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Digital delivery of Behavioural Activation therapy to overcome depression and facilitate social and economic transitions of adolescents in South Africa

Prof. Michelle Craske; Prof. Sarah-Jayne Blakemore; Prof. Heather O'Mahen; Prof. Alastair Van Heerden; Prof. Stephen Tollman ...

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Co-Principal Investigators: Prof. Kathleen Kahn, University of the Witwatersrand
Prof. Alan Stein, University of Oxford

Investigators: Prof. Michelle Craske, University of California Los Angeles
Prof. Sarah-Jayne Blakemore, University of Cambridge
Prof. Heather O'Mahen, Exeter University
Prof. Alastair Van Heerden, University of the Witwatersrand
Prof. Stephen Tollman, University of the Witwatersrand
Prof. Crick Lund, University of Cape Town/King's College London
Prof. Tholene Sodi, University of Limpopo
Dr Kate Orkin, University of Oxford
Dr Mahreen Mahmud, University of Exeter
Dr Emma Kilford, University College London
Ms Julia Ruiz Pozuelo, University of Oxford
Dr Bianca Moffett, University of the Witwatersrand
Dr Xavier Gómez-Olivé, University of the Witwatersrand
Dr Rhian Twine, University of the Witwatersrand

See list of Investigators' affiliations and contact details below

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University of the Witwatersrand, South Africa

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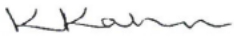
Confidentiality Statement
This document contains confidential information that must not be disclosed to anyone other than the Sponsor, Funder, the Investigator Team, host organisation, and members of the Research Ethics Committee and Regulatory Authorities unless authorised to do so.

Protocol signature page

The undersigned has read and understood the trial protocol detailed above and agrees to conduct the trial in compliance with the protocol.

Prof. Kathleen Kahn		04/04/2020
Principal Investigator (Please print name)	**Signature**	**Date**

Prof. Alan Stein		04/04/2020
Principal Investigator (Please print name)	**Signature**	**Date**

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1. KEY TRIAL CONTACTS

Co-Principal Investigators	Prof Kathleen Kahn; kathleen.kahn@wits.ac.za; +27824177373 Prof Alan Stein; alan.stein@psych.ox.ac.uk; +447947864283
Project Manager	Dr Bianca Moffett; bianca.moffett@wits.ac.za; +27730091410 Interim Project Manager (April 2021 – August 2021): Ms Shayni Geffen; shayni.geffen@wits.ac.za; +27829534920
Sponsor	Wits Health Consortium Faculty of Health Sciences University of the Witwatersrand, South Africa
Funder(s)	MRC Newton Fund UK-South Africa Joint Initiative on Mental Health (MR/S008748/1) (SAMRC) Earl Prinsloo: earl.prinsloo@mrc.ac.za; +27 21 9380317
Statistician	Prof. Eustasius Musenge School of Public Health University of the Witwatersrand, South Africa Eustasius.Musenge@wits.ac.za; +27 0117172610
Trial Steering Committee	• Prof Roz Shafran (UCL) - Chair • Prof Soraya Seedat (Stellenbosch University) • Prof Jonathan Roiser (UCL-NIMH) • Prof Jonathan Levin (University of the Witwatersrand))
Data and Safety Monitoring Board (DSMB)	Chair of DSMB: Prof Bonga Chiliza: ChilizaB@ukzn.ac.za

2. LIST OF INVESTIGATORS AFFILIATIONS AND CONTACT DETAILS

Name	Role	Affiliation	Email
Prof Kathleen Kahn	Co-Principal Investigator	Professor of Public Health and Senior Scientist, MRC/Wits Rural Public Health and Heath Transitions Research Unit (Agincourt), School of Public Health, University of the Witwatersrand	Kathleen.kahn@wits.ac.za
Prof Alan Stein	Co-Principal Investigator	Professor and Head of Section, Child and Adolescent Psychiatry, Department of Child and Adolescent Psychiatry, University of Oxford	Alan.stein@psych.ox.ac.uk
Prof Michelle Craske	Investigator	Professor of Psychology, Psychiatry and Biobehavioral Sciences at the University of California, Los Angeles (UCLA)	MCraske@mednet.ucla.edu
Prof Sarah-Jayne Blakemore	Investigator	Professor of Psychology and Cognitive Neuroscience, University of Cambridge.	sjblakemore@psychol.cam.ac.uk
Prof Heather O'Mahen	Investigator	Associate Professor in Perinatal Clinical Psychology, University of Exeter, United Kingdom	H.OMahen@exeter.ac.uk
Prof Crick Lund	Investigator	Professor of Public Mental Health, Alan J Flisher Centre for Public Mental Health, Department of Psychiatry and Mental Health, University of Cape Town; Professor of Global Mental Health and Development, Centre for Global Mental Health, Institute of Psychiatry, Psychology and Neuroscience, King's College London	crick.lund@uct.ac.za
Prof Alastair van Heerden	Investigator	Associate Professor University of Witwatersrand, and Research Fellow at Human Sciences Research Council (HSRC) South Africa	alastair.vanheerden@wits.ac.za
Prof Stephen Tollman	Investigator	Research Professor and Director, MRC/Wits Rural Public Health and Heath Transitions Research Unit (Agincourt), School of Public Health, University of the Witwatersrand	Stephen.Tollman@wits.ac.za
Prof Tholene Sodi	Investigator	Professor, Department of Psychology at the University of Limpopo	Tholene.sodi@ul.ac.za
Dr Kate Orkin	Investigator	Senior Research Fellow in Behavioural Economics at the Centre for the Study of African Economies, University of Oxford	kate.orkin@bsg.ox.ac.uk

Dr Mahreen Mahmud	Investigator	Lecturer (Assistant Professor) in Economics at the University of Exeter	M.Mahmud@exeter.ac.uk
Dr Emma Kilford	Investigator	Postdoctoral research fellow at University College London (UCL) Department of Clinical, Educational and Health Psychology	e.kilford@ucl.ac.uk
Dr Bianca Moffett	Investigator/ Project Manager	Project Manager DoBAt Study, MRC/Wits Rural Public Health and Heath Transitions Research Unit (Agincourt), School of Public Health, University of the Witwatersrand	Bianca.moffett@wits.az.za
Ms Julia Pozuelo Ruiz	Investigator/ Research Assistant	Doctoral student, Department of Psychiatry, and Research Assistant in the Centre for Studies of African Economies, University of Oxford.	julia.ruizpozuelo@psych.ox.ac.uk
Dr Rhian Twine	Investigator/ Public Engagement Officer	Head, Public Engagement Office, MRC/Wits Rural Public Health and Heath Transitions Research Unit (Agincourt), School of Public Health, University of the Witwatersrand	Rhian.Twine@wits.ac.za
Dr Xavier Gómez-Olivé	Investigator/ Agincourt Research Manager	Research Manager, MRC/Wits Rural Public Health and Heath Transitions Research Unit (Agincourt), School of Public Health, University of the Witwatersrand	f.gomez-olivecasas@wits.ac.za

3. LAY SUMMARY

Adolescence is a critical period in life when young people negotiate independence and increased responsibility and make important decisions. The incidence of depression peaks during adolescence, coinciding with the development of multiple cognitive functions in the brain.[1] Adolescent depression is a key public health concern, with high prevalence rates reported amongst rural and low resource communities in South Africa. Depression impacts young people's ability to make decisions and manage stressful situations in life.[2] It has also been linked to poor social, economic and health outcomes including early pregnancy, HIV, lower educational attainment and poverty in adulthood.[3] Evidence is urgently needed for cost-effective and scalable interventions targeting adolescent depression.

Behavioural activation (BA) is a psychological therapy which focuses on making links between mood and behaviour. It does this by identifying activities that are meaningful and positively reinforcing for the individual (activation), and addressing processes that inhibit activation (e.g. avoidance).[4] BA has been shown to be effective in treating adolescent depression, and can be adapted to diverse sociocultural contexts.[5] In addition to improving depressive symptoms, studies suggest that BA targets cognitive functions involved in depression, including executive function and social cognition.[6] These functions develop substantially during adolescence and are associated with a range of future socioeconomic outcomes.[7] Further, BA has been successfully delivered online and through trained peer mentors with limited specialist intervention, offering a scalable solution to overcome the lack of access to psychological therapies.[8,9]

The proposed trial will be a pilot randomised controlled trial to evaluate digital delivery of Behavioural Activation therapy for adolescents with depression in rural South Africa (DoBAt study). Central to the study is an iterative process to co-design the *Kuamsha* app (meaning "activate" in Swahili) through extensive formative work with adolescents from the study site. We will assess the feasibility, acceptability and determine the preliminary effectiveness of the intervention (primary objective). As a secondary objective, we will locally adapt and pilot outcome measures of mental health, cognition, risky behaviours, socioeconomic measures, and collect descriptive data to inform the development of a further larger trial.

4. SYNOPSIS

Trial Title	Digital delivery of Behavioural Activation therapy to overcome depression and facilitate socio-economic transitions of adolescents in South Africa		
Short Title	DoBAt study		
Trial registration	South African National Clinical Trials Registry (SANCTR) registration number: DOH-27-112020-5741		
Sponsor	Wits Health Consortium Faculty of Health Sciences University of the Witwatersrand, South Africa		
Funder	MRC Newton Fund UK-South Africa Joint Initiative on Mental Health (MR/S008748/1) Contact: Earl Prinsloo Email: earl.prinsloo@mrc.ac.za Phone: +27 21 9380317		
Clinical Phase	Pilot Trial		
Trial Design	Two-arm individually randomised control trial (RCT)		
Trial Participants	Adolescents aged 15-19 with mild to moderately severe depression based on scores between 5 and 19 on the 9-item Patient Health Questionnaire-Adolescent version (PHQ-A), that live in the MRC/Wits-Agincourt study area, Bushbuckridge, and from whom we obtain written informed assent and consent (including parental consent if <18).		
Sample Size	A total of 200 adolescents will be recruited, with 100 randomly allocated to each of the intervention and control arms.		
Planned Trial Period	Recruitment will provisionally commence in June 2021 (pending COVID developments). The intervention phase of the trial will run over 10 weeks, and follow-up will be conducted at 5, 11 and 24 weeks.		
Planned Recruitment	June – December 2021 *(COVID-19 permitting)*		
Aim	The aim of this study is to determine the feasibility, acceptability and initial effectiveness of a digitally delivered Behavioural Activation (BA) therapy intervention to overcome depression and facilitate socioeconomic outcomes for adolescents in South Africa.		
	Objectives	**Outcome Measures**	**Timepoints (weeks)**
Primary objectives	(1) To determine the feasibility and acceptability of a digitally delivered Behavioural Activation (BA) therapy to overcome depression.	We will assess the number of participants: recruited, assessed at baseline, randomised, completing the course of treatment, completing follow up measures. We will assess the acceptability of the recruitment method (including acceptability of randomisation),	0, 5, 11, 24

		intervention and study design through a series of in-depth interviews and an Acceptability Questionnaire with participants *(questionnaire and guides attached in HREC/OxTREC ethics application).*	
	(2) To provide preliminary evidence on the initial efficacy (direction and magnitude) of any effects of the intervention on depressive symptoms amongst adolescents with depression compared to control.	9-item Patient Health Questionnaire Adolescent version 9-item (PHQ-A).	0, 5, 11, 24
Secondary Objective	To pilot locally adapted outcome measures of mental health, cognition, risky behaviours, socioeconomic measures, and collect descriptive data to inform the development of a further larger trial.	Mental health scales: - Conor-Davidson Resilience Scale 10-item (CD-RISC) - Brief Rumination Response Scale 5-item (RRS) - Behavioural Activation for Depression Scale 25-item (BADS) - Emotional wellbeing (WEMWBS)	0,5, 11, 24
		Cognition tasks: - Affective set-shifting task - Affective go/no-go task - Affective backwards digit span - Balloon Analogue Risk Task (BART) - Matrix Reasoning Item Bank (MaRs-IB) - Emotion recognition task	0, 11
		Risky Behaviours scales: - Substance use - Sexual behaviour - Other risky behaviours Peer Influence	0, 11, 24
		Socioeconomic measures: - Employment and earnings - Consumption and finances Aspirations and expectations	0, 11, 24

		- Time preference, risk preference, and loss aversion task	
Intervention arm	The intervention arm will receive Behavioural Activation (BA) therapy via a smartphone application (the *Kuamsha* app) and supported by Trained Peer Mentors, implemented over 10 weeks. The app consists of six tailored modules (sessions) that contain BA's core principles integrated into a gamified format. Each module takes approximately 15-20 minutes to complete and is supplemented by brief "homework activities" that reinforce the concepts learnt within that module. The Kuamsha app has been developed through a process of extensive formative research and iterative co-design with adolescents in the study area to reflect the socio-cultural context in order to increase usability and acceptability. The app will be supplemented by brief phone calls (15 mins per module) from Trained Peer Mentors.		
Control arm	The control arm will receive active symptom monitoring every 2 weeks also via a smartphone application. Furthermore, the control app (*Kuchunguza* app – meaning "explore" in Swahili) will contain six 15-20 minute video clips from WildEarth-SafariLive, a locally produced wildlife documentary series that has been deemed an appropriate attentional control.		
Risk Management	A comprehensive Risk Management Protocol has been developed to ensure the safety of participants in the trial. Any participant that shows any indication of being severely depressed and/or suicidal during screening, baseline or follow-up assessments, as well as during delivery of the intervention, will be referred to the Risk Management Team. The Risk Management Team (RMT) consists of the Project Manager (a medical doctor), one Registered Counsellor, the Trial Psychologist, and three Trial Psychologist Supervisors (3 Clinical Psychologists). The RMT is responsible for overseeing all risk management aspects of the trial in consultation with the co-PIs. The RMT will immediately escalate participants at highest risk to the co-PIs and send a summative report to the investigator team on a monthly basis or more frequently as required.		

5. ABBREVIATIONS

AE	Adverse Event
BA	Behavioural Activation
CRF	Case Report Form
EF	Executive Function
DSMB	Data and Safety Monitoring Board
GCP	Good Clinical Practice
HDSS	Health and Demographic Surveillance System
HIV/AIDS	Human Immunodeficiency Virus/ Acquired Immune Deficiency Syndrome
HREC	Human (Medical) Research Ethics Committee
ICF	Informed Consent Form
MRC	Medical Research Council
NGO	Non-Governmental Organisations
PI	Principal Investigator
PIS	Participant Information Sheet
HREC	Human Research Ethics Committee
SAE	Serious Adverse Event
SC	Social Cognition
SES	Socioeconomic status
SOP	Standard Operating Procedure
TSC	Trial Steering Committee

6. BACKGROUND AND RATIONALE

Depression in a key developmental phase

Adolescence is characterised by substantial biological, cognitive, and social changes. During this time, individuals start to develop their self-identity, acquire the necessary skills to navigate future challenges, and make important decisions about their health, education, relationships, and entrance into the labour market within a context of diminishing parental control and heightened peer influence.

Executive Function (EF) and Social Cognition (SC) are the higher order cognitive functions that control the ability to strategise, set and maintain goals, pay attention, ignore distractions, empathise and regulate emotions to build successful relationships with others. These functions develop significantly during adolescence and are associated with a range of social and economic outcomes.[7] They also play a critical role in managing the high levels of negative affect and the rapid fluctuations in mood which are characteristic of adolescence.[10] EF and SC develop less well among individuals growing up in poverty, putting adolescents in low socioeconomic status (SES) groups at a lifelong disadvantage.[11]

The incidence of depression peaks during adolescence, and it is particularly problematic given the risk for greater depression chronicity across the lifespan.[1] Untreated depression can have serious consequences, as it affects interpersonal relationships, interferes with schooling, and disrupts productivity.[3] Depression, in turn, has a marked negative effect on EF and SC, with depressed individuals consistently underperforming on cognitive assessments compared to controls.[2,12] It is also associated with more than 90% of all cases of suicide, which has recently been recognized as the second largest and fastest growing cause of unnatural deaths among young people in South Africa.[13,14] Depression in adolescence also yields greater risk for substance use, poor sexual health, academic underachievement, and a significant reduction in future income.[15–17]

Poverty and mental health interact in a vicious cycle, with higher prevalence of depression in conditions of poverty. This, in turn, leads to lower education and socio-economic status, violence and insecurity, and poverty traps.[18–20] The province of Mpumalanga is characterized by high levels of poverty: it ranks fourth lowest in terms of income per capita and youth unemployment stands at 55.6%.[21] In our study site in rural Mpumalanga, South Africa, the prevalence of depressive symptoms stands at 18.2%, which is almost twice the prevalence recorded in a nationally-representative survey of adults in South Africa.[22,23] Furthermore, the prevalence of depression is expected to rise, in part due to the ongoing epidemiological transition from communicable to non-communicable diseases and co-morbidity between mental, neurological, and substance use disorders, HIV, and other chronic health conditions.[24] Evidence is urgently needed for scalable models of low-cost, effective mental health interventions for adolescents in South Africa with approaches that are not reliant on skilled mental health professionals and that are robust to threats in face-to-face delivery from public health crises such as COVID-19.

Evidence from past interventions: CBT as the gold standard

Cognitive behavioural therapy (CBT) has the most empirical evidence as a psychotherapy for depression.[25] CBT is built on the idea that the way we think affects the way we feel, and thus it targets the *content* of depressive thinking by trying to modify or replace negative, irrational thoughts with more accurate, helpful, and positive ways of thinking.

CBT is complex, and may require highly experienced and skilled psychological therapists, who are expensive to train and employ. In low- and middle-income countries (LMICs) the need for an extensive professional infrastructure of such therapists' limits access to CBT.[26] Furthermore, earlier evidence from CBT with adolescents' points to high rates of dropout, as well as a lack of engagement with this

therapy.[27] These issues are likely to be even of greater relevance in LMICs, and thus, there is a need for innovative strategies in these countries.

Modifying BA for app delivery for adolescents in the context of rural South Africa

Until recently, psychological interventions have been difficult to scale-up in LMICs, particularly given the absence of trained clinicians, and that CBT includes elements that are not well suited to non-western cultures.[28]

Behavioural Activation (BA) is a relatively simple yet effective psychological therapy for depression. BA uses behavioural strategies to target the *process* of depressed thinking and in particular, attentional control (i.e. an individual's ability to voluntarily control their attention) and depressive rumination (i.e. the tendency to repetitively think about the causes and consequences of one's negative emotional experiences). Contrary to CBT, BA does not try to change thinking, but rather identifies the ways in which negative thinking can interfere with adaptive behaviour and encourages behaviours that are action-focused, concrete, specific, and goal-directed.[4] During the treatment, participants learn to set goals, make plans, problem solve, establish routines, and reduce avoidance.

This approach has five key advantages as a potential intervention which could be scaled at a population level:

- *Simplicity:* BA is simple to explain, understand and deliver, making it relatively straightforward to incorporate into an adolescent's life. Evidence has shown effectiveness with depressed adolescents.[29] While most evidence from BA comes from adolescents in high income countries, a few studies show promising results in ethnically diverse lower income settings.[30] BA can be delivered by non-specialist health workers with limited training in under-resourced settings. It does not require extensive training or complex skills from therapists, and can be delivered by lay counsellors (i.e. task shifting).[5]

- *Efficacy when delivered online or via smartphones:* BA delivered via online programs with minimal support from lay counsellors or peer mentors has been shown to be as effective as when delivered in person.[8,9,31] Modestly priced smartphones and mobile data, coupled with a responsive system of supporters, provide a vehicle to vastly increase access to services, as shown by the rise in other internet- and phone-based psychological treatments (eHealth and mHealth).[32]

- *Cross-cultural validity:* BA fits with cultural concepts of depression in Southern Africa that place environmental stressors as the cause, and targets behavioural changes rather than beliefs and attitudes. It is thus relatively easy to adapt BA cross-culturally with potential for it to be widely used to treat depression in LMIC by a range of health care workers.[33]

- *Focus on EF and SC:* By teaching goal setting, planning and problem solving as well as establishing routines, BA is likely to directly target executive functioning. By encouraging rewarding activities and attention to experience, BA is likely to target social cognition. To date, cognitive mechanisms of BA have not been studied, although indirect evidence comes from "metacognitive therapy", which shares some features with BA, and was found to improve indices of executive functioning in a small scale study.[6] We hypothesise that an intervention that targets both EF and SC may be more effective than targeting either separately.

Proposed study

The proposed study will be embedded in the MRC/Wits-Agincourt Unit's Health and socio-Demographic Surveillance System (HDSS) study area in the rural Bushbuckridge Local Municipality of Mpumalanga Province, South Africa. The study area is located alongside the western border of Mozambique and comprises 31 contiguous villages with a population of 150,000 people in 21,000 households. As in other parts of the country, there is a high prevalence of depression amongst adolescents, and a paucity of mental health and social care services, particularly psychological therapies.[34]

We have built a multidisciplinary team of developmental and clinical psychologists, psychiatrists, epidemiologists, public health experts and economists, with a depth of global and local expertise in child and adolescent mental health, digital interventions, cognitive neuroscience, behavioural economics, and primary healthcare within the South African context.

This study is a two-arm single-blind individual-level randomised control pilot trial (n=200, with outcome assessors remaining blind). The main aim is to determine the feasibility, acceptability and initial effectiveness of a digitally delivered Behavioural Activation therapy intervention to overcome depression and facilitate socio-economic outcomes for adolescents in South Africa (DoBAt study).

Central to the study is an iterative process of co-design of the DoBAt intervention with adolescents from the Bushbuckridge context. Extensive formative research is underway to ensure that the development of the DoBAt intervention is locally and culturally relevant, appealing and easy to use. A broad array of local stakeholders have been engaged and consulted during the process of intervention and protocol development. These include adolescents and their caregivers, local health and social care providers, educators, a community advisory group, and representatives of the provincial and district Departments of Health, Education and Social Development.

A particularly innovative goal of the proposed study is to culturally-adapt and refine experimental measures of executive function and social cognition; and explore whether social cognition mediates the effects of BA on the outcomes. We will also explore alternative mediators such as resilience, rumination, and functioning. The evidence will allow us to understand the mechanisms by which the effects of the intervention are mediated and will form the basis for the refinement of treatments, towards more targeted, cost-effective and scalable therapies. The study will also allow us to pilot locally adapted outcome measures of mental health, risky behaviours, socioeconomic measures, and collect descriptive data to inform the development of a further larger trial.

If the pilot study produces promising results it will inform the development of a further larger RCT which we believe could support better management of depression among adolescents living in rural South Africa, and would align effectively with efforts by the Department of Health to strengthen primary and community-based healthcare systems.

Given the limited access to effective interventions in rural LMICs, innovative, scalable treatment delivery options are desperately needed. The DoBAt study will address this need in a number of ways. The randomized, controlled design of this study will strengthen the evidence for causality between the intervention and study outcomes. Relying on digital technology and aligning this with the evolving community-oriented primary care system, this study has the potential to deliver a tailored treatment for an understudied and vulnerable group — adolescents with depression — in rural South Africa.

7. OBJECTIVES AND OUTCOME MEASURES

All outcomes will be assessed at baseline (week 0), end of intervention (11 weeks) and 24 weeks. In addition, the primary outcome, other mental health measures and one cognitive task (emotion recognition)[1] will be assessed mid-intervention (5 weeks).

Table 1: Primary and secondary objectives of the study, outcome measures and timepoints of assessment

Objectives	Outcome Measures	Timepoints (weeks)
Primary objectives: (1) To determine the feasibility and acceptability of a digitally delivered Behavioural Activation (BA) therapy to overcome depression (2) To provide preliminary evidence on the initial efficacy (direction and magnitude) of any effects of the intervention on depressive symptoms amongst adolescents with depression compared to control.	(1) We will assess the number of participants: recruited, assessed at baseline, randomised, completing the course of treatment, completing follow up measures. We will assess the acceptability of the recruitment method (including acceptability of randomisation), intervention and study design through a series of in-depth interviews and an Acceptability Questionnaire with participants. (2) 9-item Patient Health Questionnaire Adolescent version 9-item (PHQ-A)	0, 5, 11, 24
Secondary objective: To pilot locally adapted outcome measures of mental health, cognition, risky behaviours, socioeconomic measures, and collect descriptive data to inform the development of a further larger trial.	Mental health scales: - Conor-Davidson Resilience Scale 10-item (CD-RISC) - Brief Rumination Response Scale 5-item (RRS) - Behavioural Activation for Depression Scale 25-item (BADS) - Emotional wellbeing (WEMWBS)	0,5, 11, 24
	Cognition tasks: - Affective set-shifting task - Affective go/no-go task - Affective backwards digit span - Balloon Analogue Risk Task (BART) - Matrix Reasoning Item Bank (MaRs-IB) - Emotion recognition task	0, 11

[1] Inclusion of the emotion recognition task is dependent on the outcome of a face validation study currently taking place in Limpopo University, led by Dr. Kilford, Prof. Sodi, and Prof. Blakemore.

	Risky Behaviours - Substance use - Sexual behaviour - Other risky behaviours Peer Influence scales	0, 11, 24
	Socio-economic measures: - Employment and earnings - Consumption and finances - Aspirations and expectations - Time preference, risk preference, and loss aversion task	0, 11, 24
Exploratory analysis: To test whether changes in social cognition mediate the effects of BA on adolescent depression.	- Emotion recognition task	0,5, 11

8. TRIAL DESIGN

This pilot study is a two-arm single-blind individual-level randomised control trial (RCT) to determine the feasibility and acceptability of a digitally delivered Behavioural Activation therapy intervention to overcome depression and facilitate socio-economic outcomes for adolescents in South Africa. This pilot trial will also provide preliminary evidence on the initial efficacy (direction and magnitude) of any effects of the intervention on depressive symptoms amongst adolescents with depression compared to control.

A total of 200 adolescents will be recruited through a two-stage process, with the initial screening being conducted in schools (after school hours). Those adolescents that screen positive for mild to moderately-severe depression will be invited to participate in the DoBAt study. Adolescents and guardians will be asked to provide verbal informed assent and/or consent. Participants for whom we obtain verbal assent and/or consent will subsequently be visited by a fieldworker at their household in order to obtain confirmatory written informed assent and/or consent, and to conduct the baseline assessment and enrol participants into the study.

Enrolled participants will be individually randomised into intervention or control arms of the study (100 participants each) based on computer-generated stratified random permuted blocks. Individual randomisation will be stratified by gender, age, and depression severity. A Field Supervisor (unblind) will conduct a further household visit to deliver and explain the use of the mobile phone and digital application to the participant (unblind). All outcomes assessments will be conducted by the Fieldwork/Assessment Team who will be blind to the allocation status of participants. Baseline and 11-week assessments will be conducted in-person through household visits using hand-held electronic devices to upload data to the server in real-time. Assessments at weeks 5 and 24 will be conducted electronically/telephonically.

A comprehensive Risk Management Protocol has been developed to ensure the safety of participants in the trial (see Appendix B). Any participant identified as being severely depressed and/or suicidal during screening, baseline or follow-up assessments, as well as during delivery of the intervention, will

be referred to the Risk Management Team (RMT). The RMT will ensure further assessment and management of the participant according to the Risk Management Protocol.

Graph 1: Graphic to illustrate the flow of the participant through recruitment and the study

Figure A. Recruitment timeline

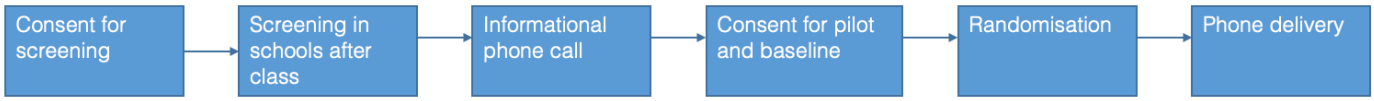
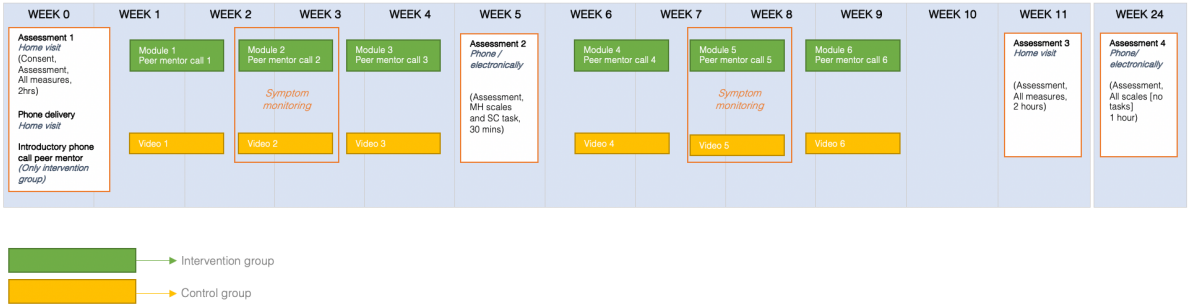


Figure B. Study timeline



9. PARTICIPANT IDENTIFICATION

9.1. Study Context

The Agincourt HDSS falls within the rural Bushbuckridge area of Mpumalanga Province and comprises approximately 31 villages with 150 000 inhabitants. Prior to 1994 it was part of the Gazankulu Homeland area and, as with other previous homeland areas in South Africa, infrastructure development still lags behind. Electricity is available in all villages, but its use is limited by cost; there is very little piped water to dwellings; sanitation is rudimentary; and few roads have been tarred.[35] Free primary and high school education is available, but the quality remains poor, and there are limited further educational and employment opportunities for graduates. Money sent home by migrant workers, as well as social grants, including the old-age pension and child support grants, remain vital sources of income for households. Data from the 2019 census shows that more than 93% of household own a cell phone and 64.7% have a smartphone. This digital landscape offers a new dimension of treatment opportunity among underserved communities in a resource poor setting.

There is a high prevalence of depression amongst adolescents in South Africa, and a paucity of mental health and social care services.[36,37] A nationally representative study of South African households found the lifetime and 12-month prevalence of *major depression* to be 9.7% and 4.9% respectively.[38] As mentioned above, a previous study amongst adolescent females in the Agincourt HDSS study reported a prevalence of depressive symptoms of 18.2%, which is almost twice the prevalence recorded in a nationally-representative survey of adults in South Africa.[22,23] Depression is rarely diagnosed in primary care[39] and suicide attempts/ parasuicide amongst adolescents are not infrequent presentations at district hospitals, although data are lacking.

Within the study subdistrict there are 2 health centres and 6 clinics, as well as 3 district hospitals within a 25-60km radius. Between these facilities there are 3 clinical psychologists and several social workers, primary healthcare nurses, and generalist medical officers. Within the province there are 3 full-time public sector psychiatrists, and no specialist inpatient psychiatric units. Inpatient mental health care is provided at 3 designated district and secondary hospitals largely run by medical officers. Several Registered Counsellors have been trained in tertiary institutions, but as yet no posts have been made available to them in the study area. Local NGOs providing social services include: GRIP (Greater Rape Intervention Programme) and VEPs (Victim Empowerment Prevention programmes) that deal with interpersonal and sexual violence, and Right to Care which provides support to persons living with HIV/AIDS. There are no specialist child or adolescent mental health services. Thus, there is a need for 'innovative' strategies that target adolescents with depression, an understudied and underserved group in rural South Africa.

9.2. Trial Participants

The participants will be adolescents aged between 15 and 19 years of age in grades 9 – 11 who screen positive for mild to moderately severe depression based on scoring between 5 and 19 on the 9-item Patient Health Questionnaire-Adolescent Version (PHQ-A), live in the Agincourt HDSS study area and supply written informed assent and consent (including parental consent if <18). Most participants will be from the Xitsonga ethnic group in South Africa, who reflect the majority of the black African population in the region. Participants from other ethnic groups may still be able to be part of the trial, as long as they are able to read and speak sufficiently in Xitsonga. Participants will be eligible for enrolment in the study provided they meet *all* inclusion criteria and *none* of the exclusion criteria.

9.3. Inclusion Criteria

- Adolescent males or females aged between 15 and 19 years in grades 9 to 11 at the beginning of the study
- Mild to moderately severe depression indicated by a score between 5 and 19 on the PHQ-A
- Able to read sufficiently in Xitsonga to use the app
- Participant (and their parent/ guardian if <18) is willing and able to give informed consent and/or assent for participation in the trial
- Participant is intending to continue to live in the study area for 12 weeks after baseline

9.4. Exclusion Criteria

- Hospitalisation for at least five days for severe psychiatric illness (specifically bipolar disorder, schizophrenia and other psychoses), or a life-threatening or other serious physical illness
- History of bipolar disorder, schizophrenia and other psychoses
- Severe depression as indicated by score >19 on the PHQ-A
- Current suicidal ideation/thoughts with specific plans and means identified
- Currently receiving a psychological treatment for a mental health problem(s)
- Lacks capacity to consent to treatment or research participation
- Lacks capacity to utilise the app whether recruited to control or treatment group
- Any other reason that the staff feel would jeopardize the health or well-being of the participant or staff or would prevent proper conduct of the study

- Adolescents who do not speak Xitsonga

10. TRIAL PROCEDURES

10.1. Community Entry

A broad array of local stakeholders have been engaged and consulted with during the process of intervention and protocol development in collaboration with the MRC/Wits-Agincourt Unit's Public Engagement Office. These include representatives from the provincial and district Departments of Health, Education and Social Development, local health and social care providers, heads of schools and educators, and a community advisory group. In addition, we have done extensive formative work with adolescents, parents/guardians and educators in the study area which has informed the iterative design and development of the intervention. We will organize further meetings with local stakeholders prior to the recruitment of participants for our pilot RCT in order to feedback the findings from our formative work and discuss/get feedback on the RCT.

Furthermore, we will gain clearance from the Departments of Health and Education to conduct the initial phase of our screening in schools (after school hours). There are 25 high schools in the HDSS catchment area. We will identify the schools with a higher share of adolescents aged between 15 and 19. The project manager and senior fieldworker will then meet with the (head) educators and governing bodies of the identified schools in order to request their participation in the screening and intervention phases of the pilot RCT.

10.2. Recruitment, Screening and Eligibility Assessment

Participants will be recruited through a two-stage recruitment process. Upon obtaining approval from the Department of Education, educators, and governing bodies of the schools, we will organise meetings at the respective high schools with parents/guardians, educators, and adolescents aged 15-19. During these meetings we will give an overview of the study and provide all parties with an opportunity to express their ideas and concerns, and to ask questions. During these meetings, we will invite all adolescents aged 15-19 in grades 9-11 to participate in the initial screening for the study and will provide written information sheets for participants (adolescents) and parents/guardians that explain the screening process. Subsequent to these meetings, we will ask educators to hand out informed consent and assent forms to adolescents aged 15-19 to take home. These consent forms will ask for telephone numbers/contact details of adolescents and their parent/guardian. We will request that those adolescents who are willing to participate in the study return their signed assent and/or consent forms to a fieldworker who will collect them at schools on another occasion.

The first stage of recruitment (Phase 1) will be conducted by trained fieldworkers in schools after school hours. All adolescents for whom we have obtained written informed assent and consent to conduct screening for the study will be invited to stay after school. We will then provide a 15-minute electronic assessment with the PHQ-A assessment and other basic sociodemographic questions (see questionnaire in the HREC/OxTREC ethics application).

Data will be transferred manually to a secure server and stored in a password protected MySQL database. The initial assessment of eligibility will involve categorising adolescents into three groups based on their PHQ-A scores as follows:

- Adolescents who score <5 on the PHQ-A and therefore have no/minimal symptoms of depression will not be eligible for the study.
- Adolescents who score between 5-19 and therefore have symptoms of mild to moderately-severe depression and meet the other eligibility criteria will be invited to take part in the study. These adolescents will be followed up by fieldworkers for the second stage of recruitment as outlined below.
- Adolescents who score >19 and therefore meet the criteria for having severe depression will not be eligible for the study. These adolescents and their parents/guardians will be contacted telephonically by Registered Counsellors specifically employed for the study. The Registered Counsellor will conduct a further risk assessment and refer the participant to a medical doctor and/or state employed clinical psychologist urgently (within 48hours) or at the participant's convenience based on whether the participant is assessed as "low suicide risk" or "high suicide risk". Further details can be found in the Risk Management Protocol in *Appendix B*.

The second stage of the recruitment process will be done with adolescents who scored between 5 and 19 on the PHQ-A and who also meet the other eligibility criteria. First, the adolescents and parents/guardians will be notified telephonically by trained fieldworkers and given further information regarding what participation in the DoBAt study would involve. Adolescents and parents/guardians will be given the opportunity to ask questions over the phone, and if they are willing to give verbal consent the fieldworker will then arrange a date and time to meet the adolescent and their parent/guardian at their home.

At the first home visit both adolescent and parent/guardian will be given the opportunity to review the participant and parent/guardian information sheets and to ask further questions. Adolescents will then be invited to participate in the trial and to provide electronic informed consent (>18) and/or assent (<18) forms. For adolescents who are under 18, we will also invite their parent/guardian to provide electronic informed consent. Those for whom we obtain informed consent from the guardian, as well as informed consent/assent from the adolescent, and who meet all the inclusion criteria and none of the exclusion criteria will be eligible to participate in the study.

10.3. Informed Consent

At both stages of recruitment we will obtain informed consent from participants aged 18 or over, and informed assent and parental/guardian consent from participants younger than 18. During the first stage of recruitment (screening in schools) we will obtain *paper-based* written informed consent or assent and parental/ guardian consent; whereas during the second stage of recruitment (for participation in the trial) we will obtain *electronic* informed consent or assent and parental/ guardian consent. Participants and guardians must personally sign and date the latest approved versions of the participant/guardian Informed Consent and/or Assent Forms before any trial specific procedures are performed.

Written and verbal Xitsonga versions of the participant and guardian Information Sheets and Informed Consent and Assent Forms will be presented to participants and parents/guardians detailing: the nature of the study; what it will involve for the participant; the implications and constraints of the protocol; potential consequences of participation, and any risks involved in taking part. It will be clearly stated that the participant is free to withdraw from the trial at any time for any reason without affecting their future care or legal rights.

The participant will be allowed as much time as they wish to consider the information, and the opportunity to question the investigator, their family or any other independent parties to decide

whether they will participate in the study. Written/electronic Informed Consent will then be obtained by means of participant dated signature and dated signature of the person who presented and obtained the Informed Consent. The person obtaining the consent will be a highly experienced and well-trained fieldworker, who has been authorised to do so by the Principal Investigator. A paper copy of the signed Informed Consent will be given to the participant. Original signed written consent forms (stage 1 of recruitment) will be retained in a locked cabinet at the trial site; whereas electronic consent forms (stage 2 of recruitment) will be retained at the trial site in a secure server (see Section 14 on data management for more information).

10.4. Enrolment and baseline assessment

In principle, all eligible adolescents from whom we obtain informed consent and assent will be enrolled in the study. In the event that there are two adolescents in one household that have met the eligibility criteria, the older adolescent will be enrolled for participation, unless we are towards the end of our recruitment process and need to enrol more younger adolescents. Enrolment and registration for the trial will be done by trained fieldworkers at the participant's household using hand-held electronic devices that connect to a web-based registration system.

The baseline assessment will be conducted during the same (first) household visit. This will consist of a brief demographic questionnaire, and completion of the primary and secondary outcome measures, and will take approximately 2 hours (questionnaire and tasks attached in HREC/OxTREC ethics application). It will be administered by highly experienced and well-trained fieldworkers using hand-held electronic tablets. Data will be uploaded to the server in real-time to ensure quality and safety. Fieldworkers will explain that participants can expect to receive a phone call to arrange a second household visit during which the mobile phone will be given to the participant.

10.5. Randomisation and allocation

Participants will be randomly allocated to intervention or control arms of the study based on computer-generated stratified random permuted blocks. Individual randomization will be stratified by gender and age. The allocation code will be held by the Senior Data Scientist. A notification will be sent to the Project Manager that a new participant has been enrolled and randomised. The Project Manager will then instruct one of the two Field Supervisors to phone the participant to arrange a date and time for a second household visit. Randomisation will be conducted after the baseline assessment visit (conducted by fieldworkers) and before the second visit (conducted by Field Supervisors) in order to maintain blinding of the Fieldwork/Assessment Team.

Field Supervisors will conduct the second household visits during which mobile phones will be given to adolescents and will explain how to use the smartphone and digital applications (apps).

Adolescents and their parents/guardians will have the opportunity to raise any questions or concerns, and will be given telephone numbers for two dedicated helplines: 1) a Phone-use Helpline: to phone in the case of any issues with respect to the phone or digital application, and 2) a Risk Management Helpline: to phone in the case of severe psychological distress and/or thoughts of self-harm or suicide. Additionally, adolescents in the intervention arm of the study will be allocated to a Trained Peer Mentor from whom they will receive a weekly phone call for the duration of the study.

10.6. Blinding and code-breaking

For practical and risk management reasons, *Field Supervisors* will be aware of which adolescents have been allocated to intervention and control groups, but they will not be involved in any outcome assessments. The two Field Supervisors are experienced senior fieldworkers who have done previous work in adolescent populations and will provide a vital link between the adolescents participating in the study, the Project Manager and Risk Management Team.

Similarly, we have decided that the *Project Manager and Risk Management Team* will not be blinded for the purposes of the pilot trial, in order to prioritise participant safety, but we will explore how this could be done in a full-scale RCT. Notably, the Project Manager, and Risk Management Team will not be involved in any collection of data relating to outcome assessments.

By using an independent *Fieldwork/Assessment Team* to conduct the baseline and follow-up assessments at separate visits to the Field Supervisors, we will ensure that all outcome assessors remain blind. Any breaches in blinding will be documented, and we will endeavour to change the fieldworker conducting subsequent assessments on a particular adolescent where unblinding has occurred.

10.7. Summary of all scheduled visits

After baseline and randomisation, the participants will receive 1 scheduled visit from one of the Field Supervisors to deliver the mobile phone and explain the use of the digital application, as detailed above. This visit will take approximately *1 hour*. In addition to this visit, follow-up assessments will be conducted at 5, 11 and 24 weeks (4 assessments in total).

Baseline and follow-up assessment at week 11 will be conducted in-person at participants' households, using hand-held electronic devices and uploaded to the server in real-time to ensure quality and safety, and will take a maximum study visit of 2 hours. Assessments at weeks 5 and 24 will be done electronically or telephonically and will take approximately *1 hour* each. We have attached a list of potential measures and will select those which are most appropriate to the local context based on the findings from previous formative work conducted in the study area.

All questionnaires will be available in Xitsonga (the predominant language in this area). All assessments will be conducted by highly experienced and well-trained Xitsonga speaking fieldworkers (Fieldwork/Assessment Team) who will be blind to the allocation status of participants. The specific measures are as per *Table 3* below.

Table 3. Measurement Schedule

Assessment	**Screen & Enrolment**	**Baseline**	**5 WKS**	**11 WKS**	**24 WKS**
Place:	Schools	Home	Electronically/ Phone	Home	Electronically/ Phone
Screening					
Sociodemographic questions & eligibility checklist	X				
Patient Health Questionnaire Adolescent version 9-item (PHQ-A)	X				
Primary Outcome					
Patient Health Questionnaire Adolescent version 9-item (PHQ-A)	X		X	X	X

Secondary outcomes					
Mental health					
Generalised Anxiety Disorder (GAD-7)		X	X	X	X
Conor-Davidson Resilience Scale (CD-RISC)		X	X	X	X
Brief Rumination Response Scale (RRS)		X	X	X	X
Emotional wellbeing (WEMWBS)		X	X	X	X
Behavioural Activation for Depression Scale (BADS)		X	X	X	X
Trauma		X			
Risky behaviour and peer influence					
Risky behaviours		X		X	X
Peer influence scales		X		X	X
Socioeconomic					
Employment and earnings		X		X	X
Consumption and finances		X		X	X
Aspirations and expectations		X		X	X
Time preference, risk preference, loss aversion task		X		X	
Brief sociodemographic questionnaire (asked to parent/guardians if <18)		X			
Cognition					
Affective set-shifting task		X		X	
Affective go/no-go task		X		X	
Affective backwards digit span		X		X	
Balloon Analogue Risk Task (BART)		X		X	
Emotion recognition task		X	X	X	
Matrix Reasoning Item Bank (MaRs-IB)		X		X	
Monitoring throughout treatment					
Mood Monitoring (only treatment group)		Throughout treatment			
Trained Peer Mentor calls (only treatment group)		7 calls (1 per module)			
Symptom Monitoring (treatment and control group)		Every 2 weeks			
Post-treatment					
Acceptability Questionnaire & IDIs				X	

10.8. Description of Measures

All measures will be translated into Xitsonga, back-translated into English, and assessed for accuracy, clarity and ease of comprehension in consultation with the MRC/Wits-Agincourt Public engagement Office and a Xitsonga speaking Clinical Psychologist on the study team (Prof. Sodi).

We will ask about mental health, trauma, and risky behaviours (e.g. sexual behaviour, substance use, and other sensitive behaviours) using Audio Computer-Assisted Self-Interviewing (ACASI) software. Participants will listen to pre-recorded survey questions through headphones and select their response on a tablet computer.

Computerised cognitive and socioeconomic tasks will be performed individually by participants on a tablet computer, in a quiet location under the instruction of a trained fieldworker. The tasks will be explained by the fieldworker via instructions embedded in the task application and then performed by the participant after some practice trials. Participants complete the tasks by responding using the tablet touch screen.

Primary outcome

Patient Health Questionnaire Adolescent version (PHQ-A). 9-item measure that assesses the severity of depressive disorders and episodes (or clinically significant symptoms of depressive disorders and episodes) in adolescents. Each item asks the adolescent to rate the severity of his or her depression symptoms during the past 2 weeks. Each item on the measure is rated on a 4-point scale (0 = Not at all; 1 = Several days; 2 = More than half the days; and 3 = Nearly every day). The total score can range from 0 to 27, with higher scores indicating greater severity of depression. This measure shown good psychometric properties with a sample of adolescents and young adults in South Africa and Kenya.[40–42]

Secondary outcomes

Generalised Anxiety Disorder (GAD-7). The GAD-7 is a 7-item questionnaire designed to assess the symptoms of Generalised Anxiety Disorder over the previous 2 weeks. The items enquire about the degree to which the respondent has been bothered by feeling nervous, anxious or on edge, not being able to stop or control worrying, worrying too much about different things, having trouble relaxing, being so restless that it is hard to sit still, becoming easily annoyed or irritable and feeling afraid as if something bad might happen. Studies from Sub-Saharan Africa examining the psychometric properties of the GAD-7 have demonstrated good internal consistency and performance characteristics with young adults in Zimbabwe and among Kenyan youth.[42,43]

Conor-Davidson Resilience Scale (CD-RISC). The CD-RISC is a 10-item questionnaire that measures the ability to cope with traumatic stress. It measures several components of resilience by measuring the ability to: (i) adapt to change, (ii) deal with what comes along, (iii) cope with stress, (iv) stay focused and think clearly, (v) not get discouraged in the face of failure, and (vi) handle unpleasant feelings such as anger, pain or sadness. CD-RISC-25 has been used a sample of South African adolescents in public schools [44] and with homeless youth in Ghana.[45]

Brief Rumination Response Scale (RRS). Rumination in the process of dwelling persistently on recurrent negative thoughts. The brief RRS comprises 5-items on brooding, defined as a passive comparison of one's current situation with some unachieved standard. This short scale is highly correlated with the full measure of the RRS, and it is known to be important in the onset and maintenance of depression.[46] The full scale has been previously used among depressed Nigerian

adolescents [47] and it is currently being used in a trial led by Prof. Stein with HIV-positive pregnant women in KwaZulu-Natal.

Warwick-Edinburgh Mental Wellbeing Scale (WEMWBS). The WEMWBS is a 14-item questionnaire to assess psychological functioning and emotional wellbeing in the general population. It covers key aspects of psychological functioning (optimism, autonomy, agency, curiosity, clarity of thought and positive relationships) and positive affect (confidence, feeling relaxed, cheerful, having the energy to spare). The scale has been used in South Africa, Tanzania, and Kenya and proved to be valid in a range of settings (e.g. public health, schools, clinical settings, etc.). The Cronbach's alpha for the WEMWBS in a sample of Kenyan adolescents was 0.70, indicating adequate reliability of this measure.[42]

Behavioural Activation for Depression Scale (BADS). The BADS is a 25-item questionnaire to measure when and how individuals become less avoidant and more activated over the course of treatment — a key variable to measure in studies of Behavioural Activation. BADS examines changes in the following areas: activation, avoidance/rumination, work/school impairment, and social impairment. Although most of the evidence comes from high income countries, several BA trials with adolescents have found an association between BADS and treatment effect.[48–50]

Trauma. Four brief questions about trauma will be included as part of the baseline assessment. These questions were initially developed for use in a study of digitally delivered CBT, supported by peer mentors, at the University of California Los Angeles (UCLA). The trauma questions will form part of our risk management response, in order to identify any participants who are currently experiencing ongoing physical, sexual or emotional abuse of interpersonal violence. Risks will be assessed and managed according to the Risk Management Protocol.

Risky behaviours and peer influence. The questions and scales include:

- *Sexual behaviour:* we will ask participants about marriage, sexual activity, use of contraception, and fertility using a subset of questions from the 2016 South Africa Demographic and Health Survey 2016 (SADHS) and Wits Reproductive Health and HIV Institute (Wits RHI) sexual behaviour survey. The SADHS is based on the standard DHS questionnaire and adapted to reflect the population and health issues relevant to South Africa. The RHRU was a national survey of 15-24 year olds in nine provinces of South Africa, including Mpumalanga.[51]
- *Substance use:* the frequency of substance use will be assessed using the Alcohol, Smoking and Substance Involvement Screening Test for Youth (ASSIST-Y).[52] The ASSIST-Y has been validated for use among young people and in a low- and middle-income country context. In addition, the ASSIST-Y will capture information on a wide range of substance use, with clinically relevant cut-off points to identify potentially harmful use.
- *Other risky behaviours:* we will ask participants about school engagement, delinquency, gambling, and dangerous driving using items from the Youth Risk Behaviour Surveillance Survey (YRBSS) and the Adolescent Risk-Taking Questionnaire.[53,54]
- *Peer influence:* We will measure peer influence in participant's engagement with risky behaviours by asking a subset of questions from the Resistance to Peer Influence Scale (RPI) and a scale of peer sexual behaviour and substance use.

Socioeconomic questionnaires and tasks:

- *Employment and earnings*: participants will be asked to report any work for payment in the past 30 days, along with the hourly wage.
- *Consumption and finances*: participants will be asked about items purchased, sources of income, and savings in last 30 days.

- *Aspirations and expectations:* we will ask participants about their aspirations in various domains (e.g. education, income, age of marriage) and how likely they think those aspirations are to occur. We will ask about self-efficacy using a single-item Self-Esteem Scale.
- *Time preference task:* participants will be asked to rank how much are they willing to give up something today in order to benefit from that in the future and will be presented with an incentivised task. This task will ask respondents to choose how much phone data to allocate to payment at an earlier date and a payment at a later date. Each question involves different amounts and different time periods. This task is meant to elicit respondents' preferences for phone data at different points in time.[55]
- *Risk preference task:* participants will be asked to rank how willing are they to take risks and will be presented with an incentivised task. Subjects will be asked to choose between a sure gain of a particular amount of data, or a draw, where they would have an equal change of earning a higher amount or earning nothing. They will be presented with different situations, each with different amounts of sure gain. This task is meant to measure risk attitudes.[56]
- *Loss aversion task:* participants will be presented with an incentivised task where they choose between a sure loss of a particular amount of phone data, or a draw, where they would have an equal chance of losing a higher amount or losing nothing. They will be presented with different situations. Each situation will increase the amount of the sure loss. This task is meant to elicit respondents' loss aversion.[56]

Cognition tasks:
Computerised cognitive tasks include computerised paradigms of affective control, social cognition, risk-taking and executive function.

- *Affective Set-Shifting:* set-shifting will be assessed with a modified version of the Wisconsin Card Sorting Task. In this version participants assign cards to one of four decks based on three sorting criteria: (i) the number of items on the card, (ii) the colour of the card, (iii) or the shape of the items (neutral version) or the emotional expression of the faces (affective version). Participants are not told the sorting rule but instead rely on the computerised feedback they receive to determine the correct rule. The sorting rules change suddenly, and participants need to adapt their sorting criterion.[57]
- *Affective Go/No-Go:* inhibition of affective information will be assessed using a face based emotional go/no-go task.[67] Participants view faces of different emotional valences (positive or negative) and have to respond via a button press to faces of a target emotion, but not respond to those that do not match the target. The non-affective task version will use non-emotional characteristics as targets (e.g. gender).
- *Affective Backwards Digit Span:* the backward digit span is an updating task in which participants are asked to recall digits that are serially presented, superimposed over neutral (e.g., scrambled face) or negative (e.g., sad face) images, in reverse order. The task assesses how many digits participants can remember in sequence and will be adapted for computerised presentation.[58]
- *Balloon Analogue Risk Task (BART):* in this incentivised task, participants earn monetary rewards for inflating a balloon and choose when to stop and claim their reward. With each pump, the potential payoff increases, however if the balloon explodes no reward is given. This task assesses risk-seeking preferences under uncertainty.[59]
- *Emotion recognition task:* Participants are shown images of faces showing different types of emotional expressions and are asked to classify the emotion that is expressed. Task difficulty is varied by adding Gaussian noise mask to the image at varying intensities.[60]
- *Matrix Reasoning Item Bank (MaRs-IB):* participants complete a measure of abstract reasoning, where they have to select one of several potential objects to complete the pattern of a matrix. The task requires participants to identify the missing element that completes a pattern and is frequently used to test fluid intelligence.[61]

Monitoring throughout treatment

- *Mood Monitoring (treatment group):* participants in the intervention arm will be asked to monitor their mood at different times throughout the treatment. Participants will be presented with different cartoon face moods within the app and will be asked to select which emotion is closest to their current mood. In-app points will be earned every time the user completes mood monitoring.
- *Trained Peer Mentor calls (treatment group):* participants in the intervention arm of the study will also receive one 15-minute phone call per week for 6 weeks from a Trained Peer Mentor (in addition to one introductory phone call). This phone call is part of the intervention design, described further below.
- *Symptom Monitoring (treatment and control group).* We will monitor symptoms every two weeks for the participants in the treatment and the control group using the PHQ-A and GAD-7. This monitoring will allow us to assess risk and safety in the study. Participants will receive an SMS with a link to a secure online survey and will receive a small amount of phone data (R10) each time they complete it (see section 18.9 for further information on compensation for participation).

If at any of the assessments or during monitoring: enrolled participants score >19 on the PHQ-A, and/or answer affirmatively to thoughts of self-harm or suicide; they will be contacted telephonically by one of the Registered Counsellors. The Registered Counsellor will conduct a further risk assessment and institute *active monitoring* and/or *active management* steps based on whether the participant is assessed as "low suicide risk" or "high suicide risk". Further details can be found in the Risk Management Protocol in *Appendix B*.

Acceptability questionnaire. During the trial, we will also collect app engagement metrics with the following information: session length, number of sessions completed, number of active users, attrition rate. At the end-of-intervention visit (11 weeks), we will conduct an acceptability questionnaire with all participants. Results from this questionnaire will provide important data to assess the feasibility, acceptability of our intervention (a primary outcome) as well as to support our Process Evaluation (understanding of what worked for whom and why). After this, we will arrange another visit to conduct in-depth interviews with a random selection of participants from both the intervention and control groups in order to garner their feedback on their experience using the app.

In addition, we will ask adolescent's parent/guardian to answer a sociodemographic questionnaire about the household during the baseline assessment. For participants age 18 or 19, we will ask this section to participants themselves.

Lastly, participant's data will be linked to the HDSS census data.

10.9. Early Discontinuation/Withdrawal of Participants

During the course of the trial a participant may choose to withdraw early at any time. This may happen for a number of reasons, including but not limited to: i) the occurrence of what the participant perceives as an intolerable adverse event (AE), ii) inability to comply with trial procedures, iii) participant decision. According to the design of the trial, participants have the following options for withdrawal:

- Participants can withdraw from the study but permit data obtained up until the point of withdrawal to be retained for use in the study analysis. No further data would be collected after withdrawal. Withdrawal from the trial treatment will not result in exclusion of data from the study analyses.
- Participants can withdraw completely from the study and withdraw the data collected up until the point of withdrawal. The data already collected would not be used in the final study analysis.

In addition, the Principal Investigators may discontinue a participant from the trial treatment at any time if they consider it necessary for any reason including, but not limited to:

- Ineligibility (either arising during the trial or retrospectively having been overlooked at screening)
- Significant protocol deviation
- An AE which requires discontinuation of the intervention or results in inability to continue to comply with trial procedures
- Worsening of the mental health condition which requires discontinuation of the intervention or results in inability to continue to comply with trial procedures

Participants who have withdrawn from the study/been discontinued by the Principal Investigators will be offered referrals to mental health and social care services if required. If the participant is withdrawn due to an AE, the Principal Investigators/Project Manager will arrange for follow-up visits or telephone calls until the AE has resolved or stabilised. Investigators will be required to follow up Serious Adverse Events (SAE) until resolution or end of trial. The type of withdrawal and reason for withdrawal will be recorded in the Case Report Form (CRF). Withdrawn participants will not be replaced.

10.10. Definition of End of Trial

The end of trial will be the date of the final (24 week) assessment of the last participant in the trial.

11. TRIAL INTERVENTIONS

11.1. Description of the Intervention and Control

Participants in the intervention arm will receive BA therapy delivered via a smartphone app (the *Kuamsha* app) supported by weekly phone calls (1 per module with a total of 7 calls (including one introductory call), each lasting 15 minutes) from Trained Peer Mentors, implemented over 10 weeks.

The BA treatment focuses on two core principles: (i) increasing activities that are meaningful and positively reinforcing for the individual (activation), and; (ii) addressing processes that inhibit activation (e.g. negatively reinforced avoidance behaviours). We used this BA framework to develop the *Kuamsha* relying on two approaches. First, we used an *iterative approach* to co-construct the app with adolescents. The intervention app has been developed through a process of extensive formative research and a participatory design with adolescents from the study site to reflect the socio-cultural context in order to increase usability and acceptability, whilst maintaining fidelity to the core principles of BA. Experts in adolescent mental health, BA and digital interventions, as well as primary healthcare and public health specialists with knowledge and experience of working in the local context have contributed to the development of the app. Drawing from the findings of this formative work,

the team decided upon a *narrative gaming approach*, in which the app relays the principles of BA to the player through an engaging story (using plot, dialogues, player choices, sounds, and humour).

The *Kuamsha* app will consist of two storylines (the Song Contest and the Football Match), each with six tailored modules ('episodes'). Both storylines allow participants to play the role of a young person who faces difficulties during their everyday life. Participants are able to make choices which affect the course of the story and allows them to see the consequences of these actions (i.e. 'in-vivo teaching'). The stories cover topics which are part of BA therapy, including problem-solving, getting enough sleep, managing negative thoughts, being connected and communication, and identifying and engaging in meaningful activities. Each 'episode' will be followed by a homework activity where the participant is encouraged to reflect on the BA principles outlined in the episode and think about ways to apply the principles to their own lives. To stimulate motivation and performance, the app will include both game design and BA elements, including mood monitoring, avatar personification, in-app points, and reminders.

Each module takes 15-20 minutes to complete and we expect adolescents to complete one module in a week. One storyline can be completed in up to 10 weeks (allowing for holidays/missed weeks/taking extra time with a specific module, etc.) Participants can complete both stories during the 10-week period if they wish. Example mock-ups of the *Kuamsha* app and a summary of each module are shown in Appendix A.

The app will be supplemented by brief phone calls (15 mins per module) from Trained Peer Mentors. The role of the Trained Peer Mentors will predominantly be to support adherence and compliance to the app, and to troubleshoot problems related to the use of the app and implementation of the homework activities. They will be encouraged *not* to provide additional advice or counselling and will conduct their calls according to a pre-determined checklist. Peer Mentors will be trained and supervised by the Trial Psychologist (described further in the next section).

The control arm will receive active symptom monitoring also via a smartphone application. Furthermore, the control app will contain 15-20-minute video clips from WildEarth-SafariLive, a locally produced wildlife series that will act as a sufficient 'placebo', as it controls for video/story-based elements whilst not containing too many "active ingredients" such as humour, absorption and learning that could be related to BA. In the given context, the control represents an enhancement of usual care since most adolescents with depression would not usually receive any intervention, let alone symptom monitoring and referral.

11.2. Recruitment, training and supervision of personnel

Trained Peer Mentors will be Xitsonga speaking students or recent graduates, from the Department of Psychology or Social Work at an accredited South African University. They will be trained, assessed and supervised by the Trial Psychologist according to the Training Manual developed specifically for the intervention (currently under development). Up to 20 Peer Mentors will be trained and up to 10 will be selected for participation in the intervention based on a competency assessment at the end of their training. All students will be given a certificate for participation in training.

Two Field Supervisors that are Xitsonga speaking senior fieldworkers with excellent knowledge of the study site will provide a vital link between participants and the Risk Management Team. They will conduct the home visits subsequent to the baseline assessment in order to explain to participants how to use the mobile phones and apps, as well as providing participants with contact details for the two Helplines. Furthermore, they will explain the role of Trained Peer Mentors to the participants and

initiate connection between Peer Mentors and participants. The Field Supervisors will also work in conjunction with the Registered Counsellors to arrange appointments and follow-ups of participants identified as having severe depression and/or suicidal ideation. They will be trained and supervised by the Project Manager.

Registered Counsellors will *not* play a role in the intervention, but will be recruited and employed for the purposes of the trial in order to provide proactive risk management to all adolescents who are identified as having severe depression (PHQ-A >19) and/or suicidal ideation, whether at screening, or during the process of the trial. At the outset of the trial one Xitsonga-speaking Registered Counsellor who is resident in the Bushbuckridge area or local vicinity will be trained and employed by the research unit for the duration of the trial. If deemed necessary, the unit will employ a second Registered Counsellor at a later stage. At present there are several Registered Counsellors in the area that have received a 4-year training and professional certification from state institutions, but for whom no government posts have yet been created. The Registered Counsellor(s) will be trained and supervised by the Trial Psychologist and Project Manager.

The *Trial Psychologist* will be a Xitsonga speaking psychologist specifically contracted for the duration of the trial. Their primary responsibility will be the training, assessment and supervision of the Peer Mentors. In addition, they will receive referrals for cases where psychological support is required as part of risk management in addition to the support of Registered Counsellors for participants in both intervention and control arms. This was deemed necessary in order to mitigate the risk of overwhelming pre-existing Department of Health resources. The Trial Psychologist will be supervised by the Trial Psychologist Supervisors (a senior Clinical Psychologists on the study team).

The *Fieldwork/Assessment Team* will conduct all outcomes assessments on participants in both intervention and control arms. They will be highly trained quantitative fieldworkers employed by the MRC/Wits-Agincourt Unit. They will be trained and supervised by the Project Manager and their training will include principles of research ethics and Good Clinical Practice.

11.3. Concomitant Medication

Participants who are receiving other psychological treatments at the start of the trial (screening and/or baseline assessment) will not be eligible for participation in the trial. Participants who were randomised and who subsequently start receiving psychological therapy, either due to referral to a psychologist as part of the Risk Management Protocol or otherwise, will not be excluded from the trial. Their data will be used in all intention-to-treat analyses, and we will record and report on all instances of other psychological treatment received.

Participants who are using anti-depressant medications, including Selective Serotonin Reuptake Inhibitors (SSRIs), Tricyclic Antidepressants (TCAs) and any other antidepressant medication recognised by National and International Drug Formularies, either at the start of the trial, or who are subsequently initiated on anti-depressant medication during the course of the trial, will not be excluded from participation in the trial as long as they meet entry criteria for depression, but a record of the dates and dosages of their medication use will be recorded.

11.4. Fidelity of the intervention

The following measures will be instituted to ensure that the intervention is delivered as intended, and to assess the degree to which fidelity is maintained throughout the trial.

*Fidelity of **delivery** of the intervention*

Key delivery *agents* will be the digital apps for both arms and the Trained Peer Mentors in intervention arm.

- *Adherence*
    - Objective: To determine the extent to which the Peer Mentors deliver the intervention according to their training protocol.
    - Outcome measures: Number of sessions that meet at least 95% of criteria for adherence according to training protocol. Independent raters will listen to a random number of recordings of Peer Mentors phone calls and assess them against the training protocol. We will also ask Peer Mentors to complete a pre-specified questionnaire after every call and send on to the Trial Psychologist for review. This questionnaire will contain concrete items for each session outlined in the Peer Mentor Training Manual. Examples of questions include: What was the focus of this session? Did the adolescent have any barriers or particular successes? What was the agreed activity to do in the next week?.
- *Competence*
    - Objective: To determine the competency of the Peer Mentors to deliver the intervention as per pre-determined competency assessment outlined in the Peer Mentor Training Manual.
    - Outcome measure: Competency of the Peer Mentors will be expressed as a percentage based on their Competency Assessment Test. This test will include a written test and observation of skills through role-playing to assess Knowledge, Attitudes and Practices. Tests will be scored by the 2 clinical psychologists (the Trial Psychologist and Trial Psychologist supervisor) using a pre-determined scoring system.

The following additional measure will be instituted to ensure that the intervention is delivered with a high degree of fidelity:

- *Training of Peer Mentors* will be conducted by the Trial Psychologist, who will themselves be trained and orientated to their role in the trial by three the Trial Psychologist Supervisors (senior Clinical Psychologists). All training will be conducted according to a Peer Mentor Training Manual which is being developed by a Clinical Psychologist who is a specialist in Behavioural Activation interventions, in collaboration with Primary Healthcare specialists familiar with the study context.
- *The Trial Psychologist* will conduct individual supervision sessions with the Peer Mentors every 2 weeks and additionally as necessary.
- Further *group supervision sessions* by the Trial Psychologist with Trained Peer Mentors will be used to revise certain key aspects of the intervention manual and provide booster training at regular intervals during the trial.

*Fidelity of **receipt** of the intervention (participants in the intervention arm)*

- *Treatment Compliance:*
    - *Treatment completion* will be defined as having opened at least 4 out of 6 of the app episodes.
    - *Treatment non-completers* will be defined as participants that open less than 4 out of 6 of the app episodes.
    - *Drop out from care* will be defined as 5 consecutive missed scheduled calls from the Trained Peer Mentor, as well as inability of the Field Supervisors to locate the

participant on two home visits, or direct verbal or written indication from the participant that they wish to withdraw from the study. In the case that a participant indicates that they no longer want to participate in the study, we will ask for permission to retain their data. We will endeavour to continue to collect data from people who move out of the area provided they give informed consent to continued participation and can be contacted. If a participant misses the 11-week follow-up assessment appointment, and the Field Supervisors is repeatedly unable to contact the participant despite home visits, they will be deemed to be *lost to follow up.*

- *Dose*
    - Objective: To determine the degree to which the participant engaged in and completed the app modules and/or Peer Mentor phone calls.
    - Outcome measure: This will be measured using a composite measure to produce a score between 1-100, to encompass the following aspects of app use/engagement:
        - Module engagement: number of times participants logged into the app, number of modules opened & completed, total time spent on app
        - Homework engagement: number of homework assignments opened, initiated, completed partly, completed entirely.
        - Mood and symptoms monitoring: number completed partly or entirely.
        - Peer mentor engagement: number of phone calls to peer mentor, total time spent on calls.

11.5. Post-trial Treatment

We will delete the Kuamsha app from participant's phone on conclusion of the pilot trial. We will not request adolescents to return the mobile phones. Participants identified as requiring urgent mental health care at the time of the final assessment, as identified by scoring 19 or higher on the PHQ-A (severe depression) and/or active suicidal ideation, will be referred to a Medical Officer and/or Clinical Psychologist at the local district hospital for further assessment and management. This has been discussed and agreed with these healthcare providers. A brief psychiatric history will be provided to health professionals to whom participants are referred, with permission from the participants. For participants with mild to moderately severe depression, we will supply them with further information and details of how to access governmental and non-governmental mental health and social care services. Participants with specific socio-economic difficulties will be referred to a designated social worker at their nearest clinic. In addition, we will advocate for the creation of posts within the public health sector for Registered Counsellors to conduct basic counselling and risk assessment and management.

12 SAFETY REPORTING

The safety reporting window for the DoBAt study will be from time of enrolment and registration into the study until the end of trial defined as completion of the 24-week assessment. Investigators will follow up all Adverse Events until event resolution/stabilisation or until the end of the trial.

12.1 Adverse Events (AEs)

Any untoward physical, psychological or social occurrence in a participant who has enrolled in the study, including occurrences which are not necessarily caused by or related to the use of the intervention/ control. These may include:

- Thoughts of self-harm or suicide with no specific plans/ means identified, no intent, no previous or current self-harm/ suicide attempts, social support available ("low suicide risk")
- Social harms such as domestic/ interpersonal violence where there is no current danger to enrolled participant
- Sexual assault of enrolled participant's family members, including other minors in the household
- Medical or psychological harms such as exposure to trauma or negative life events such as crime, accidental injuries, motor vehicle accidents or family bereavement
- Stigma causing severe psychological distress
- Inadvertent disclosure of participation status or breach of confidentiality, intentionally or unintentionally, by research staff

Adverse events have the potential to become Serious Adverse Events (SAEs) without intervention and thus require some limited active monitoring, and escalation to SAEs if assessment indicates risk of adverse outcomes is high.

12.2 Serious Adverse Events (SAEs)

A serious adverse event is any untoward physical, psychological or social occurrence that:

- Results in death
- Is life-threatening, including but not limited to suicide attempts requiring urgent medical attention
- Thoughts or acts of self-harm or suicide *with any of the following high-risk features*: specific plans/ means identified, intent to complete suicide, previous or current acts of self-harm/suicide attempts, low social support ("high suicide risk")
- Results in inpatient hospitalisation or prolongation of existing hospitalisation of > 5 days due to physical illness or injury
- Results in severe psychological or psychiatric illness requiring hospitalisation of > 5 days
- Results in persistent or significant disability/incapacity
- Results in serious social harm, specifically exposure to interpersonal violence and/or sexual assault or threats of interpersonal violence/ sexual assault where there is immediate danger or risk of ongoing danger to the participant

Other 'important medical events' may also be considered a serious adverse event when, based upon appropriate medical judgement, the event may jeopardise the participant and may require medical or surgical intervention to prevent one of the outcomes listed above.

NOTE: The term 'life-threatening' in the definition of 'serious' refers to an event in which the participant was at risk of death at the time of the event; it does not refer to an event which hypothetically might have caused death if it were more severe.

12.3 Assessment of Causality

The relationship of each adverse event to the trial intervention must be determined by a medically/psychiatrically qualified individual according to the following definitions:

- **Related**: The adverse event follows a reasonable temporal sequence from trial intervention administration and cannot reasonably be attributed to any other cause.
- **Not Related**: The adverse event is probably produced by the participant's pre-existing physical, mental or social state or related contextual factors.

12.4 Assessment of Expectedness

Expectedness will be determined according to the known risks of participation in the study and/or of the underlying condition (namely, depression), and/or arising out of living in the study context.

- **Expected** events include:
  - Possibility of worsening of symptoms of depression and/or anxiety
  - Thoughts or acts of self-harm and/or suicidal ideation and attempts
  - Stigma related to participation in the study and causing psychological distress to participants
  - Interpersonal or sexual violence given a high baseline prevalence in the study context
  - Traumatic events or bereavement given a high baseline prevalence in the study context
- **Unexpected** events include:
  - Death

12.5 Procedures for Reporting AEs

AEs occurring during the safety window for the trial that are observed by the study team or reported by the participant, will be reported on the trial Case Report Form (CRF). The following information will be reported on the CRF: description, date of onset and end date, severity, assessment of relatedness to trial intervention, suspected cause, and action taken. Follow-up information should be provided as necessary.

The severity of events will be assessed on the following scale: 1 = mild, 2 = moderate, 3 = severe. Non-serious AEs considered related to the trial intervention, as judged by a medically qualified investigator or the Sponsor, will be followed up either until resolution, or the event is considered stable.

It will be left to the co-PIs clinical judgment to decide whether or not an AE is of sufficient severity to require the participant's removal from the study. A participant may also voluntarily withdraw from the study due to what he or she perceives as an intolerable AE. If either of these occurs, the participant must undergo an end of trial assessment and be given appropriate care under medical supervision until symptoms cease, or the condition becomes stable.

12.6 Procedures for Reporting SAEs

The Project Manager will complete an SAE report form for all reportable SAEs. Where the SAE requires *immediate* reporting, the SAE report form will be scanned and emailed to both PIs immediately or within 24 hours of the Project Manager becoming aware of the event.

The in-country PI (Prof Kahn) will then report the event to the DSMB Chair and the Wits HREC Chair within a further 24 hours. The central study team will provide additional, missing or follow up information in a timely fashion.

The DSMB will perform an initial check of the report and request any additional information from the central study team. The SAE will also be reviewed at the next quarterly Trial Steering Committee meeting. SAEs that are reported late must be accompanied by an explanation for this.

12.7 Development Safety Update Reports

The Principal Investigator will submit (in addition to the expedited reporting above) a Development Safety Update Report (DSUR) once a year throughout the trial, or on request, to the Medical Research Council, Wits HREC, OxTREC, Mpumalanga Province and Sponsor.

13 STATISTICS

13.1 Description of Statistical Methods

The statistical aspects of the pilot study are summarised here with details fully described in a Statistical Analysis Plan (SAP) that will be available from the time that the first participant is recruited. The SAP will be finalised before any analysis takes place.

Qualitative data will be analysed using a thematic analysis.[62] For each in-depth interview, we will create a list of initial themes based upon the study objectives of investigating the feasibility, acceptability, and potential benefits of the intervention. Initial themes will then be adapted into a coding framework through a process of iteration, and additional themes added as determined by the data. NVivo10, a computer program that aids in the sorting and management of qualitative data, will be used to facilitate the analysis.

Quantitative data will be analysed using *Stata* Version 15.0 (Stata Corporation, College Station, Texas, USA) and/or other appropriate statistical analysis packages under the direction of the trial statistician. The primary outcome analyses will be blinded to study arm until the analysis is finalized and approved by the investigators.

Primary objective 1: Feasibility and acceptability

Recruitment

1) proportion of eligible adolescents consenting to the screening
2) proportion completing the screening phase consenting to DoBAt study
3) proportion completing the baseline assessment

Randomisation

4) number of participants randomised to treatment
5) number of participants randomised to control

Treatment

6) number of BA app modules opened and the proportion opening 4 or more sessions
7) trained Peer Mentor's adherence to the BA protocol

8) proportion of participants completing mood monitoring, symptoms monitoring & homework activities

Follow-up

9) proportion completing the follow-up assessments (5, 11, 24 week follow up)

Primary objective 2: Initial efficacy of intervention

Analysis

1) odds ratio and 95% C.I.s for recovery – with recovery defined as adolescents no longer meeting PHQ-A criteria for participants completing treatment. The confidence intervals can inform as to the effect sizes for future sample size calculation)
2) we will also compare continuous scores on the PHQ-A pre and post treatment
3) Incidence of adverse and serious adverse events.

Statistical analysis will be performed on an intention-to-treat (ITT) basis according to the recommendations in the CONSORT statement and its adaption for eHealth trials.[63,64]

Pre-specified subgroup analysis will be conducted based on socio-economic indicators, sex, and age. Sensitivity analyses will be conducted to estimate the effect of excluding unblinded participants. Severity of depression at baseline will be used as a covariate in the analysis.

Secondary objectives

As part of the secondary analyses, we will pilot locally adapted outcome measures of mental health, cognitive tasks, risky behaviours, socioeconomic measures, and collect descriptive data to inform the development of a further larger RCT. This descriptive data will include possible floor and ceiling effects, test-retest reliability, accuracy, duration, latency, and efficiency, and bivariate correlations across variables of interest.

Exploratory analysis

We will also test possible cognitive mechanisms, principally social cognition, by which the effects of the intervention are mediated. Other alternatives mechanisms such as resilience, rumination, and functioning will also be tested.

13.2 Number of participants

According to the MRC/Wits-Agincourt HDSS data, there are approximately 7,657 adolescents aged 15-19 within the study site. Taking into account the depression rates in the area as documented by previous research, we estimate around 10% to score between 5 and 19 on the PHQ-A (n=765). We estimate that 70% of those eligible will consent to take part in the study. To recruit a sample of 200 adolescents we will need to recruit from different high schools for 4 months.

13.3 Post-intervention Mixed-Methods Process Analysis

Following the pilot trial, a mixed methods Process Analysis will be conducted to help researchers and decision makers to interpret the outcomes of the pilot trial, and to facilitate further adaptations to the intervention and trial procedures for a full-scale RCT. This will be based on the recommendations

of the MRC framework for evaluation of complex interventions.[65,66] The objectives of the Process Analysis will be:

Quantitative Components:
To identify:

1. The extent to which the intervention was delivered as planned (extent of *fidelity*) in terms of dose and adherence to the intervention procedures (definitions described above).
2. For whom the intervention is effective in reducing depression by conducting a *subgroup analysis* of pre-specified subpopulations (gender, age, baseline executive function and social cognition, participants who were put on antidepressant medication during the trial period).
3. The mechanisms through which the intervention works by conducting exploratory analyses of potential mediating factors (changes in social cognition, functioning, rumination).

Qualitative Components:
To explore:

1. *Contextual factors* that may have impacted on the delivery of the intervention.
2. *Adolescents and guardians' perceptions* regarding the feasibility/usability, acceptability and appropriateness of the intervention to treat adolescent depression, as well as suggested adaptations.
3. *Study staff and local healthcare workers' perceptions* regarding the feasibility/usability, acceptability and appropriateness of the intervention to treat adolescent depression, as well as barriers and facilitators to implementation at greater scale.
4. The *extent to which the study procedures* as outlined in the protocol were found to be pragmatic and ensure quality and safety, and suggested adaptations to a full-scale DoBAt RCT.

Qualitative components will be done by conducting in-depth interviews with a purposively selected sample of participants, taken from both intervention and control groups. These participants will be selected based on a prespecified criteria (i.e. male vs. female, and treatment completion vs. dropouts). We will also hold in-depth interviews with parents/guardians, as well as interviews with study staff including peer mentors, fieldworkers, the Risk Management Team and local healthcare workers.

14 DATA MANAGEMENT

The data management aspects of the study are summarised here with details fully described in the Data Management Plan. The data will be managed by the Data Manager who will be appointed for the duration of the trial and will have direct oversight of the process supported by the co-PIs and Project Manager. The process will be detailed in the Trial Master File.

14.1 Source Data

Source documents are where data are first recorded, and from which participants' Case Report Forms (CRF) data are obtained. These include but are not limited to: data collected through electronic and or telephonic questionnaires and uploaded to the server; in-app monitoring and app-use metrics; and correspondence.

CRF entries will be considered source data if the CRF is the site of the original recording (e.g. there is no other written or electronic record of data). All documents will be stored securely, and confidentiality of participants will be maintained at all times. On all trial-specific documents, other than the signed consent, the participant will be referred to by the trial participant number only, and

not by name. Signed consent documents will be stored in a locked cabinet separate from other study documents.

14.2 Access to Data

Direct access to the trial data will be granted to authorised representatives from the Sponsor, host institution and the regulatory authorities to permit trial-related monitoring, audits and inspections.

14.3 Data Recording and Record Keeping

All essential documents enabling the conduct of the trial and the quality of the data produced to be evaluated, will be collated in a Trial Master File.

All survey data, including assessments, will be collected using NubiS, a web-based software to conduct online surveys, and stored in a MySQL database. The participants will be identified by a study specific participant number in any database. Names or initials will NOT be included in any electronic study data file. All data will be documented, and clear SOPs developed to ensure proper Quality Control of the data.

The identity of all trial participants and the link to the trial data will be kept on the password protected MRC/Wits-Agincourt Research Unit server. The unique identifier key to link with an individual will be kept in a separate, secure database that will be accessible to only the study Data Manager and co-PI based in the MRC/Wits-Agincourt Research Unit. Data users will receive data that contains only an anonymised individual identifier and will not have access to the table with personal identifiers. Special statistical identity disclosure protection measures will be used when data is shared with data users. This will include, but is not restricted to data anonymization, recoding and aggregation. Project data will be stored in the MRC/Wits-Agincourt Research Unit's data repository. (http://www.agincourt.co.za/index.php/data/)

14.4 Data Archiving

Data files will be stored on a password protected server at the MRC/Wits-Agincourt Unit for the duration of the project to enable team access. Regular back-up copies will be made on password protected file space. All data collection devices will be encrypted. Data will be input online with secure web authentication, data logging and Secure Sockets Layer (SSL) encryption. SSL provides the needed security similar to that provided by VPNs; however, SSL is preferred since it enables authorised researchers to access the system without the extra configuration complications associated with VPN clients. The MRC/Wits-Agincourt server is resilient and hardened against hacking and other forms of attacks. The server is located in a secured server room with controlled physical access. Additionally, all data traffic is encrypted, and installed network firewalls provide secure network access.

When the project is completed, the full database will be stored only on the MRC/Wits-Agincourt server. Data will be stored for a minimum of 10 years following the completion of the study. Long-term data storage will be in .csv files using a standard (simple) ASCII coding scheme for survey data, and in .rtf files for qualitative data.

15 QUALITY ASSURANCE PROCEDURES

15.1 Risk assessment

The trial will be conducted in accordance with the current approved protocol, Good Clinical Practice (GCP), relevant regulations and standard operating procedures. Risks will be assessed and managed according to the Risk Management Protocol (see *Appendix B*) which will be reviewed as necessary over the course of the trial to reflect significant changes to the protocol or outcomes of monitoring activities.

15.2 Monitoring

Regular monitoring will be performed according to the trial specific Data and Safety Monitoring Plan. (DSMP). Data will be evaluated for compliance with the protocol and accuracy in relation to source documents as defined in the DSMP. Following written standard operating procedures, the monitors will verify that the clinical trial is conducted, and data are generated, documented and reported in compliance with the protocol, GCP and the applicable regulatory requirements.

15.3 Trial committees

The following trial committees have been put in place to oversee the safety and quality assurance of all trial participants and data.

15.3.1 Trial Management Group

The Trial Management Group includes the two co-Principal Investigators and several co-investigators who are clinicians and academics with a wealth of experience in conducting clinical research and trials (see Table 1). This group includes experts in Child and Adolescent Psychiatry, Psychology, Behavioural Activation, Cognitive Neuroscience, Behavioural Economics, Public Mental Health, Public Health and Primary Healthcare within the South African context, as well as the co-directors, manager and head of Public Engagement of the MRC/Wits-Agincourt unit. The Trial Management Group will meet on weekly basis throughout the duration of the trial. The Trial Management Group will be responsible for monitoring all aspects of the conduct and progress of the trial, ensuring that the protocol is adhered to, and for taking appropriate action to safeguard participants and the quality of the trial itself.

15.3.2 Risk Management Team

The Risk Management Team consists of the Project Manager (a medical doctor), two Field Supervisors, two Registered Counsellors, the Trial Psychologist, and the Trial Psychologist Supervisor (senior Clinical Psychologists). The Risk Management Team will meet on a weekly basis throughout the trial period, with additional meetings where necessary. The Risk Management Team will be responsible for conducting the assessment and management of all risks, including AEs and SAEs according to the Risk Management Protocol (see *Appendix B*).

15.3.3 Trial Steering Committee

The Trial Steering Committee (TSC) consists of senior academic clinicians and researchers including Roz Shafran (chair of the TSC, Professor of Translational Psychology, UCL), Jonathan Roiser (Professor of Cognitive Neuroscience, UCL), Soraya Seedat (Professor of Psychiatry, Stellenbosch University), and Jonathan Levin (Professor of Biostatistics, University of Witwatersrand). The TSC had its first meeting in January 2020 and will continue to meet on a quarterly basis until the end of the study period. The role of the TSC is to provide independent oversight of the conduct of the trial, as outlined in the DoBAt Trial Steering Committee Charter.

15.3.4 Data and Safety Monitoring Board

An independent Data and Safety Monitoring Board, comprised of two mental health clinicians with experience conducting clinical trials and an independent statistician, has been put in place to provide oversight of data quality and safety management, and quality assurance aspects of the trial as outlined in the DoBAt Data and Safety Monitoring Plan. All AEs will be reported to the DSMB on a quarterly

basis and all SAEs will be reported to the DSMB within 48 hours of occurrence (as outlined in the Risk Management Protocol, *Appendix B)*. Key roles of the DSMB include:

- To pick up any trends, such as increases in un/expected events, and take appropriate action
- To seek additional advice or information from investigators where required
- To evaluate the risk of the trial continuing and take appropriate action where necessary

16 PROTOCOL DEVIATIONS

A trial related deviation is a departure from the ethically approved trial protocol or other trial document or process (e.g. consent process or intervention administration) or from GCP or any applicable regulatory requirements. Any deviations from the protocol will be documented in a Protocol Deviation Form and filed in the Trial Master File.

An SOP will be developed to describe the procedure for identifying non-compliances, escalation to the central team and assessment of whether a non-compliance /deviation may be a potential serious breach.

17 SERIOUS BREACHES

A serious breach is defined as "*A breach of GCP or the trial protocol which is likely to affect to a significant degree –*

(a) the safety or physical or mental integrity of the subjects of the trial; or

(b) the scientific value of the trial".

In the event that a serious breach is suspected the Sponsor will be contacted within 48 hours. In collaboration with the Principal investigators the serious breach will be reviewed by the Sponsor and, if appropriate, the Sponsor will report it to the Human Research Ethics Committee (HREC) within seven calendar days.

18 ETHICAL AND REGULATORY CONSIDERATIONS

18.1 Declaration of Helsinki

The Investigator will ensure that this trial is conducted in accordance with the principles of the Declaration of Helsinki to safeguard the health and rights of human participants.

18.2 Guidelines for Good Clinical Practice

The Investigator will ensure that this trial is conducted in accordance with relevant regulations and with GCP.

18.3 Approvals

Following Sponsor approval, the protocol, informed consent forms, and participant information sheets will be submitted to the University of the Witwatersrand Human Research Ethics Committee (Wits HREC), Ehlanzeni District and Mpumalanga Provincial Departments of Health and Education, and the Oxford Tropical Research Ethics Committee (OxTREC) for written approval.

The co-PIs will submit and, where necessary, obtain approval from the above parties for all substantial amendments to the original approved documents.

18.4 Reporting

The co-PIs shall submit once a year, or on request, a Progress Report to Wits HREC, OxTREC, Ehlanzeni District and Mpumalanga Provincial Departments of Health and Education, and Funder. In addition, an End of Trial notification and final report will be submitted to Wits HREC, OcTREC, Ehlanzeni District and Mpumalanga Provincial Departments of Health and Education, and the Funder within 12 months of completion of the study.

18.5 Justification for inclusion of vulnerable participants

Participants in this study are vulnerable by nature of i) being adolescents ii) having a mental health condition, namely depression, and iii) living in a low-resource setting. There is a high prevalence of depression amongst adolescents in low-resource settings and little to no treatment available, therefore it is critical that the feasibility, acceptability and effectiveness of potentially scalable psychological therapies is tested in these populations. Extensive formative work has been undertaken to ensure that the intervention is tailored to the needs of the local community.

18.6 Benefits to participants

There will not be any direct benefits for taking part of the screening (Phase 1), and participants will not be paid.

For adolescents that participate in the pilot, we know that Behavioural Activation can improve adolescent's mood and reduce depressive symptoms. However, we are not sure whether the Kuamsha app will improve participants' mood as a result of receiving the treatment in the intervention group. This study will provide preliminary evidence on the initial efficacy of the intervention.

In addition to these potential benefits to participants, the study will produce knowledge about the feasibility, acceptability and initial effectiveness of a digitally delivered and potentially scalable psychological therapy to address depression amongst adolescents and facilitate social and economic outcomes. It will also help us to adapt the intervention to better address the needs of adolescents in this community, and to plan for a full-scale clinical trial.

18.7 Mitigation of potential harms to participants

Coercion during recruitment
We will take very careful steps to prevent any coercion. In particular, we will reiterate to adolescents during the assent process that they do not have to take part, even if their parent/ guardian has consented to participation. They will be informed that they can withdraw at any time without having to tell their parent/ guardian.

Confidentiality issues
Mobile phones are often shared with friends and family members in South Africa. To protect against a breach of confidentiality, a password will be required to access the app content.

Stigma associated with depression
It is possible that some participants in the intervention arm may feel uncomfortable when discussing experiences of low mood and problems faced with the Trained Peer Mentor. We will use several strategies to minimise this. First, we will provide information sheets about mental health during the consent stage to both the participants and caregivers (separately) and give them the opportunity to ask any questions they may have. Second, we will emphasise the importance of confidentiality to all participants all throughout the trial. Researchers will be prepared to support any participants who are distressed by giving participants the opportunity to stop at any time. Third, at the outset of each phone call, Peer Mentors will be trained to ask whether participants are able to talk privately/in an environment they feel comfortable with at the time, and a contingency made if this is not possible such as calling them back at a later time. Once this has been established, a brief introduction will be given to say that it is very common to experience low mood, face problems and/or experience poor mental health.

Technological considerations
To support the DoBAt study, we will provide smartphones to adolescents. We will install a third party "nanny app" to restrict adolescents use of certain social media and other websites. This was deemed necessary in order to limit the cost of data provided to each participant. We will also provide adolescents and parents/guardians (where relevant) with internet safety guidelines appropriate to the local context when distributing the smartphones. Despite the proliferation of mobile phones in South Africa during the past decade, mobile data coverage might be unreliable. To reduce potential problems with internet access during therapy sessions, both apps (treatment and control group) will be offered in both online and offline modes. This way, users will be able to download the sessions in advance to the device internal storage and use it any other time, regardless of internet signal.

Risks of owning desirable commodities
Cell phone ownership has grown exponentially in South Africa over the last decade. Adolescents are the primary adopters, with nearly 72% of cell phone ownership occurring among 15 to 24-year olds from South Africa.[67] Data from Agincourt's 2019 census shows that 93% of households own a cellphone, and 64.7% a smartphone. Despite these trends, we are aware of the risk of theft and will work with caregivers and community leaders to minimise this risk. We recently completed a large cash transfer trial in the study area in which 2,450 adolescents were randomised to receive substantial cash grants with no associated problems. Van Heerden is a leader in the use of smartphones in longitudinal and treatment studies, including with adolescents, in low-resource African settings.

18.8 Participant Confidentiality and Informed Consent

Autonomy of participants will be upheld through ensuring a detailed and thorough informed consent and assent process, and confidentiality of all participant data and information provided to the study team.

Further details on the Informed Consent process are provided in *Section 10.3.*

The study staff will ensure that participants' anonymity and confidentiality of their data is maintained. The processing of the personal data of participants will be minimised by only using the unique participant number as an identifier on all study documents and electronic databases. All documents

will be stored securely and will only be accessible by study staff and authorised personnel. The study staff will safeguard the privacy of participants' personal data (further details are provided in *Section 13* Data Management).

Audio recordings from the weekly calls delivered by the Trained Peer Mentors will be stored in a locked cabinet in a separate office from personal data, and will be backed up on a secure network with very limited access (i.e. only to senior research team members and researchers working directly with a particular participant or directly involved in coding data). Participants will be given the option to not have any audio recordings used outside of the team of researchers and this is clearly outlined in the consent form. Publication of direct quotations from participants will always be anonymised, and specific consent sought for this use.

18.9 Compensation for participation

Participants will be provided with light refreshments, including juices and snacks, during every home visit (baseline assessment, and week 11).

All participants in the intervention and control arms will be given a low-end smartphone with either the Kuamsha (intervention) or Kuchunguza (control) app installed. Participants may keep this phone at the end of the study. Participants will be reimbursed with ZAR25 of phone data, on average, on their mobile phone provider network every week during the trial. The purpose of this is two-fold: (i) to ensure they have data to use the apps during the treatment, and (ii) to ensure that they can call/text for support. In addition, all participants will be asked to monitor their symptoms every two weeks, and they will receive a small amount of phone data (R10) every time they complete the questionnaire.

Furthermore, four assessments tasks will be incentivised (i.e. time preference, risk preference, loss aversion task, and the BART task – see section 10.2 on descriptions of measures). Evidence shows that providing incentives helps minimise potential experimenter demand effect and increases the effort put in by participants (thus increasing the quality of the data). This holds true even when these tasks are implemented with children as young as 10 years old.[68,69] Following common practices in the economics literature, we will randomly select one answer from all three tasks and participants will receive that amount as data on their phones.

The total amount of phone data provided to each participant, if they remain engaged in the study for its full duration, will be, on average, ZAR300. All benefits will be the same across study arms.

19 FINANCE AND INSURANCE

19.1 Funding

This trial is funded by MRC Newton Fund UK-South Africa Joint Initiative on Mental Health (MR/S008748/1), total award amount ZAR 8 991 863 to SA partners; GBP 215 443 to UK partners. Total award administered through Wits Health Consortium

19.2 Insurance

Insurance will be provided by Wits Health Consortium in line with the Clinical Trials Compensation Guidelines of the Association of the British Pharmaceutical Industry.

19.3 Contractual arrangements

Contractual arrangements between all Parties are outlined in the Collaboration Agreement between Wits Health Consortium and the Chancellor Masters and Scholars of The University of Oxford and University of Exeter and University of Cambridge and University of California Los Angeles and University of Cape Town and University of Limpopo.

20 PUBLICATION POLICY

The Investigators will be involved in reviewing drafts of the manuscripts, abstracts, press releases and any other publications arising from the study. Authors will acknowledge that the study was supported by the South African and UK Medical Research Councils with funds received from the South African Medical Research Council, the South African National Department of Health and the UK Government's Newton Fund. Authorship will be determined in accordance with the ICMJE guidelines and other contributors will be acknowledged. Results of the trial will be published as soon as possible after completion and ensuing publications will be made open access.

Using networks established by the MRC/Wits-Agincourt Unit, we will engage with the local community at the village and service-provider level to conduct feedback campaigns and develop simple, translated 'fact sheets' containing population-level data and study findings. These will be available for distribution at community meetings and to village leaders, fieldworkers and service providers.

21 DEVELOPMENT OF A NEW PRODUCT/ GENERATION OF INTELLECTUAL PROPERTY

Ownership of IP generated by the Project will be in accordance with i) the terms of the Award referenced MR/S008748/1 and dated 19 February 2019 (the "Head Terms") and ii) the Collaboration Agreement between Wits Health Consortium and the Chancellor Masters and Scholars of The University of Oxford and University of Exeter and University of Cambridge and University of California Los Angeles and University of Cape Town and University of Limpopo.

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23 APPENDIX A: DoBAt treatment app (Kuamsha app)

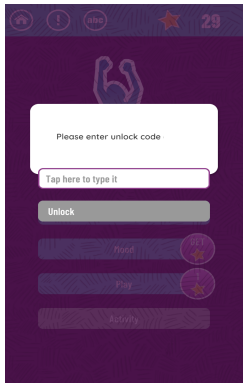
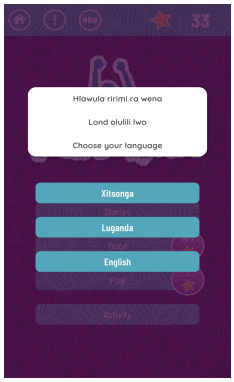
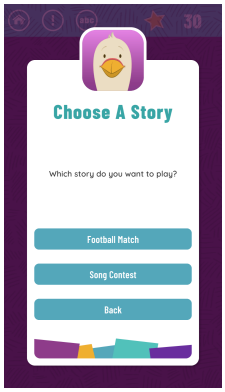
I. Story 1. The Song Contest

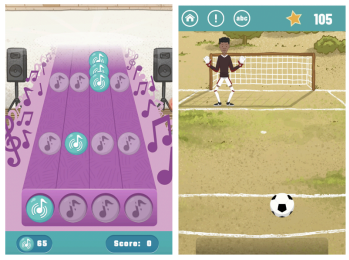
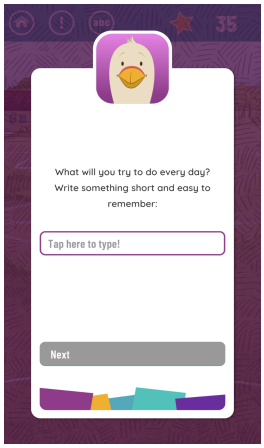
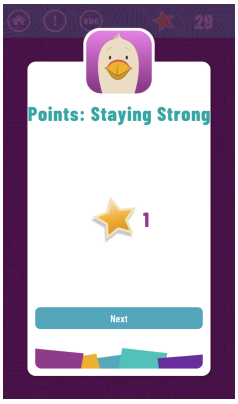
Learning module	Description of each episode	BA Learning principles
Episode 1 ("Pick a team")	Students find out about a school Song Contest. The winning prize is a voucher to shop for a new outfit at the mall. User chooses how the main character looks and picks two teammates to join the Song Contest.	Absorption TRAP-TRAC Sleep Self-confidence Relapse prevention
Episode 2 ("Find a cool tune")	First practice session with group which didn't go well because Boy Teammate (BT) fell asleep. Main character upset about that and decided to ask Miss Crane for advice. After hearing that BT's grandmother ill, main character showed leadership and compassion in how she handled BT.	
Episode 3 ("The Lure")	Desirable character invites main character to go to the tavern and she/he accepts.	
Episode 4 ("The Fallout")	Main character arrives late to practice session without homework done. Teammates get annoyed. Main character decides to apologise instead of avoiding the problem and her teammates are forgiving. Main character goes to sleep early.	
Episode 5 ("The Return")	Main character sleeps and feels recharged. Team is happy with the practice. New instruments unlocked when player answers questions about sleep. Final audio mixing task is completed. Main character learns that she has to give a presentation if they win and asks Miss Crane for advice. She learns that it's normal to be nervous and ways to deal with that.	
Episode 6 ("The Big Day")	Team feels nervous before the show. They perform and win the prize. Group reflects on journey.	

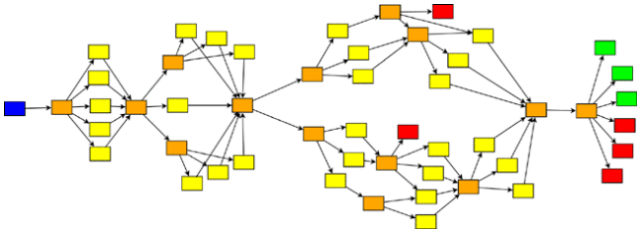
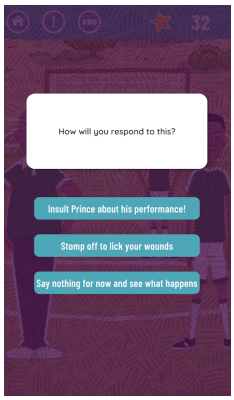
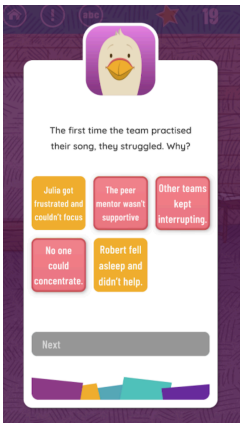
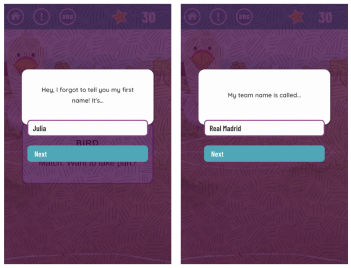
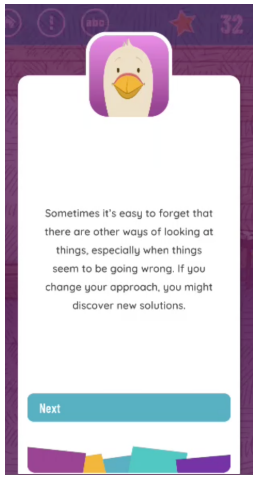
II. Story 2. The Football Match

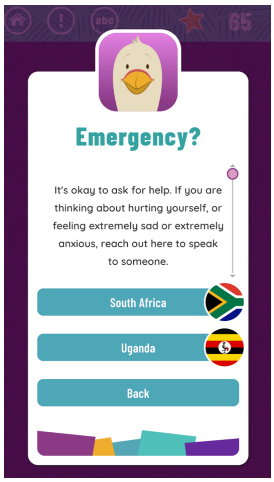
Learning module	Description of each episode	BA Learning principles
Episode 1 ("Pick a team")	Main character is the striker for the local team. User chooses how the main character looks and picks a name for the football team. User gets introduced to the football task.	Absorption Rumination TRAP-TRAC Problem-solving Negotiation
Episode 2 ("Game Over")	Main character misses some important shots. Shane is a discouraging main character because of her poor performance. Team loses the game. Main character leaves the match alone feeling upset and discouraged, ruminating over her performance during the match. Bird offers different, more positive perspective on performance but the main character not in a frame of mind to believe it.	
Episode 3 ("Hide away")	Main character is frustrated, misses school and gets a detention. Main character feels a bit better after friends visit her at her house, but apprehensive about going to school. She does a Keepy-Uppy practice which makes her feel energised enough to do her homework.	
Episode 4 ("That's okay")	She returns to school feeling more positive after a good night's sleep. She handles Shane well, but still lowers her mood. She decides to speak with Coach Bayer after school about her performance in the match. Main character learns that mistakes can be useful opportunities to learn, instead of something to avoid. She practises what she's learned (saying "That's ok. What can I learn here" after every shot) in the Shots on Goal Football Practice. She starts practice feeling more confident**.**	
Episode 5 ("Keep practising")	Main character speaks with friends before practice about what she learned from Coach Bayer and asks for help in dealing with Shane. With their supportive presence, she gets Shane to agree to stay away from her so that they can focus on football and winning. She feels confident, keeps practising, and feels ready for the re-match.	
Episode 6 ("The Big Match")	It all came together for the main character, stepping out on the pitch with new confidence. She keeps calm and greets mistakes with curiosity instead of frustration. She scores the winning goal.	

III. Graphics examples

Component	Description	Example
Home screen	This is the first screen that users will see as they open the Kuamsha app. Users will have the option to play through the stories, monitor their mood, play absorbing activities to improve focus, or report on their weekly activities (see below for further details on each of these components).	
Log-in unlock code	Kuamsha is password-protected. Users will be asked to enter a password every time they access the app.	
Language selector	Users will be able to select their preferred language. All of the text in the app underwent two rounds of translation and has been checked by a clinical psychologist for accuracy.	
Story Selection	The core of the game consists of a choice between two narrative stories. Each consists of 6 episodes that are played in sequential order. It is possible to begin one story and then switch to the other. During gameplay points are earned for the choices made and by completing other core game elements described below.	

Mood monitoring	Mood monitoring is an important part of BA and can be used as a tool for understanding how your mood is impacted and changes depending on the activities you are engaged in. Every time user complete mood monitoring they would get in-app points. Participants will be asked to monitor their mood different times (before episode and after episode, when they report homework, when they complete absorbing activity).	
Absorbing activities	We will have two different activities to teach the concept of absorption (focusing on an activity to detract from negative thoughts). Participants can decide between two different absorbing activities: • Music-absorbing activity: rhythm game where users will tap the screen in time with the music. • Football-absorbing activity: users will practice at taking shots on goal.	
Homework activity	We will ask users to think about an activity that they could do that is associated with the principle of the episode they just completed. Each homework session consists of one or two activities that expand on the BA principle covered within that session.	
In-app points	Participants will earn in-app points every time they complete an episode, report their weekly activity, monitor their mood, and play the absorbing activities. In-app points have been shown to be critical to increase app's engagement and user retention.	

Choices affect outcomes	A key principle of the game is that the player is drawn into the narrative through the use of interactive choice. Choices made by the player branch the story in ways that lead the character down different pathways in the game. To keep complexity manageable, story branches are relatively quickly merged back with the main storyline through the use of bottlenecks. 	
Lessons learned	In order to ensure that players are reflecting on the game and show some level of understanding of the concepts and choices made, each story episode ends with a summary of lessons learned. These take the form of multiple choice responses which are saved as part of the game data for later analysis and potential review by peer mentors.	
Character personalization	Users will be asked to personalise their character in the story by choosing their name, preferred pronouns, and their team's name. Character personalisation is central to how players experience the game, and it has been shown to improve engagement and user retention.	
Bird Guide	The bird character is used throughout the game as a way of having players reflect on their choices, supporting review of what as been learnt, offering suggestions and other game mechanics designed to draw the multiple components of the game into a unified whole.	

Emergency number	Kuamsha includes an "emergency button" for adolescents to call in event that they are feeling extremely sad or thinking about hurting themselves. After pressing the button, adolescents will be transferred to a toll-free National Suicide Hotline to receive support. The Kuamsha team will be notified. Depending on the severity of the situation, adolescents will be referred to either a Registered Counsellor and/or a Clinical Psychologist, both employed exclusively for this trial. A comprehensive Risk Management Protocol has been developed to ensure the safety of participants in the trial.	

24 APPENDIX B: RISK MANAGEMENT PROTOCOL

The Risk Management Protocol (RMP) outlines the **definitions** and **procedures** that will be used to *identify, respond to, mitigate and document* all risks and adverse events in the DoBAT Pilot Trial, as well as the **relevant personnel** that are responsible for *implementing and overseeing* Risk Management. The RMP reflects the experience of the trial team in the management of similar risks in previous psychological trials, and trials involving adolescents, in low-resource communities, as well as knowledge of the local study context and availability of medical, psychological and social services.

A comprehensive overview of the Safety Reporting procedures for the DoBAt Study is outlined in *Section 12* of the protocol. A brief *overview of the definitions of key terms* is given below.

24.1. Definitions

Adverse Events (AEs)

An Adverse Event is any untoward physical, psychological or social occurrence in a participant who has enrolled in the study, including occurrences which are not necessarily caused by or related to the use of the intervention/ control. These may include:

- Thoughts of self-harm or suicide with no specific plans/ means identified, no intent, no previous or current self-harm/ suicide attempts, social support available ("low suicide risk")
- Social harms such as domestic/ interpersonal violence where there is no current danger to enrolled participant
- Sexual assault of enrolled participant's family members, including other minors in the household
- Medical or psychological harms such as exposure to trauma or negative life events such as crime, accidental injuries, motor vehicle accidents or family bereavement
- Stigma causing severe psychological distress
- Inadvertent disclosure of participation status or breach of confidentiality, intentionally or unintentionally, by research staff

Adverse events have the potential to become Serious Adverse Events (SAEs) without intervention and thus require some limited active monitoring, and *escalation to SAEs if assessment indicates risk of adverse outcomes is high.*

Serious Adverse Event (SAE)

A serious adverse event is any untoward physical, psychological or social occurrence that:

- Results in death
- Is life-threatening, including but not limited to suicide attempts requiring urgent medical attention
- Thoughts of self-harm or suicide *with any of the following high-risk features*: specific plans/ means identified, intent to complete suicide, previous or current self-harm/suicide attempts, low social support ("high suicide risk")
- Results in inpatient hospitalisation or prolongation of existing hospitalisation of > 5 days due to physical illness or injury
- Results in severe psychological or psychiatric illness requiring hospitalisation of > 5 days
- Results in persistent or significant disability/incapacity

- Results in serious social harm, specifically exposure to interpersonal violence and/or sexual assault or threats of interpersonal violence/ sexual assault where there is immediate danger or risk of ongoing danger to the participant

Other 'important medical events' may also be considered a serious adverse event when, based upon appropriate medical/ psychological judgement, the event may jeopardise the participant and may require medical/ psychological intervention to prevent one of the outcomes listed above.

Assessment of Causality

The relationship of each adverse event to the trial intervention must be determined by a medically/psychiatrically qualified individual according to the following definitions:

- **Related**: The adverse event follows a reasonable temporal sequence from trial intervention administration and cannot reasonably be attributed to any other cause.
- **Not Related**: The adverse event is probably produced by the participant's pre-existing physical, mental or social state or related contextual factors.

Assessment of Expectedness

Expectedness will be determined according to the known risks of participation in the study and/or of the underlying condition (namely, depression), and/or arising out of living in the study context.

- **Expected** events include:
  - Possibility of worsening of symptoms of depression and/or anxiety
  - Thoughts or acts of self-harm and/or suicidal ideation and attempts
  - Stigma related to participation in the study and causing psychological distress to participants
  - Interpersonal or sexual violence given a high baseline prevalence in the study context
  - Traumatic events or bereavement given a high baseline prevalence in the study context
- **Unexpected** events include:
  - Death

24.2. Procedures for Risk Identification, Response, Mitigation and Documentation

An *overview* of the procedures for identifying, responding to, mitigating and documenting risks is given here with details on the management of *specific anticipated risks given in Section 24.3 below.*

Risk Identification

Risks may be identified during contact (telephonically or in-person) between the participants and the study team, including at: consent, *screening, assessments* (0, 4, 11, 24 weeks), and during the *post-intervention qualitative interviews*. Participants in the intervention group will also *receive weekly calls from the Trained Peer Mentor* to support the participant to complete the module. Given the nature of the study involving vulnerable participants, participants in both the intervention and control groups will receive *additional active symptom monitoring every two weeks* using the PHQ-A and GAD-7 to assess for worsening of mood symptoms and/or active thoughts of self-harm/ suicidal ideation. In addition, a contact number for a 24-hour *toll-free national Risk Management Helpline* will be available for participants in both groups to call in the event of severe psychological distress and/or thoughts of self-harm or suicidal ideation.

Risk Response

Risk responses will be standardised according to the Risk Management Protocol (this document). Risk responses reflect current standard of care protocols which are supported by agreements between the MRC/Wits-Agincourt Unit and local service providers, with additional support from dedicated Risk Management Team personnel where appropriate or necessary.

Where regular trial follow-up would not be sufficient to manage the risk that has been identified, additional active checking-in (***Active Monitoring***) will be done, by telephone and/or text message. *Referrals may be warranted for risk factors that could escalate into adverse events without referral*, or where expected referrals have not been completed.

Active Management will be used in situations in which the *risk is sufficiently high that follow up only by telephone would not be enough*, and the situation requires, for example, that we make in-person home visits to establish safety, directly engage with the participant, and make referrals and/or transport a person to, services for further assessment and management. These are the type of adverse events that may develop into SAEs without active management.

Risk Mitigation

Several measures have been put in place to mitigate the risks associated with participation in the trial. These include:

- Early engagement of local stakeholders including adolescents, parents, educators, local health and social care providers to determine existing state of mental health and social care services, including usual pathways to care.
- Existing and ongoing relationships between the DOH and MRC/Wits-Agincourt Unit, underpinned by an MOR between the Mpumalanga Provincial Department of Health and the University of the Witwatersrand's Faculty of Health Sciences with well-established referral pathways into medical, psychological and social services provided at the local primary healthcare clinics and district hospitals.
- An existing and ongoing relationship between the MRC/Wits-Agincourt Unit and local NGOs providing social and psychological services.
- Additional active symptom monitoring amongst participants in both intervention and control arms to allow for early detection of worsening of mood symptoms and/or active thoughts of self-harm/ suicidal ideation.
- A contact number for a 24-hour *toll-free national* Risk Management Helpline for participants to call in the event of severe psychological distress and/or thoughts of self-harm or suicidal ideation.
- Employment of dedicated Risk Management Team (RMT) personnel with training and experience in managing a range of medical, psychological and social risks; including adolescents with depression, self-harm, suicidal ideation and attempts. RMT personnel include:
    - A full time **Project Manager** who is a medical doctor with post-graduate training and experience in mental health
    - A Xitsonga speaking **Registered Counsellor** with experience in assessing and managing adolescents with depression and suicidal risk

  - A dedicated **Trial Psychologist** to provide additional psychological support as appropriate (e.g. cases of severe depression with PHQ-A score >19)
  - Two '**Field Supervisors'** (senior fieldworkers with excellent knowledge of the study site and previous experience working with adolescents) to provide a link between the RMT with the participants in the study site when necessary.
- A strong complement of senior academic clinicians to provide support and oversight including a Child and Adolescent Psychiatrist (A.Stein) and Primary Healthcare Specialist (K.Kahn), and senior Clinical Psychologists (T.Sodi, H.O'Mahen, C.Lund)
- An independent Data and Safety Monitoring Board chaired by a psychiatrist to provide oversight of all data and safety monitoring aspects of the trial
- A Trial Steeing Committee to oversee all aspects of the conduct of the study.
- Anticipation of risks associated with participation in the trial and clear SOPs for responding to these risks as outlined in the RMP (this document) as well as clear delineation of the roles and responsibilities of the Risk Management Team.
- Training of the Risk Management Team will be conducted by the Project Manager and Trial Psychologist with oversight from the Trial Psychologist Supervisors and co-PIs and will include all aspects of risk management and safety reporting.
- Training of the Fieldwork/Assessment Team, including the team conducting Informed Consent and Assent will be conducted by the Project Manager with oversight from the co-PIs and will include all aspects of risk, data and safety management.
- All trial personnel will be trained in Research Ethics and Good Clinical Practice.

Risk and Adverse Event Documentation

A comprehensive overview of the Safety Reporting procedures for the DoBAt Study is outlined in *Section 12* of the protocol. In brief, all AEs will be documented on the Case Report Form and a summary of all AEs will be submitted to the DSMB and TSC on a quarterly basis, and to the HREC on an annual basis. All SAEs will be documented on an SAE reporting form and the Project Manager will inform the co-PIs within 24hours, and the DSMB within 48 hours of the study team becoming aware of the SAE.

24.3. Management of Specific Anticipated Risks

The identification, response, mitigation, and documentation of *other specific anticipated risks* is given in *Tables 1 and 2* below. **Further details on the response to *risk of self/harm and suicide* are given in *Section 24.4***

Table 1 outlines the ***active monitoring*** and management of risks associated with ***Adverse Event***.
Table 2 outlines the ***active management*** of risks associated with **Serious Adverse Events.**

Table 1 The ***active monitoring*** and management of risks associated with ***Adverse Events***.

Adverse Event	**Expected/Unexpected** **Related/Unrelated**	**Risk Identification**	**Risk**	**Risk Response**	**Mitigation**	**Documentation**
Thoughts of self-harm or suicide with no high-risk features	**Expected** since participants have mild to moderately severe depression. In previous trials we have found that the majority of participants are not actively suicidal. In most cases risk of suicide is low. **Unrelated** as no evidence that treatment or supportive phone calls will increase thoughts of self-harm.	1. PHQ-A by recruitment team at school 2. PHQ-A by Assessment Team at home 3. Peer mentor sessions by phone 4. Mood and symptom monitoring	Low	<u>Registered Counsellor to contact participant telephonically to conduct a **risk assessment**:</u> • Determine if *current* • Determine if *low or high suicide risk* *see *section 24.3.2* <u>If *current* thoughts of self-harm/ suicide and *low suicide risk* - **active monitoring** steps:</u> • Assess for **familial or social support** • **Contract for safety** in immediate 48-hour period • Provide **emergency contact numbers** to participant • Ask to **speak to family member or friend** to confirm contract for safety, and ensure that access to means of self-harm or suicide are removed from the environment • **Notify the Trial Psychologist** • **Contact telephonically within 48 hours to reassess** • Escalate to "high suicide risk" active management **if thoughts persist after 24 hours** If *current* thoughts of self-harm *with high suicide risk escalate to active management status and manage* (see Table 2)	Full time PM with experience managing similar cases. Registered Counsellors and Trial Psychologist available to provide support as appropriate. Co-PIs and Trial Psychologist Supervisor available to support PM and Trial Psychologist in making risk judgements. MOU between DOH/ MRC/Wits Agincourt Research Unit with well-established referral protocol into DOH psychological and social services.	PM documents all AEs on Case Report Form (CRF). PM submits report of AEs to DSMB and TSC on quarterly basis. PM submits record of adverse events to ethics on annual recertification review.

Interpersonal violence	**Expected** given baseline prevalence in the study site. **Unrelated** to intervention or support calls . **If related** (a consequence of being enrolled in the intervention or support calls) managed as an SAE – see Table 2.	1. Peer mentor sessions by phone 2. Trauma questions included in baseline questionnaire (week 0)	Low	Immediate assessment of extent of risk: • Determine if currently occurring • Determine type of violence (emotional, physical, sexual) • Determine extent of threat of harm to participant *If not current:* • Assess for familial or social support • Contract for safety in immediate 48-hour period • Offer a referral and linkage to care to DOH social worker for assessment and support • Offer emergency contact numbers to call in event of danger • If symptoms of severe depression and/or thoughts of self-harm/ active suicidal ideation then for review by the Registered Counsellor If risk is *current and imminent* and there is a *threat of harm without intervention* - escalate risk to SAE status and manage (see Table 2)	Full time PM with experience managing the medical and psychosocial implications of interpersonal violence. Registered Counsellors and Trial Psychologist available to provide support as appropriate. Co-PIs and Trial Psychologist Supervisor available to support PM and Trial Psychologist in making risk judgements. Existing and ongoing relationship between DOH/ MRC/Wits Agincourt Research Unit with well-established referral protocol into DOH social services.	PM documents all AEs on CRF. PM submits report of AEs to DSMB and TSC on quarterly basis. PM submits record of adverse events to ethics on annual recertification review.
Sexual assault	**Expected** given population-based prevalence. Low incidence in prior work, most cases reported were for non- enrolled family members. Some additional referrals were required to elicit	1. Peer mentor sessions by phone 2. Trauma questions included in baseline questionnaire (week 0)	Low	Immediate assessment of extent of risk: • Determine if currently occurring • Determine type of violence (emotional, physical, sexual) • Determine extent of threat of harm to participant *If not current:* • Assess for familial or social support; • Contract for safety in immediate 48-hour period • Offer a referral and linkage to care to DOH social worker for assessment and support	Full time PM with experience of managing similar cases. Registered Counsellors and Trial Psychologist available to provide support as appropriate. Co-PIs and Trial Psychologist Supervisor available to support PM and Trial Psychologist in making risk judgements. Existing and ongoing relationship between DOH/	PM documents all AEs on CRF. PM submits report of AEs to DSMB and TSC on quarterly basis. PM submits record of adverse events to ethics on annual

	supportive counselling through Crisis Centre. **Unrelated**			• Offer emergency contact numbers to call in event of danger If risk is *current and imminent and there is a threat of harm without intervention* - escalate risk to SAE status and manage (see Table 2)	MRC/Wits Agincourt Research Unit with well-established referral protocol into DOH psychological and social services. Existing and ongoing relationship with local NGOs addressing sexual violence (GRIP, Sonke Gender Justice, Victim Empowerment Units).	recertification review.
Traumatic events or bereavement (family members)	**Expected** given mortality rates due to homicide, motor vehicle accidents and accidental injury, and disease related mortality in the study community.	1. Peer mentor sessions by phone 2. Trauma questions included in baseline questionnaire (week 0)	Low	Immediate assessment of extent of risk: • Determine if currently occurring • Determine type of trauma/ bereavement • Determine extent of threat/harm to participant If not current: • Assess for familial or social support • Contract for safety in immediate 48-hour period • Offer a referral to DOH social worker for assessment and support • Offer emergency contact numbers to call in event of danger If risk is *current and imminent and there is a threat of harm without intervention* - escalate risk to SAE status and manage (see Table 2).	Full time PM with experience of managing similar cases. Registered Counsellors and Trial Psychologist available to provide support as appropriate. Co-PIs and Trial Psychologist Supervisor available to support PM and Trial Psychologist in making risk judgements. Existing and ongoing relationships between DOH/ MRC/Wits Agincourt Research Unit with well-established referral protocol into DOH psychological and social services	PM documents all AEs on CRF. PM submits report of AEs to DSMB and TSC on quarterly basis. PM submits record of adverse events to ethics on annual recertification review.

Table 2 outlines the ***active management*** of risks associated with **Serious Adverse Events.**

Serious Adverse Event	Expected/Unexpected Related/Unrelated	Risk Identification	Risk	Risk response	Mitigation	Documentation
Participant's death	**Unexpected** given participants have mild to moderately-severe depression. **Unrelated** to intervention or support calls. If related then SUSAR.	1. Peer mentors telephone calls 2. Baseline or follow-up assessments	Low	In instances of participant death risk management steps include: • Be sensitive and supportive to the participant's family • Document information available regarding cause of death	Full time PM with extensive experience in the sensitive management of participant deaths. Full time Trial Psychologist and Registered Counsellors available to provide sensitive and timely support to family as appropriate. Members of field team and unit Public Engagement Office to attend funeral if social distancing regulations allow, otherwise to phone family with condolences.	Always reported as an SAE. PM documents detailed information on the SAE form and CRF. PM reports SAE to PI within 24hours, to DSMB within 48 hours, and to HREC within 7 days.
Participant hospitalisation >5 days ***Medical illness, injury or severe psychological or psychiatric illness*** *requiring hospitalisation*	**Unexpected** given participants have mild to moderately-severe depression. May be **unrelated** to participation in the study **or related** to participation if worsening psychological distress deemed to be caused by participation in the	1. Baseline or follow-up assessments 2. Peer mentor sessions by phone 3. Mood and/or symptom monitoring	Low	In instances where participant hospitalisation is discovered **retrospectively**: • Document information available regarding cause of hospitalisation • Offer referrals for further medical support as appropriate In instances where participation need for hospitalisation is discovered **prospectively**: • Provide support to/for referral to medical services • Assist in securing ambulance or other appropriate transport	Full time PM with experience managing medical and psychiatric emergencies. Study Team includes an experienced Child and Adolescent Psychiatrist, Trial Psychologist and Trial Psychologist Supervisor to advise and support the PM. The Agincourt Unit has a well-established clinical platform	PM documents detailed information in the CRF for records. PM reports SAEs (if hospitalisation is >5 days) to PI within 24hours, DSMB Chair within 48 hours and HREC within 7 days.

	trial. (If related then SUSAR)				to facilitate timely and appropriate referrals.	
Thoughts or acts of self-harm or suicidal ideation/ attempts with high risk features	**Expected** since participants are depressed. **Unrelated** as no evidence that treatment or supportive phone calls will increase suicidal ideation.	1. PHQ-A by recruitment team at school 2. PHQ-A by assessment interviewer at home 3. Peer mentor sessions by phone 4. Mood and/or symptom monitoring	**High**	<u>Registered Counsellor to contact participant telephonically and conduct a **risk assessment**:</u> • Determine if *current* • Determine if *low or high suicide risk* *see *section 24.3.2* <u>If *current* thoughts of self-harm/suicide and *high suicide risk* - **active management** steps:</u> • Assess for **familial or social support** and offer to set up an **assessment with the Trial Psychologist** • If **deferred assessment is agreed** contract for safety for immediate 48-hour period and request to talk with family member or friend to confirm. Family to ensure removal of access to means of suicide. Provide emergency contact numbers. • If there is **concern of low support or safety risk**, ask the participant for permission for the Trial Psychologist to visit her/ him in person to check on her/him. Stay on the phone while you contact the Trial Psychologist and *make arrangements for an immediate home visit.* • If **additional assessment by Trial Psychologist confirms low support OR no safely contract possible**, refer for in-patient care via the DOH referral system. • Make **arrangements for transport** as appropriate	2 full time Registered Counsellors with experience in conducting suicide risk assessments and referrals. Trial Psychologist and Project Manager with experience managing adolescents with self-harm and suicidal ideation/ attempts. Study Team includes an experienced Child and Adolescent Psychiatrist and Trial Psychologist Supervisor to advise and support the PM and Trial Psychologist. Additional support available from DSMB, whose chair is a Psychiatrist. Existing and ongoing relationships between DOH/ MRC/Wits Agincourt Research Unit with well-established referral protocol into DOH in-patient psychological and social services.	PM documents risks of self/harm or suicide ideation as SAE if any “high suicide risk” features are present, or AE if no high risk features present. AEs reported to DSMB on quarterly basis and to HREC on annual recertification review. Record of SAEs reported to PI within 24hours, DSMB Chair within 48 hours and HREC within 7 days. PM and Trial Psychologist maintain a CRF for recording of detailed risk management steps and ongoing .management until AE/ SAE is closed.

Social harms *Interpersonal violence* *Sexual assault*	**Expected** given baseline prevalence in study site. **May be:** **Unrelated** to intervention or support calls. **Related** as consequence of receiving treatment or support	1. Peer Mentor telephone calls 2. Participant discloses to a fieldworker or member of the project team during screening/ consenting/ assessments 3. Trauma questions included in baseline questionnaire (week 0)	Low	Assessment (Table 1) establishes risk is: • Current or recent incident • Current potential threat of harm Immediate risk management steps: • Assess for familial or social support • Contract for safety in immediate 48-hour period • Offer a referral to SAPS, social worker and medical practitioner for assessment and further management • If referral to declined request the participant meets with trial psychologist to receive psychoeducation on social, medical and legal services available • Offer emergency contact numbers to call in event of danger • If there is concern that a minor may be in danger, and the mother is refusing assistance from either the social worker or trial psychologist, trial supervisor contacts mother to explain this is notifiable and that a report will be made to social worker, to try to ensure mother cooperates and accepts assistance to ensure child's safety • If related to trial participation, trial supervisor takes steps to engage with family and other support to mediate resolution, with support from social worker or trial psychologist as appropriate.	Full time PM with experience in the management of similar cases. Trial psychologist employed by the trial for advice, referrals and home assessment. Peer Mentors, Registered Counsellors, and Trial Psychologist are trained to ensure competence in managing threat of harm from domestic or interpersonal violence Existing and ongoing relationships between DOH/ MRC/Wits Agincourt Research Unit with well-established referral protocol into DOH in-patient psychological and social services.	PM documents as AE if the outcome does not require hospitalisation; or as SAE if hospitalisation is required. AEs reported to DSMB on quarterly basis and to HREC on annual recertification review. SAEs reported to PI within 24hours, DSMB Chair within 48 hours and HREC within 7 days. PM and Trial Psychologist maintain a CRF for recording of detailed risk management steps and ongoing management until AE/ SAE is closed.
Stigma and emotional harm	**Expected** since mental health problems are frequently stigmatised	1. Peer mentors telephone calls	Low	Immediate assessment of referral needs: • Determine if trial staff involved in inappropriate behaviour and take	Full time PM with experience managing sensitive physical and mental health concerns.	PM document detailed information in the CRF (including meetings and

Result of participation *Inadvertent disclosure* *Breach of confidentiality*	**Related** if participation is the source of stigma, inadvertent disclosure or if trial staff member is involved in breach of confidentiality (intentional or unintentional)	2. Mood and symptoms monitoring via phone 3. Reports from health care providers 4. Reports received from MRC/Wits-Agincourt Unit's Community Advisory Board (CAB), Adolescent Advisory Group (AAG) or Public Engagement Office (PEO)		appropriate disciplinary and/or training steps • Determine if referral needs to be made to Trial Psychologist or DOH psychologist to manage consequences of stigma or social harm and to provide support to participant or to participants family • Trial Psychologist may offer to facilitate discussion aimed at conflict resolution with family and social supports if participants is willing. • Determine any ongoing threat of harm to participant and take steps to address. • Request input from CAB and PEO to ensure adequate resolution.	Trial psychologist employed by the trial for advice, referrals and home assessment. Confidentiality contracts signed by all Agincourt staff and all staff GCP and ethics trained. PM conducts supervision and booster training of Risk Management and Assessments Teams to ensure competence and reduction of risks.	recommendation from CAG and AAG) for records. PM documents and ensures disciplinary action is taken where appropriate. SAEs reported to PI within 24hours, DSMB Chair within 48 hours and HREC within 7 days.

24.4. Responding to Risks of Self-Harm and/or Suicide

Identification

Risk of self-harm/suicide may be identified in *screened participants* on completion of the PHQ-A during screening. Risk of self-harm/suicide may be identified in *enrolled participants* in both the intervention and control arms using the PHQ-A during *assessments* at 5, 11 and 24 weeks; as well as through symptom monitoring every 2 weeks.

The PHQ-A is able to discriminate between mild to moderately-severe depression (a score between 5-19) and severe depression (a score more than 19). In addition, the 9th question of the PHQ-A asks directly about "having had any thoughts that you would be better off dead and/or of hurting yourself". Any enrolled participants with symptoms of severe depression (PHQ-A score more than 19) and/or answering affirmatively to thoughts of self-harm and/or suicidal ideation ("Yes" to Question 9 of PHQ-A) will be contacted by a Registered Counsellor to conduct a Risk Assessment (as outlined below).

In addition to detecting risk of self-harm/suicide during assessments and monitoring, participants in the intervention arm will receive weekly calls from a Trained Peer Mentor during which participants may disclose risk of self-harm and/or suicidal ideation. In such instances the Peer Mentor will immediately report this to the Project Manager who will ensure that a Registered Counsellor calls the participant to conduct a Risk Assessment within 24 hours of the risk being identified and sooner if there is any indication of high suicide risk.

Participants in both study arms will also be provided with a contact number for a toll-free national Risk Management Helpline that will be operational 24 hours a day/ 7 days a week to use in the event of severe psychological distress and/or thoughts of self-harm or suicidal ideation.

Risk Stratification

All risks of self-harm and/or suicide will be stratified into "low suicide risk" and "high suicide risk". Participants will be deemed to be at "high suicide risk" if any *one* of the following high-risk features is present:

- The presence of **specific plans** for self-harm or suicide
- The participant identifies **specific means** to be used in self-harm/ suicide
- Participant self-reported **intent** to complete suicide, or an attempt using a lethal means
- **Current or previous acts of self-harm or suicide attempts**
- **Low social support** (the lack of a responsible and caring family member or guardian)

Risk Response

Risk of self-harm/ suicide will be managed according to the flow chart in *Figure 1* for screened participants and *Figure 2* for enrolled participants.

i) Screened Participants (see *Figure 1*)

All screened participants who are identified as having severe depression (score > 19 on the PHQ-A) and/or answer affirmatively to thoughts of self-harm and/or suicidal ideation (Yes to Question 9 of the PHQ-A) will be contacted by the Registered Counsellor who will conduct a further risk assessment to determine:

- If the participant is having thoughts of self-harm/ suicide and if any attempts have been made
- If thoughts of self-harm/ suicidal ideation are *current (i.e. "active")*
- If the participant is "low suicide risk" or "high suicide risk" (see above)

If a screened participant is assessed to be at "low suicide risk":

- Participant is given a referral letter to see a Clinical Psychologist and/or Medical Officer at Tintswalo or Mapulaneng Hospitals and a list of emergency contact details.
- If PHQ-A score between 5-19 and "low suicide risk" participant may still be eligible for enrolment into the trial.

If a screened participant is assessed to be at "high suicide risk":

- Registered Counsellor recommends participant to see a Clinical Psychologist and/or Medical Officer at Tintswalo or Mapulaneng Hospital within 48 hours and offers referral and transport arrangements.
- If participant IS willing to see Clinical Psychologist or Medical Officer within 48 hours transport and referral arrangements are made by PM to take the participant to receive care within 48 hours
- If the participant is NOT willing to see Clinical Psychologist or Medical Officer within 48hours then PM asks for permission for a member of the RMT to conduct a home visit and to establish a Contract for Safety.
- If all steps above do not seem sufficient to ensure the participant's safety – PM would support an involuntary admission to hospital.

ii) Enrolled participants (see *Figure 2*)

All enrolled participants who are identified as having severe depression (score > 19 on the PHQ-A) and/or answer affirmatively to thoughts of self-harm and/or suicidal ideation (Yes to Question 9 of the PHQ-A) will be contacted by the Registered Counsellor who will conduct a further risk assessment to determine:

- If the participant is having thoughts of self-harm/ suicide and if any attempts have been made
- If thoughts of self-harm/ suicidal ideation are *current (i.e. "active")*
- If the participant is "low suicide risk" or "high suicide risk" (see above)

If an enrolled participant is deemed to be at "low suicide risk", the following *active monitoring* steps will be taken:

- Assess for familial or social support
- Contract for safety in immediate 48-hour period
- Provide emergency contact numbers to participant
- Ask to speak to family member or friend to confirm contract for safety, and ensure that access to means of self-harm or suicide are removed from the environment
- Notify the Trial Psychologist

- Contact telephonically within 48 hours to reassess
- Escalate to "high suicide risk" active management if thoughts persist after 24 hours

If an enrolled participant is deemed to be at "high suicide risk" the following *active management* steps will be taken:

- Assess for familial or social support and offer to set up an assessment with the Trial Psychologist
- If deferred assessment is agreed contract for safety for immediate 48-hour period and request to talk with family member or friend to confirm. Family to ensure removal of access to means of suicide. Provide emergency contact numbers.
- If there is concern of low support or safety risk, ask the participant for permission for the Trial Psychologist to visit her/ him in person to check on her/him. Stay on the phone while you contact the Trial Psychologist and *make arrangements for an immediate home visit.*
- If additional assessment by Trial Psychologist confirms low support OR no safety contract possible, refer for in-patient care via the DOH referral system.
- Make arrangements for transport as appropriate

Mitigation

Steps taken to mitigate the risk of self-harm and/or suicidal ideation/ attempts include those outlined in Section 24.2.3 of this RMP. Of note, *specific measures have been put in place to facilitate **early detection and intervention*** in risk of self-harm and/or suicidal ideation/ attempts. These include i) active symptom monitoring of participants in the intervention and control arms of the study every 2 weeks, and ii) a dedicated Risk Management Helpline which participants are encouraged to call in the event of severe psychological distress and/or thought of self-harm/ suicidal ideation

Documentation

Active thoughts of self-harm and/ or suicide that are deemed to be "low suicide risk" will be documented as Adverse Events. Details will be kept in the Case Report Form and the Project Manager will submit an AE report to the DSMB on a quarterly basis and to the HREC on an annual basis. Active thoughts of self-harm and/ or suicide that are deemed to be "high suicide risk", as well as any acts of self-harm or suicide attempts, will be documented as Serious Adverse Events. Details will be recorded on the Case Report Form and on an SAE report form. The co-PIs will be notified within 24 hours and the chair of the DSMB will be notified within 48 hours.

FIGURE 1. FLOW CHART FOR SUICIDE RISK MANAGEMENT DURING SCREENING

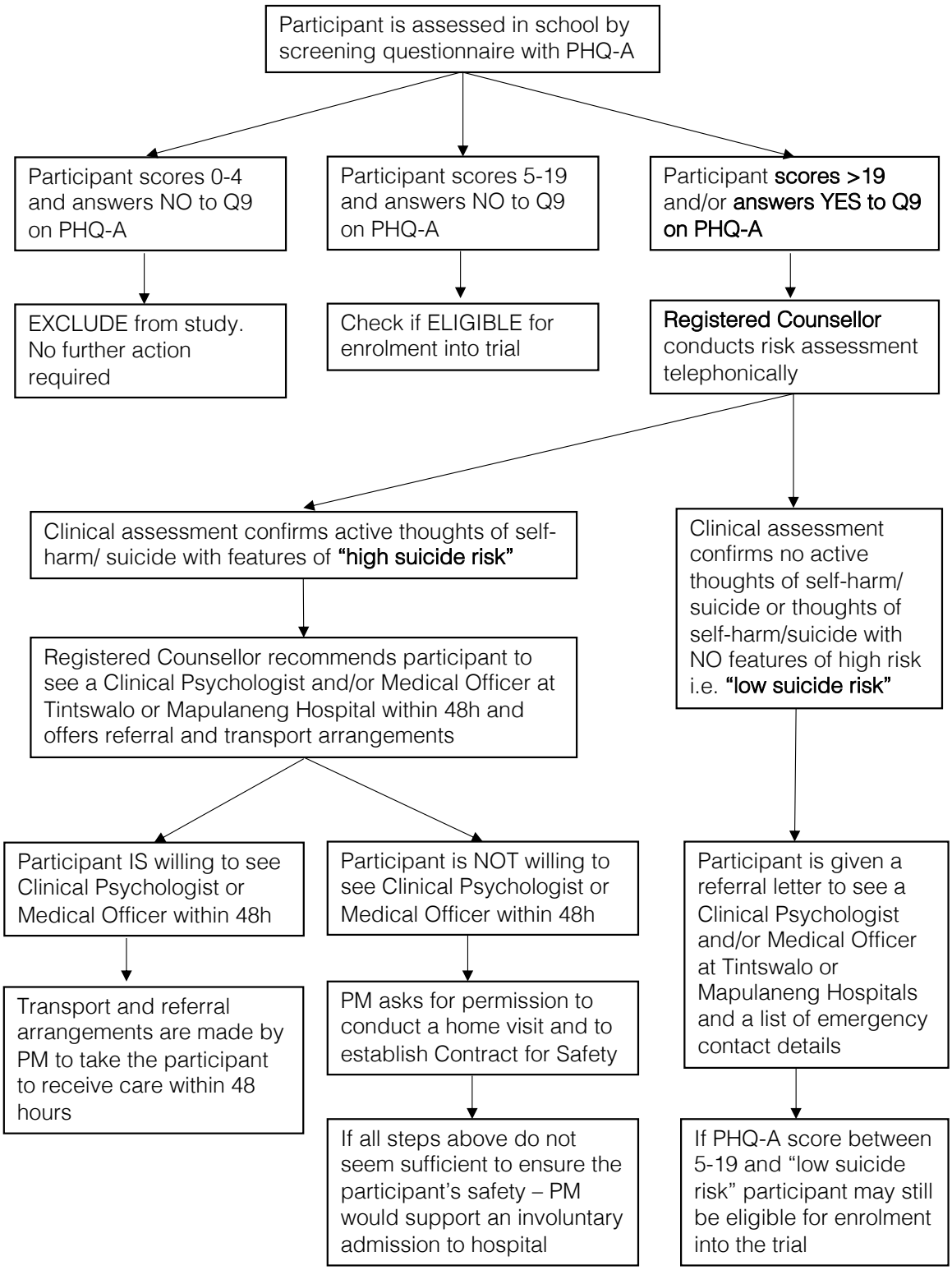
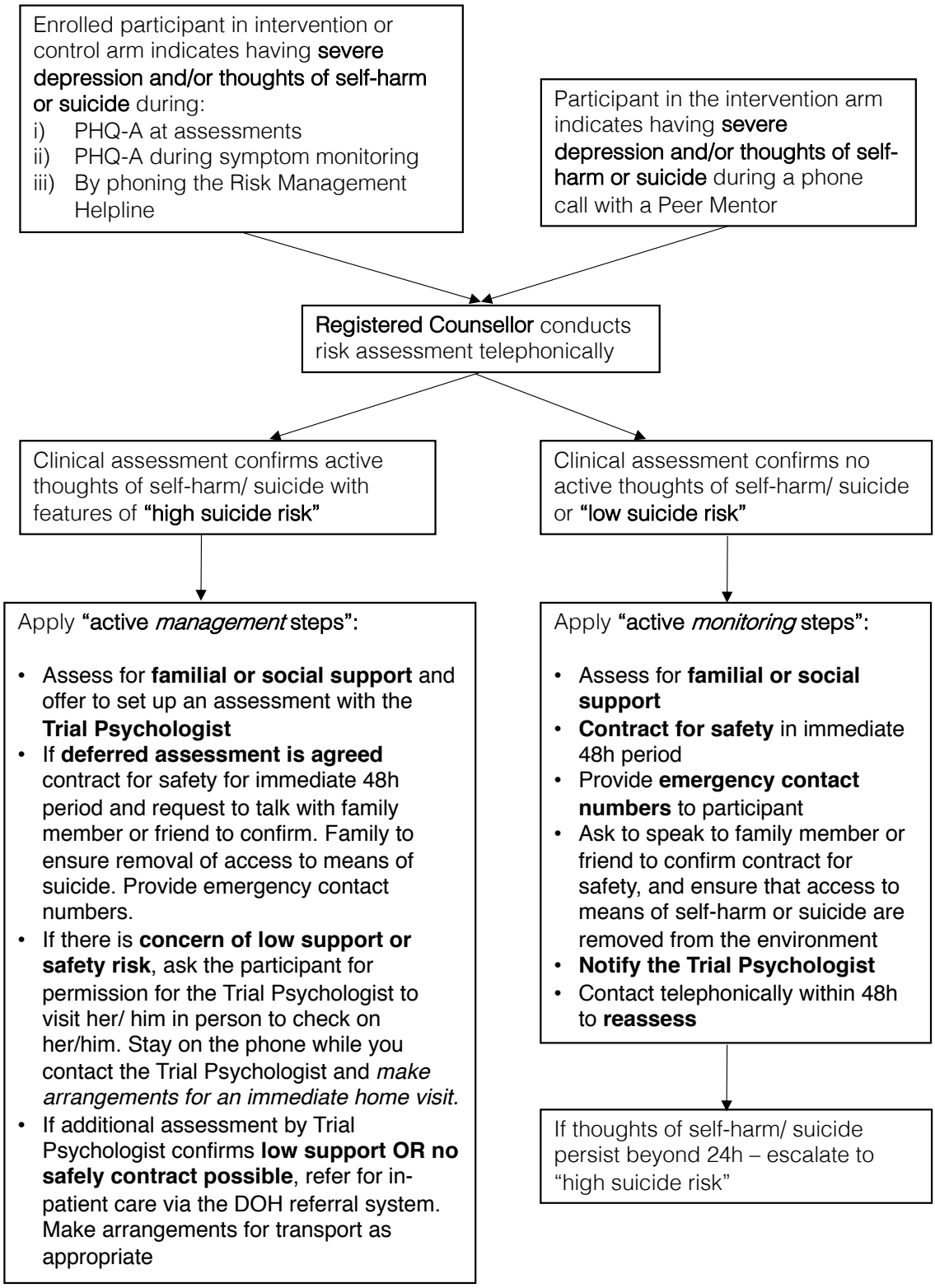


FIGURE 2. FLOW CHART FOR SUICIDE RISK MANAGEMENT DURING THE TRIAL



24.5. Risk Management Personnel

The *Risk Management Team (RMT)* is responsible for implementing all risk management aspects of the trial in accordance with the Risk Management Protocol (this document) and in consultation with the *co-Principal Investigators (co-PIs)*. Oversight of the RMT will be provided by the co-PIs and an independent *Data and Safety Monitoring Board (DSMB).*

24.5.1. Risk Management Team

The RMT consists of the Project Manager (a medical doctor), the Field Supervisors, 2 Registered Counsellors, a Trial Psychologist, and the Trial Psychologist Supervisors (senior clinical psychologists). The RMT will meet on a weekly basis throughout the trial period, with additional meetings where necessary. The RMT will immediately escalate serious risks/ adverse events to the co-PIs and DSMB. The roles and responsibilities of the RMT personnel in relation to Risk Management and Safety Monitoring are outlined in *Table 3* below.

Table 3: **Roles and Responsibilities** of members of the **Risk Management Team** in relation to Risk Management and Safety Monitoring

Role	Responsibility with regard to Risk Management and Safety Monitoring
Co-Principal Investigators (co-PIs)	The **co-PIs are responsible for and oversee the running of the trial**, work of the *Project Manager, Risk Management and Fieldwork/Assessment Teams.* Have access to only anonymised baseline data at the end of the recruitment phase. The variable indicating the allocation arm (A or B) will not be included in the baseline data. Have limited contact with participants in the intervention and control arms. **Have regular contact with the Project Manager and Risk Management and Assessment Teams.** Blinding maintained in any conversations between PI and these teams, except where AEs/ SAEs. **Receive notifications from the Project Manager of any SAEs and withdrawals within 24 hours. Review SAE forms and send de-identified SAE reports to DSMB within 48 hours.**
Project Manager (PM)	The **PM is responsible for the day-to-day running of the project** and *supervises the Fieldwork/Assessment Team and the Risk Management Team* (including the Registered Counsellors and Field Supervisors). Provides **training, supervision and support of the *Fieldwork/ Assessment Team***, whilst maintaining blinding. Together with the Trial Psychologist and Trial Psychologist Supervisor – provides **training, supervision and support to the *Risk Management Team*.** Is **notified in the event of AEs and SAEs**, **as well as any at-risk participants (those with severe depression, severe worsening of mood symptoms and/or active suicidal ideation)** by the Field Supervisors, Risk Management and Assessment Teams.

	Records AE and SAEs and prepares reports for the DSMB, Wits HREC, and SAMRC. **Reports SAEs to PIs within 24 hours** for submission to DSMB within 48 hours. Has access to the database with names and contact details of participants.
Trial Psychologist Supervisors	**Orientates the Trial Psychologist** to the project and to their supervisory role and provides **supervision and support to the Trial Psychologist and Project Manager.** May receive reports of AE and SAEs from the Trial Psychologist, and forwards these to the Project Manager within 24hours.
Trial Psychologist	**Trains, supervises and supports the Peer Mentors**. Also conducts a Competency Assessment on the Peer Mentors at the end of their training. Together with the Project Manager and Trial Psychologist Supervisors, trains and orientates the Registered Counsellors to their role within the project. **Receives referrals from the Registered Counsellors for at-risk participants** (those with severe depression, severe worsening of mood symptoms or active suicidal ideation) ***requiring additional psychological support.*** Receives information on AEs and SAEs through the Trained Peer Mentors and Registered Counsellors. Sends all AE and SAE notifications to the Project Manager within 24 hours.
Trained Peer Mentors	Trained Peer Mentors will be **responsible for providing weekly phone calls to the intervention arm participants** as per their training and a pre-determined checklist. They will be supervised by the Trial Psychologist, and will not have contact with control arm participants, or the Assessment Team. They will **report any AEs and SAEs as well as any at-risk participants (**those with severe depression, severe worsening of mood symptoms and/or active suicidal ideation) identified during the intervention sessions to the Project Manager immediately.
Registered Counsellors	Registered Counsellors will **receive referrals from the Field Supervisors, Peer Mentors and/or Assessment Team** for any participant who has severe depression, severe worsening of mood symptoms and/or active suicidal ideation at any of the assessments or during app mood/symptom monitoring. In these instances, the Registered Counsellor will be assisted by the Field Supervisors to contact the participant and make a **follow-up appointment and management plan** according to the Risk Management Protocol. The Registered Counsellors will also be responsible for **answering calls from the Risk Management Helpline.** They will be trained, supervised and supported by the Trial Psychologist and Project Manager They will report AEs and SAEs to the Project Manager within 24 hours.

Field Supervisors	Two Field Supervisors that have a good knowledge of the study area will provide a vital link between participants and the Risk Management Team. They will be trained and supervised by the Project Manager. They will conduct the home visits subsequent to the baseline assessment in order to **explain to participants how to use the mobile phones and digital applications**, as well as providing participants with contact details for the 2 Helplines. They will also connect participants in the intervention arm to the Peer Mentor. They will **work in conjunction with the Registered Counsellors to arrange appointments and follow-ups of at-risk participants** (those identified as having severe depression, severe worsening of mood symptoms and/or active suicidal ideation.) In the event that a participant is lost to follow-up, the Field Supervisors will attempt to trace the participants and enquire about the reasons for this. They will report AEs and SAEs to the Project Manager within 24 hours.
Assessment Team	A Fieldwork/ Assessment Team will be trained to **conduct the consenting and screening processes, as well as baseline and follow up assessments.** They will be trained, supervised and supported by the Project Manager, with whom they will maintain blinding. If they identify AE or SAEs during the follow up assessments they will report these to the Project Manager immediately/ within 24 hours. They *will have no role in randomization and will do all follow up assessments without knowing the allocation status of the participants*. It is possible that during the follow up assessments the adolescents mention receiving a phone call or a feature of the Kuamsha application. The training will stress that fieldworkers should as far as possible ignore that information. However, if unblinding occurs, another fieldworker will be allocated for the respective participant's subsequent follow-up assessments.

24.5.2. Data and Safety Monitoring Board

An independent Data and Safety Monitoring Board (DSMB) has been established to monitor the data emerging from the trial, in particular as they relate to the safety of participants, and to advise the Trial Steering Committee on whether there are any reasons for the trial not to continue. The DoBAt Pilot Trial DSMB consists of two senior mental health clinicians with experience conducting clinical trials and an independent statistician. The DSMB is the only body involved in the trial that has access to the unblinded comparative data during the trial.

All SAEs will be reported to the DSMB within 48 hours of the Central Study Team being notified of them. In addition, the trial statistician will prepare a comprehensive report for each DSMB meeting. This will be circulated in advance of the meeting to allow DSMB members time to study the data. The DSMB will then be required to undertake the following:

- to determine if additional interim analyses of trial data should be undertaken
- to consider the data from interim analyses, unblinded if considered appropriate, plus any additional safety issues for the trial and relevant information from other sources including SAE report forms
- after considering interim analyses and ensuring that the safety, rights and wellbeing of the trial participants are paramount, to report (following each DSMB meeting) to the Trial Steering Committee and to recommend on the continuation of the trial
- to consider any requests for release of interim trial data and to recommend to the Trial Steering Committee on the advisability of this
- in the event of further funding being required, to provide to the Trial Steering Committee and MRC appropriate information and advice on the data gathered to date that will not jeopardise the integrity of the study.

The DSMB will conduct its proceedings in accordance with a Data and Safety Monitoring Plan developed specifically for the purposes of the DoBAt Pilot Trial.

24.5.3. Staff Leave and Handovers

Before staff take any planned leave from their role they are responsible for giving a thorough handover of outstanding cases to the team. The Trained Peer Mentor calls will be used to verify that the ongoing schedules have been appropriately delegated. Handovers must be authorised by the Project Manager and the Trial Psychologist Supervisor. Leave and handover of work by the Trial Psychologist must be authorised by the Trial Psychologist Supervisor.

In incidences where emergency leave is required, the Counselling and Fieldwork Calendars will be used to make ad hoc arrangements for ongoing cases. In the case of termination of employment, handover will be carefully managed by the co-Principal Investigators and the Project Manager.

Failure of staff to report cases according to this Risk Management Protocol may result in disciplinary action

25 APPENDIX C: AMENDMENT HISTORY

Amendment No.	Protocol Version No.	Date issued	Author(s) of changes	Details of Changes made
1	V1.1	13/06/20	Julia Ruiz Pozuelo	Included additional socioeconomic measures (self-esteem, problem-solving, goal-setting, negotiation)
2	V1.2	19/04/2021	Julia Ruiz Pozuelo	Changes to: • **Project timeline** • **Questionnaire**: (a) Changed substance use measure from AUDIT to ASSIST-Y; (b) Included four brief questions about trauma assessed at baseline; (c) Included a brief sociodemographic questionnaire for adolescent's parents/guardians at baseline assessment, (d) Modified one socioeconomic task (risk preference task), (e) Add one additional introductory phone call between peer mentors and participants. • **Data collection**: (a) Use of ACASI software to deliver mental health and trauma questionnaire; (b) Change in data management platform from RedCap or OpenDataKit to NubiS; (c) Electronic questionnaire in school survey; (d) Electronic consent/assent forms. • **Risk Management**: Provide participants with national 24-hour toll-free helpline • **Control app** video clips changed from Planet Earth to WildEarth – SafariLive.