components of the Wilson Cleave Model. METHODS: 212 persons with a variety of advanced cancer from the McGill University Health Center (MUHC) were evaluated using nine patient-reported outcomes and seven direct measures over a course of 18 months. As an attempt to minimize measurement error, Rasch measurement was used to model symptoms, function, general health perceptions (GHF), and overall quality of life (QoL) latent constructs. Additionally, biological variables were measured. The latent QoL construct was then modeled over time using “group-based modeling”. Probability of group membership was finally predicted using the different biological, symptoms, function, and GHF constructs of the Wilson-Cleave model at study entry, which coincided with the time of cancer diagnosis. RESULTS: The Rasch QoL model over time resulted in 5 distinct trajectories: a linear increasing trajectory representing 26% of the sample, two flat and medium high trajectories representing 26% and 17% respectively, a quadratic increasing trajectory representing 25% of the sample, and a linear decreasing trajectory representing 5% of the sample. The latent constructs from the time of diagnosis that statistically significantly predicted group membership were age, sex, cancer type, recalled weight loss, CRF, social support, emotional status, and fatigue. CONCLUSIONS: Using Rasch group-based trajectory modeling, and linear regression, we were able to discriminate between relevant QoL subgroups of patients. Most importantly, we were able to identify trajectories that enabled us to make preliminary conclusions about the most important contributors to QoL over time, and emphasize the importance in assessing these constructs in people with cancer.

PMR68 BIAS WHEN ADJUSTING FOR SURROGATES OF CONFOUNDERS

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OBJECTIVES: High-dimensional propensity score (HDPS) methods have been used in health economic evaluations, but data in an attempt to control confounding bias are imprecise and expensive. A large number of covariates that may be proxies for unobserved factors. We have previously shown that PS models are biased with non-linear link functions. We conducted a Monte Carlo simulation study to assess the performance and bias of PS estimators for a large number of covariates that are children of unmeasured confounders and other unmeasured parent of the outcome variable (colliders) may bias the relationship between exposure and outcome by estimating mean bias, and standard errors. METHODS: We used directed acyclic graphs to replicate the causal network of plausible confounding scenarios. We simulated a scenario where the outcome variable Y is a function of a confounder, C, and another parent, U, but not of exposure X (function of C). Covariate Z is a function of parents C and U. All variables had normally distributed random errors. We conducted Monte Carlo simulations of the causal network, with varying strengths of each of the causal relations, and estimated the effect of X on Y, using linear regression models, while adjusting for covariate Z. RESULTS: Correctly specified mean bias of the PS estimator. Bias was large in situations with X only and Z only (bias ≥ 5 with a variable standard error). There was some reduction in bias in some situations where Z was highly correlated with the confounder, C, but increased bias when much of the variance in Y was determined by U. CONCLUSIONS: Adjustment for colliders that are children of unmeasured determinants of the outcome variable, but not of the exposure, may also increase bias. This is of great importance in observational studies, particularly when using HDPS to adjust for large numbers of variables that are not measured directly. Researchers should always use causal knowledge when using data to make causal inference.

PMR69 SIZE DISTORTION OF HYPOTHESIS TESTS FOR TWO-STAGE LEAST SQUARES MODEL: WHAT THE RULE OF THUMB CAN’T GIVE YOU

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OBJECTIVES: Big data approaches may lead to multiple strong instrumental variables (IVs), significantly improving the performance of two-stage least squares model (TSLS). The current rule of thumb for detecting weak IV is based on the goal of keeping relative bias of TSLS less than 0.1. With the increasing number of IVs, we need to examine the impact of weak IV on hypothesis testing. We investigated whether or not the rule of thumb can be efficient enough to prevent size distortion of hypothesis testing for TSLS. METHODS: We used a Monte Carlo approach to create 28 original data sets for different models with the number of IVs varying from 3 to 30. For each model, we created 2000 observations and conducted 50,000 iterations to reach a converged outcome. The relationship between the endogenous variable and IVs was carefully adjusted to let the F statistics for the first stage model equal 10 (rule of thumb). The mean value of relative bias and percent of false rejection for each model were recorded and compared across all the models. RESULTS: The relative bias of TSLS equaled 0.1 constantly across all the models in the study. However, the likelihood of rejecting a true hypothesis increased when the number of IVs in the model increased while holding the F statistics for the first stage equal to 10. And this likelihood exceeded 10% when TSLS had 24 IVs and exceeded 15% when TSLS had 30 IVs. CONCLUSIONS: When more IVs were added into the TSLS model, the rule of thumb was no longer an efficient guarantee for good performance of hypothesis testing. A more restricted margin for F statistics is needed to be explored to improve the rule of thumb, especially when the number of IVs could be large in the context of big data.

PMR70 DEPRESSION AND COMORBID OBESITY AND HYPERTENSION IN UNITED STATES CHILDREN

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OBJECTIVES: To investigate the association between depression and comorbid obesity and hypertension in US children over a 8-year period using data from the National Health and Nutritional Examination Survey among those with depression or hypertension. METHODS: We built a logistic regression model using a sample of 727 respondents aged 0-18 between 2005 and 2012. RESULTS: Out of 727 subjects, 49.2% were female, 50.1% were male, 11.5% were between the ages of 0-5, 37.8% between the ages of 6-10, 26% between the ages of 11-15, 24.5% between the ages of 15-19 years. 71.3% were non-White, 16.4% were obese and 3.6% had hypertension. Obesity and hypertension are significant predictors of depression. Children who are obese are about 2.9 times more likely (p<0.005) to be depressed than children who are not obese, and children who suffer from hypertension are approximately 4.6 times more likely (p<0.001) to experience depression than those who do not have hypertension. Other significant predictors of depression in children are gender (p<0.001), OR=0.486) and family size (p=0.06, OR=0.673). CONCLUSIONS: Obesity and hypertension are associated with depression after controlling for other factors. This finding has important implications for depression management in children. It brings into focus the maintenance of a healthy body mass index (BMI) in mitigating depression.

PMR71 ANXIETY AND COMORBID OBESITY AND HYPERTENSION IN UNITED STATES BACKGROUND & OBJECTIVES: Accurate identification of major malformation cases from administrative databases is crucial for perinatal epidemiology. In Quebec, most of major malformations are detected in hospital, however administrative databases capture diagnoses data from both hospitals and other medical facilities. We aimed to compare the prevalence of major congenital malformations identified from administrative databases diagnostic codes (ICD-9 and ICD-10) with definitions: diagnoses made in hospital only vs. diagnoses made in hospital and other medical facilities. We evaluated the impact of including each definition to quantify the association between maternal use of asthma controller medications and the prevalence of major malformations at birth and during the first year of life. METHODS: A cohort of pregnancies from asthmatic women between 1990 and 2010 was formed through the linkage of administrative databases from Quebec. We calculated the prevalence of major malformations identified in the 1st year of life of the newborn using the 2 case definitions. We also calculated the crude odds ratio (OR) of major malformations associated with maternal use of inhaled corticosteroids (ICS) and long-acting beta,-agonists (LABA) in the 1st trimester of pregnancy. RESULTS: From 30655 pregnancies, 2060 (6.8%) major malformations were identified with hospital diagnostic codes only vs. 2748 (9.0%) with hospital and other medical facilities diagnostic codes. The OR of major malformations associated with ICS was 1.1 (95%CI: 1.0-1.2) with the first and 1.1 (95%CI: 1.0-1.2) with the second case definition. Corresponding results were 1.3 (95%CI: 1.0-1.6) and 1.1 (95%CI: 0.9-1.4) for LABA exposure. CONCLUSIONS: The case definition of congenital malformations had a considerable impact on the prevalence of major congenital malformations, but less impact on the associations examined. The percentage of false positive cases when using all medical facilities diagnostic codes in the case definition is unknown and should be the objective for future research.

PMR73 SURVIVAL MODELING FOR THE ESTIMATION OF TRANSITION PROBABILITIES IN MODEL-BASED ECONOMIC EVALUATIONS IN THE ABSENCE OF INDIVIDUAL PATIENT DATA: A TUTORIAL

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OBJECTIVES: Survival modeling techniques are increasingly being used as part of decision modeling for health economic evaluations. With limited availability of appropriate survival modeling techniques to estimate transition probabilities, for use in model-based economic evaluations, in the absence of individual patient data. The use of the proposed tutorial is illustrated based on the final progression-free survival (PFS) analysis of BOLERO-2 trial in metastatic breast cancer (mBC).

METHODS: An algorithm was adopted from Goyet and colleagues, and was then run in the statistical package R to reconstruct individual patient data (IPD), based on the final
RESERCH ON METHODS – Patient Reported Outcomes Studies

PM7/5
PSYCHOMETRIC VALIDATION OF PATIENT-REPORTED OUTCOME MEASURES OF PAIN IN UNITED STATES PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS
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OBJECTIVES: Increasingly, economic evaluations of progressive diseases have adopted the approach of partitioned survival analysis. In three state cancer models (prospective - pre-progression, post-progression and death) the proportion of patients in each state are often obtained from survival functions for progression free (PFS) and overall survival (OS). The proportion in the pre-progression state is estimated from the PFS curve, and the proportion in the post-progression state is the proportion between OS and PFS. Based on simulated data reflecting the results from recent randomized clinical trials, this study explored the accuracy of this method. METHODS: Three clinical scenarios were considered based on varying OS. Clinical trial data sets were simulated for a standard and a novel treatment assuming substantive benefit with the new treatment in terms of slowing progression but no impact on treatment on mortality compared with the controls. The objective was to assess whether observed survival rates were assumed and represent plausible values. Results: Survival analysis of the pre-progression state was performed. The difference between actual results based on complete follow up and results based on curtailed follow up of various durations using both traditional Markov modelling and partitioned survival analysis was assessed. RESULTS: In the moderate survival scenario (median OS ~12 months), the ICUR for the new treatment based on the raw simulated data was ~119,600. With trial follow up of 9 months the ICUR for new treatment was ~120,600 with Markov modelling and ~87,500 with partitioned survival analysis. With 18 months follow up, the figures were ~122,500 and ~103,000 respectively. Results with different durations of follow up found a consistent pattern as did results for both the short and long term survival scenarios. CONCLUSIONS: Analyses based on partitioned survival analysis have an inherent bias in favor of treatments which impact disease progression, not within health state mortality. They should not be considered an appropriate basis to facilitate reimbursement decisions.

RESEARCH ON METHODS – Patient Reported Outcomes Studies

PM7/6
PSYCHOMETRIC PROPERTIES OF THE WORLD HEALTH ORGANIZATION’S QUALITY OF LIFE BREF INSTRUMENT (WHOQOL-BREF) AMONG ADULTS WITH AUTISM
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OBJECTIVES: The purpose of this study was to assess construct validity of the WHOQOL-BREF instrument among adults with autism. Reliability and floor and ceiling effects of the WHOQOL-BREF instrument in this population were also assessed. METHODS: A cross-sectional online survey (using Qualtrics survey system) of adults with autism enrolled with the International Autism Research Network was performed for adults with autism registered with the IAN, those aged 18 years and above and having the capacity to self-report with little or no proxy help were identified and targeted for the study. The WHOQOL-BREF instrument was validated using confirmatory factor analysis. Convergent and discriminant validity was assessed based on relevant item-total correlation. Known groups validity was tested by comparing WHOQOL-BREF scores among group differing in autism severity. Cronbach’s alpha was used to assess internal consistency reliability. Floor and ceiling effects were determined based on percentage ≥15% of responses with lowest and highest possible score on the instrument, respectively. RESULTS: The final sample included 262 adults with autism. Based on the unidimensional hierarchical model of WHOQOL-BREF instrument was considered the best fitting model among adults with autism (chi-square=428.00, df=242; RMSEA=0.054; CFI=0.993). Corrected item-total correlation suggested good convergent and discriminant validity of the WHOQOL-BREF instrument. WHOQOL-BREF varied significantly by autism severity, indicating adequate known-groups validity. High internal consistency reliability (Cronbach’s alpha=0.914) was observed. The floor and ceiling effect are acceptable with the exception of one item which displayed floor effect and six items which displayed ceiling effects. CONCLUSIONS: Study results indicated that the WHOQOL-BREF is a psychometrically sound instrument to assess quality of life among adults with autism.

PM7/7
DO EQ-5D AND SF-6D ASK THE RIGHT QUESTIONS IN MENTAL HEALTH? A CONTEXTUAL VALIDATION USING INTERVIEWS WITH PATIENTS
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OBJECTIVES: The purpose of this study was to assess construct validity of the EQ-5D and SF-6D against what individuals with mental health problems perceive to be important to their quality of life using rigorous qualitative methods. METHODS: We first undertook a systematic review of qualitative research undertaken with people with mental health problems. The review was based on the methodological framework for undertaking structured in-depth interviews undertaken with 19 people who had a broad range of mental health problems at varying levels of severity drawn from primary and secondary care services (including mood disorders and psychosis) in the UK. The interviews were analysed thematically using framework analysis. RESULTS: A framework analysis of 13 qualitative studies revealed six major themes: well-being and ill-being; control, autonomy and choice; self-perception, belonging; activity, and hope. These themes comprised the types and severity of mental health problems studied, our interview data fitted well with the themes from the review, any differences tended to be within the themes and related to the degree of impact of the themes on different levels of severity. CONCLUSIONS: Any themes and severity of mental health problems, our interview data fitted well with the themes from the review, any differences tended to be within the themes and related to the degree of impact of the themes on different levels of severity.