**Clinical Trial Protocol**

**Excluded Medical Device**

Improving Access to Care for Australian Children – The Online Mental Health Check:

Two School Based Randomised Controlled Trials

Version 9: 13th January 2023

Professor Jennie Hudson

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# **General Information**

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| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Protocol Title** | | | | | | | | | | | | | | |
| Improving Access to Care for Australian Children – The Online Mental Health Check: Two School Based Randomised Controlled Trials | | | | | | | | | | | | | | |
| **Protocol identifying number** | | TBD Ethics in preparation | | | | | | | | | | | | |
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| **Version Number** | |  | | | | **Version date** |  | | | | | | | |
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| **Human Research Ethics Committee** | | | | | | | | | | | | | | |
| **Name** | UNSW | | | | | | | | | | | | | |
| **Status of ethical review** | **Approved**  **In progress**  **To be submitted** | | | | | | | | | | | | | |
| **Trial Sites** |  | | | | | | | | | | | | | |
| **Funding for the Clinical Trial** | | | | | | | | | | | | | | |
| **Funding Body Name** | AMP Foundation ($50,000)  Johnston Foundation ($325,695) | | | | | | | | | | | | | |
| **Amount of Funding** | $375,695 | | | | | | | | | | | | | |
| **Regulatory Requirements** | | | | | | | | | | | | | | |
| **Therapeutic Goods Administration Clinical Trial Notification** | | | | | | | | | | | **Yes**  **No** | | | |
| **Insurance for Clinical Trial** | | | | | | | | | | | | | | |
| **Insurer** | UNSW | | | | | | | | | | | | | |
| **Type of Insurance** | Clinical trials are not automatically covered by UNSW insurance, and confirmation must be obtained by completing the [Clinical Trials Spreadsheet](https://www.fin.unsw.edu.au/sites/default/files/content/clinicaltrials.xlsx) and sending it to the UNSW Insurance manager ([peter.mccarthy@unsw.edu.au](mailto:peter.mccarthy@unsw.edu.au)).  Once insurance has been confirmed, attach a copy of the insurance certificate to the trial protocol. | | | | | | | | | | | | | |
| **Confirmation of Insurance** | **Attached**  **In progress**  **To be submitted** | | | | | | | | | | | | | |

# **Safety and Monitoring Contacts**

|  |  |
| --- | --- |
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| **Trial Management Group** | |
| Professor Jennie Hudson, Dr Deanna Francis, Dr Annabel Songso, Dr Chloe Lim, Ms Abigail Allsop, Ms Emma McDermott | |

**Delegation of Clinical Trial Duties**

Responsibilities for the conduct and oversight for the trial are delegated to you as the Coordinating Principal Investigator. You may delegate trial related responsibilities to the listed Principal Investigator(s) and any trial-related personnel. All trial-related duties delegated by the Coordinating Principal Investigator or Principal Investigator(s) and trial-related personnel must only be delegated to those that are qualified by experience and training. Delegated responsibilities must 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 is to 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 has the potential to 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 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.
* 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**

The overarching goal of this research is to evaluate an Online Mental Health Check designed for children in Grades K to 6. The mental health check will be a way for parents and/or children to report on anxiety and depression. Parents will receive a report with the results and triage services for support (e.g., psychoeducation, links to services, psychologists, evidence-based care). We plan to conduct a school-based study with two independent randomized controlled trials to answer the following research questions:

1. Does personalized triaging significantly improve access to evidence-based mental health care for children aged 6 to 12 years compared to children aged 6 to 12 years receiving standard care?
2. Does the mental health check significantly impact stigma for children aged 6 to 12 years and their parents, compared to children who do not complete regular mental health checks and their parents?

# **Background Information**

This project has the potential to improve access to mental health care for Australian children aged 6 to 12 years with anxiety and/or depression. Anxiety and depression impact around 7 to 14% of Australian children (Lawrence et al., 2015), yet many children do ***not***receive appropriate evidence-based care to support their needs. Indeed, a recent study showed that only 19.5% of children experiencing anxiety accessed evidence-based therapy to support their mental health (Ghandi et al., 2021). This means that an alarming proportion of children with anxiety and depression are unsupported, which is concerning given that we know untreated mental health problems are associated with poor outcomes for children that frequently persist into adulthood (Cresswell et al., 2020; Ford et al., 2007). We also know that early detection and access to care improves outcomes for young people. However, there are many barriers impacting capacity to access evidence-based care, including 1) limited mental health knowledge – especially *where* to seek help, 2) perceived self and public stigma and embarrassment, 3) negative perceptions regarding the therapist and issues with trust, and 4) financial cost, service availability, long waitlists exacerbated by Covid-19, and logistical barriers (Radez et al., 2021). We aim to address some of these concerns in the current study.

Currently, there is wide interest in online screening tools to identify anxiety and depression symptoms in young people. Preliminary evidence is underway to evaluate an online screening and intervention tool for children aged 4 to 7 years in the United Kingdom (e.g., MY-CATS; Reardon et al., 2022), and similar screening tools have been developed for adolescents (e.g., Youth StepCare; Parker et al., 2020) and adults (e.g., Practitioner Online Referral and Treatment Service [PORTS]; Titov et al., 2020). While the MY-CATS tool is currently being evaluated, there is preliminary evidence to support the efficacy of Youth StepCare. Youth StepCare is a web-based universal screening service that was developed to identify anxiety and depression symptoms in patients aged 14 to 17 years presenting to GP clinics (Parker et al., 2020). Evaluation of Youth StepCare in a 12-week uncontrolled trial revealed that the service was useful for identifying patients aged 14 to 17 years with unidentified symptoms of anxiety and depression. In terms of PORTS, evaluation revealed that the service improved access to **one third** of adults with mental health difficulties who are not currently accessing care (Titov et al., 2020). Thus, the limited number of online screening tools available seem to be promising in their ability to detect anxiety and depression in adolescents and adults.

A clear limitation of the existing literature is that there are no online mental health assessment tools to identify anxiety and depression symptoms in Australian children aged 6 to 12 years. We aim to fill this gap in the current study by developing an online mental health check which will be an assessment and triage service for children aged 6 to 12 years. This online mental health check aims to **identify and detect symptoms of anxiety and depression in children,** while triaging aims to **increase children’s access to evidence-based care to support children’s mental health.** We aim to evaluate whether the mental health check and the **provision of triage information** increases access to care by conducting a school based randomised controlled trial. We also aim to evaluate whether the mental health check alone significantly impacts stigma in children aged 6 to 12 years by conducting a school-based cluster randomised controlled trial.

**References:**

Lawrence, D., et al., 2015. The mental health of children and adolescents: Report on the second Australian child and adolescent survey of mental health and wellbeing. *Department of Health, Canberra*, p. 4-5.

Radez, J., et al., 2021. Why do children and adolescents (not) seek and access professional help for their mental health problems? A systematic review of quantitative and qualitative studies. *Eur Child Adolesc Psychiatry, 30*(2), 183-211. <https://doi.org/10.1007/s00787-019-01469-4>

Reardon, T., Dodd, H., Hill, C., Jasper, B., Lawrence, P. J., Morgan, F., Rapee, R. M., Ukoumunne, O. C., Violato, M., Davey, E., Halliday, G., Jones, B., Martineau, L., McCall, A., Niekamp, N., Placzek, A., Potts, R., Weisser, T., & Creswell, C. (2022). Minimising young children's anxiety through schools (MY-CATS): protocol for a cluster randomised controlled trial to evaluate the effectiveness and cost-effectiveness of an online parent-led intervention compared with usual school practice for young children identified as at risk for anxiety disorders. Trials, 23(1), 1-15. [149]. <https://doi.org/10.1186/s13063-022-06010-8>

Parker, B. L., Achilles, M. R., Subotic-Kerry, M., & O’Dea, B. (2020). Youth StepCare: a pilot study of an online screening and recommendations service for depression and anxiety among youth patients in general practice. BMC Family Practice, 21(1), 1-10.

Titov, N., et al.. 2020. Evaluation of The Practitioner Online Referral and Treatment Service (PORTS): the first 18 months of a state-wide digital service for adults with anxiety, depression, or substance use problems. *Cogn Behav Ther, 49*(4), 307-326. https://doi.org/10.1080/16506073.2019.1666162

# **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 design is a school-based study where we aim to conduct an (1) individual randomized controlled trial with two intervention arms, and 2) a cluster randomized controlled trial with two intervention arms. These trials are two independently run studies. Trial 1 will collect data during baseline assessment and follow-up assessments at 5 and 10 weeks. For trial 2, data will be collected during a baseline assessment and follow up assessments at 6 and 12 weeks. Parent and child report data will be collected using standardized questionnaires delivered online. Details of the Trial 1 and 2 designs are shown in the below flowcharts:

Diagram

Description automatically generated

Diagram

Description automatically generated

***Description of the Intervention***

The mental health check is a questionnaire delivered on a website that offers a way for parents and children to answer questions on symptoms of anxiety and depression. The responses will be automatically and immediately scored using algorithms, and the data will be transformed into a PDF report (e.g., test description, scores). The report also includes “triage” information about services and resources that can support the child (e.g., psychoeducation, parenting resources, links to services, recommendations to see a psychologist or GP). Parents can email, download, or print the report. The scoring and report will be generated automatically using a computer algorithm that is being developed by the IT team at BDI. Completion of the mental health check and triage differs depending on the trial and treatment allocation.

***Trial 1: Triage vs Standard Care.*** The key difference in this trial is who receives the *triage information.*

|  |  |  |
| --- | --- | --- |
|  | **Triage** | **Standard care** |
| **Screening** | Demographic/background questionnaire | Demographic/background questionnaire |
| **Baseline** | Mental health check  **Triage information**  Outcome ax (access to care, help seeking, stigma) | Mental health check  Outcome ax (access to care, help seeking, stigma) |
| **5 weeks** | Mental health check  Outcome ax (access to care, help seeking, stigma) | Mental health check  Outcome ax (access to care, help seeking, stigma) |
| **10 weeks** | Mental health check  Outcome ax (access to care, help seeking, stigma) | Mental health check  Outcome ax (access to care, help seeking, stigma) |

***Trial 2: Monitor vs Control.*** The key difference in this trial is whether the assessment of stigma is completed before or after the mental health check

|  |  |  |
| --- | --- | --- |
|  | **Monitor** | **Control** |
| **Screening** | Parent questionnaire | Parent questionnaire |
| **Baseline** | Mental health check  Outcome ax (stigma) | Outcome ax (stigma)  Mental health check |
| **6 weeks** | Mental health check  Outcome ax (stigma) | Outcome ax (stigma) |
| **12 weeks** | Mental health check  Outcome ax (stigma) | Outcome ax (stigma)  Mental health check |

*Note.* ax = assessment

***Description of the Mental Health Check***

***Mental Health Check.*** The mental health check (see Appendix A) will comprise brief questionnaires assessing symptoms of anxiety and depression. The questionnaire differs according to the person completing the questionnaire (i.e., parent or child) and the age of the child. For children and their parents in Grades 3 – 6, we will use the Revised Child Anxiety and Depression Scale-Child (RCADS-C-25) and Revised Child Anxiety and Depression Scale-Parent (RCADS-P-25; Ebesutani etal., 2012, 2017). For children in Grades K to 2, parents will complete the Preschool Anxiety Scale (PAS; Spence et al., 2001), and the Preschool Feelings Checklist (PFC; Luby et al., 2004). An example of the report and triage information is also provided in Appendix A.

**Grades 3 to 6:** The RCADS-C/P-25 contains 15 items assessing anxiety and 10 items assessing depression. Evaluation of the psychometric properties indicate adequate internal consistency in community and clinical samples (alphas = 0.70 – 0.82). The anxiety scale is structurally valid and internally consistent (alpha = 0.82) with test-retest reliability (r = .78 - .86) and criterion validity considered acceptable (Klaufus et al., 2020). Items on the RCADS-C/P-25 are scored on a 4-point Likert scale ranging from 0 to 3, with raw scores tallied and converted into T scores using age and gendered normative data from the United States. T scores greater than 65 are considered “borderline clinical threshold for anxiety”. Cildren scoring above 65 on either parent or child report will be considered as experiencing “above threshold” anxiety and/or depression symptoms. We are also including additional questions to measure how much anxiety interferes with the child’s daily life (three additional questions in the child report; two in the parent report).

**Grades K to 2:** The PAS contains 28 items assessing five factors of anxiety (social anxiety, separation anxiety, generalised anxiety, physical injury fears, and obsessive-compulsive disorder). Items on the PAS are completed by parents of children aged 2.5 to 6.5 years and are scored on a 5-point Likert scale ranging from 0 (*not true at all*) to 4 (*very often true*), with a maximum total score of 112, where higher scores indicate greater levels of anxiety.

Raw scores for the total scale and each subscale are tallied and converted into T scores using age and gendered normative data from Australia. T-scores greater than 60 are considered “elevated”. The PAS has good construct validity, moderately correlating with the CBCL (r = 0.59, r = 0.68; p < 0.001). Each PAS subscale also correlates significantly with the CBCL (r’s = 0.37 to 0.61), however it is recommended to use the total scale, as the five factor model using all scales provides a significantly better fit of data than each one-factor model (Spence et al., 2001).

A 29th Yes/No item in the PAS asks, *“Has your child ever experienced anything really bad or traumatic (e.g., severe accident, death of a family member/friend, assault, robbery, disaster)”*; if the parent responds “Yes”, then a further 5 questions assessing post-traumatic stress disorder (PTSD) are included. These 5 items are also scored on the same 5-point Likert scale as the first 28 items , with a maximum total score of 20, yet these items are not scored as they are for clinicial interest only (Spence et al., 2001).

**Grades K to 2:** The PFC contains 16 items assessing depressive symptoms in children aged 3 to 6 years. Internal consistency for this scale has been reported to be good, (α = 0.85; Silver et al., 2021). The maximum sensitivity (i.e., ability to correctly identify depression in children; 0.92) and specific (i.e., not falsely identifying children who are not depressed; 0.84) are adequate (Luby et al., 2004). The PFC’s convergent validity is adequate via associations with Preschool Age Psychiatric Assessment (depressive disorders; r = .25, r = .27; p < .001), and the CBCL Affective Problems Scale (r = .47, r = .29; p < .001) in ages 3 and 6, respectively (Silver et al., 2021). It is important to note the latter study comprised a small proportion of children with depressive symptoms (i.e., 10 from 80 children). Items are completed by parents of children aged 3 to 6 years and are scored on a dichotomous scale with response options of “Yes” and “No” (scored as Y = 1, N = 0). An example of one item is as follows, Q12) “Often seems to be very tired and has low energy”. Scores range from 0-16. Higher scores indicate greater symptoms of depression.

# **Sample Size**

The plan is to enrol 432 child-parent dyads to complete Trial 1. The nominated sample is based on the ability detect a moderate effect with 80% power at alpha .05, N = 360 child-parent dyads are required to detect an effect size of .5, with *N =* 432 child-parent dyads required to account for 20% attrition.

We plan to enroll 440 child-parent dyads to complete Trial 2. To detect a small effect with 80% power at

alpha .05, N = 352 completers are required to detect an effect size of .3, with a total sample size of N = 440 child-parent dyads to allow for 20% attrition. We estimate to recruit participants from a sample of approximately 18 to 20 schools.

# **Selection and Withdrawal of Subjects**

## **Inclusion/Exclusion Criteria**

***Trial 1 participants:***

* **Children** in Years 3 to 6 who is able to access a device to complete the study questions, can consent and complete questions online (with help if needed)
  + Note: children in Year K to 2 do not have sufficient cognitive capacity to independently answer the check or outcome assessments
* **Parents/carers** of a child in Year K to 6 who is able to access a device to complete the study questions, can consent and complete questions online (with help if needed)

***Trial 2 participants:***

* **Schools**: mainstream Government or Independent primary schools in Australia with the capacity to provide children with a device (i.e., laptop, desktop, tablet) to complete the assessments
* **Classes**: where schools have more than one Year class, all Year classes will be invited to participate. Classes will range from 15 to 35 students per class and will include a mix of co-ed and single sex schools from both rural and non-rural areas.
* **Children**: child attends Government or Independent Primary School in Australia and is in Year 3 to 6 with the capacity to answer questions online via a device (i.e., laptop, desktop, tablet), can consent and complete questions online (with help if needed), and their parent/carer has not opted-out
  + Note: children in Year K to 2 do not have sufficient cognitive capacity to independently answer the check or outcome assessments

**Parents/carers**: Parents of children in Year K to 6 who attends Government or Independent Primary School in Australia, has the capacity to answer questions online via a device (i.e., laptop, desktop, tablet) and complete questions online (with help if needed), and is able to provide informed consent

## **Recruitment Strategy**

***Trial 1 recruitment:*** To identify eligible children and parents/carers we will recruit through Australian schools using the following methods (see Appendix F for Trial 1 advertisements):

|  |  |
| --- | --- |
|  | **Parents of children in K – 6 and children in Y3 - 6** |
| **Step 1** | * Online advertisement targeting parents with a link to the study website * School link newsletter advertisement – a state government initiative that links schools and local health services. Interested parents will be able to register their interest through the website or contact the research team via email for more information. * Emailing and phoning NSW schools (admin/reception) to provide details about the study. To reduce the risk of coercion, the school administrator will be asked to forward the email invitation to the principal on the research team’s behalf. This reduces the risk of the principal perceiving non-participation as impacting their relationship with the research team. * Schools will be asked to email the following materials to parents: links to a video description of the study and the study website * Contacting school organisations such as P&C (https://www.pandc.org.au/) and the Black Dog Institute School Advisory Group, and inviting leads to share the study link with details about the study to their network. Interested participants can register their interested participants can register their interest and sign-up to participate via the study website * Parents can register their interest for the study via a link to the study website. The RAs will contact interested parents to provide more information about the study, who will then be sent a link to complete the consent forms (parent and/or child) online. * Follow-up reminders will be sent to parents who provide their consent but do not start the screening questions or baseline questionnaire. * Follow-up reminders will be sent to parents who have not completed the study questionnaires at any of the data collection periods (baseline, 5 weeks, and 10 weeks). * These reminders will be limited to **two follow-up reminders at each time-point** to ensure that the recipients do not feel inundated by reminders. These reminders will be restricted to two emails. * At each timepoint that participant receives an email reminder, they will also receive an SMS prompt. These SMS prompts ensure the participant is aware of the survey being made available to them, in the case that the email reminder is in the participant’s junk/spam folders. Therefore, participants will also receive **two follow-up SMS prompts at each time point.** See Appendix U. * In the event that the trial is re-opened, participants who previously registered but did not complete the surveys will be contacted to notify them the study is open again * The research team can be contacted at any time to ask questions * There are no risks or discomforts associated with this recruitment strategy. Parents are free to withdraw from the study at any time, and it will be explicitly stated by the research team that participation is entirely voluntary. * The PDF withdrawal form will be made available in the emails sent to participants. Participants will be withdrawn from the study upon the research team receiving the completed PDF form via email. |
| **Step 2** | * We will instigate additional Australia-wide arms-length methods to boost recruitment if we have not reached 50% of our target sample by October 2022. Trial 1 will be advertised via the following channels:   + Black Dog Institute website and social media channels (e.g., Twitter, Instagram, and Facebook)   + Conference presentations   + Professional networks such as school counsellor forums   + Word of mouth discussions   + P&C (<https://www.pandc.org.au/>)   + Black Dog Institute School Advisory Group   + Parent blogs and networks (e.g., Raising Children’s network), parenting social media groups (e.g., parenting NSW)   + Child and Family East (CAFE) at Sydney Children’s Hospital, Randwick   + Child Development Unit (CDU) at Children's Hospital at Westmead |

***Trial 2 recruitment (see Appendix G for Trial 2 advertisements)***

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Schools** | **Children in Y3 - 6** | **Parents in YK - 6** |
| **Criteria** | * Varied demographic profiles from a range of rural and urban regions in Australia. | * Attending participating school in Y3 to 6 | Parents of children in YK to 6 of a participation school |
| **Process** | * Government school research applications (SERAP for NSW schools, QERI for QLD schools, RAAC for TAS schools, and Research Conducted on Department of Education Sites by External Parties Policy process for WA schools) * Independent schools through known contacts * Identify schools through publicly available information provided by the state Departments of Education. * The schools recruited for Trial 2 will be different to the schools approached for Trial 1 | * Schools will be asked to email these materials to parents: links to a video description of the study, information sheet, opt-out consent, parent information and consent, and parent questionnaire * Parents will be invited to attend an online information session with the research team to hear more details about the study * We will ask schools to send a reminder to participating classes (via SMS or email) to encourage those who do not wish to take part to return the opt-out consent forms – at least 2 weeks before the scheduled participation * If parents do not provide opt-out consent, but do **not** complete the parent questionnaire, then children will be excluded from the study. | * Schools will be asked to email these materials to parents: links to a video description of the study, information sheet, opt-out consent, parent information and consent, and parent questionnaire |
| **Participation** | * The research team will email copies of the information sheets to school administrators (see Appendix I) – we may call the school administrator first to confirm the best email to send the information sheet * School staff can register their interest in the study via a website or contact the research team. The study will be advertised on social media (see Appendix G). The research team will contact those who register their interest to provide more information about the study * The research team can be contacted at any time to discuss the study requirements | * Where parents do not opt-out, children will be invited to take part in the research at school as part of a whole class activity. * The research team will ask schools to provide a list of the children who can participate. * Before participating, the teacher will read a verbal script (see Appendix L) to children explaining the study and offer an opportunity for children to ask questions. | * Interested parents can complete the parent questionnaire and consent form online via the online platform (Qualtrics). * Two follow-up reminders will be sent to parents who provide their consent but do not start the screening questions or baseline questionnaire. * Two follow-up reminders will be sent to parents who have not completed the study questionnaires at any of the data collection periods (baseline, 6 weeks, and 12 weeks). * These reminders will be limited to **two follow-up reminders each** to ensure that the recipients do not feel inundated by reminders. These reminders will be restricted to one email and one phone call, or two email reminders. * The research team can be contacted at any time to ask questions * There are no risks or discomforts associated with this recruitment strategy. Parents are free to withdraw from the study at any time, and it will be explicitly stated by the research team that participation is entirely voluntary. * The PDF withdrawal form will be made available in the emails sent to participants. Participants will be withdrawn from the study upon the research team receiving the completed PDF form via email. |

## **Screening**

***Trial 1***

After providing consent, parents will be invited to complete a parent questionnaire to ensure that they (and their child) meet eligibility criteria for the trial. The questionnaire includes 13 items and will be completed online via a suitable online platform (Research engine). The questionnaire will take approximately 10 minutes to complete. If the parent and/or child do not meet eligibility criteria for the trial, the research team will contact the parent (phone and email) to thank them for their time and advise that they unfortunately do not meet criteria for enrolment into the study.

***Trial 2***

After providing consent, school principals will complete a school questionnaire to ensure that their school is eligible to participate in the trial. Following this, parents will be invited to complete a parent questionnaire. Both questionnaires will be hosted on a suitable online platform (Qualtrics). If the parent and/or child do not meet eligibility criteria for the trial, the research team will contact the parent (phone and email) to thank them for their time and advise that they unfortunately do not meet criteria for enrolment into the study.

## **Consent**

***Trial 1 Consent***

|  |  |  |
| --- | --- | --- |
|  | **Children in Y3 - 6** | **Parents in YK - 6** |
| **Informed consent** | * Parents/carers provide online consent (see Appendix H) * Children will be asked the following question: “are you happy to answer these questions about your mental health? If you start and decide to stop that is OK (Yes/No)” - to indicate their willingness to take part in the study. | * Parents/carers provide online consent (see Appendix H) * Parents/carers can contact the PIs to ask questions about the study |
| **Screening** | * N/A – completed by parent/carer | * Parents/carers will be emailed a link to a demographic background questionnaire to determine their/their child’s eligibility for the trial |
| **Eligible** | * Randomly allocated to condition and parents will be emailed link for child to complete mental health check and outcome assessments (baseline, 5 weeks, 10 weeks) | * Randomly allocated to condition and will be emailed link to complete mental health check and outcome assessments (baseline, 5 weeks, 10 weeks) |
| **Not eligible** | * N/A – parent advised | * Following the eligibility questionnaire, the participant will be promptly taken to a webpage stating that they are not currently eligible for the study. |

***Trial 2 Consent (see Appendices I to K for Trial 2 Consent Forms)***

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Schools** | **Children in Y3 - 6** | **Parents in YK - 6** |
| **Informed consent** | * Principals provide online consent (see Appendix I) Principals will be encouraged to read the information sheet and consult with others, contact the research team, and attend an information session before providing their consent. * Contact details of the research team are included for participants to raise questions for discussion. | **Parents**   * Parents provide opt-out consent online if they **do not** want their child to participate in the study * Parents will be emailed an information statement that states participation is presumed unless the opt-out consent form is completed online (see Appendix K). * Parents can attend an information session with the research team via Microsoft Teams to answer any questions about the study, and explicitly discuss the opt-out consent process. * Links to the opt-out consent form will be emailed to parents by school staff at least 2 weeks prior to the research activity to allow sufficient time for parents to decline participation. * Opt-out consent is a practical and feasible consenting procedure in schools. It reduces the burden on school staff and increases student participation.   **Teachers**   * Read a plain language statement that explains the research, what to do, and opportunity to decline participation (see Appendix L)   **Children**   * Where parents do not opt-out, written assent will be obtained from children * Can decline participation by selecting “no” on the landing page of the study | * Parents/carers provide online consent (see Appendix J) |
| **Screening** | * Principals will then be invited to complete the brief background screening questionnaire to determine school eligibility. | * Children will answer 6 demographic questions to capture information about their socioeconomic status. Children will not be excluded based on these responses. |  |
| **Eligible** | * Notified by PIs by telephone * Identify contact person to liaise with the research team | * Randomly allocated to condition and will be emailed link to complete mental health check and outcome assessments (baseline, 6 weeks, 12 weeks) to complete at school | * Randomly allocated to condition and will be emailed link to complete mental health check and outcome assessments (baseline, 6 weeks, 12 weeks) |
| **Not eligible** | * Following the eligibility questionnaire, the school contact will be promptly taken to a webpage stating that their school is not currently eligible for the study. | * N/A – parent contacted |  |

## **Withdrawal of Consent or Participant**

Participants may withdraw from Trial 1 or 2 at any time by completing the Form for Withdrawal of Participation at the end of the PISCF. The PDF withdrawal form will be made available in the emails sent to participants. Participants will be withdrawn from the study upon the research team receiving the completed PDF form via email. They are informed of this, and that their decision whether to take part or not to take part, or to take part and then withdraw, will not affect their relationship with the UNSW or the Black Dog Institute (BDI; See PISCF).

Participants are informed in the PISCF that if they withdraw from the study, the research team will destroy any information that has been collected. However, they are also informed that if they withdraw after group results have been combined in a way that does not identify them, the research team will not be able to withdraw their responses from the aggregated results.

# **Treatment of Subjects**

An overview of the difference in research procedures that participants will be asked to complete is described in the table below.

**Trial 1**

|  |  |  |
| --- | --- | --- |
|  | **Triage** | **Standard care** |
| **Parents** | * Complete screening questionnaire * Baseline: complete mental health check **and receive triage information** and outcome assessment (Access to Care, GHSQ, stigma) * Complete 5- and 10-week assessments (mental health check, Access to Care, GHSQ, stigma) | * Complete screening questionnaire * Baseline: complete mental health check and outcome assessment (Access to Care, GHSQ, stigma) * Complete 5- and 10-week assessments (mental health check, Access to Care, GHSQ, stigma) * Option to receive triage information after week 10 |
| **Children** | * Complete baseline assessment (mental health check, Access to Care, GHSQ, stigma) * Complete 5- and 10-week assessments (mental health check, Access to Care, GHSQ, stigma) | * Complete baseline assessment (mental health check, Access to Care, GHSQ, stigma) * Complete 5- and 10-week assessments (mental health check, Access to Care, GHSQ, stigma) |

**Trial 2**

|  |  |  |
| --- | --- | --- |
|  | **Monitor** | **Control** |
| **Parents** | * Complete screening questionnaire * Complete baseline assessment (mental health check, stigma) * Complete 6-week assessments (mental health check, stigma) * Complete 12-week assessments (mental health check, stigma) | * Complete screening questionnaire * Complete baseline assessment (stigma, mental health check) * Complete 6-week assessments (stigma) * Complete 12-week assessment (stigma, mental health check) |
| **Children** | * Complete baseline assessment (mental health check, stigma) * Complete 6-week assessments (mental health check, stigma)   Complete 12-week assessments (mental health check, stigma) | * Complete baseline assessment (stigma, mental health check) * Complete 6-week assessments (stigma)   Complete 12-week assessment (stigma, mental health check) |

## **Investigational Medical Product and Trial Intervention**

Trial 1 and 2 are evaluating the newly developed “Mental Health Check” for children. The mental health check is a questionnaire delivered on a website that offers a way for parents and children to answer questions on symptoms of anxiety and depression. The Check includes three main components:

1. Parents and children answer questions to assess and identify symptoms of anxiety and depression
2. Parents are provided with a report that describes the tests, responses, and scores, with a descriptor (e.g., coping vs struggling; terminology to be decided). Parents can email, download, or print the report.
3. Parents are also provided with triage information about services and resources that can support the child (e.g., psychoeducation, parenting resources, links to services, recommendations to see a psychologist or GP). The scoring and report will be generated automatically using a computer algorithm that is being developed by the IT team at BDI. Completion of the mental health check and triage differs depending on the trial and treatment allocation (see Section 11 Treatment of Subjects)

## **Storage, dispensing and product accountability.**

The website hosting the Mental Health Check with be developed and maintained by IT and Development teams at BDI. All accountability and management of the Mental Health Check will be managed by research team.

## **Randomisation and Allocation**

***Trial 1.*** Participants will be individually randomized using minimization procedures to ensure balance across the conditions (i.e., triage or standard care) on the following variables: 1) socioeconomic status using the Index of Community Socio-Educational Advantage level (ICSEA; <1000 versus => 1000), 2) location (metropolitan vs rural/remote), and 3) gender identity (male, female, non-binary). Minimisation will be completed in Research Engine.

***Trial 2.*** Schools will be assigned to a single condition (cluster design) for administrative feasibility. Assignment will be carried out by an external researcher not involved in the study activities. Assignment will occur after the school principals provide consent for participation. During the consent process, principals will be advised that their school may be allocated to one of two treatment conditions. A minimization approach will be used to ensure balance across the conditions (i.e., triage or standard care; monitor or control) on the following variables: 1) socioeconomic status of the school using the Index of Community Socio-Educational Advantage level (ICSEA; <1000 versus => 1000), 2) location of the school (metropolitan vs rural/remote), and 3) gender mix of the school (single vs mixed gender schools). Minimisation will be completed in a statistical package. Schools and researchers will not be blinded to the assignment, but participating parents and children will not be informed of their school’s allocation. The method developed and implemented by Carter and Hood [2008] will be used to ensure balance between intervention arms. This enumerates all possible divisions of the available schools into two groups and calculates a balance index for each of these groupings. Groupings with an acceptable level of balance will be retained (maximum 10) and the allocation schedule will be selected at random from these.  Should any additional schools become available, they will be assigned using minimisation based on the balance factors and taking into account assignments made in the initial allocation.

Carter, B. R., & Hood, K. (2008). Balance algorithm for cluster randomized trials. BMC Medical Research Methodology, 8, 65. doi:10.1186/1471-2288-8-65

# **Safety and Monitoring**

## **Assessment of Safety Event Report Forms**

Safety reports will be assessed on the seriousness, causality, and expectedness of the event to the trial treatment(s), intervention(s), investigational medical product(s), investigational medical device(s). The following are known and expected adverse effects, harms, risks, or discomforts associated with trial procedures, treatments, or interventions.

1. Known Adverse Effects

It is possible that participants may experience psychological distress induced by trial assessments (completion of online questionnaires).

1. Known Harms, Risks or Discomforts
2. It is possible that participants may experience psychological distress induced by trial assessments (completion of online questionnaires).

## **Adverse Events**

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 medical device.

AEs 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.

Adverse event reports must be reported to the Coordinating Principal Investigator within immediately, within 24 hours. All adverse event reports must be recorded in the [UNSW Safety Monitoring Register Template](https://research.unsw.edu.au/document/UNSW%20Safety%20Monitoring%20Register%20Template.xlsx).

We will report any of the following adverse events following the HREC reporting procedure:

* For children in all groups, we will evaluate responses on the mental health check and identify if there are any significant (i.e., >1SD) increases in anxiety and/or depression symptoms from baseline to 5 weeks (trial 1) or 6 weeks (trial 2), or 5 weeks to 10 weeks (trial 1) or 6 weeks to 12 weeks (trial 2). A 1 SD increase is considered an adverse event as this increase may be due to the monitoring (i.e., regular completion of mental health check) over the course of the trial. In such cases, the research team will notify the parent, discuss the result and provide them with the option to withdraw their child from the study should they wish. In the event we are not able to contact the parent/ carer to discuss the result, the child will be automatically withdrawn from the study.
* Parent withdrawal due to severe distress (parent or child) and the need for crisis management support
* Distress due to not receiving triage information – triage information will be provided to the family and the participant withdrawn from the trial
* Any protocol deviations or violations will also be reported to the HREC. Safety event reports, including adverse and serious adverse events will be reported by Francis, Songco or Hudson. Significant safety issues and urgent safety measures will be reported to the UNSW Sponsors Delegate (humanethics@unsw.edu.au) immediately but no later than seven days. The Trial Management Group (comprised of all investigators) will meet regularly to discuss any potential safety issues or concerns relating to adverse events. Research Assistant Lim, Project Manager Allsop and Research Assistant McDermott will immediately notify Francis, Songco and Hudson if there are any indications of protocol deviations, violations, safety issues or adverse events that may arise. Single case reports of Adverse Events and Serious Adverse Events will not be reported to the UNSW Sponsors delegate, though all case reports will be recorded in the Safety Monitoring Register, assessed as per trial safety standards, and be reported to the UNSW Sponsor’s Delegate at the conclusion of the study.
* The research team’s process to assess whether the event was related to the clinical trial, its procedures, or the interventions, is as follows: Any investigator who receives information sufficient for an adverse event or safety issue regarding a participant is required to report this to Francis, Songco and Hudson, where this will be recorded in the Safety Monitoring Register. The Data Safety Monitoring Board will be periodically tracking participant data to observe any unexpected trends in participant measures and report their findings to the Trial Management Group. In the case of an adverse event, upon ensuring the provision of support has been provided to the participant, the Trial Management Group will investigate if there were any errors in the performance of the trial relating to clinic error, misuse, or operational difficulties (e.g., instructions provided). This will be disclosed to our committee established for assessing safety monitoring reports.

## **Adverse Device Effect**

An adverse device effect (ADE) is related to the use of an investigational medical device. Including adverse events resulting from insufficient or inadequate Instructions for Use, deployment, implantation, installation, or operation, or any malfunction of the investigational medical device. This definition includes any event resulting from use error or from intentional misuse of the investigational medical device.

ADE 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.

ADE must be reported to the Coordinating Principal Investigator within immediately, within 24 hours. All adverse event reports must be recorded in the [UNSW Safety Monitoring Register Template](https://research.unsw.edu.au/document/UNSW%20Safety%20Monitoring%20Register%20Template.xlsx).

## **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 investigational medical product, the trial intervention, or procedures:

* 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 and are 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 Investigator within 48 hours of the event occurring. SAR reports must be recorded in the [UNSW Safety Monitoring Register Template](https://research.unsw.edu.au/document/UNSW%20Safety%20Monitoring%20Register%20Template.xlsx).

## **Serious Adverse Device Effects**

A Serious Adverse Device Effect (SADE) is an SAE that is related to the investigational medical product, the trial intervention, or procedures. SAR reports are classified following the safety assessment flowchart and are assessed by Sponsors Independent Medical specified in section 2 of the protocol. The sponsors independent medical expert must determine whether the SAR was expected or unexpected. The Sponsors Independent Medical cannot delegate this responsibility to other research personnel.

#### **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 investigational medical product or intervention safety information are classified as a SAR report. SAR reports are reported to the Coordinating Principal Investigator as soon as possible but no later than 7 days for multicentre clinical trials. Serious Adverse Reaction reports must 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 investigational medical product, the trial intervention, or procedures for use safety information are classified as a SUSAR.

Fatal or life-threatening Australian SUSAR reports are reported to the Therapeutic Goods Administration, the Coordinating Principal Investigator, and the sponsor’s delegate 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 are to be reported to the Therapeutic Goods Administration, the Coordinating Principal Investigator, and the sponsor’s delegate within 15 calendar days after being made aware of the case follow up information reported within a further 8 calendar days. SUSAR reports must be recorded in the [UNSW Safety Monitoring Register Template](https://research.unsw.edu.au/document/UNSW%20Safety%20Monitoring%20Register%20Template.xlsx).

## **Significant Safety Issue (SSI**)

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

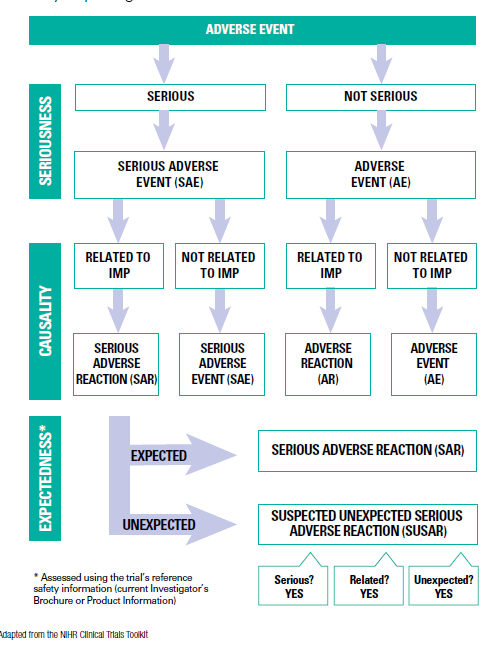
## **Urgent Safety Measure (USM)**

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 Therapeutic Goods Administration, Human Research Ethics Committee and the Sponsor’s Delegate must be notified of any significant safety issues that meet the definition of an urgent safety measure should be notified 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).

## **Safety** **Assessment Flow Chart Investigational Medical Device Trials**



## **Register of Clinical Trial Safety Monitoring Reports**

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

## **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 must be recorded in a safety monitoring register and are reported to the UNSW Sponsor’s Delegate annually.

#### **Emerging Safety Issues**

## The Trial Management Group, Trial Safety Committee or the Data Safety Monitoring Board 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 Management Group, Trial Safety Committee, or the Data Safety Monitoring Board must seek the advice of the human research ethics committee and sponsor’s delegate.

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

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

* Documented evidence that the Trial Management Group, Trial Safety Committee, or the Data Safety Monitoring Board (e.g., meeting minutes) confirming that regular reviews of safety occurred.
* Analysis of the trial intervention(s) 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 has the potential to) result in participant harms.

## **Reporting Protocol Deviations**

* Protocol deviations occurring at a site must be documented in site files and reported by the principal site investigator to the Coordinating Principal Investigator.
* The Coordinating Principal Investigator must 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 must 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**

* A serious breach occurring at a participating site must be reported by the site Principal Investigator to the Coordinating Principal Investigator within a specified timeframe.
* The Coordinating Principal Investigator must 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 must 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 must 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 must be recorded. Written records and copies of documentation sent to the sponsor must be retained in the Investigator Site File.
* Copies of protocol deviation and serious breach reports must 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, to establish whether the proposed CAPA is appropriate and establish whether there is or will be an ongoing impact on the 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 whether 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**

***Trial 1***

Statistical analyses will be conducted using IBM SPSS statistics 28. Participant characteristics and scores on outcome measures (mental health check, access to care, general help seeking) at each time point (baseline, 5 weeks, 10 weeks) will be presented using descriptive statistics: mean, standard deviation, and 95% confidence intervals. Interim analysis of the primary outcome data will be conducted in the event that the target sample size is not recruited. If a significant result is identified in this interim analysis, the trial will be prematurely stopped. Where futility is identified, the study will be abandoned and where the interim analysis shows an inconclusive finding, recruitment would be re-opened.

To investigate within group changes in the triage group from baseline to 5 weeks to 10 weeks, mixed-model repeated measures (MMRM) will be used for each outcome measure (mental health check, access to care, general help seeking). Time will be treated as a within-groups factor (baseline, 5 weeks, 10 weeks) and condition as the between-group factor (intervention vs. control).. This approach handles missing data by including all available data from each subject into the analysis and assumes missing data are missing at random. An unstructured covariance matrix accommodated within-participant dependency and degrees of freedom will be estimated using the Kenward-Roger method. Where necessary, data will be transformed in order to meet the normality assumptions of model residuals in order to establish the robustness of conclusions reached using raw scores. Between-groups effect sizes will be calculated as the modelled standardized mean difference at each occasion of measurement. All analyses will be two tailed, with statistical significance set at *p* < .05. Effect sizes will be calculated to determine the size of the within group changes between baseline, 5 weeks, and 10 weeks of the intervention for each outcome measure.

To investigate between group differences in changes in clinical outcomes from baseline to 5 weeks to 10 weeks in the triage group compared to the standard care group, mixed-model repeated measures (MMRM) will then be used to evaluate differences in outcome measures across the groups.

***Trial 2***

Statistical analyses will be conducted using IBM SPSS statistics 28. Participant characteristics and scores on outcome measures (stigma) at each time point (baseline, 6 weeks, 12 weeks) will be presented using descriptive statistics: mean, standard deviation, and 95% confidence intervals.

To investigate within group changes in the monitor group from baseline to 6 weeks to 12 weeks, mixed-model repeated measures (MMRM) with effects attributable to schools included as a random intercept will be used for the outcome measure (stigma). Time will be treated as a within-groups factor (baseline, 6 weeks, 12 weeks) and condition as the between-group factor (intervention vs. control). This approach handles missing data by including all available data from each subject into the analysis and assumes missing data are missing at random. An unstructured covariance matrix accommodated within-participant dependency and degrees of freedom will be estimated using the Kenward-Roger method. Between-groups effect sizes will be calculated as the modelled standardized mean difference at each occasion of measurement. All analyses will be two tailed, with statistical significance set at *p* < .05. Effect sizes will be calculated to determine the size of the within group changes between baseline, 6 weeks, and 12 weeks of the intervention for each outcome measure.

Interim analyses with the Data Safety Monitoring Board will be conducted when 50% target sample has been recruited for each trial.

To investigate between group differences in changes in clinical outcomes from baseline to 6 weeks to 12 weeks in the monitor group compared to the control group, mixed-model repeated measures (MMRM) will then be used to evaluate differences in stigma between the groups. We will include school as a random effect to accommodate clustering effects.

# **Data Handling, Ownership and Access**

# **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.

# **Authorship**

Requirements for authorship include a significant contribution to the study in terms of design, development, and analyses.

# **Recording and Reporting Data**

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

Participants will be assigned a participant ID, and data will be reported using an online platform (Research Engine and Qualtrics). Once all data is collected through the platform, data will be downloaded, and personally identifiable information will be removed from the dataset by the research team. The de-identified data will be stored on the UNSW OneDrive with access restricted to research staff via password protection. OneDrive is appropriate for research data classified from Public to Highly Sensitive. Any change or correction to data should be dated, initialled, and explained (if necessary) and should not obscure the original entry (i.e., an audit trail should be maintained); this applies to both written and electronic changes or corrections.

Data will be retained on the UNSW secure servers for up to 15 years after study completion, or until the participants reach 25 years of age (as per the retention period for clinical trials involving children) and stored within Australia. In the UNSW OneDrive, the data is encrypted in the cloud; a secure link is required to access and share the data. Only members of the UNSW and Black Dog Institute research team listed on this protocol will have access to the data.

1. Confidentiality

Information collected in the trial must be handled following the requirements of the Privacy and Personal Information Protection Act 1998 (NSW). Trial subjects have right of access to personal information held about them by the UNSW and can request correction and amendment of it. The UNSW requirements to ensure that personal information is protected is available in the [UNSW Privacy Management Plan](https://www.legal.unsw.edu.au/compliance/privacyhome.html).

1. Direct Access to Source Data and Documents

Site principal investigator(s) and institution(s) will permit trial-related monitoring, audits, HREC review, and regulatory inspection(s), providing direct access to source data/documents. The sponsor will not have access to source data however, site(s) and institutions will allow the sponsors monitor or auditor access to source documentation for auditing purposes.

# **Trial Management Group, Data Safety Monitoring Board, Independent Safety Committee**

The Trial Management group will meet weekly to fortnightly to trouble shoot any issues or concerns that arise relating to the trial. Notes and documents arising from these meetings will be stored securely on UNSW OneDrive.

The Data Safety Monitoring Board will -

* Periodically review aggregate subject data related to safety, attrition, withdrawals, data integrity and overall conduct of the trial and discuss via telephone conference;
* Provide recommendations to continue, modify or terminate the trial
* Maintain records of all activities.

Outcomes from analyses and any meeting minutes will be stored securely on UNSW OneDrive.

**Monitoring Quality Control and Quality Assurance**

The Coordinating Principal Investigator and Principal Investigator(s)’ responsibility is to monitor the clinical trial. The Coordinating Principal Investigator and Principal Investigator(s) 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 is 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 must ensure that agreements are executed at each of the following sites before site initiation, recruitment, and data collection commences.

Templates for clinical trial research agreements can be downloaded using the following link:

* <https://www.medicinesaustralia.com.au/policy/clinical-trials/clinical-trial-research-agreements/>
* All agreements are to be negotiated with [Research Grants and Contracts](https://research.unsw.edu.au/research-grants-and-contracts-rgc) once the clinical trial protocol has been developed, human ethics approval has been established, and, where applicable, the UNSW Clinical Trials Sponsor’s Delegate has confirmed that UNSW will act as clinical trial sponsor.
* Signed CTRAs and other agreements must be included in the list of GCP essential documents. Recruitment and data collection for a clinical trial must not commence without an executed CTRA in place.

# **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**

Coordinating Principal Investigators, Principal Investigators and all site personnel or trial-related staff must have current Good Clinical Practice Training. 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 retained by all trial investigators.

## **Qualifications and Curriculum Vitae**

Copies of CVs for all principal investigators will be stored as an essential document. The [TransCelerate CV template](https://research.unsw.edu.au/document/TransCelerate%20CV%20template.pdf) can be used as a template.

# **Clinical Trial Delegation and Responsibilities Log**

| **Protocol / Study Number:** | TBA – in preparation | **Sponsor Name:** | UNSW |
| --- | --- | --- | --- |
| **Principal Investigator Name:** | Prof Jennie Hudson | **Site Number:** | N/A |
| **Site Name (if applicable)** | Black Dog Institute | | |

**\*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.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Name** | **Principal Investigator’s Signature** | **Initials** | **Start**  **(dd/mmm/yyyy)** | **End**  **(dd/mmm/yyyy)**  **(complete only if prior to end of study)** |
| Prof Jennie Hudson |  | JH | 01/07/2022 |  |
|  |  |  |  |  |

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)** |
| --- | --- | --- | --- | --- | --- | --- | --- |
| Dr Deanna Francis |  | DF | Trial management | 1, 2, 3, 14, 18, | 01/07/2022 |  | \_\_/\_\_\_/\_\_\_\_\_ |
| Dr Annabel Songco |  | AS | Trial management | 1, 2, 3, 14, 18, | 13/1/2023 |  |  |
| Miss Chloe Lim |  | CL | General Project Assistance | 1, 2, 3, | 01/07/2022 |  | \_\_/\_\_\_/\_\_\_\_\_ |
| Mrs Abigail Allsop |  | AA | General Project Assistance | 1, 2, 3, | 12/8/2022 |  | \_\_/\_\_\_/\_\_\_\_\_ |
| Ms Emma McDermott |  | EM | General Project Assistance | 1, 2, 3 | 31/10/2022 |  | \_\_/\_\_\_/\_\_\_\_\_ |
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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. |

|  |
| --- |
| **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:**  **Date:**  23/05/2022 |

**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)\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ |
| 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.

# **Corrective and Preventive Action Form**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Raised by: | Assigned to: | | | Date: | Remarks: |
| Description: | | | | | |
| Proposed immediate action (correction): | | | | | |
| Completed by: | | Date: | Remarks: | | |
| Root cause analysis required: Yes  No | | | | | |
| Underlying / root cause: | | | | | |
| Determined by: | | Date: | Remarks: | | |
| Proposed action for long term solution (corrective/preventive action): | | | | | |
| Completed by: | | Date: | Remarks: | | |
| Comments on effectiveness of action taken: | | | | | |
| Closed out by: | | Date: | Remarks: | | |