Iowa Summer Institute in Biostatistics

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Iowa Summer Institute in Biostatistics Presentations

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Assessing Imaging Data from the Michael J. Fox Foundation's Parkinson's Progression Markers Initiative for use in Future Clinical Trials

Globally, more than 10 million people are living with Parkinson's Disease (PD) making it the second most common neurodegenerative disorder. Parkinson's Disease affects the central nervous system, often causing unilateral symptoms: tremors, rigidity, and imbalance of the body, later progressing to bilateral symptoms affecting an individual's ability to complete daily routines. Data collected through The Michael J. Fox Foundation provides a critical opportunity for research. The foundation has created a Parkinson's Progression Markers Initiative (PPMI) to find biomarkers that will allow for an earlier diagnosis of Parkinson's Disease, improved disease tracking, and aid the planning of treatments and therapies. The goal of the Michael J. Fox Foundation Parkinson's Progression Markers Initiative is to identify biomarkers that predict Parkinson's progression as this would shorten the time to treatment discovery, thereby lowering the costs of studies. DaTSCAN is a type of biomarker that is used for diagnosing Parkinson's through tracking dopamine transmitters (DaT) that accumulate in the striatum, caudate, and putamen regions of the brain. This study looks to model the PPMI DaTSCAN data in order to make predictions about the sample size and study duration needed in a clinical trial for potential Parkinson's disease-modifying treatments.

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Intervening in *Clostridium difficile* Infections in California Hospitals

Background:
Clostridium difficile infection (CDI) poses a serious health threat for hospitalized patients. Individual risk factors include advanced age, prolonged antibiotic use, and severe illness. Environmental risk factors of CDI include bathroom sharing with infected patients, patient transfers, and seasonal trends. Despite several clinical trials testing various strategies for reducing CDI rates, most have been unsuccessful or provided short-term success.

Methods:
We used a linear mixed effects model to predict CDI rates 24 months out. Using this prediction model, we tested strategies for selecting healthcare facilities to participate in a clinical trial. Our goal was to find an intervention method that effectively reduced CDI cases given an arbitrary cost constraint. Strategies under consideration included targeting hospitals with high CDI rates, larger proportions of patients over 65, and high levels of centrality within the hospital network.

Results:
Most, but not all, of the proposed strategies outperformed a random selection of hospitals to treat. The various strategies considered led to an average reduction in CDI cases ranging from 1207.596 to 2095.729, compared to an average reduction of 1263.206 for random selection of hospitals to treat.

Conclusion:
Our results suggest that strategic targeting of certain hospitals within a network to participate in a treatment intervention program can be beneficial to decreasing CDI cases. Targeting hospitals which have the highest incidence of CDI performed best among all tested strategies. This study provides strong evidence that convenience samples of hospitals to treat is an inefficient approach to implementing a clinical trial.

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Understanding the Opioid Crisis in Iowa through Data

The issue of opioid abuse and overdose has become a nation-wide epidemic in recent years, resulting in a tremendous economic burden of an estimated $78.5 billion per year. According to the National Institute of Health, more than 115 people in the United States die from opioid overdose daily. Prescription patterns of legal opioids after surgeries and other medical procedures have contributed to the epidemic, as previous studies have observed that patients who are prescribed doses exceeding 50 Morphine Milligram Equivalent (MME) per day have twice the risk of overdose than those who are not prescribed doses as high. As a preliminary exploration of the issue of high-dosage prescriptions in the state of Iowa, MME per day rates by surgery category were summarized and visually mapped using the INLA package in R, which is an alternative approach to the Bayesian Markov Chain Monte-Carlo method for inference. Geographical hot spots for high dosage prescription rates in the state were located and visualized, showing intensity of high dosage prescriptions throughout the state of Iowa. We also consider adjusting for demographic covariates such as age, race, and population size.

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The Role of Lithium in Suicide Prevention

In the U.S., 4.6% of people report having attempted suicide at least once, and 1.2% of all deaths are attributed to suicide. Studying the factors associated with suicide is important, because for every completed suicide there are 25 suicide attempts. Lithium is commonly used to decrease the risk of suicide. Along with environmental factors, genetics also plays a role in suicide risk. Human embryonic kidney (HEK) cell lines were split into four treatment groups. The four groups were lithium treatment for 7 days, lithium treatment for 21 days, control treatment for 7 days, and control treatment for 21 days. In each of these groups, the gene expression levels were measured using RNA sequencing. This study was focused on identifying genes with significant changes in expression after treatment with lithium. We investigated changes at each time point separately, as well as the interaction between treatment and time. At 21 days, there were 2,315 significant genes, 105 of which were brain specific. At 7 days, 4,872 genes were significant; of these, 225 were brain specific. For the group where the interaction was investigated, there were 3,660 significant genes, and 183 were brain specific. Gene set analyses revealed consistent expression patterns among several gene groups, indicating that lithium decreases activity in the NMDA receptor complex and increases activity in the mitochondria. Ongoing work includes comparing these results to previous genome-wide association and whole exome sequencing studies to identify genes with multiple types of experimental evidence pointing to their role in suicidal behavior.

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Radiomics for Disease Characterization: An Outcome Prediction in Cancer Patients

Lung cancer is one of the most pervasive forms of cancer in the United States, with 234,030 new cases expected in the country in 2018. As awareness of lung cancer and cancer-associated habits has increased in recent years, the number of people receiving screening for lung cancer has also grown. For this reason, it is necessary to both examine and improve upon the screening methods which are being used to determine if an abnormal mass within a patient's lung is cancerous or benign. Particularly, there is a need to reduce the number of false positive results at the screening stage in order to avoid performing invasive procedures (i.e. biopsy, surgery, etc.) unnecessarily. In this analysis, two-hundred patients from the University of Iowa Hospital were screened with CT scans to see if the nodules found in their lungs were cancerous. From these scans, over 400 quantitative imaging biomarkers were available for statistical analysis. We combined these biomarkers with patient demographic information in a variety of linear, nonlinear, and ensemble models to predict whether screened lung nodules are cancerous or benign. In our presentation, we will compare the predictive performances of our models in terms of cross-validated ROC, provide a synopsis of top performing models, discuss the impact of data pre-processing, and present a strategy for optimization of classification sensitivity and specification.

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Spatial Analysis of Risk Factors Affecting State Rates of Suicide in Young Americans

According to the Center for Disease Control, suicide was ranked the second leading cause of death in Americans ages 15 through 24 years in the United States. This project applies Generalized Linear Models (GLMs) and Spatial Generalized Linear Mixed Models (SGLMMs) to assess the relationships between several predictor variables and the suicide rates for young Americans in U.S. states. Statewide predictor variables considered included demographics, availability of mental health facilities, and gun control laws. We found that states with higher proportions of counties without mental health facilities tend to have a higher risk of death by suicide. Furthermore, Amerindians and Whites have a significantly higher rate of suicide, and even after controlling for income data and proportions of rural versus urban residents, the proportions of whites are positively associated with a higher suicide rate. In addition, certain categories of gun laws were found to be associated with decreased rates of suicide.

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Siri Neerchal
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Assessing the Descriptive Epidemiology of Idiopathic Clubfoot in Iowa

Idiopathic talipes equinovarus, or clubfoot, is a common musculoskeletal birth defect. Despite nearly 50 years of study, major risk factors for clubfoot (other than perhaps cigarette smoking during pregnancy) remain elusive. The goals of this project were to examine trends in prevalence, identify geographic hotspots, and estimate associations with selected child and parental characteristics for clubfoot using Iowa Registry for Congenital and Inherited Disorders (IRCID) clubfoot data and Iowa birth data from 1997-2016. The IRCID conducts statewide surveillance for major structural birth defects diagnosed among pregnancies of Iowa residents. A simple linear regression model and a spline model were constructed to estimate statewide prevalence over the 20-year time period, and multilevel Poisson regression analyses were used to estimate relative risk of clubfoot over space and time. Prevalence ratios for various child and parental characteristics were estimated using logistic regression analyses. Sub-analyses stratified by clubfoot laterality were also performed.

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