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Bipolar disorder prediction with sensor-based semi-supervised learning

D1.1 – Use Cases with Psychiatric Scenarios

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History

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12-MAY-2022	0.1	Task assignments and integrated version of the document
26-JUN-2022	0.2	Scenarios for locomotor sensors added
18-SEP-2022	0.3	Version for internal review
30-SEP-2022	1.0	Version ready for submission
14-Oct-2022	1.1	Version with revised description of pilot with acoustic data

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Executive summary

This deliverable outlines the results of Task 1.1 activities during the first nine months of the BIPOLAR project, which were driven by the BIPOLAR team in cooperation with advisors representing the medical domain. To this end, all participants of the BIPOLAR team collaborated with two experienced professionals in psychiatry, namely Dr Monika Dominiak from Department of Affective Disorders, Institute of Psychiatry and Neurology in Warsaw, Poland and Prof. Svetlozar Haralanov from University Hospital for Neurology and Psychiatry "St. Naum" in Sofia, Bulgaria. This interdisciplinary team formalized five psychiatric scenarios, which were briefly described in the Grant Agreement. These psychiatric scenarios need to be addressed by the BIPOLAR package.

The analysis of each psychiatric scenario allowed for the definition and refinement of the project's scope. It also led to better understanding and agreement between the team members on which psychiatric needs will be addressed by the BIPOLAR project. Based on the common understanding of the functionality of the BIPOLAR package under development, its functionality was documented in the form of use cases, which describe the interactions between actors (persons, devices or digital entities), the assumptions and the expected outcomes after the execution of a flow of actions. Further functional and non-functional requirements will be identified based on the expertise and experience of all partners. This manual includes 5 use cases forming 2 pilots.

In the future, BIPOLAR's key performance indicators will be specified based on the identified use cases and requirements in order to be able to measure the outcome of the pilots and provide input for the technical evaluation of the project results.

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List of acronyms

Acronym	Explanation
BIPOLAR	Bipolar disorder prediction with sensor-based semi-supervised learning project
BD	Bipolar disorder

1.Introduction

1.1.About this document

The aim of the use case analysis report is to document and analyse the context and all subjects needed for the design and implementation of the software package proposed within the BIPOLAR project. In order to extract the fundamental requirements for the project, we have conducted |interviews with experienced medical experts of the two pilots of the project, that are:

1. **Acoustic Data Pilot (ADP)**: **Acoustic data collected from smartphones of bipolar disorder patients**
2. **Locomotor Data Pilot (LDP): Locomotor data collected from sensor of bipolar disorder and unipolar depression patients**.

Based on gathered information from literature and doctors, five psychiatric scenarios for bothpilots were defined. Later on, for every psychiatric scenario, use cases were formulated against which requirements fulfilment will be verified and interactions with BIPOLAR package components will be tested. Simple use case diagrams, identifying primary actors and activities that form each system, were prepared. After psychiatric scenarios and use cases were formulated, requirements were collected, defined, verified (whether they are clear, complete, and consistent), classified (functional, non-functional, etc.) and analysed.

This deliverable is the result of the activity carried out in T1.1. (Preparing psychiatric scenarios). It also uses some results obtained in T4.1 (Requirement analysis and software package prototype architecture). The results of this deliverable will influence design of methods and components in WP2-WP3, and later on for T4.2 (Development of fuzzy semi-supervised learning models) and T4.3 (Software package implementation and modules integration).

The information identified up to the delivery date of this deliverable is included, but completing and updating necessary information will be continued throughout the project.

The document is divided into four sections. The first is an introduction that covers the purpose of the BIPOLAR project and the methodology for defining the use cases and requirements. In sections 2 and 3 psychiatric scenarios and use cases, grouped by the pilots defined in the project, are described and analysed. Finally, in section 4 summary, an overall conclusion and future work are provided.

1.2.Scope of BIPOLAR project

BIPOLAR aims to develop a software package containing a set of computational methods that will support engineering of information from sensors and semi-supervised learning to provide accurate prediction of shifts from euthymia to depression, mania and mixed states.

BIPOLAR will be tested for datasets with acoustic and locomotor features collected from smartphones and wearable sensors. Recent related work confirms that these types of data are considered as promising markers of depressive or manic symptoms[1]. In particular, smartphone sensor-based system incorporating sensor modalities covering different disease-relevant aspects of the human behavior are expected to facilitate the life of bipolar disorder patients and support their treatment[2]. Furthermore, psychomotor disturbances (PMDs) which are cardinal symptoms of endogenous depressions, which are objectively measurable and might reflect their neurobiological mechanisms[3].

Below we provide a short description of terms like pilot, psychiatric scenario, use cases, and requirements which are extensively used across this report.

Table 1. Basic terms used to define psychiatric scenarios identified in the BIPOLAR project.

Term	Definition
Use case	Use case specification includes (among other): (i) actors (persons, devices or digital entities) that interact and participate in the use cases; (ii) requirements, assumptions and/or pre-conditions to be satisfied for the use case to be performed; (iii) flow of events between actors, and sequences of interactions focusing on differences from current operations, and (iv) expected outcomes after the use case execution.
Psychiatric scenario	Psychiatric scenario identified in the BIPOLAR project is described using the template from Table 2.
Requirement	"A requirement is a statement that identifies a system, product or process characteristic or constraint, which is unambiguous, clear, unique, consistent, stand-alone (not grouped), and verifiable, and is deemed necessary for stakeholder acceptability."[4]

[1] Antosik-Wójcińska, A.Z., Dominiak, M., Chojnacka, M., Kaczmarek-Majer, K., Opara, K., Radziszewska, W., Olwert, A., Święcicki, Ł. ***Smartphone as a monitoring tool for bipolar disorder: a systematic review including data analysis, machine learning algorithms and predictive modelling*** . International Journal of Medical Informatics, (2020) 138:04131. https://doi.org/10.1016/j.ijmedinf.2020.104131

[2] Grünerbl A, Muaremi A, Osmani V, Bahle G, Ohler S, Tröster G, Mayora O, Haring C, Lukowicz P. ***Smartphone-based recognition of states and state changes in bipolar disorder patients*** **.** IEEE J Biomed Health Inform. 2015 Jan;19(1):140-8. https://10.1109/JBHI.2014.2343154 . 2014 Jul 25.

[3] Haralanov S, Haralanova E, Milushev E, Shkodrova D. ***L ocomotor movement-pattern analysis as an individualized objective and quantitative approach in psychiatry and psychopharmacology: clinical and theoretical implications*** . Psychiatry and Neurosciences Vol. III, Chapter32. Springer Nature Switzerland AG. 2019. pp.387-416. https://doi.org/10.1007/978-3-319-95360-1_32

[4] ***Systems Engineering Handbook: A Guide for System Life Cycle Processes and Activities***. Version 3.2.1. San Diego, CA, USA: International Council on Systems Engineering (INCOSE), INCOSE-TP-2003-002-03.2.1: 362.

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1.3. Methodology

The Volere methodology[5] provides several templates to deal with the different techniques and activities that it includes. In a quick view, the Volere Requirement Process suggests a methodology that can be summarised as follows:
(1) Define the purpose of the project
(2) Stakeholder identification and analysis
(3) Business scenarios
(4) Use cases
(5) Writing the requirements: functional requirements and non-functional requirements
(6) Validation of requirements: completeness, relevance, testability, coherency, traceability
(7) Communicating the Requirements
(8) Requirement completeness (verification by other work packages).

In BIPOLAR project, all scenarios are dedicated to support a particular medical domain that is psychiatry, and thus, they are called psychiatric scenarios in the remaining of this document. Each psychiatric scenario identified in the BIPOLAR project is described using the template from Table 2. In this table, the guidelines on how to fill the template are provided. Scenarios should be written from the point of view of an external viewer that should understand the problem/case without in-depth knowledge about the project.

For each pilot in BIPOLAR, an UML use case diagram will be created that will outline the key actors. Use cases are related to psychiatric scenarios that can be viewed as "components" to achieve the goal which are set by the psychiatric scenarios. A use case diagram is a diagram that shows the relationships among actors within a pilot. This diagram aims at facilitating a preliminary overview of the functionality, that the BIPOLAR package should have, and discovering/specifying the related actors.

Finally, requirements for BIPOLAR will be gathered. Requirement is "a statement that identifies a product (includes product, service, or enterprise) or process operational, functional, or design characteristic or constraint, which is unambiguous, testable or measurable, and necessary for product or process acceptability." [6] According to the Volere methodology, there are various types of requirements. Within BIPOLAR, we aim at distinguishing **functional requirements.**

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[5] ***Volere Requirements: How to Get Started*** https://www.volere.org/wp-content/uploads/2018/12/VolereGettingStarted.pdf

[6] Systems and Software Engineering - **Recommended Practice for Architectural Description of Software Intensive Systems.** Geneva, Switzerland: International Organization for Standards (ISO)/International Electrotechnical, Commission (IEC), ISO/IEC 42010:2007

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Table 2. Template for the psychiatric scenarios identified in the BIPOLAR project.

Scenario ID *#1*	**Scenario name** *Self-explanatory. Choose short title*	
Illustration of system's behaviour in a specific situation, flow of events	*Write here the scenario: description of users' interaction with a system in users' perspective, covering a short story of an individual user(s), interacting with a system, to achieve a specific outcome, under specific circumstances, over a certain time interval. Check that the scenario covers at least the following elements.*	
	User/users:	*What are the characteristics of the user(s)? (e.g., age, gender, education, technical skills) Are they producer or consumer with respect to the system/service?*
	Setting / context	*What is the physical environment? (e.g., place, location, another person(s) involved).*
	Interacting system	*If possible, give an overview of the technical environment (e.g., devices and network, services and platform, etc.).*
	Users' goals	*What the user(s) wants to achieve?*
	Initial status	*What is the initial condition of the interacting system, or*
	Interactions	*How the user(s) interacts with the system? (in addition, a schematic of the interacting system, if relevant, could be helpful)*
	Data	*What information (data) is produced and /or consumed?*
	Motivation	*Why to choose the particular way to act?*
	Time	*When? How long? At what frequency?*
System functionalities	**General description**: *Short description of the main functionalities needed for this business scenario shown above.*	

Functional requirements are the fundamental subject matter of the system and are measured by concrete means like: data values, decision-making logic, and algorithms. We also gather and specify requirements related to all identified psychiatric scenarios. Non-functional requirements are the behavioural properties that the specified functions must have, such as performance, usability, etc. Non-functional requirements can be assigned to a specific measurement.

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2.Pilot 1: Predict bipolar disorder with Acoustic Data collected from smartphones Pilot (ADP)

Acoustic Data Pilot (ADP) aims at uncertainty-aware prediction of bipolar disorder states based on acoustic features extracted from voice of bipolar disorder patients. Acoustic features are extracted from voice signal using a dedicated mobile application BDMon for patients' smartphones. Figure 1 shows an illustrative overview of data collection within this pilot.

Figure 1. Illustrative overview of the smartphone-based collection of acoustic data.

The application required a smartphone with Android system. The patient's voice signal was divided into 20ms frames (within one frame it is approximately stationary). The extended Geneva Minimalistic Acoustic Parameter Set (eGeMAPS) for voice research was extracted from each frame. This set comprises 86 features including time-domain descriptors (such as e.g., zero-crossing rate, amplitude statistics) and spectral features (such as e.g., mel-cepstral coefficients, fundamental frequency and its harmonics).

In Figure 2, an UML use case diagram is created for ADP pilot.

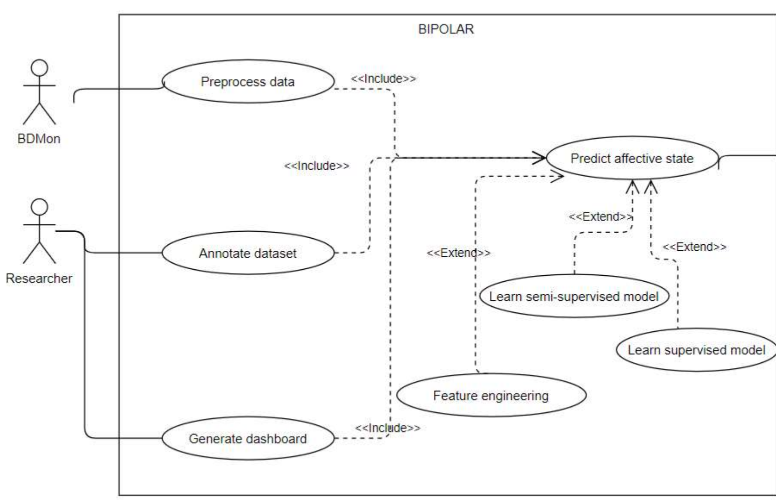

Figure 2. Use case diagram for ADP dedicated to Predicting bipolar disorder with acoustic data collected from smartphones.

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Psychiatric scenarios can be viewed as "components" to achieve the goal which are set by the use case. A use case diagram facilitates a preliminary overview of the functionality, that the BIPOLAR package should have, and discovering/specifying the related actors. Actors for this ADP pilot are gathered in Table 3.

Table 3. Main actors identified in the Acoustic Data Pilot (ADP).

Actor (type)	Description
BDMon (system)	Smartphone application able to extract features from speech, remove the interlocutor speech.
Researcher with programming skills (person)	A professional, either from academia or business, interested in using BIPOLAR package. Basic programming skills in a high-level programming language such as R/Python are required to interact with the software component. Typical examples of such researchers would be (I) a psychiatrist/psychologist willing to explore their data, (ii) a software engineer with advanced programming skills using BIPOLAR package in a broader programmatic context.
Doctor (person)	A professional expert in medical domain willing to get more information about a patient. He/she is in particular interested to know more about acoustic features related to patients' state, which are most discriminative, how this particular patients looks compared to other patients and what is the affective state of the patient predicted by the BIPOLAR software.

2.1.ADP-PS1: Uncertainty-aware annotation of sensors data with psychiatric information

The key goal of the first psychiatric scenario is to intelligently combine unsupervised data from sensors with labels from external label source and to estimate uncertainty related with this process. The uncertainty is expressed by a **confidence factor** assigned to each observation that became supervised in the result of the aforementioned process. The confidence factor is a fraction ranging from 0 to 1 which describes a level of confidence we assign to the supervised assumption that a given observation belongs to the certain class (e.g., that the specific call belongs to the "depression" phase of bipolar disorder).

Such indirect annotation of **unsupervised data from sensors** (e.g. voice characteristics recorded by a smartphone application during a phone call) with information from **external label source** (in this case, a psychiatrist's assessment of the current disease phase obtained during stationary visit) is a frequent approach in the literature[7]. The merging of information in this use

[7] Dominiak M, Kaczmarek-Majer K, Antosik-Wójcińska AZ, Opara KR, Olwert A, Radziszewska W, Hryniewicz O, Święcicki Ł, Wojnar M, Mierzejewski P. **Behavioral and Self-reported Data Collected From Smartphones for the Assessment of Depressive and Manic Symptoms in Patients With Bipolar Disorder: Prospective Observational Study**. J Med Internet Res. 2022 Jan 19;24(1):e28647. doi: 10.2196/28647. PMID: 34874015; PMCID: PMC8811705.

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case is performed based on the time domain. Data from a pre-defined "ground truth period" around the date of psychiatric assessment (e.g. a time frame spanning from 7 days before the visit up to 2 days after the visit) are assigned the label from the visit.

Our BIPOLAR package is taking into account the inherent uncertainty related to the process of label extrapolation. Using all available information provided by the user, the confidence factor is estimated for each observational unit that became supervised in the result of "ground truth period" annotation. The higher the confidence factor, the higher our confidence that the observational unit is truly representative of the assumed supervised class. Note that BIPOLAR software estimates the confidence factor in a fully automatic and data-driven way, and does not require user to provide any type of expert assessment.

In Table 4, the main characteristics of this scenario for **Uncertainty-aware annotation** are summarized.

This scenario requires two datasets to be provided initially: (1) **unsupervised data from sensors** (further referred to as X; in this use case these are voice characteristics from phone calls), identified by a composite key [patient ID, datetime of the call], and (2) **categorical labels from psychiatric assessment of patient** (a value from a pre-defined set of possible disease phases, e.g. {"euthymia", "mania", "depression", "mixed"}) identified by a composite key [patient ID, datetime of the visit]. The requirements for quality and shape of the datasets will be further described in Section 4 and during the completion of the project. The user may need to wrangle their data before being able to use the BIPOLAR software.

To interact with the system, the user must recreate a programming environment on his device of choice according to the documentation provided by the authors of BIPOLAR. The software component will require the user to set values for the a priori parameters of the method, e.g. the length of the "ground truth period".

Potential extensions for the future include a **time-weighing** mechanism of the "ground truth period" definition. Current approaches consider a binary inclusion/exclusion mechanism, while the time domain could be used to weigh the contribution of the phone calls further from the visit differently than those closer to the visit. The user would need to choose one of the available weighing options.

It must be noted the outcome of this system, a new dataset with partially supervised observations and confidence factor about the certainty of the supervision, may be used in many ways. One can limit themselves only to exploring the differences between highly confident calls and these that are deemed less confident per the confidence factor estimated by BIPOLAR. On the other hand, the estimated confidence factor can be used in uncertainty-aware statistical learning to increase the impact of highly confident supervised observations in finding classification rules.

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Table 4. Main characteristics of the Psychiatric scenario ADP-PS1: **Uncertainty-aware annotation of sensor data with psychiatric information.**

Psychiatric scenario: ADP-PS1		
Scenario	**Uncertainty-aware annotation of sensor data with psychiatric information**	
Illustration of system's behavior	User wants to annotate their unsupervised data from sensors with labels obtained from psychiatrists during stationary visits in an uncertainty-aware manner. To interact with the system, user must recreate programming environment per the BIPOLAR documentation. Then, the user is supplying two datasets: (I) unsupervised data from sensors, (ii) label information from psychiatric assessments. The datasets must comply with the requirements described in the documentation. The key requirement is the merging composite key: [identifier of a patient, time when information was recorded]. To run BIPOLAR algorithm, the user must set a priori values for certain parameters of the method that require expert assumptions, such as the length of the ground truth period. As the outcome, the user receives the dataset (I) with added information about labels and the confidence	
	User/users:	researcher with programming skills
	Setting / context	The user interacts with the system on their own; the user is providing their own data to the system.
	Interacting system	BIPOLAR component will be available as an R library that can be installed from github repository following BIPOLAR component's documentation.
	Users' goals	User wants to annotate their unsupervised data and obtain a confidence factor for each annotation that express uncertainty about label's validity.
	Initial status	Two datasets are required from user: (I) unsuperivsed data from sensors, (ii) labels from psychiatric assessments, that can be combined based on common keys. User must provide a priori values for some of the parameters of BIPOLAR that require expert assumptions.
	Potential extension for the future	Including a time-weighing mechanism for the ground truth period.
System functionalities	1. Label extrapolation (annotation of unsuperivsed data from sensors with information from additional label source) based on ground truth period. 2. Estimating uncertainty of extrapolated labels by means of a confidence factor.	
Owner	KK	

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2.2.ADP-PS2: Semi-supervised prediction of the mental state

This psychiatric scenario aims at prediction of affective state for partially labeled datasets. The primary goal of this scenario is prediction of the affective state incorporating both, the uncertainty about psychiatric labelling and some completely unlabeled acoustic data.

In the majority of the state of the art, the episode prediction problem is stated as a supervised learning task. Supervised techniques require a lot of labeled data (results of the psychiatric assessment in this context), and providing these data on a day to day basis is almost infeasible in the bipolar disorder monitoring context. On the other hand, unsupervised learning techniques such as clustering algorithms or statistical process control overcome these limitations since they try to find the structure information in unlabeled data to construct a classifier or a control chart. However, due to absence of labeled information on data distribution, clustering methods may give inconsistent data partitions that include instances from different classes. Hopefully, semi-supervised learning algorithms have the potential to improve classification performance by using a combination of both labeled and unlabeled data. Recently, to alleviate the problems of uncertainty about patients' state and limited data, Kamińska et al [8] showed that advanced approach to handling uncertainty about psychiatric assessments and feature engineering enables to increase the accuracy of episode prediction. Similarly, Casalino et al. [9] applied dynamic incremental fuzzy semi-supervised clustering. Preliminary results are very promising but it is also observed that the results depend on the randomly selected chunks (the solution is not robust). Therefore, further research is needed to investigate its benefits and limitations and next experiments on larger sample size. This scenario focuses on fuzzy semi-supervised learning to capture uncertainties related to partially labeled data collected from sensors. The key idea of semi-supervised learning is to equip unsupervised learning with a partial supervision mechanism that provides a useful guide during the process of knowledge discovery from data. The supervised information used in semi-supervised fuzzy clustering can be represented by a small amount of labeled data or by pairwise constraints that two instances belong to one cluster or not. In the literature there has been relatively little focus on semi-supervised approaches applied in the BD monitoring context.

Table 5. Main characteristics of the Psychiatric scenario ADP-PS2: **Semi-supervised prediction of the mental state.**

Psychiatric scenario: ADP-PS2	
Scenario	**Semi-supervised prediction of the mental state**
Illustration of system's behaviour in a specific	Systems aims to predict what is the mental state given partially labeled acoustic data. Once a portion of new data (e.g., for a new day) is collected, the system updates whether the state change occurred conditional on his current state. Synthetic data or simulation approaches

[8] Kamińska, O., Kaczmarek-Majer, K., Hryniewicz, O. **Acoustic Feature Selection with Fuzzy Clustering, Self Organizing Maps and Psychiatric Assessments.** Proceedings of the IPMU 2020: Information Processing and Management of Uncertainty in Knowledge-Based Systems, (2020) 342-355. DOI:10.1007/978-3-030-50146-4_26

[9] Casalino, G., Dominiak, M., Galetta, F., Kaczmarek-Majer, K. (2020) **Incremental Semi-Supervised Fuzzy C-Means for Bipolar Disorder Episode Prediction**, IEEE Conference on Evolving and Adaptive Intelligent Systems (EAIS), Bari, Italy, 2020, pp. 1-8,

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	may be used to improve the overall performance of the semi-supervised learning. The outcome of this scenario is the prediction whether the mental state is changing or will be changing in the coming days in particular direction. At least two fuzzy semi-supervised clustering algorithms that enable taking datasets from ADP-PS1 as input are compared.	
	User/users:	Researcher/programmer that is designing and implementing system that aims at monitoring of mental state change using sensor data.
	Setting / context	The system has historic data about smartphone usage and some history about psychiatric visits.
	Interacting system	The system uses partially labeled data.
	Users' goals	The end user needs to implement whether the mental state has changed or is likely to change soon.
	Initial status	Datasets about smartphone usage and about psychiatric states.
	Potential extension for the future	(1) Semi-supervised federated learning (2) Real-time distributed semi-supervised uncertainty-aware prediction
System functionalities	1. Feature selection (Uncertainty-aware approach) 2. Semi-supervised learning 3. Comprehensive cross-validation of sensor and psychiatric data ✓ leave-last-visit-out validation ✓ leave-one-patient-out validation ✓ leave-last-day-out validation	
Owner	KKM	

2.3. ADP-PS3: Dashboard for monitoring mental state change with smartphone data

This psychiatric scenario aims at readable visualization about current patients' data both from patients visits and mobile recordings. Dashboard, here also defined as report characterized with legible important information on foreground, is aimed to present:

(1) basic patients' information gathered during the visit;
(2) phone call statistics;
(3) and results received from executed algorithms with its visualizations.

The dashboards developed within this scenario are aimed to provide information in a simple and transparent way, which can be helpful e.g., for psychiatrics. As a pre-requirement of a dashboard is to select a patient number. Then, there will be presented the most important information about the given patient with a prediction whether the mental state is changing or will be changing in the coming days. Information will be presented using charts and easy to interpret statements in natural language. Then, dashboard will also contain a section with patient basic information gathered during the visit, like last BD states, taken medications, or remaining information describing mood. A dashboard will present tables and charts with basic statistic about patients' mobile recordings like number

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of incoming, outgoing, missed phone calls broken down into several different time periods, e.g., week, month. Those basic information could indicate patients activity during the study.

Next, we are going to present series of simulation with results received from executed semi-supervised algorithm like comparing prediction to remaining data or in comparison to the rest of patients. Most of it will be presented using, charts or tables. At the end of dashboard there will be presented features importance and explanation for particular patient' states to indicate which acoustic features could change the patient's condition.

Examples of patients' results will be carefully analyzed to maximize the interpretability of provided dashboards. There will be visible a short outline with structures of that dashboard with links to particular section of the reports (like prediction, basic information etc.) to be able to use this dedicated tool easily.

Table 6. Main characteristics of the Psychiatric scenario ADP-PS3: **Dashboard for monitoring mental state change with smartphone data**

Psychiatric scenario: ADP-PS3		
Scenario#3	**Dashboard for monitoring mental state change with smartphone data**	
Illustration of system's behaviour in a specific	The outcome of this scenario is a report (dashboard, web summary) about the patient status and potential change generated for selected patient. Data from patients visit and from mobile recording will be used for generating the dashboard. Information like patients history, mobile recording statistics and result received using algorithm will be presented on dashboard using mostly tabels and charts to improve comprehension of data.	
	User/users:	Medical doctor that is leading patient's treatment and monitoring
	Setting / context	Patient uses smartphone on a daily basis and transfer data to the system. System has some historic information about smartphone usage and history of his psychiatric visits.
	Interacting system	The system verifies whether a change is observed. The outcomes from this verification are presented on a simple dashboard with remaining information.
	Users' goals	If the patient is in euthymia, the question is whether he stays in euthymia or a change is observed. If he is in affective state (disease episode), the question is whether he stays in this affective state or whether he returns to euthymia (stable state). The end user needs to know: (1) Whether the change occurred (2) What is the current state – basic information about patient (3) Why the system predicts this affective state (e.g., features explanations)

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	Initial status	Information about the patient current state with main indicators defined (about his smartphone usage and about his psychiatric state)
	Potential extension for the future	(1)End User gets daily notifications whether a change of the patient state is detected. (2)End user (medical doctor) approves or disapproves the alarms judging on the information presented
System functionalities	1.Generation of the web-based summary about patient historic data (sensor and psychiatric data combined) and about his/her current status 2.Generation of the web-based summary about the observed mental state and main outcomes of the predictive modeling.	
Owner	OK	

3.Pilot 2: Predict depression with Locomotor Data collected from sensors Pilot (LDP)

This pilot aims at predicting depression with locomotor data collected from wearable sensors. It consists of two main components: learning model for prediction and generating dashboard. In Figure 3, an UML use case diagram is created for the Locomotor Data Pilot (LDP).

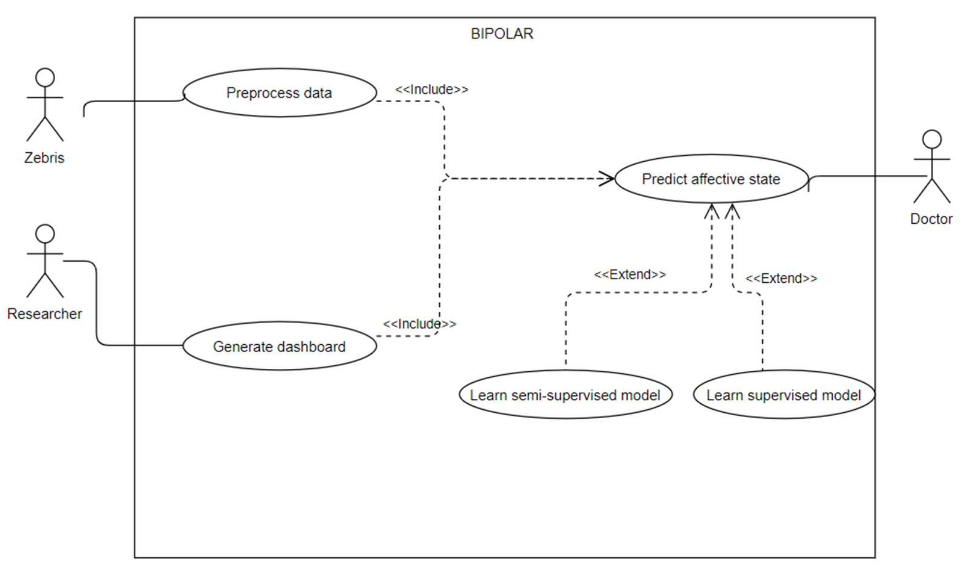

Figure 3. Use case diagram for BIPOLAR in Pilot 2 aiming at predicting depression with locomotor data collected from wearable sensors.

Main actors are described in Table 7.

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Table 7. Main actors of LDP pilot

Actor (type)	Description
Zabris (system)	Zebris software with wearable sensors able to extract features from movements.
Researcher (person)	The typical user is **a researcher with some basic programming skills**. The system will be implemented as a library in one of the high-level programming languages (Python or R). The user must know how to interact with the library in a given programming language, but the basic programming skills are considered enough. Hence, it can be either (I) **a psychiatrist with programming skills** that wants to explore available data, or (ii) **a (trained) software engineer** building a separate tool using this system to preprocess the data.
Doctor (person)	Psychiatrist that needs more information about one considered patient.

Analysis is based on data received from Unterberger stepping test[10 11 12 13]. It is a 1 min stepping in place with arms stretched forward as in the Romberg standing test. Figures 4 and 5 illustrate this stepping test and the station with Zebris equipment needed to perform it.

Figure 4. Illustration of the stepping test.

[10] https://www.cambridge.org/core/journals/journal-of-laryngology-and-otology/article/abs/unterberger-stepping-test-a-useful-indicator-of-peripheral-vestibular-dysfunction/31641D94757D800E77D74C5BD453B6FA

[11] Haralanov S, Haralanova E, Milushev E, Shkodrova D. ***L ocomotor movement-pattern analysis as an individualized objective and quantitative approach in psychiatry and psychopharmacology: clinical and theoretical implications*** . Psychiatry and Neurosciences Vol. III, Chapter32. Springer Nature Switzerland AG. 2019. pp.387-416. https://doi.org/10.1007/978-3-319-95360-1_32

[12] https://www.tandfonline.com/doi/abs/10.3109/00016485909129172?src=recsys

[13] https://www.tandfonline.com/doi/full/10.3109/02703181.2015.1128510?src=recsys

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Figure 5. Station with the Zebris equipment for performing the stepping test.

BIPOLAR has access to the locomotor data from stepping test gathered by the team of Prof. Svetlozar Haralanov from University Hospital for Neurology and Psychiatry "St. Naum" in Sofia, Bulgaria. In particular, 527 people have been tested in two goups. First group: 322 patients with depression (depressive episode and recurrent depressive disorder). Second group: healthy 205 people (healthy controls).

Classical Unterberger stepping test (with eyes closed) has been extended by some additional variants, from which the most systematically studied are the simplified variant (with eyes open) and the complicated cognitive or motor variants (with eyes closed but with additional performance of cognitive or motor tasks). The different test variants are marked horizontally in order of consequence as: CE = closed eyes; OE = open eyes; CognTask (100-1) CE = Dual task: stepping in place *with closed eyes* + cognitive task consisting in reverse counting from 100 downwards (100, 99, 98, etc.); CognTask (100-1) OE = Dual task: stepping in place *with open eyes* + cognitive task consisting in reverse counting from 100 downwards; Motor task DDK CE = Dual task: stepping in place *with closed eyes* + motor task consisting in diadochokinesis (successive pronation or supination of the hands investigating alternate motion rates); Motor task DDK OE = Dual task: stepping in place *with open eyes* + motor task, consisting in diadochokinesis (successive pronation or supination of the hands that investigates alternate motion rates). The head movements of the investigated persons are recorded directly during the execution of each psychomotor test and thereafter they are analysed automatically by the computer program of Zebris.

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In principle we use various scales to measure psychometrically the degree of depression severity. These scales could be for self-assessment, i.e. Beck Depression Inventory (BDI) or for observer rating. The most used observer rating scales are the Hamilton Depression Rating Scale ($HAMD_{17}$) and the Montgomery-Asberg Depression Rating Scale (MADRS). They are used mainly in clinical trials for antidepressant drugs. The simplest assessment in the real clinical practice is by the clinical global impression severity ratings (CGI-S). As our patients are rated by different scales during the years, the most common assessment is by CGI-S $\geq$ 5 points. That means: moderate and marked depression: cut-off for MADRS: $\geq$ 25 and cut-off for $HAMD_{17}$: $\geq$ 20. In our data-base are selected patients with more clinically oriented criteria, which are much more relevant than the standard rating scales, since they calculate much more factors as: family anamnesis, premorbid functioning, initial manifestations of the illness, course (trajectory) of the illness, number of depressive episodes, frequency of these episodes, etc. The investigated patients are dynamically observed during the years as well as during the index episode until the achievement of clinical remission (longitudinal instead of cross-sectional approach). Therefore, we could be sure that the patients included are with major depressive episode and more concretely with recurrent depressive disorder (but not with bipolar disorder).

3.1.LDP-PS4: Prediction of depression using loco-motor sensors

Based on the analysis of the data from the results of the stepping test, the BIPOLAR makes it possible to support end user in distinguishing healthy controls from depressive patients.

Table 8. Main characteristics of the Psychiatric scenario LDP-PS4: **Prediction of depression using loco-motor sensors.**

Psychiatric scenario	
Scenario #4	Prediction of depression using loco-motor sensors
Illustration of system's behavior	Systems aims to predict what is the depression level given partially labeled locomotor data. Once a portion of new data (e.g., for a new patient) is collected, the system updates what is the mental state of this patient. Synthetic data or simulation approaches may be used to improve the overall performance of the semi-supervised learning algorithms. Background information about the medical context of this scenario: (1) Doctor is in a position to recognize that the patient is in a depression, based on the results of the tests. (2) For the moment lateral sway and steps are very important locomotor parameters for discriminating between patients and controls as well as between activated and inhibited depressive patients. (3) LatS (lateral sway parameter): It's measured in cm; It reflects the unconscious (involuntary/automatic) psychomotor reactivity. Higher values mean *slowed down* unconscious (involuntary/automatic) psychomotor reactivity (hypo-reactivity). (4) Steps parameter (number of steps per minute; speed of locomotion; 1 minute stepping in place with arms stretched forward): It reflects the conscious (volitional) psychomotor/locomotor activity. Higher

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	values mean *speeded up* psychomotor/locomotor activity (hyper-activity). Correspondingly, lower values mean *slowed down* psychomotor/locomotor activity (hypo-activity). (5) We're interested in the main parameters (lateral sway and steps) as compared between subgroups (predominant/smaller/relatively small) and between test variants (CE:closed eyes+CognTask:counting from 100 to 1 and OE:open eyes+CognTask: counting from 100 to 1). Some examples of abnormal locomotor/psychomotor behavior: two poles of activation vs. retardation as measured by lateral sway, two poles of activation vs. retardation as measured by steps, two poles of dissociation between them, two poles of longer vs. shorter longitudinal deviation, two poles of right-sided vs. left-sided angular deviation, two poles of right-sided vs. left-sided self-spin. two poles of dissociation between them, etc.	
	User/users:	Medical doctor that is leading patient's treatment and monitoring
	Setting / context	Doctor uses Zebris/Unterberger stepping test and makes an assessment based on the data collected by sensors and their analysis carried out using the software developed within the project.
	Interacting system	System carries out analysis of collected data. Depending on the configuration and elevated/lowered values of the measured parameters doctor obtains some results supporting the diagnosis of the lack or presence of depression.
	Users' goals	(1) Patient's state assessment – ill (depression) / healthy (no depression) (2) Information about the predictive process
	Initial status	System has access to a database enabling learning mental state based on results of a stepping test.
	Potential extension for the future	As a next step (in the future) we could include analogous data from patients with bipolar depression. Within the groups of depressive patients and healthy controls the data analysis could discover not only over-activated and over-inhibited locomotion but also two poles of asymmetric locomotion - right-sided vs. left-sided angular deviation and/or self-spin, as well as some case of dissociated asymmetry: right-sided angular deviation combined with left-sided self-spin or left-sided angular deviation combined with right-sided self-spin.
System functionalitie s	(1) Prediction of affective state (2) Data annotation	
Owner	IZ	

3.2.LDP-PS5: Dashboard for monitoring mental state change with locomotor data

This psychiatric scenario aims at delivering a report (also known dashboard) for the medical doctor. Medical doctor will receive information about the results of Unterberger stepping test and the predicted mental status.

Preliminary content planned for the dashboard for a single patient consists of the following blocks:

1. Chance (%) that the patient is in depression based on the stepping test"s resultsSummary about important variables (e.g., lateral sway and steps);
2. Results received from previous visits (if any);
3. Visualization of the obtained results together with a comparison to other patients.

The dashboard is designed to present information about a single patient at a time. It's supposed to help the doctor in assessing whether the patient is at risk of depression. The patient's profile should contain information about important target parameters (e.g. lateral sway or number of steps). The results are presented graphically and legibly for the doctor. The comparison visualizations will take a form of 2-d scatterplots showing relevant historical data from other healthy and unhealthy individuals and the new data point. Such plots can be produced for pairs of variables, e.g. lateral sway and number of steps.

The doctor receives a report which can be a base for a further, in-depth diagnosis. At a later stage, the developers, in collaboration with the doctors, decide which parameters are included in the report and in which graphical form. They are going to make a decision regarding possible variants for a one patient of data, as well as which ones and in what range it's going to appear in the report. Possible interpretations of individual parameters will also be the subject of further work.

Table 9. Main characteristics of the Psychiatric scenario LDP-PS5: **Dashboard for monitoring mental state change with locomotor data**

<table>
<tr><td colspan="3">Psychiatric scenario</td></tr>
<tr><td>Scenario#5</td><td colspan="2">Dashboard for monitoring mental state with locomotor data</td></tr>
<tr><td rowspan="4">Illustration of system's behaviour in a specific</td><td colspan="2">Dashboard summarizes the results for a given patient. The outcome of this scenario is visualization of the patient history and prediction about the mental state based on the results from Unterberger stepping test. Dashboard enables also to compare the data of a given patient to other available measurements, and calculates chances that the patient is in an affective mental state (e.g. in depression in the case of unipolar depression).</td></tr>
<tr><td>User/users:</td><td>Medical doctor</td></tr>
<tr><td>Setting / context</td><td>The system has historic data locomotor sensors and mental state of bipolar disorder, unipolar depression and healthy controls.</td></tr>
<tr><td>Interacting system</td><td>The interacting system is a report with interactive capabilities. The report will be a single file (e.g. a HTML</td></tr>
</table>

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		page) that can be opened in a web browser. The report will be delivered upon request (e.g. when a visit occurs and new data is collected).
	Users' goals	The end user needs a dashboard that support the diagnosis of the mental state.
	Initial status	Datasets about locomotor sensors and about outcomes of the psychiatric evaluation (mental states).
	Potential extension for the future	1. Adding more parameters received from Unterberger test beside lateral sway or number of steps. 2. Possibility of predicting a bipolardisorder additionally 3. A more interactive form of a report (e.g. R Shiny application),
System functionalitie s	1. Summarizing information from Unterberger stepping test in a form of a comprehensive report for the doctor; 2. Predicting chances of the patient being in affective state (e.g. depression in unipolar depression) based on the database of Unterberger stepping test results for healthy and unhealthy individuals.	
Owner	KKM	

4.Future work

BIPOLAR is not yet a distributed IT system, but a software component for computational purposes. Nonetheless, we foresee that BIPOLAR will be further developed after the completion of the project and in the long term will form a part of a comprehensive IT system in which hundreds of actors will be involved from different medical centers worldwide.

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