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How genetics, behaviour, and environment can contribute to a condition called metabolic syndrome in people who are taking antipsychotic medication

Submission date
08/03/2023

Recruitment status
No longer recruiting

Registration date
11/07/2023

Overall study status
Completed

Last Edited
17/03/2025

Condition category
Mental and Behavioural Disorders

[X] Prospectively registered
[X] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[X] Record updated in last year

Plain English summary of protocol
Background and study aims
Many people with mental illnesses in both childhood and adulthood take AntiPsychotics (APs) to treat their symptoms, but this medication can put them at risk for physical illnesses like Metabolic Syndrome (MetS). Several factors can contribute to this risk, including biological and lifestyle factors, underutilization of health care services, side effects of medication, and substance use. However, we don't know much about the predictors and consequences of MetS in AP users.

To address this issue, the RISKMet project aims to achieve three goals:
1. Identify risk factors for MetS in AP users by comparing two groups of subjects: those with MetS (Cases) and those without (Controls). The project will look at familiar history of MetS and psychological and functional risk factors such as disability, quality of life, and sleep quality.
2. Conduct a thorough clinical and biological evaluation of patients with and without MetS. The project will examine body parameters and their influencing factors using physical exams and blood samples. Additionally, RISKMet will analyze pharmacological treatments and genetic variability associated with MetS symptoms.
3. Identify behavioral patterns of both patients and healthy individuals using a prospective cohort design. The project will monitor physical activity and eating behaviors in both groups over a three-month period, using wrist-worn accelerometers and a mobile-based Experience Sampling Method (ESM). Participants will provide information about their mood, stressors, eating behaviors, and psychosocial environment.

The RISKMet project will provide insight into potential risk and protective factors associated with the development of MetS in clinical populations, which will help health workers better manage patients taking APs. The project aims to expand current knowledge about the comorbidities associated with AP treatment and improve early diagnosis by identifying specific risk factors and pathways.

Who can participate?
Patients treated with SGA for at least 1 year, with a diagnosis of schizophrenia, bipolar disorder or neurodevelopmental Disorders; parents of patients treated with SGA; siblings of patients treated with SGA; healthy controls.

What does the study involve?
The study involves clinical assessment, monitoring of dietary habits through a smartphone app, monitoring of physical activity using a wearable device, blood samples at two different times (T0 and after 3 months, T3).

What are the possible benefits and risks of participating?
While we cannot state that there will be any direct health benefits to study participants, thanks to the careful clinical evaluation to be carried out (as well as lab analyses) we may discover situations of potential clinical interest (such as an undiagnosed disorder requiring intervention) to be communicated to each participant. This can facilitate early diagnosis and subsequent therapeutic intervention.
Participation in this study entails some risks, listed below:
1. Blood sample collection: the risks associated with blood sample collection are the same as those of routine blood draws. It is possible that the patient may feel weak or experience slight pain, bruising, or redness at the site of the blood draw. In rare cases, infection may occur. In isolated cases, dizziness or fainting may occur. To avoid these minor complications, the precautions taken in all routine situations will be taken.
2. Smartphone app: completing the questionnaires via smartphone may lead to moments of distraction in everyday life and/or the interruption of an ongoing activity, which could pose some risks. To minimize these risks, the use of the smartphone is usually prohibited when driving or using heavy machinery.

Where is the study run from?
Ministero della Salute (Italy)

When is the study starting and how long is it expected to run for?
March 2023 to November 2025

Who is funding the study?
Ministero della Salute (Italy)

Who is the main contact?
Dr Giovanni de Girolamo, gdegirolamo@fatebenefratelli.eu

Contact information

Type(s)
Principal investigator

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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
PNRR-MAD-2022-12375751

Study information

Scientific Title
Metabolic syndrome in people treated with antipsychotics: a multimethod investigation of genetic, behavioural and environmental risk factors

Acronym
RISKMet

Study objectives
1. Patients treated with selected Second Generation Antipsychotics (SGA) or mood stabilizers have a high risk of developing MetS.
2. Specific psychotropic medications have a higher risk of developing MetS in treated patients compared to other psychotropic drugs.
3. Several risk factors (e.g., familiarity, diet, physical activity, substance use disorders, others) may moderate the risk of MetS in people treated with specific SGA or mood stabilizers.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 27/03/2023, Comico Etico (CEIOC) of IRCCS San Giovanni di Dio Fatebenefratelli in Brescia (25125 BRESCIA - Via Pilastroni, 4, Italy; +39 (0)30/3501586; ceioc@fatebenefratelli.it), ref: PNRR-MAD-2022-12375751

Study design
Multicenter observational including a case-control study, a cross-sectional study and a cohort study

Primary study design
Observational

Study type(s)
Diagnostic

Health condition(s) or problem(s) studied
Genetic, behavioural and environmental risk factors of metabolic syndrome in people treated with antipsychotics (schizophrenia, bipolar disorder, neurodevelopmental disorder)

Interventions
1. To identify risk factors for metabolic syndrome (MetS) using a case-control design. We will recruit (among both adult and paediatric population) two groups of subjects: "Cases" (MetS+) and sex- and age-matched "Controls" (MetS-). This aim will include an assessment of familiarity for MetS and both psychological and functional risk factors (e.g. disability, quality of life, functioning levels, quality of sleep).

2. To perform an in-depth clinical and biological characterization of patients with (MetS+) and without (MetS-) MetS. This aim will study body parameters and their influencing factors at the whole organism level. At two time points (T0 and after 3 months, T3), participants will undergo a structured physical examination and blood sampling (e.g. body weight, height, waist and hip circumferences, heart rate, systolic and diastolic blood pressure, fasting blood glucose, C-peptide, HbA1c,triglycerides, HDL cholesterol, LDL cholesterol and total cholesterol, oxidized LDL and high-sensitivity C-reactive protein, AST, ALT, gammaGT, and zonulin concentration). Moreover, we will deeply assess pharmacological treatments and will examine genetic variability associated with predisposition to sensitivity or resistance to MetS symptoms.

3. To identify behavioural patterns of both patients and healthy individuals using a prospective cohort design. Behavioural markers will be assessed twice: at T0 and at 3-month FU (T3) in both MetS+ and MetS- and in healthy control sample. Both at T0 and T3, for seven days, PA will be monitored with a wrist-worn accelerometer that will be wear for a 24-hour period, while eating behaviour (daily caloric intake, binge eating episodes, night-time eating, cravings, fast food consumption, and satiety) will be monitored using a mobile-based Experience Sampling Method (ESM). Participants (or caregivers) will provide information about their mood, stressors, eating behaviours, dietary restraint, and various other assessments of the psychosocial environment.

Intervention Type
Other

Primary outcome(s)
Part 1 (case-control study)
Familiarity for MetS and both psychological and functional risk factors:
1.1. BPRS to assess the presence and severity of psychopathology
1.2. CGI to measure illness severity (CGIS).
1.3. WHODAS 2.0 to measure the impact of health conditions on functioning in six life domains (Cognition, Mobility, Self-care, Getting along, Life activities, Participation).
1.4. SLOF: (1) physical functioning, (2) personal care skills, (3) interpersonal relationships, (4) social acceptability, (5) activities of community living and (6) work skills.
1.5. ECI: method for categorizing medical comorbidities based on ICD categories.
1.6. LEDS: in-depth, semi-structured interview investigating the number, nature and severity of acute (events) and ongoing stressors (difficulties) around ten key life domains experienced in a set study period.
1.7. EQ5D: Health questionnaire to evaluate quality of life
1.8. PSQI: to evaluate the quality and patterns of sleep

1.9. SF-36: self-reported measure of quality of life
1.10. DBC-P: to assess behavioural and emotional problems of young people aged 4-18 years with developmental and intellectual disabilities (UO2).
1.11. Tanner Staging Scale: used to rate sexual maturity in children, adolescents and adults based on external primary and secondary sex characteristics (UO2).
1.12. PedsQL: brief, 23-item measure of health-related quality of life in children and young people, to be filled by parents (Proxy Report) as well as children and young people (Self-Report) (UO2).
1.13. DAWBA: package of interviews, questionnaires and rating techniques designed to generate ICD-10 and DSM-IV or DSM-5 psychiatric diagnoses on 2-17 year olds; we will use only the background section for the assessment of family and environmental risk factors (UO2).
1.14. WHOQOL-BREF: self-administered questionnaire comprising 26 items on the individual's perceptions of their health and well-being over the previous two weeks.
1.15. CBCL: is a widely used caregiver report form identifying problem behavior in children (UO2).
1.16. SDQ: brief behavioural screening questionnaire about emotional symptoms, conduct problems, hyperactivity/inattention,peer relationship problems and prosocial behaviour (UO2).
1.17. PCC: a 16-item measure to assess family relationships, specifically inter-parental conflict in terms of parents ability to agree and cooperate when performing parenting duties (UO2).

Part 2 (cross-sectional study)
In-depth clinical and biological characterization of patients at two time points (T0 and after 3 months, T3):
2.1. Structured physical examination
Body weight (kg), height (cm), waist and hip circumferences (cm), heart rate (bpm), systolic and diastolic blood pressure (mmHg)
2.2. Blood sampling
Fasting blood glucose, C-peptide, HbA1c, triglycerides, HDL cholesterol, LDL cholesterol and total cholesterol, oxidized LDL and high-sensitivity C-reactive protein, AST, ALT, gammaGT, and zonulin concentration
2.3. Assess pharmacological treatments using treatment history form
2.4. Examine genetic variability associated with predisposition to sensitivity or resistance to MetS symptoms using blood samples

Part 3 (cohort study)
Behavioural patterns at two time points (T0 and after 3 months, T3):
3.1. For seven days, PA will be monitored with a wrist-worn accelerometer that will be worn for a 24-hour period
3.2. Eating behaviour (daily caloric intake, binge eating episodes, night-time eating, cravings, fast food consumption, and satiety) will be monitored using a mobile-based Experience Sampling Method (ESM).
3.3. Participants (or caregivers) will provide information about their mood, stressors, eating behaviours, dietary restraint, and various other assessments of the psychosocial environment using Experience Sampling Method (ESM) with a specific app.

Key secondary outcome(s))
There are no secondary outcome measures

Completion date
14/11/2025

Eligibility

Key inclusion criteria
Age groups: 6-17 years; 18-45 years; and 46-65 years
In each stratum, using medical records we will select 25 "cases" treated with APs for at least 1 year. For each case, we will recruit a matched "control".

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Mixed

Lower age limit
6 years

Upper age limit
65 years

Sex
All

Key exclusion criteria
1. Intention to move in the subsequent year
2. Severe cognitive impairment
3. Severe substance use disorder

Date of first enrolment
01/05/2024

Date of final enrolment
15/07/2025

Locations

Countries of recruitment
Italy

Study participating centre
IRCCS San Giovanni di Dio Fatebenefratelli
Via Pilastroni 4
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Study participating centre
Associazione La Nostra Famiglia - IRCCS Eugenio Medea
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Sponsor information

Organisation
Ministero della Salute

ROR
https://ror.org/00789fa95

Funder(s)

Funder type
Government

Funder Name
Ministero della Salute

Alternative Name(s)
Italian Ministry of Health, Italy Ministry of Health, Ministry of Health of Italy, Ministry of Health - Italy, Ministry of Health, Italy

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
Italy

Results and Publications

Individual participant data (IPD) sharing plan
The final dataset will be stored in a public repository (Zenodo).

IPD sharing plan summary
Stored in publicly available repository

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes
Protocol file			09/03/2023	No	No
Study website	Study website	11/11/2025	11/11/2025	No	Yes