missions. Often it is mentioned that in order to obtain unbiased estimates based on indirect comparisons the distribution of characteristics of the patients included in the different trials needs to be similar, as well as the study design. By means of directed acyclic graphs (DAGs), which are often used in epidemiology for inferences, it is explained that indirect and mixed treatment comparisons are biased when differences in patient characteristics and trial design do act as an effect modifier of the treatment effect. Furthermore, the graphs can be used to differentiate between heterogeneity, selection, and confounding bias. DAGs for indirect comparisons of RCTs are compared with DAGs for head-to-head randomized designs and meta-analysis of RCTs.

**RESEARCH ON METHODS & CONCEPTUAL PAPERS—Cost Studies**

**Methods for Estimating Confidence Intervals of Per Member Per Month (PMPM) Utilization Rates**

**Saverno K,1 Goodman M2**

1University of Arizona College of Pharmacy, Tucson, AZ, USA. 2Xcenda, Woodbury, MN, USA

**OBJECTIVES:** Per member per month (PMPM) utilization rates are commonly reported in the medical literature to compare differences in costs and other outcomes across various health care technologies and interventions. A limitation of PMPM estimates is that a confidence limit around the point estimate is not obvious or available from standard statistical software. Our objective is to demonstrate various methods of calculating confidence intervals for PMPM utilization rates. **METHODS:** Several methods were used to estimate confidence intervals surrounding PMPM estimates including Fieller’s method and Monte-Carlo (MC) simulation. Women with at least one prescription fill for alendronate, risedronate, or ibandronate during 2006 in a large managed care data set were used as a sample to generate PMPM estimates and 95% confidence intervals for bisphosphonate drug cost, all hospitalization cost, hospital days, and number of hospital admissions during the calendar year of 2006. **RESULTS:** There were 34,675 women in our sample. The PMPM estimate of bisphosphonate drug cost was $23.48. The 95% confidence intervals generated by the Fieller and MC methods were ($23.21, $23.75) and ($23.45, $23.87), respectively. The PMPM hospitalization cost was $242.28: Fieller and MC 95% confidence intervals were ($221.53, $263.03) and ($227.74, $259.99), respectively. The PMPM estimate of hospital days was 0.108 days: Fieller and MC 95% confidence intervals were (0.098, 0.118) and (0.100, 0.116), respectively. The PMPM point estimate for number of hospital admissions was 0.013: Fieller and MC 95% confidence intervals were (0.0131, 0.0142) and (0.0133, 0.0142), respectively. **CONCLUSION:** The Fieller and MC simulation methods produced similar confidence intervals for PMPM estimates for each of the outcomes of interest. Use of these methods would improve the utility of PMPM point estimates in comparing health care technologies.


**Fang C, Cohen JT, Neumann PJ**

Tufts-New England Medical Center, Boston, MA, USA

**OBJECTIVE:** To review and critically evaluate published cost-utility analysis (CUA) research on pharmaceuticals for the past three decades. **METHODS:** We examined data from the Tufts-NEMC Cost-Effectiveness Analysis Registry (www.tufts-nemc.org/cearegistry), which contains detailed information on over 1100 CUAs and 3000 cost-utility ratios (in $US2005) published from 1976–2005. **RESULTS:** Of 1164 CUAs published through 2005, 518 (44.5%) pertain to pharmaceuticals. The proportion of all CUAs that focus on pharmaceuticals increased from 32% prior to 1990 to 48% from 1990–2005. **CONCLUSIONS:** There were 34,675 women in our sample. The PMPM estimate of bisphosphonate drug cost was $23.48. The 95% confidence intervals generated by the Fieller and MC methods were ($23.21, $23.75) and ($23.45, $23.87), respectively. The PMPM hospitalization cost was $242.28: Fieller and MC 95% confidence intervals were ($221.53, $263.03) and ($227.74, $259.99), respectively. The PMPM estimate of hospital days was 0.108 days: Fieller and MC 95% confidence intervals were (0.098, 0.118) and (0.100, 0.116), respectively. The PMPM point estimate for number of hospital admissions was 0.013: Fieller and MC 95% confidence intervals were (0.0131, 0.0142) and (0.0133, 0.0142), respectively. **CONCLUSION:** The Fieller and MC simulation methods produced similar confidence intervals for PMPM estimates for each of the outcomes of interest. Use of these methods would improve the utility of PMPM point estimates in comparing health care technologies.

**The Adoption and Diffusion of Cost-Effectiveness Acceptability Curves in Published Economic Evaluations**

**Greenberg D,1 Cohen JT2, Neumann PJ2**

1Ben-Gurion University of the Negev, Beer-Sheva, Israel. 2Tufts-New England Medical Center, Boston, MA, USA

Cost-effectiveness acceptability curves (CEACs) plot the probability that one treatment is more cost-effective than another, as a function of a societal threshold willingness to pay for additional units of efficacy (e.g., life-year or QALY gained). **OBJECTIVES:** To assess the adoption and diffusion rates of CEACs within the field of economic evaluations. **METHODS:** We used the Tufts-New England Medical Center registry of 620 published cost-effectiveness analyses (CEA), presenting an original cost/QALY ratio from 2002–2005 (http://www.tufts-nemc.org/cearegistry/). For each CEA we recorded the year of publication, journal’s name, study origin (country), and a subjective assessment of overall study quality ranging from 1 (low) to 7 (high). We used univariate analyses (chi-square and t-test), to assess differences in CEAC use by year of publication, study origin and quality. We also compared practices in journals publishing a high-volume (n ≥ 10) versus low-volume (n < 10) of CEAs during the study period. We used multivariable logistic regression to identify factors predicting CEAC use. **RESULTS:** Approximately one fifth (20.2%) of CEAs presented a CEAC. The adoption of CEACs has increased over time from 5.3% (2002) to 30.4% (2005) (p < 0.0001). Studies using CEAC were of higher quality (4.6 ± 1.0 vs. 4.1 ± 0.9; p < 0.0001) and more prevalent in high-volume journals (30.7% vs. 16.4%; p < 0.0001). CEACs were more frequently used in UK studies (48.8%) versus studies from Sweden (24.1%), The Netherlands (17.9%), United States (11.7%), and Canada (9.1%). Significant predictors for using CEACs were study quality (OR 1.96; 95% CI 1.53–2.51), publication in a high-volume journal (OR 1.85; 95% CI 1.18–2.89), and year of publication. **CONCLUSIONS:** CEACs have been rapidly adopted, especially among UK-based investigators. If CEACs turn out to be a useful tool to decision makers, this trend is encouraging, but means to achieve more rapid deployment should be identified.