variable. CONCLUSIONS: Logistic regression using a generalized multinomial logit link appears to provide a good propensity score from which pseudo-randomization into three groups can be performed in a retrospective sample.

PRM45 NETWORK META-ANALYSIS OF STUDIES WITH OUTCOMES AT MULTIPLE TIME POINTS USING FRACTIONAL POLYNOMIALS
Veiastra da Silva MC1, Jansen JP2
1Mapi Consultancy, Boston, MA, USA, 2Mapi Consultancy / Tufts University School of Medicine, Boston, MA, USA
OBJECTIVES: Network meta-analysis of randomized controlled trials (RCTs) are often based on one effect measure per study. However, many studies have data available at multiple time points. Furthermore, not all studies might have measured the outcomes at the same time points. As an alternative to network meta-analysis based on the results at one time point, a network meta-analysis method is presented that allows for the simultaneous analysis of outcomes at multiple time points.
METHODS: The development of outcomes over time of interventions compared in a RCT are modeled with fractional polynomials, and the difference between the parameters of these polynomials within a trial are synthesized across studies with a Bayesian network meta-analysis. RESULTS: The proposed models are illustrated with an analysis of RCTs evaluating interventions for osteoarthritis of the knee. Fixed and random effects first and second order fractional polynomials were evaluated. CONCLUSIONS: Network meta-analysis with models where the treatment effect is represented with several parameters using fractional polynomials can be used to simultaneously analyze results at multiple follow-up times that are not consistent across studies.

PRM46 CONTROLLING FOR MULTICOLLINEARITY IN PURSUIT OF A PRO-BASED LABEL WHEN MULTIPLE PROS ARE ASSESSED
Cole JC
Covance Market Access Services, Inc., San Diego, CA, USA
OBJECTIVES: The FDA’s final Guidance for industry on patient reported outcome (PRO) use in support of labeling claims was issued in December, 2009. In their Guidance, the FDA noted that a study’s endpoint model must consider the hierarchy of multiple endpoints, including how PROs used for a label claim fit into this hierarchy. Researchers should be knowledgeable of the various ways familial error is influenced and how best to control for it with an informed multiplicity plan as part of their endpoint model.
METHODS: Outcomes from previously published literature were examined for the influence of various familial error error issues and related multiplicity controls, including analytic issues, gatekeeping, and precision alpha control (vs. Bonferroni or Hochberg). RESULTS: In a study with one clinical and three PRO outcomes, A Bonferroni correction resulted in just one significant result. A gatekeep between primary and secondary outcomes resulted in two significant findings. Finally, when using either an adjustment for known-levels of correlation to adjust alpha (Tukey's test of statistical certainty) or using a repeated measures ANOVA vs. change-score analysis, three of the outcomes were classified as significant. CONCLUSIONS: Researchers should understand the implications of their multiplicity control in order to make informed decisions about their analyses, organization of their endpoint model, and ultimately make the best plans to ensure their PRO-based label claims have the most accurate demonstration of their statistical probability.

PRM47 BAYESIAN REGRESSION MODELS FOR ESTIMATION OF ILLNESS-ATTRIBUTABLE COST FROM AGGREGATE DATA
Mittakazu N1, Tomlinson C2
1Toronto Health Economics and Technology Assessment (HTA) Collaborative, Toronto, ON, Canada, 2Toronto General Research Institute, Toronto, ON, Canada
OBJECTIVES: In Health Economics, the estimation of disease specific attributable cost is of major importance. For this estimation, cost data of cases (patients with the disease) and comparable controls (patients without the disease) are often utilized. Without the individual level data, the cost of a patient’s illness and the total cost of choosing and treating different diseases may lead to errors in subsequent inference. The author will juxtapose contrasting cases of how best to control for it with an informed multiplicity plan as part of their endpoint model.
RESULTS: The proposed models are illustrated with an analysis of RCTs evaluating interventions for osteoarthritis of the knee. Fixed and random effects first and second order fractional polynomials were evaluated. CONCLUSIONS: Network meta-analysis with models where the treatment effect is represented with several parameters using fractional polynomials can be used to simultaneously analyze results at multiple follow-up times that are not consistent across studies.

PRM48 DIAGNOSTIC TOOLS FOR THE ASSESSMENT OF THE UNDERLYING MODEL ASSUMPTIONS IN THE STUDY OF HEALTH CARE COSTS
Juneau P
Thomson Reuters, Boyd, MD, USA
OBJECTIVES: It is a common practice to use a log link and assume a gamma distribution when performing regressions of health care costs as an outcome on a set of potential predictors. In many circumstances, this approach is reasonable and performs well; however, do circumstances exist where these assumed model characteristics are untenable? If so, do simple diagnostic procedures exist that can assess the appropriateness of model assumptions for regression models involving health care costs as an outcome? METHODS: Application of residual analyses available in common statistical software packages (e.g., SAS) afford practitioners the ability to graphically and analytically evaluate whether the choice of a link is appropriate in a given cost model regression scenario. These same tools can also assist with an assessment of the appropriateness of the model fit. RESULTS: The model fit will justly depend on where the choice of a generalized linear model with a log link and an assumed gamma distribution are defensible and where these assumptions are not met and may lead to errors in subsequent inference. CONCLUSIONS: With the use of these readily available diagnostic procedures found in common software packages, it is possible to easily evaluate whether underlying model assumptions are tenable and if the choice of a simpler, more common approach may actually demonstrate higher fidelity to its underlying model assumptions than the commonly used generalized linear model with a gamma distribution and a log link.

PRM49 HOW TO PRESENT THE PROBABILITY OF BEING THE BEST TREATMENT IN THE CONTEXT OF A BAYESIAN NETWORK META-ANALYSIS OF PARAMETRIC SURVIVAL CURVES
Cope SI, Vieira da Silva MC1, Jansen JP2
1Mapi Consultancy, Boston, MA, USA, 2Mapi Consultancy / Tufts University School of Medicine, Boston, MA, USA
OBJECTIVES: Increasingly, network meta-analysis (NMA) of published survival data are based on parametric survival curves as opposed to reported hazard ratios to avoid relying on the proportional hazards assumption, which may not be valid. One approach to a Bayesian approach to NMA is that the probability of being the best treatment out of all those compared can be calculated. This directly supports decision-making. However, in the context of survival analysis multiple options are available. METHODS: Based on a case study in oncology, the probability that each treatment is best varies with the different alternatives. With methods 1-4 the probability that a certain treatment is best is calculated and presented based on the following underlying results: 1) the hazard over time, 2) the cumulative hazard over time, 3) the survival proportions over time, 4) the expected survival over time, 5) the expected survival at maximum follow-up, 6) expected survival when all patients have died, and 7) median survival. RESULTS: Since the NMA of survival curves results in changing hazard and survival estimates over time for the compared interventions, calculations of the probability that a certain treatment is best varies with the different alternatives. With methods 1-4 the probability that a certain treatment is best will vary as a function of follow-up, which provides relevant information. With methods 5-7 only one probability of being the best is obtained for each treatment, which is easier to understand. Method 1 does not directly relate to the survival proportion, which makes it not very intuitive. Method 7 discards a lot of information. CONCLUSIONS: Different approaches to present the probability of being the most efficacious treatment for finding which obtained with a NMA of survival curves have pros and cons. The probability that a certain treatment is best as a function of survival proportions over time, as well as expected survival over time seem the most useful and intuitive.

PRM50 META-REGRESSION MODELS TO ADDRESS HETEROGENEITY AND INCONSISTENCY IN NETWORK META-ANALYSIS OF SURVIVAL OUTCOMES
Cope SI, Jansen JP2
1Mapi Consultancy, Boston, MA, USA, 2Mapi Consultancy / Tufts University School of Medicine, Boston, MA, USA
OBJECTIVES: As an alternative to network meta-analysis (NMA) of survival data based on the single constant hazard ratio (HR), NMA with a multi-dimensional treatment effect were introduced recently. With these models the HR is modeled as a function of time, and violations of the transitivity assumption are less likely. Bias is still present, however, if there are systematic differences in effect modifiers across comparisons. The objective of this paper is to extend multidimensional NMA models for survival data with treatment-by-covariate interactions to adjust for confounding bias. METHODS: By means of an example network of randomized controlled trials evaluating different interventions for melanoma, three different approaches (7) for the analysis of overall survival (OS) are compared: 1) NMA assuming a constant HR between treatment and control group for each study; 2) a two-dimensional NMA model assuming survival outcomes are described by a Weibull function; and 3) an extension of method 2 with treatment-by-covariate interactions to adjust for systematic differences across studies. RESULTS: The models with the multi-dimensional treatment effect (method 7) are not comparable to the data as the model with the constant HR (approach 1). Adding treatment-by-covariate interactions for the scale parameter of the two-dimensional NMA models reduced inconsistency. CONCLUSIONS: Adding treatment-by-covariate interactions to multi-dimensional NMA models for published survival curves is worthwhile to explain systematic differences across studies and reduce inconsistencies. An additional advantage is that heterogeneity in survival data can be addressed.