Clinical Risk Management Plan

Mobio Interactive Pte Ltd

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Document Management

Revision History

Version	Date	Summary of Changes
0.1	2020-06-01	Draft 1
1.0	2020-07-17	Reviewed and approved

Reviewers

This document must be reviewed by the following people:

Reviewer name	Title / Responsibility	Date	Version
Mark Thoburn	Chief of Design and Regulatory Affairs, serving as Clinical Safety Officer	2020-07-17	1.0
Bechara Saab	Chief Scientist	2020-07-17	1.0

Approved by

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Name	Title	Date	Version
Mark Thoburn	Chief of Design and Regulatory Affairs, serving as Clinical Safety Officer	2020-07-17	1.0

Related Documents

These documents provide additional information and are specifically referenced within this document.

Ref	Doc Reference Number	Title	Version
	CRM-CRMS	MI Clinical Risk Management System	1.0
	CRM-CSHL	AmDTx Clinical Safety Hazard Log	1.0
	CRM-CSCR	Am MI Clinical Safety Case Report	1.0
	AM-CRMF	Clinical Risk Management File	1.0
	CRM-CSHL	AmDTx Clinical Safety Hazard Log	1.0
	CRM-CSCR	Am MI Clinical Safety Case Report	1.0

Contents

Introduction

The purpose of the Clinical Risk Management Plan (CRMP) is to define the implementation of, and any variation to, the MI Clinical Risk Management System (CRMS). It describes how MI will conduct clinical risk management to ensure patient safety with respect to services provided.

In fulfilling this purpose, any variation to the standard practices and procedures to be followed, as defined by the CRMS, when performing the activities of the programme are documented here in this document.

This CRMP identifies the means by which AmDTx (also “Am”) shall be controlled to ensure that Am’s clinical safety management is of high quality, conforms to the requirements of the CRMS, and any specific programme requirements.

This document will be updated when the plan changes in any way as to deviate from what has been committed to deliver. This will be decided by MI and its Clinical Safety Team.

AmDTx Overview & Clinical Safety

Program Overview:

AmDTx (also “Am”) is a mobile app that administers psychotherapy, primarily in the form of mindfulness meditation, through audio recordings. The app allows users to self-assess their mood and stress, and log personal comments. Users’ computer vision stress assessments inform the personalisation of their training.

- AmDTx has demonstrated clinical efficacy with student and patient populations in two randomized controlled trials. (Walsh et al., 2019; Subnis et al 2020). See Appendix A of this document for study results.
- Am’s computer vision stress assessment is now able to objectively quantify stress with 86% accuracy (Al-Jebrni et al., 2020). See Appendix A of this document for study results.

As AmDTx allows the user to view unique stress measures, it falls in scope of DCB0129, as there could be adverse effects of this information displaying incorrectly.

Clinical Risk Management File

MI's relevant clinical safety documentation, the Clinical Risk Management File (CRMF), is managed by the Clinical Safety Officer (CSO) and contains:

- AmDTx Clinical Safety Hazard Log
- Am MI Clinical Safety Case Report

The CRMF folder is securely stored in MI's Clinical Risk Folder.

Individual project areas and associated assurance approaches:

MI's CRMP manages risks associated with the use of Am's computer vision assessment of stress. Assurance is conducted via the following activities:

Risk Discovery:

- The primary vehicle for the discovery of risk associated with the use of AmDTx is randomized controlled trials, where Am is rigorously tested with clinical populations who are screened for adverse effects via medically validated psychological surveys.
- Prior to the release of a new version of AmDTx, the device is tested by members of the "Am tribe", a dedicated group of Am users who provide feedback to the development team via online surveys and report bugs and adverse events experienced during testing.
- The engagement and performance of real-world users of Am is monitored for risks associated with the use of Am.

Risk Assessment and Control:

- Identified risks are entered into the Hazard Log and assessed. Control measures are approved through regular, or extraordinary, meetings of the Clinical Safety Board (CSB).
- Regular meetings of the CSB are conducted quarterly. Extraordinary meetings are arranged within a week of the identification of a Risk level 3, and within 3 days of the identification of a Risk Level 4 or 5.

Post market Surveillance:

- As detailed above in Risk Discovery, use of Am by all users is monitored for risks via an internal tool that outputs anonymised, aggregated user data, including psychobiometrics. Identified risks inform Risk Assessment and Control activities in a continuous feedback loop

Resources / Personnel

The Clinical Safety Officer is responsible for ensuring the clinical safety of AmDTx through the application of clinical risk management.

Key responsibilities include:

- approval of the Clinical Risk Management Plan to confirm that the plan is appropriate and achievable in the context of AmDTx development and modification;

- ensuring that clinical risk management activities are completed in accordance with the Clinical Risk Management Plan (this document);
- reviewing and approving of all safety documentation including Clinical Safety Case Reports and Hazard Logs;
- reviewing evidence in the Clinical Risk Management File to ensure it is complete and supports the Clinical Safety Case Report;
- escalating any unacceptable safety risks.

Table 1 Roles and responsibilities

Development Team		Assurance Team	
Safety Engineer	Ramya Loganathan	Chief Scientist	Bechara Saab
CTO	Avetis Muradyan	Clinical Safety Officer	Mark Thoburn

Clinical Risk Evaluation and Management

The clinical risk evaluation and management process can be found in Appendix A. The hazard assessment process will follow the MI's CRMS approach.

Hazards may be identified in other ways during the development and use of AmDTx such as:

- Discovery during design of a solution by supplier;
- Testing of amended functionality;
- Ad hoc testing of live service functionality;
- Reporting of an incident or problem within the live service; and
- Identification by a member of staff within the supplier

For each identified hazard, the following information will be defined and recorded and summarised on the Hazard Log:

- Hazard number;
- Hazard name;
- Hazard description;
- Potential clinical impact – this will describe the effect of the hazard in the care setting and potential impact on the patient;
- Possible causes – these may be technical, human, error etc. A hazard may have a number of causes; and

- Existing controls – these are identified existing controls or measures that are currently in place and will remain in place post implementation that provide mitigation again the hazard, i.e. will be used as part of the initial Hazard Risk Assessment.

Each Hazard will be discussed by MI's Clinical Safety team and any other appropriate people. They will perform the following tasks and record the outcome in the Hazard Log:

- Estimation of clinical risks;
- Clinical risk evaluation; and
- Clinical risk control option management.

Estimation of clinical risks.

For each identified hazard estimation will be made of the clinical risk. This will include the severity of the hazard, the likelihood of the hazard and the resulting clinical risk.

Appendix A – Risk Classification Matrix

Clinical Risk Management Risk Matrix

Likelihood						
	Very High	3	4	4	5	5
	High	2	3	3	4	5
	Medium	2	2	3	3	4
		1	2	2	3	4
	Very Low	1	1	2	2	3
		Minor	Significant	Considerable	Major	Catastrophic
		Consequence				

Risk Matrix key - Severity

5	Unacceptable level of risk.
4	Mandatory elimination or control to reduce risk to an acceptable level
3	Undesirable level of risk Attempts should be made to eliminate or control to reduce risk to an acceptable level. Shall only be acceptable when further risk reduction is impractical.
2	Acceptable where cost of further reduction outweighs benefits gained.
1	Acceptable, no further action required

Hazard likelihood definitions

Likelihood Category	Interpretation
Very high	Certain or almost certain; highly likely to occur
High	Not certain but very possible; reasonably expected to occur in the majority of cases
Medium	Possible
Low	Could occur but in the great majority of occasions will not
Very low	Negligible or nearly negligible possibility of occurring

Hazard Consequence definitions

Consequence Classification	Interpretation	Number of Patients Affected
Catastrophic	Death	Multiple
	Permanent life-changing incapacity and any condition for which the prognosis is death or permanent life-changing incapacity; severe injury or severe incapacity from which recovery is not expected in the short term	Multiple
Major	Death	Single
	Permanent life-changing incapacity and any condition for which the prognosis is death or permanent life-changing incapacity; severe injury or severe incapacity from which recovery is not expected in the short term	Single
	Severe injury or severe incapacity from which recovery is expected in the short term	Multiple
	Severe psychological trauma	Multiple
Considerable	Severe injury or severe incapacity from which recovery is expected in the short term	Single
	Severe psychological trauma	Single
	Minor injury or injuries from which recovery is not expected in the short term.	Multiple
	Significant psychological trauma.	Multiple
Significant	Minor injury or injuries from which recovery is not expected in the short term.	Single
	Significant psychological trauma	Single
	Minor injury from which recovery is expected in the short term	Multiple
	Minor psychological upset; inconvenience	Multiple
Minor	Minor injury from which recovery is expected in the short term; minor psychological upset; inconvenience; any negligible severity	Single

Appendix B – Study results

- Walsh et al. (2019) JMIR Mental Health

  Background: Mindfulness training (MT) includes a variety of contemplative practices aimed at promoting intentional awareness of experience, coupled with attitudes of non-judgment and curiosity. Following the success of 8-week, manualized group interventions, MT has been implemented in a variety of modalities, including smartphone apps that seek to replicate the success of group interventions. However, although smartphone apps are scalable and accessible to a wider swath of population, their benefits remain largely untested.

  Objective: This study aimed to investigate a newly developed MT app called Wildflowers, which was codeveloped with the laboratory for use in mindfulness research. It was hypothesized that 3 weeks of MT through this app would improve subjective well-being, attentional control, and interoceptive integration, albeit with weaker effects than those published in the 8 week, manualized group intervention literature.

  Methods: Undergraduate students completed 3 weeks of MT with Wildflowers (n=45) or 3 weeks of cognitive training with a game called 2048 (n=41). State training effects were assessed through pre- and post session ratings of current mood, stress level, and heart rate. Trait training effects were assessed through pre- and post intervention questionnaires canvassing subjective well-being and behavioral task measures of attentional control and interoceptive integration. State and trait training data were analyzed in a multilevel model using emergent latent factors (acceptance, awareness, and openness) to summarize the trait questionnaire battery.

  Results: Analyses revealed both state and trait effects specific to MT; participants engaging in MT demonstrated improved mood (r=.14) and a reduction of stress (r=−.13) immediately after each training session compared with before the training session and decreased post session stress over 3 weeks (r=−.08). In addition, MT relative to cognitive training resulted in greater improvements in attentional control (r=−.24). Interestingly, both groups demonstrated increased subjective ratings of awareness (r=.28) and acceptance (r=.23) from pre- to post intervention, with greater changes in acceptance for the MT group trending (r=.21).

  Conclusions: MT, using a smartphone app, may provide immediate effects on mood and stress while also providing long-term benefits for attentional control. Although further investigation is warranted, there is evidence that with continued usage, MT via a smartphone app may provide long-term benefits in changing how one relates to their inner and outer experiences.

- Subnis et al. (2020) JMIR Protocols

  The Principle Investigator reports that AmDTx is as effective as group psychotherapy for the prevention of mental illness in cancer patients. While the final results are not yet publicly available, the protocol describing the trial is listed above.

- Al-Jebrni et al. (2020) Biomedical Signal Processing and Control.

  Background: Accurate measurement of human stress at scale is a major mHealth challenge. Here we explore the potential for deep neural networks (DNNs) to improve remote and objective quantification of stress from voluntary selfie videos captured through mobile device front-facing cameras. Methods: Two DNNs were trained with

heart rate (HR) and heart rate variability (HRV) data obtained through photophlethysmographic imaging (PPGI) of 11,823 mobile device selfie videos captured in tandem with self-assessments of stress, and compared to contemporary algorithms used to estimate stress from HR and HRV data.

Results: A classification DNN and predictive DNN determined self-reported stress with 86 % accuracy and a mean absolute error of 0.001, respectively. Both DNNs performed far better than other recently described approaches when applied to the identical dataset.

Conclusions: Well-trained DNNs can objectively and remotely quantify stress at scale. Future efforts may concentrate on the measurement of additional enigmatic cognitive states.