whichever came first. Patients were excluded if they had type-1 diabetes or were pre-
scribed rosiglitazone or troglitazone during the study period, or had stroke, MI, or
brain injury prior to index date. Cox proportional hazards model was used to estimate
risk for stroke or MI controlling for demographics, baseline comorbidities, medication use
and other factors. RESULTS: A total of 12,753 patients with T2DM were included; total of 9,053 (10.62%) patients were on PIO and 7,620 on Non-TZD cohort; a total of 178 (1.97%) patients who initiated PIO were hospitalized for stroke or MI compared to 1,383 (2.41%) patients in the Non-TZD cohort (P < 0.001) during the follow-up period. The unadjusted incidence rates for stroke or MI hospitalization associated with PIO relative to Non-TZD was 0.789 (95% CI: 0.677-0.921). After adjusting for baseline covariates in the multivariate analysis PIO patients were less likely to have stroke or MI hospitalization than Non-TZD patients, adjusted hazard ratio was 0.959 (95% CI: 0.732-1.26). CONCLUSIONS: T2DM patients initiated on pioglitazone were at reduced risk of having stroke or MI hospitalization than Non-TZD patients during the follow-up period. The result is consistent with clinical trial metaanalyses demonstrating lower risk of stroke or MI with pioglitazone com-
pared to other oral antidiabetic agents.

**PODUM SESSION IV: MODELING METHODS – HANDLING UNCERTAINTY**

**MO9 HANDLING UNCERTAINTY IN THE CASE OF COMBINED END-POINTS**

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Trials powered to show significant differences in a combined end-point invariably lack power to evaluate the individual endpoints. Analyzing them separately leads to wide uncertainty margins which may have important consequences, especially when death is included. OBJECTIVES: To develop methods which recognize the process underlying the occurrence of endpoints and to analyze whether such methods lead to different point estimates and different results in probabilistic sensitivity analyses (PSA). METHODS: Two methods are compared with the “usual” approach, where individual events are modeled as the outcomes of a multinomial distribution. The first method heroinically assumes that the risk reduction of the combined endpoints can be applied to the total event rate after which a partial multinomial model can be used for the events. The second method uses a Bayesian meta-regression which is programmed in Winbugs and includes data from earlier trials in the same area with and without the inclusion of explanatory variables. The two methods are illus-
trated using MI/stroke free survival as an endpoint from studies concerning lipid lowering therapy and studies concerning platelet inhibition. In the first, lipid levels are included as explanatory variables, in the second an unobserved common process is assumed. RESULTS: Analysis of data from six cholesterol trials and five platelet studies shows that assuming that the risk reduction applies to all events reduces the uncertainty by between 12-22% without affecting the point estimates. When using the Bayesian meta-regression models, the uncertainty is decreased by between 30%-80% with explanatory variables and between 16-45% without explanatory variables. However, point estimates may change more substantially as guided by the evidence from previous observations. CONCLUSIONS: Using Bayesian meta-regression to capture the dependence between endpoints in a combined endpoint-study may reduce the uncertainty of PSA results substantially. The magnitude of the reduction seems greater than when making heroic assumptions concerning the underlying dependence.

**MO10 EARLY MODELLING: METHODS IN THE ECONOMIC ANALYSIS OF PRE-PHASE II PRODUCTS**

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OBJECTIVES: Economic evaluations are increasingly used as tools to inform decision-makers about the cost-effectiveness of health technologies. Such evaluations are often undertaken during the late stages of the technology development (i.e. around the time of product launch or, in some cases, post-launch). However, there is an increasing need for the manufacturers of the technology to appraise the likely cost effectiveness of the intervention before making decisions on price and indication, as well as to inform the development of clinical trials. METHODS: Due to the simplified nature of such ‘early analyses’, there is no availability of Phase III trial data, or evidence of subtle interferences between parameters. The purposes of such an analysis are to allow the user to determine the relative importance of different parameter inputs, in order to inform decisions on pricing, target populations and further research. This presentation outlines the key advantages and limitations of early modelling, and how the decision maker should interpret such analyses. RESULTS: This study demonstrates that early modelling is a vital exercise even (and, sometimes, especially) when there is a significant lack of cost and effectiveness data. Early models can be an effective tool for determining price and target indications. A variety of outputs are demonstrated that will maximise the usefulness of such models to the decision maker. CONCLUSIONS: Even when there is a lack of Phase III data, economic models are a useful tool. However, the approach to modelling in such circumstances is significantly different to that when ‘full’ models are prepared. This study demonstrates how the value of early models can be increased, using a number of key outputs.