:** We investigate both the impact of the add value and the regulation in the pricing of the anticancer drugs. To do so, we estimate a country fixed effects model: Yi,j= a + B,j + Ei,j with (i,j =1…n) Where Yi,j is a price for a drug i in a country j. Xi,j is the vector of drugs characteristics, and B,jis the country fixed effects. **RESULTS:** A total of 207 drugs prices were observed across all countries in the study. Our model evaluated the impact of twelve variables considered most likely to impact the prices setting. The model fitted the data well (R2=55%). As expected the therapeutic added value had a significant effect on the prices, with one month of Progression free survival gained increasing the Prices with 80 € (p<0,001). For the clinical evidence, the design of clinical trial shows a coefficient of 510 € (p<0,001). The form and the drug age has a significant impact on the prices. The fixed effect demonstrates that the level of pricing disparities reflects the differences in the pricing regulations **CONCLUSIONS:** This study demonstrates that the level of pricing disparities, in most cases reflect the therapeutic added value and the differences in the prices mechanisms.

BREAKOUTS – SESSION IV

MEDICATION ADHERENCE STUDIES

AD1
REAL-WORLD IMPACT OF GENDER, AGE AND SOCIO-ECONOMIC STATUS ON TYPE-2 DIABETES MELLITUS (T2DM) PATIENTS DISEASE ENGAGEMENT AND ADHERENCE WITH TREATMENT REGIMENS
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OBJECTIVES: It is hypothesised that gender, age and socio-economic status (SES) play key roles in engagement with disease, life-style choices and adherence. This analysis investigated the impact of these non-modifiable factors amongst T2DM patients. **METHODS:** Data were drawn from the 2015 Adelphi Diabetes Disease Specific Programme (DSP) in T2DM across 5EU/USA. The DSP is a real-world, cross-sectional survey involving diabetes specialists, primary care physicians (PCPs), and