

Principal Investigator

First Name: Jayesh
Last Name: Kamath
Degree: MD PhD
Primary Affiliation: University of Connecticut Health Center
E-mail: jkamath68@gmail.com
Phone number: 8606796727
Address: 263 Farmington Avenue


City: Farmington
State or Province: CT
Zip or Postal Code: 06030
Country: USA

2016-0725

General Information

Key Personnel (in addition to PI): **First Name:** Grace
Last name: Chan
Degree: PhD
Primary Affiliation: University of Connecticut Health Center

Are external grants or funds being used to support this research?: No external grants or funds are being used to support this research.

 [jayesh_kamath_coi_with_signature.pdf](#)

 [grace_chan_coi_with_signature.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

Associated Trial(s): [NCT00334126 - A Randomized, Double-blind, Placebo-controlled, Parallel Group Study to Evaluate the Efficacy and Safety of Paliperidone ER Compared to Quetiapine in Subjects With an Acute Exacerbation of Schizophrenia](#)
[NCT00645307 - A Randomized, Double-Blind, Placebo-Controlled, Parallel-Group Study With an Open-Label Extension Evaluating Extended Release OROS® Paliperidone in the Prevention of Recurrence in Subjects With Schizophrenia - Open Label Phase](#)
[NCT00589914 - 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](#)
[NCT00590577 - A Randomized, Double-Blind, Placebo-Controlled, Parallel-Group, Dose Response Study to Evaluate the Efficacy and Safety of 3 Fixed Doses \(25 mg eq., 100 mg eq., and 150 mg eq.\) of Paliperidone](#)

[Palmitate in Subjects With Schizophrenia](#)[NCT00119756 - A Randomized, Crossover Study to Evaluate the Overall Safety and Tolerability of Paliperidone Palmitate Injected in the Deltoid or Gluteus Muscle in Patients With Schizophrenia](#)[NCT00210548 - A Randomized, Double-Blind, Placebo-Controlled, Parallel-Group, Dose-Response Study to Evaluate the Efficacy and Safety of 3 Fixed Doses \(50 mg eq., 100 mg eq., and 150 mg eq.\) of Paliperidone Palmitate in Subjects With Schizophrenia](#)[NCT00101634 - A Randomized, Double-blind, Placebo-controlled, Parallel-group, Dose-response Study to Evaluate the Efficacy and Safety of 3 Fixed Doses \(25 mg eq, 50 mg eq, and 100 mg eq\) of Paliperidone Palmitate in Patients With Schizophrenia](#)[NCT00397033 - A Randomized, Double-blind, Placebo-controlled, Parallel-group Study to Evaluate the Efficacy and Safety of Two Dosages of Paliperidone ER in the Treatment of Patients With Schizoaffective Disorder](#)[NCT00412373 - A Randomized, Double-blind, Placebo-controlled, Parallel- Group Study to Evaluate the Efficacy and Safety of Flexible-dose Paliperidone ER in the Treatment of Patients With Schizoaffective Disorder](#)[NCT00077714 - A Randomized, Double-blind, Placebo- and Active-controlled, Parallel-group, Dose-response Study to Evaluate the Efficacy and Safety of 2 Fixed Dosages of Paliperidone Extended Release Tablets and Olanzapine, With Open-label Extension, in t](#)[NCT00083668 - A Randomized, Double-blind, Placebo- and Active-controlled, Parallel-group, Dose-response Study to Evaluate the Efficacy and Safety of 3 Fixed Dosages of Paliperidone Extended Release \(ER\) Tablets and Olanzapine, With Open-label Extension.](#)[NCT00074477 - A Randomized, Double-Blind, Placebo-Controlled Study to Evaluate the Efficacy and Safety of 50 and 100 Mg-eq of Paliperidone Palmitate in Patients With Schizophrenia](#)

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

Research Proposal

Project Title

Investigation of Racial and Ethnic Differences in Cardiometabolic Health of Patients with Schizophrenia/Schizoaffective Disorder

Narrative Summary:

Patients with schizophrenia have higher risk of weight gain and related health consequences (e.g. diabetes) compared to the general population. Research shows that racial/ethnic differences exist in obesity and obesity-related adverse health problems. It is possible that patients with schizophrenia of certain race/ethnicity carry higher risk of these health problems compared to similar patients of other races/ethnicities. We propose to analyze the data available in the YODA project to identify any racial/ethnic differences in weight and related health problems in adult patients with schizophrenia/schizoaffective disorder enrolled in studies conducted at sites in the United States.

Scientific Abstract:

Background: Patients with schizophrenia carry higher risk of weight gain and metabolic syndrome (MetS) compared to the general population. Separately, studies have documented racial/ethnic differences in obesity and prevalence of MetS with certain races/ethnicities having higher risk of these health problems. It is unknown if racial/ethnic differences exist in the risk of weight and MetS in patients with schizophrenia/schizoaffective disorder.

Objective: To investigate racial/ethnic differences in body mass index (BMI) and MetS, factors contributing to the risk of MetS, and MetS-related health outcomes in patients with schizophrenia/schizoaffective disorder enrolled in studies conducted at sites in the US.

Study Design: Retrospective, cross-sectional review of records of adult patients with schizophrenia/schizoaffective disorder enrolled in studies conducted at the US sites.

Participants: Records (screening and baseline) of all adult patients with schizophrenia/schizoaffective disorder enrolled in the studies conducted at US sites will be eligible for the proposed analyses.

Outcome measures: The primary outcome measures include the BMI and MetS components. The secondary outcome measures include MetS-related health consequences.

Statistical analyses: One-way ANOVA will be used to test the main racial/ethnic effect in BMI and all 5 components of MetS among schizophrenia/schizoaffective disorder patients. Generalized linear models will be used to investigate racial/ethnic differences in factors contributing to MetS and MetS-related health outcomes

Brief Project Background and Statement of Project Significance:

Metabolic syndrome (MetS), a significant public health problem, is associated with high risk of diabetes and other adverse metabolic and cardiovascular outcomes [1]. Patients with schizophrenia carry higher risk of MetS compared to the general population [2]. As a result, cardiovascular deaths are significant cause of mortality in patients with schizophrenia [3]. Numerous factors contribute to risk of MetS in patients with schizophrenia. These factors include genetic factors, lifestyle factors and as well as use of certain antipsychotic (APs) medications [2]. Evidence suggests that certain genes that increase the risk of serious mental illness might also heighten the risk of cardiometabolic disorders [4]. Additionally, patients with Schizophrenia have a high incidence of lifestyle factors contributing to MetS and related cardiometabolic risks, such as poor diet, smoking, stress and lack of exercise [5]. It is also well documented that certain APs are associated with significant weight gain and add substantial cardiometabolic risks in these patients [2].

According to a survey conducted by the United States (US) census Bureau in 2008, approximately 33%, or more than 100 million people, identified themselves as belonging to a racial or ethnic minority population [6]. Evidence suggests that there are race/ethnic differences in obesity and prevalence of MetS, with higher rates among African American and Hispanic populations [7]. It is unknown if such differential risk also exists in patients with schizophrenia based on their race/ethnicity. It is known that certain factors such as access to better nutrition, access to health care, and stress are further compromised in racial/ethnic minorities due to diverse economic and psychosocial stressors. These factors may exacerbate risk of weight gain and MetS in patients with schizophrenia of certain race/ethnic background. It is also possible that in patients with schizophrenia of certain race/ethnicity, specific genetic factors may have a differential contribution, increasing their risk of weight gain and MetS. Other psychosocial factors may play a role. For example, a recent study reported racial/ethnic disparities in monitoring of MetS in patients with schizophrenia in Veterans Health Administration [8].

It is important to investigate prevalence of MetS in patients with schizophrenia based on their race/ethnicity and evaluate any differential impact of factors contributing to MetS in these patients. This will improve and personalize management of this serious health problem affecting the lives of patients with schizophrenia. The purpose of the proposed project is to investigate racial/ethnic differences in MetS in patients with schizophrenia enrolled in schizophrenia/schizoaffective disorder studies conducted in the United States (US). The proposed study will also investigate racial/ethnic differences in factors contributing to MetS risk in these patients and differences in MetS related health outcomes such as cardiometabolic outcomes.

Specific Aims of the Project:

Hypotheses: Racial/ethnic differences have an impact on risk of MetS in patients with schizophrenia and schizoaffective disorder. Patients with schizophrenia/schizoaffective disorder of certain races/ethnicities carry higher risk of MetS compared to other races/ethnicities.

Specific Aims: In a cross-sectional, retrospective review of records of patients enrolled in schizophrenia/schizoaffective disorder studies at the US study sites-

1. Investigate racial/ethnic differences in body-mass index (BMI) and other MetS components in patients with schizophrenia and schizoaffective disorder.
2. Investigate racial/ethnic differences in factors contributing to the risk of MetS in patients with schizophrenia and schizoaffective disorder.
3. Assess racial/ethnic differences in MetS-related health outcomes in patients with schizophrenia and schizoaffective disorder

What is the purpose of the analysis being proposed? Please select all that apply. Preliminary research to be used as part of a grant proposal

Participant-level data meta-analysis

Participant-level data meta-analysis uses only data from YODA Project

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

Records of patients enrolled in the schizophrenia/schizoaffective disorder studies at the US sites (available in the YODA project) will be eligible for the study. In the multi-site studies such as the ones available in the YODA project, comprehensive assessments of all patients enrolled in the study are conducted at screening and baseline (prior to initiation of any study intervention). Such assessments include assessment of demographic/clinical characteristics, lifestyle factors, medical/psychiatric comorbidities and comprehensive laboratory investigations. The proposed analyses will utilize data available from screening/baseline assessments of patients enrolled in these studies.

Inclusion/Exclusion Criteria:

Inclusion criteria- Records of adult (age 18 and above) patients enrolled in schizophrenia/schizoaffective disorder studies at any US site

Exclusion criteria- Records of child/adolescent (less than 18 years of age) patients or patients enrolled at non-US sites

Based on brief information available from the YODA Project Trials webpage, over 4,000 adult study participants from six Paliperidone trials and six Paliperidone palmitate trials satisfied the above criteria

Main Outcome Measure and how it will be categorized/defined for your study:

Primary Outcome measures (from screening/baseline evaluations data source):

1. Body mass index
2. Five Components of MetS: Fasting glucose, high-density-lipoprotein (HDL) cholesterol, triglycerides, blood pressure, and waistline

Secondary Outcome measures (from screening/baseline evaluations data source):

1. Other health related data such as heart rate, QTc interval gathered
2. Health outcomes including diabetes, cardiovascular illness, cerebrovascular illness and other medical comorbidities

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

Self-reported racial/ethnic from screening or baseline evaluations will be used to define the main predictor, a four-level categorical variable: Caucasian, African-American, Hispanic, and Other.

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

Other variables of interest and potential confounders (if available from screening/baseline evaluations data):

1. Demographic variables such as age, gender, socioeconomic status, geographic location, and other psychosocial factors
2. Lifestyle factors such as smoking, other substance use, diet, exercise
3. Psychiatric comorbidities and relevant psychiatric symptomatology at baseline
4. Family medical history (e.g. history of diabetes, cardiovascular/cerebrovascular illness)
5. Any available data on health care utilization, access to health care and quality of life

Statistical Analysis Plan:

Specific Aim 1: One-way ANOVA will be used to test the main racial/ethnic effect in BMI and all 5 components of MetS among schizophrenia/schizoaffective disorder patients. A four-level racial/ethnic categorical variable will be considered: Caucasian, African-American, Hispanic, and Other.

Specific Aim 2: General linear models with racial/ethnic main effect, MetS risk factor main effect, and racial/ethnic by MetS risk factor interaction will be used to determine if there are racial/ethnic-specific MetS risk factor. MetS risk factors will include age, gender, socioeconomic status, living environment, past and current substance use, diet and exercise habit, comorbid medical and psychiatric problems and family history.

Specific Aim 3: Generalized linear models will be used to examine how MetS-related outcomes such as QTc interval, diabetes, cardiovascular and cerebrovascular illness differ by racial/ethnic categories after adjusting for potential confounding covariates.

Project Timeline:

Data analyses will start as soon as study data is available. . It will require approximately 4-6 months from the point of data access. Approximately 4-6 months will then be required for dissemination including presentation and publication of study outcomes.

Dissemination Plan:

Study outcomes will be presented at national or international meetings (e.g. ASCO or ACNP meeting) and published in psychiatry journals (e.g. Journal of Psychiatric Research).

Bibliography:

[1] Rutter MK, Meigs JB, Wilson PW. Cardiovascular risk and the metabolic syndrome. *Metab Syndr Relat Disord*. 2006; 4(4):252-60.

- [2] Meyer JM, Stahl SM. The metabolic syndrome and schizophrenia. *Acta Psychiatr Scand*. 2009; 119(1):4-14.
- [3] Newcomer JW. Antipsychotic medications: metabolic and cardiovascular risk. *J Clin Psychiatry*. 2007; 68 Suppl 4:8-13.
- [4] Gough SC and O'Donovan MC. Clustering of metabolic comorbidity in schizophrenia: A genetic contribution? *Journal of Psychopharmacology*. 2005; 19(suppl 6), 47-55.
- [5] Meyer J, Koro CE and L'Italien GJ. The metabolic syndrome and schizophrenia: A review. *International Review of Psychiatry*. 2005; 17(3), 173-180.
- [6] U.S. Census Bureau, American FactFinder. American Community Survey. 2008 American Community Survey 1-year estimates [Internet]. ACS demographic and housing estimates: 2008. Available from: <http://factfinder.census.gov>.
- [7] Beltrán-Sánchez H, Harhay MO, Harhay MM, McElligott S. Prevalence and trends of metabolic syndrome in the adult U.S. population, 1999-2010. *J Am Coll Cardiol*. 2013; 62(8):697-703.
- [8] Phillips KL, Copeland LA, Zeber JE, Stock EM, Tsan JY, MacCarthy AA. Racial/Ethnic disparities in monitoring metabolic parameters for patients with schizophrenia receiving antipsychotic medications. *Am J Geriatr Psychiatry*. 2015; 23(6):596-606.