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Are external grants or funds being used to support this research?: External grants or funds are being used to support this research.
Project Funding Source: National Institute of Mental Health (pending council review)
How did you learn about the YODA Project?: Internet Search

Conflict of Interest

https://yoda.yale.edu/system/files/yoda_project_coi_form_huo.pdf
https://yoda.yale.edu/system/files/yoda_project_coi_form_miller_0.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. NCT00645099 - R076477SCH3020 - A Prospective Randomized Open-label 6-Month Head-To-Head Trial to Compare Metabolic Effects of Paliperidone ER and Olanzapine in Subjects With Schizophrenia
2. NCT01606228 - R076477SCH3033 - An Open-Label Prospective Trial to Explore the Tolerability, Safety and Efficacy of Flexibly-Dosed Paliperidone ER among Treatment-Naive and Newly Diagnosed Patients with Schizophrenia
3. NCT00334126 - R076477SCH3015 - 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
4. NCT00086320 - R076477-SCH-301 - A Randomized, Double-blind, Placebo-controlled, Parallel-group Study With an Open-label Extension Evaluating Paliperidone Extended Release Tablets in the Prevention of Recurrence in Subjects With Schizophrenia

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5. NCT00650793 - R076477-SCH-703 - A Randomized, DB, PC and AC, Parallel Group, Dose-Response Study to Evaluate the Efficacy and Safety of 3 Fixed Dosages of Extended Release OROS Paliperidone (6, 9, 12 mg/Day) and Olanzapine (10 mg/Day), With Open-Label Extension, in the Treatment of Subjects With Schizophrenia - Open Label Phase
6. 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
7. 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
8. NCT00590577 - R092670PSY3007 - 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
9. NCT00111189 - R092670PSY3001 - A Randomized Double-blind Placebo-controlled Parallel Group Study Evaluating Paliperidone Palmitate in the Prevention of Recurrence in Patients With Schizophrenia. Placebo Consists of 20% Intralipid (200 mg/mL) Injectable Emulsion
10. 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
11. NCT00119756 - R092670PSY3005 - 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
12. NCT00210548 - R092670PSY3003 - 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
13. NCT00101634 - R092670PSY3004 - 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
14. NCT00249132 - RIS-INT-3 - A Canadian multicenter placebo-controlled study of fixed doses of risperidone and haloperidol in the treatment of chronic schizophrenic patients
15. NCT00216476 - RISSCH3001 - CONSTATRE: Risperdal® Consta® Trial of Relapse Prevention and Effectiveness
16. NCT00083668 - R076477-SCH-305 - 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, in the Treatment of Patients With Schizophrenia
17. NCT00074477 - R092670-SCH-201 - 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
18. NCT00078039 - R076477-SCH-303 - Trial Evaluating Three Fixed Dosages of Paliperidone Extended-Release (ER) Tablets and Olanzapine in the Treatment of Patients With Schizophrenia
19. NCT00253136 - RIS-USA-121/CR006055 - Risperidone Depot (Microspheres) vs. Placebo in the Treatment of Subjects With Schizophrenia
20. NCT01529515 - R092670PSY3012 - A Randomized, Multicenter, Double-Blind, Relapse Prevention Study of Paliperidone Palmitate 3 Month Formulation for the Treatment of Subjects With Schizophrenia
21. NCT01662310 - R076477-SCH-3041 - Paliperidone Extended Release Tablets for the Prevention of Relapse in Subjects With Schizophrenia: A Randomized, Double-Blind, Placebo-Controlled, Parallel-Group Study
22. NCT00524043 - R076477SCH4012 - A Randomized, Double-Blind, Placebo- and Active-Controlled, Parallel-Group Study to Evaluate the Efficacy and Safety of a Fixed Dosage of 1.5 mg/Day of Paliperidone Extended Release (ER) in the Treatment of Subjects With Schizophrenia
23. NCT00645307 - R076477-SCH-701 - 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
24. NCT00249223 - RIS-INT-61 - Risperidone Depot (Microspheres) vs. Risperidone Tablets - a Non-inferiority, Efficacy Trial in Subjects With Schizophrenia
25. NCT01157351 - R092670SCH3006 - A Fifteen-month, Prospective, Randomized, Active-controlled, Open-label, Flexible Dose Study of Paliperidone Palmitate Compared With Oral Antipsychotic Treatment in Delaying Time to Treatment Failure in Adults With Schizophrenia Who Have Been Incarcerated

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26. NCT01081769 - R092670SCH3005 - A 24-month, Prospective, Randomized, Active-Controlled, Open-Label, Rater-Blinded, Multicenter, International Study of the Prevention of Relapse Comparing Long-Acting Injectable Paliperidone Palmitate to Treatment as Usual With Oral Antipsychotic Monotherapy in Adults With Schizophrenia
27. NCT01281527 - R092670SCH3010 - A 6-month, Open Label, Prospective, Multicenter, International, Exploratory Study of a Transition to Flexibly Dosed Paliperidone Palmitate in Patients With Schizophrenia Previously Unsuccessfully Treated With Oral or Long-acting Injectable Antipsychotics
28. NCT01051531 - R092670SCH3009 - Safety, Tolerability, and Treatment Response of Paliperidone Palmitate in Subjects With Schizophrenia When Switching From Oral Antipsychotics
29. NCT01527305 - R092670SCH4009 - An Open-Label, Prospective, Non-Comparative Study to Evaluate the Efficacy and Safety of Paliperidone Palmitate in Subjects With Acute Schizophrenia
30. NCT01299389 - PALM-JPN-4 - A Randomized, Double-Blind, Placebo-Controlled, Parallel-Group, Fixed-Dose, Multicenter Study of JNS010 (Paliperidone Palmitate) in Patients With Schizophrenia
31. NCT01258920 - PALM-JPN-5 - A Long-Term, Open-Label Study of Flexibly Dosed Paliperidone Palmitate Long-Acting Intramuscular Injection in Japanese Patients With Schizophrenia
32. NCT00216671 - RISSCH4045 - Early Versus Late Initiation of Treatment With Risperdal Consta in Subjects With Schizophrenia After an Acute Episode
33. NCT00369239 - RISSCH4043 - Is Premorbid Functioning a Predictor of Outcome in Patients With Early Onset Psychosis Treated With Risperdal Consta?
34. NCT00216632 - RISSCH4026 - Treatment Success in Patients Requiring Treatment Change From Olanzapine to Risperidone Long Acting Injectable (TRESOR)
35. NCT00236379 - RIS-USA-275 - A Six-month, Double-blind, Randomized, International, Multicenter Trial to Evaluate the Glucoregulatory Effects of Risperidone and Olanzapine in Subjects With Schizophrenia or Schizoaffective Disorder
36. NCT00216528 - RIS-KOR-66 - A Prospective, Open-Label Study to Evaluate Symptomatic Remission in Schizophrenia With Long Acting Risperidone Microspheres (Risperdal Consta)
37. NCT00269919 - RIS-KOR-64 - Effect on Efficacy, Safety and Quality of Life by Long-Term Treatment of Long-Acting Risperidone Microspheres in Patients With Schizophrenia
38. NCT00236353 - RIS-USA-305 - An Open-label Study of the Efficacy and Safety of RISPERDAL Long-acting Microspheres (RISPERDAL CONSTA) Administered Once Monthly in Adults With Schizophrenia or Schizoaffective Disorder
39. NCT00495118 - RIS-INT-80 - Risperidone Depot (Microspheres) in the Treatment of Subjects With Schizophrenia or Schizoaffective Disorder - an Open-label Follow-up Trial of RIS-INT-62 and RIS-INT-85
40. NCT01855074 - RISSCH4186 - Evaluation of Efficacy and Safety of Risperidone in Long-acting Microspheres in Patients With Schizophrenia, Schizophreniform or Schizoaffective Disorders Diagnosed According to the DSM-IV Criteria, After Switching Treatment With Any Antipsychotic Therapy With Long-acting Microspheres of Risperidone
41. NCT00236457 - RIS-INT-62 - Randomized, Multi-center, Open Label Trial Comparing Risperidone Depot (Microspheres) and Olanzapine Tablets in Patients With Schizophrenia or Schizoaffective Disorder
42. NCT00236587 - RIS-USA-265 - An Open Label, Long Term Trial of Risperidone Long Acting Microspheres in the Treatment of Patients Diagnosed With Schizophrenia
43. NCT00297388 - RIS-SCH-401 - A 52-wk Prospective, Randomized, Double-blind, Multicenter Study of Relapse Following Transition From Oral Antipsychotic Medication to 2 Different Doses (25 or 50 mg Every 2 Wks) of Risperidone Long-acting Microspheres (RISPERDAL CONSTA) in Adults With Schizophrenia or Schizoaffective Disorder
44. NCT00821600 - RIS-SCH-1012 - Single-Dose, Open-Label Pilot Study to Explore the Pharmacokinetics, Safety and Tolerability of a Gluteal Intramuscular Injection of a 4-Week Long-Acting Injectable Formulation of Risperidone in Patients With Chronic Stable Schizophrenia
45. NCT00299702 - RISSCH4060 - A 2-year, Prospective, Blinded-rater, Open-label, Active-controlled, Multicenter, Randomized Study of Long-term Efficacy and Effectiveness Comparing Risperdal® Consta® and Abilify® (Aripiprazole) in Adults With Schizophrenia
46. NCT00526877 - RISSCH4119 (RISC-TWN-MA10) - Evaluation of Efficacy and Safety of Long-acting Risperidone Microspheres in Patients With Schizophrenia or Schizoaffective Disorders, Who is Receiving Psychiatric Home-care Treatment, When Switching From Typical Depot or Oral Antipsychotics to Long-acting Risperidone Microspheres
47. NCT00034775 - RIS-USA-259 - Open-Label Trial Exploring A Switching Regimen From Oral Neuroleptics, Other Than Risperidone, To Risperidone Depot Microspheres
48. NCT00460512 - R076477SCH3017 - An Open-label Prospective Trial to Explore the Tolerability, Safety and Efficacy of Flexibly Dosed Paliperidone ER in Subjects With Schizophrenia

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49. NCT00566631 - R076477SCH3018 - Tolerability, Safety and Treatment Response of Flexible Doses of Paliperidone ER in Acutely Exacerbated Subjects With Schizophrenia
50. NCT01515423 - R092670PSY3011 - A Randomized, Multicenter, Double-Blind, Non-inferiority Study of Paliperidone Palmitate 3 Month and 1 Month Formulations for the Treatment of Subjects With Schizophrenia
51. NCT02713282 - R092670SCH3015 - A 52-Week, Open-Label, Prospective, Multicenter, International Study of a Transition to the Paliperidone Palmitate 3-Month Formulation In Patients With Schizophrenia Previously Stabilized on the Paliperidone Palmitate 1-Month Formulation

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

Research Proposal

Project Title

Inflammation and the Metabolic Syndrome in Psychosis

Narrative Summary:

The metabolic syndrome (MetS), which is associated with cardiovascular disease morbidity and mortality and a state of low-grade inflammation, is highly prevalent in patients with psychosis, but whether baseline levels of inflammatory markers predict incident metabolic adverse effects of antipsychotic treatment is unclear. In this project, we will perform meta-analyses of the association between inflammation and prevalent and incident metabolic syndrome in patients with psychosis. Results of the proposed study may identify a potential biomarker of patients with psychosis ata= heightened risk of adverse cardiometabolic effects of antipsychotics towards personalized medicine approaches.

Scientific Abstract:

Background: The metabolic syndrome (MetS) is a constellation of metabolic risk factors associated with the development of atherosclerotic cardiovascular disease, and is highly common in patients with psychosis. The MetS is also associated with a state of inflammation. Blood white blood cell (WBC) counts—even within the normal range—serve as a marker of inflammation. Psychosis is associated with increased inflammation, including increased total and differential WBC counts. The adverse metabolic effects of atypical antipsychotics, which increase MetS risk, may potentiate aberrant levels of blood inflammatory markers.

Objective: To perform meta-analyses of the relationship between inflammation and the MetS in patients with psychosis, including OPTICS Project data .

Study Design: This is a systematic review and meta-analysis of the association between total and differential WBC counts and prevalent MetS in psychosis.

Participants: Studies will be identified through two approaches. From the OPTICS Project, we have identified over 50 trials for potential inclusion in the meta-analysis. Second, we will systematically search Medline, PsycInfo, Web of Science, and ScienceDirect.

Main Outcome Measures: MetS (and its individual criteria).

Statistical Analysis: We will perform random-effects meta-analyses of the relationship between inflammation and 1) prevalent, and 2) incident MetS in patients with psychosis. We will also investigate the predictive value of inflammation for incident MetS, using receiver-operating characteristic (ROC) analysis.

Brief Project Background and Statement of Project Significance:

The metabolic syndrome (MetS) is a constellation of metabolic risk factors associated with the development of

atherosclerotic cardiovascular disease morbidity and mortality. MetS is highly common in patients with psychosis, with a prevalence of over 40% at the baseline visit of the Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE) schizophrenia study. Cardiovascular disease is the leading cause of mortality in patients with psychosis, with a >2-fold increased risk of death compared to the general population. Given the tremendous burdens of both MetS comorbidity and premature mortality in psychosis, a novel potential biomarker that may identify—prior to treatment—patients with psychosis at heightened risk for incident adverse cardiometabolic effects of antipsychotics is a compelling opportunity and a public health priority.

MetS is also associated with a state of low-grade inflammation. Blood white blood cell (WBC) counts and ratios—even within the normal range—serve as a marker of inflammation. Psychosis is associated with increased inflammation, including increased total and differential WBC counts and ratios, as well as the acute phase reactant C-reactive protein (CRP). In the CATIE schizophrenia study, WBC counts were significantly positively correlated with CRP levels. The adverse metabolic effects of atypical antipsychotics, which increase MetS risk, may also potentiate aberrant levels of blood inflammatory markers. Several large population-based samples found that total and differential WBC counts were associated with prevalent and incident MetS and its individual criteria. There is evidence for associations between inflammation and the MetS in psychosis, but compared to the general population, relatively less is known, especially whether baseline levels of WBCs predict incident metabolic adverse effects of antipsychotic treatment. An important limitation of previous studies of inflammation and the MetS in psychosis is the non-standardized antipsychotic treatment within and across individual studies.

A particular advantage of the OPTICS Project is the large number of patients with psychosis treated with either risperidone or its active metabolite paliperidone , which would permit subgroup analyses that minimize potential confounding effects of non-standardized antipsychotic treatment. In screening data from the YODA project, over 50 trials (19000 patients) with potentially relevant individual-level data were identified, including measurement of total and differential WBC counts for at least two time points, to study the association between inflammation and the MetS.

Given the burden of the metabolic syndrome (MetS) and premature cardiovascular disease mortality in psychosis, a novel potential biomarker that may identify—prior to treatment—patients at heightened risk for incident adverse cardiometabolic effects of antipsychotics is a compelling opportunity and a public health priority. We propose to investigate a marker that is that is widely available, routinely ordered, inexpensive, and easy to interpret, thereby representing a “next-step” towards personalized medicine approaches for these patients.

Specific Aims of the Project:

Aim 1: To perform meta-analyses of the relationship between inflammation (white blood cell [WBC] and the metabolic syndrome (MetS) in patients with psychosis, including data from the OPTICS Project.
a. Test the hypothesis that in patients with psychosis, baseline total and differential WBC counts predict current MetS and its components
b. Test the hypothesis that in patients with psychosis, baseline total and differential white blood cell counts predict incident MetS and its components following antipsychotic treatment.
c. To investigate the predictive value of total and differential WBC counts for incident MetS, using receiver-operating characteristic (ROC) analysis (exploratory secondary aim).

What is the purpose of the analysis being proposed? Please select all that apply.
Participant-level data meta-analysis
Participant-level data meta-analysis pooling data from YODA Project with other additional data sources

Research Methods

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

This is a systematic review and meta-analysis of the association between total and differential WBC counts and prevalent MetS in psychosis. Studies will be identified through two approaches. From the OPTICS Project, we have identified 54 trials, for potential inclusion in the meta-analysis. Second, we will systematically search Medline, PsycInfo, Web of Science, and ScienceDirect from inception until the present, and the reference lists of identified studies (PLEASE NOTE WE HAVE YET NOT PERFORMED THIS SEARCH, SO CANNOT PROVIDE THE REQUESTED TRIAL IDs, ALTHOUGH WE WILL INCLUDE OUR OWN PUBLISHED DATA: PUBMED IDs

30407600, 30433271, AND 33285266.

For all studies (both OPTICS Project trials and those identified by the systematic review), the inclusion criteria will be studies with data on baseline total and or differential WBCs and prevalent MetS (or its individual criteria) in adults with psychosis (schizophrenia or schizoaffective disorder). Exclusion criteria will be absence of data on: 1) WBCs, 2) MetS (or its individual criteria), and 3) fasting blood samples, which are needed for the triglyceride, HDL cholesterol, and glucose criteria for MetS.

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

The Main Outcome Measure is the MetS (and its individual criteria). We will apply the AHA/NHLBI criteria to determine the presence or absence of the MetS and its individual criteria for each subject at each time point. MetS is defined as meeting ?3 of the following 5 criteria: 1) waist circumference (WC) ?102 cm (males) or ?88 cm (females), 2) fasting triglycerides ?150 mg/dL, 3) fasting HDL <40 mg/dL (males) or <50 mg/dL (females), 4) systolic or diastolic blood pressure (?130 or ?85 mmHg, respectively, or antihypertensive treatment), and 5) fasting glucose ?100mg/dL. If data on WC are not available, we will use a linear model derived from the large NHANES cohort that predicts WC from BMI with 88% accuracy,29 as these two measures are highly correlated.

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

The Main Independent Variable will be total (and differential) WBC counts at study baseline.

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

Continuous variables that will be included in the analyses, as available, are age, sex (% male), body mass index (BMI), socioeconomic status (SES), duration of illness, psychopathology scores, and study quality scores (based on the sum of the presence or absence of thirteen factors [one point for each]: whether data are included on age, sex, race, BMI, SES, alcohol and other substance use, smoking, duration of illness, levels of psychopathology, family history, medications [antipsychotics, mood stabilizers, and antidepressants]).

Geographic region (by continent), race, alcohol use, smoking, family history, and medications will be modeled as categorical variables, as available.

Statistical Analysis Plan:

We will test for normality of total and differential WBC counts for each trial using a one-sample Kolmogorov-Smirnov test. Any marker that is non-normally distributed will be log-transformed prior to analyses. For each trial, binary logistic regression models will be used to evaluate total and differential WBCs as predictors of the MetS and its individual criteria (odds ratios [ORs] and 95% confidence intervals [95% CIs]), after controlling for the above-mentioned potential confounding/moderating factors. For each study identified in the systematic literature review, we will extract data on effect size (ORs and 95% CIs) for the association between total and/or differential WBCs as predictors of the MetS or its individual criteria. Two study team members will perform double data entry, and Dr. Miller will verify the results.

We will then perform a series of meta-analyses to estimate pooled effect size estimates (ORs and 95% CIs) for associations between total and differential WBCs and prevalent MetS (and its individual criteria) using the random effects method. Random effects methods are considered to be more representative of real-world data in comparison to the alternative fixed effect approach, and provide a more conservative estimate of the average weighted OR. The null hypothesis will be an OR=1.00 (i.e., no association between WBC counts and the MetS). In total, we will perform 24 separate primary meta-analyses (4 different WBC counts—total WBC, neutrophils, monocytes, and lymphocytes—for each of 6 different metabolic parameters: MetS and the five individual MetS criteria, as per our previous publications). We will also perform an a priori subgroup analysis for OPTICS Project trials only. In an exploratory secondary analysis, we will also perform meta-analyses of the neutrophil-lymphocyte ratio (NLR), another marker of inflammation that is abnormal in psychosis and a proxy marker of systemic inflammation, and prevalent MetS.

The meta-analysis procedure also calculates a chi-2 value for the heterogeneity in effect size estimates, which is based on Cochran’s Q-statistic, and I2, the proportion of the variation in effect size attributable to between-study

heterogeneity. Between-study heterogeneity chi-2 will be considered significant for p<0.10. For each meta-analysis, if the OR is significant and between-study heterogeneity chi-2 is also significant, we will perform a sensitivity analysis. Sensitivity analysis will be performed by removing one study at a time and repeating the meta-analysis procedure, to examine its impact on the OR estimates and between-study heterogeneity. If between-study heterogeneity remains significant after removing each individual study, we will then remove all combinations of two different studies and repeat the meta-analysis procedure.

We will then perform a series of meta-regression analyses to investigate potential moderating variables. Meta-regression assesses and adjusts the effects of potential moderating variables on the pooled OR from the meta-analysis. A positive slope (i.e., regression coefficient) means that the pooled OR from the meta-analysis and the moderator variable change in the same direction, and a negative slope means they change in the opposite direction. Continuous variables that will be included in meta-regression analyses will be age, sex (% male), BMI, SES duration of illness, psychopathology scores, and study quality scores. Geographic region (by continent), race, alcohol use, smoking, family history, and medications will be modeled as categorical variables. These variables may be associated with inflammation and the MetS (e.g., age) or may be a proxy measure for other residual moderating factors, such as genetics, diet, exercise, and psychosocial stress (e.g., geography). The potential for publication bias will be examined by means of Sterne's funnel plot analysis and Egger's regression intercept. All statistical analyses will be performed in Stata 10.0.
Software Used:
STATA

Project Timeline:

The study will begin in July 2021. For the Aims, we will apply for access to the OPTICS Project YODA trial bundle, and conduct a systematic search of the literature over the first 3 months of the study. We will then extract and enter data from all identified studies over the next 12 months, starting in October 2021, which will be completed by October 2022. Data analysis and draft manuscript preparation will follow thereafter, which will be submitted for publication (and with results reported back to the YODA Project) in July 2023. We will also update the YODA Project quarterly on the status of the project, coincident with NIMH progress reports.

Dissemination Plan:

The target audience is clinicians and researchers working with patients with psychosis treated with antipsychotics. We aim to produce two study manuscripts, for the meta-analyses of total and differential WBC counts and: 1) prevalent, and 2) incident MetS.
Potentially suitable journals for the manuscripts are JAMA Psychiatry, the American Journal of Psychiatry, Schizophrenia Bulletin, Schizophrenia Research, NPJ Schizophrenia, and the Lancet Psychiatry.

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Supplementary Material:

https://yoda.yale.edu/sites/default/files/4517781_egrant.pdf