Protocol

Development of a Cohesive Predictive Model for Substance Use Disorder Rehabilitation Using Passive Digital Biomarkers, Psychological Assessments, and Automated Facial Emotion Recognition: Protocol for a Prospective Cohort Study

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Abstract

Background: Substance use disorder (SUD) involves excessive substance consumption and persistent reward-seeking behaviors, leading to serious physical, cognitive, and social consequences. This disorder is a global health crisis tied to increased mortality, unemployment, and reduced quality of life. Altered brain connectivity, circadian rhythms, and dopaminergic pathways contribute to sleep disorders, anxiety, and stress, which worsen SUD severity and relapse. Factors like trauma and socioeconomic disadvantages heighten risk. Digital health technologies, including wearables and machine learning, show promise for diagnosis, monitoring, and intervention, from relapse prediction to early detection of comorbidities. With high relapse rates and younger patient cases, these innovations could enhance the treatment outcomes of SUD.

Objective: The objective of this study is to develop and validate a predictive model with machine learning for the duration of therapy and the rehabilitation or relapse in patients with SUD, using digital physiological measurements, psychological profiles, automatic facial emotion recognition, and the emotional state during craving.

Methods: The study will be conducted with adult male patients with SUD at a rehabilitation center and control volunteers. Participants will undergo a self-reported demographic and psychological assessment, a clinician-administered craving and emotional reaction test, and will also be monitored using a smartwatch. SUD participants will be monitored for a total of 18 months (6 months during rehabilitation, an additional 12 months post discharge), and control participants for a total of 6 months. All participants will be reassessed at the sixth month of monitoring. The collected data will then be used to train models with a neural network, which will then be validated against other models and compared with other algorithms. Demographic, psychological, digital biomarkers, and craving profiles will be created, correlations will be analyzed, and they will be compared with controls to generate a digital phenotype of SUD. When the model achieves adequate validity (area under the curve of ≥0.80), a graphic user interface will then be designed for clinical use.

Results: The study is supported by the Program for the Improvement of Working Conditions for Members of the SNII and SNCA (PROSNII U006EST), and APPAC-VII-CUCS-2025 for Article Publication Fees, from the University of Guadalajara. The research protocol was approved by the University of Guadalajara (reference CI-01225) in January 2025. Recruitment of patients with SUD and control participants will take place from January 2025 through January 2027.

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Conclusions: As shown in recent studies, accessible and affordable wearables, like commercial smartwatches, combined with psychological, demographic, and emotional state data, used with a machine learning predictive model, may be able to be used as tools to enhance SUD rehabilitation and prevent relapse.

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Introduction

Substance user disorder (SUD) is characterized by the excessive consumption of a substance, persevering and repetitive conducts of reward-seeking and reinforcing, regardless of the harmful physical, cognitive, behavioral, and social consequences. The disturbances created by SUD are related to alterations in brain connectivity, even after successful remission of substance use [1].

Worldwide, SUD is considered a multidimensional and critical health crisis phenomenon, connected with an increase in mortality, development of diseases, reduction of safety, increase in unemployment rates, and reduction of quality of life [2].

Research has suggested a link between the alteration of circadian rhythms and SUD in its earlier stages, that in time, due to the alteration of dopaminergic and glutamatergic pathways [3], results in sleep disorders. The development of these has been found to be a pivotal factor in the progression, severity, and relapse of SUD. These findings confirm a bidirectional relationship between SUD and sleep disorders [4-6].

Increased levels of anxiety and stress have also been associated with SUD, specifically in the abstinence and craving stages of the addiction cycle [7-12]. Anxiety and stress have also been related to an increase in heart rate, sweating, oxygenation levels, and atypical patterns of physical activity, all of which have been found in SUD [13-17].

In addition to physiological biomarkers, psychological evaluation has identified critical changes in executive function, decreased emotional regulation, and heightened levels of anxiety and depression [18-22]. Furthermore, environmental factors have been recognized to increase the risk of developing this disorder, like adverse experiences during childhood, violent or traumatic events, and disadvantageous economic conditions [23-29].

The first studies using digital technologies in mental health disorders were done on patients with major depressive disorder (MDD) through ecological moment assessment questionnaires through mobile devices, increasing a better treatment adherence [30-33]. After this study, various researches have been carried out, using varying methodologies and with objectives going from early diagnosis to prognosis of various complex pathologies, such as Alzheimer disease and major neurocognitive disorders some of the areas, where wearables and virtual reality have been used, allowing to observe cognitive decline and behavioral patterns [34-39].

Machine learning (ML) has also been used as a tool for the diagnosis of anxiety disorders with the use of speaking patterns, gaming activities, and self-reports [40-49]. It has also allowed researchers to measure the severity and variability of that disorder in varying environments through wearables, allowing remote intervention and through simulations [30,48,50-52]. It has also been used in predictive models for early depression diagnosis through smartphone use, severity, and progression through physical activity, sleep, and social interaction data [53-61]. In addition, ML models (MLM) have been trained to detect relapse in MDD and risk of suicide [62-64]. Similarly, it has been used to predict the start of a psychotic episode 5 days before it by using patterns of movement and sleep disturbance [63,65].

With a 60% relapse rate, an average of 5 recovery attempts required for full remission, and a growing number of new patients with SUD presenting at younger ages [2], this disorder represents a significant opportunity for digital health technologies. These tools, often used in managing cognitive and mood disorders commonly comorbid with SUD, have the potential to enhance treatment effectiveness and reduce relapse rates.

This study aims to integrate physiological, behavioral, and psychological data through digital technologies to develop comprehensive digital profiles of individuals with SUD. These profiles will be analyzed using ML tools to identify clinically relevant patterns. The resulting models are intended to serve as complementary tools in clinical practice, supporting treatment decisions, improving prognostic accuracy, and facilitating the monitoring of patients in remission.

Methods

Goal and Objectives

The purpose of this study is to develop and validate a predictive model of substance use relapse or rehabilitation with ML in patients with SUD. This will be through using digital physiological measurements (digital biomarkers), demographic and psychological profiles, automatic facial emotion recognition, and the emotional state during craving (ESDC).

Study Design

This study adopts a prospective cohort design, using data collected from nontraditional experimental groups to develop a MLM aimed at predicting clinical outcomes in the rehabilitation or relapse of patients with substance use disorders. The model will rely on comparative analyses between groups,

identifying patterns in physiological, psychological, and emotional reactivity data to enhance predictive accuracy.

No interventions will be implemented in either group as part of this study, ensuring that all collected data reflect naturalistic conditions and minimizes external influence on the observed outcomes.

Participant Identification and Randomization

Participants in both groups will be randomly assigned a unique identification number, which will be used throughout the study to ensure anonymity and meet the inclusion criterion of randomization. Psychological assessments conducted at the rehabilitation center will be conducted through self-reported questionnaires, administered in a traditional pen-and-paper format, overseen by the institution's psychologists, who will use only the assigned ID numbers during the digitization of all data. Control participants will complete all psychological tests in a self-reported computer-based format, using their ID numbers, which will be randomly assigned at the start of the monitoring period.

A secondary randomization process will be conducted to create k-clusters of data before training the ML algorithm. This step will also include the selection of test data for verification purposes, ensuring robust validation of the model.

Blinding

Due to the nature of this study, neither the participants nor the first group of research staff will be blinded to group assignments. However, the group allocation of participant ID clusters will remain concealed from the second group of researchers. This second group will be responsible for data management, training the ML algorithm with the predictive model, and conducting validation, verification, and testing of the highest-performing models.

Timeline

This study will include 2 types of observations: continuous passive monitoring and active surveys conducted at specific time points. Passive monitoring will occur continuously for 6 months in both groups, followed by an additional year for participants with SUD after their discharge from the treatment facility. Active surveys will be conducted at three time points: (1) baseline session or baseline, (2) 3 months after baseline, and (3) 6 months after baseline.

For digital monitoring purposes, smart bands provided to participants will be synchronized with a smartphone at the baseline session. Psychological assessment will be conducted within the first 15 days after baseline. Retesting will take place during the 15 days prior to the 6 months after baseline. Emotional reactions to cravings will be assessed at two points: (1) 3 months after baseline and (2) at 6 months after baseline (Figures 1A-1F).

Figure 1. Timeline of experimental procedures. (A) Demographic and psychological assessment, a battery of interviews and tests will be applied at 2 timepoints. (B) Digital measurements with the smart band Xiaomi Redmi Smart Band 8, starting on day one for controls, and after the first month of treatment for substance use disorder. (C) Evaluation of the emotional state during craving halfway through the digital monitoring period (third month), and at the end of it. (D) Data preprocessing is required for all 3 data sources. (E) Training in a machine learning predictive model in neural networks. (F) creation of a graphic user interface for clinical use.
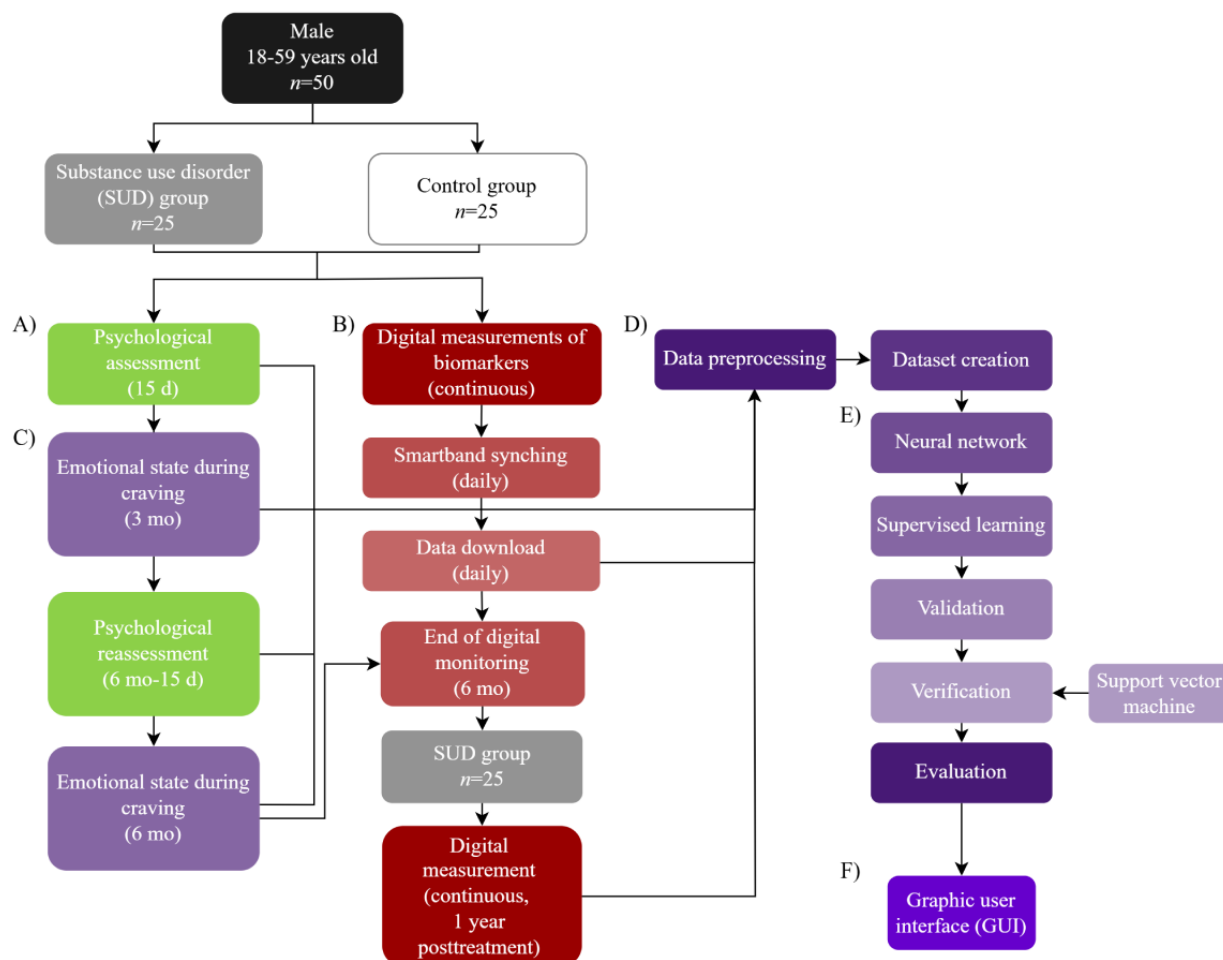
Participants and Study Setting

Sample Size

The minimum sample size was determined using Epidat 4.2 software (Xunta de Galicia), following the equation for estimating the comparison between independent means. The calculation was based on data reported by Rykov et al [30], in a study where patients were screened using wearable devices, and (MLMs were applied (Textbox 1).

Textbox 1. Sample characteristics.

- Variance: distinct
- Standardized mean difference=2.54
- Expected SD of population 1=1.6
- Expected SD of population 2=3.21
- Ratio between sample sizes=1
- CI=95%
- Statistical power=80%

In addition, based on the rule of one-to-ten for artificial neural network (ANN) models suggested by Kavzoglu and Mather [31], in which a sample should be at least 10-100 times the numbers of independent variables (4 in this study, based on the 4 suggested profiles), a sample of 40-400 participants was obtained. Therefore, a minimum sample size of 25 was determined for each group. Participants will be recruited within 2 years of the beginning of the study, aiming for recruitment greater than 25 per group.

Recruitment

Participants for the SUD group will be recruited from a male-only, age-restricted inpatient drug rehabilitation facility in Cajititlán, Mexico. Eligibility criteria include being male, aged 18-59 years, and actively participating in a therapeutic community treatment program for SUD, with a cognitive behavioral therapy approach. Furthermore, candidates must undergo their first rehabilitation attempt within this specific program and be under medication management for any possible mental health comorbidity diagnosed with the Mini International Neuropsychiatric Interview (MINI) or physical disease. Finally, participants are required to review the privacy and safety terms and provide informed consent before joining the study. Smartwatches will be synchronized with a community smartphone by the personnel of the rehabilitation center, in accordance with the restricted access to smartphones.

Control Participants

Control group participants will be recruited through an open call for volunteers in the ZMG area, restricting the sampling to similar sex and age characteristics of the patients from the rehabilitation facility. To be eligible, individuals must be male, aged 18-59 years, have no history of SUD, either diagnosed or self-reported, with no current use of substances, excluding caffeine. They must review and agree to the privacy and safety terms, as well as the requirements for active participation. In addition, participants are required to commit to a six-month study period, synchronize and upload their data weekly, and attend scheduled meetings with the research team. In case an individual is interested in participating in the study, but does not have access to a personal smartphone, a device will be provided.

Exclusion Criteria

The exclusion criteria have been established for both groups equally. Individuals with physical conditions that significantly affect mobility, impede the use of a smart band or the registry of facial expressions, such as facial (eg, craniofacial abnormalities, facial nerve palsies, or severe neurological conditions) or neurological disorders, are ineligible. In addition, patients with a history of heart conditions, breathing issues, as well as significant vision and hearing impairment will be excluded, as these conditions might affect the measurements.

Withdrawal Criteria

Participants will be withdrawn from the study under the following circumstances: failure to use or misuse of the smart band for more than 5 consecutive days or exceeding 20% of the six-month period will result in the cessation of monitoring, with participants being notified, the device retrieved, and the data discarded. Relapse in substance use for the SUD group or the onset of addictive behavior for controls will also lead to immediate withdrawal; if the exact timing of such behavior cannot be determined, the corresponding data will be excluded. Finally, participants who voluntarily drop out of the study or request the removal of their data will be withdrawn, and their data will be discarded.

Study Setting

Participants will be evaluated in person at the key time points outlined in Figure 1 by health care professionals trained in conducting clinical interviews, administering psychological tests, and assessing the ESDC. For patients with SUD, assessments will take place in a designated area within the rehabilitation treatment facility, ensuring both privacy and comfort. Control group participants will be assessed at the University Center of Health Sciences, University of Guadalajara, in Guadalajara, Mexico, by trained health professionals.

Passive monitoring of biological and digital measurements using a smart band will be conducted for at least 22 hours per day, allowing a threshold of 2.4 hours (20%) of lost daily data, 7 days a week. Participants will be required to wear the device during sleep. Participants' physiological activity will be recorded during various activities and across diverse locations.

Data Collection, Storage, and Protection

Digital measurements will be downloaded from a Xiaomi account as a password-protected zip file. The csv files containing data from the linked devices will be processed and coded before being securely stored for future use. Clinical data will be entered into the database under a unique study ID number, either directly from source materials or from the instruments used for assessment.

In compliance with ISO (International Organization for Standardization)/IEC (International Electrotechnical Commission) 29100 guidelines and the General Data Protection Regulation (GDPR) [66,67], all data will be stored in encrypted storage units housed within the Department of Neuroscience at CUCS, University of Guadalajara. In addition, all files will be backed up on an encrypted cloud system hosted by the University of Guadalajara servers. During the study, access to these databases will be restricted to authorized study staff with the necessary training and permissions, ensuring the privacy and confidentiality of participants.

Instruments

The study instruments that will be used in this protocol to measure each assessment category referred to in the timeline (Figure 1), are presented in Table 1.

Table 1. Study instruments.

Instrument	Period				
	Baseline	3 Months	6 Months	18 Months	Continuous
Wearable: Xiaomi Redmi Smart Band 8[a]	✓	✓	✓	✓ [b]	✓
Demographic survey[c]	✓				
The Adverse Childhood Experiences Assessment (ACEs)[d]	✓				
The University of Rhode Island Change Assessment Scale (URICA)[d]	✓				
The Alcohol, Smoking and Substance Involvement Screening Test (ASSIST)[d]	✓				
The Beck Depression Inventory (BDI-II)[d]	✓				
The Beck Anxiety Inventory (BAI-II)[d]	✓				
The Pittsburgh Sleep Quality Index (PSQI)[d]	✓		✓	✓ [b]	
Wechsler Adult Intelligence Scale IV (WAIS-IV): Digit Span and Letter-Number Sequencing subscales[d]	✓		✓		
Emotional Pictures Database (EmoMadrid)[e]		✓	✓		
Mannheimer Craving Scale (MaCS)[e]	✓	✓	✓		
Automatic facial emotion recognition software (FER)[e]		✓	✓		

[a]Digital measurement of biomarkers.

[b]Substance use disorder group only.

[c]Demographic assessment.

[d]Psychological assessments.

[e]Emotional state during craving assessment.

Digital Measurement of Biomarkers

The Xiaomi Redmi Smart Band 8 will be worn on the user's nondominant hand, positioned 2 cm below the wrist bone and secured at a comfortable level, as instructed by the user manual. The device will be worn for a minimum of 22 hours per day, allowing for an anticipated loss of up to 2 hours of data due to activities such as recharging the device, synchronization with a smartphone, showering, and other routine tasks.

Physiological data, including heart rate (HR), peripheral capillary oxygen saturation, physical activity, stress, and sleep, will be collected using the device's shortest available measurement intervals. Data will capture periods of both high and low activity, during self-reported exercise, regular physical activity, and rest, and will identify any abnormalities in activity patterns.

Data synchronization, which facilitates upload to the associated Xiaomi account, will occur every 72 hours for all participants during the 6- or 18-month study period, as applicable. This data will be downloaded, preprocessed, and stored securely on an encrypted external hard drive and the institution's server for access by authorized research staff within 48 hours (Figures 2A-2E). Participants will receive a reminder notification if synchronization is not completed within 5 days.

Raw data will be used to compute digital the physiological features proposed in a MLM study by Rykov et al, [30] (Table 2).

Figure 2. Scheme of smart band data retrieval. (A) Data from the smart band Xiaomi Redmi Smart Band 8 via Bluetooth to the smartwatch it's been linked to for synchronization. (B) Through the Xiaomi app Mi Fitness, the data of the monitored period will be uploaded to the account's cloud to be downloaded by the researchers. (C) Raw data will be extracted, labeled, and preprocessed. (D) All data will be saved in an assigned encrypted server, property of Universidad de Guadalajara. (E) Alternatively, a second copy will be done on an encrypted external hard drive.
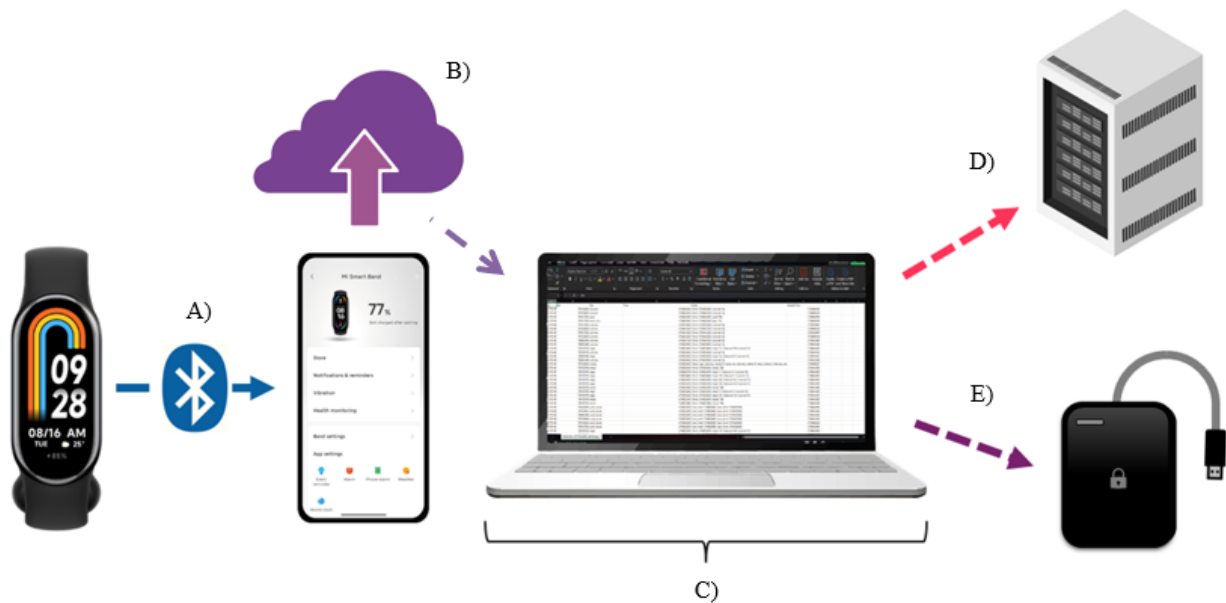
Table 2. Summary of raw measurements and physiological features.

	Raw data	Physiological features
Physical activity	Calories, steps, vitality, and time standing up	Daily footsteps, sedentary time, light physical activity, moderate physical activity, and vigorous physical activity
Heart rate (HR)	Beats per minute (BPM), maximum and minimum BPM, and single measure	HR resting HR, daytime HR, nighttime HR, HR delta, and HR root-mean-square successive differences
Sleep	Type of sleep, wake-up time, bedtime, and awake	Coefficient variance, time in bed, total sleeping time, sleep efficiency, sleep onset latency, waking after sleep onset, and sleep midpoint
Rhythm	Activity peaks	Circadian rhythm: COSINOR and nonparametric measurements
Oxygenation	SpO_2[a] during daytime, single measures of SpO_2, and sleep time SpO_2	—[b]
Stress	Stress level and single stress measurements	—

[a]SpO_2 : peripheral capillary oxygen saturation.

[b]Not available.

Demographic and Psychological Assessment

Demographic information, such as age, place of birth, education, occupation, civil status, household income, housing characteristics, as well as medical and family history, will be collected at baseline. A form will be filled in by the participant, assistance from the trained research staff will be provided if it is required.

The psychological tests will be administered at baseline within the first 15 days of participation. A battery of self-report questionnaires has been chosen to assess for a history of childhood trauma (Adverse Childhood Experiences Assessment [ACEs]) [68], the presence of depression or depressive symptoms (Beck Depression Inventory [BDI-II]) [69], anxiety and stress (Beck Anxiety Inventory [BAI-II]) [70], sleep

disorders (Pittsburgh Sleep Quality Index [PSQI]) [71], and short-term memory (Wechsler Adult Intelligence Scale IV [WAIS-IV] subtests: Digit Span and Letter-Number Sequencing) [72]. Substance use–specific tests will aim to determine the type of substance, frequency and quantity of used drugs (Alcohol, Smoking and Substance Involvement Screening Test [ASSIST]) [73], level of substance craving (Mannheimer Craving Scale [MaCS]) [74], as well as the stage or frame of mind of the individual starting the therapeutic process (University of Rhode Island Change Assessment Scale [URICA]) [75].

To obtain a comparative measurement after treatment, depression, anxiety and stress, sleep disorders, short-term memory, stage of change and craving, will be reevaluated within fifteen days before the sixth month period of digital tracking ends (Figure 3).

Figure 3. Flowchart of the psychological test battery. WAIS-IV: Wechsler Adult Intelligence Scale IV;.
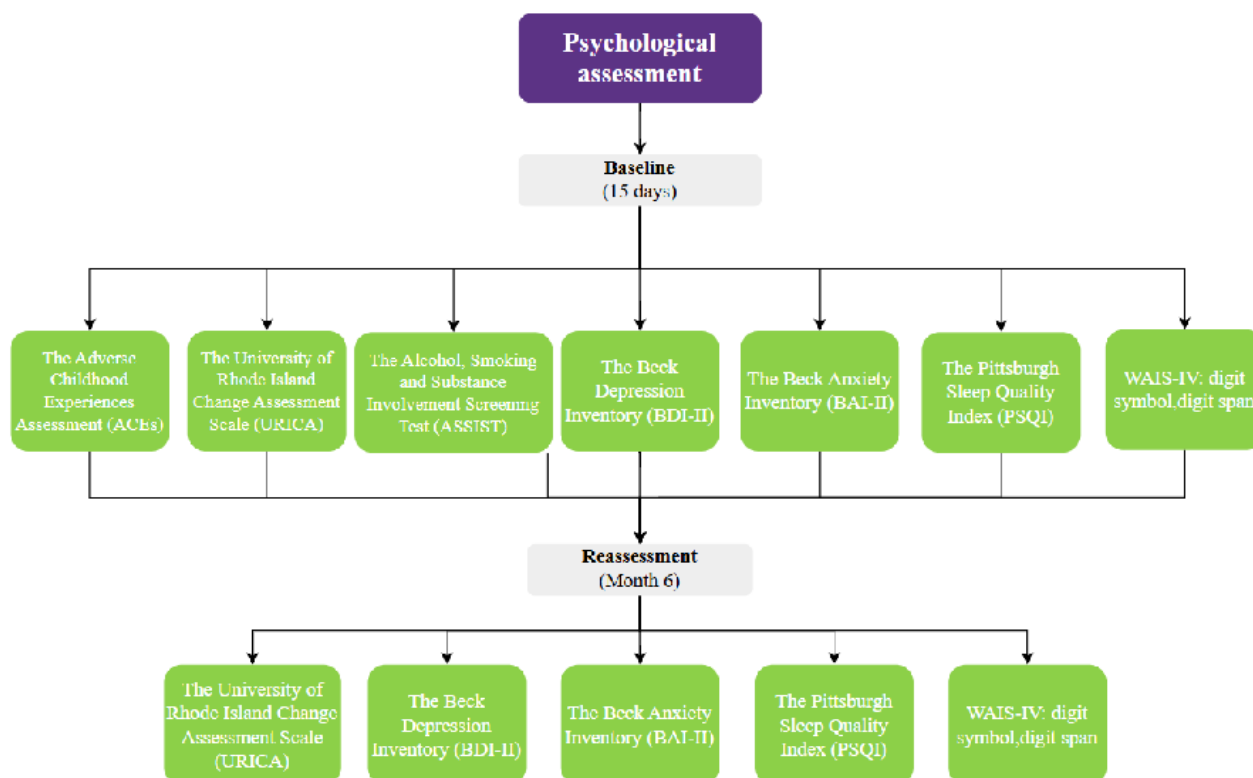
Emotional State During Craving

Given the significance of craving in SUD, a profile of the ESDC will be developed. Participants will be shown images from the Emotional Picture Database (EmoMadrid), designed by CEACO, which will be used as stimuli to elicit an emotional response [76]. Participants will be recorded all throughout the test, and Facial Emotion Recognition (FER) software. Software will provide an objective, real-time measure of participants' emotional expressions, which we will analyze in conjunction with their self-reported "Emotional State during Craving" data. The FER software is a personal script written in python, which automatically detects emotions by analyzing changes of facial expression of dataset that consists of 48×48 pixel grayscale images (32,298 images) of faces (FER-2013). Craving levels will be measured both before and after the test.

An experimental setup will be arranged to ensure optimal conditions for the test. This setup will include a white screen for image projection, an HD camera for recording the participant, and a controlled environment with low lighting and sound insulation to minimize distractions. A trained researcher will administer the test in this environment.

At the start of the experiment the FER software will be activated and participants will respond to items 9 to 11 of the MaCs scale (Table 1), which assesses craving-related anxiety levels, the effort required to resist urges, and impulses to consume substances. Following this brief questionnaire, the instructions for the experiment will be presented both visually and verbally to ensure the participant's full understanding.

A modified version of the protocol has been designed to suit the characteristics of the study population. Fifty images have been selected and categorized as positive, negative, neutral, or substance-use-related. These images have been further customized to align with the substance use profile of the participant group. Each image will be displayed for 1 second, after which participants will score it based on valence and activation. Once a score is provided, the next image will be shown. The procedure will be divided into 2 sets of 25 images, with a 30-second rest period between sets.

After the image presentation, participants will be reassessed using the same 3 MaCs scale items. In addition, they will be asked whether they experienced any changes in their emotional state after viewing the images and to provide a qualitative description of any observed shift (Figures 4A-4D).

All data obtained from the FER analysis, MaCS EMA, the EmoMadrid emotional response assessment and physiological data obtained by the smart band, will be used to observe the relationship between exposure to emotional and substance use visual stimuli, emotional response and craving.

Figure 4. Flowchart of emotional reaction to craving assessment. Steps of the brief craving assessment, in addition to a modified version of the emotional pictures database for valence and activation, including a sample of the chosen images of each category. (A) Positive images (n=15). (B) Negative images (n=16). (C) Neutral images (n=10). (D) Substance use-related images (n=9).
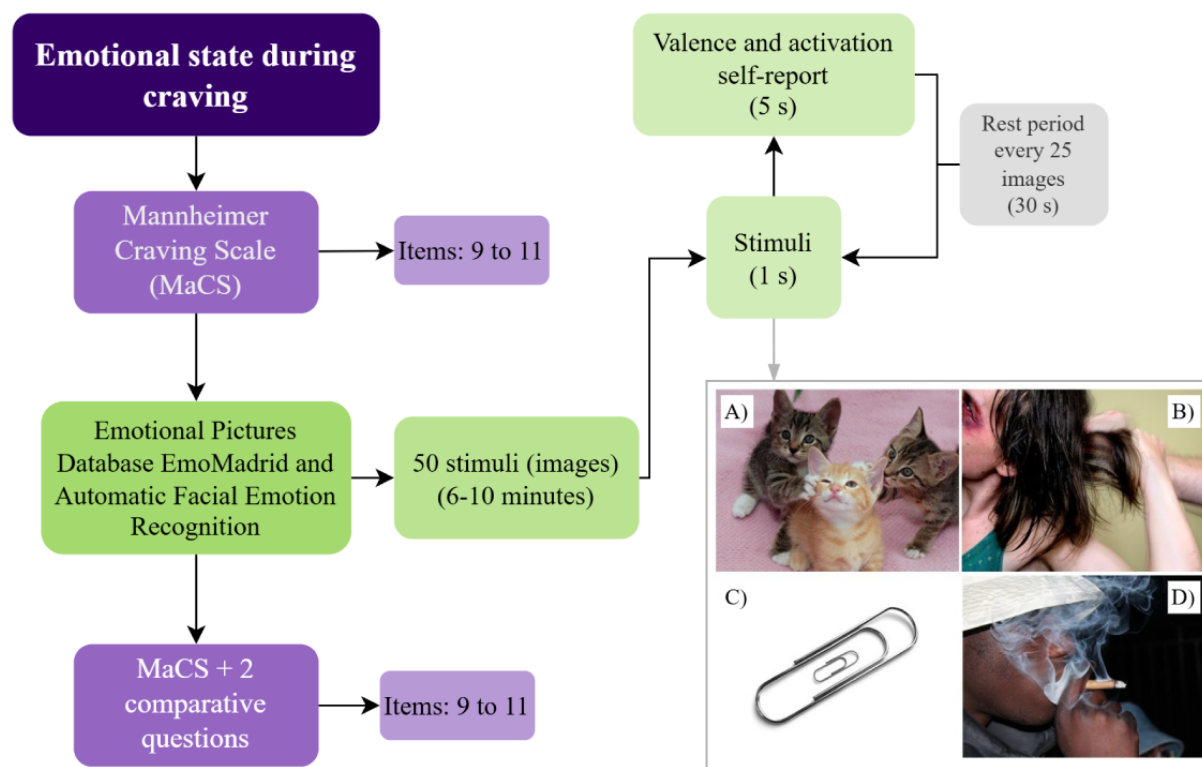
Statistical Analysis

Statistical analysis will be conducted using R-Studio IDE (version 4.3.1; Posit PBC), Prism GraphPad (version 9, GraphPad Software Inc), and MATLAB (version R2025a, MathWorks Inc). A descriptive analysis of normality (Shapiro-Wilkin normality test) means and medians, SD and error, variance (ANOVA or Kruskal-Wallis tests) will be performed. Correlation analyses (Spearman or Pearson) will be conducted to gain a preliminary understanding of the interactions between variables, as well as using time series analysis descriptive models to identify patterns, trends and cycles of activities by participants, and by groups. MATLAB will be used for advanced data processing and visualization, ensuring robust and comprehensive analysis.

Data Exclusion

Missing data will be addressed through imputation. If more than 20% of daily data samples are missing, they will be excluded. For missing data below this threshold, linear interpolation and neighbor mean imputation (k-nearest neighbor) will be applied during preprocessing using MATLAB.

The quality of data collected from the smart band will be assessed by correlating heart rate at randomly selected timestamps with oxygen saturation, activity levels, self-reported exercise, and sleep type during sleep hours. If atypical correlations are identified, 10 data points before and after the anomaly, along with 5 additional randomly chosen timestamps, will be reviewed. A day with more than 20% of faulty measurements will be excluded from the dataset.

Data will also be excluded in cases of device misuse, such as exchanging the device with other participants or nonparticipants, switching the wearing side without prior notice, or removing the device for more than 5 hours without informing the research team.

If the total sum of missing and excluded data exceeds 20% of the 6-month period, the participant's data will be removed from the study. Finally, for SUD participants, any measurements obtained during periods of substance use will be excluded, and their participation in the study will be terminated.

MLMs

Predictive MLMs for classification and regression will be designed, trained, and tested following the methodology outlined by Luo and colleagues [77] in their Guidelines for Developing and Reporting Machine Learning Predictive Models in Biomedical Research.

Data Preprocessing

Databases and labeling will initially be managed using Microsoft Excel (version 2412), after which MATLAB (version 2025a, MathWorks, Inc) will be used for data preprocessing. This process will include data cleaning and preparation to ensure the dataset is suitable for ML training.

Feature selection will be done following a filter methodology after correlation analysis to assess the correlation with the target

and statistical measures. All data obtained through the wearable device, psychological assessment and ESDC will be scaled through a z-score standardization for dimensionality reduction and integration across all modality.

The data will be divided into training, validation, and test datasets using a k-fold cross-validation approach. The dataset will be split into k folds, with 2 folds randomly selected: one for validation and another for testing. The remaining k-2 folds will be used for training. The number of folds will vary depending on the specific model, enabling a broader experimental variance and improved model evaluation.

Algorithms

Modeling will be conducted using MATLAB, with ANN serving as the base algorithm. Additional algorithms, including decision trees, random forests, and support vector machines, will be used for validation. This multialgorithm approach will facilitate a comprehensive comparison of predictive accuracy across various models.

Output

The primary objective of this study is to develop a MLM capable of predicting clinical outcomes in patients. To achieve this, the data will be segmented and classified into 5 categories (Figure 5). Around 2 of these categories will correspond to the first layer, which pertains to the duration of the therapeutic process, while the remaining 3 will focus on the latency of relapse, if any.

Figure 5. Model's possible outputs. These categories will be used as output labels of the predictive model and will allow the evaluation of the patterns detected from the input.
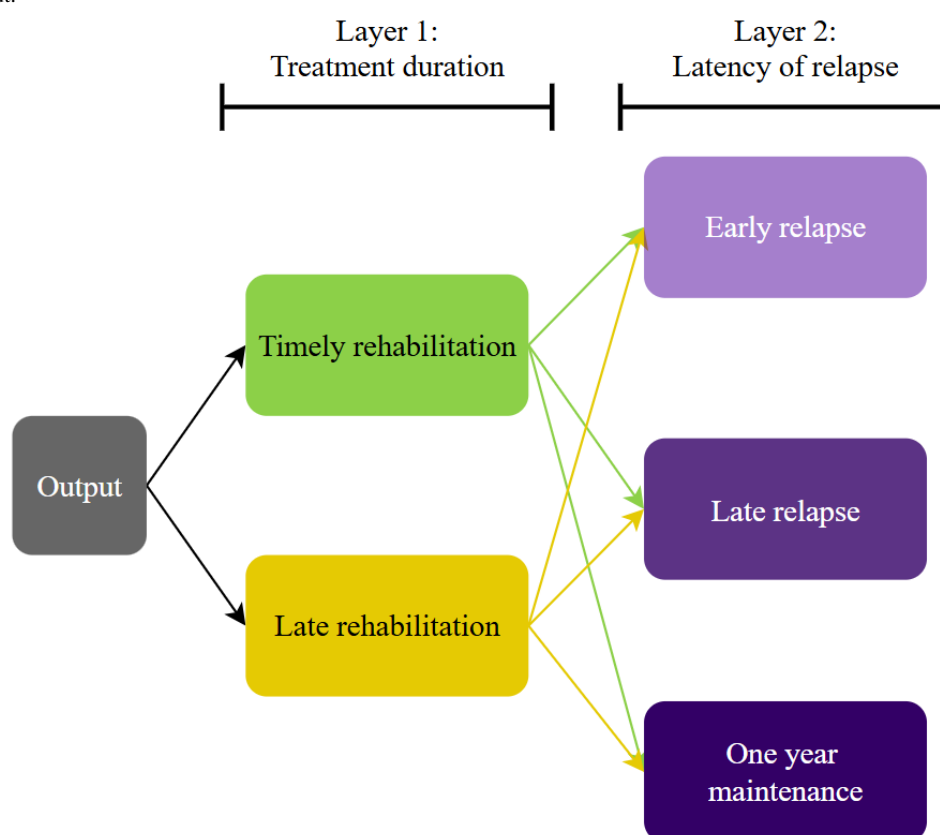
For the duration of the therapeutic process, the following labels will be used:

1. Timely rehabilitation: patients with SUD who complete the rehabilitation protocol within 7 months.
2. Late rehabilitation: patients with SUD who complete the protocol in 7 months or longer.

Regarding relapse latency, the labels will include the following:

1. Early relapse: substance use occurring within the first 6 months post discharge.
2. Late relapse: substance use occurring after 6 months but before the completion of 18 months post discharge.

3. One-year maintenance: patients who have abstained from substance use at the end of the 18-month postrecovery period.

Validation and Verification

All models and algorithms will undergo validation, verification, and testing using MATLAB's tools for model evaluation and hyperparameter optimization. These processes will assess precision, performance, and recall metrics. Optimal model performance will be defined by achieving an area under the curve (AUC) of ≥0.80 and F2 score of ≥0.8.

The output categories will serve as benchmarks to evaluate the validity, reliability, and precision of the models. The validation dataset will be used to perform initial comparisons both within

individual models of each algorithm and across different algorithms, replicating models with distinct architectures to refine performance.

For model verification, the test dataset will be used to determine final AUC and F2 scores. This final evaluation will confirm the models' effectiveness as ML tools for predicting rehabilitation outcomes and informing clinical decision-making.

Outcomes

Profiles

A total of 4 distinct subprofiles will be generated based on the results of the statistical analysis: (1) demographic, (2) psychological, (3) craving, and (4) digital biomarkers. These profiles will subsequently be integrated to create digital phenotypes for individuals with SUD.

Predictive Model

A predictive model will be developed to distinguish between healthy individuals and patients with SUD. In addition, the model will predict the duration of a rehabilitation therapeutic program and the length of sobriety adherence for individuals rehabilitated using the center's methodology. A minimum performance threshold of AUC≥0.8 and F2≥0.8 has been established to evaluate the model as fully functional.

Graphical User Interface

As an outcome of this study, a graphical user interface will be developed using MATLAB to enable practical application of the predictive tool within the rehabilitation center where this research is being conducted. The graphical user interface will facilitate clinical use of the model and allow for further training and refinement, expanding its potential utility in similar settings.

Ethical Considerations

This study has been approved by the Research, Ethics in Research and Biosafety committees of the Centro Universitario de Ciencias de la Salud, Universidad de Guadalajara (registry number 25-06; approval ID CI01225). This certifies that the research protocol adheres to the principles outlined in the Declaration of Helsinki of ethical research involving human participants, with a satisfactory quality and relevancy of the research.

Candidates will be provided with detailed materials in both written and digital formats for review before confirming their participation. All participants will be provided with an informed consent reviewed by the previously mentioned committees, signed by the participant, researchers, and two witnesses. Participants have the right to withdraw their consent at any time and may request the removal of their data from the study, in compliance with the Federal Law on Personal Data Protection and Article 16 of the Federal Constitution of the United States of Mexico [78,79].

All identifying participant information will be anonymized through a numeric ID system. Subsequently, the obtained data will be securely stored, either locked in a filing cabinet or in encrypted digital files and retained for a minimum of 5 years before being destroyed, as required by the Official Mexican Norm for Clinical Files (NOM-004-SSA3-2012) [80]. This information will only be accessible for purposes related to contact by the research group.

Participation in this study is entirely voluntary, and no financial incentives will be provided for joining or continuing in the study.

Results

The study is supported by the Program for the Improvement of Working Conditions for Members of the SNII and SNCA (PROSNII U006EST), and APPAC-VII-CUCS-2025 for Article Publication Fees, from the University of Guadalajara. The research protocol was approved by the University of Guadalajara (reference CI-01225) in January 2025. Recruitment of patients with SUD and control participants will take place from January 2025 through January 2027. As of June 2025, we have enrolled 35 participants, 18 patients with SUD and 17 controls. Data obtained from the device, as well as psychological and demographic data at baseline assessments and at 3 months are at the labeling and preprocessing stage of the data analysis. Results are expected to be published by the summer of 2028.

Discussion

Principal Findings

This study aims to evaluate the viability and efficacy of a predictive model designed to estimate the duration of a rehabilitation process and predict the likelihood of early, late, or no relapse in substance use, based on the digital phenotype of SUD. The hypothesis posits that an AUC of ≥0.80 and F2 of ≥0.8 will demonstrate that data collected from an affordable commercial smart band, demographic questionnaires, psychological tests included in the institution's base protocol, and the proposed use of FER combined with valence and emotional activation scoring during craving episodes can effectively support the creation of this predictive model.

The potential of this project is supported by several premises. Wearable devices have become increasingly accessible and seamlessly integrated into daily life. As of January 2024, GSMA Intelligence reported 125.4 million cellular connections in Mexico, and GWI estimated that 31% of internet users aged 16-56 years use a smartwatch or smart band [81]. Considering that the device used in this study is among the most affordable commercial smart bands and compatible with any mobile operating system, the development of a viable predictive model could introduce this tool as a complementary aid in SUD rehabilitation, enhancing the effectiveness of treatment strategies.

Wearable devices and MLM have been successfully applied to various mental health conditions. For example, passive physiological activity measurements and MLMs have distinguished depressive patients from healthy controls by correlating variations in circadian rhythms, nocturnal HR, and higher depression test scores [30]. Similarly, MLMs using passive data have predicted depressive, manic, or hypomanic episodes in patients with bipolar disorder (BD) by identifying sleep disturbances, circadian rhythm changes, and physical activity variations [82]. Furthermore, facial emotion recognition

combined with MLMs has been used to diagnose and predict alexithymia with an AUC of 0.80 [83]. In the context of SUD, MLMs have demonstrated potential by evaluating participant engagement, correlating stress and craving during recovery, and providing insights into treatment outcomes [84].

Psychological assessments remain a cornerstone for diagnosing and quantifying symptom severity in SUD, projecting recovery trajectories, and supporting research protocols. The psychological tests included in this study have been previously validated in SUD research, translated into Spanish, and recommended for clinical and diagnostic use [85-90]. Despite potential biases in self-reports, these tools have also been engaged in mental disorders such as schizophrenia and mood disorders like major depression and BD to develop MLMs and support symptom monitoring through digital technologies [30,46,60,91-96].

Digital tools for long-term symptom monitoring and clinical support during remission have been widely accepted in studies involving high-risk populations. For example, US veterans at risk of suicide provided valuable data on physiological activity and behavioral patterns surrounding suicide attempts through digital monitoring [64]. Similarly, high levels of acceptance have been observed among patients with BD, schizophrenia, anxiety, and major neurocognitive disorders, highlighting the feasibility of using such technologies in mental health research and clinical practice [34,37,56,60,93,97-102].

Limitations and Considerations

This study is subject to several limitations and potential risks of bias that must be acknowledged. Participants will be selected through convenience sampling of patients with SUD in a rehabilitation facility, limiting participation to cisgender male individuals between 18 and 59 years of age in both groups, therefore limiting the generalizability of results. The experimental status will be disclosed to them beforehand as well. This awareness could influence self-reporting in psychological tests and responses during exposure to visual stimuli related to substance use, potentially introducing bias.

While the Xiaomi Redmi Smart Band 8 has been selected for its cost efficiency and suitability for future clinical applications in rehabilitation centers, its sensors may have higher measurement errors compared to research-grade devices. Studies have indicated that similar consumer-grade devices generally exhibit lower precision. However, this trade-off is justified by the need to prioritize accessibility and scalability in clinical settings.

To identify events of physical activity, such as exercise, and atypical behavior, this study will rely in self-reporting through the app included in the Xiaomi Smart Band 8 device in the control group. Activity of participants with SUD will also be assessed by classifying their behavior according to the fixed schedule at the rehabilitation facility. Data will be clustered time-wise according to the time of the day and the reported activity accordingly, to reduce possible noise created by this variability. Since these events will rely on self-reported activities, a margin of error might be present in the observations in this time window.

Data clustering by groups before final testing introduces a potential risk that research staff may infer group assignments prematurely, which could influence the interpretation of results. The reliability of data used for training the models also depends on participants' proper use of the device and the accuracy of self-reported information, both of which carry inherent risks of bias that may impact outcomes.

The characteristics of the data and the results of ML training, validation, and verification may affect the algorithm's performance. There is a possibility that the baseline algorithm designed for this project might not achieve the desired accuracy or generalizability, based on the participants recruited by the cutoff time of recruitment. In addition, the possibility of an algorithm better suited for smaller sample sizes could be considered at a later stage of this study based on the available data.

To address these risks, the study will follow established guidelines for developing and reporting ML predictive models in biomedical research [103]. These guidelines provide a comprehensive framework for reporting in research articles and outline structured steps for model development, aiming to reduce bias and ensure robustness in predictive modeling [77].

Conclusion

As shown in recent studies, accessible and affordable wearables, like commercial smartwatches, combined with psychological, demographic, and emotional state data, used with a ML predictive model, may be able to be used as tools to enhance SUD rehabilitation and prevent relapse.

Authors' Contributions

DFQ performed conceptualization, formal analysis, software management, and supervision. APGP performed data curation, investigation, methodology, visualization, and contributed to writing the original draft and review and editing. KMP contributed to investigation, visualization, and writing—review and editing. JGE and SL were responsible for funding acquisition and provided resources. DEMF and SL handled project administration. DEMF also contributed to supervision.

Conflicts of Interest

None declared.

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Abbreviations

ACE: Adverse Childhood Experiences Assessment
ANN: artificial neural network
ASSIST: Alcohol, Smoking and Substance Involvement Screening Test
AUC: area under the curve
BAI-II: Beck Anxiety Inventory
BD: bipolar disorder
BDI-II: Beck Depression Inventory
EmoMadrid: Emotional Pictures Database
ESDC: emotional state during craving
FER: facial emotion recognition
GDPR: General Data Protection Regulation
HR: heart rate

IEC: International Electrotechnical Commission
ISO: International Organization for Standardization
MaCS: Mannheimer Craving Scale
MDD: major depressive disorder
MINI: Mini International Neuropsychiatric Interview
ML: machine learning
MLM: machine learning model
PSQI: Pittsburgh Sleep Quality Index
SUD: substance use disorder
URICA: University of Rhode Island Change Assessment Scale
WAIS-IV: Wechsler Adult Intelligence Scale IV