**Clinical Trial Protocol**

**Physiological, Psychological, Psychiatric, Surgical or Health Interventions**

The MyMood&Me Project: Using text data to infer mental health

Version 4 (21/01/22)

Dr Bridianne O’Dea

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# **General Information**

|  |
| --- |
| **Protocol Title**  |
| The MyMood&Me Project: Using text data to infer mental health  |
| **Protocol identifying number** | UNSW HREC HC210397ANZCTRN: To be updated upon submission. |
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| **Human Research Ethics Committee**  |
| **Name** | UNSW Human Research Ethics Committee |
| **Status of ethical review** | [x] Approved[ ]  In progress [ ]  To be submitted |
| **Trial Sites** | N/A |
| **Funding for the Clinical Trial** |
| **Funding Body Name** | The National Health and Medical Research Council (GNT1165233/RG180562) |
| **Amount of Funding** | $352 000 |
| **Interests that the funding body has in the clinical trial** | The funding body is independent to the project and is not involved in the trial design, execution, data analysis or manuscript preparation.  |
| **Insurance for Clinical Trial**  |
| **Insurer** | University of New South Wales  |
| **Type of Insurance**  | Clinical Trials Insurance  |
| **Confirmation of Insurance**  | [x] Attached [ ]  In progress [ ]  To be submitted |

# **Safety and Monitoring Contacts**

|  |
| --- |
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| **Independent Safety Monitoring Board or Data Safety Monitoring Board Members** |
| * This trial utilises a Trial Management Group to monitor the safety of the trial. The members of this group are outlined below.
 |
| **Trial Management Group/Trial Steering Commitee** |
| * Dr Bridianne O’Dea
* Dr Mark Larsen
* Professor Nick Glozier
* Professor Michael Berk
* Professor Philip Batterham
* Professor Helen Christensen
* Dr Michelle Tye
* Dr Sophie Li
* Ms Cassandra Chakouch
 |
| **Sponsors Independent Physician/Medical Expert**  |
| **Name** | To be confirmed |
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| **Address** |  |
| **Pharmacy, Clinical Laboratory, Radiology, Pathology and other medical and/or technical departments involved in the trial**  |
| **Name** | N/A |
| **Telephone**  |  |
| **Email** |  |
| **Address** |  |

# **Delegation of Clinical Trial Duties**

Responsibilities for the conduct and oversight for the trial are delegated to the Coordinating Principal Investigator (Dr Bridianne O’Dea). Trial related responsibilities will be delegated to the listed Principal Investigators and any trial-related personnel by the Coordinating Principal Invesitgator. All trial-related duties delegated by the Coordinating Principal Investigator or Principal Investigators and trial-related personnel will only be delegated to those that are qualified by experience and training. Delegated responsibilities will be retained in the [UNSW Clinical Trial Delegation Log](https://research.unsw.edu.au/document/Clinical%20Trial%20Delegations%20Log.docx). The UNSW Sponsor's Delegate will be notified of the following:

* Protocol deviation reports outlined in the UNSW Research Misconduct Procedure.
* Any serious breach of Good Clinical Practice, the clinical trial protocol, the clinical trial standard operating procedures, or the human ethics approval that is likely to affect to a significant degree the safety or rights of participants or the reliability and robustness of the data generated in the clinical trial.
* Significant safety issues that are likely to (or have the potential to) affect to a significant degree the safety or rights of participants or the reliability and robustness of the data generated in the clinical trial.
* Urgent safety measures implemented to remove or prevent a significant safety issue.
* Safety reports relating to the continuation, suspension, or discontinuation of the clinical trial for safety reasons.
* Non-compliance with the protocol, SOPs, GCP, and applicable regulatory requirement(s) significantly affects or can potentially affect human subject protection or reliability of trial results significantly.
* Participant complaints or concerns received concerning the conduct of the research.
* Significant modifications to the clinical trial are likely to affect a significant degree the safety or rights of participants or the reliability and robustness of the data generated in the clinical trial.
* Addition of participating trial sites, contractual arrangements at participating sites or modifications to legal agreements.
* The intention to conduct the trial in other countries.

# **Trial Objectives and Purpose**

This experimental pilot project aims to explore the potential of text data for producing valid and reliable linguistic markers of depression and anxiety among adults with mental illness. The research questions that this study seeks to address are:

1. What is the relationship between participants’ symptoms of mental health, their completion of the brief text tasks, and the linguistic features expressed in their responses?
2. What type of text data (e.g., SMS, social media posts, expressive writing, image reflections) is most useful for generating linguistic markers?
3. What is the level of acceptability and engagement in completing repetitive text tasks of this kind for generating linguistic markers of mental health?

**Hypotheses**

**H1:** At the group-level, mental health symptomatology will be marked by weak correlations with the linguistic features (rs=.01–.1) expressed by participants.

**H2**: At the individual-level, mental health symptomatology will be marked by strong correlations between linguistic features and symptoms (rs=.7–.9).

**H3:** Correlated linguistic features will be different for each individual but consistent across the writing tasks.

# **Background Information**

Worldwide, depression and anxiety are leading causes of disability and represent major health and economic burdens (Mathers & Loncar, 2006). This is due in part to the detrimental effects of these mental illnesses on functioning, but also the low levels of help-seeking due to low mental health literacy among individuals, the inability to recognise symptoms, poor help-seeking attitudes, and a lack of access to care (Burgess et al., 2009; Oliver et al., 2005; Wright et al., 2007). There is a need to look to new ways of detecting mental illness in the population to increase treatment uptake and outcomes, reduce severity, and prevent death (Arango et al., 2018).

Personalised medicine is founded on the established principle that everyone has unique characteristics of illness (Snyderman, 2012). This approach aims to account for the heterogeneity that occurs within diagnostic categories, particularly depression (U. Ozomaro et al., 2013). Defined as “objective, quantifiable characteristics that can be measured accurately and reproducibly, and observed from outside the patient”, markers provide clinically relevant information about an individual which can be used to infer their need for treatment. In the context of depression, mainly biomarkers and genetic markers have been investigated to date, with significant delay and cost (Ripke et al., 2013). There is a need for new investigations that aim to identify more readily accessible, low-cost markers.

**Linguistic markers of mental illness**

There has been significant enthusiasm in the potential of text data for generating markers of mental health as it is a readily available and naturally occurring data source. Psycho-linguistic theory postulates that the words and features used in everyday language can reveal individuals’ thoughts, emotions, and motivations (Litvinova et al., 2016; Pennebaker, 2011; Pennebaker et al., 2014). It has been hypothesised that the language and features expressed in text content may indicate an individual’s mental state. Linguistic analysis, in contrast to self-report, has the advantage of tapping into implicit signals of low mood and other emotional states. A recent meta-analysis confirmed that depression is correlated with an increased use of first-person pronouns (r=0.13) (Edwards & Holtzman, 2017). Emerging research indicates that there may be a range of other linguistic features, topics, and sentiment within text that may indicate an individual’s mental health. Computerised communication and validation of automated linguistic tools (e.g., Linguistic Inquiry and Word Count; LIWC) now means that text data can be easily collected and analysed with minimal human effort, and at very low cost. However, it remains unknown how much text data is needed, and which type is the most useful for producing valid and reliable linguistic markers for mental health. The current study aims to determine this.

This research is significant because it will help determine the feasibility of brief writing tasks for generating linguistic markers of mental illness. If deemed acceptable and engaging, these tasks may be adapted for delivery alongside therapy interventions, to be used to monitor for recovery and remission of common mental disorders like depression and anxiety.

# **Statement of Compliance**

The clinical trial will be conducted in compliance with the following guidelines and documentation:

* [ICH Guidelines for Good Clinical Practice (GCP)](https://www.tga.gov.au/publication/note-guidance-good-clinical-practice)
* [National Statement on Ethical Conduct in Human Research](https://nhmrc.gov.au/about-us/publications/national-statement-ethical-conduct-human-research-2007-updated-2018) (National Statement)
* As approved by the Human Research Ethics Committee (HREC), the clinical trial protocol is responsible for monitoring the trial's conduct.
* The responsibilities set out by the UNSW Sponsors Delegate.
* The onsite or remote monitoring standard operating procedures as put in place by the clinical trial sponsor.

# **Trial Design**

The study is a pilot randomised crossover design of a total of 9 weeks duration (i.e., 56 days of intervention and one additional week to complete study assessments). Table 1 outlines the crossover sequencing design for the current study.

**Table 1. Crossover sequencing design of the current study.**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Task type** | **Sequence order** | **Period 1** | **Period 2** | **Period 3** | **Period 4** |
| Repetitive writing tasks | Sequence 1 (ABCD) | A | B | C | D |
|  | Sequence 2 (BCDA) | B | C | D | A |
|  | Sequence 3 (CDAB) | C | D | A | B |
|  | Sequence 4 (DABC) | D | A | B | C |
|  |  | **Day 1** | **Day 14** | **Day 28** | **Day 42** |
| One-off writing tasks | Sequence 1 (VWXY) | V | W | X | Y |

Notes: Each intervention period lasts for 14 days.

All subjects will be allocated to a random sequence of four repetitive stimulated writing tasks, and a set sequence of four one-off stimulated writing tasks (see Appendix 1 for a detailed outline of the nature and repetition of the writing tasks). The total intensity and frequency of writing tasks will be the same for all participants; however, the order in which the repetitive writing tasks are completed will be different. A random-number generator will be used to generate the sequence as well as randomisation codes. This will be conducted by the trial statistician who will not be involved in the day-to-day operations of the trial. Participants will be randomised after providing their consent to participate. Participants and the research operations team will remain blinded to participants’ allocation until they complete the study.

There are four intervention periods in the current study, each lasting 14 days, with two types of writing tasks scheduled in each intervention period.

In addition to the randomised writing tasks, participants will also be asked to complete five fortnightly mental health surveys, scheduled on days 1, 14, 28, 42, 56. The one-off stimulated writing tasks will be scheduled to be completed at the same time as the corresponding fortnightly mental health survey (on days 14, 28, 42, and 56), but the writing task will be administered first to reduce any carryover effect of the symptom scales. There is no wash out period as there is nil to limited evidence of a carryover effect for the proposed writing interventions; However, the repetitive stimulated writing tasks will not be scheduled within two days (before or after) of the fortnightly health survey, given the impacts that symptom scales (i.e., triggering reflection on negative mood states) may have on participants’ writing.

This methodology is appropriate to answer the research questions because increasing research indicates that individuals have their own unique markers of mental health. A cross-over trial therefore allows each individual to serve as their own control, while also allowing us to examine overall group differences and similarities in linguistic markers. This study design will also enable us to determine which type of text data, and the minimum volume of data needed, is likely to yield reliable and valid linguistic markers of mental health. Our findings can then be used to inform future studies on the use of this approach.

# **Sample Size**

The sample size for analysis was set at N=100. This is based on detecting moderate correlations (*r*=0.3-0.5) between linguistic features and mental health outcomes (primary outcome). Given that the study design is intensive, a conservative estimate of 40% attrition has been used. As such, the recruitment target for the trial is N=140.

# **Selection and Withdrawal of Subjects**

All inclusion and exclusion criteria will be assessed through a self-report questionnaire hosted on the study website. Excluded participants will be provided with a generic message and details on mental health services and other trusted mental health organisations (e.g., Black Dog Institute, Beyond Blue). Appendix 3 outlines the screening protocol.

Please note: To mitigate the potential of participants “gaming” the inclusion criteria (i.e., making multiple attempts to enter the study by various combinations of inclusion/exclusion criteria), the Participant Information Statement and Consent Form (PISCF) will not stipulate the exact details of the inclusion and exclusion criteria, and will instead give generalized indications. As outlined, we will also provide generic feedback on reasons for exclusion.

## **Inclusion Criteria**

1. Currently 18 years of age or older (confirmed by self-report)
2. Currently located in Australia
3. Have an active mobile phone number and email address (for receipt of study invitations and reminders)
4. Have at least moderate symptoms of depression or anxiety (i.e., total score ≥ 10 on the PHQ-9 or GAD-7).

## **Exclusion Criteria**

1. Participants who report a suicide attempt in the past six months (i.e., Have you made a suicide attempt in the past six months? Answered ‘Yes’ or ‘No’)
2. Participants who report extreme and unmanageable emotional distress (i.e., “Are you currently experiencing extreme and unmanageable emotional distress?” Answered ‘Yes’ or ‘No’)

## **Recruitment Strategy**

This study will utilise an online recruitment strategy. Recruitment will take place until the desired sample size is achieved. All recruitment materials are outlined in Appendix 4. A website for the study will be established and the URL will be included in all study materials. All study adverts will direct participants to the study website, where they will access the PISCF and undertake the screening. Study advertisements will be published on the Black Dog Institute website and social media channels including Facebook, Twitter, and Instagram.

Participants will also be recruited via the Black Dog Institute Online Clinic. The Online Clinic is a web-based platform that adults (18 years +) can use to assess their mental health. Interested adults access the clinic via a website (https://onlineclinic.blackdoginstitute.org.au) and complete a range of clinical assessments for common mental health conditions. At the end of this process, individuals receive a personalised report with suggested support services and free or low-cost resources for them to access. Responses are completely anonymous; however, participants have the option to provide their contact details if they would like opportunities to get involved with Black Dog Institute research projects. Participants who satisfy the inclusion criteria and provide consent to be contacted for research purposes will be contacted by this research team and invited to participate in the study. The research team (using a generic study email address) will email these participants using a standard study invitation that will direct potential participants to the study website, where they will be asked to re-screen and complete the consent procedure. The initial invitation will be followed up with one reminder, sent 5 days after the initial invitation.

The research team will also contact relevant mental health organisations independent of the research team to recruit participants to take part in the study. These organisations will be asked to “share” the study advertisements on their organisation’s communication channels (e.g., website, social media, newsletters, mailing list) using the same adverts outlined in Appendix 4. Support to assist with recruitment will be assumed by the organisation's agreement to post or disseminate recruitment materials. No organisations will know whether a person agrees to participate or not as the recruitment materials will direct potential participants to the study website which hosts participant information statement and consent form which will include further instructions on how to provide consent.

The study will also utilise a paid advertising campaign on Twitter, Facebook, Instagram, and Google, for the duration of recruitment. This campaign will use the same adverts outlined in Appendix 4.

## **Screening**

The study website will list all information from the PISCF so that participants are aware of the study conditions prior to completing the screening questions. To determine whether a participant is eligible to take part in the study, interested participants will complete a self-report checklist hosted on the study website (see Appendix 3). Participants will be informed that the responses to the screening questionnaires will be anonymous but stored for reporting purposes. Consent to undergo the screening procedure will be implied based on individuals’ completion of the questions. Once a potential participant is determined to be eligible, the participant will be invited to take part in the study and the online consent process will be actioned. Ineligible participants will receive a short thank you message advising them that the study is not the right fit for them at this time.

## **Consent**

Upon completion of the screening, eligible participants will be required to read through the full consent form again and give final consent by selecting the required boxed on the website. After this, participants will proceed to the baseline survey. A copy of the PISCF will be emailed to all consenting participants for their reference. Participants will not be reconsented at the beginning of each fortnightly survey due to the short duration of the study period and to reduce participant burden.

Participants will have sufficient time to consider the study participation because the baseline survey remains open for a period of 7 days. Therefore, there is no obligation for the participant to complete the baseline survey immediately after providing consent. Further, participants can easily cease the study at any time by discontinuing with the online survey. Participants will not be reconsented at the beginning of each fortnightly survey due to the short duration of the study period and to reduce participant burden. However, study withdrawal information will be included in study invitation emails.

This consent process is appropriate for the data collection method (i.e., online survey) and participant group because participants are being recruited via online methods, and therefore online consent procedures align with their expectations of research participation. In addition, this is an internet trial (i.e., all study procedures conducted online, thus, an online consent form is consistent with the study activities).

Participants will not be reconsented at the beginning of each fortnightly survey due to the short duration of the study period and to reduce participant burden. However, study withdrawal information will be included in the initial study invitation email.

## **Withdrawal of Consent or Participant**

Participants will be able to withdraw from the study at any time by emailing the research team. Participants will also be provided with instructions on how to actively withdraw in the initial study invitation email sent when they register to take part in the study. By clicking on the URL at the bottom of the welcome email, participants can withdraw and actively remove all data from the study without making direct contact with the research team. Participants can also withdraw by emailing the research team.

Once withdrawn from the research study, all the participants data will be removed, and no further information will be collected from them. Withdrawn subjects will not be recontacted or followed-up.

Failure to complete the survey will be considered lost to follow-up for that timepoint but will not withdraw participants from future surveys or study activities.

# **Treatment** **of Subjects**

The trial is conducted entirely online, as such there will be no face-to-face contact with participants or contact with participants outside of the email and SMS communications.

* 1. **Trial Intervention**

**One-off Writing Tasks & Outcome Measures**

As mentioned in Section 7 all participants will be asked to complete a one-off writing task on days 14, 28, 42 and 56 (see Table 1). The details of the one-off writing tasks are outlined in Appendix 1. Upon completion of the writing task, participants will be asked to complete a mental health survey. Appendix 2 outlines the mental health survey

Participants will be asked to complete the mental health survey on 5 occasions (on days 1, 14, 28, 42 and 56). At baseline (i.e., day 1) and endpoint (i.e., day 56), the mental health survey includes standardised, self-reported psychometric scales for depression (Patient Health Questionnaire-9), anxiety (Generalised Anxiety Disorder Scale -7), rumination (Ruminative Response Scale), and mastery (Perceived Mastery Scale). At baseline only, participants will also complete a demographics questionnaire, motivations for participation, and a brief validated screener for personality disorders. At baseline and final endpoint, participants will complete the rumination and mastery questionnaires. The survey will take no more than 10 minutes to complete. Each survey will stay open for 48 hours. Participants will receive an initial invitation (via email and SMS) to complete, followed by two reminders for non-completers (sent via email and SMS).

Participants will not be provided with any feedback on their symptoms; however, all participants will receive a “thank you” message and information on where and how to seek help.

Adherence to the writing tasks will not be monitored throughout the study period. Participants will receive scheduled reminders (up to 3) to complete the writing tasks and surveys. An acceptability questionnaire will be delivered after participants complete each writing task for the first time (i.e, total of 8 acceptability questionnaires) to measure the level of acceptability for each task.

**Experiment Conditions**

The brief writing tasks are outlined in Appendix 1. These tasks were selected for inclusion in the current study based on the tasks’ ability to generate linguistic markers of mental health in prior research. There will be no word limit for these tasks, with the participants encouraged to write as much as they wish. Participants will be reminded not to worry about spelling, sentence structure or grammar, to just write freely as instructed. There will be no time limit, but participants will be advised to allocate 5 minutes to each task. Participants can complete the tasks at any time during the task collection period. Participants will be reminded that all data is confidential and will not be linked to their personal information (email or mobile phone) for analyses. The repetitive writing tasks will remain open for completion for 24 hours, with participants receiving 1 initial invitation to complete, followed by 2 reminders for non-completers. The one-off writing tasks will remain open for completion for 48 hours, as they are delivered as part of the fortnightly mental health survey.

# **Safety and Monitoring**

1. Assessment of Safety Event Report Forms

Safety reports will be assessed on the seriousness, causality, and expectedness of the event to participation in the MyMood&Me trial. The following are known and expected adverse effects, harms, risks or discomforts associated with the trial.

1. Known Adverse Effects

Given the clinical target population of the trial its expected that participants may experience adverse effects related to suicidal ideation.

1. Known Harms, Risks or Discomforts

The study involves two expressive writing tasks that are “negatively anchored” i.e., require participants to reflect on events that caused them emotional distress. While a systematic review has demonstrated that these writing tasks can have a positive impact on mood (i.e., a therapeutic effect), there is a small possibility that these tasks may lead to psychological discomforts or harms for some participants. Examples of these psychological discomforts and harms include:

* + Increased feelings of worthlessness and distress due to the reflection of sensitive or distressing events.
	+ Increased worry and rumination due to the reflection of sensitive or distressing events.

To minimise the risk of these discomforts/harms, the researchers will adopt the following processes:

1. Participants can cease participation in the writing tasks or mental health survey at any time. At the completion of each survey, participants will be provided with information on mental health services and supports to promote help-seeking (for details, see Appendix 2).
2. The exclusion criteria will ensure that the study excludes participants with recent suicidality and extreme psychological distress. Excluded participants will receive information about mental health services and supports.
3. For the emotionally anchored writing tasks, participants will be asked to indicate their mood before and after the task using ecological momentary assessment of mood. This will provide a measure of mood change that can be used by the research team to examine any potential negative impacts of the experimental conditions on participants’ mood.
4. As this is an observational study, participants will not receive any feedback on their writing tasks or their mental health survey responses. Instead, all participants will receive a thank you message and links to mental health information and support services.

The benefits outweigh the potential risks of discomfort and harm because the evidence suggests that these writing tasks are more likely to improve, not worsen mood, and the current study includes minimal exposure to these writing tasks. Furthermore, the current study includes measures of symptoms and other related outcomes (e.g., acceptability) to capture any harms associated with this study. Lastly, there is no evidence to suggest that answering questions about your mental health has a negative impact on mood or wellbeing.

1. Adverse Events or Adverse Reactions

Adverse events (AE) are considered any untoward medical occurrence in a patient or clinical trial participant administered the intervention, which does not necessarily have a causal relationship with this treatment.

Data on AEs related to suicidal ideation will be collected at all five data-collection timepoints (days 1, 14, 28, 42, and 56) through self-report outcome measurements. Severe suicidal ideation will be defined as the self-report of suicidal thoughts or thoughts of self-harm nearly every day. This will be indicated by a score of 3 on item-9 of the PHQ-9. Data on other AEs will not be routinely collected through self-report measures.

Adverse Reactions (AR) are considered untoward and unintended responses to the trial intervention related to any intervention procedures.

AEs and ARs are assessed using the safety monitoring flow chart. Those classified as "not serious" are assessed by the qualified physician/medical expert specified in section 2 of the protocol. The Qualified Physician cannot delegate this responsibility to other research personnel. Additionally, participants will be presented at the following questions at the end of the trial to assist the relation of AEs and ARs to the trial.

“Were you hospitalised at any point during your enrolment in the MyMood&Me trial?” Yes / No

“Do you feel that being involved in this trial made your symptoms of depression, anxiety, and/or suicidality worse?” Yes / No

Adverse event reports will be reported to the Coordinating Principal Investigator within 7 days. All adverse event reports will be recorded in the [UNSW Safety Monitoring Register Template](https://research.unsw.edu.au/document/UNSW%20Safety%20Monitoring%20Register%20Template.xlsx).

1. Serious Adverse Events

Serious Adverse Events(SAEs) that result in or lead to one or more of the following and the event is not related to the trial intervention:

* The death of a trial participant.
* A life-threatening illness or injury involving a trial participant.
* A participant's permanent impairment of body structure or body function.
* In-patient or prolonged hospitalisation (not for a pre-existing condition or an elective surgery) of a trial participant.
* Medical or surgical intervention to prevent life-threatening illness or injury or permanent impairment to a body structure or function of a trial participant.
* Fetal distress, fetal death or congenital abnormality or birth defect.

SAE reports are classified following the safety assessment flowchart will be assessed by Sponsors Independent Medical specified in section 2 of the protocol. The Sponsors Independent Medical cannot delegate this responsibility to other research personnel. SAE reports are reported to the Coordinating Principal within 7 days. SAR reports will be recorded in the [UNSW Safety Monitoring Register Template](https://research.unsw.edu.au/document/UNSW%20Safety%20Monitoring%20Register%20Template.xlsx).

1. Serious Adverse Reactions

A Serious Adverse Reactions (SAR) is an SAE that is related to the trial intervention. SAR reports are classified following the safety assessment flowchart and will be assessed by Sponsors Independent Medical specified in section 2 of the protocol. The sponsors independent medical expert will determine whether the SAR was expected or unexpected. The Sponsors Independent Medical will not delegate this responsibility to other research personnel. Any participant that experiences an SAR and/or AR will be emailed by a clinical psychologist from the Black Dog Insititue and offered a telephone consulation and risk assessment.

#### **Expected Serious Adverse Reaction**

A serious adverse reaction by its nature, incidence, severity, or outcome is anticipated and identified in the current version of the intervention safety information are classified as a SAR report. SAR reports will be reported to the Coordinating Principal Investigator within 7 days. Serious Adverse Reaction reports will be recorded in the [UNSW Safety Monitoring Register Template](https://research.unsw.edu.au/document/UNSW%20Safety%20Monitoring%20Register%20Template.xlsx).

#### **Suspected Unexpected Serious Adverse Reaction (SUSAR)**

A serious adverse reaction by its nature, incidence, severity, or outcome is unanticipated and not identified in the interventions instructions for use or safety information are classified as a SUSAR.

Fatal or life-threatening Australian SUSAR reports will be reported to the Coordinating Principal Investigator, the sponsor's delegate and the approving HREC within 7 calendar days after being made aware of the case follow up information reported within a further 8 calendar days.

All other Australian SUSAR reports will be reported to the Coordinating Principal Investigator, the sponsor's delegate and the approving HREC within 15 calendar days after being made aware of the case follow up information reported within a further 8 calendar days. SUSAR reports will be recorded in the [UNSW Safety Monitoring Register Template](https://research.unsw.edu.au/document/UNSW%20Safety%20Monitoring%20Register%20Template.xlsx).

1. Significant Safety Issue (SSI)

A safety issue that could adversely affect participants' safety or materially impact the trial's continued ethical acceptability or conduct. The Human Research Ethics Committee and Sponsor's Delegate will be notified of all significant safety issues within 15 calendar days of the sponsor instigating or being made aware of the issue**.** SSI reports will be recorded in the [UNSW Safety Monitoring Register Template](https://research.unsw.edu.au/document/UNSW%20Safety%20Monitoring%20Register%20Template.xlsx).

1. Urgent Safety Measure (USM)

A measure that is taken to eliminate an immediate hazard to a participant's health or safety. Significant safety issues where an urgent safety measure is required to be taken to eliminate

an immediate hazard must be classified as a significant safety issue requiring an urgent safety measure. The Human Research Ethics Committee and the Sponsor's Delegate will be notified of any significant safety issues that meet the definition of an urgent safety measure within 72 hours. Examples include:

* a serious adverse event that could be associated with the trial procedures and that requires modification of the conduct of the trial
* a patient population hazard, such as lack of efficacy of an intervention used for the treatment of a life-threatening disease.

USM reports must be recorded in the [UNSW Safety Monitoring Register Template](https://research.unsw.edu.au/document/UNSW%20Safety%20Monitoring%20Register%20Template.xlsx).

1. Safety Assessment Flow Chart Investigational Medical Product Trials



1. Register of Clinical Trial Safety Monitoring Reports

A register of all event reports assessed and classified will be retained by the Coordinating Principal Investigator and reported to the trial sponsor annually and the HREC if required.

1. Reporting of Clinical Trial Safety Monitoring Reports

Single case reports of Adverse Events Adverse Reactions, Serious Adverse Events (SAEs), Serious Adverse Reactions (SARs), reports do not need to be reported to the UNSW Sponsor's Delegate or the HREC. All single case reports will be recorded in a safety monitoring register and will be reported to the UNSW Sponsor's Delegate annually.

Due to the low-risk nature of this trial, a formal Data and Safety Monitoring Committee (DSMC) will not be convened. In lieu of the of the DMSC, a Trial Steering Committee (TSC) will be employed for all monitoring and reporting. Adverse events and serious adverse events will be reported to the Trial Steering Committee (see Appendix 6 for details) when they meet monthly.

Any SUSAR’s will be reported immediately to the Sponsors’ independent expert. If the independent expert classifies/confirms the report as an unexpected serious adverse reaction, they will report this immediately to the Coordinating Principal Investigator. They will report the SUSAR to the UNSW Sponsors’ delegate as soon as possible and within 7 days of being made aware of the SUSAR.

If a SSI arises during the trial that requires an urgent safety measure, this will be documented and reported to the UNSW ethics committee and the UNSW sponsors delegate as soon as possible and within 7 days.

#### **Emerging Safety Issues**

For this trial, the Trial Steering Committee is responsible for reviewing the safety information to identify any serious emerging safety concerns. If safety concerns are identified, this body will establish a plan to minimise the time participants may be placed at excess risk of harm. Before implementing the plan, the Trial Steering Committee will seek the advice of the human research ethics committee and sponsor's delegate.

#### **Annual assessment of safety**

The following information will be provided in a report to the sponsors delegate annually:

* Documented evidence that the Trial Steering Committee confirmed that regular safety reviews occurred.
* Analysis of the trial and its implications for participants considering all available safety data and relevant clinical or non-clinical studies results.
* Any reports of emerging safety issues and a description of any measures taken or proposed to minimise risks.
* A copy of the safety monitoring register.

# **Non-compliance, Protocol Deviation and Serious Breaches of Good Clinical Practice**

## **Protocol Deviation**

A protocol deviation is defined as any breach, divergence or departure from the requirements of Good Clinical Practice, the clinical trial protocol, the clinical trial standard operating procedures, or the human ethics approval that does not have a significant impact on the continued safety or rights of participants or the reliability and robustness of the data generated in the research or clinical trial. Protocol deviations are events that do not occur persistently or systematically and do not potentially result in participant harms. Examples of protocol deviations include but are not limited to:

* Deviations because of participant adherence to the protocol, including rescheduled study visits, participants refusal to complete scheduled research activities or failure to complete self-report questionnaires required by the study protocol.
* Blood samples obtained or clinical trial testing occurring at times close to, but not precisely at the time points specified in the protocol.
* The completion of consent forms, safety monitoring report, case report forms or data collection tools in a manner that is not consistent with the protocol instructions or failure to make reports within the required reporting timeframes.
* Administration of the clinical trial investigational medical product or device in a manner that is not consistent with the manufacturer's instructions for use.
* Use of an unapproved version of the participant information statement or recruitment of participants using unapproved recruitment procedures.
* Inclusion of a participant that does not meet the inclusion criteria.
* An urgent safety measure must be taken to eliminate an immediate hazard to a participant's health or safety.

## **Serious Breach of Good Clinical Practice**

A serious breach is defined as a breach of Good Clinical Practice, the clinical trial protocol, the clinical trial standard operating procedures, or the human ethics approval that is likely to affect to a significant degree the safety or rights of participants or the reliability and robustness of the data generated in the clinical trial. Examples of serious breaches include but are not limited to:

* Persistent or systematic non-compliance with the instructions for completing consent forms, safety monitoring forms, case report forms or data collection tools that result in continued missed or incomplete data collection.
* Failure to record or report adverse events, serious adverse events, suspected unexpected serious adverse reactions, significant safety issues where urgent safety measures were implemented.
* Failure to conduct clinical trial procedures following the clinical trial delegation log.
* Widespread and uncontrolled use of protocol waivers affecting eligibility criteria, which leads to harm to trial subjects.
* Failure to report investigational medical product or device defects to the clinical trial sponsor or any relevant regulatory body.
* Failure to conduct research following the issued approvals, permits or licences by required laws, regulations, disciplinary standards, and UNSW policies relating to the responsible or safe conduct of research.
* Concealing or facilitating breaches (or potential breaches) of the Research Code by others.
* Researching without the requisite approvals, permits or licences required by laws, regulations, disciplinary standards, and UNSW policies related to the responsible or safe conduct of research.
* Failure to conduct research as approved by an ethics review body where that conduct leads to (or has the potential to) results in participant harms.
* Researching without ethics approval as required by the National Statement on Ethical Conduct in Human Research where that conduct leads to (or has the potential to) result in participant harms.
* Any breaches as outlined in the UNSW Research Misconduct Procedure or the Australian Code for responsible conduct of research that leads to (or can potentially) result in participant harms.

## **Reporting Protocol Deviations**

* Protocol deviations occurring at a site will be documented in site files and reported by the principal site investigator to the Coordinating Principal Investigator.
* The Coordinating Principal Investigator will review the protocol deviation and the clinical trial protocol to establish the corrective actions and preventative steps to prevent the deviation from reoccurring.
* The protocol deviation and corrective action plan will be reported to the UNSW Sponsor's Delegate by the Coordinating Principal Investigator or Coordinating Research Team using the protocol deviation report form.

## **Reporting of a Serious Breach**

* The Principal Investigator will report any serious breaches occurring at a participating site to the Coordinating Principal Investigator within a specified timeframe.
* The Coordinating Principal Investigator will review the serious breach, along with the clinical trial protocol, to develop a Corrective and Preventive Action (CAPA) that defines the steps to prevent the serious breach from reoccurring.
* The serious breach report and the CAPA will be provided to the approving HREC, and the UNSW sponsors delegate for review and approval.

## **Reporting of Serious Breaches by Third Parties**

* A Suspected Breach is a report judged by the reporter as a possible serious breach but has yet to be formally confirmed as a serious breach by the sponsor.
* A Suspected Breach form will be completed when a third party (e.g., individual/institution) wishes to report a suspected breach of Good Clinical Practice or the protocol and should be reported directly to the reviewing HREC without reporting through the sponsor.
* Recording of Protocol Deviation and Serious Breach Reports
* A register of protocol deviation and serious breach reports will be recorded. Written records and copies of documentation sent to the sponsor will be retained in the Investigator Site File.
* Copies of protocol deviation and serious breach reports will be recorded, written records and copies of documentation sent to the sponsor, referrals made to the HREC or establishing whether a breach of the Australian Code for Responsible conduct of research must be retained in the Master Site File.

# **Review of a Protocol Deviation and a Serious Breach**

* The UNSW Sponsor's Delegate will review reports to establish whether the event meets the definition of a protocol deviation or serious breach,  establish whether the proposed CAPA is appropriate and establish whether there is or will be ongoing impact reliability and robustness of the data generated.
* The UNSW Sponsor's Delegate will seek advice from the approving HREC on the corrective and preventive actions.
* Protocol deviation or serious breach reports where a UNSW researcher, staff or student is responsible for the protocol deviation or the serious breach will be reviewed as per the [UNSW Research Misconduct Procedure](https://www.gs.unsw.edu.au/policy/documents/researchmisconductproc.pdf) to establish a breach of the [UNSW Research Code of Conduct](https://www.gs.unsw.edu.au/policy/documents/researchcode.pdf) has occurred.
* Protocol deviation or serious breach reports where the UNSW Sponsor's Delegate determines that site personnel are responsible for a protocol deviation or the serious breach will be referred onto their responsible institution for review under their Research Misconduct procedures to establish whether a breach of the [Australian Research Code for the Responsible Conduct of Research](https://www.nhmrc.gov.au/about-us/publications/australian-code-responsible-conduct-research-2018) has occurred.

# **Statistics**For analyses, participants’ text data will be exported from the survey platform and analysed using Linguistic Inquiry and Word Count (LIWC) (Pennebaker et al., 2007), a robust and widely validated tool for extracting linguistic features from text. This software analyses text and calculates the percentage of words that reflect different emotions, thinking styles, social concerns, and parts of speech captured by the LIWC program dictionary (Tausczik & Pennebaker, 2010). This will result in a set of 68 linguistic features for each post which will then be correlated with mental health scores. The tool also calculates the total number of words within the text that match the program dictionary, reported as “dictionary words”. LIWC scores will be averaged across each text task, and then combined for an overall LIWC score. This will result in dataset consisting of participants’ symptom scores matched with their averaged LIWC scores for the same period. This dataset will be anonymised and published for open access. Latent Dirichlet Allocation (LDA) will be used for topic analysis. A generative model that allows sets of observations in text to be explored. It posits that each document is a mixture of a small number of topics and that each word is attributable to one of the document’s topics. Affective Norms for English Words (ANEW) will be used for emotional sentiment. This allocates a valence and arousal score for each English word. The dimension of valence ranges from highly positive to highly negative and arousal ranges from calming to agitating. For the inferential modelling, bayesian context models and machine learning methods will be employed to extract, for each participant, the linguistic features, emotional sentiment, and topics that highly correlate with their mental health. Bivariate analyses will be undertaken to investigate the correlation between the linguistic features and symptom scores between individuals. We will perform multivariate analysis between multiple linguistic features using partial-least squares (PLS) regression. Because our past research has shown that these group-level inferences do not always generalise to intra-individual changes in symptom scores over time, we will test the PLS regression model constructed on group-level data on repeated measures of single participants using a two-staged approach. We will first use the group-level model to predict the symptom scores at each time point at which linguistic features were extracted and symptoms were assessed and correlated the predicted and observed symptom scores across time points for each participant. We will then compare the correlation coefficients estimated for each participant at the group level. To do this, we will convert the correlation coefficients using Fisher's z transformation and compare the z-scores against zero using a one-sample t-test.

# **Data Ownership**

All research data collected during this trial is governed and handled following the Research Data Governance and Materials Handling [policy](https://www.gs.unsw.edu.au/policy/documents/researchdatagovernancepolicy.pdf). UNSW, rather than any individual or Organisational Unit, is the Custodian of data and materials and any information derived from the data. Original research data and primary materials generated in the research conducted at the University will be owned and retained by the University subject to any contractual, statutory, ethical, or funding body requirements.

# **Handling and Reporting Data**

Principal Investigators will be responsible for maintaining adequate and accurate source documents and trial records that include all pertinent observations on each site's trial subjects. Source data will be attributable, legible, contemporaneous, original, accurate, and complete.

All aspects of the study, including data collection and storage will be administered through the Black Dog Institute Research Engine. The Research Engine stores data on secure servers commissioned by the University of New South Wales IT and is hosted on the GovDC Data Centres located in Silverwater, Sydney. The data is stored in a SQL Server 2016 database which is backed up daily on a drive on the server. The drive itself is backed up daily to a tertiary location. Server backups are performed daily and weekly. The daily backups are retained for 2 weeks, the weekly backups for 6 weeks, the monthly backups for 6 months and half yearly backups for 7 years. Access to the servers is strictly controlled and only authorised UNSW IT and Black Dog Institute IT staff can access the servers (VPN) using Two Factor Authentication. UNSW servers are penetration tested regularly for security vulnerabilities and UNSW IT also perform regular security patches and updates on the servers. The Research Engine itself is only accessible to authorised personnel, including the Chief Investigators and the Black Dog Institute IT and data analytics team. Upon completion of the study, participants’ data will be exported, de-identified analysed using various statistical software packages.

The Black Dog Research Engine automatically generates a unique ID code for each participant that is included in all reports. This enables de-identification of the dataset for analysis. For analysis, a copy of the data (via a Microsoft Excel spreadsheet) is exported from the Research Engine and saved as a password protected file on One Drive in a folder only accessible to the co-investigators named on this project. Individual identifiers will then be removed from the data using the following method: Indirect (e.g. email address, mobile phone number, IP addresses) identifiers will be separated from the dataset by an approved member of the research team listed on this application. The master list for the de-identification will be stored separately to the de-identified data, in a password protected file, stored on OneDrive, and only accessible by the Coordinating Principal Investigator and research officer approved on this project. A separate spreadsheet consisting of participants’ email addresses and mobile phone numbers will also be stored in a password protected file, in a private folder on One Drive to enable the GiftPay vouchers to be sent to participants.

As this study is collecting personal information (e.g., mobile phone numbers and email addresses), this information is protected in accordance with the Australian Privacy Act 1988. Participants have the right to access and destroy any personal information collected by this study. If participants have concerns about the way their data has been handled, they are encouraged to notify the Coordinating Principal Investigator and the UNSW HREC. This information is outlined for participants in the PISCF.

All data will be retained for 15 years after study completed. Data may be used for future research purposes or shared with other researchers only for studies related to this general research topic. In addition to the above, the following processes will be followed:

* + The researchers will nominate a member of the research team to be responsible for data sharing (a data custodian) and this person is Dr Bridianne O’Dea.
	+ Individual identifiers will be removed from the data using the following method: Indirect (e.g. email address, mobile phone number, IP addresses) identifiers will be separated from the dataset by an approved member of the research team listed on this application. The master list for the de-identification will be stored separately to the de-identified data, in a password protected file, stored on OneDrive, and only accessible by Coordinating Principal Investigator and research officer approved on this project.
	+ The study data will be provided to other researchers in a de-identified format via a private OneDrive file. In addition, participants actual text responses (i.e., their raw text data) will not be shared with any researchers for secondary research purposes. Only analysed data (e.g., linguistic features, topics analysis, or sentiment) will be shared.
	+ Where possible, the researcher will ask others who wish to access the data for a copy of their ethics approval to do so before the data is shared for secondary research purposes. The researcher will maintain a copy of other researchers' ethics approval for their records.
	+ The researcher will transfer the data to other researchers by sharing a link to a secure UNSW OneDrive folder or providing a downloadable, de-identified locked data file (e.g. published as part of open access journal requirements).
	+ The researcher will report to the HREC the number of times the data has been accessed for a secondary research purpose on their Annual Monitoring Report or the number of times the aggregated data has been published, which is required to be completed annually as a condition of approval for all research projects. Please note – this will not be possible for all secondary data analyses as many journals require the dataset to be published alongside the paper. Therefore, we are not able to track all use of the data but can report the number of datasets published.
	+ Participants will be able to opt into this secondary research via the online consent form.

## **Direct Access to Source Data and Documents**

Site principal investigators and the Black Dog Institute will permit trial-related monitoring, audits, IRB/IEC review, and regulatory inspection(s), providing direct access to source data/documents.

# **Monitoring Quality Control and Quality Assurance**

The Coordinating Principal Investigator and Principal Investigators 'responsibility are to monitor the clinical trial. The Coordinating Principal Investigator and Principal Investigators are responsible for undertaking or participating in site initiation or protocol-specific training before recruitment and data collection commences. A monitoring report demonstrating regular compliance monitoring with the clinical trial protocol, procedures, and HREC approval will be provided to the UNSW Sponsor's Delegate annually.

Root, cause, analysis reports are to be completed by the Coordinating Principal Investigator for reports of non-compliance and serious breaches. A corrective and preventative action plan must be developed and actioned for any reports of non-compliance and serious breaches.

# **Clinical Trial Research Agreement**

The Coordinating Principal investigators will ensure that agreements are executed at each of the following sites before site initiation, recruitment, and data collection commences.

# **Research Governance Site Authorisation**

Site authorisation is to be obtained, or if a research site is added, a site authorisation letter from the delegated authority of an institution responsible for any participating site is obtained. It is to be stored as a GCP essential document before participants are recruited at a participating site.

# **Good Clinical Practice Requirements**

It is recommended that the Coordinating and Principal Investigators' ensure that all investigators and trial-related staff have current Good Clinical Practice Training. Once completed, the evidence of training confirmation is to be stored as a GCP essential document.

It is the responsibility of the Coordinating and Principal Investigators to familiarise themselves with the requirements of the [Guideline for Good Clinical Practice (E6, R2)](https://database.ich.org/sites/default/files/E6_R2_Addendum.pdf)

# **Essential Documents for the Conduct of a Clinical Trial**

All essential documents referred to in section 8.2 of the [Guideline for Good Clinical Practice (E6, R2)](https://database.ich.org/sites/default/files/E6_R2_Addendum.pdf)  are to be retained by all trial investigators.

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| --- | --- | --- |
| **Trial Documentation**  | **Version** | **Date** |
| Human Research Ethics Committee Approval | V1 | 09.07.2021 |
| HC210397 UNSW Risk Assessment Human Research Ethics Application | V3 | 06.07.2021 |
| HC210397 Project Description | V4 | 31.08.2021 |
| Appendix 1 – Description of the text tasks | V3 | 31.08.2021 |
| Appendix 2 – Online mental health survey  | V2 | 31.08.2021 |
| Appendix 3 - Screening protocol  | V3 | 31.08.2021 |
| Appendix 4 - Study adverts  | V2 | 29.06.2021 |
| Appendix 5 - Participant Information Statement and Consent Form | V4 | 31.08.2021 |
| Appendix 6 – Trial Steering Committee Terms of Reference | V1 | 29.06.2021 |
| Appendix 7 – Standard operating procedures | V1 | 29.06.2021 |
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| **Legal Agreements and Regulatory Information** | **Version** | **Date** |
| Insurance Certificate | V1 | 15.07.2021 |

# **Clinical Trial Delegation and Responsibilities Log**

| **Protocol / Study Number:** | UNSW HREC HC210397 | **Sponsor Name:** | University of New South Wales |
| --- | --- | --- | --- |
| **Principal Investigator Name:** | Dr Bridianne O’Dea | **Site Number:** | NA |
| **Site Name (if applicable)** | NA |

**\*THIS FORM IS TO BE COMPLETED BY ALL PERSONNEL INVOLVED IN THE STUDY AFTER RECEIVING PROPER STUDY TRAINING AND BEFORE TAKING PART IN ANY STUDY ACTIVITIES**

**Principal Investigator (PI)**

By signing, I confirm/acknowledge that the tasks listed below will only be delegated to appropriately trained, skilled and qualified staff. I will remain responsible for the overall study conduct and reported data, ensuring study oversight. All associates, colleagues, and employees assisting in the conduct of the study are informed about their obligations and have not performed any study tasks before appropriate delegation and completion of appropriate training. Mechanisms are in place to ensure that site staff receives the appropriate information and training throughout the study and that a 2-way communication channel exists between staff and self. Any changes in staff or delegation in staff will be recorded promptly.

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| **Name** | **Principal Investigator’s Signature** | **Initials** | **Start****(dd/mmm/yyyy)** | **End****(dd/mmm/yyyy)** **(complete only if prior to end of study)** |
| Bridianne O’Dea | A black and white logo  Description automatically generated with low confidence | BOD | 14/10/2021 |  |

Site Staff

| **Name** | **Signature** | **Initials** | **Study Role** | **Key Study Task(s)****(choose from list below)** | **Start****(dd/mmm/yyyy)** | **End****(dd/mmm/yyyy) (complete only if prior to end of study)** | **PI Initials & Date****(dd/mmm/yyyy)** |
| --- | --- | --- | --- | --- | --- | --- | --- |
| Cassandra Chakouch |  | CC | Research Officer | Subject selection and recruitment; Evaluate study related results/outcomes; Maintain essential documents | 14/10/2021 |  |  BOD14/10/2021 |
| Cesar Anonuevo |  | CA | Technical/IT support | Technical support | 14/10/2021 |  |  BOD14/10/2021 |
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| **Comments:**  |
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| **Electronic Signature Declaration for Principal Investigator and Site Staff**1. My electronic signature as it applies to entering electronic data or signing records in sponsor-owned or sponsor -outsourced computer systems is the legally binding equivalent of my handwritten signature.
2. I will not share password(s) assigned to me for this study with any other persons.
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| **Principal Investigator's End of Study Declaration**I hereby confirm that the above information is accurate and complete, and that I authorised the delegation of study-related tasks to each individual as listed above. **Principal Investigator’s Signature:** A black and white logo  Description automatically generated with low confidence **Date:**  14/10/2021 |

**Task Key:**

|  |  |
| --- | --- |
| 1. Obtain informed consent \* | 12. Sample collection |
| 2. Subject selection/recruitment\* | 13. Sample processing and/or shipment |
| 3. Confirm eligibility (review inclusion/exclusion criteria)\* | 14. Evaluate study-related test results \* |
| 4. Obtain medical history (source documents) | 15. Use IWRS/IVRS  |
| 5. Perform physical exam\*  | 16. Make entries/corrections on (e)CRFs |
| 6. Conduct study visit procedure as outlined in the protocol\* | 17. Sign- off (e)CRFs\* |
| 7. Make study-related medical decisions\* | 18. Maintain essential documents |
| 8. Assess AEs/SAEs\* | 19. Perform study-related assessments as per protocol \* |
| 9. Dispense study drug\* | 20. Complete company- specific log ( if applicable) |
| 10. Perform drug accountability | 21. Other (specify) Technical support |
| 11. Study drug storage and temperature monitoring | 22. Other (specify) \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ |

\*These tasks may only be performed by qualified individual as permitted by local law, medical or standard of care practices, or applicable required training as per job description or designation.

# **Safety Monitoring Register Template**

* [UNSW Safety Monitoring Register Template](https://research.unsw.edu.au/document/UNSW%20Safety%20Monitoring%20Register%20Template.xlsx)
* [UNSW Adverse Event or Incident Event Case Report Form](https://research.unsw.edu.au/document/Adverse%20Event%20Incident%20Report%20Form%20September%202019%20.docx) Example.
1. **References and Literature**

Arango, C., Díaz-Caneja, C. M., McGorry, P. D., Rapoport, J., Sommer, I. E., Vorstman, J. A., McDaid, D., Marín, O., Serrano-Drozdowskyj, E., Freedman, R., & Carpenter, W. (2018). Preventive strategies for mental health. *The Lancet Psychiatry, 5*(7), 591-604. [https://doi.org/10.1016/S2215-0366(18)30057-9](https://doi.org/10.1016/S2215-0366%2818%2930057-9)

Burgess, P. M., Pirkis, J. E., Slade, T. N., Johnston, A. K., Meadows, G. N., & Gunn, J. M. (2009). Service use for mental health problems: findings from the 2007 National Survey of Mental Health and Wellbeing. *Aust. N. Z. J. Psychiatry, 43*(7), 615-623.

Dickert , N., & Grady , C. (1999). What's the Price of a Research Subject? Approaches to Payment for Research Participation. New England Journal of Medicine, 341(3), 198-203. [https://doi.org/doi:10.1056/NEJM199907153410312](https://doi.org/doi%3A10.1056/NEJM199907153410312)

Edwards, T., & Holtzman, N. S. (2017). A meta-analysis of correlations between depression and first person singular pronoun use. *Journal of Research in Personality, 68*, 63-68. <https://doi.org/10.1016/j.jrp.2017.02.005>

Geladi, P., & Kowalski, B. R. (1986, 1986/01/01/). Partial least-squares regression: a tutorial. Analytica Chimica Acta, 185, 1-17. [https://doi.org/https://doi.org/10.1016/0003-2670(86)80028-9](https://doi.org/https%3A//doi.org/10.1016/0003-2670%2886%2980028-9)

Litvinova, T., Seredin, P., Litvinova, O., & Zagorovskaya, O. (2016). Profiling a set of personality traits of text author: what our words reveal about us. *Research in Language, 14*(4), 409-418. <https://doi.org/10.1515/rela-2016-0019>

Mathers, C. D., & Loncar, D. (2006). Projections of global mortality and burden of disease from 2002 to 2030. *PLoS Medicine, 3*. <https://doi.org/10.1371/journal.pmed.0030442>

Oliver, M. I., Pearson, N., Coe, N., & Gunnell, D. (2005). Help-seeking behaviour in men and women with common mental health problems: cross-sectional study [10.1192/bjp.186.4.297]. *British Journal of Psychiatry, 186*(4), 297-301. <http://bjp.rcpsych.org/content/186/4/297.abstract>

Ozomaro, U., Wahlestedt, C., & Nemeroff, C. B. (2013, May 16). Personalized medicine in psychiatry: problems and promises. *BMC Medicine, 11*, 132. <https://doi.org/10.1186/1741-7015-11-132>

Pennebaker, J. (2011). *The secret life of pronouns: what our words say about us*. Bloomsbury.

Pennebaker, J., Chung, C., Frazee, J., Lavergne, G., & Beaver, D. (2014). When Small Words Foretell Academic Success: The Case of College Admissions Essays. *PloS One, 9*(12), e115844. <https://doi.org/10.1371/journal.pone.0115844>

Reips, U. D. (2002). Standards for Internet-based experimenting. Experimental Psychology, 49(4), 243-256. https://doi.org/10.1026/1618-3169.49.4.243

Ripke, S., Wray, N. R., Lewis, C. M., Hamilton, S. P., Weissman, M. M., Breen, G., Byrne, E. M., Blackwood, D. H., … & Sullivan, P. F. (2013, Apr). A mega-analysis of genome-wide association studies for major depressive disorder. *Molecular Psychiatry, 18*(4), 497-511. <https://doi.org/10.1038/mp.2012.21>

Snyderman, R. (2012). Personalized health care: From theory to practice. *Biotechnol. J, 7*(8), 973-979. <https://doi.org/10.1002/biot.201100297>

Tausczik, Y. R., & Pennebaker, J. W. (2010). The psychological meaning of words: LIWC and computerized text analysis methods. Journal of Language and Social Psychology, 29, 24-54.

Varoquaux, G., Raamana, P. R., Engemann, D. A., Hoyos-Idrobo, A., Schwartz, Y., & Thirion, B. (2017). Assessing and tuning brain decoders: cross-validation, caveats, and guidelines. NeuroImage, 145, 166-179.

Wright, A., Jorm, A. F., & Kelly, C. M. (2007). Improving mental health literacy as a strategy to facilitate early intervention for mental disorders. *Medical Journal of Australia, 187*(7), S26.

**Appendix 6: Trial Steering Committee**

**The MyMood&Me Project: Using text data to infer mental health**

**Trial Steering Committee**

**Version 1 (29th June 2021)**

## Administrative details

|  |  |
| --- | --- |
| **Title:** | The MyMood&Me Project: Using text data to infer mental health |
| **Sponsor:** | University of New South Wales (UNSW) |
| **HREC:** | University of New South Wales Human Research Ethics Committee |
| **Chief Investigator:** | Dr Bridianne O’Dea, Black Dog Institute, UNSW |
| **Research Manager:** | Ms Cassandra Chakouch, Black Dog Institute |
| **Data Steward:** | Dr Bridianne O’Dea, Black Dog Institute, UNSW |
| **Funding body:** | National Health and Medical Research Council |
| **HREC Reference number:**  | HC210397 |
|  |  |
| **ANZCTR Number:** | To be confirmed |
| **Number of Sites:**  | 0 |
| **Number of Participants:**  | 140 |

## **Summary**

The MyMood&Me project aims to explore the role of text data for producing reliable linguistic markers of depression and anxiety among adults with mental illness. Over 9 weeks, participants will be randomly assigned to receive a series of writing tasks alongside fortnightly self-report mental health assessments. The linguistic expression within the text data will be analysed to examine if it is sufficient to identify any existing linguistic markers of depression and anxiety.

Using online recruitment, 140 participants will be recruited from a clinical population. All participants will be aged 18 years or older and have at least moderate symptoms of depression or anxiety (i.e., total score ≥ 10 on the PHQ-9 or GAD-7).

## **Design**

This trial is a pilot randomised crossover design of 9 weeks duration (i.e., 56 days of intervention and one additional week to complete study assessments). There will be four intervention periods, each lasting 14 days, with two types of writing tasks (a repetitive stimulated writing task and a one-off stimulated writing task) scheduled for each intervention period. In addition to the randomised writing tasks, participants will be asked to complete five fortnightly mental health surveys, scheduled on days 1, 14, 28, 42, 56.

## **Aims**

The current trials primary aim is to examine the potential of brief writing tasks for producing valid and reliable linguistic markers of depression and anxiety among adults with mental illness. The primary outcome will be assessed by examining correlations of linguistic features with symptoms. The trial will also aim to examine:

1. The type of text data (e.g., SMS, social media posts, expressive writing, image reflections) that is most useful for generating linguistic markers.
2. The level of acceptability and engagement in completing repetitive text tasks of this kind for generating linguistic markers of mental health.

## **Data**

All participants will complete self-report questionnaires, including:

* Demographics (baseline only)
* History of mental health (baseline only)
* Motivations for participation (baseline only)
* Personality (The Standardised Assessment of Personality; baseline only)
* Rumination (Ruminative Response Scale; RRS-short form; baseline and endpoint)
* Mastery (The Perceived Mastery Scale; baseline and endpoint)
* Depressive Symptoms (Patient Health Questionnaire; PHQ-9; baseline, 2 weeks, 4 weeks, 6 weeks, endpoint)
* Generalised Anxiety (Generalised Anxiety Disorder; GAD-7; baseline, 2 weeks, 4 weeks, 6 weeks, endpoint)
* Mood Monitoring (Multidimensional Mood Questionnaire; MDMQ)
* Acceptability (mid-endpoint only)

**Trial Steering Committee (TSC)**

**Overview**

* The TSC will function in accordance with the principles of the following documents: Good Clinical Practice (GCP) Guidelines, Declaration of Helsinki 2000, NHMRC National Statement on Ethical Conduct in Human Research, NHMRC Guidance Safety and Monitoring of Clinical Trials involving a Therapeutic Good, and University of New South Wales HREC guidelines.
* Members will disclose conflicts of interest and will be cleared of significant conflicts of interest and potential conflicts of interest. No member should have financial, proprietary, professional, or other interests that may affect impartial, independent decision-making by the TSC.
* Composition of membership will reflect expertise in clinical, statistics and the specific scientific expertise relevant to the study, in this case, suicidality ad suicidal ideation.
* A quorum group of two must be present for closed sessions and subsequent decisions and/or recommendations made by the committee.

**Roles and responsibilities**

The purpose of the Trial Steering Committee (TSC) is to supervise of the overall conduct of the trial, by safeguarding the interests of study participants and assessing the safety and efficacy of the trial protocol.

The TSC will provide:

* Advice, guidance, and consultation on trial design and conduct
* Consultation on trial roadblocks and issues
* Oversight of trial processes
* Consultation on scientific quality and integrity
* Final sign-off on Trial Protocol
* Oversight of compliance with Good Clinical Practices

The investigators will:

* Assure the proper conduct of the study.
* Assure collection of accurate and timely data.
* Report relevant data to the TSC prior to scheduled meetings.
* Promptly report safety concerns to the TSC.
* Communicate with regulatory authorities (e.g., HREC) as necessary.

### **Composition**

TSC membership for the trial will be established prior to recruitment commencing.

**Meetings**

Prior to recruitment commencing, the TSC members will form an understanding of the protocol and study endpoints. The TSC will meet monthly once the trial commences, and will be held face-to-face if practicable, or otherwise by video conference. Prior to each meeting, a report will be sent to the TSC outlining the points of discussion and trial updates.

**Reporting**

A serious adverse event (SAE) for this trial is defined as any untoward occurrence that involves hospitalisation or death (suicide or otherwise). As per the NHMRC Safety Monitoring and Reporting Guidelines, any suspected unexpected SAEs or reactions will be reported to the TSC and the UNSW Human Research Ethics Committee within 24 hours of the research team becoming aware, using the Adverse Event Form provided by the UNSW HREC. All AEs, both solicited and spontaneous, will be reported to the TSC.

A breach of protocol is defined as something likely to affect the rights and safety of a trial participant (for example, the sharing of data to those outside those with approved access), or the reliability or robustness of the data is compromised. Any serious breaches of protocol will be reported to the TSC and UNSW HREC within 24 hours of the research team becoming aware, using the Suspected Serious Breach Report Form.

**Confidentiality**

All information and data provided to the TSC will be considered privileged and confidential. The TSC will agree to use these data to accomplish the responsibilities of the TSC and will not use it for any other purpose without written consent from the Chief Investigator or trial sponsor.

**Safety analyses**

The primary safety endpoints are:

* Severe Suicidal ideation, as measured by percentage of participants scoring 3 on item-9 of the PHQ-9.

**Stopping guidelines**

The primary charge of the TSC is to monitor the study for participant safety. As such, the TSC may recommend pausing or terminating the trial if they have concerns for participant safety, based on (but not limited to) a higher than anticipated rate for one or more of the primary endpoints.

# **Appendix 7: Standard operating procedures**

**The MyMood&Me Project: Using text data to infer mental health**

**Standard operating procedures**

**Version 1 (29th June 2021)**

**Procedures for eliciting reports of and for recording and reporting adverse event and intercurrent illnesses.**

**Adverse Events and Serious Adverse Events**

For this current trial, an adverse event (AE) is defined as any untoward medical or clinical occurrence in a participant without regard to the possibility of a causal relationship. All AEs will be collected after a participant has consented and enrolled into the trial. AEs may include severe suicidal ideation as reported on fortnightly mental health surveys (days 1, 14, 28, 42, and 56). Severe suicidal ideation will be defined as self-reports of suicidal thoughts or thoughts of self-harm nearly every day, indicated by a score of 3 on item-9 of the PHQ-9.

A serious adverse event (SAE) for this trial is defined as any untoward occurrence that involves hospitalization or death (suicide or otherwise) without regard to the possibility of a casual relationship.

**Reporting Adverse Events**

The trial will maintain a record of any reported adverse events or serious adverse events. A summary of adverse events will be reported to the trial’s qualified expert (as named in Section 1). A summary of serious adverse events will be reported annually to the UNSW sponsors delegate and UNSW ethics committee.

Due to the low-risk nature of this trial, a formal Data and Safety Monitoring Committee (DSMC) will not be convened. In lieu of the of the DMSC, a Trial Steering Committee (TSC) will be employed for all monitoring and reporting. Adverse events and serious adverse events will be reported to the Trial Steering Committee (see Appendix 6 for details) when they meet monthly.

Any suspected unexpected serious adverse reactions (SUSAR) will be reported immediately to the Sponsors’ independent expert. If the independent expert classifies/confirms the report as an unexpected serious adverse reaction, they will report this immediately to the coordinating principal investigator (CPI). The CPI will report the SUSAR to the UNSW Sponsors’ delegate as soon as possible and within 7 days of being made aware of the SUSAR.

If a significant safety issue (SSI) arises during the trial (e.g., any issue that could adversely affect the safety of participants or materially impact on the continued ethical acceptability or conduct of the trial), that requires an urgent safety measure (e.g., any action taken to eliminate an immediate hazard to a participants health), this will be documented and reported to the UNSW ethics committee and the UNSW sponsors delegate as soon as possible and within 7 days.

In accordance with UNSW requirements, the Chief Investigator will also notify the UNSW Sponsor’s delegate of:

* Protocol Deviation reports outlined in the UNSW Research Misconduct Procedure.
* Any serious breach of Good Clinical Practice, the clinical trial protocol, the clinical trial standard operating procedures, or the human ethics approval that is likely to affect to a significant degree the safety or rights of participants or the reliability and robustness of the data generated in the clinical trial.
* Safety Reports relating to the continuation, suspension, or discontinuation of the clinical trial for safety reasons as they arise.
* Participant complaints or concerns received in relation to the conduct of the research.
* Any significant modifications to the clinical trial that are likely to affect to a significant degree the safety or rights of participants or the reliability and robustness of the data generated in the clinical trial.
* Amendments to clinical trial research agreements or service level agreements.
* Revisions to regulatory requirements including correspondence with the Therapeutic Goods Administration, clinical trial registries or the FDA.

**Procedure for the type and duration of the follow-up of subjects after adverse events**

The current trial will recruit participants from a clinical population, it’s expected that feelings of anxiety and/or depression, and suicidal thoughts or thoughts of self-harm will be common. Included at the end of each fortnightly mental health survey are suggested resources and contact details for services, should participants become distressed and need assistance. These services include Lifeline, Beyond Blue, and Kids Helpline as well as a range of resources and support from the Black Dog Institutes website. Participants that experience an AR and/or SAR will be contacted by an independent psychologist for a telephone consultation and risk assessment.

**Procedure for accounting for missing, unused, and spurious data**

All data will be collected via online surveys, rather than pencil-and-paper responses, reducing the amount of missing data or errors within the data set. To maintain data integrity frequency tables of all variables (including time and date information) will be collected and checked to ensure that scale items have only legal values. These legal values will also be checked for coherency (i.e., do end times/dates occur after corresponding ‘start’ time/dates.

Any missing items will be flagged with a value that cannot be confused as a legal value. Additionally, a present/absent indicator variable will be created for each data collection timepoint to track missing data due to participant absence. For partially answered inventories, respondents that answer at least 50% of items on a scale and still have a valid score will be allowed (Bell &Fairclough, 2014). Respondents that have less than 50% of items on scale completed will be assigned as missing values. The research team will be guided by the trial statistician in data analysis.

**Procedures for reporting any deviation(s) from the original statistical plan (any deviation(s) from the original statistical plan should be described and justified in protocol and/or in the final report, as appropriate)**

Any deviation for the original statistical plan will be submitted to the University of New South Wales HREC for approval before implementation.