Principal Investigator

First Name: Hwanhee
Last Name: Hong
Degree: PhD
Primary Affiliation: Duke University
E-mail: hwanhee.hong@duke.edu
State or Province: NC
Country: USA

General Information

Key Personnel (other than PI):
First Name: Elizabeth
Last name: Stuart
Degree: PhD
Primary Affiliation: Johns Hopkins Bloomberg School of Public Health
SCOPUS ID:
Requires Data Access? Unknown

First Name: Trang
Last name: Nguyen
Degree: PhD
Primary Affiliation: Johns Hopkins Bloomberg School of Public Health
SCOPUS ID:
Requires Data Access? Unknown

First Name: Leon
Last name: Di Stefano
Degree: MS
Primary Affiliation: Johns Hopkins Bloomberg School of Public Health
SCOPUS ID:
Requires Data Access? Unknown

First Name: Carly
Last name: Lupton-Smith
Degree: MS
Primary Affiliation: Johns Hopkins Bloomberg School of Public Health
SCOPUS ID:
Requires Data Access? Unknown

First Name: Ting-Hsuan
Last name: Chang
Degree: MS
Primary Affiliation: Johns Hopkins Bloomberg School of Public Health
SCOPUS ID:
Requires Data Access? Unknown

First Name: Tengjie
Last name: Tang
Degree: BA
Primary Affiliation: Duke University
SCOPUS ID:
Requires Data Access? Unknown

First Name: Congwen
Last name: Zhao
Degree: MS
Primary Affiliation: Duke University
SCOPUS ID:
Requires Data Access? Unknown

First Name: Elena
Last name: Badillo-Goicoechea
Degree: MS
Primary Affiliation: Johns Hopkins Bloomberg School of Public Health
SCOPUS ID:
Requires Data Access? Unknown

First Name: Qiao
Last name: Wang
Degree: PhD
Primary Affiliation: Dr. Hwanhee Hong
SCOPUS ID:
Requires Data Access? Unknown

First Name: Elaona
Last name: Lemoto
Degree: PhD Student
Primary Affiliation: Duke University
SCOPUS ID:
Requires Data Access? Unknown

First Name: Wenshan
Last name: Yu
Degree: PhD
Primary Affiliation: Duke University
SCOPUS ID:
Requires Data Access? Unknown

First Name: Kyungeun
Last name: Jeon
Degree: MSc
Primary Affiliation: Duke University
SCOPUS ID:
Requires Data Access? Unknown

How did you learn about the YODA Project?: Internet Search

Conflict of Interest

https://yoda.yale.edu/wp-content/uploads/2019/08/coi_carlyluptonsmith.pdf
https://yoda.yale.edu/wp-content/uploads/2018/09/coi_congwen_zhao.pdf
https://yoda.yale.edu/wp-content/uploads/2020/02/coi_hwanheehong.pdf
https://yoda.yale.edu/wp-content/uploads/2016/05/coi_leon_di_stefano.pdf
https://yoda.yale.edu/wp-content/uploads/2018/12/coi_stuartelizabeth.pdf
https://yoda.yale.edu/wp-content/uploads/2017/07/coi_tengjietang.pdf
https://yoda.yale.edu/wp-content/uploads/2017/05/coi_tinghsuanchang.pdf
https://yoda.yale.edu/wp-content/uploads/2017/03/coi_trangnguyen.pdf
https://yoda.yale.edu/wp-content/uploads/2019/04/coi-ebg.pdf
https://yoda.yale.edu/wp-content/uploads/2019/12/coi_form_qw.pdf

https://yoda.yale.edu/wp-content/uploads/2017/08/coi_form_el.pdf
https://yoda.yale.edu/wp-content/uploads/2018/12/coi_form_kj.pdf
https://yoda.yale.edu/wp-content/uploads/2022/01/coi_form_WY.pdf
https://yoda.yale.edu/wp-content/uploads/2022/01/coi_form_KJ.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. NCT00589914 - R092670PSY3006 - A Randomized, Double-Blind, Parallel-Group, Comparative Study of Flexible Doses of Paliperidone Palmitate and Flexible Doses of Risperidone Long-Acting Intramuscular Injection in Subjects With Schizophrenia
2. NCT00604279 - R092670PSY3008 - A Randomized, Open-Label, Parallel Group Comparative Study of Paliperidone Palmitate (50, 100, 150 mg eq) and Risperidone LAI (25, 37.5, or 50 mg) in Subjects with Schizophrenia
3. NCT00210717 - R092670PSY3002 - A Randomized, Double-Blind, Parallel Group, Comparative Study of Flexibly Dosed Paliperidone Palmitate (25, 50, 75, or 100 mg eq.) Administered Every 4 Weeks and Flexibly Dosed RISPERDAL CONSTA (25, 37.5, or 50 mg) Administered Every 2 Weeks in Subjects With Schizophrenia

Research Proposal

Project Title

Combining data sources to identify effect moderation for personalized mental health treatment

Narrative Summary:

Identifying effect moderators is crucial for personalized delivery of treatment and prevention interventions, but doing so is incredibly difficult using standard study designs. This work will synthesize, extend, and apply methods for identifying effect moderators when multiple studies are available, with a particular focus on the complexities in mental health research.

Scientific Abstract:

Background: Identifying effect moderators is crucial for personalized delivery of treatment and prevention interventions, but doing so is incredibly difficult using standard study designs.
Objective: This work will synthesize, extend, and apply methods for identifying effect moderators when multiple studies are available, with a particular focus on the complexities in mental health research.
Study Design: This work will synthesize, extend, and apply methods for identifying effect moderators when multiple studies are available, with a particular focus on the complexities in mental health research. The methods will apply broadly and will be illustrated in an example: estimating the effects of medication treatment for schizophrenia (using 3 randomized controlled trials). In addition, we will synthesize experimental data with non-experimental data from the Duke University and Johns Hopkins Health System electronic health record.
Participants: Adult patients with schizophrenia
Main Outcome Measure(s): For schizophrenia studies, key outcomes of interest include PANSS, CGI-S,

PSP, adverse events, and hospitalization.
Statistical Analysis: The work will: 1) Extend moderation methods for scenarios with multiple randomized experiments, and 2) Develop methods for using data from combined datasets with both experimental and non-experimental designs to identify effect moderation. Two types of methods will be developed. First, machine learning methods (developed already in the single study setting to estimate the conditional additive treatment effect as a function of covariates) will be extended to cases with multiple trials. Second, a Bayesian meta-analysis approach using individual level patient data will also be used.

Brief Project Background and Statement of Project Significance:

Determining ?what works for whom? is a key goal in prevention and treatment across a variety of areas, including mental health. By understanding which individuals benefit most from which treatments we have the possibility of directing scarce resources to those who will most benefit, and of reducing the ?churn? of individuals attempting multiple treatments before finding the one that works for them. Identifying effect moderators?factors that relate to the size of treatment effects--is crucial for delivery of treatment and prevention interventions, but doing so is incredibly difficult using standard study designs. By developing methods to take full advantage of both experimental and non-experimental data this work has the potential to move towards personalized mental health, thus improving how we prevent and treat mental health challenges in the population.

Specific Aims of the Project:

Aim 1: Develop methods to identify effect heterogeneity using multiple randomized experiments.
Aim 2: Develop methods to identify effect heterogeneity using data from combined datasets with both experimental and non-experimental studies.

Research Methods

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

We will be analyzing data on Vivli. The four other studies that will be used on Vivli include NCT01153009, NCT01140906, NCT00672620, and NCT00635219.
Male or female; Age >= 18; schizophrenia according to DSM-IV; baseline PANSS total score 60-120; BMI >= 15 kg/m^2; interventions including paliperidone palmitate and risperidone LAI

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

Outcome measures of interest include PANSS, CGI-S, PSP, adverse events, and hospitalization. The primary outcome will be PANSS and the remaining outcomes will be secondary outcomes. To measure treatment effects, we will consider changes in PANSS, CGI-S, and PSP scores between randomization and the end of the study and consider the number of adverse events and hospitalization.

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

We will consider effect moderators and confounders that are collected across the RCTs and EHR data. Possible effect moderators include co-occurring disorders such as fibromyalgia, coronary artery disease, diabetes, obesity, hypertension, and other mental health conditions (bipolar, anxiety, PTSD); demographics such as age, race, and gender; height, weight, and BMI; information on substance use, including drugs and alcohol; and indicators of severity of disease.

Other Variables of Interest that will be used in your analysis and how they will be categorized/defined for your study:

n/a

Statistical Analysis Plan:

Our proposed project spans a broad spectrum that includes on one end the situation where putative effect moderators have been specified and on the other end the situation where effect moderation is assumed to be via some unknown function of a set of covariates. We use Bayesian parametric models to handle the former case and nonparametric machine learning methods to handle the latter case. In addition, to deal with the problem that RCTs are generally not powered to test moderation effects, we propose to combine data from multiple studies: multiple RCTs, and RCTs plus non-experimental
electronic health records (EHR) data. We will develop advanced statistical methods that are built based on Bayesian meta-analysis approaches and Bayesian variable selection models with individual participant-level data (IPD) [Riley et al. 2010, Hong et al. 2015, Seo et al. 2021] and existing machine learning methods for effect modeling (developed for the single study setting) [Tan et al. 2021] to handle multiple studies.

Project Timeline:

Anticipated project start date: 1/1/2022
Analysis completion date: 5/31/2025
We plan to write multiple manuscripts over the course of project. We aim to submit first publication using the YODA data in the early 2023.

Dissemination Plan:

First, the newly developed methods will be disseminated through journal articles, conference talks, and a website to both statistical and medical audience. Second, we will develop (and publish in journals relevant to mental health researchers) several tutorials to provide general guidance on how to use the methods to combine data sources when examining effect moderation. Third, we will disseminate the methods through teaching at Johns Hopkins, Duke, and more broadly.

Bibliography:

Riley RD, Lambert PC, and Abo-Zaid G, (2010). Meta-analysis of individual participant data: rationale, conduct, and reporting. BMJ: British Medical Journal, p. 340:c221.
Hong H, Fu H, Price KL, and Carlin BP. (2015). Incorporation of individual patient data in network meta-analysis for multiple continuous endpoints, with application to diabetes treatment. Statistics in Medicine, 34(20), 2794-2819.
Seo M, White IR, Furukawa TA, Imai H, Valgimigli M, Egger M, Zwahlen M, Efthimiou O. (2021). Comparing methods for estimating patient-specific treatment effects in individual patient data meta-analysis. Statistics in Medicine, 40(6):1553-1573.
Tan X, Chang CC, Tang L. A tree-based federated learning approach for personalized treatment effect estimation from heterogeneous data sources. arXiv preprint arXiv:2103.06261. 2021 Mar 10.