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Requires Data Access? Yes

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/2025/04/YODA-Cyrus-Hsia-COI-form.pdf
https://yoda.yale.edu/wp-content/uploads/2025/04/YODA-Benjamin-Chin-Yee-form.pdf
https://yoda.yale.edu/wp-content/uploads/2025/05/YODA-Jenyvette-Hsia-COI.pdf
https://yoda.yale.edu/wp-content/uploads/2025/05/YODA-Ella-Derkzen-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. NCT00650806 - 28431754OBE2001 - A Randomized, Double-Blind, Placebo-Controlled, Parallel-Group, Dose-Ranging Study to Investigate the Safety and Efficacy of JNJ-28431754 in Nondiabetic Overweight and Obese Subjects
2. NCT02243202 - 28431754OBE2002 - A Randomized, Double-Blind, Placebo-Controlled, Parallel-Group Study to Investigate the Safety and Efficacy of the Co-administration of Canagliflozin 300 mg and Phentermine 15 mg Compared With Placebo for the Treatment of Non-diabetic Overweight and Obese Subjects
3. NCT00236639 - TOPMAT-OBES-002 - A Randomized, Double-Blind, Placebo-Controlled, Multicenter, Parallel Group, Dose-Response Study to Assess the Efficacy and Safety of Topiramate in the Treatment of Patients With Obesity
4. NCT00236600 - TOPMAT-OBES-004 - A Multicenter, Randomized, Double-Blind, Placebo-Controlled, Parallel-Group Study of Efficacy and Safety of Topiramate in Weight Loss Maintenance in Obese Patients Following Participation in an Intensive, Non-Pharmacologic Weight Loss Program
5. NCT00231530 - TOPMAT-OBDM-003 - A Multicenter, Randomized, Double-Blind, Placebo-Controlled, Parallel-Group Study to Assess the Safety and Efficacy of Topiramate in the Treatment of Obese, Type 2 Diabetic Patients on a Controlled Diet
6. NCT00236665 - TOPMAT-OBHT-001 - A Multicenter, Randomized, Double-Blind, Placebo-Controlled, Parallel Group Study of the Efficacy and Safety of Topiramate in the Treatment of Obese Patients With Mild to Moderate Essential Hypertension
7. NCT00210808 - CAPSS-220 - A Multicenter, Randomized, Double-blind, Placebo-controlled, Flexible-dose Study to Assess the Safety and Efficacy of Topiramate in the Treatment of Moderate to Severe Binge-eating Disorder Associated With Obesity
8. NCT00231647 - TOPMAT-OBD-202 - A Randomized, Double-Blind, Placebo-Controlled, Multicenter, Parallel-Group Study to Assess the Efficacy and Safety of Topiramate OROS Controlled-Release in the Treatment of Obese, Type 2 Diabetic Subjects Managed With Diet or Metformin
9. NCT00231621 - TOPMAT-OBDL-001 - A Multicenter, Randomized, Double-Blind, Placebo-Controlled, Parallel Group, One-year Study of the Efficacy and Safety of Topiramate in the Treatment of Obese Subjects With Dyslipidemia
10. NCT00236626 - TOPMAT-OBDM-001 - A 9 Month, Double-Blind, Placebo-Controlled Study With a Blinded Crossover Transition to Open-Label Extension, Evaluating the Safety and Effectiveness of Topiramate on Insulin Sensitivity in Overweight or Obese Type 2 Diabetes Patients
11. NCT00231660 - TOPMAT-OBDM-002 - A Multicenter, Randomized, Double-Blind, Placebo-Controlled, Parallel-Group Study of the Efficacy and Safety of Topiramate in the Treatment of Obese, Type 2 Diabetic Patients Treated With Metformin
12. NCT00231634 - TOPMAT-OBDM-004 - A Multicenter, Randomized, Double-Blind, Placebo-Controlled, Parallel Group Study of the Efficacy and Safety of Topiramate in the Treatment of Obese, Type 2 Diabetic Patients Inadequately Controlled on Sulfonylurea Therapy
13. NCT00231608 - TOPMAT-OBMA-001 - The Safety and Efficacy of Topiramate in Male Patients With Abdominal Obesity: A 6-Month Double-Blind, Randomized, Placebo-Controlled Study With a 6-Month Open-Label Extension
14. NCT00236613 - TOPMAT-OBES-001 - A Randomized, Double-Blind, Placebo-Controlled, Multicenter, Parallel Group, Dose-Response Study to Assess the Efficacy and Safety of Topiramate in the Treatment of Patients With Obesity

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

Research Proposal

Project Title

Characterizing Laboratory Abnormalities in Response to Obesity: A Patient-Level Data Meta-analysis

Narrative Summary:

Obesity is highly prevalent in the general population in industrialized countries. Obesity is associated with many adverse health related outcomes and diseases from hypertension, diabetes, obstructive sleep apnea and heart disease. Further, obesity has been associated with changes in laboratory parameters such as the complete blood count (CBC), inflammatory markers, and iron indices. However, data are often limited to retrospective population data. This study aimed to evaluate the laboratory abnormalities of patients with obesity at baseline and during treatment for obesity. (Please see supplementary materials section.)

Scientific Abstract:

Background: Obesity is a growing global public health issue associated with multiple comorbidities and hematologic laboratory abnormalities. However, data on the patterns and clinical relevance of these changes remain sparse and inconsistent across studies.

Objective: To assess the prevalence and trajectory of laboratory and hematologic abnormalities in obese individuals participating in clinical trials and to identify correlations between these changes and therapeutic outcomes.

Study Design: Individual participant data meta-analysis of obesity trials.

Participants: We will enroll participants with obesity in all available obesity trials regardless of type of treatments. Laboratory abnormalities will be based on World Health Organization definitions.

Primary and Secondary Outcome Measures: The primary outcome will be the prevalence of laboratory abnormalities including elevated white blood cell count (WBC), red blood cell count (RBC), hemoglobin (Hb), hematocrit (Hct), platelet count (Plt), absolute neutrophil count (ANC), C-reactive protein (CRP), and ferritin at baseline. Secondary outcomes will include changes in these parameters in relation to body mass index (BMI) over time, specifically evaluating whether weight loss achieved through treatment is associated with improvements in these laboratory markers.

Statistical Analysis: Descriptive statistics will be used to summarize baseline laboratory findings. (Please see Supplementary Materials section.)

Brief Project Background and Statement of Project Significance:

Obesity is a growing global public health issue associated with multiple comorbidities, including cardiovascular disease, diabetes, and metabolic syndrome. Laboratory abnormalities--particularly in hematologic parameters--have been increasingly reported among individuals with obesity, including leukocytosis, thrombocytosis, anemia of chronic disease, and changes in inflammatory markers (Sung et al., 2019; Farhangi et al., 2018; Herishanu et al., 2006). Obesity induces a pro-inflammatory state that affects hematologic parameters, including white blood cell (WBC) count, red blood cell (RBC) count, platelet count, and thrombotic risk (Purdy et al., 2020). Mechanisms such as elevated interleukin-6 levels and leptin's role in myeloid differentiation contribute to leukocytosis and thrombocytosis in obese individuals (Purdy et al., 2020). Further obese individuals may have altered iron metabolism, potentially due to increased hepcidin levels, leading to reduced iron absorption and storage (Zhao et al., 2015). These laboratory changes may reflect not only the underlying inflammatory state of obese patients but their increased risk of cardiovascular outcomes (Farhangi et al., 2013).

In clinical trials, especially those targeting weight loss or metabolic improvement, changes in these lab values may serve as indirect indicators of systemic inflammation, metabolic stress, or therapeutic response (Purdy et al., 2020, Farhangi et al., 2013). However, data on the patterns and clinical relevance of these changes remain sparse and inconsistent across studies. A better understanding of how hematologic markers evolve in clinical trials involving obese individuals is critical for interpreting safety and efficacy outcomes and for understanding the pathophysiology of obesity-related complications.

Specific Aims of the Project:

To assess the prevalence and trajectory of laboratory and hematologic abnormalities in obese individuals participating in clinical trials and to identify correlations between these changes and therapeutic outcomes.
Specific Hypotheses:
1. Obesity is associated with increases in white blood cells (WBCs).
2. Obesity is associated with increases erythrocyte count (ERCs).
3. Obesity is associated with increases in hemoglobin (Hb).
4. Obesity is associated with increases in hematocrit (Hct).
5. Obesity is associated with increases in platelet counts (Plts).
6. Obesity is associated with increases in absolute neutrophil counts (ANC).
7. Obesity is associated with increases in C-reactive protein (CRP).
8. Obesity is associated with increases in erythrocyte sedimentary rates (ESR).
9. Obesity is associated with increases in ferritin.
10. For increases in body mass index (BMI), there are incremental increases in CBC (WBC, ERC, Hb, Hct, Plts, ANC), CRP, ESR, Ferritin.
11. Treatment of Obesity decreases CBC (WBC, ERC, Hb, Hct, Plts, ANC), CRP, ESR, Ferritin.
12. Smoking affects the above laboratory values.
13. Impact of obesity and smoking are synergistic on the above laboratory values.
14. There are laboratory changes by age, sex, and race.

Study Design:

Methodological research

What is the purpose of the analysis being proposed? Please select all that apply.

New research question to examine treatment effectiveness on secondary endpoints and/or within subgroup populations

New research question to examine treatment safety

Participant-level data meta-analysis

Meta-analysis using only data from the YODA Project

Research Methods

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

We will perform pooled data analysis using individual participant data from the 14 trials on obesity.

Inclusion criteria of trial: We will include trials that have a minimum of body mass index (BMI) and at least one CBC (WBC, ERC, Hb, Hct, Plts, ANC), CRP, ESR, or Ferritin value. This will ensure that we can capture the effects of BMI on at least one laboratory variable. If additional variables of age, sex, race, weight, height, smoking, or another measure of obesity is provided, that will be beneficial to assess secondary objectives but are optional.

Exclusion criteria of trial: We will exclude trials that do not measure BMI and at least one CBC (WBC, ERC, Hb, Hct, Plts, ANC), CRP, ESR, or Ferritin value.

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

Primary outcome:
To assess the baseline laboratory and hematologic abnormalities CBC (WBC, ERC, Hb, Hct, Plts, ANC), CRP, ESR, Ferritin in obese individuals participating in clinical trials.

Secondary outcomes:
To determine if obesity, measured by increases in body mass index (BMI) or other measures in the trials, are associated with incremental increases in CBC (WBC, ERC, Hb, Hct, Plts, ANC), CRP, ESR, Ferritin.
To determine if treatment of obesity decreases CBC (WBC, ERC, Hb, Hct, Plts, ANC), CRP, ESR, Ferritin.
To determine if smoking increases CBC (WBC, ERC, Hb, Hct, Plts, ANC), CRP, ESR, Ferritin.
To determine if obesity and smoking are synergistic on CBC (WBC, ERC, Hb, Hct, Plts, ANC), CRP, ESR, Ferritin.
To determine effect of laboratory changes by age, sex, and race.

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

The main independent variables will be BMI, smoking, age, sex, and race.
Major dependent variables will be laboratory abnormalities in CBC (WBC, ERC, Hb, Hct, Plts, ANC), CRP, ESR, and Ferritin. Abnormal laboratory values will be defined as values outside of the laboratory reference intervals (ranges).
Eg. White blood cells (WBCs) above or below laboratory reference interval.

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

None

Statistical Analysis Plan:

We plan to use individual participant data from the 14 obesity trials. Descriptive statistics will be performed for the baseline characteristics of the participants and laboratory values in the trials and the subgroups of patients with abnormal laboratory parameters. We will use the chi-square test for categorical variables and Mann--Whitney test for continuous variables to compare populations. We will use paired t-tests or Wilcoxon signed-rank tests to assess within-group changes and ANOVA or mixed-effects models to assess between-group differences over time. We will use Pearson or Spearman correlation for continuous outcomes (e.g., change in BMI vs. WBC count) and multivariate regression models to adjust for confounders (age, sex, comorbidities). All statistical tests will be two-tailed, and p-values <0.05 will be considered statistically significant.

Software Used:

STATA

Project Timeline:

The proposed research will begin once approved. Data analyses will be completed within 3 months. Manuscript drafting will take a further 3 months and we will prepare for manuscript submission. Once manuscript submitted, results will be reported back to the YODA Project.

Dissemination Plan:

These results will be impactful and expected to be shared with healthcare providers to inform the impact of obesity on baseline laboratory parameters and expected changes with treatment of obesity. We plan to submit to top Laboratory or Hematology journals, such as Blood Advances, Blood VTH, Lancet Hematology, American Journal of Hematology, Annals of Hematology, or International Journal of Laboratory Hematology. If data analysis shows impact on a broader audience, we may consider a General Internal Medicine or General Medicine journal.

Bibliography:

1. Sung, K. C., et al. (2019). Hematologic parameters and metabolic syndrome: Findings from a large cross-sectional study. Clinical Biochemistry, 67, 53-58.

2. Farhangi, M. A., et al. (2018). White blood cell count and inflammatory markers in relation to obesity and body composition in Iranian adults. Journal of Health, Population and Nutrition, 37(1), 1-8.

3. Herishanu, Y., et al. (2006). Obesity and Leukocytosis: A Study of 327 Patients. American Journal of Hematology, 81(10), 763--765.

4. Zhao, X., et al. (2015). Obesity and Iron Deficiency: A Systematic Review and Meta-Analysis. Obesity Reviews, 16(2), 108--118.

5. Farhangi, M.A., et al. (2013). White Blood Cell Count in Women: Relation to Inflammatory Biomarkers, Hematological Profiles, Visceral Adiposity, and Other Cardiovascular Risk Factors. Journal of Health, Population and Nutrition, 31(1), 58--64.

Supplementary Material:

https://yoda.yale.edu/wp-content/uploads/2025/04/2025-0260-Supplementary-Materials_Narrative-Summary-and-Abstract.docx