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General Information

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Are external grants or funds being used to support this research?: No external grants or funds are being used to support this research.
How did you learn about the YODA Project?: Scientific Publication

Conflict of Interest

https://yoda.yale.edu/wp-content/uploads/2021/09/reza_ahmadi_-_coi.pdf
https://yoda.yale.edu/wp-content/uploads/2019/01/saeed_ghodsi_-_coi.pdf

Certification

Certification: All information is complete; I (PI) am responsible for the research; data will not be used to support litigious/commercial aims.
Data Use Agreement Training: As the Principal Investigator of this study, I certify that I have completed the YODA Project Data Use Agreement Training

1. NCT00488631 - A Phase 3 Multicenter, Randomized, Placebo-controlled, Double-blind Study to Evaluate the Safety and Efficacy of Golimumab Maintenance Therapy, Administered Subcutaneously, in Subjects With Moderately to Severely Active Ulcerative Colitis

What type of data are you looking for?: Individual Participant-Level Data, which includes Full CSR and all supporting documentation

Research Proposal

Project Title

Efficient Learning of Continuous-Time Hidden Markov Models with Discrete-Time Irregular Observations for Healthcare Intervention Planning

Narrative Summary:

Disease progression models provide a mechanism for understanding and predicting the impact of interventions on the health state of patients. CT-HMMs have recently attracted attention, as they are able to handle the complexities of real-world data. The main contribution of this research project is to propose a CT-HMM disease progression model, which incorporates the effect of interventions, and to present an efficient approach for learning the parameters of this model based on the EM algorithm (https://escholarship.org/content/qt3gz0c7qx/qt3gz0c7q). We believe Ulcerative Colitis is an appropriate disease for demonstrating the advantages of our model.

Scientific Abstract:

Background: Disease progression models provide a mechanism for understanding and predicting the impact of interventions on the health state of patients. In this study, we develop a statistical disease progression model that is capable of handling the shortcomings of the existing methods.
Objective: Provide a statistical framework for tracking disease progression in response to treatment.
Primary and Secondary Outcome Measure(s): Statistical error of the model in predicting ulcerative colitis remission.
Study Design: Methodological research
Participants: The inclusion and exclusion criteria that are mentioned on the project's main page are appropriate for our study. We include patients who have been diagnosed with Ulcerative Colitis. The statistical model is capable of incorporating covariates (e.g. age, gender, ethnicity, etc.) naturally. Therefore, we do not have restrictions on the demographics. Since our model captures the treatment effect over time, we require all the patients in all 4 treatment groups in the study.
Statistical Analysis: We present a Continuous-Time Hidden Markov Model for tracking the course of the disease (https://escholarship.org/content/qt3gz0c7qx/qt3gz0c7qx.pdf).

Brief Project Background and Statement of Project Significance:

The availability of vast amounts of healthcare data has inspired an increasing interest in data-driven healthcare intervention planning methods. Disease progression models provide a mechanism for understanding and predicting the impact of interventions on the health state of patients. Most traditional Markovian state-transition models perform poorly on real-world data since they are incapable of capturing complexities such as the unobservability of the underlying health state and irregularity of observation times. Moreover, most of the existing frameworks are unable to explicitly model the effect of interventions on disease progression. CT-HMMs have recently attracted attention, as they are able to handle these complexities. The main contribution of this research is to propose a CT-HMM disease progression model, which incorporates the effect of interventions, and to present an efficient approach for learning the parameters of this model based on the Expectation-Maximization algorithm.

Specific Aims of the Project:

We'll track the progression of the disease in response to the treatment over time. The model is supposed to provide guidelines for predicting disease remission.

Research Methods

Data Source and Inclusion/Exclusion Criteria to be used to define the patient sample for your study:

We include patients who have been diagnosed with Ulcerative Colitis. The statistical model is capable of incorporating covariates (e.g. age, gender, ethnicity, etc.) naturally. Therefore, we do not have restrictions on the demographics. Since our model captures the treatment effect over time, we require all the patients in all 4 treatment groups in the study. The inclusion and exclusion criteria that are mentioned on the project's main page (https://clinicaltrials.gov/ct2/show/NCT00488631) are appropriate for our study.

Primary and Secondary Outcome Measure(s) and how they will be categorized/defined for your study:

As the primary outcome, we will measure the statistical error of the model in predicting disease flare-ups and remissions, defined as Mayo scores of [6, 12] and [0, 6], respectively. Our multi-layered Markovian model also uses the patient-reported outcome measure (e.g. IBDQ score) as the secondary outcome associated with the observed layer of the HMM.

Main Predictor/Independent Variable and how it will be categorized/defined for your study:

The main observation variables (outcomes) that the model tracks are the patient-reported outcomes (e.g. IBD score) as well as clinical outcomes (e.g. endoscopy score). Since we're using a Markvian model that tracks the disease state over time, we do not have a classical regression analysis with independent variables. However, our model will use the medication data as well as control variables such as demographics (e.g. age, gender), lab tests (e.g. C-reactive protein), hospitalization history, etc.

Statistical Analysis Plan:

We have already developed the statistical model as well as a statistical inference algorithm for fitting data into the model. The mathematical details are available online at https://escholarship.org/content/qt3gz0c7qx/qt3gz0c7qx.pdf. In summary, we divide the patients into training and validation sets randomly and estimate the parameters of the Markovian model using the training set based on the developed EM algorithm. Afterwards. we evaluate the predictive power of the trained model on the validation set. The evaluation metric will be the error of predicting both patient-reported outcomes and clinical outcomes (e.g. endoscopy score) using the entire available history of the patient.

Project Timeline:

We expect the analysis to take 6-12 months depending on the possible complexities that arise while working with real-world data. The mathematical results are ready as mentioned earlier.

Dissemination Plan:

We plan to publish the work in healthcare - machine learning or healthcare - AI journals.

Bibliography:

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