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Youth-GEMS: Understanding genetic and environmental interactions in youth mental health

Submission date
21/12/2023

Recruitment status
Recruiting

Registration date
30/01/2024

Overall study status
Ongoing

Last Edited
04/02/2026

Condition category
Mental and Behavioural Disorders

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

Plain English summary of protocol

Background and study aims
The first symptoms of mental illness usually begin during youth, the developmental stage between 12 and 24 years of age. The first manifestations of mental illness are often subtle and do not meet diagnostic criteria for specific diagnoses. This period is critical because early detection and treatment can maximize recovery and may even prevent the progression of illness. However, there is not enough knowledge about how early symptoms may predict later mental health, which poses difficulties in deciding treatment plans and assessing risk. The Youth-GEMs project aims to bridge this gap by studying young people who are in the first stages of mental illness during two years, with the objective of developing a model that will allow predicting the individual's risk and aid in prevention and treatment.

Who can participate?
People between 12 and 24 years of age who are attending specialised mental-health services for the first time.

What does the study involve?
Participants will fill in a questionnaire about their health, life experiences, symptoms and coping mechanisms every 3 months for 2 years. At baseline, they will also undergo a clinical interview with a mental health professional, a test on attention and memory (among other cognitive functions), and will give a blood or saliva sample.

What are the possible benefits and risks of participating?
This study is not testing any intervention or drug, therefore we do not expect any benefit of participating other than the experience of helping advance scientific knowledge. The risks are considered minimal. A common risk of blood extractions is a small bruise in the place where blood was taken, but it often resolves spontaneously in a few days. Another risk is a possible data breach. However, all scientists involved in this study have received training in data protection and are using the safest servers to store data to minimize this risk.

Where is the study run from?
The study is run from six sites in Europe: Madrid (Spain), Maastricht (The Netherlands), Oulu (Finland), Belgrade (Serbia), Split (Croatia) and Tartu (Estonia). All the sites will be coordinated from the leaders from Hospital General Universitario Gregorio Marañón (Spain) and Oulu University (Finland).

When is the study starting and how long is it expected to run for?
June 2021 to December 2026

Who is funding the study?
The European Union (EU)

Who is the main contact?
Dr Covadonga Martínez Díaz-Caneja, covadonga.martinez@iisgm.com

Contact information

Type(s)
Scientific, Principal investigator

Contact name
Dr Covadonga Martínez-Díaz Caneja

Contact details
Instituto de Psiquiatría y Salud Mental
Hospital General Universitario Gregorio Marañón
C. de Ibiza, 43
Madrid
Spain
28009
+34 (0)915 86 80 00
covadonga.martinez@iisgm.com

Type(s)
Scientific, Principal investigator

Contact name
Prof Ian Kelleher

ORCID ID
https://orcid.org/0000-0003-1484-651X

Contact details
Centre for Clinical Brain Sciences (CCBS)
University of Edinburgh
Kennedy Tower
Royal Edinburgh Hospital
Edinburgh
United Kingdom

EH10 5HF
+44 (0)131 465 9585
ian.kelleher@ed.ac.uk

Type(s)
Public, Scientific

Contact name
Mr Renzo Abregú-Crespo

ORCID ID
https://orcid.org/0000-0001-5325-0992

Contact details
Instituto de Psiquiatría y Salud Mental
Hospital General Universitario Gregorio Marañón
C. de Ibiza, 43
Madrid
Spain
28009
+34 (0)914265095
renzo.abregu@iisgm.com

Additional identifiers

Protocol serial number
101057182

Study information

Scientific Title
Gene-Environment interactions in Mental health trajectories of Youth (Youth-GEMs Cohort)

Acronym
Youth-GEMs-Cohort

Study objectives
1. The researchers will be able to characterise multidimensional latent risk and resilience mental health trajectories in a trans-syndromal sample of help-seeking young people.
2. The quality of life trajectories will have genetic, environmental, biological, clinical, cognitive and digital predictors.
3. The researchers will be able to cross-validate clinical and digital predictors in help-seeking youth.

Ethics approval required
Ethics approval required

Ethics approval(s)
1. approved 07/02/2024, Comité de Ética de la Investigación con Medicamentos (CEIm) Hospital General Universitario Gregorio Marañón / Ethics Committee in Research with Drugs Gregorio

Marañón Hospital (C/ Dr. Esquerdo 46, Pabellón de Gobierno, Madrid, 28007, Spain; +34 (0)91 586 7007 - 91 426 9378; ceim.hgugm@salud.madrid.org), ref: 313/23

2. approved 14/03/2024, Klinika za neurologiju i psihijatriju za decu i omladinu (Ethics Committee of the Clinic for Child and Adolescent Neurology and Psychiatry in Belgrade) (Dr Subotića starijeg 6, Belgrade, 11000, Serbia; +381 11 2658 355; ana.kesic.npk@gmail.com), ref: 193/3

3. approved 29/04/2024, Etičko povjerenstvo Medicinskog fakulteta Sveučilišta u Splitu (Ethics Committee of the Faculty of Medicine, University of Split) (Šoltanska ul. 2A, Split, 21000, Croatia; +385 (0)21 557 929; uzz@mefst.hr), ref: 2181-198-03-04-24-0048

4. approved 14/01/2025, University of Tartu Research Ethics Committee (Raekoja plats 9, Tartu, 51004, Estonia; +372 (0)737 6215; eetikakomitee@ut.ee), ref: 394/T-32

5. approved 09/12/2024, Regional Medical Research Ethics Committee of the North Ostrobothnia Welfare Region (c/o OYS Tutkimuspalveluyksikkö N5, Research Service Unit N5 PO Box 10, OYS, 90029, Finland; +358 (0)50 448 4955; tutkimuspalvelut@pohde.fi), ref: OTE 11/2024

6. approved 24/01/2025, Medisch-ethische toetsingscommissie (Medical Ethics Review Committee) (P. Debyelaan 25, Postbus 5800, Maastricht, 6202 AZ, Netherlands; +31 (0)43 387 6009; secretariaat.metc@mumc.nl), ref: METC 24-018

Study design
Multicenter non-interventional observational study

Primary study design
Observational

Study type(s)
Other, Prevention, Quality of life, Treatment

Health condition(s) or problem(s) studied
Non-chronic emerging mental health symptoms

Interventions
Current methodology as of 04/02/2026:
Participants will be referred to the study by experienced mental health professionals. If they agree to participate, research staff will cite them in-site for informed consent procedures and baseline visit. During the baseline visit, participants will undergo a blood extraction, clinical interview and neurocognitive assessment with a trained psychologist or psychiatrist of the study. They will also download the app under their guidance and have the opportunity to ask questions. Finally, they will be asked to complete a self-report questionnaire in REDCAP. The follow-up visits will be conducted remotely through the REDCAP survey, although all participants will be able to contact their site project coordinator to ask questions, request a telephone call to guide them through the questionnaire or troubleshoot REDCAP issues. If participants prefer, follow-up visits will be conducted in person at the center. Participation will end after the 24-month follow-up assessment.

Previous methodology:
Participants will be referred to the study by experienced clinicians. If they agree to participate, research staff will cite them in-site for informed consent procedures and baseline visit. During

the baseline visit, participants will undergo a blood extraction, clinical interview and neurocognitive assessment with a trained psychologist or psychiatrist of the study. They will also download the app under their guidance and have the opportunity to ask questions. Finally, they will be asked to complete a self-report questionnaire in REDCAP. The follow-up visits will be conducted remotely through the REDCAP survey, although all participants will be able to contact their site project coordinator to ask questions, request a telephone call to guide them through the questionnaire or troubleshoot REDCAP issues. Participation will end after the 24-month follow-up assessment.

Intervention Type
Genetic

Primary outcome(s)
Quality of life, with general wellbeing, daily functioning, relationships with friends, relationships with family and coping as subdomains, measured with the MyLifeTracker outcome measure at baseline, 3, 6, 12, 18 and 24 months follow-up

Key secondary outcome(s))
Current secondary outcomes as of 04/02/2026:
Clinical dimensions:
1. Anxiety and depression measured with the RCADS at baseline, and 3, 6, 12, 18 and 24 months follow-up
2. Distress tolerance measured with the DTS-short at baseline, and 3, 6, 12, 18 and 24 months follow-up
3. Current mania measured with the Altman Self-rating Mania Scale (ASRM) and Rapid Mood Screener (RMS) at baseline, and 3, 6, 12, 18 and 24 months follow-up
4. Psychotic-like symptoms measured with the Psychosis Experiences Inventory (PEI) at baseline, and 3, 6, 12, 18 and 24 months follow-up
5. Dissociative symptoms measured with the Dissociative Experiences Scale (DES) at baseline, and 6, 12, and 24 months follow-up
6. Suicidality measured with the Columbia Suicide Severity Rating scaleat baseline, and 24 months follow-up
7. Non-suicidal self-harm measured at baseline, and 24 months follow-up
8. General psychopathology measured with the Strengths and Difficulties Questionnaire (SDQ) at baseline, and 3, 6, 12, 18 and 24 months follow-up
9. Eating disorders measured with the Eating Disorder Screen for Primary Care at baseline, 12, and 24 months follow-up
10. Obsessions and intrusive thoughts measured with the Children’s Obsessional Compulsive Inventory Revised (ChOCI-R) at baseline, and 3, 6, 12, 18 and 24 months follow-up
11. Stressful life events measured with an ad-hoc questionnaire at baseline, 12, and 24 months follow-up
12. Childhood Trauma measured with the Childhood Trauma Questionnaire - Short version, Juvenile Victimization Questionnaire (JVQ), and Childhood Experience of Care and Abuse (CECA) at baseline
13. Bullying and cyberbullying measured with an ad-hoc questionnaire at baseline.
14. PTSD symptoms measured with the UCLA PTSD Reaction Index for DSM-5 Brief form at baseline.
15. Family and social environment measured with an ad-hoc questionnaire at baseline and 12 and 24-month follow-up.
16. Parental bonding measured with the Relationship Structures (ECR-RS) questionnaire and peer bonding measured with the Community and Youth Collaborative Institute (CAYCI) at

baseline and 12 and 24-month follow-up.
17. Alcohol use and abuse measured with the AUDIT at baseline, and 3, 6, 12, 18 and 24 months follow-up
18. Drug use and abuse measured with the DUDIT at baseline, and 3, 6, 12, 18 and 24 months follow-up
19. Loneliness emotion with the Loneliness 3 item scale at baseline, 12 and 24 months follow-up.
20. Emotions and affect with Positive and Negative Affect Schedule (PANAS) at baseline, 3, 6, 12, 18 and 24 months follow-up.
21. Clinical impression measured with the Clinical Global Impressions Scale (CGI) at baseline, and 3, 6, 12, 18 and 24 months follow-up
22. Social and ocuppational measured with the Social and Occupational Functioning Assessment Scale (SOFAS) at baseline, and 3, 6, 12, 18 and 24 months follow-up
23. Mental health symptoms measured with DSM-5 Dimensional Cross-Cutting Symptom Assessment (DSM5-CC) at baseline, and 6, 12, 18 and 24 months.
24. Premorbid Adjustment measured with the Premorbid Adjustment Scale (PAS) at baseline.
25. Pregnancy and early development measured with the APGAR measure and ad hoc questions at baseline
26. Obstetric complications measured with the Scale of Obstetric Complications by Lewis at baseline
27. Development milestones with ad hoc questions at baseline

Lifestyle and behavioural factors:
1. Internet and social media use measured with the Social Media Disorder Scale (SMDS-9) at baseline, and 3, 6, 12, 18 and 24 months follow-up
2. History of crime and violent behaviour measured with an ad hoc questionnaire at baseline, and 3, 6, 12, 18 and 24 months follow-up
3. Reward response measured with Behavioral Inhibition and Behavioral Activation System (BIS /BAS) Scales at baseline, and 3, 6, 12 and 24 months follow-up

Physical health:

1. General health measured with the EQ-5D-Y at baseline, and 3, 6, 12, 18 and 24 months follow up
2. Disability measured using 12-item Self-Report World Health Organization Disability Assessment Schedule (WHODAS) at baseline, and 3, 6, 12, 18 and 24 months follow-up
3. Sleep and circadian alterations measured with the REACH study at baseline, and 3, 6, 12, 18 and 24 months follow-up
4. Physical activity measured with the REACH study at baseline, and 3, 6, 12, 18 and 24 months follow-up

5. Menstrual cycle measured with the Menstrual Distress Questionnaire (MDQ) at baseline, and 3, 6, 12, 18 and 24 months follow-up

Psychological mechanisms, subjective experience and existential dimensions:

1. Coping mechanisms measured with Coping Orientation to Problems Experienced Inventory (Brief-COPE) at baseline, and 3, 6, 12, 18 and 24 months follow-up.
2. Resilience measured with the Brief Resilient Coping Scale (BRCS) at baseline, and 3, 6, 12, 18 and 24 months follow-up
3. Self-esteem measured with the Multidimensional Wellbeing in Youth Scale – self-confidence dimension at baseline, and 3, 6, 12, 18 and 24 months follow-up
4. Well-being measured with the EPOCH measure of adolescent well-being at baseline, and 3, 6,

12, 18 and 24 months follow up
5. Callous/unemotional traits measured with the Inventory of Callous-Unemotional Traits and Antisocial Behavior (INCA) for Young People at baseline, and 3, 6, 12, 18 and 24 months follow-up
6. Reward responsiveness measured with the BAS Reward Responsiveness & Frustrative Nonreward Responsiveness Subscale at baseline, and 3, 6, 12, 18 and 24 months follow-up
7. Irritability measured with the Affective Reactivity Index (ARI) at baseline, and 3, 6, 12, 18 and 24 months follow-up

8. Reflective functioning measured with the Reflective Functioning Questionnaire (RFQ) at baseline, and 3, 6, 12, 18 and 24 months follow-up.

Neurocognitive functioning
1. Estimated IQ, assessed using the Wechsler Intelligence Scales (WAIS and WISC) at baseline.
2. Sustained attention, cognitive flexibility, working memory, visual memory, sensorimotor ability, and motor speed, assessed using an ad hoc neuropsychological battery at baseline.

Previous secondary outcomes:
Clinical dimensions:
1. Anxiety and depression measured with the RCADS at baseline, and 3, 6, 12, 18 and 24 months follow-up
2. Distress tolerance measured with the DTS-short at baseline, and 3, 6, 12, 18 and 24 months follow-up
3. Current mania measured with the Altman Self-rating Mania Scale at baseline, and 3, 6, 12, 18 and 24 months follow-up
4. Psychotic-like symptoms measured with the Prodromal Questionnaire (PQ-16) and the PEI at baseline, and 3, 6, 12, 18 and 24 months follow-up
5. Dissociative symptoms measured with the DES-B at baseline, and 3, 6, 12, 18 and 24 months follow-up
6. Suicidality measured with the Columbia Suicide Severity Rating scaleat baseline, and 3, 6, 12, 18 and 24 months follow-up
7. Non-suicidal self-harm measured at baseline, and 3, 6, 12, 18 and 24 months follow-up
8. General psychopathology measured with the Strenghts and Difficulties Questionnaire (SDQ) at baseline, and 3, 6, 12, 18 and 24 months follow-up
9. Eating disorders measured with the Eating Disorder Screen for Primary Care at baseline, and 3, 6, 12, 18 and 24 months follow-up
10. Obsessions and intrusive thoughts measured with the Obsessional Compulsive Inventory - Child self report at baseline, and 3, 6, 12, 18 and 24 months follow-up
11. Childhood Trauma measured with the Childhood Trauma Questionnaire - brief at baseline
12. Stressful life events measured with an ad-hoc questionnaire at baseline, and 3, 6, 12, 18 and 24 months follow-up
1. Bullying and cyberbullying measured with an ad-hoc questionnaire at baseline and 3, 6, 9 and 12 months follow-up
2. PTSD symptoms measured with the UCLA PTSD Reaction Index for DSM-5 Brief form at baseline and 12 months follow-up
3. Family and social environment measured with an ad-hoc questionnaire at baseline
4. Parental bonding measured with the Relationship Structures (ECR-RS) questionnaire and peer bonding measured with the Attachment Questionnaire for Children (AQC) at baseline and 12 and 24-month follow-up.
5. Alcohol use and abuse measured with the AUDIT at baseline, and 3, 6, 12, 18 and 24 months follow-up
6. Drug use and abuse measured with the DUDIT at baseline, and 3, 6, 12, 18 and 24 months follow-up

Lifestyle and behavioural factors:
1. Internet and social media use measured with the Social Media Disorder Scale at baseline, and 3, 6, 12, 18 and 24 months follow-up
2. Gaming disorder measured with the Nine-Item Internet Gaming Disorder Scale at baseline, and 3, 6, 12, 18 and 24 months follow-up
3. History of crime and violent behaviour measured with an ad hoc questionnaire at baseline, and 3, 6, 12, 18 and 24 months follow-up

Physical health:
1. General health measured with the EQ-5D-Y at baseline, and 3, 6, 12, 18 and 24 months follow up
2. Disability measured using 12-item Self-Report World Health Organization Disability Assessment Schedule (WHODAS) at baseline, and 3, 6, 12, 18 and 24 months follow-up
3. Sleep and circadian alterations measured with the PROMIS Sleep Disturbance and Sleep-Related Impairment in Adolescents at baseline, and 3, 6, 12, 18 and 24 months follow-up

Psychological mechanisms, subjective experience and existential dimensions:
1. Coping mechanisms measured with the Brief COPE at baseline, and 3, 6, 12, 18 and 24 months follow-up
2. Resilience measured with the Brief Resilient Coping Scale at baseline, and 3, 6, 12, 18 and 24 months follow-up
3. Self-esteem measured with the Multidimensional Wellbeing in Youth Scale – self-confidence dimension at baseline, and 3, 6, 12, 18 and 24 months follow-up
4. Well-being measured with the EPOCH measure of adolescent well-being at baseline, and 3, 6, 12, 18 and 24 months follow up
5. Callous/unemotional traits measured with the INventory of Callous-Unemotional Traits and Antisocial Behavior (INCA) for Young People at baseline, and 3, 6, 12, 18 and 24 months follow-up
6. Reward responsiveness measured with the BAS Reward Responsiveness & Frustrative Nonreward Responsiveness Subscale at baseline, and 3, 6, 12, 18 and 24 months follow-up
7. Irritability measured with the Affective Reactivity Index at baseline, and 3, 6, 12, 18 and 24 months follow-up

Completion date
31/12/2026

Eligibility

Key inclusion criteria
Current inclusion criteria as of 04/02/2026:
1. Age between 12-24 years
2. New appointment with a mental health service within the past 2 months
3. Good command of the languages used in the study, as most of the clinical assessment will be based on self-reported questionnaires
4. Written informed consent by the participant, their parents if minors, or legal representatives if appropriate

Previous inclusion criteria:
1. Aged 12-24 years
2. Less than 1 month from the first contact with mental health services
3. Good command of the languages used in the study

4. Written informed consent by the participant and their parents and legal representatives, when appropriate

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Mixed

Lower age limit
12 years

Upper age limit
24 years

Sex
All

Total final enrolment
0

Key exclusion criteria
Current exclusion criteria as of 04/02/2026:
1. Previous contact with a mental health service at the same level of care (primary, secondary, tertiary, quaternary) within the past 12 months
2. Intellectual disability with associated functional impairment
3. Severe neurological or medical condition
4. Genetically confirmed neurobehavioral syndromes
5. Significant difficulties in completing the self-reported questionnaires

Previous exclusion criteria:
1. Intellectual disability with associated functional impairment
2. Severe neurological or medical condition
3. Genetically confirmed neurobehavioral syndromes
4. Significant difficulties in completing the self-reported questionnaires

Date of first enrolment
02/03/2024

Date of final enrolment
31/12/2026

Locations

Countries of recruitment
Croatia

Estonia

Finland

Netherlands

Serbia

Spain

Study participating centre
Fundacion para la Investigacion Biomedica del Hospital Gregorio Maranon
Doctor Esquerdo 46
Madrid
Spain
28007

Study participating centre
Sveuciliste U Splitu Medicinski Fakultet
Šoltanska 2
Split
Croatia
21000

Study participating centre
Clinic for Neurology and Psychiatry for Children and Youth
dr Subotića starijeg 6
Belgrade
Serbia
112112

Study participating centre
Tartu Ulikool
Ravila 14a
Tartu
Estonia
50411

Study participating centre
Universiteit Maastricht
Minderbroedersberg 4
Maastricht

Netherlands
6200 MD

Study participating centre
University of Oulu
Pentti Kaiteran katu 1
Linnanmaa
Oulu
Finland
PO Box 8000

Sponsor information

Organisation
Hospital General Universitario Gregorio Marañón

ROR
https://ror.org/0111es613

Organisation
University of Edinburgh

ROR
https://ror.org/01nrxwf90

Organisation
University of Split

ROR
https://ror.org/00m31ft63

Organisation
Clinic for Neurology and Psychiatry for Children and Youth

Organisation
Maastricht University

ROR
https://ror.org/02jz4aj89

Organisation
Tartu Ulikool

Funder(s)

Funder type
Research council

Funder Name
HORIZON EUROPE European Research Council: HORIZON-HLTH-2021-STAYHLTH-01 Grant Agreement number: 101057182

Alternative Name(s)
European Research Council, Horizon Europe - European Research Council, EU - Horizon Europe - ERC, European Research Council (ERC), Conseil européen de la recherche, Consejo Europeo de Investigación, Det Europæiske Forskningsråd, Europäischer Forschungsrat, ERC, CER, CEI, EFR

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study will be available upon request from Dr Covadonga Martínez (covadonga.martinez@iisgm.com)

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Study website	Study website	11/11/2025	11/11/2025	No	Yes