Protocol Title: Kintsugi Voice Device Pilot Study

Sponsor: Kintsugi Mindful Wellness, Inc.

1569 Solano Avenue No. 365
Berkeley, CA 94707

Principal Investigator: Grace Chang
Co-Investigators: Herbert J. Harman, MD, Roshanak Ramezani, MD

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Statement of Compliance

The study will be conducted in accordance with the International Conference on Harmonisation guidelines for Good Clinical Practice (ICH E6), the Code of Federal Regulations on the Protection of Human Subjects (45 CFR Part 46). All personnel involved in the conduct of this study have completed human subject's protection training.

SIGNATURE PAGE

The signature below constitutes the approval of this protocol and the attachments, and provides the necessary assurances that this trial will be conducted according to all stipulations of the protocol, including all statements regarding confidentiality, and according to local legal and regulatory requirements and applicable US federal regulations and ICH guidelines.

Principal Investigator: Grace Chang
Co-Investigators: Herbert J. Harman, MD, Roshanak Ramezani, MD

Signed: Grace Chang Date:

Signed: Herbert J. Harman, MD Date:

Signed: Roshanak Ramezani, MD Date:

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Key Roles

Principal Investigator	Grace Chang Kintsugi Mindful Wellness, Inc. 1569 Solano Avenue, No. 365 Berkeley, CA 94707 grace@kintsugihealth.com (310) 598-1553
Co-Investigator	Herbert Harman, MD Vituity Herbert.Harman@Vituity.com (541) 250-6368
Co-Investigator	Roshanak Ramezani, MD Vituity Roshanak.Ramezani@Vituity.com (858) 414 3774
Research Coordinator:	Mei-Hsin Cheng, PhD Kintsugi Mindful Wellness, Inc. 1569 Solano Avenue, No. 365 Berkeley, CA 94707 mace@kintsugihealth.com (650) 762-5087
Research Coordinator:	Danielle Faruq Kintsugi Mindful Wellness, Inc. 1569 Solano Avenue, No. 365 Berkeley, CA 94707 danielle@kintsugihealthhello.com (305) 215-0299
Research Coordinator:	Alexa Mazur Kintsugi Mindful Wellness, Inc. 1569 Solano Avenue, No. 365 Berkeley, CA 94707 alexa@kintsugihealth.com (610) 724-1431

Research Coordinator:	Do Hyung Kim Kintsugi Mindful Wellness, Inc. 1569 Solano Avenue, No. 365 Berkeley, CA 94707 david@kintsugihealth.com (314) 745-2316
Research Coordinator:	Alice Kim Kintsugi Mindful Wellness, Inc. 1569 Solano Avenue, No. 365 Berkeley, CA 94707 alice@kintsugihealth.com
Research Coordinator:	Bhavana Sreeram Kintsugi Mindful Wellness, Inc. 1569 Solano Avenue, No. 365 Berkeley, CA 94707 bhavana@kintsugihealth.com
Research Associate:	Rima Seiilova-Olson Kintsugi Mindful Wellness, Inc. 1569 Solano Avenue, No. 365 Berkeley, CA 94707 rima@kintsugihealth.com
Research Associate	Irina Vanzhula, PhD Johns Hopkins School of Medicine ivanzhu1@jhu.edu

Abbreviations

AE:	Adverse Event
AI:	Artificial Intelligence
API:	Application Programming Interface
ASADE:	Anticipated Serious Adverse Device Effect
CFR:	Code of Federal Regulations
DSM-5:	Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition
FDA:	Food and Drug Administration
GAD-7:	General Anxiety Disorder-7
GCP:	Good Clinical Practice
HCP:	Healthcare Provider
ICF:	Informed Consent Form
IRB:	Institutional Review Board
MDD	Major Depressive Disorder
PHQ-9:	Patient Health Questionnaire-9
PI	Principal Investigator
SAE:	Severe Adverse Event
SCID:	Structured Clinical Interview for DSM Disorders
USADE:	Unanticipated Serious Adverse Device Event

Glossary

Term	Definition
Accuracy	Rate of correct predictions made by the Device on a set of voice samples. Accuracy is estimated by using independent data that was not used at any time during the training process.
AE	An Adverse Event (AE) is any untoward medical occurrence, unintended disease or injury, or untoward clinical signs (including abnormal laboratory findings) in participants, users or other persons, whether or not related to the investigational Device.
Algorithm	A process or set of rules to be followed in calculations or other problem-solving operations, especially by a computer.
Anxiety Disorders	Anxiety disorders involve anxiety that does not go away and can get worse over time. Symptoms can interfere with daily activities. There are multiple types of anxiety disorders including generalized anxiety disorder, panic disorder, and various phobia-related disorders.
API	The Application Programming Interface is a type of software interface offering a service to other pieces of software. The API can be electronically interfaced and perform analysis with data transferred from computer-based applications.
Case Report Form	Printed or electronic document designed to record protocol-required information on each participant in a clinical study.
Device	In this protocol, the Device refers to the Kintsugi Voice Device.
Device Operator	Individual who operates the Device.
Dropout	After consenting to participation in trial (and therefore enrolling), a study subject discontinues participation in the trial (e.g., due to lack of interest, medical condition,

	adverse event). Dropout may simply be lost to follow up.
DSM-5	Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition; standard classification of mental disorders for clinicians for diagnosis of neurobehavioral and psychiatric disorders.
Endpoint	Key outcome measure in a clinical study.
GAD-7	General Anxiety Disorder-7, a widely used rating scale to measure the severity of anxiety based on participant responses to seven questions.
GCP	Good Clinical Practice.
Ground Truth	Data assumed to be correct by direct observation or measurement. In this study, the clinical Ground Truth involves the clinician evaluation via SCID.
ICF	Informed Consent Form is used to provide subjects with the information they need to make a decision to volunteer for a research study. ICF will include a summary of the research, potential risks, and potential benefits.
Indeterminate	The model does not have high confidence to classify the participant for depression and / or anxiety. Up to 20% of the results are expected to be indeterminate.
IRB	The Institutional Review Board is a group that has been formally designated to review and monitor biomedical research involving human subjects.
MDD	Major Depressive Disorder is a mood disorder that causes a persistent feeling of sadness and loss of interest. It affects how you feel, think, and behave and can lead to a variety of emotional and physical problems. Also called clinical depression.
ML	Machine Learning is the study of computer algorithms that can improve automatically through experience and by the use of data instead of being explicitly programmed. It is

	seen as a part of artificial intelligence. Machine learning algorithms build a model based on sample data, known as training data, in order to make predictions or decisions without being explicitly programmed to do so.
Phonemes	Distinct units of sounds.
PHQ-9	Patient Health Questionnaire-9 is a widely used rating scale to measure the severity of depression based on participant responses to nine questions.
PI	A Principal Investigator is the individual responsible for supervising the conduct of the clinical investigation, including protecting the rights, safety, and welfare of participants in a clinical trial.
PII	Personally Identifiable Information. Any representation of information that permits the identity of an individual to whom the information applies to be reasonably inferred by either direct or indirect means.
SAE	A Serious Adverse Event is an adverse event that leads to death or serious deterioration in the health of the participant.
SCID	Structured Clinical Interview is a semistructured interview guide for making the major DSM-5 diagnoses.
Sensitivity	Measure of the proportion of participants truly having clinically significant depression or clinically significant depression as verified by a clinician who are correctly identified by the Device as Positive for depression or anxiety (or True Positive Rate). Sensitivity = (True Positive) / (True Positive + False Negative)
Specificity	Measure of the proportion of participants truly not having depression or anxiety as verified by a clinician who is correctly identified by the Device as Negative for depression or anxiety (or True Negative Rate). Specificity = (True Negative) / (True Negative

	+ False Positive)
Standard of care	Medical or psychological treatment guideline that specifies appropriate treatment based on scientific evidence and collaboration between medical and/or psychological professionals in the treatment of a given condition.
Study Survey	A web-based study survey that will be administered to study participants.

Background Information

Major Depressive Disorder (MDD) is the leading cause of disability worldwide.[1,2] Depression and anxiety disorders are among the most prevalent of all mental disorders.[3] Approximately eight percent of adults in the United States reported having at least one major depressive episode and 18.1% of adults in the US have anxiety disorder.[3,4] Depression and anxiety disorders are a frequent comorbidity for patients suffering from chronic medical diseases, such as diabetes, cancer, and inflammatory bowel disease.[5-7] Multiple studies show a 2-3 fold increase in the cost of treating these chronic conditions, if their depression goes undiagnosed or untreated. Early detection of disorders is key to both better health and economic outcomes.[8] Diagnosing depression and anxiety can be challenging since there is no current biomarker test used to detect the possible presence of these conditions. The PHQ-2 / PHQ-9 screener, which can either be self-administered or administered by a clinician, is the most commonly used diagnostic instrument. Even though the US Preventive Services Taskforce and the American Academy of Family Physicians recommend screening in individuals 12 and older,[9,10] with the US primary care visit averaging 16 minutes, mental health screening is frequently skipped,[11] and only an estimated 4.2% of primary care patients are screened for these conditions.

The DSM-5, the standard classification of mental disorders used by mental health professionals in the US, has definitions for MDD and anxiety disorders. However, reliability of psychiatric diagnosis is still low, even among psychiatrists.[12] Because psychiatric diagnoses are often based on inferences derived from observation of patient behavior and patient self-reports, interrater reliability are moderate, typically ranging between kappa values of 0.4 to 0.6.[13]

Primary care clinicians provide the majority and an increasing percentage of mental health care.[11] If the agreement between psychiatrists, specialists trained specifically on mental health care is low - the expectation is that it will be even more challenging for primary care clinicians to diagnose depression and anxiety. According to a global Lancet study, the General Practitioners' sensitivity is 47.3%.[14] Multiple studies describe the underdiagnosis of depression and anxiety, which is even more pronounced among the more medically disenfranchised demographic groups such as the elderly and racial minorities.[15]

Kintsugi, a digital health technology company based in Berkeley was founded to address these challenges. Kintsugi initially started by creating a consumer application, a voice journaling wellness app that is available on the Apple App Store. This app allows users to journal by speaking, interact with community members who share similar challenges, and track their wellness and mental health over time to promote mental wellbeing. Based upon their preliminary work and user engagement, the Kintsugi team applied for and was awarded several National Science Foundation Small Business Innovation Research (SBIR) grants to develop new Artificial Intelligence (AI) technologies in healthcare. Most recently, the team is developing an AI-based algorithm that is able to detect signs of depression and anxiety from short clips of free-form speech. The Kintsugi Voice Device is the result of these efforts.

Voice biomarker technologies provide a unique way to scale access to mental healthcare by assisting clinicians with the screening and triage especially in high-volume environments where administrative burdens are high and mental health conditions are often overlooked. Researchers have attempted to find objective methods to increase the accuracy of depression and generalized anxiety disorder diagnoses, and voice-based biomarkers are attractive because of their non-invasive nature and ability to provide passive monitoring.

Study Device Description

The Kintsugi Voice Device ("Device") is a software API that allows the clinician to upload a voice sample for analysis from an individual ≥ 22 years old. The API can be electronically interfaced and perform analysis with data transferred from computer-based applications. The Kintsugi Voice Device output is adjunct to clinical assessment and provides a sensitive reliable estimate of the presence of vocal characteristics consistent with a significant depressive episode and/or a clinically significant anxiety state, which are a necessary condition for the diagnosis of lifetime mood disorders, such as major depressive disorder and/or generalized anxiety disorder. The Kintsugi Voice Device is not to be used in-lieu of full patient evaluation or relied upon to make or confirm diagnosis but offers objective signals in the global assessment of mood and anxiety disorders.

The Device comprises of the following:

- An API that can be integrated into different clinical workflows. Input of the API is a patient voice sample that is at least 60 seconds
- Underlying machine learning algorithm that drives the Device outputs ("Algorithm")
- Depression and Anxiety are separate algorithms

The Device output is the following:

- For depression:
    - The voice sample contains characteristics of depression (the model has high confidence that the speaker has depression),
    - The voice sample does not contain characteristics of depression (the model has high confidence that the speaker does not have depression),
    - Indeterminate (the model doesn't have high confidence to classify the patient as depressed or not depressed)
- For anxiety:
    - The voice sample contains characteristics of anxiety (the model has high confidence that the speaker has anxiety),
    - The voice sample does not contain characteristics of anxiety (the model has high confidence that the speaker does not have anxiety),
    - Indeterminate (the model doesn't have high confidence to classify the patient as anxious or not anxious)

Principles of Operation

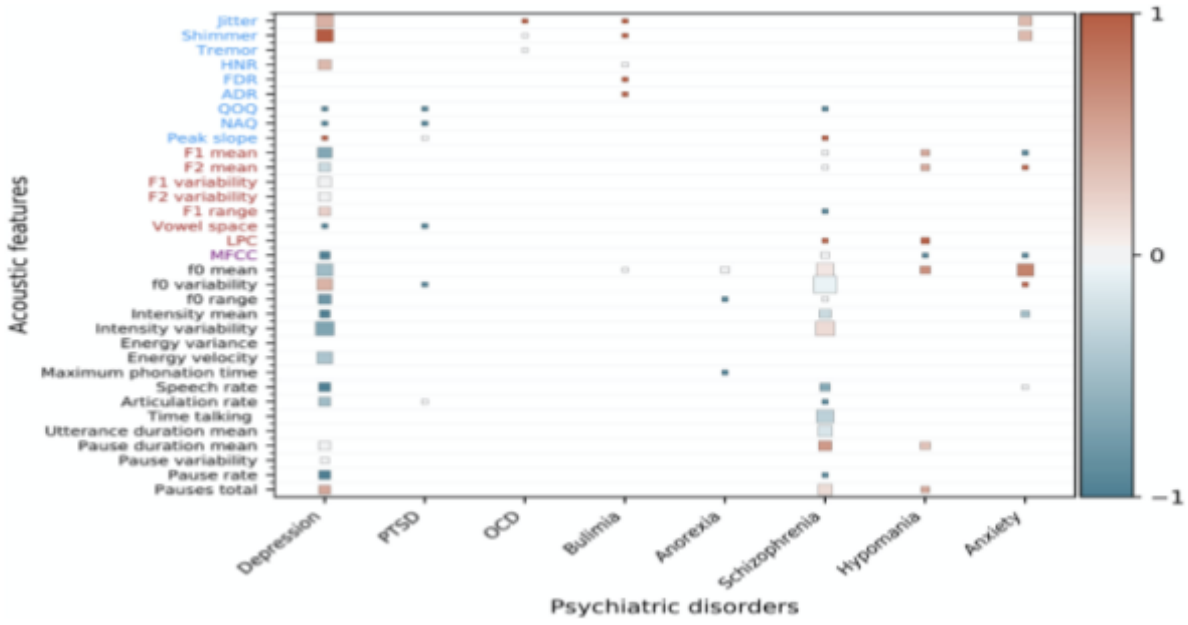
The Kintsugi Voice Device technology is based on a large and growing body of research on voice biomarkers and their ability to detect and predict various neurological and mental disorders.[16–18] Voice biomarkers are a set of acoustic features extracted from voice signals.[19]

Producing speech involves coordination of various cognitive and motor processes therefore samples of speech provide insight into the state of physical and mental health. Speech has

been studied for a variety of health conditions including dementia, aphasia, Parkinson's, Alzheimer's disease, and various psychiatric conditions.[19–24]

There have been studies on the relationship between voice and cognitive behavior since the 1920s. Individuals with depression have been reported to have lower pitch, more monotonous tone, lower sound intensity, and lower speech rate as well as more hesitations, stuttering, and whispering.[25] Longer speech pause times were correlated with depression and the reduction in speech pause times was used to identify clinical improvement among both unipolar and bipolar patients with depression.[26,27] More recently, Mundt et al. demonstrated in a landmark study of 105 patients that it was possible to collect speech samples from an automated telephone system and measure the severity of depression and treatment response by using voice biomarkers.[28] Since then, multiple groups have created models to study the effects of depression on phonemes, which is the unit of sound that can distinguish one word from another.[29,30] Articulatory-phonetic units of speech can capture the effects of different psychiatric symptoms and be used to deduce the severity of psychiatric symptoms from the human voice.[29] In a review of 1395 studies on using speech to identify the presence or severity of cognitive disorders, Low et al. 2020 analyzed 127 of these studies and synthesized the features that had predictive power for multiple cognitive disorders, including depression, anxiety, schizophrenia, and hypomania (Figure 1).[31] As shown in Figure 1, every acoustic feature that had predictive power for depression also had predictive power for anxiety, which serves as the fundamental basis for the Device's operation.[31]

Figure 1: Synthesis of Null-Hypothesis Testing Studies Across Psychiatric Disorders from Low et al. 2020



Adapted from Low et al.[31]

System or Device Components Description

The Device is composed of a neural network-based algorithm that analyzes voice recordings to screen for signs of depression and anxiety. The audio files that are used as input to the algorithm are recorded by general use computing platforms (e.g., cellphone, tablet, laptop) and are stored as uncompressed audio in raw form. It is then pre-processed using the following process:

- resample the data to match specifications
- evaluate the quality of the speech sample
- normalize the loudness of the audio
- transcode the audio from the original encoding to linear pulse-code modulation
- trim the pauses at the beginning and end of the audio file

Once processed, vocal features are extracted from the audio and inputted into the neural network models. The software interprets the acquired signals using signal processing and an artificial neural network to quantitatively evaluate voice characteristics for presence of indicators correlated to depression and anxiety. The Kintsugi Voice Device then generates an output for signs of depression and anxiety which is displayed to the Device Operator. The Kintsugi Voice Device output will be positive for depression or negative for depression and positive for anxiety or negative for anxiety. The outcome can also be “uncertain” or within an “indeterminate range” if the Device cannot provide a high-confidence result.

Study Objectives

This study seeks to evaluate the ability of the Device to aid clinical assessment for depression and anxiety by comparing its output with the established diagnostic standard consisting of a diagnosis made by a specialist clinician based on DSM-5 criteria.

This is a prospective study of up to 100 subjects, ages $\geq$22 years of age.

We are striving for a 50%/50% split of subjects who have depression and/or anxiety and subjects who do not have depression and/or anxiety.

Study Endpoints

Effectiveness Endpoints

The primary endpoints of this study are to:

1. Determine the specificity and sensitivity of the Device in discriminating the presence of a significant depressive episode using the Structured Clinical Interview for DSM-5 Clinical Trial Version as the established diagnostic standard (“gold standard”)
2. Determine the specificity and sensitivity of the Device in discriminating the presence of a clinically significant anxiety state using the SCID-5-CT as the established diagnostic standard

The secondary endpoints of this study are:

- Measurement of the percentage of all adults for whom the Device provided no result
- Determine the specificity and sensitivity of the Device in discriminating the presence of a significant depressive episode compared to the PHQ-9
- Determine the specificity and sensitivity of the Device in discriminating the presence of a clinically significant anxiety state compared to the GAD-7

Safety Endpoints

Adverse events (AEs) and serious adverse events (SAEs) will be collected and reported from enrollment, which is determined by informed consent signature, through the completion of the study.

Study Duration

The study is expected to last up to 8 months. The duration of each individual subject’s involvement in the study will be approximately 2 hours total consisting of a screening call followed by a psychiatrist clinical evaluation and online survey. However, participants could be active on the study for up to 2 weeks to schedule a SCID assessment.

Study Design and Procedures

This is a prospective fully remote, decentralized clinical study to measure the sensitivity and specificity of the Device predictions against clinical ground truth for major depressive disorder and for generalized anxiety disorder. Up to 100 participants will undergo investigational and comparator assessments for major depressive disorder and a clinically significant anxiety state.

The research coordinator will schedule a time with the participant for the evaluation. There will be a two-part evaluation: a web-based study survey and a specialist clinician evaluation via the SCID assessment. The SCID assessment will include questions about the past medical history of the participant as well as questions from the Clinical Global Impression - Severity scale. The order of the two evaluations will be randomized to minimize any potential bias.

The Device output will be positive for depression, negative for depression, or indeterminate for depression and positive for anxiety, negative for anxiety, or indeterminate for anxiety. PHQ-9 and GAD-7 scores will also be collected through the Study Survey.

Participants will also be evaluated by a specialist clinician via the SCID assessment. The psychiatrist performing the SCID assessment will be a board-certified psychiatrist. The clinical evaluation via the SCID assessment will be recorded and the channel-separated audio file of the participant during this assessment will be used as the Device input. The input for the Device will be obtained by the clinical research team and will be at least one minute of audio taken from the SCID assessment where the participant is asked about their current illness history and treatment history. The results of these assessments will act as the clinical comparator for comparison with the Device output.

Clinicians and participants will both be blinded to the participant the Device output and the participant assessment results (SCID, PHQ-9, GAD-7). Further, a SCID reviewer may review the recorded SCID assessment and standard clinical assessment and completed SCID template to minimize interrater variability.

Subject Identification and Recruitment, Process of Consent
Subjects may be recruited through various mediums including but not limited to social media, Craigslist, and/or specialized clinical trial recruitment groups. At the time of enrollment, the mental status of the participant will not be known. Subjects may be recruited from populations that self-select as interested in mental health. Potential subjects will be provided with detailed study information so that they are able to make an informed decision.

If subjects wish to enroll, they will need to answer brief pre-screening questions about the inclusion/exclusion criteria to determine if they meet the study inclusion/exclusion criteria. Subjects ineligible for the study will be told they do not qualify. Subjects eligible for the study will receive an informed consent form if they are interested in participating. Participant identity will be verified before enrollment.

Participants will then schedule a time for the SCID assessment and to take the web-based study survey within the same day. Study participants can choose to end participation in the study at any time. The clinical research coordinator will also answer any questions on the study that participants have prior to enrollment.

Participants will also provide basic information such as their physical address, emergency contact, age, and email. Only the necessary participant information and medical history required for the study will be collected.

Recruitment will continue until up to 100 participants have SCID results or until the Sponsor terminates the study. The Sponsor may collate interim results at any time during the study to determine whether the study should continue.

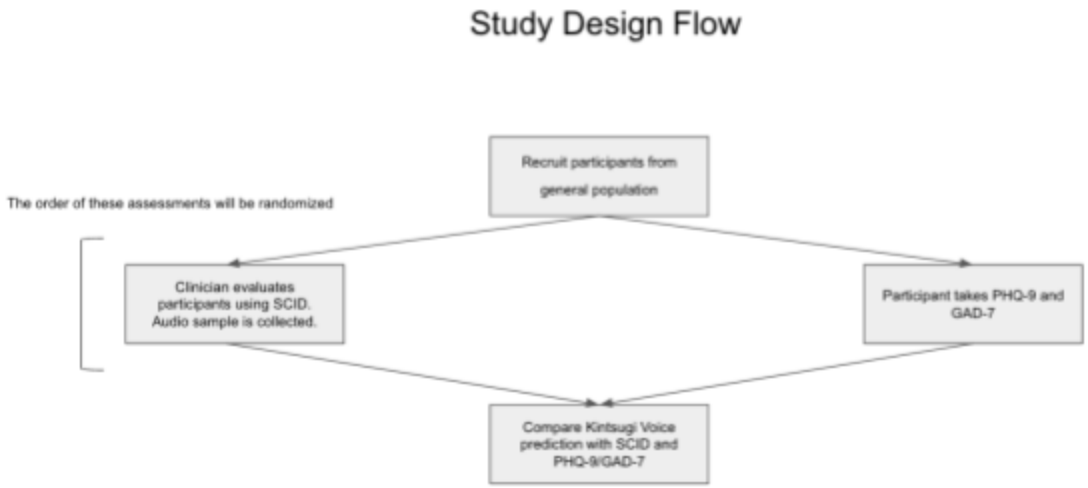
Process of Consent

The participant will be given access to the informed consent from. The informed consent form serves to ensure that participants understand the purpose of the study, assessments the participants will be asked to undertake as part of the study, the risks and benefits of participating, and the voluntary nature of their participation. The informed consent form will inform the participants that they will provide a recording of their voice and video as part of the study. The informed consent form will also inform the participants that their specialist SCID assessments conducted over a HIPAA-compliant video-conferencing platform will be recorded for the purposes of the study and research. A copy of the consent form will be provided to the participant after they consent. A clinical research coordinator will be available to answer participant questions about the study.

Randomization

The order in which the online survey and SCID assessment occur will be randomized. All participants will participate in investigational (Kintsugi Voice Device) and comparator assessments (SCID assessment, PHQ-9, and GAD-7).

Figure 2: Study Design Flow



A schematic of the study steps is illustrated in Figure 2.

Participants will be considered enrolled once they have signed the informed consent form.

Participants will receive instructions on completing our web-based Study Survey. If the audio sample from the SCID assessment is not scorable (e.g. poor microphone quality, insufficient length, excessive background noise), the participant may be asked to submit an additional audio sample. A clinical research team member will run the audio sample through the Device. Participants will fill out the PHQ-9 and GAD-7 questionnaires as part of the Study Survey. The Device output, PHQ-9, and GAD-7 results will not be shared with the clinicians. Similarly, the Device output, the PHQ-9, and GAD-7 results will not be shared with the participants.

Participants will complete a SCID assessment immediately after or immediately before the web-based Study Survey. A clinical research coordinator will be available to support the participant if they run into issues with the Study Survey.

The SCID assessment will be conducted by a specialist. Specialists will have board certification in psychiatry and have at least two years of experience diagnosing depressive and anxiety disorders. Specialists will also undergo psychiatric assessment scoring training for the SCID assessment prior to providing diagnoses for the study to minimize discrepancies in scoring.

Participants will complete the SCID assessment through a HIPAA compliant teleconferencing application such as Zoom Meetings. The meeting will be recorded, and the participant will need to consent to the recording in order to participate in the study. After the SCID assessment, the specialists will determine a diagnosis based on whether the participant meets the DSM-5 criteria for Major Depressive Disorder and Generalized Anxiety Disorder.

Once the Study Survey (voice sample, PHQ-9, GAD-7) and the specialist-evaluated SCID are complete, the participant will receive an Amazon gift card of $50 for their time.

Study Population

This study will enroll up to 100 subjects ≥22 years old. Only subjects who meet all eligibility criteria and sign the informed consent will be enrolled.

Inclusion Criteria

- Subjects ≥22 years of age at the time of informed consent
- Participant must be able to read, understand and sign the Informed Consent Form
- Access to a laptop, smartphone, tablet, or other Device with a functioning microphone
- Participants must be willing to be videotaped as part of the study
- Stated willingness to comply with all study procedures and availability for the duration of the study
- Fluency in English
- Availability for the duration of the study
- The participant must reside within the state of California

Exclusion Criteria

Participants with at least one of the following conditions will be excluded:

- Any impairment that would prevent participants from completing an online survey and/or engage in clinician assessment interviews (e.g., visual impairment, motor impairment, hearing impairment, acute intoxication)
- Any known history of neurodegenerative or Central Nervous System disorders
- Any known history of schizophrenia, psychosis, or severe cognitive deficits
- Any known presence of disorders that may lead to false signal of depression or anxiety including Multiple Sclerosis, Amyotrophic Lateral Sclerosis, Parkinson's Disease, Stroke, Traumatic Brain Injury
- Presence of voice disorders that may impact vocal cords such as acute or chronic laryngitis, vocal cord paresis or paralysis, or spasmodic dysphonia
- Any known history of vocal cord injury or cerebrovascular accident or head trauma with residual dysarthria in the past year
- Past or active heavy smokers if there is impact on the vocal cords
- Any known history of congenital deafness
- Subjects who do not speak English
- Subjects who do not live in the United States
- Subjects who have previously participated in any Kintsugi-sponsored study.

Data Collection and Storage

Data will be retained in accordance with federal and institutional policies. Participants will be assigned a unique participant ID for de-identification. All data for analysis will be identified by participant ID number instead of personal identifiable information (PII).

The recruitment data with participant names, phone numbers, emails, location, and emergency contact will be password protected and only accessible to the research team.

Authorized representatives of institutions participating in the study, the Sponsor, the reviewing IRB and other groups or organizations that have a role in the study including reviewers of the structured interviews, regulatory bodies (e.g. the US Food and Drug Administration (FDA), Department of Health and Human Services (DHHS) agencies) will have access to and may view a participant's study information. They will be subject to regulations protecting patient confidentiality (e.g. HIPAA).

The data repository for this study includes:

- Device input
    - Voice sample provided as an audio recording
- Device output
- Video recording of the diagnostic assessment for clinically significant depression and clinically significant anxiety according to the DSM-5 criteria (SCID)
- Results from the PHQ-9 and GAD-7 questionnaire participant self-assessment
- Medical history relevant to the inclusion/exclusion criteria

At the conclusion of the study, the data will be retained in accordance with institutional policy. Identifiable data will be kept for 7 years after the completion of the study. De-identified data will be kept indefinitely.

Potential Risks and Benefits

Potential Risks

Risks related to the study are minimal.

The main potential risk to study participants is loss of confidentiality. Measures to protect the confidentiality of study participants will be implemented as described in the Data Collection and Storage section.

Participants may feel discomfort answering questions or being interviewed.

An emergency contact will be collected for each participant, in the rare case that there is imminent danger to the participant as determined by the psychiatrist and, as stated in the consent, that 911 may be called if the clinician determines there is an emergency. The clinician will refer the participant to local resources should there be an emergency but will not provide ongoing care.

Potential Benefit

Knowledge gained from the study could potentially benefit patients in the future.

Participation in this study might lead to identification of clinically significant depression or clinically significant anxiety, enabling earlier therapy known to positively impact outcomes.

Adverse Events Reporting

Definitions

Term	Definition
Adverse Event (AE)	Any untoward medical occurrence, unintended disease or injury, or untoward clinical signs (including abnormal laboratory findings) in participants, users or other persons, whether or not related to the investigational Device (ISO 14155-1).
Serious Adverse Event (SAE)	Adverse event that a) Led to death, b) Led to serious deterioration in the health of the participant, that either resulted in 1) A life-threatening illness or injury, or 2) A permanent impairment of a body structure or a body function, or 3) In-patient or prolonged hospitalization, or 4) Medical or surgical intervention to prevent life-threatening illness or injury or permanent impairment to a body structure or a body function, c) Led to fetal distress, fetal death or a congenital abnormality or birth defect (ISO 14155-1).
Anticipated Serious Adverse Device Effect (ASADE)	An anticipated serious adverse Device effect (ASADE) is any SAE on health or safety or any life-threatening problem or death caused by, or associated with the Device, if that effect, problem, or death was previously identified in nature, severity, or degree of incidence in the investigational plan, informed consent, operator manual, other risk analysis documentation or regulatory application; or any other serious problem associated with a Device that relates to the rights, safety, or welfare of subjects.
Unanticipated Serious Adverse Device Effect (USADE)	Any serious adverse effect on health or safety or any life-threatening problem or death caused by, or associated with, a Device, if that effect, problem, or death was not previously identified in nature, severity, or degree of incidence in the investigational plan or application (including a supplementary plan or application), or any other unanticipated serious problem

	associated with a Device that relates to the rights, safety, or welfare of participants 21 CFR 812.3(s).

Recording of AEs/ADEs and SAEs/SADEs

All suspected adverse events (AEs) will be evaluated and recorded in the participant's study case report form. The AEs/ADEs/SAEs/SADEs may be observed by the investigator and/or clinical research staff or volunteered by the subject. All observed and volunteered adverse signs and symptoms, anticipated or unanticipated, regardless of severity or frequency will be recorded in the case histories (i.e. case report form). The reports of the AEs/ADEs/SAEs/SADEs will include the description of the event of symptom, date of onset, date of resolution, severity, anticipated or unanticipated, the relationship to the study Device, the action taken (if any), and the outcome. AEs/ADEs will be reported to the IRB only if the study clinicians, Dr. Herbert J. Harman and Dr. Roshanak Ramezani, determine that the event is possibly or definitely related to the Device. All SAEs/SADEs, anticipated or unanticipated, must be reported to the sponsor and reviewed by the IRB as soon as possible, but no later than 10 working days after the initial event was recorded. The study clinicians, Dr. Herbert J. Harman and Dr. Roshanak Ramezani, will review all adverse events to determine the severity and relationship to study Device.

Follow-up of Subjects after AEs

All reported AEs/ADEs/SAEs/SADEs should be followed until resolution of the event or until the subject's participation in the study ends. Resolutions of the events should be documented in the appropriate case report form.

Data Analysis Plan

This is a prospective study with up to 100 subjects who meet the inclusion criteria and who do not meet any of the exclusion criteria.

The analysis set includes all enrolled subjects who provide a sample of their voice and are evaluated by a specialist. Device-related adverse events will be tabulated and analyzed.

Study Management

Investigator, Clinician, and Research Staff Selection

Investigator(s) and research staff will be invited to participate in the study based on their medical specialty and experience conducting clinical research studies. Specialists will have board certification in psychiatry and have at least two years of experience diagnosing depressive and anxiety disorders.

Training and Monitoring

Investigator(s) and research staff, including clinical research coordinators and clinicians, will be trained on the study procedures. Clinicians administering the assessment will also receive training for the SCID to minimize discrepancies in scoring.

Informed Consent

An IRB-approved informed consent document will be provided to subjects through an electronic signature software tool. Subjects must sign the informed consent document before they can participate in the Study Survey or participate in a clinician evaluation. Clinical research coordinators will inform the subjects on the purpose of the study, expected duration, potential risks and benefits from the study, as well as making it clear that participants are free to refuse participation in this clinical study.

Participant Withdrawal Criteria

Participation in this study is voluntary and participants can withdraw from the study at any time. In order to withdraw, a participant will need to:

1. Call or email the research coordinator.
2. Let the research coordinator know about their intention to withdraw.

A participant that withdraws from the study prior to completion of study will not be paid.

A subject will be considered lost to follow up after 2 unsuccessful attempts to contact the subject.

If a participant withdraws from the study prior to its completion, their data will not be deleted; they will still be used for the research study.

Protocol Amendments

Any amendments to this study protocol must be communicated clearly in writing, signed, and dated by the sponsor and the principal investigator. IRB approval will be obtained for all study amendments.

Study Discontinuation

The study Sponsor has the right to terminate this study at any time.

Subject Confidentiality

This study preserves the confidentiality of all subjects under the Health Insurance Portability and Accountability Act of 1996 (HIPAA) Privacy Rule. The following safeguards will be in place to protect the privacy of the individuals who are the subjects of the health information to be used in the research and the confidentiality of that information: The subjects will be informed by the investigator or the investigator's designee that their medical records will be kept as confidential as possible but may be subject to review by: (1) Kintsugi, or its representative; (2) reviewing IRB; and/or (3) by appropriate regulatory bodies (e.g. the US Food and Drug Administration (FDA), Department of Health and Human Services (DHHS) agencies).

Only minimum personal information required for purposes of the study will be collected. The personal information will be collected and used to ensure subject eligibility for study participation, to conduct the study, and to provide compensation to participants after completion of the study requirements. Permission to use or disclose personal information, except for that has been collected and relied on may be canceled by the subject by written notice. If the subject is withdrawn from the study, the information collected to that time may still be used to preserve the scientific integrity of the study. There is no expiration date to this authorization.

Subjects' identities will be kept confidential. Subjects will be assigned a unique study code that will not reveal the subjects' identity, and this code will be used on all study documents.

Financial Considerations

Subject Compensation:

The participant will be compensated $50 for their participation upon completion of both the Study Survey (PHQ-9 and GAD-7) and the specialist clinical evaluation.

Costs to the Subject:

The specialist clinician evaluation will be covered by the Company sponsoring the study. Any additional services will not be covered by the sponsor.

Clinician / Specialist Compensation:

Specialist clinicians will be compensated by the clinician evaluations / assessments they complete. Reviewing specialist clinicians will be compensated per independent review of cases.

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