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Executive Summary

This document describes the NEC - POPD - Requirement No. 2 (Protection of Personal Data) for the AI related medical research "Digital Phenotyping for Psychiatric Disorders from Social Interaction", a Pilot Research Project within the GAIN project. Aside from the target topic of the deliverable "Protection of Personal Data", it contains other relevant sections of the Ethics Protocol as well, such as Study Objectives and Design, Participant Selection and Enrolment, Data Collection and Management, etc.

The study plan has been elaborated by the Project Ethics Advisor (D 1.1) in cooperation with the partners from INRIA, and was approved without changes by Tbilisi State Medical University Biomedical Research Ethics Committee on 2 March, 2023 (meeting protocol #1-2023/102).

Document History			
Version	**Date**	**Contributors**	**Description**
1	11/03/2023	G. Giorgobiani – MICM, E. Chkonia - Central Psychiatric Hospital, Tbilisi Mental Health Center; A. Konig - INRIA	Deliverable 1. 2. NEC - POPD - Requirement No. 2 (Protection of Personal Data)
2	23/03/2023	G. Giorgobiani – MICM, E. Chkonia - Central Psychiatric Hospital, Tbilisi Mental Health Center; A. Konig – INRIA; B.E. Wirth - DFKI	Deliverable 1. 2. NEC - POPD - Requirement No. 2 (Protection of Personal Data)
3	26/03/2023	G. Giorgobiani – MICM, E. Chkonia - Central Psychiatric Hospital, Tbilisi Mental	Deliverable 1. 2. NEC - POPD - Requirement No. 2 (Protection of Personal Data)

		Health Center; A. Konig – INRIA; B.E. Wirth - DFKI	
4 (final)	11/10/2023	G. Giorgobiani – MICM, E. Chkonia - Central Psychiatric Hospital, Tbilisi Mental Health Center; A. Konig – INRIA; B.E. Wirth - DFKI	Deliverable 1. 2. NEC - POPD - Requirement No. 2 (Protection of Personal Data)

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INTRODUCTION

The Pilot Research Project at MICM is the part of the Twinning Research and Innovation Programme (TRIP) of the HE funded project GAIN, based on (but not limited to) the bilateral (INRIA-DFKI) large-scale project MePheSTO (Digital Phenotyping for Psychiatric Disorders from Social Interaction), which naturally integrates the TRIP research directions and enables MICM to submerge its research personnel into the running cutting-edge European research endeavor.
MePheSTO is an interdisciplinary research project that envisions a scientifically sound methodology based on AI methods for the identification and classification of objective, and thus measurable, digital phenotypes of psychiatric disorders, such as mental, affective, and mood illnesses/disorders. MePheSTO tackles several scientific challenges on the overlap of such scientific disciplines as Natural Language Processing, Computer Vision, Semantic Speech Analysis, with the application potential in Health.
The Pilot Research Project at MICM with the same title "Digital Phenotyping for Psychiatric Disorders from Social Interaction" will be conducted in Georgia. The main responsible institution of the task is the Central Psychiatric Hospital (Tbilisi Mental Health Center), where the clinical data will be initially collected. The data will be stored on the computer server at MICM for further investigation by the project partners and will be handled in accordance to the Consortium Agreement, GDPR and this protocol.
The Pilot Research Project at MICM will be guided and monitored by the GAIN Project Steering Board (GPSB). Principal investigators of the pilot project are Prof. Eka Chkonia (Central Psychiatric Hospital, Tbilisi Mental Health Center) and Dr. Alexandra König (Stars Team, INRIA).
The Ethics Protocol is an adapted version of the MePheSTO Ethics Protocol.

Approval of the Ethics Protocol

The Ethics Protocol of the Pilot Research Project at MICM "Digital Phenotyping for Psychiatric Disorders from Social Interaction" is an adapted version of the Ethics Protocol of the INRIA-DFKI joint research with the same title conducted within the project MePheSTO.
The GAIN version of the Ethics Protocol was adapted and translated into Georgian by the Ethics Advisor of the GAIN project, Prof. Eka Chkonia with consultancy of Dr. Alexandra König, an author of the MePheSTO version.
The study plan was assessed and approved without changes by the Biomedical Research Ethics Committee of Tbilisi State Medical University on 2 March, 2023 (meeting protocol #1-2023/102, see Figure 1).

Letterhead

Tbilisi State Medical University Biomedical Research Ethics Committee

#1-2023/102 meeting protocol

extract

2 March 2023

Study plan assessment: Digital Phenotyping for Psychiatric Disorders from Social Interaction

Principle Investigators/responsible persons:

Eka Chkonia, TSMU Associate professor, Department of Psychiatry

Alexandra König, Neuropsychologist, French National Research Institute for Research in Digital Science and Technology (INRIA).

Discussion:

Study plan assessment: Digital Phenotyping for Psychiatric Disorders from Social Interaction

Committee Concluded:

Approved without changes.

/ Givi Javashvili / Head of the Committee

Signature

I, Levan Namoradze, certify that I am fluent (conversant) in the English and Georgian languages, and that the above/attached document is an accurate translation of the document attached entitled the Extract.

LEVAN NAMORADZE

3/11, Politkovskaya str., Tbilisi, 0186, Georgia

Figure 1. meeting protocol #1-2023/102

Remark: It should be noted that as the medical data collection will be performed in Georgia, a non-EU country, the abovementioned approval (by the National Ethics Committee) of the study and the fact that the analogous study is approved and conducted in the EU countries Germany and France comply with the EU requirements for the involvement of **Non-EU countries**.

STUDY OBJECTIVES

- Primary objective

The aim of the study is to create a longitudinal multimodal corpus of patient-clinician interactions within the context of psychiatric disorders (namely major depressive episode and schizophrenia). The collected data will be annotated and clinically labelled for further use.

- Secondary objective

The secondary objective is to identify and formalize a set of novel multimodal digital biomarkers derived from the interaction data allowing reliable phenotyping of the target psychiatric disorders that goes significantly beyond the state-of-the-art. To this end, a set of methods/models for the extraction of those biomarkers from multimodal data is developed. On this basis, prognostic models for **predicting the patient's status** (e.g., relapse prediction) can be built.

- Exploratory objectives

- To validate automatic audiovisual behavior descriptors of psychiatric symptoms
- To automatically detect disruption and discontinuity in clinical interaction
- To predict evolution of symptoms (for differential diagnosis)
- To objectively assess the therapeutic alliance with multimodal digital phenotyping
- To predict adherence to treatment as well as treatment outcome based on objective evaluation of therapeutic alliance
- To measure levels of social synchrony, involvement behavior, behavioral mirroring, and relationship quality between clinician and patient.

STUDY DESIGN

This is a prospective longitudinal multicenter observational study across the clinical site.

STUDY PROCEDURE

Participants will be recruited in the participating clinics (inpatient and outpatient clinics) via their treating psychiatrists or a member of the research team. The participant will receive a detailed information sheet about the study, its process, potential risks, and benefits. They will be given at least 24 hours to decide on participating in the study. Participants will provide informed consent via a consent form. This will require the participants to provide their name and a contact phone number which will be stored on the clinics' servers. The information to be stored will be clearly described to participants in the participant information sheet and they will be asked to explicitly consent for this data to be stored. Participants will then be asked to provide key demographic details: sex, age, years of education and living status (e.g., living alone, as a couple, with family) and medical history. Participants will also be asked to provide the names of their current medications. This will be done to be able to control for any medications that may interfere with the behaviors to be studied in the analysis.

If participants agree, they will be asked to reply to self-surveys sent via text messages to their smartphone after discharge during the length of the study. The short surveys will help to gather additional information on the participants' state (mood, arousal, cognition, stressful events, depressive symptoms, negative symptoms, social participation, etc.). Wearable sensors will be provided to a subgroup of participants to capture physiological measures (heartrate, electrodermal activity, etc.), sleep quality, activity over the day, behavioral data during the study participation.

On receipt of a completed consent form, a member of the research team will arrange a first study appointment with the research participant. At the start of this baseline assessment the research team member will review the study information and the consent form and confirm whether the participant understands the purpose of the study and what is expected of their participation and whether they are happy to continue with the study. If the participant does not have the capacity to consent to their participation in the study, they will not continue in the study. All technical equipment usage will be reviewed and explained.

It is important to ensure that participants have the capacity to consent to the study at study entry. On receipt of a consent form from the participant, we will arrange a study visit and spend the first part of this visit discussing the information sheet, giving the participant opportunity to ask any questions they have. We then ask participants to describe their understanding of the study. Only participants who are able to comprehend the information, communicate a clear understanding about what the study involves for them, and communicate their willingness to enroll in the study will be considered to have capacity to take part. Once consent has been confirmed, the researcher will remind the participant that all clinical interactions will be video and audio recorded (except if the participant requests not to be recorded). Additionally, wearable sensors will be worn by participants and the clinician during the recorded interaction.

Prior to the start of the recording, any missing demographic data, medical history, or medication information will be collected from all participants. Sex, age, education (years), living status, and current medications will be recorded. Thus, the researchers will be able to control for any medications that may interfere with the social behavior to be analyzed during recordings. The different steps of the study are presented in Figure 2. and should be completed in the following order:

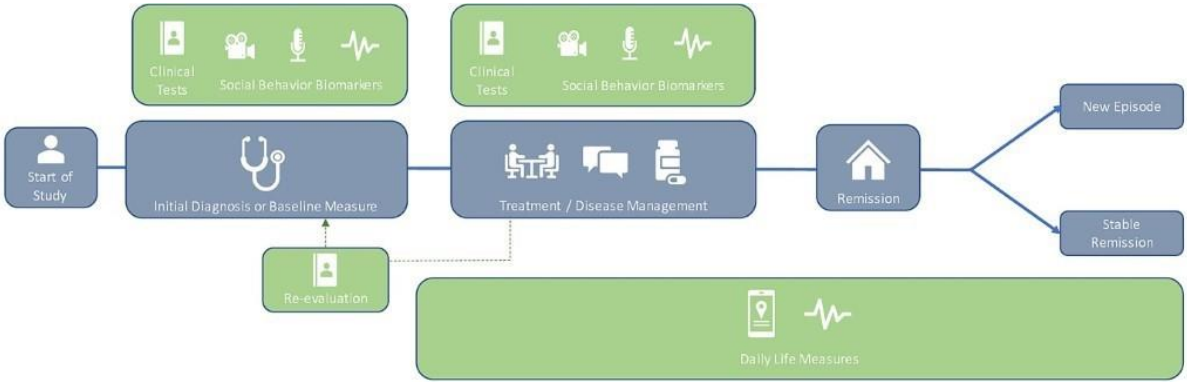


Figure 2. Overall study design

A) Baseline assessment: The research team member will start with a general screening interview (to last approximately 1h30 to 2 hours) with the participant using the Structured Clinical Interview for DSM-Disorders (SCID-CV) tool or the comprehensive assessment of at-risk mental states (CAARMS). The screening interview will be recorded (video and audio, physiological measures).
B) The participant will be briefed in the usage of the smartphone to answer the online surveys and ecological momentary assessments (EMA) in form of text messages as well as in the use of the wearable sensors
C) If the diagnosis criteria of major depressive episode (MDE) and/or schizophrenia are met (additional subsamples of high risk (HR) and ultra high risk (UHR) individuals likely to develop schizophrenia will be included), further psychiatric assessments will be performed using classical standard questionnaires and scales:

<u>For those with Major Depressive Episode:</u>

- self-assessment of depression symptoms
- semi-structured interview for depressive symptomatology

<u>For those with schizophrenia:</u>

- self-assessment of negative and positive symptoms
- semi-structured interview for positive and negative symptomatology

<u>For both:</u> Subjective quality of life
Additional assessments can be administered according to the site.

D) Every participant will undergo a short cognitive test battery.
E) Afterwards the participants will undergo their standard clinical pathway with its regular consultations. This includes medical and therapeutic consultations (weekly for hospitalized patients and monthly for ambulatory patients) which will be each time recorded for the length of the study (which is one month for inpatient clinics and 6 months for outpatient clinics). During the consultation, clinician and participant will be equipped with a wearable sensor to collect physiological measures (heartrate variability, electrodermal activity, accelerometer, body temperature).
Before each recording session the patient will be asked on his or her current medication status (if there were any modifications since the last recording).
F) Post recording session ratings (3 – 5 items) will be completed after each recorded session by patient and clinician on their perceived quality of the clinical interaction.
G) Daily life measures will be collected via the mobile phone (or via e-mail) in form of short regular surveys and ecological momentary assessments (EMA). A wearable device will be provided to a subsample of participants to record additional information on sleep quality, physical activity, etc.

H) For inpatient clinics: End of study participation at discharge (approximately at M12)
   a. A minimum psychometric assessment will be performed (for symptom improvement, therapy success) at all clinical sites; see C) consisting of
      i. A semi-structured interview and a self-report
      ii. An assessment of the overall perceived quality of care.

   For outpatient clinics: End of study participation (approximately at M6)
   b. A minimum psychometric assessment will be performed (for symptom improvement, therapy success) at all clinical sites; see C) consisting of
      i. A semi-structured interview and a self-report
      ii. assessment of the overall perceived quality of care.

I) Follow up / re-evaluation
   At M3, M6, M12 after the end of the study participation (via phone, video-conference or face to face consultation):
   a. Minimum psychometric assessments (for symptom improvement, therapy success) at all clinical sites; see D)
   b. Screening for medication adherence, any clinical care in between (hospitalization, outpatient counseling, relapse, etc.)

Description of setting

The recording setup will be as minimal as possible to be not invasive and still ensure a natural behavior during the interactions. The room in which the recordings take place will be a regular consultation room at the clinics. They require to be relatively quiet and bright in order to capture audio and video of sufficient quality for further analyses.

The patient will sit in front of the clinician at least 2 meters apart from each other, eventually with a table in between them. Small discrete cameras will be placed on the table between them.

EQUIPMENT

4.2.1 Audio recording

The speech of the participants and their interactions with the clinicians will be recorded as audio files via a microphone. We will directly record the speech of the patient and the clinician with the device placed in between them. From the audio files, we will use automatic speech recognition (ASR) and manual transcriptions to obtain textual transcripts of the recordings. A subset or all of the data will be manually transcribed for comparison between automated and manual transcriptions.

We will use either the internal microphone of the device (PC or tablet) or an external microphone for better recording quality. The recorded data are automatically stored on the secured server.

4.2.2 Video recording

We intend to support the proposed speech analysis by a complementary computer-vision based analysis. This analysis exploits advanced methods related to automated face analysis, motion tracking, detection, and recognition, as well as human behavior analysis.
Firstly, we plan to record 2D video-data and depth data (RGBD) from all participants for the computer vision-based analysis. Then we intend to study this data in order to find facial/gestural behaviors and facial/gestural activities that are representative for psychiatric symptoms during a social interaction.
We intend to acquire the video data using an external camera. The recorded data are automatically stored on the secured server. For a subsample of patients, follow-up evaluations will be made via a video-conference system which will allow to gather additional audio and video data.
The video data collected will allow us to perform eye tracking analysis on a subsample.

4.2.4 Physiological measures

We would like to explore the use of additional objective markers of stress levels within this study. For this we will extract physiological data during the recorded clinical interactions:

- Electro-dermal activity (EDA): measures sympathetic nervous system activity manifested through the skin, by measuring the constantly fluctuating changes in certain electrical properties of the skin;
- Heart rate Variability (HRV): derived from measuring blood volume pulse (BVP);
- Peripheral skin temperature: measured using and integrated infrared thermopile;
- 3-axis accelerometer: captures motion-based activity, which identifies intensity and frequency of movements that could be a seizure.

4.2.5 Online questionnaires

Participants will receive text messages on their mobile phones or email addresses with a link to go on a specific website to remotely complete clinical questionnaires on their current symptoms as well as questions on daily life activities, so called ecological momentary assessments (EMA). In addition, participants will be asked to record short audio samples.
The information will be stored on a secured server.

4.2.6 Videoconference system

The system is a web-based platform fully dedicated to diagnosing, screening and monitoring mental disorders. This tool is developed by INRIA using the latest advances in information and communication technologies to provide remote care through a web platform using any internet browser. This web platform allows an easy and direct connection between a clinician and their patient. Both connect to the web platform using their respective identifiers and passwords.

STUDY POPULATION

NUMBER OF PARTICIPANTS

Up to 100 participants will be invited to this study. Participants will be recruited through the Central Psychiatric Hospital, Tbilisi Mental Health Center.

INCLUSION CRITERIA

According to SCID diagnosed with either major depressive episode or schizophrenia, aged between 18 and 65.

EXCLUSION CRITERIA

- Do not have capacity to consent
- Acute suicidal tendencies or in a major crisis
- Not native speakers or had any major hearing or language problems.

CO-ENROLMENT

Co-enrolment in all study types will be allowed.

PARTICIPANT SELECTION AND ENROLMENT

IDENTIFYING PARTICIPANTS

Participants will either be identified by their treating psychiatrists or a member of the study team of the involved clinics. Either psychiatrist or clinical researchers will contact them to see if the study may be suitable for them. The initial information sheet will be given to participants. Interested participants will be given the opportunity to discuss any questions with the research team upfront.

CONSENTING PARTICIPANTS

Participants will be invited to participate in this study during their consultation in the clinic. The participant information sheet will be provided to the participants (in paper version or by e-mail, depending on their preference), and they will be given at least 24 hours to decide on participating in the study. Participants will provide informed consent via on consent form. This will require the participants to provide their name and a contact phone number which will be stored on the clinics' servers. This information will be clearly described to participants in the participant information sheet and they will be asked to explicitly consent for this data to be stored.

On receipt of a completed consent form, a member of the research team will arrange a first study appointment with the research participant. At the start of this baseline assessment the research member will review the study information and the consent form and will confirm whether the participant

understands the purpose of the study and what is expected of their participation and whether they are happy to continue with the study. If the participant does not have the capacity to consent to their participation in the study, they will not continue in the study.
Members of the research team are experienced in working with this population and assessing capacity. Only appropriately trained staff will be delegated to this task. Senior staff will be available to discuss any concerns about a participant's capacity to consent.

- Withdrawal of Study Participants

Participants are free to withdraw from the study at any point or a participant can be withdrawn by the investigator. If withdrawal occurs, the primary reason for withdrawal will be documented in the participant's case report form, if possible. The participant will have the option of withdrawal from all aspects of the trial but continued use of data collected up to that point. To safeguard personality rights, only the minimal amount of personally-identifiable information will be collected. Participants can withdraw their data up to the point of conversion to numerical files. After this point, it is not possible to identify the participants and therefore data cannot be withdrawn.

DATA COLLECTION

General clinical data will be collected at the baseline and at the end of study participation and 3 months, 6 months, and 12 months after study participation.
Demographic and medication data will be recorded on electronic case report forms.
All questionnaire and clinical data will be collected using paper-based or online forms.
Survey and wearable data will be collected over the smartphone.
If participants have no access to the internet at home, a paper-based version of the questionnaires will be posted to them with a self-addressed envelope to return to the research site. Apart from this case, there will be no paper-based documentation for this study.

Data collection during clinical Face-to-Face interviews:

SPEECH DATA: The speech of the participants will be recorded as audio files during clinical interactions. Depending on the situation, the recorded speech is either free speech or direct answers to questions.
Procedure: We will directly record the speech of the patients. From the audio files, we will use automatic speech recognition (ASR) to obtain textual transcripts of the recordings. A subset or all of the data will be manually transcribed for comparison between automated and manual transcriptions.
Materials: We will use either the internal microphone of the device (PC or tablet) or an external microphone for better recording quality. The recorded data are automatically stored on the secured server.

VIDEO DATA: We intend to support the proposed speech analysis by a complementary computer-vision based analysis. This analysis exploits advanced methods related to automated face analysis, tracking, detection and recognition, as well as human behavior analysis.
Procedure: Firstly, we plan to record 2D and 3D video-data from all participants for the computer vision-based analysis. Then we intend to study this data in order to find facial movements and expression, as well as body gestures and postures that are representative for social behaviors typically found in the targeted psychiatric disorders.
Material: We intend to acquire the data using an internal device camera. The use of an external web-camera connected to a PC is also considered. In both cases, the recorded data are automatically stored on the secured server.

PHYSIOLOGICAL DATA: We intend to record physiological measures of the patient and the clinician during clinical interviews. The following measures will be recorded via a device placed on the body:

- Electro-dermal activity (EDA): measures sympathetic nervous system activity manifested through the skin, by measuring the constantly fluctuating changes in certain electrical properties of the skin;
- Heart rate variability (HRV): derived from measuring blood volume pulse (BVP);
- Peripheral skin temperature: measured using and integrated infrared thermopile;
- 3-axis accelerometer: captures motion-based activity, which identifies intensity and frequency of movements that could be a seizure.

Procedure: The data will be recorded on the device and sent to a secured server.
Material: We will use noninvasive devices such as wristbands and/or skin adhesive collars (or electrodes)

Additionally, after discharge, daily life measures will be collected via short regular surveys and ecological momentary assessments (EMA) sent to the patients' phones.

Data collection during clinical remote interviews:

When the interviews are done remotely, we will use a web-based telemedicine (videoconference) tool. We will record the same data as in the face-to-face interviews.
Procedure: When the interview starts, the recording of speech and video are directly starting and the data are stored directly on secured servers.
Material: The data will be recorded using the device used to connect to the telemedical interface (PC or tablet). Speech and video data will be recorded using the cameras and microphones embedded in or plugged to the device. Physiological data will be recorded in the same way as in the face-to-face interviews, idem for the forms and questionnaires.

DATA MANAGEMENT

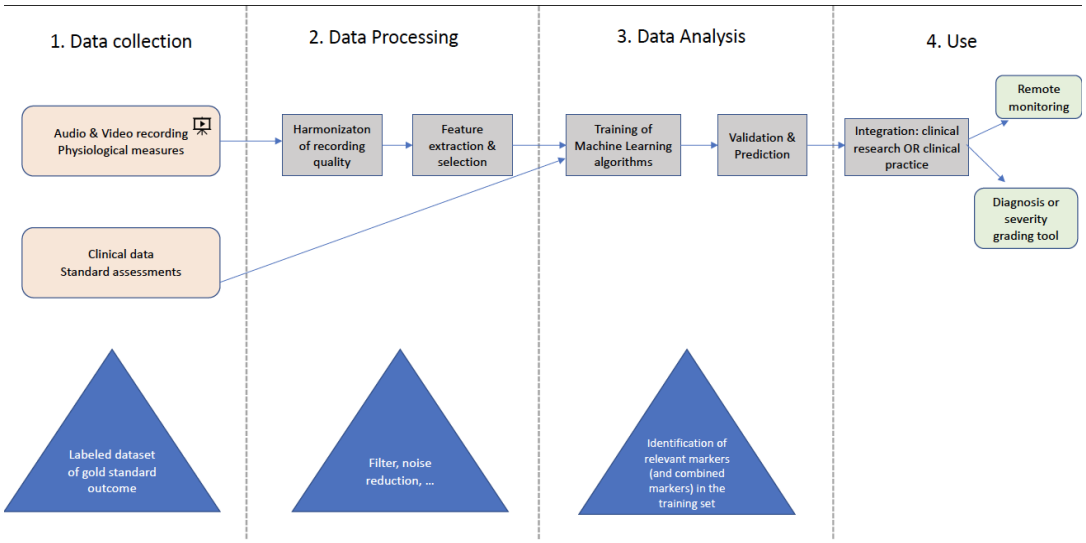
All Investigators and study site staff involved in this study must comply with the requirements of the appropriate data protection legislation (including the General Data Protection Regulation and Data Protection Act) with regard to the collection, storage, processing, and disclosure of personal information.

Personnel data

We will store the following data about participants:

- Name
- Phone number
- **Sociodemographic data:** age, gender, education, marital status, domiciliary status drug use, etc.
- **Medical history & biological treatment**: antipsychotic, antidepressant, anxiolytic drugs prescribed (Clozapine, Risperidone, Olanzapine, etc.)
- **Therapeutic treatments:** CBT, cognitive remediation, psycho-analysis
- **Neuropsychological/cognitive assessment**
- **Neuropsychiatric Assessment**: Specialized scales andquestionnaires according to the patients' profiles
    - **Audiovisual recordings** (face to face & videoconference)
    - **Physiological measures**
    - Additional **ecological momentary assessments (EMA).**

Data Information Flow



Data flow diagram

Data acquisition and security

Data collection will be conducted via the different recording devices. Digital data (audio or speech, video, physiological measures, recorded scores, answers to questionnaires) as well as paper data (written records) will be collected.

Concerning the paper data, they will be stored at a designated place with limited access to clinicians participating in the study (a key is needed for access). Each involved clinical partner will store these papers in their clinic. The data will be digitized through a web-platform in order to conduct the research work. In the following paragraphs, we provide details about the security of all digital data.

Concerning the digital data, demographic, medication and all clinical data will be stored in the secured and certified Health Data Hosting infrastructures of each clinical partner. However, regarding the remaining digital data (speech, video and physiological), we have to consider the data acquisition and security in the two cases of Face-to-Face and remote setups.

- ### Data acquisition and security during Face-to-Face interviews:

During the Face-to-Face interviews, the recording of data will be done on local servers, not connected to the internet outside the clinics. All the data remain in the intranet of the clinical facility. The local servers will be encrypted and the access is contingent on an authorized password.

- ### Data acquisition and security during remote interviews:

To perform the remote interview, a secured connection to the web-platform is required by both clinicians and participants. The secured and encrypted connection (i.e., HTTPS) requires authentication with an e-mail address and an encrypted password. Only limited e-mail addresses' domains will be allowed to connect to the web-platform. The clinician should have a professional e-mail, which is provided by their organization. The allowed domains should be those of clinical partners involved in the clinical study.

The enrolled subjects will have an authorized access to the web-platform with their e-mail and a temporarily generated password valid only for the time of their participation in the study. The password will be entered by the person accompanying the subject (a clinician, member of the clinical study) to connect the subject to the platform. A unique identifier to replace the e-mail will be provided to subjects without an e-mail address.

The collected data during the study are stored in a secured encrypted database. The server of the clinical partner performing the inclusions will host the database within the clinical facilities, which are secured and respond to all norms of security. Authorized and certified IT personnel will manage the security of the server.

An IT technician will manage the database and will manage the rights on the database:

- Create/delete/edit the list of clinicians who can access the web-platform.
- Create/delete/edit the list of subjects participating in the clinical study.

The authorized clinicians will have the right to access to the web-interface, which will allow them to perform the study. The collected data are automatically stored in the database.

The access to the stored data is strictly reserved to the clinicians with a secured account. The type of the database is a MySQL DataBase. The security of the database is ensured by its encryption using AES (Advanced Encryption Standard) techniques. The following rules will be applied:

- the database is accessible from trusted hosts only,
- no use of data from input without filtering,
- all type of data is protected,
- the administrator of the database (the IT technician) is not a user of the web platform.

Security of transmission between clinicians and participants during study sessions: After the clinician and the participant are connected to the platform, video streams are circulating in both directions. Video streams are protected by integrating the following rules:

- The sessions of the clinical study are scheduled by the involved clinicians and are not publicly known.
- We add a signaling protocol that provides an encryption of signaling traffic.
- The connection between the clinician and the patient is a P2P connection, the media contents (audio and video channels) are transmitted between peers directly in full duplex. Thus, as the signaling server maintains the number of peers in communication, we monitor the connection for addition of suspicious peers in a call session. If the number of peers actually present on the signaling server is more that the number of peers interacting on the connection, then it could mean that someone is eavesdropping secretly and should be terminated from session access by force.
- Request permission from both sides to use the camera and the microphone.

Transfer of Data

To transfer data from the clinical recording sites to the technical partners, we will employ an end-to-end encryption methodology, using asymmetric encryption, as detailed in the guidelines of the BSI. Data will be encrypted at the clinical sites on the recording computer that is not connected to the internet. After copying this encrypted data to a computer that is connected to the internet, the data will be transferred via the internet to the technical partners. The data will be kept encrypted at the technical sites and only be de-crypted right before de-crypted data is needed (e.g. to re-structure, annotate, extract features, or train machine learning models with the data).

Data Controller

The Central Psychiatric Hospital and MICM are the data controllers along with any other entities involved in delivering the study that may be a data controller in accordance with applicable laws and the GAIN Consortium Agreement.

STATISTICS AND DATA ANALYSIS

SAMPLE SIZE CALCULATION

A total sample size of up to 100 participants will be recruited. This amount of participants, together with the number of participants collected at other sites during the MePheSto project, will provide sufficient data for algorithm development work (primary outcome). Any additional data beyond that would be beneficial to further refine the algorithms.

Generally, comparison studies like the present one require sufficient data to validate new practice methods. In case of highly representative data, the size of data needed for investigative studies might be of limited quantity, which serves real life studies like ours, that require the time-intense acquisition and enrollment of each patient.

PROPOSED ANALYSES

In this study, we will mainly work on the analysis of the following types of data: clinical scores (questionnaires and scales either obtained during face to face visits or remotely), speech, video and physiological measures.

To achieve the primary objective of the study, comparison analyses will be performed between the new digital markers and the standard clinical measures. We will as well perform a multi-modal analysis using combined data modalities.

GOOD CLINICAL PRACTICE

ETHICAL CONDUCT

The study will be conducted in accordance with the principles of the International Conference on Harmonisation Tripartite Guideline for Good Clinical Practice (ICH GCP). Before the study can commence, all required approvals will be obtained and any conditions of approvals will be met.

INVESTIGATOR RESPONSIBILITIES

The investigator is responsible for the overall conduct of the study at the site and compliance with the protocol and any protocol amendments. In accordance with the principles of ICH GCP, the following areas listed in this section are also the responsibility of the investigator. Responsibilities may be delegated to an appropriate member of the study site staff. Delegated tasks must be documented on a Delegation Log and signed by all those named on the list prior to undertaking applicable study-related procedures (wet ink, Docusign or Abode Sign signatures will all be accepted).

- ### Informed Consent

The investigator is responsible for ensuring informed consent is obtained before any protocol specific procedures are carried out. The decision of a participant to participate in clinical research is voluntary and should be based on a clear understanding of the study components.
Participants must receive adequate oral and written information – appropriate participant information and informed consent forms will be provided. The oral explanation to the participants will be performed by the investigator or qualified delegated persons, and must cover all the elements specified in the participant information sheet and consent form.
The participants must be given every opportunity to clarify any points they do not understand and, if necessary, ask for more information. The participants must be given sufficient time to consider the information provided. It should be emphasized that the participants may withdraw their consent to participate at any time without loss of benefits to which they otherwise would be entitled.

- ### Study Site Staff

The investigator must be familiar with the protocol and the study requirements. It is the investigator's responsibility to ensure that all staff assisting with the study are adequately informed about the protocol and their trial related duties.

- ### Data Recording

The principal investigator is responsible for the quality of the data recorded for the purposes of the study.

- ### Investigator Documentation

The principal investigator will ensure that the required documentation is available in the investigator site files (ISF). The ISF may be held electronically or in paper form.

- ### Confidentiality

All study data must be identified in a manner designed to maintain participant confidentiality. All records must be kept in a secure storage area with limited access. Clinical information will not be released without the written permission of the participant. The investigator and study site staff involved in this study may not disclose or use for any purpose other than the conduct of the study, any

data, record, or other unpublished information, which is confidential or identifiable, and has been disclosed to those individuals for the purpose of the study.

- Data Protection

All Investigators and study site staff involved with this study must comply with the requirements of the appropriate data protection legislation (including the General Data Protection Regulation and Data Protection Act) with regard to the collection, storage, processing and disclosure of personal information.
Computers used to gather the data will have limited access measures via user names and passwords.
Published results will not contain any personal data and re-identification of any participants from the publications will not be possible.

Annex 1: Declaration on independence and absence of conflicts of interest

The undersigned Eka Chkonia, appointed as independent Ethics Advisor for the project [GAIN] [GA 101078950], declares that:

- She will execute her responsibilities in full independence of other professional and academic commitments;
- She is not affected by any conflict of interest arising in particular from any economic or professional interests, from family or other personal links, or from any other relationships or common interests which may compromise the independent nature of the report provided;
- there are no other professional or financial constraints to carry out the required assignment or that would compromise the independent nature of the report provided:
- She will notify the Beneficiary/Coordinator/Principal Investigator without delay if the above situation changes, particularly in such a way as to compromise the independent nature of the report.
- She will not reveal any information about the project's activities and its outcomes, without the express written approval of the Beneficiary/ies or the Commission/Executive Agency/Funding Body.

Date: 11.10.2023

Signature: