RESEARCH ON METHODS – Study Design

PMR209
HOW DO CENTRES INCLUDED IN RANDOMISED CONTROLLED TRIALS WITH PARALLEL ECONOMIC EVALUATIONS IN THE UK?

Gheorghe A, Roberts TE, Fletcher BR, Calvert M
University of Birmingham, Birmingham, UK

OBJECTIVES: The proportion of centres participating in randomised controlled trials (RCTs) may affect the generalisability of economic evaluation results if it is biased, but there is limited evidence on how trialists currently include centres in RCTs. Our aim was to investigate how trialists reported on centres for selection in RCTs with parallel economic evaluations in the UK.

METHODS: We systematically reviewed and meta-summarised centre selection information in full-length protocols of RCTs with parallel economic evaluations funded by the UK National Institute of Health Research (NIHR) Health Technology Assessment programme (NIHR-HTA) and initiated between January 2005 and January 2012. Free text information on centre selection was extracted, abstracted and categorised; effect sizes (%) were calculated for the emerging categories as a measure of prevalence relative to the number of included studies. RESULTS: Of 365 reviewed studies, 129 trial protocols were included in the systematic review with a total target sample size of 317,000 participants. The meta-summary identified 53 centre selection considerations, grouped under three categories: diversity and representativeness, centre characteristics and trial participation. A total of 78 (60%) protocols provided a rationale for centre selection. A total of 31 (24%) protocols explicitly considered representativeness, for example in terms of the target population (11%) and delivered services (12%). Fifty-seven (44%) protocols required particular centre characteristics, such as size (17%) and research experience (15%). Thirty-seven (29%) protocols envisaged considerations that would ensure successful trial participation, such as the willingness to participate (7%) and ensuring recruitment (13%). CONCLUSIONS: The rationale for centre selection in RCTs with parallel economic evaluations is currently under-reported. Centres are primarily enrolled on pragmatic and less so with a view to ensuring generalisability. There are little reasons to believe that economic results from RCTs are informed by a representative sample of centres, thus questioning the representativeness of their findings.

PMR210
RECRUITING PATIENTS WITH A RARE BLOOD DISORDER AND THEIR RECRUITMENT媒體

Milena Di Benedetto1,2, Colles TM1, Sharma T1
1Weill Cornell Medicine, New York, NY, USA; 2Truven Health Analytics, Cambridge, MA, USA

OBJECTIVES: Recruiting research participants with experiences relevant to rare diseases (patients and caregivers) remains a constant challenge. Researchers often rely on patient advocacy or support groups as well as clinician referrals, which each present unique recruitment issues. Social media sites, such as Facebook, can potentially be helpful in recruiting patients for many study types, particularly those involving hard-to-reach populations. However, little is known about the value of social media in recruiting. In this study, Facebook was used to recruit adult patients and parents of children with hemophilia A for participation in a Web-based survey.

METHODS: A cross-sectional study was developed to better understand patient and caregiver experiences and behaviors related to hemophilia A. Exclusion criteria included: ages 18 years or younger and/or have been recruited in a previous study or for which hemophilia A. Members of three local or national blood disorder organizations in the United States and Canada were invited to complete a Web-based survey via postings on the organizations’ social media accounts. Two organizations posted advertisements about the study on their respective Facebook pages. A nominal donation was made to each organization for their assistance in study recruitment.

RESULTS: Of the 145 individuals who responded to survey invitations, 101 (70%) completed the survey questionnaire. More than half of respondents (56%) were parents of children with hemophilia A, and the remainder were adult patients. Of the 101 respondents, 63 (62%) were provided with a study advertisement on Facebook. A total of 26 (25%) respondents were reached through ads on Facebook. Of the 26 respondents, 8 (8%) were reached through ads on Facebook. Of the 26 respondents, 8 (8%) were reached through ads on Facebook. Of the 26 respondents, 8 (8%) were reached through ads on Facebook. Of the 26 respondents, 8 (8%) were reached through ads on Facebook.

CONCLUSIONS: This study used an online tool to quickly assess the impact of various criteria. The data demonstrate how shorter CE understimates treatment effect, related hospitalizations, and overall burden of illness in a chronic population.

PMR211
THE EFFECTS OF EXCLUDING TREATMENTS FROM NETWORK META-ANALYSIS

Mills G1, Kanters S2, Thorlund K1
1Stanford University, Palo Alto, CA, USA; 2University of British Columbia, Vancouver, BC, Canada

OBJECTIVES: To investigate the effect of omitting treatments from network meta-analyses on overall treatment effects and treatment rankings. METHODS: We selected published network meta-analyses that met the following criteria: compared ≥2 drugs, had ≥2 loops, ≥2 studies and set to a primary question of interest. More than one network was identified per publication if multiple networks were included within a single publication. Of the 126 included networks, 46 included ≥2 drugs. Within a network, each drug was dichotomized as a logical outcome. The network was analyzed systematically with the removal of one node at a time. Nodes that were ≥50% of studies were not removed. Impact of node exclusion was measured using the relative change in treatment effect estimates, changes in top-three ranked treatments, and changes in probability of being the best treatment. Relative changes in effect size were expressed as fold-deviations. For each network with excluded node(s), we measured the maximum and geometric mean of fold-changes. RESULTS: In total, 19 networks were selected for analysis. Approximately half the networks had average fold-change larger than 1.0 (greater than 10% relative change in treatment effects). Approximately half of the networks also had changes in the top three ranks and substantial changes in treatment rank probabilities. Within these networks, the maximum fold-change was generally larger than 1.2. In networks with no changes in top-three ranked treatments, the best treatment mostly had probability >70% of being the best. Two features were consistent across the nodes leading to the largest change in probabilities and effects: they were among the most connected nodes and tended to have a 0% probability of being the best treatment.

CONCLUSIONS: Network meta-analytic methods are still in their infancy. Our results suggest that failing to include one or more treatments within a network can lead to important changes in conclusions reached.

PMR212
USING AN ONLINE DATA ANALYTIC TOOL TO INFORM STUDY DESIGNS FOR CHRONIC DISEASE POPULATIONS: A CASE STUDY WITH CLL

Foley E1, Hansen LL1
1Truven Health Analytics, Cambridge, MA, USA; 2Truven Health Analytics, Northwood, NH, USA

OBJECTIVES: Chronic lymphocytic leukemia (CLL) accounts for almost 40% of all leukemias. Current treatments have high rates of adverse events requiring hospitalization. With promising treatments on the horizon, the need for well-designed studies of treatment patterns and adverse events will increase. Designing studies can be challenging given the long-term nature of CLL. This study uses an online analytic tool to explore the necessary observation period to accurately assess treatment and hospitalization rates. METHODS: Using the Treatment Pathways tool and data from an 8-year oncology subset of the 2004–2012 MarketScan databases, we identified patients with two plus claims for CLL, one year prior enrollment, no prior treatment. Four follow-up groups were estimated: continuous enrollment (CE), 365 days before the first (F/R/C), 3 years before the first (F/R/C/R), 4 years before the first (F/R/C/R). Treatment and hospitalization rates and the time between diagnosis, treatment, and hospitalization were calculated.

RESULTS: A total of 4886 patients met all inclusion criteria: 3984 had 1 year, 2201 had 2 years, 1451 had 3 years, and 874 had 4 years CE. Bendamustine use increased from 4% among those with 1 year CE to 5% for all other CE groups. F/R/C/R increased from 21% among those with 1 year to 27% among those with 4 years CE. Hospitalization rates increased from 41% to 49% for bendamustine, and 38% to 44% for F/R/C from 1 year to 4 years CE. Among those with 4 yrs CE, median time to first treatment was 4.3 years for benzimidate, 14 years for F/R/C; median time to first hospitalization was 98 and 365 days, respectively.

CONCLUSIONS: This study used an online tool to quickly assess the impact of various criteria. The data demonstrate how shorter CE understimates treatment, related hospitalizations, and overall burden of illness in a chronic population.

PMR213
USING REAL-WORLD CLAIMS DATA FOR PLANNING ONCOLOGICAL CLINICAL TRIALS

Foley E1, Hansen LL1
1Truven Health Analytics, Cambridge, MA, USA; 2Truven Health Analytics, Northwood, NH, USA

OBJECTIVES: To understand the value of quickly estimating the impact of certain inclusion/exclusion criteria on a potential clinical trial population using real-world administrative data. METHODS: Using the Treatment Pathways tool and data from the 8-year oncology subset of the 2004 – 2012 MarketScan databases, we identified patients with castrate-resistant prostate cancer (CRPC) with at least 6 months of history. From these patients, we identified cohorts with definitive exclusion criteria and primary care pathways and time-dependent exclusions (based on radiation or treatments). Seven of 12 exclusion criteria were identifiable within the claims database. RESULTS: Inclusion criteria identified patients with CRPC and excluded patients with CRC based on time to first diagnostic surgical castration and receipt of docetaxel. Of them, 1370 (59%) had 6 months of follow-up data for evaluation of exclusion criteria. Among the 1370 patients, 248 (18%) met none of the exclusion criteria, while 482 patients (35%) had brain metastasis and/or other cancers. The remaining 640 (47%) had at least one time-dependent exclusion, including 534 receiving corticosteroids, 136 receiving androgen receptor and reductase inhibitors, 86 receiving radiation and 31 with both treatments.

CONCLUSIONS: These patients could be trial-eligible depending on the timing of treatment cessation and trial recruitment. This study demonstrates a method to understand the impact of specific inclusion/exclusion criteria on a potential clinical trial population in just a few hours using an online pathway creation tool and administrative data representing millions of patients. Using this method, trial planners can evaluate different scenarios to quickly and easily determine estimated attrition rates helping them to maximize potential recruitment success. Limitations exist due to the timing of exclusions and data on lab results included in the exclusion criteria that were unavailable in this subset of claims data.

PMR214
USE OF A NOVEL ADJUNCTIVE CLINICAL TRIAL DESIGN TO EXAMINE EFFICACY, SAFETY OF ARMOFAFINIL FOR THE TREATMENT OF BIPOLAR I DEPRESSION

Calabrese JR1, Ketter TA2, Yang K3, Frye MA4
1University Hospitals Case Medical Center, Cleveland, OH, USA; 2Stanford University School of Medicine, Stanford, CA, USA; 3Teva Pharmaceutical Industries Ltd., Frazer, PA, USA; 4Mayo Clinic, Rochester, MN, USA

OBJECTIVES: Patients in randomized, controlled trials of bipolar depression are generally not representative of a clinical population. This study attempted to examine a large sample of patients more representative of patients seen in clinical practice. This report presents baseline patient characteristics from a