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Exploring the link between bipolar disorder and medical diseases: an investigation of risk factors and biological characteristics for better prevention and treatment

Submission date
08/03/2023

Recruitment status
Recruiting

Registration date
18/04/2023

Overall study status
Ongoing

Last Edited
06/06/2025

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
Bipolar Disorder (BD) is a common and long-lasting mental health problem that causes a lot of difficulties for people who have it. This is because it often happens alongside other health problems, both physical and mental. The BIPCOM project wants to study these other problems and find better ways to diagnose and treat them in people with BD.

The project has three main goals:
1. To learn more about how common these other problems are in people with BD, what causes them, and how they change over time. This will be done by looking at data from Nordic biobanks and medical records, as well as asking people with BD about their experiences.
2. To do a study with 400 people who have BD to find out how likely they are to develop certain physical health problems over the course of a year. This will help doctors know what to watch out for and how to prevent these problems from getting worse.
3. To create a tool that doctors can use to make personalized treatment plans for people with BD and other health problems. This tool will be based on the results of the project and will be developed with input from patients and their families.

The project will work closely with patients and other stakeholders to make sure that the results are useful and can be put into practice. If the project is successful, it could lead to better health outcomes for people with BD and fewer serious complications. It could also help doctors make better treatment plans that are tailored to each person's needs.

Who can participate?
Patients aged 18 – 65 years with BD.

What does the study involve?
The study includes the use of questionnaires, blood sampling, and, for selected individuals, the use of an accelerometer for three weeks each year.

What are the possible benefits and risks of participating?
Information from the questionnaires and blood tests will be shared with study participants who can use it for diagnostic purposes.
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: The use of the APPetite-mobile-app 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 prohibited when driving or using heavy machinery.

Where is the study run from?
ERA PERMED (France)

When is the study starting and how long is it expected to run for?
February 2023 to July 2026

Who is funding the study?
1. Fondazione Regionale per la Ricerca Biomedica (Italy)
2. Bundesministerium für Bildung und Forschung (Germany)
3. VINNOVA (Sweden)
4. Norges Forskningsråd (Norway)
5. Agence Nationale de la Recherche (France)
6. Departament de Salut, Generalitat de Catalunya (Spain)
7. Sächsisches Staatsministerium für Wissenschaft und Kunst (Germany)

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

Study website
https://bipcom.eu/

Contact information

Type(s)
Principal Investigator

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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
ERAPERMED2022-087

Study information

Scientific Title
Medical comorbidities in bipolar disorder: clinical validation of risk factors and biomarkers to improve prevention and treatment

Acronym
BIPCOM

Study objectives
Metabolic Syndrome (MetS) in Bipolar Disorder (BD) patients has been chosen as a ‘pilot case’ because it has important implications for prevention, personalized treatment and effective patient management. Unfortunately, most healthcare delivery systems are neither comprehensive nor configured to detect, diagnose, treat and manage medical comorbidities, including MetS, in patients with mood disorders. This leads to a loss of useful information for appropriate patients stratification and disease prediction and prevention. The BIPCOM study aims to address such gaps by piloting personalized medicine approaches in BD patients and defining innovative individualised care models transferrable to clinical practice.

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 06/06/2023, Comitato Etico IRCCS San Giovanni di Dio - Fatebenefratelli (Via Pilastroni, 4,, Brescia, 25125, Italy; +390303501586; ceioc@fatebenefratelli.eu), ref: 36-2023

Study design
Multicenter observational cross-sectional cohort study

Primary study design
Observational

Secondary study design
Cohort study

Study setting(s)
Hospital, Medical and other records

Study type(s)
Diagnostic

Participant information sheet
Not available in web format, please use the contact details to request a patient information sheet.

Health condition(s) or problem(s) studied
Medical comorbidities (and in particular Metabolic Syndrome, MetS) in people with bipolar disorder

Interventions
BIPCOM uses a multifaceted and integrated approach to study Metabolic Syndrome (MetS), and other medical comorbidities (MC), in Bipolar Disorder (BD). There are several primary studies assessing one or a few specific comorbidities in BD. However, there are few register studies specifically focusing on physical comorbidities in people with BD. Through the case-register studies, we will shed new light on the prevalence and course characteristics of treated medical disorders and mortality rates among patients with BD, and it will be possible to develop prediction models. BIPCOM will follow a Personalized Medicine approach, providing new tools, which will allow us to tailor preventions and treatment to individual characteristics, rather than a "one size fits all"approach. (2) So far, most studies in this area have relied on self-reporting questionnaires. In self-reports, participants might avoid, forget, or not be aware of their MC (furthermore, pre-symptomatic stages per definition cannot be assessed), failing to identify a proportion of comorbidities, especially before they have become clinically evident. Our direct, standardized, in-depth medical assessment of recruited subjects and their follow-up with passive activity monitoring (accelerometer) will allow identification of emerging medical conditions, clarify their course, and facilitate ascertainment of possible risk factors. (3) A set of specific biomarkers will be screened using comprehensive proteomic and metabolomic analyses from biological samples. Data collected through the Experimental Clinical Study, combined with the identification of biomarkers, should provide new insights into mechanisms underlying MC.

Tests to be run: a “Patient Schedule” (PS) will include each participant’s socio-demographic, clinical and treatment-related data at baseline (T0) and at 1-year follow-up (T1). The PS includes: (1) World Health Organization Disability Assessment Schedule 2.0, 12-items, self-report version (WHODAS 2.0); (2) Specific Levels Of Functioning (SLOF); (3) Elixhauser Comorbidity Index (ECI); (4) Life Events and Difficulties Schedule; (5) EQ5D Health questionnaire; (6) Pittsburgh Sleep Quality Index (PSQI); (7) SF-36. Course of the disorder will be evaluated with the retrospective and prospective (during the 1-year follow-up), The Life Story Interview. Other areas to be assessed include: history of alcohol or drug abuse using a standardized tool; lifestyle habits, such as PA using accelerometers; dietary habits using the Short Form of the Food Frequency Questionnaire (SHFFQ) as well as the APPetite-mobile-app

Patient recruitment and baseline assessment for the Experimental Clinical Study: Each of the five recruiting sites will enrol 80 participants aged 18-65 years with a DSM-5 diagnosis of BD I or BD II from the lists of patients with BD who will have at least one contact with the service in the last year; immediately after recruitment and signature of the informed consent, each patient will undergo baseline examinations (T0). At this stage the first assessment takes place through the

administration of the questionnaires described above (tests to be run), and blood samples will be taken to investigate the specific biomarkers of METS. They will also undergo a general internist examination. At least 20 subjects/site, stratified in Mets+ and MetS-, will be asked to wear an accelerometer for one week 3 times a year, in order to compare total psysical activity (PA), intensity specific PA, sedentary time and circadian rhythms in the two groups (i.e., patients with or without MetS). In the same subjects who will conduct PA monitoring we will also study eating behaviour using the APPetite-mobile-app.

One-year follow up: 1-year monitoring will start immediately after baseline assessment and will be performed until February 2026, at this stage patients will be reassessed with the same questionnaire and biomarkers of the baseline and patients.

Intervention Type
Other

Primary outcome measure
At baseline (T0) and one year (T1):
1. Assessment for health and disability measured using World Health Organization Disability Assessment Schedule 2.0, 12-items, self-report version (WHODAS 2.0);
2. Assessment of real-life functioning measured using Specific Levels Of Functioning (SLOF);
3. Index od comorbidities of patients measured using Elixhauser Comorbidity Index (ECI);
4. Life events measured using Life Events and Difficulties Schedule;
5. Subjective health status measured using EQ5D Health questionnaire;
6. Assessment of sleep quality and disturbances measured using Pittsburgh Sleep Quality Index (PSQI);
7. Subjective health status measured with Short Form Health Survey (SF-36);
8. Evaluation of the disorder course with the retrospective and prospective (during the 1-year follow-up) measured using The Life Story Interview
9. Evaluation of: history of alcohol or drug abuse using a standardized tool; lifestyle habits, such as PA using accelerometers; dietary habits using the Short Form of the Food Frequency Questionnaire (SHFFQ) as well as the APPetite-mobile-app.
10. MetS diagnostic criteria:
10.1. Waist circumference based on population or country-specific definitions
10.2. Elevated triglycerides (or current drug treatment for high triglycerides) >150 mg/dL (1.7 mmol/L)
10.3. Reduced HDL-cholesterol <40 mg/dL (1.0 mmol/L) in males and <50 mg/dL (1.3 mmol/L) in females
10.4. Elevated blood pressure (or current antihypertensive drug treatment) systolic >130 and/or diastolic >85 mm Hg
10.5. Elevated fasting glucose (or ongoing drug treatment) >100 mg/dL (5.5 mmol/L)

Secondary outcome measures
At baseline (T0) and one year (T1):
1. Fatty liver index, assessed after FLI, included in the table on biomarkers.
2. Liver fibrosis, assessed after FIB-4, included in the table on biomarkers.
3. Physical Activity assessment and comparison of two groups (MetS+/MetS- patients): total PA, intensity specific PA, sedentary time and circadian rhythms in the two groups and associations between PA and sedentary activity with selected clinical markers, through accelerometer.

Overall study start date
01/02/2023

Completion date
01/07/2026

Eligibility

Key inclusion criteria
1. Primary diagnosis of BD I or BD II
2. At least one contact with the mental health service in the last year
3. Age 18-65 years
4. Signed informed consent.

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Upper age limit
65 Years

Sex
Both

Target number of participants
400

Key exclusion criteria
1. Plan to relocate in the subsequent year
2. Severe psychiatric comorbidities (schizophrenia spectrum disorders)
3. Severe cognitive impairment
4. Severe substance/alcohol misuse

Date of first enrolment
02/05/2024

Date of final enrolment
02/10/2025

Locations

Countries of recruitment
France

Germany

Italy

Norway

Spain

Sweden

Study participating centre
IRCCS Centro San Giovanni di Dio Fatebenefratelli
VIA PILASTRONI 4
Brescia
Italy
25125

Study participating centre
University Hospital Frankfurt
Heinrich-Hoffmann-Str. 10
Frankfurt am Main
Germany
60528

Study participating centre
Örebro University
School of medical sciences Campus USÖ S-701 82 Örebro
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70182

Study participating centre
University of Oslo
Kirkeveien 166
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Norway
0407

Study participating centre
Fondation Fondamental
Hôpital Albert Chenevier
40 rue de Mesly
Pole de psychiatrie

Créteil
France
94000

Study participating centre
Institut De Recerca-Hospital De La Santa Creu I Sant Pau
Sant Quinti 89
Barcelona
Spain
08041

Study participating centre
Deutsche Gesellschaft für Bipolare Störungen (GSBD)
GSBD, c/o Klinik für Psychiatrie, Psychosomatik und Psychotherapie
Heinrich-Hoffmann-Str. 10
Frankfurt am Main
Germany
60528

Study participating centre
University Hospital Carl Gustav
Fetscherstr. 74
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Sponsor information

Organisation
ERA PERMED

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Sponsor type
Research organisation

Website
https://erapermed.isciii.es/

Funder(s)

Funder type
Charity

Funder Name
Fondazione Regionale per la Ricerca Biomedica

Alternative Name(s)
Lombardy Foundation for Biomedical Research, Regional Foundation for Biomedical Research, FRRB

Funding Body Type
Private sector organisation

Funding Body Subtype
Trusts, charities, foundations (both public and private)

Location
Italy

Funder Name
Bundesministerium für Bildung und Forschung

Alternative Name(s)
Federal Ministry of Education and Research, BMBF

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
Germany

Funder Name
VINNOVA

Alternative Name(s)

Swedish Governmental Agency for Innovation Systems

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
Sweden

Funder Name
Norges Forskningsråd

Alternative Name(s)
Forskningsrådet, Norwegian Research Council, Research Council of Norway

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
Norway

Funder Name
Agence Nationale de la Recherche

Alternative Name(s)
French National Research Agency, French National Agency for Research, ANR

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
France

Funder Name
Departament de Salut, Generalitat de Catalunya

Alternative Name(s)
Department of Health, Generalitat de Catalunya, Department of Health, Government of Catalonia

Funding Body Type
Government organisation

Funding Body Subtype
Local government

Location
Spain

Funder Name
Sächsisches Staatsministerium für Wissenschaft und Kunst

Alternative Name(s)
Saxon State Ministry for Science and Art, SMWK

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
Germany

Results and Publications

Publication and dissemination plan
Planned publication in a high-impact peer-reviewed journal

Intention to publish date
01/02/2027

Individual participant data (IPD) sharing plan
The datasets generated will be uploaded to an online repository (Zenodo)

IPD sharing plan summary
Stored in publicly available repository

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol article		04/05/2024	07/05/2024	Yes	No