COST-EFFECTIVENESS OF INTENSIVE STATIN THERAPY COMPARED TO MODERATE STATIN THERAPY IN PATIENTS WITH ACUTE CORONARY SYNDROME: ANALYSIS FROM CANADA, GERMANY AND THE UK
Drummond MF 1, Schwartz JS 2, Koren M 3, Cannon C 4, Davie A 5, Shui AI, Murphy S 6, Graff J 7
1 University of York, York, Heslington, UK, 2University of Pennsylvania, Merion Stn, PA, USA, 3Memorial Hospital, Jacksonville Heart Center, Jacksonville Center for Clinical Research, Jacksonville, FL, USA, 4Brigham and Women’s Hospital and Harvard Medical School, Boston, MA, USA, 53 Innovus, Uxbridge, Middlesex, UK, 6Pfizer, Inc, New York, NY, USA

OBJECTIVES: The PROVE IT-TIMI 22 trial demonstrated clinical benefit of intensive lipid lowering (atorvastatin 80 mg) vs. moderate lipid lowering (pravastatin 40 mg) in patients with acute coronary syndrome (ACS). Prior US analysis found lower net costs for intensive Rx. The objective of this analysis was to evaluate cost-effectiveness of intensive vs. moderate statin therapy in ACS patients in the UK, Germany and Canada where generic pravastatin is available and hospitalization costs lower than in the US. METHODS: Hospitalization and length of treatment were obtained from PROVE-IT case report forms. Hospitalizations were classified by relevant DRG system and multiplied by associated hospitalization costs in the UK, Germany and Canada. Drug costs were obtained from each country’s public or tariff prices. RESULTS: Compared with moderate pravastatin therapy, intensive atorvastatin therapy was associated with fewer hospitalizations (1301 vs. 1444; 0.62/pt vs. 0.70/pt). Total costs (hospital + drug) per patient of intensive vs. moderate therapy were £3184 vs. £3236 (UK), €6524 vs. €6515 (Germany) and CA$7386 vs. CA$8087 (Canada), with savings per patient of £56, €284 and CA$701 respectively over the 2-year study period. Thus, increased drug acquisition costs were more than offset by reduced hospitalization costs in all three countries. Sensitivity analysis on treatment pattern variations, events and costs will be conducted. If the PROVE-IT results are generalizable to all ACS patients, the savings from intensive vs. moderate statin therapy per two years of treatment would be £5.6 million, €28.4 million and CA$70.1 million for every 100,000 ACS patients in the UK, Germany and Canada, respectively. CONCLUSIONS: As observed in PROVE-IT, intensive atorvastatin therapy reduced clinical events and costs compared to moderate pravastatin therapy among ACS patients in the UK, Germany and Canada and thus is clinically beneficial at a lower overall cost among PROVE-IT ACS patients, allowing allocation of resources to other therapy options.

ASSESSING COST-EFFECTIVENESS BEFORE MARKETING: A CASE-STUDY OF RIMONABANT FOR REDUCTION OF CARDIOMETABOLIC RISK IN PATIENTS WITH DYSLIPIDEMIA IN THE UK
Caro RJ 1, Getsios D 2, Proskorovsky I 3, Nicholls C 4, McEwan P 5
1 Caro Research Institute, Concord, MA, USA, 2 Caro Research Institute, Halifax, NS, Canada, 3 Caro Research Institute, Dorval, QC, Canada, 4 Sanofi-Aventis, Guildford, Surrey, UK, 5 Cardiff Research Consortium, Cardiff, UK

OBJECTIVE: Often cost-effectiveness analyses must be undertaken before a price for the product has been set. This study evaluated the expected cost-effectiveness of rimonabant, the first selective CB-1 receptor blocker, for treatment of patients with dyslipidemia in the UK under various price assumptions.

METHODS: A Markov model (SHAPE) was developed using data from clinical trials, published risk equations and UK patient profiles from the Health Outcomes Data Repository Database (HODaR) registry. Patients transition from At Risk or Diabetes to CVD based on UKPDS 68 or Framingham Heart study equations, or to death based on UK life-tables, and to diabetes (San Antonio Heart study) and subsequent CVD events (Saskatchewan equations). UK costs for acute resource use upon transition as well as longer term routine management are accrued in 2005 GBP. Age-dependent utilities are calculated and tariffs for all events and states are applied. Rimonabant effects on cardiometabolic risk factors were taken from the RIO Lipids trial. Ten year and lifetime horizons were examined; all outcomes were discounted at 3.5%/yr. Extensive probabilistic sensitivity analyses were carried out. RESULTS: Over ten years, >13% of patients are expected to suffer a cardiovascular event with a loss of more than $1045 QALYs and a cost above £600,000 per 1000 patients. Adding rimonabant to diet & exercise for only one year is estimated to gain >100 QALYs over a lifetime. Preliminary cost-effectiveness ratios remained acceptable (less then £20,000/QALY) under a wide range of assumptions and when testing hypothetical prices as high as $8 per day. CONCLUSIONS: Based on the reductions in total to HDL cholesterol ratio, weight and other risk factors seen in RIO Lipids trial, rimonabant should substantially reduce cardiovascular risk in obese or overweight patients with dyslipidemia and result in an acceptable cost-effectiveness ratio.

GROWTH, CHARACTERISTICS, AND QUALITY OF THE COST-UTILITY LITERATURE THROUGH 2003
1 Tufts-New England Medical Center, Boston, MA, USA, 2 Tufts University School of Medicine, Boston, MA, USA, 3 University of Nebraska Medical Center, Omaha, NE, USA, 4 University of Rochester, Rochester, NY, USA, 5 Ben-Gurion University of the Negev, Beer-Sheva, Israel, 6 Harvard University, Cambridge, MA, USA, 7 Harvard School of Public Health, Boston, MA, USA

OBJECTIVES: 1) To quantify and characterize the cost-utility analyses (CUAs) published in the scientific literature through 2003; and 2) to examine methodological practices used in these CUAs. This paper builds upon our previous analyses that evaluated CUAs from 1976 through 2001. METHODS: We systematically searched Medline and the Health Economic Evaluations Database (HEED) for original CUAs written in English and published during 2002–2003 to update a comprehensive registry of CUAs (www.tufts-nemc.org/cearegistry). Two trained readers independently extracted data on the characteristics and methodology of each study. We compared recently published (2002–2003) with previously published (1976–2001) data.

RESULTS: Our previous search identified 533 original CUAs published during 1976–2001; a finding of 262 studies published during 2002–2003 increased the sample by almost 50%. In the 1976–2001 and 2002–2003 data, most studies were based in the US (61%, 53%) and written by academics (90%, 92%). Studies examined treatment (63%, 62%) more than primary (14%, 16%) and secondary (22%, 21%) prevention. The most frequent condition studied was cardiovascular disease (21%, 18%). Percentage of funding by the pharmaceutical and device industry did not change substantially (19%, 23%). Studies improved with time across the two datasets: disclosing funding source (65% vs. 71%), stating year of currency (76% vs. 82%), reporting incremental ratios (59% vs. 79%), and using probabilistic sensitivity analyses (9% vs. 28%). CONCLUSIONS: The publication of
CUAs has accelerated in recent years. Use of recommended methods has increased, although a sizeable number of analyses still do not adhere to best practice. Continued monitoring of these trends is crucial to enhancing the quality of the field.

**MC2**

**15DS—A NEW DYNAMIC QUALITY OF LIFE TOOL WITH INCREASED SENSITIVITY AND IMPROVED COMPOSITE STRUCTURE FOR RECALL BIAS AND RESPONSE SIFT ADJUSTMENTS**

Soini El1, Rymanen OP2

1Department of Health Policy and Management, Department of Social Pharmacy, University of Kuopio, Kuopio, Finland. 2General Practice, Department of Public Health and Clinical Nutrition, University of Kuopio, Kuopio, Finland

**OBJECTIVES:** Response sift (RS) and recall bias (RB) cause problems in patient-reported outcomes (PRO). RS refers to the change of meaning in health-related quality of life (HRQoL) in pretest-posttest design. RB is the result of variation in the recall of earlier HRQoL states, satisfaction and symptoms. To present a new composite HRQoL tool for integrating contemporaneous items with recall/response items. The innovative aim of the generic 15Ds tool is the adjustment of RB/RS. **METHODS:** The widely utilized 15D tool yields both 15-dimensional health profiles and an overall HRQoL index. The 15D was promoted by the WHO health definition and the additive valuation of multiattribute utility theory (MAU) to produce quality-adjusted life years (QALY). The 15Ds was invented by the literature and pragmatic experience with the 15D. **RESULTS:** The 15Ds contains 15 contemporary dimensions with five states (i.e. the conventional 15D), 15 recall/response dimensions with six states for transitions, and three validation dimensions. The recall/response dimensions adjust subjects’ contemporary states for RB/RS. The validation dimensions contain a comparison of the subject’s general health state to the health of a same-age population (5 states), RB/RS comparison for health transitions (6 states), and comparison for the level of healing (illness conceptualization, 5 states). A preliminary analysis revealed that patients have more sensitivity for changes measured as the recall/response items than for changes in the contemporary items over time. The 15Ds gives slightly better outcomes in the index changes and offers higher discrimination for the changes of HRQoL when compared with the conventional 15D. **CONCLUSIONS:** The 15Ds can produce 15-dimensional contemporary health profiles, 15-dimensional recall/response health profiles, overall HRQoL index for both 15Ds and 15D, and approximations for the validation of transitions, health and illness. The 15Ds is recommended for recall (e.g. acute conditions when no baseline HRQoL is obtainable) and RB/RS adjustment.

**MC3**

**USING SIMULATIONS TO EXPLORE THE INFLUENCE OF COMPETING RISK ON TREATMENT-EFFECT**

Kent OM1, Hayward RA2

1Tufts-New England Medical Center, Boston, MA, USA. 2University of Michigan, Ann Arbor, MI, USA

**OBJECTIVES:** In previous work, we explored through computer-aided simulated clinical trials how heterogeneity of baseline risk can lead to heterogeneity of treatment-effect under a variety of assumptions. We now explore how heterogeneity of competing risks affect treatment-effect heterogeneity under a variety of assumptions. **METHODS:** Using simulated clinical trials in which the intervention has a constant effect on disease-specific risk (odds ratio = 0.7) but no effect on competing risk and in which outcomes in individuals are determined by varying 2 parameters: (1) the overall risk of the outcome of interest and (2) the ratio between the competing risk and the disease-specific (i.e. treatment-responsive) risk. **RESULTS:** Under conditions in the simulations, the odds ratio of the treatment-effect on the overall outcome is highly dependent on the ratio of the competing and disease-specific risk, decreasing as this ratio increases. Although the absolute treatment-effect increases with increasing overall risk, the odds ratio for the treatment decreases as the overall risk increases (holding constant the ratio between disease-specific and competing risk). When disease-specific outcomes are measured, a similar relationship between treatment-effect and overall risk is observed, although the decrease in the odds ratio with increasing risk is greatly attenuated. Detecting significant treatment-effect heterogeneity (on the odds ratio scale) based on competing risk is likely to occur only when competing risk is very high or when patients can be sub-grouped by variables which distinguish between disease-specific and competing risk. **CONCLUSION:** The ratio of competing risk to disease-specific risk in a population can have an important impact on the measured treatment effect, even when disease-specific outcomes are measured. Detection of competing-risk-based treatment-effect heterogeneity may depend on the identification of risk factors that differentiate disease-specific from competing risk. Simulations can be useful to anticipate the magnitude of these effects when planning a clinical trial.

**MC4**

**BREAKING THE SILENCE: THE EFFECTS OF EXPLICIT INSTRUCTIONS ON INCORPORATING INCOME IN TTO EXERCISES**

Krol M1, Brouwer W1, Sendi P2

1The institute for Medical Technology Assessment, Rotterdam, The Netherlands. 2Institute for Clinical Epidemiology, Basel, Switzerland

**OBJECTIVES:** The recommendation of the US Panel to incorporate productivity costs in terms of health effects (QALYs) in a cost-effectiveness analysis aroused quite some debate. A crucial yet under-explored question in this debate is whether people include effects of ill-health on income in health state valuations (HSV). The same holds for the actual inclusion in HSV of the effects of ill-health on leisure. This study aims to test whether respondents to health-state valuations using TTO questions include the effects of ill-health on income and leisure when the measure is silent on both. Moreover, it tests the consequences of explicit instructions to either include or exclude the income-effects in HSV. **METHODS:** Three questionnaires were developed and administered among the general public. Respondents were asked to value three distinct EQ-5D health-states using TTO. In version 1 respondents did not receive instructions on including or excluding income-effects in their valuations, but inclusion was assessed afterwards. In versions 2 and 3 respondents were instructed upfront to incorporate income-effects or to assume that income would not change. They were furthermore asked whether they included the effects of ill-health on leisure-time in their HSV. **RESULTS:** In version 1 64% of the respondents spontaneously included income-effects in their HSV. In version 2 and 3 88% included leisure-time. There were no differences in the valuations of respondents including or excluding income-effects, also in case of explicit instruction. Inclusion of leisure-time resulted in a significantly lower TTO-value in only one of the three health-states. **CONCLUSIONS:** Respondents do not consistently include income- and leisure-effects in their valuations. Including income-effects (spontaneously or instructed) does not seem to affect TTO-valuations and may therefore best be placed on the cost-side of the cost-effectiveness ratio. Leisure-