



Dottorato IAMED
Coordinatore: Prof. Domenico Russo
Supervisor: Prof. Stefano Calza
Co-Supervisor: Dott.ssa Marika Vezzoli

Date: 28 May 2025

Candidate: Carnevale Martina

**MEDICAL COMORBIDITIES IN
NEUROPSYCHIATRIC DISORDERS:**

**CLINICAL VALIDATION OF RISK FACTORS
AND BIOMARKERS TO IMPROVE
PREVENTION AND TREATMENT.**

- i. Investigate risk factors and clinical profiles of Medical Comorbidities
- ii. Study of **physical activity** as it represents a modifiable behavioural factor strongly associated with the risk and progression of medical comorbidities in individuals with Neuropsychiatric Disorders
- iii. Develop a Clinical Support Tool (CST) for the personalized management of the disease

Bridge the gaps in healthcare delivery systems, enable appropriate patient stratification, disease prediction and prevention, **and improve overall patient care and outcomes**



Utrecht Summer School
Causal Inference
August 2024



3 Years Collaboration
IRCCS Fatebenefratelli (BS)
Dr. **De Girolamo Giovanni**, Psychiatrist
Former Scientific Director - Head Unit of Psychiatric



6 Months Collaboration
LMU University of Munich
Department of Psychiatry and Psychotherapy
Prof. **Dr. Falkai Peter** & LMU group
Clinic Director



- Foundational concepts of Causal Modeling
- Data problems from Causal Inference POV
- Causal Inference and Causal Modeling



- PABOARD
- DIAPASON
- BIPCOM



- AMPSCZ
- INTERNAL PROJECT



Trials, 2024

STUDY PROTOCOL

Open Access



Physical Activity in young female outpatients with BORderline personality Disorder (PABORD): a study protocol for a randomized controlled trial (RCT)

RESEARCH ARTICLE

WILEY

Burnout, working alliance, and ward atmosphere: A multisite study of mental health professionals and patients with schizophrenia

Stress & Health, 2024

Brain, Behavior, and Immunity, 2024

Association of Weight Status and Waist Circumference with Physical Activity in people with Schizophrenia Spectrum Disorders and healthy controls



FATEBENEFRATELLI

• DIAPASON

UNVEILING THE DYNAMICS OF **PHYSICAL ACTIVITY AND MOOD** IN **SCHIZOPHRENIA** SPECTRUM DISORDERS: A **BAYESIAN NETWORK** APPROACH FROM THE MULTICENTRIC DIAPASON PROJECT

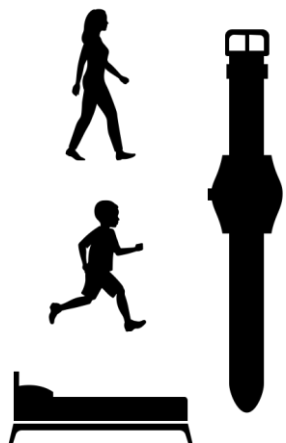
UNVEILING THE DYNAMICS OF PHYSICAL ACTIVITY AND MOOD IN SCHIZOPHRENIA SPECTRUM DISORDERS: A **BAYESIAN NETWORK** APPROACH FROM THE MULTICENTRIC DIAPASON PROJECT

Schizophrenia spectrum disorders (SSD) are severe and chronic psychiatric conditions affecting approximately 1% of the global population

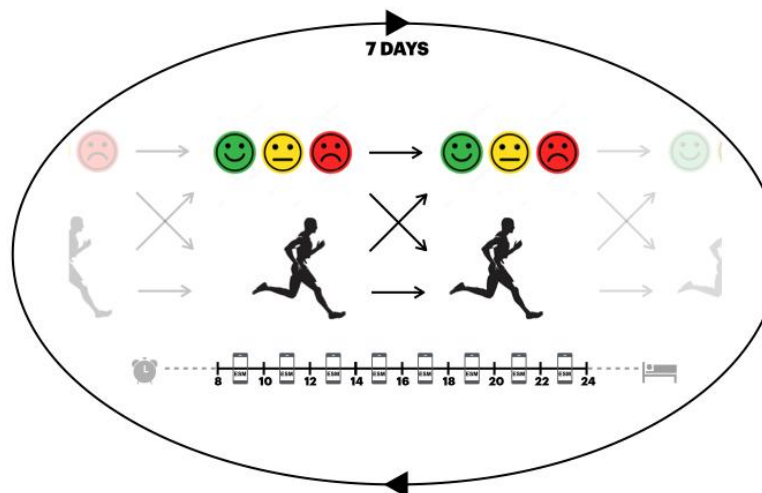
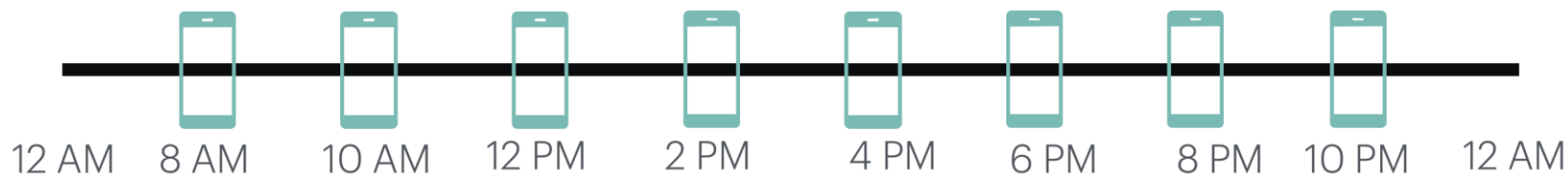
- Reduces life expectancy
- Medical comorbidities
 - Type 2 diabetes
 - Cardiovascular disease (CVD)
 - Metabolic syndrome (MetS)
- Among the modifiable risk factors, **physical inactivity** is particularly concerning, as it significantly contributes to poor outcomes in SSD
- Research has shown that lower PA levels are associated with greater severity of negative symptoms (e.g., anhedonia, blunted affect) and higher levels of depressive symptoms

Urgent need for comprehensive and innovative treatment approaches

UNVEILING THE DYNAMICS OF PHYSICAL ACTIVITY AND MOOD IN SCHIZOPHRENIA SPECTRUM DISORDERS: A **BAYESIAN NETWORK** APPROACH FROM THE MULTICENTRIC DIAPASON PROJECT



113 HC
120 SSD

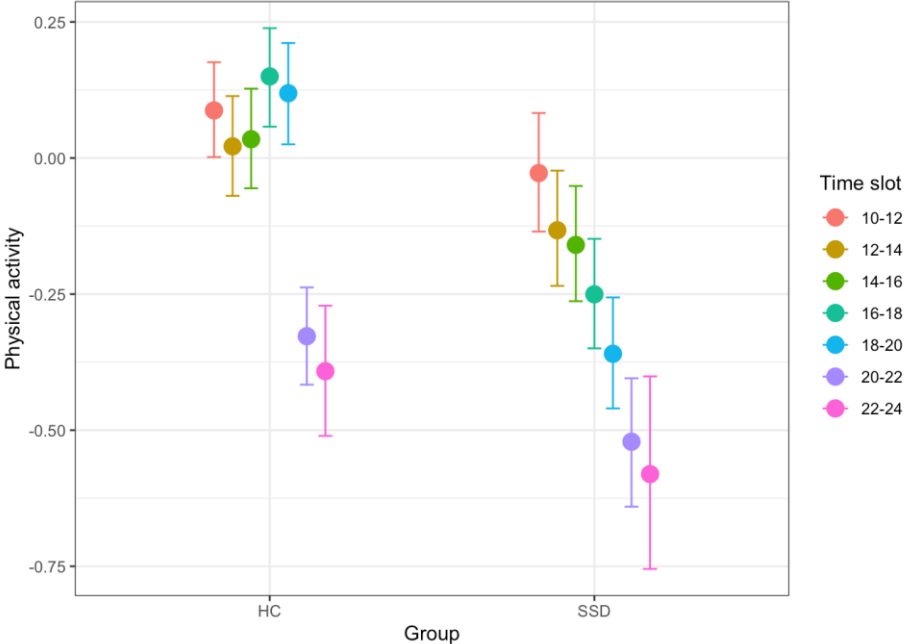
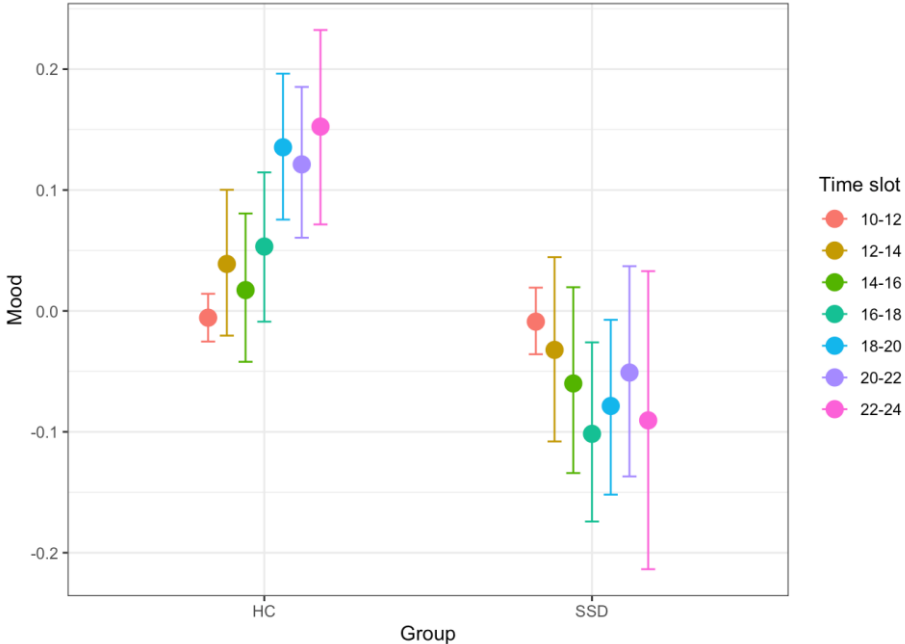


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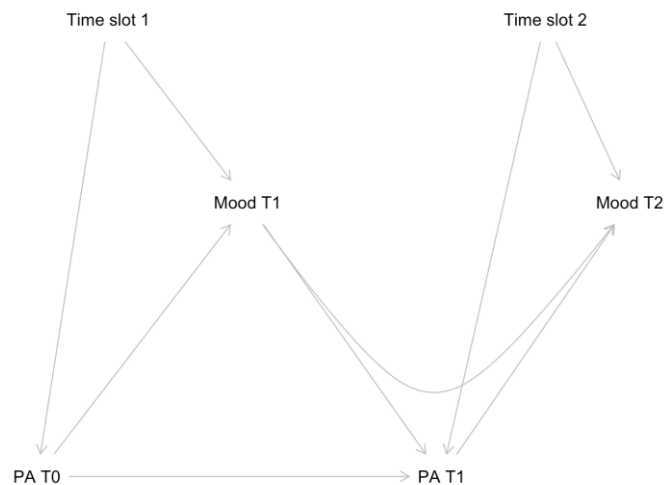
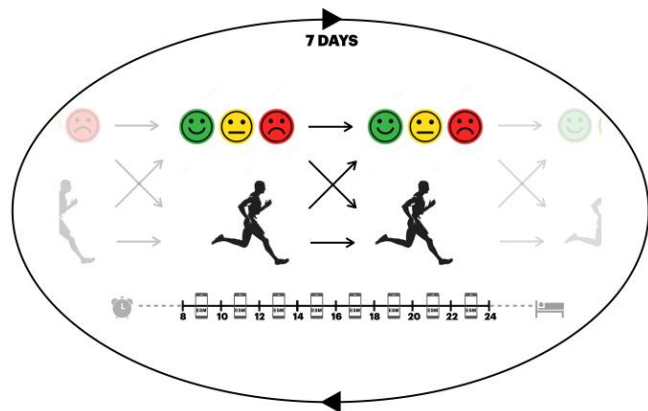
GLMM

Variables	Estimates	CI 95%	p-value
Daily PA*	-0.11	-0.24; -0.03	0.135
Type of Participant (SSD)	-0.33	-0.53; -0.12	0.002
Daily PA × Type of Participant (SSD)	0.11	-0.009; 0.30	0.290

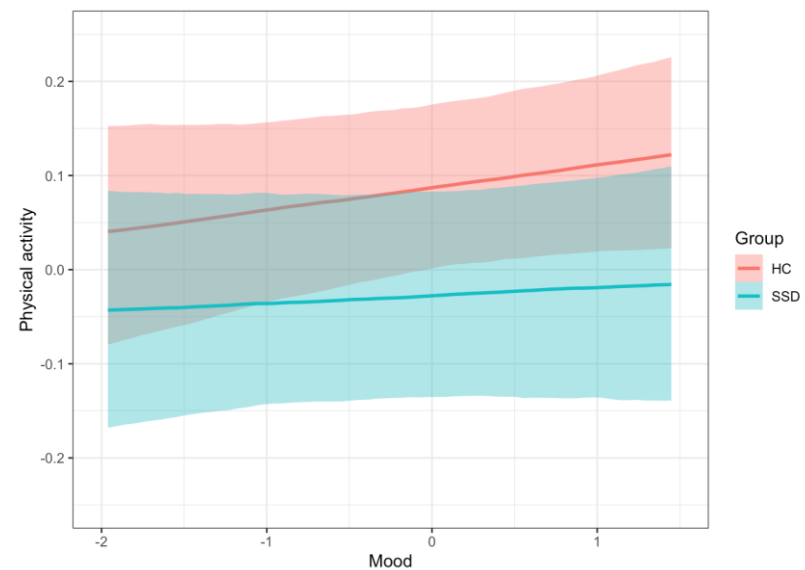
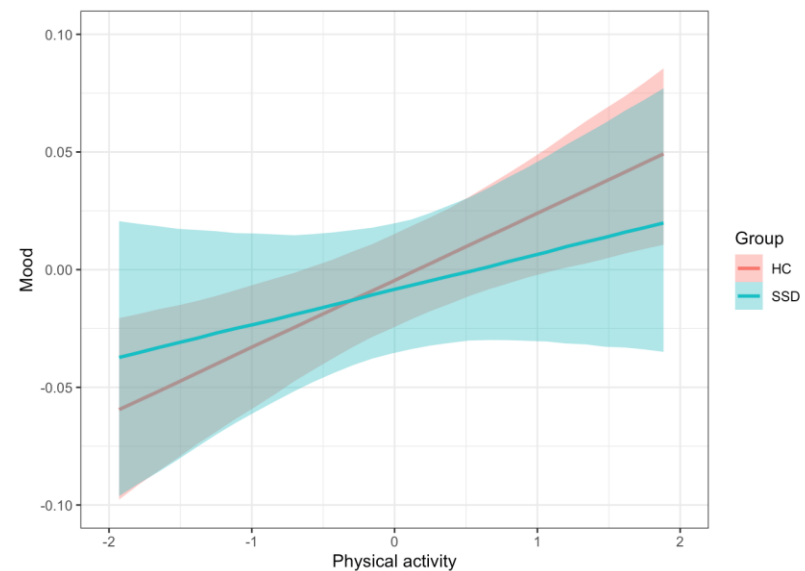
**Median daily PA after standardization*



UNVEILING THE DYNAMICS OF PHYSICAL ACTIVITY AND MOOD IN SCHIZOPHRENIA SPECTRUM DISORDERS: A **BAYESIAN NETWORK** APPROACH FROM THE MULTICENTRIC DIAPASON PROJECT



DAG

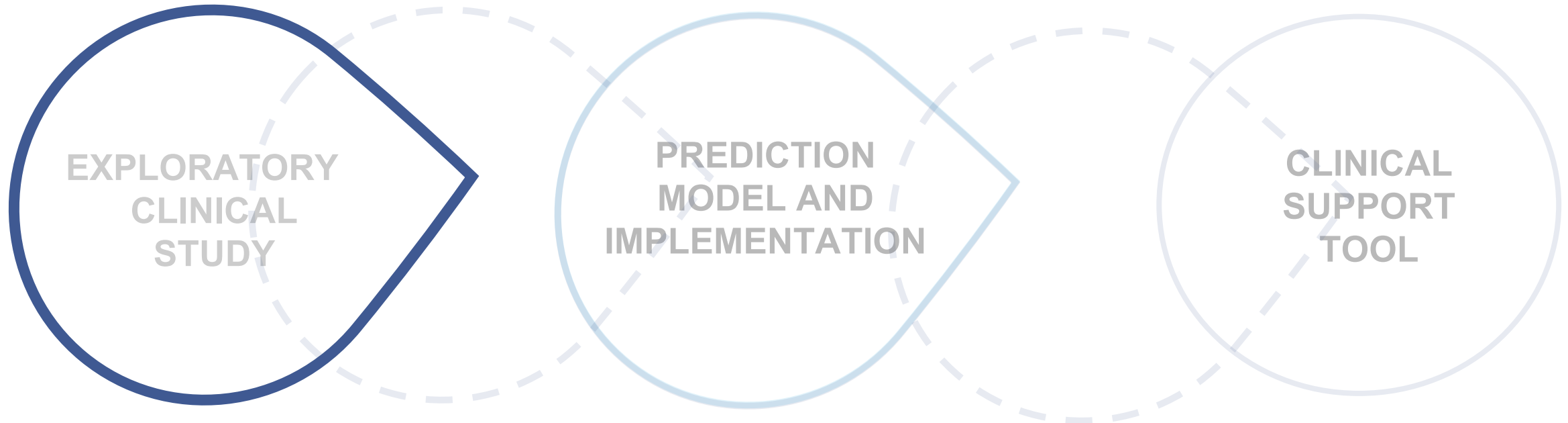




- PABOARD
- DIAPASON
- **BIPCOM**

Complex genetic disorder with a multifactorial origin characterized by **severe, chronic, and recurring** symptoms

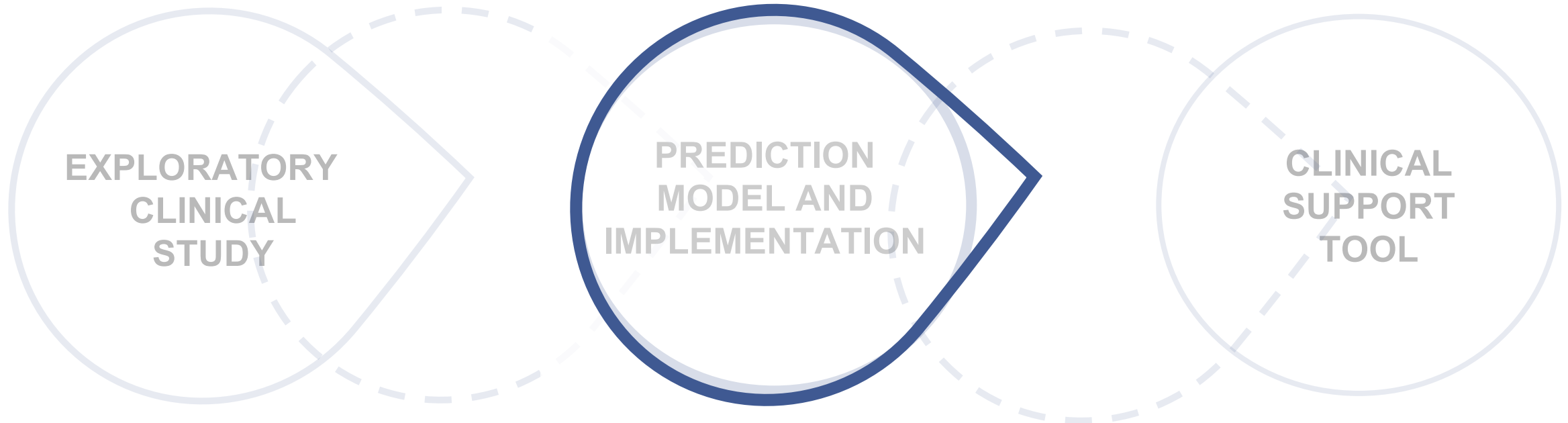
- Reduces life expectancy of 10-20 years
- High disability rate, and association with both psychiatric and medical comorbidities (MC)
 - Type 2 diabetes
 - Cardiovascular disease (CVD)
 - **Metabolic syndrome (MetS)**
- The range of risk factors and biomarkers associated with MC in people with BD has not been explored in sufficient detail
- Medical needs related to comorbidities are often neglected in favour of managing core BD symptoms



- Enrol 430 participants with BD from five countries France, Italy, Germany, Norway, Spain
- Identify which criteria among the MetS diagnostic are most associated with each other among patients with BD

- Improved prediction and stratification algorithms
- Actigraph and ESM analysis

- Personalized **risk calculator**
(PA, BMI, job type, diet, lifestyle, biomarkers)
- An electronic risk questionnaire
 - A personalized educational sheet for the patient's risk profile



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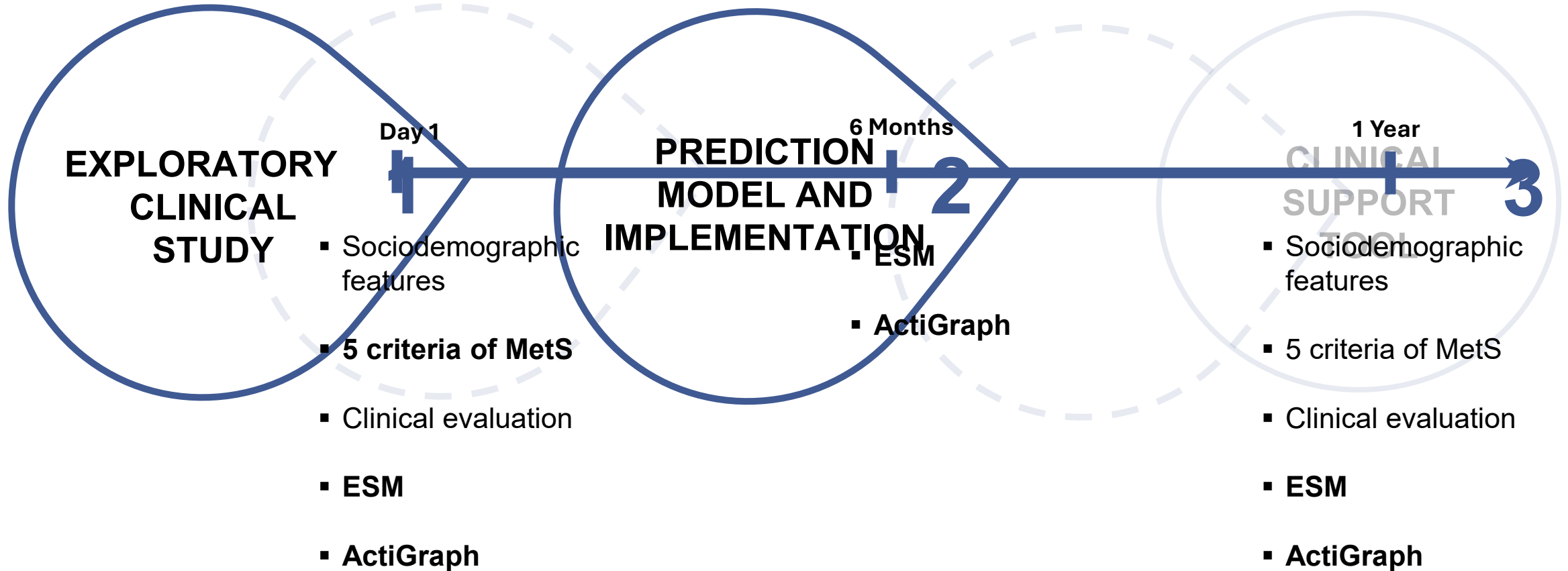


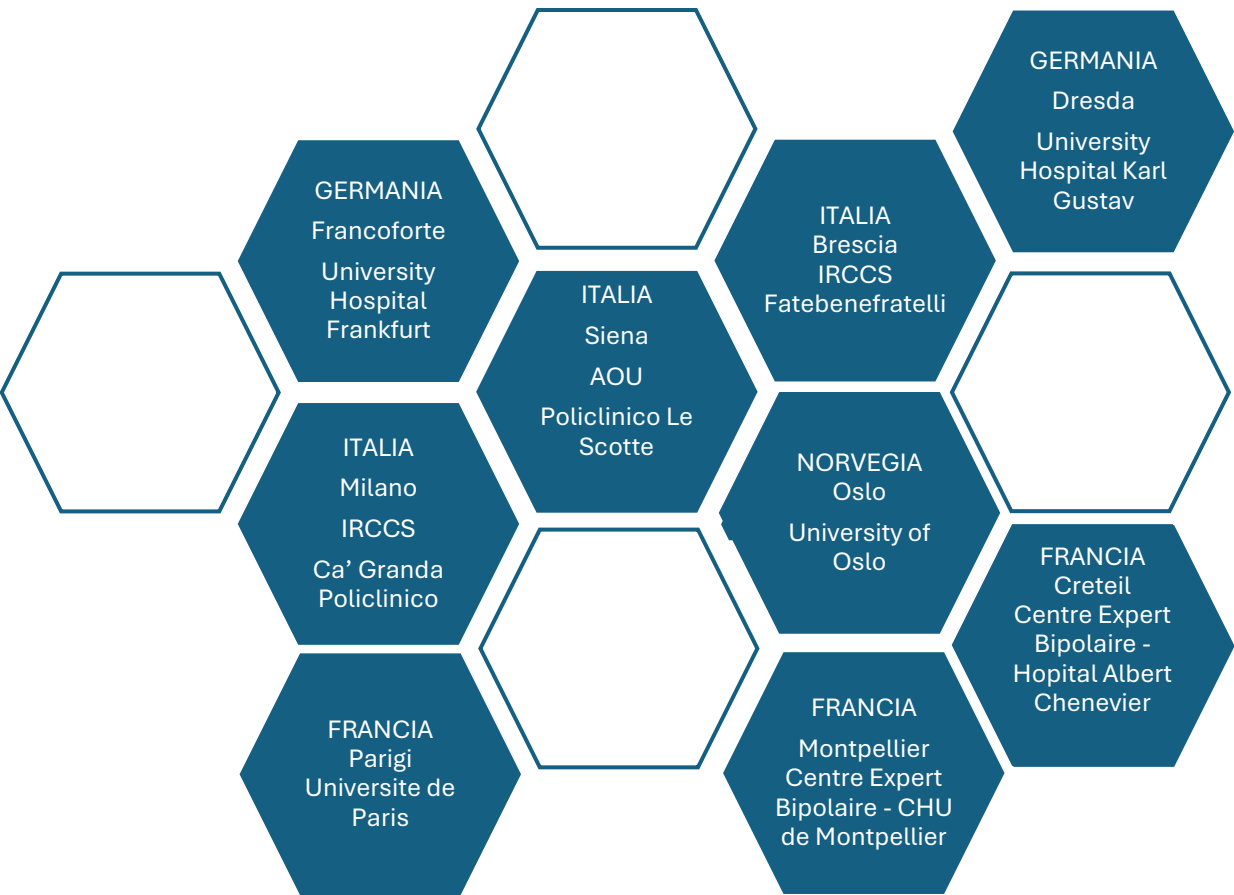
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Characteristic	Controllo N = 21 [†]	Pazienti N = 261 [†]
Age		
Mean (SD)	41.4 (14.2)	43.3 (13.4)
Median (Min; Max)	35.0 (23.0; 66.0)	44.0 (18.0; 65.0)
(Missing)	0	3
Sex		
Femmina	13 (62%)	154 (59%)
Maschio	8 (38%)	107 (41%)
Marital status		
Celibate/Maiden, cohabiting	11 (52%)	37 (18%)
Celibate/Maiden, not cohabiting	3 (14%)	83 (41%)
Divorced	2 (9.5%)	35 (17%)
Married	4 (19%)	45 (22%)
Widower/Widow	1 (4.8%)	1 (0.5%)
(Missing)	0	60
[†] n (%)		

Characteristic	Controllo N = 21 [†]	Pazienti N = 261 [†]
Education		
High school	3 (14%)	80 (40%)
Middle school	2 (9.5%)	37 (18%)
Post Graduate Training	8 (38%)	13 (6.4%)
University degree	8 (38%)	72 (36%)
(Missing)	0	59
Occupation		
Full time job	12 (57%)	84 (42%)
Housewife	1 (4.8%)	7 (3.5%)
Part time job	4 (19%)	36 (18%)
Retired	3 (14%)	25 (13%)
Student	1 (4.8%)	14 (7.0%)
Training	0 (0%)	3 (1.5%)
Unemployed	0 (0%)	31 (16%)
(Missing)	0	61
BMI		
Mean (SD)	24.0 (3.1)	27.2 (5.3)
Median (Min; Max)	23.7 (18.4; 30.2)	26.0 (17.7; 50.1)
(Missing)	0	72
[†] n (%)		



- **AMPSCZ**
- INTERNAL PROJECT

Recruitment began June 2022
CHR participants: **1977**
Healty control participants: **640**
Aged between 12-30



ProNET: Psychosis-Risk Outcomes Network



Scott Woods Carrie Bearden John Kane
Yale University University of Northwell Health
California,
Los Angeles

DPACC: Data Platform with Data Processing, Analysis, & Coordination Center



Martha Shenton Harvard University	Rene Kahn Icahn School of Medicine at Mount Sinai
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PRESCIENT: Trajectories and Predictors in the Clinical High-Risk for Psychosis Population



Barnaby Nelson
University of Melbourne

Goals

1.Developing tools for predicting individual outcomes

The AMP SCZ program aims to biomarkers, that can be used to predict the likelihood of progression to psychosis

2.Establishing a global research network

The AMP SCZ program will establish an international research network focused on recruiting young people who are at clinical high risk for schizophrenia.

3. Setting the stage for testing new preventive treatments

Research framework that can help researchers design better clinical trials, develop better approaches for measuring treatment response, and create better tools for detecting early-stage risk.

4.Creating an accessible data repository

Research data from the AMP SCZ program will be available to the broader scientific community through the National Institute of Mental Health (NIMH) Data Archive.

Procedure	Visit 1	Visit 2	Visit 3	Visit 4	Visit 5	Visit 6	Visit 7	Visit 8	Visit 9	Visit 10	Visit 11	Visit 12	Visit 13	Visit 14	Visit 15	Visit 16	Conversion
Month	-3 to -1	0	1	2	3	4	5	6	7	8	9	10	11	12	18	24	-
Consent Form																	
Interview/ Questionnaire																	
Cognitive Tasks																	
MRI*																	
EEG*																	
Blood and Saliva Samples*																	
Actigraphy (daily)																	
Digital Data (daily passive sensing, EMA, audio diary)																	
Free Speech Sampling (audio and facial recording)																	
PSYCHS (audio recording)																	

* In-person visit



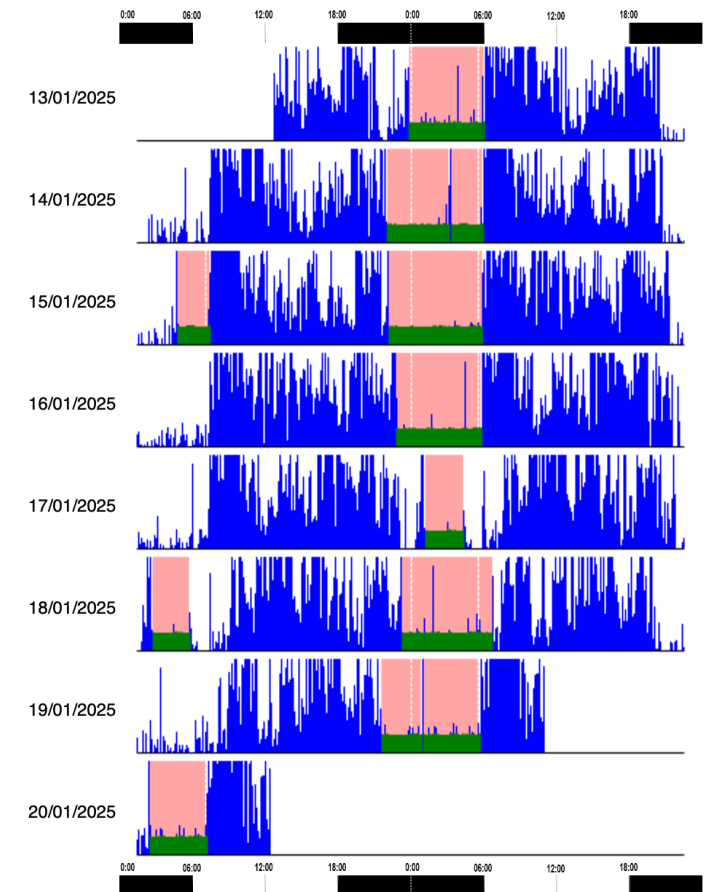
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Does PA change in three months in Schizophrenia patients with a tailored training plan?



Date	Activity kcal	Average Hourly kcal	Axis 1 Counts	Axis 2 Counts	Axis 3 Counts	Vector Magnitude	Steps
13/01/2025	440.303	36.692	778963	720739	1068421	1505912	8343
14/01/2025	1189.137	49.547	1579688	1694012	1620442	2826822	17981
15/01/2025	1130.016	47.084	1622381	1693852	1921005	3031751	17381
16/01/2025	1254.272	52.261	1793372	1671459	2065573	3205706	20623
17/01/2025	1500.360	62.515	1927115	1878047	2499708	3672788	20863
18/01/2025	1303.040	54.293	1669216	1621538	1794726	2938828	20251
19/01/2025	932.225	38.843	1300712	1337887	1590464	2451809	14907
20/01/2025	788.933	65.744	958946	934506	1003523	1673301	7866

Sleep Graphs



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