# Developing and Evaluating a Stepped Change Whole-University approach for Student Wellbeing and Mental Health: trial of unguided internet rumination CBT to prevent depression and anxiety in students (Reducing Worry)

**Trial Protocol Version 1.0 dated 05/06/2023**

**This protocol has regard for the HRA guidance and order of content**

**Funded by: UKRI – MRC Adolescence, Developing mind and Mental Health scheme**


**RESEARCH REFERENCE NUMBERS**

**IRAS Number: Not applicable**

**ISRCTN: 86795807**

**Ethics application ID: 523085**

**Sponsor protocol number: 2022-23-28**

**Table 1 PROTOCOL VERSION NUMBER AND DATE**

| Version | Date | Changes from previous version |
|---|---|---|
| 0.1 | 10/1/2022 | Based on HRA template as advised by sponsor |
| 0.2 | 18/7/2022 | Updates and edits by PI |
| 0.3 | 10/8/2022 | Updates from statistician |
| 0.4 | 15/8/2022 | Updated in light of data privacy feedback from DPO |
| 0.5 | 28/9/2022 | Updated with more detail on screening messages and honorarium and TSC |
| 0.6 | 11/11/2022 | Edits for minor corrections and reduce repetition |
| 0.7 | 04/01/2023 | Edits following the first Steering Committee meeting where the committee agreed that DMEC should be separate from main Steering Committee group plus other amendments |
| **1.0** | **05.06.2023** | Key contacts update. Removal of committee member names. Addition of TikTok as a social media advertising avenue. Section 7.1.3 payment amounts clarified. Section 7.4 clarification of who is blinded and unblinded. Section 9 Adverse event reporting requirements changed in line with Exeter Clinical Trials Unit SOP and AE and SAE examples updated. SAE reporting flowchart updated. Section 10.2 Revised recruitment end date specified. Minor revisions, typing errors, layout and formatting updated throughout. GP letters removed and stand-alone documents created. SAE form removed as out of date (revised version available electronically on database). |
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**Table 2 PROTOCOL AMENDMENTS**

| Amendment | Date | Changes from previous version | Date Authorised |
|---|---|---|---|
| **Non-substantial amendment 1 (CTU)** | **05.06.2023** | Key contacts update. Removal of committee member names. Addition of TikTok as a social media advertising avenue. Section 7.1.3 payment amounts clarified. Section 7.4 clarification of who is blinded and unblinded. Section 9 Adverse event reporting requirements changed in line with | **02.07.2023** |

| | | | |
|---|---|---|---|
| **V2.0 Amendment (REC)** | | Exeter Clinical Trials Unit SOP and AE and SAE examples updated. SAE reporting flowchart updated. Section 10.2 Revised recruitment end date specified. Minor revisions, typing errors, layout and formatting updated throughout. GP letters removed and stand-alone documents created. SAE form removed as out of date (revised version available electronically on database). | |
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**SIGNATURE PAGE**

The undersigned confirm that the following protocol has been agreed and accepted and that the Chief Investigator agrees to conduct the trial in compliance with the approved protocol and will adhere to the principles outlined including clinical trial regulations, GCP guidelines, the Sponsor's SOPs, and other regulatory requirements.

I agree to ensure that the confidential information contained in this document will not be used for any other purpose other than the evaluation or conduct of the clinical investigation without the prior written consent of the Sponsor.

I also confirm that I will make the findings of the trial publicly available through publication or other dissemination tools without any unnecessary delay and that an honest accurate and transparent account of the trial will be given; and that any discrepancies and serious breaches of GCP from the trial as planned in this protocol will be explained.

**For and on behalf of the Trial Sponsor:**

Signature: Date: .

Name (please print): Ms Pam Baxter

.....

Position: Senior Research Governance Officer

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**Chief Investigator:**

Signature:  Date: 18/7/2022.

Name (please print):

Edward Watkins.....

## KEY TRIAL CONTACTS

**Table 3 Key contacts**

| | |
|---|---|
| Chief Investigator | Professor Ed Watkins, Sir Henry Wellcome Building for Mood Disorders Research, School of Psychology, College of Life and Environmental Sciences, University of Exeter, EX4 4QG. 01392 724692, e.r.watkins@exeter.ac.uk |
| Project Manager | Nicole Madeley, Sir Henry Wellcome Building for Mood Disorders Research, School of Psychology, College of Life and Environmental Sciences, University of Exeter, EX4 4QG. 01392 |
| Trial Co-ordinator/manager | Dawn Phillips, Exeter Clinical Trials Unit, College of Medicine and Health, University of Exeter, College House, St Luke's Campus, Magdalen Road, Exeter, Devon, EX1 2LU d.phillips4@exeter.ac.uk |
| Sponsor | University of Exeter<br>Sponsor's Representative<br>Ms Pam Baxter<br>Senior Research Governance Officer<br>University of Exeter, Research Ethics and Governance Office, Lafrowda House<br>St Germans Road, Exeter, Devon EX4 6TL<br>Email: p.r.baxter2@exeter.ac.uk<br>Tel: 01392 723588<br>Mobile: 07485042117 |
| Funder(s) | UKRI Medical Research Council |
| Clinical Trials Unit | Lynne Quinn/Siobhan Creanor, Exeter Clinical Trials Unit, College of Medicine and Health, University of Exeter, College House, St Luke's Campus, Magdalen Road, Exeter, Devon, EX1 2LU, 01392 726 037 https://ctu.exeter.ac.uk |
| Key Protocol Contributors | Professor Ed Watkins, Dr Lexy Newbold, Professor Gordon Taylor, Dr Fiona Warren |
| Statistician | Professor Gordon Taylor, College of Medicine and Health, University of Exeter, College House, St Luke's Campus, Magdalen Road, Exeter, Devon, EX1 2LU, 01392 726 037<br><br>Dr Fiona Warren, Institute of Health Research, University of Exeter, Devon, 01392722749, f.c.warren@exeter.ac.uk |
| Site Team | University of Exeter (Trial Manager, project administrator and chief investigator (contacts above) |
| Other sites: recruitment only | University of Oxford, King's College London, University of Newcastle, Southampton University, Cardiff University |

## CONTENTS LIST

## i. LIST OF ABBREVIATIONS

Define all unusual or 'technical' terms related to the trial. Add or delete as appropriate to your trial. Maintain alphabetical order for ease of reference.

| | |
|---|---|
| AE | Adverse Event |
| AR | Adverse Reaction |
| CA | Competent Authority |
| CI | Chief Investigator |
| CRF | Case Report Form |
| CRO | Contract Research Organisation |
| CTA | Clinical Trial Authorisation |
| CTIMP | Clinical Trial of Investigational Medicinal Product |
| CTU | Clinical Trials Unit |
| DMC | Data Monitoring Committee |
| DMEC | Data Management and Ethics Committee |
| DMP | Data Management Plan |
| DoW | Description of Work (Annex 1 of the Grant Agreement) |
| DSUR | Development Safety Update Report |
| EAB | External Advisory Board |
| EC | Emotional Competence |
| ECom | European Commission |
| eCRF | Electronic Case Report Form |
| EU | European Union |
| EUCTD | European Clinical Trials Directive |
| EudraCT | European Clinical Trials Database |
| GA | General Assembly |
| GCP | Good Clinical Practice |
| GMP | Good Manufacturing Practice |
| IB | Investigator Brochure |
| ICF | Informed Consent Form |
| IMB | Innovation Management Board |

| | |
|---|---|
| IP(R) | Intellectual Property (Rights) |
| ISF | Investigator Site File (This forms part of the TMF) |
| ISRCTN | International Standard Randomised Controlled Trials Number |
| ITR | Individualised Treatment Rules |
| LIDAS | Lifetime Depression Assessment Self-report questionnaire |
| MA | Marketing Authorisation |
| MS | Member State |
| PI | Principal Investigator |
| PIC | Participant Identification Centre |
| PIS | Participant Information Sheet |
| PMT | Project Management Team |
| QA | Quality Assurance |
| QC | Quality Control |
| QP | Qualified Person |
| RCT | Randomised Controlled Trial |
| REC | Research Ethics Committee |
| RFCBT | Rumination Focused Cognitive Behavioural Therapy |
| SAE | Serious Adverse Event |
| SAP | Statistical Analysis Plan |
| SAR | Serious Adverse Reaction |
| SC | Steering Committee |
| SDV | Source Data Verification |
| SOP | Standard Operating Procedure |
| SSI | Site Specific Information |
| SUSAR | Suspected Unexpected Serious Adverse Reaction |
| TMF | Trial Master File |
| TMG | Trial Management Group |
| TP | Trial Protocol |

| | |
|---|---|
| TSC | Trial Steering Committee |
| WP(L) | Work Package (Lead) |
| YAB | Youth Advisory Board |

**Location/Collaborator Abbreviations**

| | |
|---|---|
| EXCTU | Exeter University Clinical Trials Unit |
| UNEXE | University of Exeter |
| UCARD | University of Cardiff |
| UOXF | University of Oxford |
| UNEW | University of Newcastle |
| KCL | King's College London |
| USOTON | University of Southampton |

**ii Project Summary**

Our overall aim is to develop and evaluate an acceptable, effective, cohesive system of whole-university and stepped care student wellbeing and mental health support. Our main objective is to resolve uncertainties as to which elements and steps within this approach are most acceptable and effective for promoting good mental health in university students, how they interact, and which work best for whom. We will derive an evidence-based model of integrated approaches to inform best practice and policy recommendations for delivering inclusive, effective, sustainable, scalable student wellbeing mental health support.

Key cross-cutting objectives include to:
(1) Examine acceptability, uptake, adherence, effectiveness across different initiatives at different levels of stepped support (at Step 1 compassionate education; online mental health literacy (MHL); digital self-monitoring; at Step 2 guided, unguided self-help; at Step 3 digital self-monitoring in mental health services).
(a) Evaluate whether building compassion into university culture, organisation and coursework is feasible and improves wellbeing, academic outcomes and inclusivity across diverse groups.
(b) Assess whether a digital self-monitoring tool improves emotional self-awareness, wellbeing, and access to appropriate support.
(c) Assess whether an online MHL course is engaging, increases mental health knowledge, healthy behaviours, access to support and reduces stigma.
(d) Test whether unguided digital rumination-focused self-help intervention prevents depression in high-worry students.
(e) Compare the efficacy and acceptability of different digital self-help and book-based self-help for students with elevated anxiety and depression.
(f) Evaluate whether adding a digital self-monitoring tool to routine student mental health services improves student engagement, care management and outcomes.

(2) Map the student journey along the stepped pathway to identify barriers, facilitators and gaps and to understand what events, symptoms and mechanisms influence student transitions between initiatives.

(3) Understand how student wellbeing and mental health needs vary across diverse groups (e.g. gender, sexuality, socioeconomic background, ethnicity, prior mental health history) over time and barriers and facilitators to accessing support for these diverse groups.
(a) Create a large representative longitudinal dataset (n>5000) of students across diverse groups and universities, with biannual assessment of wellbeing, mental health, process mechanisms, preferences, knowledge and behaviour re mental
health and access to support services.

(b) Assess the ongoing impact of COVID-19 and its consequences (social distancing, blended educational approaches) on student wellbeing.
(4) Better understand heterogeneity of intervention effects for students.
(a) Explore which subgroups of students with elevated anxiety and depression are particularly responsive to unguided digital interventions.
(b) Identify predictors of who benefits from different digital interventions.
(c) Produce exploratory Individualised Treatment Rules (ITRs) to guide the selection of treatments most likely to be helpful for students.

(5) Identify which hypothesized mechanisms for the promotion of good mental health are most associated with positive outcomes to guide which active components to enhance and include in stepped care model. Test the extent to which increasing (a) emotional self-awareness; (b) self-compassion; (c) mental health knowledge; (d) sense of belonging; (e) use of helpful cognitions and behaviours mediate positive outcomes across all initiatives.

(6) Develop and refine existing initiatives in partnership with students with co-creation workshops for digital self-monitoring tool, online MHL, strengths-based guided self-help.

(7) Develop a rich understanding of students' perspective and experience of stepped care through qualitative analysis of student focus groups and interviews.

Our research involves a rigorous evaluation of whole-university and stepped care frameworks to promote good mental health in students using a multi-disciplinary approach drawing on the humanities, psychology, psychiatry, information technology and statistics, working collaboratively across 6 universities.

To address objective 1, we will introduce different whole-university (embedding compassion in education; online mental health literacy course) and stepped care interventions (digital self-monitoring) in a phased way across collaborating universities.

To address objectives 2,3,5, a repeated biannual online student wellbeing survey at the start and end of the academic year, with cross-sectional and longitudinal components, will collect self-report quantitative data (demographics, mental health outcomes, process measures, attitudes, knowledge of and behaviours related to stepped care) from students across multiple institutions. Students can use a digital self-monitoring tool and electronic personal health record prospectively, with brief measures of wellbeing, stress, symptoms and use of support to address objective 2. We will test whether this tool helps students to better use stepped care. Observational experiments will collect pre- and post-intervention quantitative and qualitative data using a core set of outcome measures and examine data from biannual surveys to assess the impact of introducing each intervention.

To address objectives 6, 7, focus groups will explore students' experiences of these initiatives including positives, negatives, areas to improve and relevance to diverse groups.

To address objectives 1,4,5, randomised trials will compare different variants of digital self-help including guided vs unguided self-help.

To address objective 4, pre-randomisation measures will assess potential predictors of heterogeneity of treatment effect. Repeated weekly web surveys within the trials will assess change in putative mediators to support objective 5.

This specific trial of unguided i-Rumination Focused Cognitive Behavioural Therapy (RFCBT) to prevent anxiety and depression will specifically test objective 1 (d) and 5.

**Table 4 Summary of Study**

| | | |
|---|---|---|
| Trial Title | **Developing and Evaluating a Stepped Change Whole-University approach for Student Wellbeing and Mental Health: trial of unguided internet rumination-focused CBT to prevent depression and anxiety in students** | |
| Internal ref. no. (or short title) | **Nurture-U: Reducing worry and Building Confidence in University Students** | |
| Clinical Phase | III | |
| Trial Design | Phase III superiority parallel 2-arm randomised multicentre, randomized controlled trial (RCT) | |
| Trial Participants | UK university students with elevated worry and rumination | |
| Planned Sample Size | 648 for overall cohort. | |
| Treatment duration | Unguided self-help digital intervention, typically completed over 6-12 weeks | |
| Follow up duration | Over 12 months: three months, twelve months<br>The primary time point is 12 months | |
| Planned Trial Period | 30 months (starting recruitment to final follow up) | |
| | **RCTs & measures** | **Outcome domains** |
| **Primary outcome** | Incidence of major depression episode during follow-up period (LIDAS) | Indices of well-being and poor mental health |
| **Secondary outcomes** | Depression PHQ9<br>Anxiety GAD-7<br>Functioning – WSAS<br>Wellbeing – WEMWBS (7-item)<br>Brooding<br>Worry (PSWQ-Short)<br>Use of services/treatment –<br>Academic outcomes -self-report | Non-specific indices of poor mental health |

| | | |
|---|---|---|
| | Stress<br>Resilience | |
| Mediators | rumination, habit change, self-compassion, behavioural coping skills | |
| Intervention | One intervention group<br>usual practice plus existing unguided internet-delivered rumination-targeting CBT<br>The active intervention is all entirely self-help and provides psychoeducation, tips, advice and strategies for well-being promotion.<br>Control is usual practice | |
| Route of Administration | Online access via smartphone, tablet, PC, laptop | |

**iii. Funding and Support**

**Table 5 Funding and Support in Kind**

| **FUNDER(S)** | **FINANCIAL AND NON FINANCIALSUPPORT GIVEN** |
|---|---|
| **UKRI MRC** | £3780,000 |

## iv. ROLE OF TRIAL SPONSOR AND FUNDER

**Role of Funder**

The research funder has the responsibility to ensure that there is a proper use of the funds they control. The study is funded by the UKRI/MRC. The Funder has conducted a review of the study, provided feedback to the consortium, and has established that the research is worthwhile, of high scientific quality and represents good value for money. The research funder has assessed the experience and expertise of the Chief Investigator, other key researchers on the programme and has deemed that there is appropriate infrastructure for the research to be carried out.

The funder plays no further role in the design of this individual study and will have no role in data analysis or interpretation, or writing up of findings of the study. The funder will be sent all outputs prior to dissemination, but has no role in the decision to submit for publication.

**Role of Sponsor**

The study sponsor will ensure that the research team has access to resources and support to deliver the research as proposed and that responsibilities for management, monitoring and reporting of the research are in place prior to the study commencing. The sponsor will ensure that there is agreement on recording, reporting and reviewing significant developments as the research proceeds and approve any modifications to design, obtaining requisite regulatory authority.

The sponsor will assume responsibility for operating the management and monitoring systems of the research. Prior to the study commencing the sponsor will be satisfied that:

- The research will respect the dignity, rights, safety and well-being of participants and the relationship with healthcare professionals.
- The research will be reviewed and approved by the appropriate Research Ethics Committee.
- The Chief Investigator, and other key researchers have the requisite expertise and have access needed to conduct the research successfully.
- The arrangements and resources proposed for the research will allow the collection of high quality, accurate data and the systems and resources will allow appropriate data analysis and data protection.
- Organisations and individuals involved in the research agree the division of responsibilities between them.
- Arrangements are in place for the sponsor and other stakeholder organisations to be alerted to significant developments during the study, whether in relation to the safety of individuals or scientific direction.
- There are arrangements for the conclusion of the study including appropriate plans for the dissemination of findings.

The sponsor plays no role in the design of this study, and will have no role in data analysis or interpretation, or writing up of findings of the study.

## v. ROLES AND RESPONSIBILITIES OF TRIAL MANAGEMENT COMMITEES/GROUPS & INDIVIDUALS

There are a number of workstreams within the overall University Mental Health project – the relevant workstream for this trial is Workstream 4 (WS#4): Guided and unguided self-help cognitive-behavioural therapy (CBT) for student wellbeing and MH (leads Watkins, Farrand;+Gallop, Robinson, Taylor).

This trial protocol document focuses on governance and structure related to the conduct of the trials only.

The University of Exeter will act as the sponsor for the study; the study will be hosted in the Mood Disorders Centre and the Exeter Clinical Trials Unit, which has experience in the successful delivery of internet and prevention trials.

**The Trial Management Group**

The Trial management group will oversee and manage the randomised controlled trials and consists of the chief investigator, the project manager, the study manager, the statisticians, the data team and representatives from the EXCTU management team. A subset of the group will meet fortnightly, with a monthly meeting to review progress and milestones.

**Table 6 Members of the Trial Management Group**

| Name | Institution | Contact details |
|---|---|---|
| Trial Manager | EXCTU | Teamnurture-U@exeter.ac.uk |
| Lead statistician(s) | EXCTU | |
| IT Support | EXCTU | |
| Ed Watkins (Chief Investigator) | UNEXE | e.r.watkins@exeter.ac.uk |
| Senior trial manager/trial manager lead | EXCTU | |
| Project administrator | UNEXE | |
| Data management & IT | EXCTU | |

**The Nurture-U Prevent Trial Steering Committee (TSC)**

The TSC will be chaired by an independent chair, with relevant clinical and academic experience and will also include current members of our Student Advisory Board with representatives from specialist mental health professionals. The TSC will meet at the beginning of the trial and it is proposed that it meets every 6 months thereafter to oversee its conduct. It will include the trial PI, trial manager, trial statistician plus at least 3 independent members, where possible, members of the independent Expert Advisory Board. The Trial Steering Committee (TSC) will have a monitoring and decision-making role for the trial, including recruitment, progress and other milestones. The TSC will report to the funder and trial sponsor, and has the authority to recommend the suspension or discontinuation of the trial to the sponsor. The Trial Steering Committee will be quorate if at least 50% of the independent membership are present. Minutes of the meeting will be prepared by the Chair and circulated for agreement by the full membership over e-mail within a reasonable time following the meeting. All members of the TSC will contribute to discussion and decisions but to ensure that in decision making >50% of the membership is independent, co-investigators and collaborators will not have voting rights.

**TSC Terms of Reference**

1. To monitor recruitment and supervise the progress of the trial towards its objectives;
2. To consider recommendations of the relevant Research Ethics Committee;
3. To inform the funders (UKRI/MRC) on the progress of the trial;
4. To advise funders and trial Study Management Group on publicity and the presentation of all aspects of the trial;
5. In the event of further funding being required, to provide to the funders appropriate information and advice on the data gathered to date without jeopardising the study;
6. To ensure appropriate oversight of, and involvement in, trial management from lay advisers who have relevant lived experience.

**Trial Data Monitoring and Ethics Committee (DMEC)**

An independent DMEC will consist of an independent statistician/methodologist and at least two independent clinician/researcher members, (with the Chair of the committee coming from one of the methodologist or clinician). The DMEC will meet every 6 months and if necessary, in response to any serious untoward incidents. The DMEC will review adverse events and monitor data with access to group allocation with respect to recruitment, retention, and safety, and report to the TSC. The DMEC will be responsible for monitoring serious adverse effects, protocol violations and any risks emerging from the trial. It has the capacity to conduct an unblinded analysis if concerned about serious adverse effects.

**Terms of Reference**

1. To determine if interim analyses of trial data should be undertaken
2. To consider the data from interim analyses (un-blinded if appropriate);
3. Consider any safety issues for the trial and recommend appropriate contingencies
4. To consider any requests for release of interim trial data
5. To monitor data, risk, and adverse outcomes in the trial

**University Mental Health External Advisory Board (EAB)**

The role of the EAB is to periodically review the progress and results of the overall project from a variety of angles and provide advice on ongoing and future work. The EAB will be composed of internationally renowned scientists, representatives for student mental health and stakeholders involved in the delivery of mental health and wellbeing support within higher education including clinical professionals, students, policymakers and senior management. Specifically, the EAB will provide independent advice on (i) managing the project and maximising its scientific, technological and health-related impact; (ii) the exploitation of the most promising results and planning

and supporting future implementation and impact The EAB shall also assist and facilitate the strategic decisions made by the project steering group and provide tactical recommendations on management, impact or methodology to the Steering group. The chair and membership of the EAB will set their terms of reference in liaison with the Project Management Team. The EAB will meet at least annually either in person or via videoconference.

Meetings: The project's budget includes a line to cover the travel and subsistence costs of EAB members invited to attend project events. Each EAB member will be required to sign a confidentiality agreement. The Consortium Agreement will fix in detail the governance rules and procedures.

**vi. Protocol contributors**

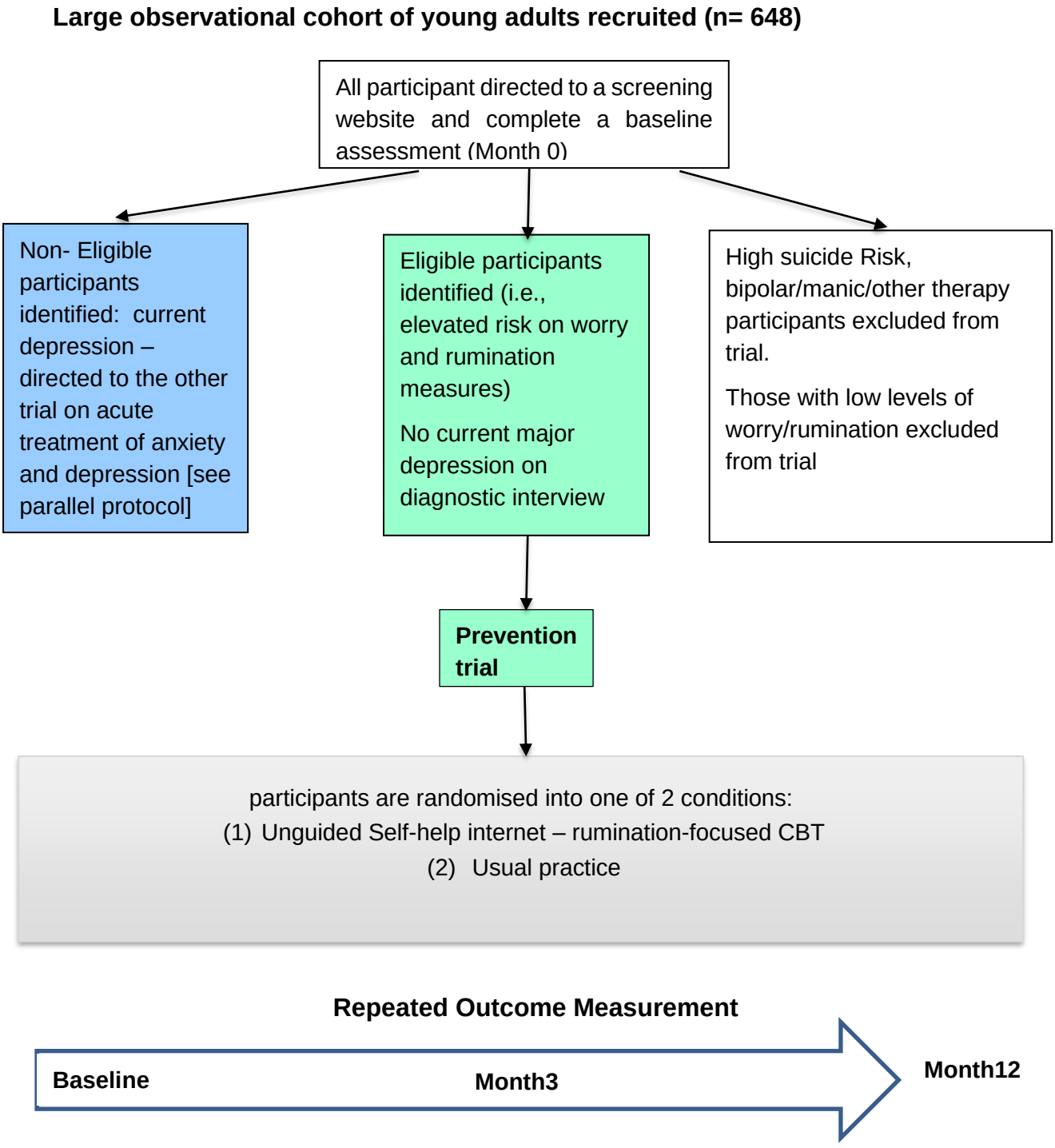
This protocol has been written by the chief investigator and lead PI for the trial Professor Ed Watkins and trial manager Dr Lexy Newbold with the assistance of Lynne Quinn (Operations Manager) from the University of Exeter Clinical Trials Unit. Tim Eames have contributed to the data management sections and Professor Gordon Taylor (Exeter CTU Co-director) and Dr Fiona Warren (trial statistician) to the statistical analysis sections.

**vii. KEY WORDS:**

**Promotion, Prevention, internet delivery, CBT, rumination, worry, unguided self-help, depression, anxiety**

**viii. TRIAL FLOW CHART**

**Figure 1Illustration of randomised controlled trial for unguided internet-RFCBT**



# 1 BACKGROUND

University provides an opportunity for young people to develop independence, positive self-identity, good coping skills and social-emotional resources to stand them in good stead through their lives, as they face challenges like leaving home, meeting academic standards, making new friends, managing finances. However, university is also a high-risk period for stress and poor mental health (MH), which can result in increased drop-out, poorer academic outcomes, diminished employment opportunities and long-term disadvantage[1-3]. MH concerns are increasing amongst university students, with anxiety, depression, self-harm and alcohol/substance abuse most common [4-8]. These MH concerns are likely to increase further because of the COVID-19 pandemic [9] and resulting uncertainties, loneliness, and restrictions. Therefore, improving student wellbeing and promoting good MH provides a key window of opportunity to promote flourishing and generate long term benefit for our students and wider society.

Our vision is for all higher education students to have ready access to inclusive, effective, integrated, and tailored wellbeing promotion and MH support developed in partnership with students. This vision meets the call's remit by addressing several inter-related challenge areas: prevention and intervention; inter-individual heterogeneity focused on who may be more likely to engage and respond to different initiatives and addressing the needs of diverse student groups including potentially vulnerable subgroups; societal transformation focused on the impact of COVID-19; examining the education environment to explore how university environments can foster wellbeing.

Our aim is to bring together expertise and initiatives from different institutions to develop and evaluate a cohesive, scalable and sustainable system of whole-university and stepped student wellbeing and MH support.

Key objectives include to: (a) examine acceptability, uptake, adherence, and effectiveness across different initiatives at different levels of stepped support; (b) map the student journey along the stepped pathway to identify barriers, facilitators, and gaps and how different steps and initiatives interact; (c) derive an evidence-based model of integrated approaches to inform best practice for effective and sustainable delivery of inclusive university MH and wellbeing support.

Across these objectives, a key issue is understanding how MH needs vary across diverse groups (by gender, sexuality, socioeconomic background, ethnicity, MH history, international students, carer status) and what different support elements are more likely to engage and help individuals from these diverse groups. We will explore which approaches work best for which individuals or subgroups.

# 2 RATIONALE

University MH services report a dramatic increase in the number of students seeking help for MH concerns and a growing disparity between student demand and current resources

[8,10,11]. Since most students with MH problems access services via their university rather than the NHS, there is now a major treatment gap. The organization, provision and means for students to access MH services varies across institutions. None of the different models of services [8,11] nor most student MH initiatives have been systematically evaluated and are often applied without a direct evidence base. Major challenges for enhancing student MH include: (Challenge 1: C1) incomplete mapping of the scope and complexity of MH need, especially with respect to inclusivity and diversity11; (C2) absence of proven effective prevention and wellbeing promotion initiatives[12,13]; (C3) a need to improve student engagement: most students experiencing poor MH do not seek formal support from university or NHS services8; (C4) long wait-times for counselling and therapy support[11]; (C5) a lack of integrated support planning and proactive follow-up; (C6) traditional face-to-face interventions alone lack sufficient capacity to address the full spectrum of need; (C7) community MH services do not align well with student need given peripatetic nature of student life, with poor continuity of care between University and NHS services.

Despite increasing research into student MH, there remain sizeable knowledge gaps as to the prevalence and drivers of MH problems in UK university students, with respect to which agpproaches work and are acceptable to students, including for diverse and minority groups (e.g., BAME, LGBTQ+, international, MH history, socioeconomic background) and critically, as to what overarching model of organized MH support for students works best. The recent University Mental Health Charter[14], a product of research synthesis, stakeholder consultation, and student co-creation recommended a systemic whole-university approach to MH, arguing that institutional environment, organisational culture, course content and delivery are important for MH, along with the integration of promotion and prevention and the provision of specialist support (see also[8]). In parallel, recent reports[11] and the Universities UK StepChange framework[15] recommended stepped care tailored to the university environment to address the capacity and complexity of MH support needs. Stepped care typically involves access to and movement between different levels of intensity based on need, ranging from predominantly community-led prevention and promotion approaches for individuals without symptoms (Step 1) to low-intensity self-help interventions for individuals with mild-to-moderate symptoms (Step 2) to psychotherapy or counselling for those with elevated symptoms (Step 3). However, to date, neither the whole-university nor the stepped change approach have been systematically evaluated within and/or across universities.

Our programme therefore advances the field by providing the first attempt to systematically investigate a coherent model of MH promotion and support for the diverse university student population. We will address major support gaps and key knowledge gaps by investigating multiple initiatives all coordinated within a systemic whole-university and stepped change framework to promote student wellbeing and good MH. We will reduce uncertainty in the evidence base and tackle the challenges identified above through diverse methodologies including focus groups, pilot studies to assess feasibility and adherence, and proof-of-concept randomised controlled trials (RCTs). Our programme is novel and provides

added translational value and value for money by investigating and integrating complementary initiatives (each a specific workstream) at each level along a stepped change pathway and their interactions: at Step 1 compassionate education, MH literacy; at Step 2 guided vs unguided self-help; at Step 3 enhanced care for students experiencing common MH conditions. To inform the scope and trends in student MH need and evaluate transitions through the stepped initiatives, a cross-cutting workstream uses (a) repeated electronic student wellbeing surveys; (b) a digital self-monitoring tool, which may itself improve access to support and promote integrated support planning. Each initiative will be embedded in existing structures or practice (e.g. teaching, wellbeing services) or use proven and available digital interventions to make the research cost-effective and support sustainable implementation beyond the grant. Through five intercoordinated workstreams, our integrative central research question is: What combination(s) of approaches within this framework is/are most acceptable and effective at promoting good student MH, for whom, and how do these different steps interact? Crosscutting research questions across all workstreams ask for each initiative: Can it be feasibly implemented? What is the uptake and experience among students from diverse backgrounds? What is its effect on wellbeing, symptoms, academic performance? How does it influence students accessing other parts of the stepped support framework? What are the mechanisms-of-action?

**CONCEPT AND METHODOLOGY**

**Overall Concept**: **Guided and unguided self-help cognitive-behavioural therapy (CBT) for student wellbeing and MH (leads Watkins, Farrand;+Gallop, Robinson, Taylor).**

Low-intensity (LI) self-help CBT, with or without support from a MH professional (e.g. a psychological wellbeing practitioner, PWP), delivered via books or digitally (at Step 2) is proven effective for treating common MH difficulties[30-32], improves access and reduces delivery costs (e.g., NHS IAPT programme). Further, digital self-help is highly scalable and usable anywhere, anytime, potentially addressing treatment barriers and challenges C4, C6, C7 around treatment access, capacity, convenience, and availability. Digital CBT for mild-to-moderate anxiety and depression is efficacious in students[33]. Students generally view online interventions positively[34]. Despite this, self-help CBT has been less frequently incorporated and evaluated within university student MH support services and when used does not always adhere to established LI-CBT precepts and is not typically adapted for students.

To optimise the use of self-help CBT for students, we will first investigate LI self-help CBT specifically designed for students: in partnership with student-led focus groups, Farrand has adapted booklet-delivered, strengths-based self-help from high-intensity CBT. As university students face many developmental and transitional challenges, we hypothesize that identification of their own strengths and learning to apply these to overcome difficulties will be

a relevant and effective way to promote wellbeing (complementing WS#3). The next step is to investigate its feasibility and acceptability.

Second, a key uncertainty within digital self-help is heterogeneity of treatment effects (HTE) i.e., variations in individual treatment response to particular treatments [33,35]: understanding which digital self-help interventions are most acceptable and work best for which students could help to tailor self-help interventions, plan the care pathway, and improve outcomes. A critical question is how much and what kind of support from a practitioner is needed: unguided self-help has greater reach, sustainability and scalability as it is not limited by therapist capacity, opening up the potential for massive cost-effective open online interventions [36] but may have less engagement and efficacy than guided interventions[35,37,38], although there is heterogeneity[33,35], with a subset of individuals helped as much by unguided self-help as guided self-help[38,39]. Identifying such a subset would be of enormous value in increasing treatment scalability, tackling C4, C6.

Third, to tackle challenge C2, we will investigate self-help for wellbeing promotion and prevention of poor MH. Recent feasibility work led by Watkins suggests that unguided self-help digital CBT, specifically designed to target rumination/worry in students (see here) may prevent anxiety and depression[39,40] but this needs evaluation in a proof-of-concept trial to test its potential as a highly scalable approach[36]. Worry/rumination is a good target to help students because it is a vulnerability factor that predicts later depression, anxiety, alcohol misuse and eating disorders in students [41], is elevated in students experiencing stress [41], easily recognised by students without stigma, and can be successfully reduced [39-41].

Fourth, the mechanisms-of-action of these self-help CBT interventions remain unresolved. Hypothesized mechanisms include (a) improved emotional self-awareness; (b) increased self-efficacy; (c) learning new cognitive and behavioural coping skills and (d) social support (for guided treatment). For example, in rumination-targeting CBT, the hypothesized mechanisms-of-action are that users learn to spot triggers for worry/rumination and then learn to engage in helpful cognitions and behaviours as an alternative to the rumination habit, with self-compassion one alternative response[39-41] (cf WS#2). Delineating mechanistic insights enables individual interventions to be further enhanced and the stepped care model to be planned to target all active mechanisms.

Hence, RQ8: Is strengths-based guided self-help feasible and acceptable to students?;
RQ9: Which digital interventions are acceptable to which students and do they reduce symptoms and demand for other services?;
RQ10: What subsets of students are particularly responsive to unguided digital interventions?;
RQ11: Can targeted unguided self-help for high worriers prevent onset of depression?

This trial is focused on RQ11.

**METHODS OVERVIEW:**
To answer RQ#11 and test our hypothesis that unguided self-help targeting users' vulnerability to rumination/worry will prevent depression better than usual practice, a proof-of-concept 2-arm superiority parallel-arm individual-level single-blind RCT will randomize high ruminating students to usual practice alone versus usual practice plus existing unguided internet-delivered rumination-targeting CBT[39,40]. Participants will be 648 students recruited across all universities scoring above previously established cut-offs on standardized self-report measures of worry and rumination [39,40], who do not currently meet diagnostic criteria for major depression or have histories of drug/alcohol dependence, bipolar disorder or psychosis, and not receiving psychological treatment. Follow-ups will occur at 3 and 12 months. Incidence of major depression over 12 months will be the primary outcome, indexed by a well-validated questionnaire/interview assessing diagnosis retrospectively across the follow-up period. Secondary outcomes include self-reported depression, anxiety, wellbeing, and educational attainment. To investigate putative mediators and test hypotheses about mechanisms (e.g., unguided CBT hypothesized to work via learning new cognitive and behavioural coping skills), eight weekly 5-minute web surveys will be used during the intervention period to monitor relevant brief process measures (subset of WS#1 process measures), treatment engagement, anxiety, and depression.

## 3 OBJECTIVES AND OUTCOME MEASURES/ENDPOINTS

### Trial Objectives

To evaluate the effectiveness of an unguided internet-delivered (mobile app) rumination-focused CBT intervention package as targeted public health approach to prevent anxiety and depression in university students with elevated levels of worry and rumination. The intervention has the potential to be scalable, easily available, low cost, convenient, acceptable, and to tackle equality of access (see also Kazdin, 2015).

More specifically, the objective is to compare the effect of usual practice against usual practice plus the unguided i-RFCBT mobile app package over a 12 month follow-up. Outcomes will be self-reported/interview assessed incidence of major depression (primary outcome) as well as resilience, depression, anxiety symptoms, social functioning, and educational achievement (secondary outcomes).

### 3.1 Primary/secondary objectives and research hypotheses

The primary objective in the trial will be to evaluate poor mental health as indexed by incidence of depression at the 12 month follow up (*primary endpoint*) in university students who are

potentially vulnerable for poor mental health because of elevated levels of worry and rumination at baseline.

The *primary outcome measure* will be the incidence of major depression across the 12-month follow-up as indexed by a diagnostic interview or self-reported equivalent.

**Hypotheses**

(1) For university students with elevated worry and rumination, unguided i-RFCBT (delivered via mobile app) added to usual practice will outperform usual practice in

- reducing incidence of depression across 12 months (1a; primary outcome, as index of poor mental health; PHQ-9);
- reducing symptoms of depression at 3 and 12 months (2a; secondary outcome, as index of poor mental health; PHQ-9);
- reducing symptoms of anxiety at 3 months and 12 months (2b); (secondary outcome, as index of poor mental health; GAD-7)
- increasing mental well-being (WEMWBS), social and occupational/academic functioning (WSAS), worry, and rumination at 3 and 12 months (2c). (secondary outcome).

**Secondary objectives** will be: (1) to assess the effects of the intervention on secondary outcomes over long-term (12-months follow up) and (2) at all time points (3 and 12 months) The same hypothetical structure as above will be used.

Additional secondary outcome measures will assess anxiety, mental well-being, social functioning, and educational achievement (see **Table 7**).

**Demographic information**

Demographic information will be collected at baseline including participant age, sex, country of birth, country where currently reside, ethnic group, educational level, occupation, and parent's occupation. Occupational status of participant and their parent(s) will be used as an index of socio-economic status.

### 3.3 Outcome measures

**Table 7 Outcome measures for Nurture-U i-RFCBT prevention trial**

| Measure | Description | Reliability and Validity |
|---|---|---|
| **PRIMARY OUTCOME** | | |
| Incidence of major depression across the follow-up period<br><br>**LIDAS (Lifetime Depression Assessment Self-Report Questionnaire)** | LIDAS self-report questionnaire /interview means of checking current diagnosis – to be determined based on evaluation of which is briefer, more reliable, able to distinguish both past and current MDE.<br><br>The Lifetime Depression Assessment Self-report questionnaire (LIDAS), Bot et al, 2017) assesses lifetime major depression (MDD) diagnosis according to DSM criteria, and is largely based on the widely used Composite International Diagnostic Interview (CIDI). It has been proven to be effective for determining history of depression through self-report in an online digital format, matching the needs for the current study. LIDAS is a promising tool for rapid determination of lifetime MDD status in large samples, such as needed for genomics studies. In the current study, it was used to more accurately determine past and current diagnostic status for depression at baseline and at 3 month and 12month follow-ups. It consists of a conditional sequence of pre-programmed questions assessing all the diagnostic criteria for depression, with logic cut-outs so that subsequent questions are determined by prior questions – as such participants can answer between 3-30 questions. | Incidence of depression over 3 and 12 months assessed by well-validated questionnaire reflecting structured clinical interview (CIDI or LIDAS to be determined)<br><br>Sensitivity and specificity were adequate. User-friendliness of the instrument was rated high. Median completion time was 6.2 min. Sensitivity and specificity for lifetime MDD were 85% [95% confidence interval (CI) 80–91%] and 80% (95% CI 72–89%), respectively, against a reference of the standard CIDI diagnostic interview. The instrument gave a prevalence of lifetime MDD in line with reported population prevalence, (Bot et al., 2017). |

| Measure | Description | Reliability and Validity |
|---|---|---|
| | | |
| **SECONDARY OUTCOMES** | | |
| **Warwick-Edinburgh Mental Well Being Scale** (**WEMWBS**; Tennant et al., 2007; Stewart-Brown et al., 2009) | 7-item participant rated questionnaire assesses psychological and eudemonic well-being, each rated on a 4 point scale, with anchors at 1= None of the time, 2= Rarely, 3= Some of the time, 4= Often, 5 = All of the time. Unidimensional scale. | Leading measure of well-being. 14-item version validated from age 16 upwards; Cronbach's α =0.89, test-retest reliability ICC over 1 week = 0.83. Good convergent validity: positive correlations with EQ-5D VAS, PANAS-PA, satisfaction with life scales (all r's >0.72); negative correlations with PANAS-NA and GHQ-12 (r >-0.53). |
| ***Patient Health Questionnaire-9*** (***PHQ-9***; Kroenke et al., 2001) | 9-item participant rated questionnaire assessing frequency of symptoms of depression over the last 2 weeks. 4-point scale for each item, with anchors at 0=not at all, 1 = several days, 2= more than half the days, 3 =nearly every day. Unidimensional scale. | Leading measure of depression widely used in clinical trials, clinical practice, and as part of the NHS Quality and Outcomes Framework (QOF) for UK primary care, and Improving Access to Psychological Treatments (IAPT) Minimum Data Set (MDS). Cronbach's α =0.89 in primary care, test-retest reliability (ICC) 0.84 after 48 hours. Validation studies indicate positive correlations with measures of functional status (r=0.73), disability days (r=0.39), and symptom-related difficulty (r=0.55) At cut-off of ≥ 10, excellent specificity (0.88) and sensitivity (0.88) with diagnoses of major depression by structured interview, replicated in a UK population (sensitivity 0.80; specificity 0.92). |
| ***Generalized Anxiety Disorder-7 (GAD-7***; Spitzer et al., 2006) | 7-item participant rated questionnaire assesses frequency of symptoms of anxiety over the last 2 weeks. 4point scale for each item, with anchors at 0=not at all, 1 = several days, 2= more than half the days, 3 =nearly every day. Unidimensional scale. | Leading measure of anxiety widely used in clinical trials, clinical practice, and as part of the UK NHS IAPT MDS. Cronbach's α =0.92, test-retest reliability ICC = 0.83. Convergent validity good, r =.72 with Beck Anxiety Inventory, r = 0.74 with Symptom Checklist-90 anxiety scale. |

| Measure | Description | Reliability and Validity |
|---|---|---|
| ***Work and Social Adjustment Scale (WSAS***; Mundt et al., 2002) | 5-item participant rated questionnaire assesses impaired functioning, rated from 0 not at all impaired to 8 severely impaired, with respect to work/education, home management, social leisure, private leisure and close relationships. Unidimensional scale. | Leading measure of functioning, widely used in clinical practice, and as part of the UK NHS IAPT MDS. Cronbach's α range from 0.70 to 0.92, test-retest reliability ICC = 0.73. Interactive voice response administration correlated 0.81 to 0.86 with clinician interviews. |
| Use and application of intervention | Developed for study (3-items) | Use and application of intervention |
| Satisfaction with intervention | Adapted Client Satisfaction with Treatment Questionnaire-8 | |
| Use of services /treatment received– questionnaire to be developed incorporating NHS and student services | To understand level of treatment sought and received – from list of student, NHS, and other options | Use of services /treatment received– questionnaire to be developed incorporating NHS and student services |
| 5-item Brooding scale | Secondary outcome | Test whether intervention reduces worry and rumination |
| Short-form Penn State Worry Questionnaires | Secondary outcome | |
| Brief Resilience Scale) | Secondary outcome | |
| Academic grades self-report | Secondary outcome to assess impact on academic studies | |
| Measures of stress (PSS, PSSI) | Secondary outcome | |
| ***Demographics*** | Date of birth, gender, country in which live; **Gender identity (M/F/neither/both); sexual orientation, race/ethnicity; birthplace, educational attainment, topic of study** | |
| ***Educational achievement*** | Academic outcomes from students either via Self-report or consent to access student records – academic grades self-report | |

| Measure | Description | Reliability and Validity |
|---|---|---|
| AEQ Adverse Events Questionnaire | The Adverse Events questionnaire is a brief measure designed to assess stressful events in young people, relevant to the population under study in the current cohort (Carver, 1998). It consists of 3 questions asking about relevant adverse experiences (bad experiences concerning academic study; bad experiences concerning relationships; other bad experiences) rated from 0 “No”, 1 “yes, happened once”, 2”yes happened twice”, 3 “yes, happened more than twice”. A fourth item asks about minor problems or hassles ranging from 0 “minor problems” to 4 “large number of minor problems and hassles”. We used the measure to assess levels of stress concisely and to examine whether stress is a potential predictor of subsequent depression and a moderatro of any treatment effects. We adapted the questionnaires to include work experience as well as academic study and to be focused on last 3 months and added a separate question about changes or transitions in life. | Carver (1998) found that this measure predicted subsequent depressive symptoms six weeks later in undergraduates and interacted with cognitive vulnerability factors to predict depression, as did Beevers and Carver (2003) in a subsequent study, |
| **Current medications, healthcare utilization, lifetime mental health treatment** (age of onset, duration, type, hospitalisations – CIDI); | | Treatment use |

| Measure | Description | Reliability and Validity |
|---|---|---|
| **high current stress severity, stress reactivity (perceived stress scale)**; | Perceived Stress Scale (PSS)[38,39] 7 items;<br>PSSI measure | Stress |
| **Brooding subscale of Ruminative Response scale (5-item)** | | Coping styles |

**Additional measures: potential mediators of clinical outcomes**

We will assess potential mediator of intervention by providing brief measures weekly for 8 weeks post-randomisation, taking less than 5 minutes to complete. **Mediator measures** – repeated weekly for 8 weeks post-randomisation, taking less than 5 minutes to complete, 23 items to rate

**Table 8 Mediator measures for i-RFCBT Prevention Trial – see also Appendix B**

| **Measure** | **Rationale** | **Further information** |
|---|---|---|
| **PHQ-2 (see L in appendix below** | **Brief measure of depression** | **2-item scale** |
| **GAD-2 (see L in appendix below)** | **Brief measure of anxiety** | **2-item scale** |
| **Stress**<br><br>**How much stress have you had in your life over the <u>past 7 days</u>?**<br>**(StressSev).**<br>**Scored as: Very severe (4), severe (3), moderate (2), mild (1), none (0), list with circle to select** | **Single item to assess stress** | **laid out with ratings as choice buttons along horizontal paralleling other questions in this section** |
| **During the past 7 days in a stressful or upsetting situation:** | **Use of cognitive and behavioural skills, 6-items, these reflect different potential strategies that individuals may use and** | **Brief questions to capture cognitive and behavioural strategies from** |

| | | |
|---|---|---|
| **a) How often did you take a moment to question your interpretation of what was happening when you got upset (e.g., look for a more positive or balanced explanation; weigh up different accounts, try and put things in perspective)?**<br>**0= Never, 1=Rarely, 2=Occasionally, 3=Sometimes, 4=Often, 5= Very often, 6= Always;**<br><br>**(b) How helpful was this in making you feel better?**<br>**0=Not at all helpful, 1 = Slightly helpful, 2=Somewhat helpful, 3=Moderately helpful, 4= Fairly helpful, 5=Very helpful, 6=Extremely helpful, N/A=Didn't do this last week**<br><br>**During the past 7 days in a stressful or upsetting situation:**<br>**(a) How often did you plan and/or do activities you knew you would enjoy?**<br>**0= Never, 1=Rarely, 2=Occasionally, 3=Sometimes, 4=Often, 5= Very often, 6= Always;** | **that may be provided within the intervention** | **Cognitive and Behavioral Response to Stress Scale (CB-RSS) Miner et al., 2015, with addition based on student feedback, see Appendix M for example of questionnaire** |

| | | |
|---|---|---|
| **(b) How helpful was this in making you feel better?**<br><br>**0=Not at all helpful, 1 = Slightly helpful, 2=Somewhat helpful, 3=Moderately helpful, 4= Fairly helpful, 5=Very helpful, 6=Extremely helpful, N/A=Didn't do this last week**<br><br>**During the past 7 days in a stressful or upsetting situation: (a) How often did you use relaxation or similar techniques to soothe, focus or calm yourself (e.g., meditation, breathing, focusing attention, imagery)?**<br><br>**0= Never, 1=Rarely, 2=Occasionally, 3=Sometimes, 4=Often, 5= Very often, 6= Always;**<br><br>**(b) How helpful was this in making you feel better?**<br><br>**0=Not at all helpful, 1 = Slightly helpful, 2=Somewhat helpful, 3=Moderately helpful, 4= Fairly helpful, 5=Very helpful, 6=Extremely helpful, N/A=Didn't do this last week** | | |

| | | |
|---|---|---|
| **During the past 7 days worry is something that**<br>**"I do automatically"**<br>**"I do without thinking"**<br>**"I start doing before I realise I'm doing it"**<br>**Each of 3 items rated on 1 to 7 scale from Strongly disagree to Strongly agree [Strongly disagree, Moderately Disagree, Slightly Disagree, Neither Agree or Disagree, Slightly Agree, Moderately Agree, Strongly Agree)** | **Change in habit applied to worry, 3 items – to assess whether rumination/worry becomes more or less of a habit; the intervention focuses on changing habit** | **Adapted items from SRHI index, Gardner et al., 2012, laid out with ratings as choice buttons along horizontal paralleling other questions in this section** |
| **During the past 7 days problem solving is something that**<br>**"I do automatically"**<br>**"I do without thinking"**<br>**"I start doing before I realise I'm doing it"**<br>**Each of 3 items rated on 1 to 7 scale from Strongly disagree to Strongly agree**<br>**(Strongly disagree, Moderately Disagree, Slightly Disagree, Neither Agree or Disagree, Slightly Agree, Moderately Agree, Strongly Agree)** | **Change in habit applied to problem-solving, 3 items – to assess whether more helpful responsive becomes more or less of a habit** | **Adapted items from SRHI index, Gardner et al., 2012, laid out with ratings as choice buttons along horizontal paralleling other questions in this section** |

| | | |
|---|---|---|
| **Please indicate how often you behaved in the stated manner during the past 7 days on a scale from 1 (Almost never) to 5 (Almost always).**<br>**"When I'm going through a very hard time, I give myself the caring and tenderness I need";**<br>**"When I feel inadequate in some way, I try to remind myself that feelings of inadequacy are shared by most people"** | **Self-compassion, 2-items; the intervention includes a self-compassion element** | **Selected items from SCS-SF (Self-Compassion Scale – Short Form), items from Self-kindness and Common humanity scales – see N in appendix for example of shortened questionnaire** |
| **2-items from Brooding questionnaire – "Indicate whether you never, sometimes, often or always thought or did each of the following when you felt sad, down or depressed over the past 7 days.**<br>**A. Think "Why do I always react this way?"**<br>**B. Think "Why can't I handle things better?"** | **Rumination, 2-items** | **Adapted from the RRS-B-Brooding 5-item questionnaire,**<br>**Treynor et al., 2003, see Appendix A for the full questionnaire – this uses two items from it** |
| **"In the last seven days I feel better prepared to handle situations I could not handle before" rated using a seven-point Likert scale ranging from −3 ("absolutely not true), 0 ("neither nor") and +3 ("absolutely true").** | **Self-efficacy/Mastery** | **Laid out as horizontal rating scale underneath the description item** |
| **"In the last seven days, I understand myself and my problems better" rated using a seven-point Likert scale ranging from −3** | **Problem clarification** | **Laid out as horizontal rating scale underneath the description item** |

| | | |
|---|---|---|
| **(“absolutely not true), 0 (“neither nor”) and +3 (“absolutely true”).** | | |

### 3.4 Primary endpoint/outcome

The primary endpoint of the trial is at 12 months post randomisation.

### 3.5 Secondary endpoints

The secondary endpoint is the 3 month follow up.

### 3.6 Exploratory endpoints

There are no exploratory endpoints.

### 3.7 Endpoints/outcomes

**Table 9 Endpoints/outcomes**

The following table displays which measures are collected at each of the assessment points:

| Measure | Detail | Size | Screening | Baseline | 3 months | 12 months |
|---|---|---|---|---|---|---|
| 5-item Brooding scale | Above previously established cut-offs for worry and rumination; brood >= (defined as scoring in top quartile in one measure and at least top tercile in other measure). This is 40 on the full measure so needs recalculating for 5-item. For 5-item scale (range 5-20), cut-off is >=10 (Cook et al., 2019 | 5 items | X | X | X | X |
| Short-form Penn State Worry Questionnaires | Above previously established cut-offs for worry and rumination; PSWQ >= (defined as scoring in top quartile in one measure and at least top tercile in other measure), this is 50 on the full scale, needs recalculating for short-form | 7 items | X | X | X | X |
| LIDAS self-report questionnaire /interview means of checking | Screening for current and past depression and primary outcome; To be eligible for prevention study, at | Conditional questionnaire asked ever and last 3 months ranging | X | | X, last 3 months | X, last 12 months |

| | | | | | | |
|---|---|---|---|---|---|---|
| current diagnosis inclusion exclusion criteria items | screening do not currently meet diagnostic criteria for major depression (in the last month, 30 days); As a prevention study, need to exclude those with current episode of major depression – likely to be eligible for acute treatment trial; Includes contingent questions so will vary in length depending on prior answers | 4 questions to 22 depending on answers<br>3 Conditional risk questions<br>7 other items<br>On past health; | | | | |
| PHQ9 | Secondary outcome measure; as screening measure - check that not overly-elevated current depression symptoms – exclude if >20 | 9-item plus 3 conditional risk questions<br>parental past health 2 items | X | X | X | X |
| Self-reported check on history of diagnosis (CIDI-SR?) | No history of drug/alcohol/ substance dependence; exclusion criteria | | X | | | |
| Self-reported check on history of diagnosis | No history of psychosis; exclusion criteria | | X | | | |
| Self-reported check on history of diagnosis | No history of bipolar disorder; exclusion criteria | | X | | | |

| | | | | | | |
|---|---|---|---|---|---|---|
| Self-reported check | Not currently receiving psychological treatment at point of entry into study; exclusion criteria | | X | | | |
| Question re university of study (drop-down list – with 6 primary universities then other -with text option) | University student - Necessary to provide independent informed consent | | X | | | |
| Age | 16 or older - Necessary to provide independent informed consent | | X | | | |
| Access to PC/smart phone/internet | Necessary for delivery of intervention | | X | | | |
| Gender identity (M/F/neither/both); sexual orientation, race/ethnicity; birthplace, educational attainment, topic of study | Demographic measures to explore diversity of sample and representativeness against student body | | | X | | |
| Past history of depression; | Obtained from LIDAS/CIDI or equivalent | | X | | | |
| Current medications, healthcare utilization, lifetime mental health | | | | X | X | X |

| | | | | | | |
|---|---|---|---|---|---|---|
| treatment (age of onset, duration, type, hospitalisations – CIDI); | | | | | | |
| high current stress severity, recent stressful life events (AEQ), stress reactivity (perceived stress scale; PSS); | | | | X | X | X |
| WEMWBS | Secondary outcome | 7-item | | X | X | X |
| GAD7 | Secondary outcome measure | 7-item | | X | X | X |
| WSAS | General Functioning | 5-item | | X | X | X |
| ADSUS-adapted<br>Physical health demographic | Estimate of health costs | 2-14 items<br>1 item | | X | X 3mth | X 12mth |
| AEQ /stress (PSS, ATQ) | Adverse events/stressful life events | 5 item, 5 item | | | X | X |
| Self-report or consent to access student records | Academic records/Self-reported academic outcomes | | | X | X | X |
| Use and application of intervention | | Developed for study (3-items) | | | X | X |

| | | | | | | |
|---|---|---|---|---|---|---|
| Adapted Client Satisfaction with Treatment Questionnaire-8 | Satisfaction with intervention | | | | X | |
| Use of services /treatment received– questionnaire to be developed incorporating NHS and student services | To understand level of treatment sought and received – from list of student, NHS, and other options | | | X | X | X |

## 4 TRIAL DESIGN

**Design**
We will undertake a Phase III superiority parallel 2-arm randomised multicentre randomized controlled trial. Our study design follows MRC Complex Interventions Guidelines and the theoretical mechanisms targeted by intervention have been confirmed. The design of the trial is illustrated in **Figure 1**.

***Conditions.*** Appropriate participants (see inclusion/exclusion criteria below) will be randomly allocated on 1:1 to the following two conditions using an intention-to-treat (ITT) approach:

(A) Offered an unguided internet-delivered RF-CBT package via an online platform (mobile app) in addition to usual practice (*experimental intervention group*)

(B) Usual practice alone (usual practice control group)

***Assessment points.*** Within the prospective cohort, the same outcome measures will be obtained at baseline (M0), 3 months (M3) and 12 months (M12) follow-up (each post-randomisation).

## 5 TRIAL SETTING

The recruitment centres are the University of Exeter, UK, which provides the coordinated central hub through which participants will be screened, randomised, data collected, treatment offered and follow-up assessments delivered, and the other universities in the project, who will all provide sources of recruitment into the study (e.g., advertising the study locally, in lectures, via websites, via social media): University of Oxford, University of Cardiff, King's College London; University of Newcastle, University of Southampton. There will also be an option for students to access the trial from other universities [Other option, e.g., direct response to social media advertising).

All participants will be directed to the trial recruitment website where they can find out more information about the study. Those interested will then link to the screening feature, where their eligibility will be assessed with a brief set of measures – if eligible, the participants then proceed to give full informed consent and complete the baseline assessment. The interventions will be provided through a licensed internet provider in which the RFBCT treatment is configured in the content management system, using a mobile app format: at randomisation, participants will be given access to the internet platform and encouraged to sign up. Follow up data will be collected online through the programmed electronic data capture system (EDC) and then collected by, stored, and organised by the EXCTU.

Researchers at each site will promote participation in the study. All queries, intervention and assessment follow-ups will be dealt with centrally from Exeter. All processes are centrally run from Exeter. The only role and responsibility for the other universities is to advertise and publicise the trials – alongside other activities they are doing for the wider Nurture-U project.

## 6 PARTICIPANT ELIGIBILITY CRITERIA

The sample will be a selected group of university students (no age limit, as long as able to provide informed consent, i.e., older than 16), who indicate potential increased vulnerability for mental illness at the screener completed on the online/app test battery in the form of more extreme scores on standardised measures of worry and rumination. Thresholds will be set so that those scoring in the top (worst) 25-33% on the measures for worry and rumination are eligible for the trial (i.e., those scoring above risk thresholds; risk thresholds will be based on worst performing quartile/tertile on each measure,

based on prior studies finding this to predict increased risk, e.g. Topper et al., 2017 – in practice, this means scores of >11 for worst tercile, > 12 for worst quartile on the brooding scale and >24 for top tercile and >26 for top quartile on the Penn State Worry Questionnaire short-form ).

We will exclude those individuals reporting current episode of major depression on screening measures that provide diagnostic indices – as the primary outcome is prevention of depression, we need to exclude those with current major depression. Those with current episodes of major depression or any history of mania or psychosis will not enter the trial and will be directed to their GP and signposted to national and local services and where appropriate to other relevant Nurture-U trials (e.g., for individuals with elevated symptoms of anxiety and depression) We will monitor screening and demographic information (age, gender, ethnicity) across included and excluded participants to inform the implementation phase.

### 6.1 Inclusion criteria

**Inclusion criteria**

(1) Aged 16 plus based in the UK, attending university (predominantly one of the six partner universities or other HE institution e.g., associated HE institution, e.g., Falmouth University for University of Exeter).
(2) Reporting elevated levels of worry and rumination on standardised questionnaires (scoring in at least worst tercile and worst quartile on brooding scale and PSWQ: this means scores of >11 for worst tercile, > 12 for worst quartile on the brooding scale and >24 for top tercile and >26 for top quartile on the Penn State Worry Questionnaire short-form)
(3) basic literacy in English as indicated by ability to complete consent and online questionnaires (12year old reading age or better).
(4) Ability to provide informed consent
(5) Available for the full duration of the study (12 months)
(6) Regular access to a relevant smart phone, tablet, PC or laptop necessary to use the intervention (using android or IOS systems)

### 6.2 Exclusion criteria

**Exclusion criteria**

(1) Meeting criteria on self-report electronic screening questionnaires for any of the following
    a. current episode of major depressive disorder
    b. active suicidality; or
    c. any history of severe mental health problem (i.e., bipolar/psychosis/mania/drug/alcohol dependence);
(2) Currently receiving psychological therapy or counselling or antidepressants or other psychiatric medication.

## 7 TRIAL PROCEDURES

University students meeting inclusion criteria will be enrolled in the cohort via the study website. Once enrolled and consented, each participant will be followed for a minimum of 12 months, with assessments at each of 3 and 12 months. UNEXE will have overall responsibility for the monitoring of the delivery of the recruitment and retention into the cohort.

All baseline assessments will be online through a serious of questionnaires created within the EDC system (Redcap). The trial website will host a welcome screen with Instagram feed and informational videos. The website will link to the privacy and data protection policy for the trial and this will be downloadable.

The EDC system will host:

- Pre-screening. There will be a set of pre-screening questions to quickly check if participant may be eligible for the study (and relative eligibility for other Nurture-U trials) [if elevated worry, rumination; if not currently depressed – see ***Table 8*** for details). Participants complete a brief consent to complete these measures. Those meeting eligibility than proceed to the full consent and baseline measures. Full details of the questions asked and information provided in the help pages can be found in Appendix.
- In the consent (a) questionnaire the information sheet will be presented and consent form with fields for completion. Consent A asks for consent to take part in the screening for the trial. Recruits will be asked for their contact details during the consent process and if consent is given then they can screen for eligibility and are assigned a Screening ID number unique to them. The recruit will automatically be emailed or provided with a copy of the information sheet, the privacy policy and the consent form for their records.
- Those excluded will be automatically routed to pages detailing why, with links to sources of help. There will be pages tailored for current/past depression, suicide risk, mania/psychosis.
- Those meeting eligibility criteria will be asked to consent to take part in the trial.
- Those providing consent will be asked to complete a series of questionnaires designed to assess their relevant baseline demographics and outcome measures.
- Participants can at any time during the assessment save what they have done and will have been emailed when they gave consent A so that they can complete their assessment in stages. The link is live for 2 weeks so they have that long to complete the assessment and read the materials before consenting to take part in the trial (consent b). Two weeks was chosen as some of the questionnaires ask about wellbeing in the last 2 weeks so if the time period was longer, those results would be out of date.
- When the participant has completed their assessment, a trigger is sent to the CTU database which signals it to collect all the participant's data through the EDC.
- A message is also sent to participants to confirm that they have completed the assessment.
- When participants consent to take part in the trial and complete the baseline assessment, participants will be randomised into one of the 2 conditions: usual practice versus usual practice plus unguided i-RFCBT (the novel experimental intervention) and assigned a new study ID number unique to them.
- Randomisation will be via an automated system programmed into the database system.
- The proposed process for eligible and consented participants to access the internet treatment is via being signed up into the platform by a therapist/administrator who can add the patient to the treatment platform using their email address via the dashboard. This will require an automated message to the relevant staff member informing them of need to set-up participant, with access to protected database to do so. It also requires an email to go to participant to inform him/her of their randomisation and what will happen.
- Participants randomised to the internet RFCBT will set their own password and work through the mobile app package at their own pace, without support.
- The Exeter EDC system will host the follow up assessments and the system will automatically email reminders to participants with a link to access the site so that they can complete follow ups at month 3, and 12 months. The data will automatically be collected and stored on the EXCTU database.
- The mediator questions also need to be sent out weekly from week 1 to week 8 post-randomisation.

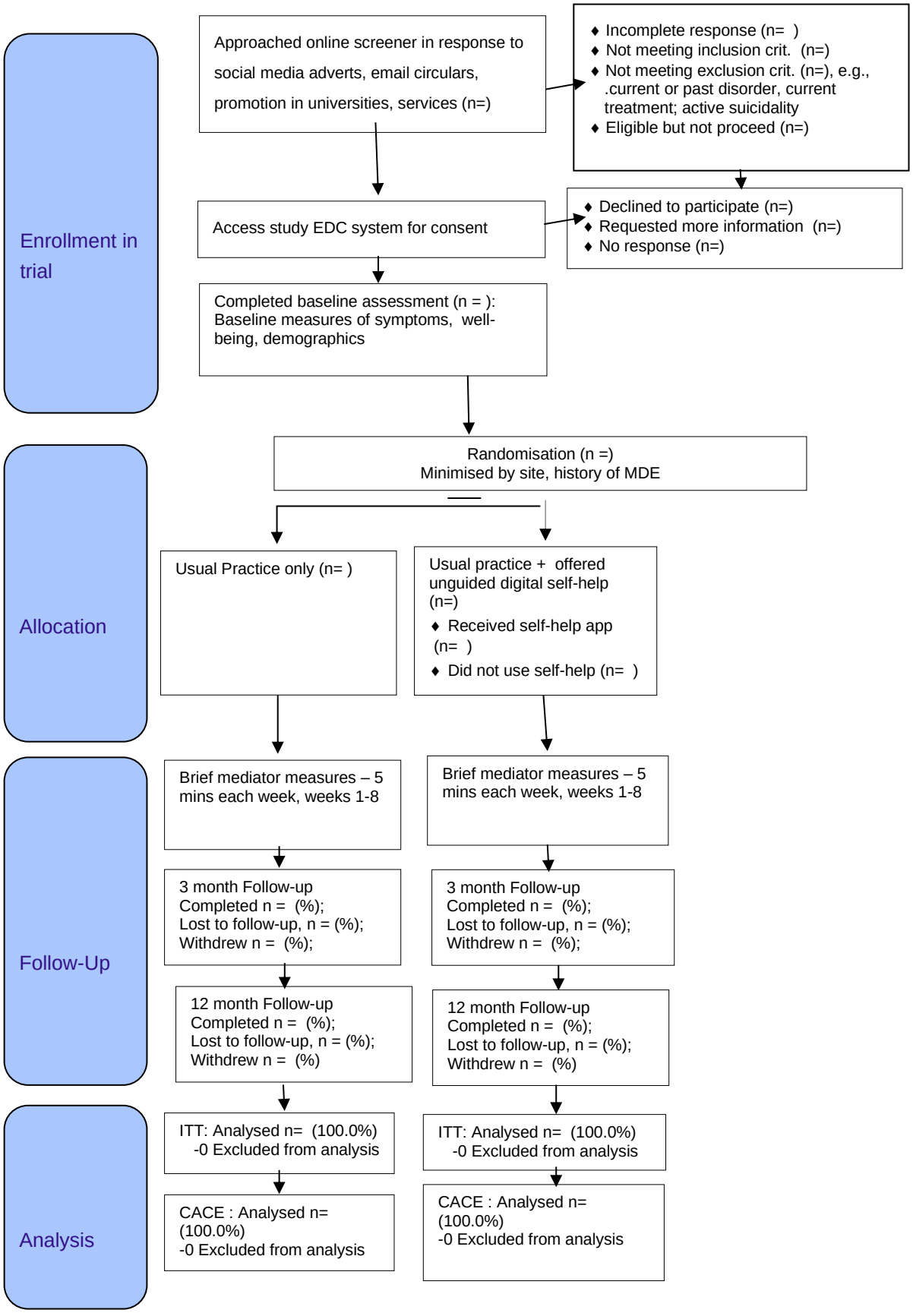
## 7.1 Recruitment

### Recruitment strategy

The consort diagram for the full trial can be found in **Figure 2**:

**Figure 2 CONSORT FLOW DIAGRAM for i-RCBT PREVENTION randomised controlled trial**

Reporting of the study and of statistical analyses will follow the CONSORT standard (Schulz, Altman, & Moher, 2010). Trial will be registered in advance and study protocol will be published.



### 7.1.1 Participant identification

We will recruit from the general university population initially across the 6 partner Universities in the grant. Posters, emails, websites, presentations, and social media will all advertise the study for students who wish to build self-esteem and confidence and reduce worry and stress. We will look for participants with self-identified concerns with self-esteem, confidence, stress, worry, and rumination to oversample this higher-risk group. The recruited sample is likely to be predominantly female based on prevalence of risk for anxiety and depression and prior studies; we will actively seek to recruit more male participants.

Recruitment of the cohort will follow successful models (e.g., http://www.mappiness.org.uk/, 66,000 participating), with study and app advertised as a means to enhance one's own confidence and reduce worry.

Using proven methods, and as recommended by the UK Young adult's Mental Health Advisory Group (YPMHAG) and the University of Exeter's emergent Young Adults' Lived Experience Group (YPLEG), site researchers will recruit participants through

- multiple traditional and social media (posting and advertising on Facebook, YouTube, Instagram, SnapChat, Google, MySpace, Twitter, TikTok, study website, through media influencers/vloggers, etc adjusted by cost/frequency as needed); social media analytics will be used to enhance recruitment;
- app store, Googleplay store;
- email circulars and local promotion (posters, emails, newsletters, signposting by staff) to university departments;
- snowballing approaches;
- promotion to at risk groups, targeted adverts (e.g. by geographical area), health portals, and via relevant charities over 12 months across the recruitment sites

The internet, a national digital community available anywhere at any time, overcomes access difficulties due to geographical location, cost, poor mobility, lack of time, and supports privacy. Self-referral avoids potential "gatekeepers" to help and other potential barriers such as requiring access to services. It is consistent with young adult's high internet usage.

All partner universities will recruit to electronic surveys (WS#1) and RCTs (WS#4). For each of the survey, online MHL course, and RCTs, following student-led engagement/awareness campaigns, we will invite relevant students at each university into the study via campus emails, local advertisements, social media and recruitment websites and ask them to consent electronically to participate.

We will work with our Student Advisory Board to develop engaging and meaningful student-led engagement and recruitment campaign materials for the trial. We will also use the wider campaign for the overall project and parallel studies to support recruitment into the trial – for example, we will seek for 1000s of students to complete our mental health survey x 2 times a year and this will include measures that can signpost relevant participants to this trial. Similarly, for greater efficiency, there will be transfer between workstreams (e.g., students in surveys scoring above symptom cut-offs directed to RCTs; those excluded from one RCT directed to other RCTs if appropriate).

The student mental health project will activate accounts in several social media to provide information about the project, all linked to the Nurture-U brand. These accounts will be used to aid recruitment in the trial:

- YouTube:
- Twitter:
- Facebook:
- Instagram:
- Vimeo:
- Linkedin:
- Google
- TikTok

No participants will be recruited through or at NHS or medical organisations or personnel.

In response to promotion and advertising or word-of-mouth, potential participants click on a link that goes to trial electronic data capture system that provides information about the study and screening for suitability in a logical conditional sequence. Individuals who met these eligibility criteria proceed to more detailed information and provide consent to join the TRIAL. The baseline assessment is automatically provided through this online platform. We will ask about usual care received by participants at baseline and then again at follow ups. Once judged eligible for the study and having consented to participate, a participant is randomised and set-up on the intervention if randomised to that arm.

**Past evidence**
Our multiple recruitment routes have each proven effective. Online and social media advertising is effective (1500 participants recruited for well-being study over 2 months via Facebook adverts, Cobb & Poirier, 2014). We have good evidence on conservative estimates that we can recruit at an approximate rate of 14 young persons per week at each site on average, making feasible an overall target of 684 participants recruited into the cohort over 16 months. In previous digital intervention studies in the UK, we recruited on average 14 participants per week for internet treatment using Facebook adverts and at least 20 a week using email circulars to universities for a self-help mental health intervention for undergraduates (Freeman et al., 2015). In the ECoWeB project, we principally recruited through social media advertising and through circulations within universities and we recruited n=3800 across 4 countries (n=1200 in UK only) across 9 months (1/3 meeting high risk criteria similar to this study -i.e., n=1266 – i.e., in UK based at one university recruited 33+ a week). A recent pilot trial for an app to help with worry that sought to recruit students with elevated worry recruited 236 participants in 6 months with limited direct advertising and recruitment focused in one university (i.e., 10 a week).

### 7.1.2 Screening
Participants will be screened by an EDC system set-up and managed by Exeter CTU for university students - those under 16 will automatically be screened out pre-assessment. Website users who report having current risk will be taken to the feedback screen where they will be advised that we are sorry to hear that they are feeling that way, to please contact their GP and to give them sources of online help and support. For those with current depression that are not indicating risk we will provide information on where to get help for symptoms of depression and advise that they contact their GP and direct them to another Nurture-U trial focused on acute treatment of depression and anxiety.

### 7.1.3 Payment
Participants will be paid in electronic vouchers for taking part in the two follow up assessments; we will pay 10 pounds for completing the mediational measures over 8 weeks, 10 pounds for completing the 3 month follow up and 10 pounds for completing the 12 month follow up.

Researchers will be able to run reports on the Exeter CTU database to identify which participants have completed follow ups at the key payment points (after 3 month and 12 month follow ups). Site

researchers will arrange for the payment of participant using electronic shopping vouchers, which can be emailed or sent by text or via direct bank transfer. No travel expenses are anticipated for participants as all assessment and intervention contents are provided remotely via digital platforms (website, app).

### 7.2 Consent

We anticipate that university students will be autonomous independent young adults who are legally recognized as being at or above the age of majority and able to provide their own informed consent to their participation in research (aged 16 or over for the UK).

Young people will be initially routed to or seek out the study website and will be provided with the participant information sheet (which will be submitted with the protocol), consent form A and data protection policy to review on the screening website, prior to completing screening measures. There will be a check box at the bottom of the information sheet which participants will need to check before they can sign the consent form. Participants will then be asked to read, date, and electronically sign consent form A and provide their contact details. Consent form A asks for consent to undertake the screening assessment and confirmation that the participation understands the nature of the study (the consent forms will be submitted for review with this protocol).

When consent is given they will automatically be emailed a copy of the consent form, information sheet and data protection /privacy policy.

Participants will then be asked to complete brief background screening measures to determine eligibility on the online screening website. Non-excluded recruits can stop and save their assessment at any time and be emailed a link to return to the assessment. The participant will have 2 weeks in which to be able to return to their part completed assessment. After this time, they would need to start the assessment again if they wanted to take part.

If a participant completes the screening assessment and is eligible for the trial then they will be presented with consent form B3 which asks them to consent to taking part in the trial. Recruits are advised that they can take time to consider taking part and can save their assessment whilst they do so.

Once participants have consented to take part in the trial, then they are provided with the baseline assessment for the trial to complete. On completion of the baseline assessment, participants will be randomized automatically and then participants are advised that they have completed the baseline assessment and that they will be contacted to be informed of their randomisation. At this stage the recruit is randomised and be given a unique participant trial number.

All participants will be given the option to seek further information from the research team, with contact details to the relevant research team provided (email, and/or telephone number as available). This information will be provided on all versions of the information sheet and on the help menu of the study website.

Our proposed procedures for recruiting and screening students have previously been approved by local and national ethics committees, and we will obtain approval before commencing the study. The sponsor will take out civil liability insurance to protect participants.

### 7.3 The randomisation scheme

At the point of randomisation participants will be automatically registered on to the trial using the EDC system. Randomisation is after the online consent, the screening process and after the online baseline assessment. There is a two-part consent process which in the first part asks for permission to screen and take part in the assessment. The second part of consent at the end of the screening assessment asks for agreement that the participant wants to take part in the main study. Participants can stop the assessment at any stage and be emailed a link to return the screening website. This allows them to have time to consider the participant information which they have read on screen and which is emailed to them. The email link will be live for 14 days. After this time the participant will need to contact the site to ask for the link to be reset.

Random selection to the 2 arms (usual care vs usual care plus unguided i-RFCBT) will be conducted automatically by means of a secure service created and managed by the Exeter Clinical Trials Unit (CTU) in conjunction with the trial statistician. This will be independent of the trial researchers.

To promote balance across key participant characteristics across groups, we will stratify allocation by trial site (reflecting source of recruitment – Exeter, Oxford, Southampton, Newcastle, KCL, Cardiff, Other), and history of depression (no history vs past history of depression – given that this is a strong predictor of future depression and was used in a prior study – Cook et al., 2019). Stratification will be used (on these two variables) and blocking will be used with minimum block size of 4 and maximum block size of 6, occurring at random to maintain concealment. Minimisation will not be used.

**Protection from bias**

We will adopt prior registration and publication of the trial protocol. Independent web-based computerised randomisation will be conducted to ensure generation of an unpredictable allocation sequence and concealment of participant allocation and of allocation sequence and prevent selection bias and confounding. We will use standardised assessments with data collected automatically through the website. The use of self-administered measures will eliminate observer bias. A detailed statistical analyses plan will be prepared and agreed with Trial Steering Committee and Data Monitoring and Ethics Committee before any analysis is conducted. The trial statistician will remain blinded to group allocation until the main data analyses have been undertaken and interpretation of the trial results have been agreed by the relevant committees. Attrition bias will be minimised by having robust trial procedures to prevent data loss such as email, text, and phone reminders to encourage follow ups.

#### 7.3.1 Method of implementing the randomisation/allocation sequence

Participants will be randomised by a programmed system within the Exeter CTU EDC system and database (programmed in RedCap). This will be an automated process. The Exeter CTU EDC system will contact an unblinded team member (administrator/therapist) indicating when an individual [by study ID] has been randomized to the active intervention. This team member will then access the relevant details in the EXCTU database and manually set up the participant in the internet treatment platform using administrator rights via the internet platform dashboard. An email will also need to go to the participant indicating the condition to which they are randomised and informing them what to expect. The relevant unblinded team member will also be able to monitor if the participant has accessed the intervention and check if there are any difficulties and encourage to sign-up.

Detailed procedure for randomisation:

1. Participants are randomised on a 1:1 basis into the 2 arms on an intention-to-treat basis: usual practice plus unguided i-RFCBT (the experimental intervention), usual practice versus continuing with usual practice. Site and history of depression are used for stratification.

2. The system must record the allocation and the date randomised.

3. The trial manager and at least one other researcher remain blind to the allocation; the participant will be aware of which intervention received. Thetherapist/administrator will be unblinded in order to set-up participant on internet platform.

4. On successful randomisation, a finish page is displayed with a message telling the participant to look for an email message from the trial team.

### 7.4 Blinding

The follow up data will be routinely collected online using the website/EDC system (and the reminders for this will be sent out automatically by email from the EDC system). This will prevent the follow up results being affected by the site researcher.

Trial researchers who will be blind to treatment allocation include the CI and Trial Manager. The Trial Manager will be in direct contact with participants to answer technical queries. The trial therapists will be unblinded and will be in direct contact with participants to follow up risk. It is possible that a researcher could become unblinded during those (infrequent) conversations if the participant mentions details of the intervention.

Should a blinded researcher become unblinded then this will be logged as an unblinding and any telephone-based chasing of follow up data for that participant in future will be conducted by another blinded researcher at the site (if available). Therefore, only blinded researchers will attempt to collect the primary outcome measures by telephone if the participant is unwilling to use the electronic platform for this purpose. Unblinded researchers will not discuss information relating to condition with blinded researchers. During any contact with participants the blinded researcher will remind them not to divulge to which condition they were allocated. In the event that there are no unblinded researchers and telephone collection of follow up primary outcome is possible, this data will be collected, but will be logged and clearly marked as ‘collected unblinded’. This will allow the statisticians to control for this in their analysis. The statisticians and the Steering Committee will be blinded to intervention until the analysis is done and they are interpreting the results.

### 7.5 Emergency Unblinding

It is extremely unlikely that a researcher other than the administrator/therapist responsible for setting participants up on the intervention would need to be unblinded, even in cases of risk. The trial code would only need to be broken for valid medical or safety reasons, for example, in the case of a serious adverse event, where it is necessary for the investigator or DMEC to know whether there is a relationship between condition and adverse events. In these circumstances, the research team will remain blinded. Where a person raises clinically relevant concerns or reports risk, and where knowing the trial condition is relevant, one of the project team dealing with this participant can potentially be unblinded to the participant’s condition to support their care and further support them – in many cases, it may not be necessary to know the condition. The action taken according to the risk protocol would be the same, regardless of condition. The PI will be able to request the condition from the CTU if there are any adverse events within a week. In the

case of a serious adverse event, it will be necessary for principal investigator / site-relevant clinician to be unblinded for safety reasons and for accurate reporting onto the DMEC.

The DMEC will be unblinded in aggregate to cases of serious adverse events (i.e., knowing condition for those reporting serious adverse events, but no other personal information) to have an overview of the relationship between condition and risk.

### 7.6 Baseline data

The CRF for the collection of baseline is available as a separate Appendix. These data will be collected after the screening section of the screening website. The measures used have been described previously in Section 3.

### 7.7 Trial assessments

Assessment will take place at baseline and then at 3 and 12-months post randomisation. The 12-month follow up will be the primary endpoint. All assessments will be through Exeter CTU managed EDC system. Only if participants have not responded to email and text prompts to complete their follow ups at 3 or 12-months will they be contacted by phone and asked to provide the primary outcome measures only on the telephone. (We have found that in previous studies participants are often willing to provide these measures on the phone rather than complete the full online assessment). The results of the assessments are only to collect research data for the trial and will not be provided to medical practitioners. The only exception to that would be if a participant indicates suicide risk and asks us to provide their assessment results to their medical practitioner. They would need to give written consent for this and provide us with the contact details to do so. See risk protocol in Appendix 16.

### 7.8 Long term follow-up assessments

Participants will be followed up at 12 months following randomisation. The structure and nature of this follow up will be the same as the 3 month follow up. There will not be any follow up after 12 months.

**Table 10 The Schedule of Procedures**

| **Procedures** | **Screening** | **Baseline (at same time as screening)** | **3 month follow up** | **12 month follow up** |
|---|---|---|---|---|
| Informed consent | Yes | Yes | Yes | Yes |
| Further Demographics | Yes DOB University | Yes Education level, ethnicity, sexuality | NO | NO |
| Mental Health History | Yes | No | No | No |
| Current Physical conditions | No | Yes | NO | No |
| Current medications | No | Yes | Yes | Yes |
| Eligibility assessment | Yes | No | No | No |
| Randomisation | No | Yes | No | No |
| Access to intervention | No | No | Yes | Yes |
| Compliance with intervention | N/A | N/A | No | No |
| Assessment of wellbeing and depression | Y | N | Y | Y |
| Assessment of current functioning | N | Y | Y | Y |
| Assessment of service use | N | Y | Y | Y |
| Adverse event assessments | N | N | Y | Y |

**Strategies to ensure retention in the study**

Attrition is often high in internet studies, especially those solely conducted through electronic media (see Andrews et al., 2010; Van Ballegooijen et al., 2014). Based on previous studies including our guided internet study for rumination (74% retention at 36 months) and internet self-help feasibility study (70% retention at 15 months), where the greatest loss-to-follow-up occurred at first follow-up and only marginally declined between later follow-ups, we have powered for a 20% loss-to-follow-up at 12 months. This possible attrition has been factored into our calculation of power and sample size.

To maximise retention, we plan to update participants and other key stakeholders about the study's progress through social media and the study website. Participants will be offered an online/app voucher or direct bank transfer in recognition of their time spent on the completion of questionnaires and interviews. Follow-up attrition will be reduced by directly contacting participants through the website and by sending regular updates and news, and by obtaining (with participant permission), relevant electronic contacts (e-mail; mobile telephone), repeated automated attempts to contact, use of text reminders for completing follow-up assessments, and an honorarium for each completed assessment. These approaches have been effective in our previous trials. For example, in earlier studies using online interventions with adolescents we were able to retain 83% of participants in the intervention and 81% of

participants in the study until the 12-month follow-up (Topper et al., 2017) and 70% of adults at 15 months (Montero-Mayin et al., 2016).

### 7.10 Withdrawal criteria

Participants can choose whether they want to stop using the internet/app intervention, or if they want to withdraw from the trial completely (including all assessments) at any time. Participants will also be withdrawn from the trial if the site clinical advisor, or the participant's medical practitioner advises that this is best for their wellbeing. A log will be kept of the participant number, reason for and date of all withdrawals from the trial. Participants who met the inclusion and exclusion criteria at baseline will not be replaced. Participants who did not meet the criteria at baseline can be replaced and their data removed from the data set. Participants who withdraw from the trial will not be followed up. Once a participant withdraws, all email and text notifications that are set on auto will be removed.

### 7.11 End of trial

The final follow ups are due in May 2025 and the project will end on 31st August 2025. Any early termination of the trial will be reported to the ethics committee, TSC and sponsor within 15 working days.

## 8 TRIAL ARMS

**Unguided internet-RFBCT (experimental intervention group)**

The experimental arm is unguided internet-delivered rumination-focused cognitive behavioural therapy (i-RFCBT), delivered via an online treatment platform in a mobile app format. This intervention has previously been tested in guided versions successfully in prior RCTs (Topper et al., 2017; Cook et al., 2019).

The self-help i-RFCBT will be delivered online and can be accessed on smartphone, tablet, PC or laptop to maximise means to access self-help, to benefit from increased engagement by allowing users to choose their preference of which to use, and to utilise the relative advantages of the medium (portability for app). The intervention includes text, pictures, audio-recordings, animations, audio-exercises to practice, questionnaires with tailored feedback and quizzes. It will be designed for iOS and Android use. The content will focus on providing psychoeducation, tips, advice, strategies, and reflective exercises and learning tests relevant to reducing worry and rumination. It has been adapted to be usable in a mobile app format.

Overall, the intervention targets the shift away from maladaptive rumination and worry to more adaptive problem-solving. This treatment builds on evidence-based developments that focus on identifying warning signs and repeated practice to train people out of unhelpful habits (rumination, self-criticism) and build helpful habits for resilience (problem-solving, self-compassion) (Watkins, 2008; Watkins et al., 2008, 2009, 2011, 2012). The intervention utilises well-established and proven cognitive-behavioural therapy principles and builds on existing effective guided web-based interventions (Topper et al., 2017). The app self-help coaches and advises participants to spot warning signs for rumination, worry, and stress and to repeatedly rehearse and practice an alternative strategy to such signs, using implementation intentions (If-Then plans) e.g., being more concrete, opposite action, problem-solving, relaxation, self-compassion, assertiveness. This innovative training approach is well-suited to unguided self-help as it involves easy-to-follow simple rehearsal of skills linked into daily life: it is a stepwise departure rather than a proxy to therapy. In addition, focusing on habit change may produce prolonged and amplified benefit beyond 1 year (Watkins et al., 2011). The combination of a focus on easily

identifiable non-stigmatising, and motivating risk factors for young adults (e.g., worry, low self-esteem), the simple rationale, tips and exercises, and targeting habit change together make this variant of self-help potentially more efficient and engaging. The intervention is effectively split into 6 modules with participants encouraged to take approximately 1 -2 weeks to work through each module. The internet package provides automated contingent feedback to the answers provided by the participants and it also sends automated reminders to participants who haven't logged into the intervention package each week.

The content and design will be refined for university students in light of focus groups with the Student Advisory Board, by making changes in internet platform content management system. This includes delivering it in a mobile app platform format. For further details on the package see Cook et al., 2019.

**Usual practice control *(Usual practice control group)***
Usual practice control is carrying on as normal, i.e., receiving usual care and 3 and 12 month assessments delivered via the screening website. This could be no intervention, NHS interventions or support from university wellbeing or welfare services. We will thus assess what participants received during the follow-up period.

### 8.1 Trial restrictions

Participants will need to be aged over 16, resident in UK, and attending a UK university. Participants with current depression, suicide risk or a past history of psychosis or mania or substance/alcohol dependence at baseline will be excluded. Participants will need to have basic literacy in English, and access to a smart phone or computer or tablet to access the intervention.

### 8.2 Assessment of compliance with treatment

Brief questions during the 8 week mediator assessment will include questions about use of the intervention where appropriate.

There will be regular downloads from the internet-treatment platform which will be compiled in a data base hosted by Exeter CTU. This will be to safeguard the data. This data will need to include both (a) user data – i.e., what the participant enters into the internet platform in terms of answers to questions and text boxes; (b) usage data – i.e., time spent on the internet platform, what completed and when.

The therapist will monitor the progress of participants in the intervention so that any problems can be identified. If resources allow, site researchers may email, text or telephone participants who are not using their app to see if they need help downloading or using it.

## 9 ADVERSE EVENTS

Participant welfare and safety

There is no known health risk associated with any of the assessments or unguided self-help. The risk concerning participation in this study is believed to be low. Further, we anticipate that the self-help will reduce vulnerability and the risk for developing poor mental health and improve well-being and resilience. In our experience from previous projects, participants are happy to participate and enjoy the assessment tasks. We will strive to use tasks that the participants experience as motivational and reinforcing whenever possible. This will also ensure a low attrition rate.

Because the trial is examining well-being promotion and prevention of poor mental health, the initial screening process will exclude anyone with history of current major depression, and diagnoses of bipolar disorder and psychosis and those reporting elevated suicidality. These individuals will be automatically guided towards appropriate information and sources of help. This process means that individuals likely to have significantly increased risk (e.g., for self-harm and suicidality), and/or for whom more intensive psychological and psychiatric treatment is appropriate, will not be included in the study.

Other than the intervention failing to produce an effect, there is nothing in the literature to suggest possible adverse effects of the assessments and interventions for the young people involved. Versions of components within the intervention have been previously used with no detected harmful effect.

As with all psychological interventions, individuals reflect on their difficulties, which can produce temporary increases in distress, but no more than would commonly occur in daily life. Prior work has provided positive feedback on the rumination self-help intervention and indicated reductions in poor mental health over 12 months, with no serious adverse events reported: as such, the intervention within the trial may benefit individual participants. The likeliest outcome for users who do not find the intervention of benefit is their disengagement from it. In addition, all participants receive more intensive monitoring, with processes to identify and direct all relevant participants to potential sources of help.

As part of our policy for addressing risk and prioritizing the welfare of participants, participants are provided with links to online support, access to contact the trial team, and automatic signposting to help and guidance if reporting risk (e.g., suicidal thoughts, as indexed in items within outcome measures such as the Patient Health Questionnaire-9, PHQ-9 on the screening or follow-up websites) or levels of symptoms suggesting a need for help within any of the assessments within the cohort study. These messages include general information on the presenting symptom, recommended actions to make themselves safe, and advice to seek medical help, and direct links to relevant national sources of help (see Appendix A).

The main indicators of harm will be the completion of questionnaires by the participants at all assessments (baseline, 3 months, 12 months). Questionnaires will be automatically screened for signs of severe distress (for example, defined as scores above 20 on PHQ-9 for depression or reports of suicidal ideation), with automatic programmed questions following up to ascertain aspects of risk and to automatically provide users with recommended advice and signpost towards help (family doctor, local hospital, relevant charities; e.g., website link to the Samaritans in the UK. Other indicators would be report of worsening symptoms or suicidality in direct contact from participants to the research team.

Individuals reporting severe levels of symptoms or meeting diagnostic criteria for depression will be offered guidance to seek appropriate help from their GP/family doctor, occupational health or student well-being service should this seem necessary.

For those who enter the trial and then indicate risk there will be the option to contact a researcher via e-mail or telephone to seek advice. This advice will include guidance to seek appropriate help from their GP/family doctor, occupational health or student well-being service should this seem necessary. Project researchers will be trained in and provided with a protocol to assess risk and with standard useful responses in these circumstances (see Appendix A). The University of Exeter trial site has a designated senior clinician(s) [clinical psychologist] who will be available as a resource to researchers to provide guidance on clinical issues arising from participants either through standardized measures or contacts

initiated by the participant. If the researcher has serious concerns about a participant, where appropriate, after discussion with the clinician, the clinician or researcher will contact the participants (by email, telephone) to review the situation, provide guidance and offer to write a referral letter to the participants GP, subject to participant consent. These procedures will be made explicit in all information sheets. Any concerns detected this way will be recorded on a standardised pro forma, a copy which will be sent to the DMEC and sponsor for the trial. The same process will be activated in response to any concerns raised by participants at other times, either spontaneously or in responses during the assessments.

We will record both serious and non-serious adverse events as defined by the National Research Ethics Service (e.g. deaths; self-harm; serious violent incidents, referral to crisis care or admission to psychiatric hospital) within both groups and report them to the DMEC and Research Ethics Committee to determine whether events are related to the treatments and to take appropriate action.

### 9.1 Definitions

**Standard definitions for adverse events etc are in Table 11.**

Because the current interventions are digital self-help rather than a medicinal product and involve no biological agent, it is not appropriate to define adverse events etc re any untoward medical occurrence – rather as a psychological intervention, appropriate adverse events would include those related to mental state and behaviour:

i) Serious adverse events (SAEs) including death, suicide attempt, self-harm, serious accident or violent incident, referral to crisis care or admission to psychiatric hospital.

ii) Adverse Events (AE) may include significant worsening symptoms of anxiety, worsening symptoms of depression, as operationalized by a reliable deterioration of movement from 'mild' to 'severe' or 'moderate' to 'severe' levels of symptoms on GAD7 or PHQ9 AND a change of ≥4 points on GAD7 or ≥6 points on PHQ9 from baseline assessment to 3 months assessment or from 3 months assessment to 12 months assessment, new instance of self-harm, new instance of suicidality.

The following definitions are therefore adapted in light of this – see below.

**Table 12 Definitions of Events**

| Term | Definition |
|---|---|
| **Adverse Event (AE)** | Standard: Any untoward medical occurrence in a participant to whom a medicinal product has been administered, including occurrences which are not necessarily caused by or related to that product.<br>*Adapted: Any deterioration in mental state or behaviour in a participant to whom the intervention has been administered, including occurrences which are not necessarily caused by or related to the intervention*. |

| | |
|---|---|
| **Adverse Reaction (AR)** | Standard: An untoward and unintended response in a participant to an investigational medicinal product which is related to any dose administered to that participant.<br><br>The phrase "response to an investigational medicinal product" means that a causal relationship between a trial medication and an AE is at least a reasonable possibility, i.e,. the relationship cannot be ruled out.<br><br>All cases judged by either the reporting medically qualified professional or the Sponsor as having a reasonable suspected causal relationship to the trial medication qualify as adverse reactions.<br><br>*Adapted: An untoward and unintended response in a participant to an intervention which is related to any dose of the intervention administered to that participant.*<br><br>The phrase "response to an intervention" means that a causal relationship between an intervention and an AE is at least a reasonable possibility, i.e. the relationship cannot be ruled out.<br><br>All cases judged by either the reporting appropriately clinically qualified professional or the Sponsor as having a reasonable suspected causal relationship to the intervention qualify as adverse reactions. |
| **Serious Adverse Event (SAE)** | Standard: A serious adverse event is any untoward occurrence that:<br><br>• results in death<br>• is life-threatening<br>• requires inpatient hospitalisation or prolongation of existing hospitalisation<br>• results in persistent or significant disability/incapacity<br>• consists of a congenital anomaly or birth defect<br><br>Other 'important events' may also be considered serious if they jeopardise the participant or require an intervention to prevent one of the above consequences.<br><br>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. |
| **Serious Adverse Reaction (SAR)** | Standard: An adverse event that is both serious and, in the opinion of the reporting Investigator, believed with reasonable probability to be due to one of the trial treatments, based on the information provided. |
| **Suspected Unexpected Serious Adverse Reaction (SUSAR)** | Standard: A serious adverse reaction, the nature and severity of which is not consistent with the information about the medicinal product in question set out in the reference safety information: |

| | |
|---|---|
| | • in the case of a product with a marketing authorisation, this could be in the summary of product characteristics (SmPC) for that product, so long as it is being used within it's licence. If it is being used off label an assessment of the SmPCs suitability will need to be undertaken.<br>• in the case of any other investigational medicinal product, in the investigator's brochure (IB) relating to the trial in question<br><br>*Adapted: A serious adverse reaction, the nature and severity of which is not consistent with the information about the intervention in question set out in the reference safety information* |

## 9.2 Adverse event reporting and management

### 9.2.1 Operational definitions for (S)AEs

These have been provided in section 9.1

## 9.3 Recording and reporting of AEs, SAEs, SARs AND SUSARs

All serious adverse events that are trial or treatment related will be recorded and immediately reported to the Chief Investigator and within 1 working day (24 working hours) to the ExeCTU Trial Manager. If these are also classed as unexpected they will be reported to the relevant ethics committees.

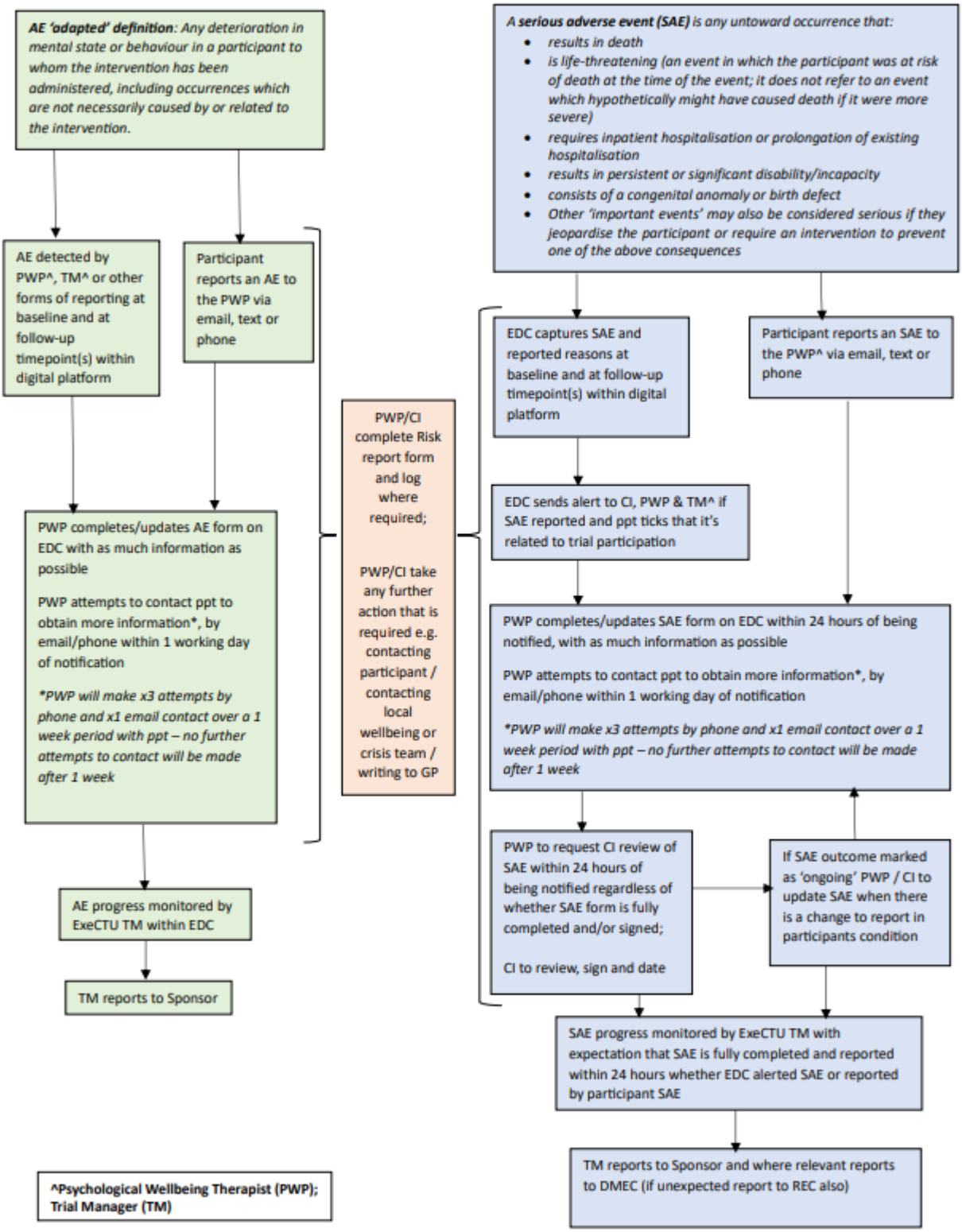
The SAE form will capture the following data:

- Date and time of onset
- Date and time investigator became aware
- SAE category
    - Death i.e. (homicide, suicide, accident, illness, all appropriate options) etc.)
    - Life threatening i.e. (suicide attempt, serious assault, self- harm)
    - Hospitalisation or prolongation of existing hospitalisation
    - Persistent or significant disability or incapacity i.e. (include development of problematic substance/ alcohol abuse; onset of new Axis I disorder)
    - Congenital anomaly or birth defect
    - Other i.e. (potentially dependent life events, e.g. job loss divorce)
- The intensity will be specified as mild, moderate or severe
- The SAE will be determined as intermittent or continuous
- The SAE outcome will be determined as resolved with a date provided, resolved with sequelae, ongoing (with dates for agreed follow ups specified) or died (if died the cause of death will be specified)
- The SAE relationship to the study or trial procedures will be determined as not related, unlikely to be related, possibly related, definitely related or unknown
- A detailed description of the event will be provided and this field will also be used to document the dates and number of attempts made to contact a participant by phone and/or email in order to obtain details about the event, the discussion that took place during any successful phone calls/emails and subsequent actions agreed or discussed between the participant and researcher/clinician

- The CI will report on their assessment of the implications (if any) for the safety of study participants and how they will address the implications
- The form must be signed and dated by the CI

We will, in line with other complex intervention studies, monitor non-serious adverse events, serious adverse events that are not trial or treatment related, serious deterioration, and active withdrawals from treatment, with specific questions in the follow-up and in response to specific participant-initiated reports. Symptoms of depression or anxiety will not be defined as adverse events unless suicidal ideation, plans or an attempt has been made. The reporting period for all events and reactions will be from referral to 12 month post baseline follow-up. Data on any adverse events will be collected by a member of the research team at each assessment and entered directly into the EDC.

**Figure 3 Safety reporting flowchart**



### 9.4 Responsibilities

Researchers at central site (University of Exeter) to check for SAEs, AEs and ARs when participants complete digital treatment / follow-up, potentially in response to automated feedback from website.

Chief Investigator (CI) is responsible via liaison with research team at central site for:

1. Ensuring that all SAEs are recorded in EDC and reported to the ExeCTU Trial Manager within 24 working hours / 1 working day of becoming aware of the event and provide further follow-up information as soon as available.

2. Ensuring that SAEs are chased with ExeCTU Trial Manager if a record of receipt is not received within 2 working days of initial reporting.

3. Ensuring that AEs and ARs are recorded and reported to the ExeCTU Trial Manager in line with the requirements of the protocol.

1. 4. Immediate review of all SUSARs.
2. 5. Review of specific SAEs and SARs in accordance with the trial risk assessment and protocol as detailed in the Trial Monitoring Plan.

Sponsor (NB where relevant these can be delegated to CI and ExeCTU Trial Manager)

1. Central data monitoring and verification of AEs, ARs, SAEs, SARs and SUSARs according to the trial protocol within the database (EDC).
2. Reporting safety information to the CI, delegate or independent clinical reviewer for the ongoing assessment of the risk / benefit according to the Trial Monitoring Plan.
3. Reporting safety information to the independent oversight committees identified for the trial (Data Monitoring Ethics Committee (DMEC) and / or Trial Steering Committee (TSC)) according to the Trial Monitoring Plan.
4. Reporting SAEs that are related to the trial and unexpected, by email to the research ethics committee.
5. Expedited reporting of SUSARs to the Competent Authority (MHRA in UK) and REC within required timelines.
6. Notifying Investigators of SUSARs that occur within the trial.
7. Preparing standard tables and other relevant information in collaboration with the CI and ensuring timely submission to the MHRA and REC.

Data Monitoring Ethics Committee (DMEC):

In accordance with the Trial Terms of Reference for the DMEC, periodically reviewing overall safety data to determine patterns and trends of events, or to identify safety issues, which would not be apparent on an individual case basis.

### 9.5 Notification of deaths

All deaths will be reported to the ExeCTU Trial Manager who will report to the Sponsor irrespective of whether the death is related to the trial or an unrelated event. If the event is unrelated to the trial then this will be reported to the sponsor within one week, and if it thought to be related to the trial the report will be submitted within 2 working days.

### 9.6 Reporting urgent safety measures

If any urgent safety measures are taken the CI/Trial Manager shall immediately and in any event no later than 3 days from the date the measures are taken, give written notice to the relevant ethics committee and other appropriate bodies where relevant (e.g., MHRA) of the measures taken and the circumstances giving rise to those measures.

### 9.7 The type and duration of the follow-up of participants after adverse reactions.

In the event of any reported adverse reaction to the intervention the participant will be contacted by the site researcher or clinician within 2 working days to review status and options.

## 10 STATISTICS AND DATA ANALYSIS

### 10.1 Sample size calculation

Sample sizes are estimated based on Minimum Clinically Important Difference (MCID) for the primary outcome at primary endpoint allowing for power at 0.80 and alpha at 0.05. The Primary outcome is Onset of MDE over 12 months: total sample required N=648, assume MCID = absolute risk reduction in incidence of MDE 10%; assuming incidence MDE 25% in control group, 20% follow-up attrition, then require n=324 per arm.

### 10.2 Planned recruitment rate

Recruitment will take place over 18 months across 6 university sites (1/10/2022 to 31/5/2024) updated from June 2023 to end of November 2024. It is estimated that an average of 14 potential participants (eligible for one of the trials and consenting to participate) will be recruited per week, from past experience, which exceeds the required recruitment of 648 potential participants (assuming recruitment across all weeks and 20% follow-up attrition – 9.5 participants in total per week would reach this target).

### 10.3 Statistical analysis plan

A detailed statistical analysis plan (SAP) is to be produced; the main points of the statistical analysis are summarised here. The SAP will be approved by the TSC prior to end of participant recruitment. Any amendments to the TSC will be documented and approved by the TSC on an ongoing basis.

#### 10.3.1 Summary of baseline data and flow of patients

The analysis and presentation of the trial will be in accordance with CONSORT guidelines (Schulz et al., 2010). Recruitment, intervention uptake, outcome completion rates and attrition will be reported (with 95% CIs) and shown on a flow diagram.

Premature discontinuation of intervention may be instigated by the participant or by an investigator. Participants may elect to withdraw from the study if they wish to do so at any time and for any reason (including perceived harms or lack of efficacy of intervention). Researchers may also request that trial intervention be discontinued for reasons of participant safety at any time; such requests will be made to and approved by the PI or an appointed deputy where possible.

Advice on a case-by-case basis may be sought from the DMEC where necessary. A participant will be withdrawn from the study entirely in the event that they are discovered to have been ineligible at the time of recruitment, in which case usual practice will continue to be provided.

As a self-help psychological intervention, we do not anticipate significant iatrogenic effects or side-effects requiring individual discontinuation. Participants who elect to discontinue their allocated intervention will be requested to continue to provide outcome data. If a participant wishes to withdraw from the study entirely (and not provide further follow-up data), they can do so without giving a reason, but we will keep any data they have already provided.

### 10.3.2 Primary analysis

The primary and secondary outcomes will be compared at 3-month and 12-month follow-up. The primary and secondary continuous outcomes will be reported descriptively (mean and standard deviation (SD)) and inferential comparisons will be reported between the two treatment contrasts: ((1) usual practice plus unguided i-RFCBT; (2) usual practice alone.

All analyses will be based on an intention to treat principle (i.e., according to original allocation irrespective of intervention adherence) and will include participants with complete outcome data at 3-month and 12-month follow-up and will adjust for baseline outcome score (where relevant) and stratification variables (site, history of depression). Furthermore, we will adjust for any baseline participant characteristics that are substantively unbalanced at baseline (defined as a difference ≥10 percentage points across categories for a categorical variable, or a difference in means >1 SD for continuous variables), and if the characteristic is thought to be predictive of outcome. Binary secondary outcomes (occurrence of major depressive disorder; generalized anxiety disorder) will be reported as proportions and analysed used logistic regression.

Multilevel mixed models will be used to analyse process measures and investigate mediating processes, provide insights about the types of users helped most by different types of intervention and for pre-post initiative comparisons.

All the RCTs will follow MRC Complex Interventions Guidelines and relevant CONSORT reporting requirements with a pre-registered trial protocol and use intention-to-treat as primary analysis. Randomisation will be in equal allocation (i.e., 1:1) using independent computerised randomisation, stratifying for baseline variables as relevant (e.g., history of depression, recruitment site).

Primary inferential analyses will compare trial arms across outcomes using multilevel mixed models adjusting for baseline score. Secondary analyses will include Complier Average Causal Effect analysis to estimate the effects of adherence with self-help. The extent of missing data will be considered and where necessary, in agreement with Trial Steering Committee (TSC), multiple imputation will be used. The trial statistical analysis plans will be prepared before any formal analyses and reviewed and approved by Data Monitoring Committee (DMC) and TSC, with trial statistician and research team blinded to allocation until primary analyses are completed.

Primary analyses will use multilevel mixed-effect models, which enable us to examine nested hierarchies in the data (individual, intervention, university), across time (examining pre-to-post change), to capture dependencies in the data, to investigate individual trajectories (random intercepts, random slopes), and which have less restrictive assumptions re missing data. Secondary analysis for prevention RCT will be Cox regression model. Statistical/methodological advice sought and provided by Exeter CTU and Prof Taylor. Sample sizes calculated for Minimum Clinically Important Difference for the primary outcome at primary endpoint for power at 0.80 and alpha at 0.05.

### 10.3.3 Secondary analyses

A number of secondary analyses will be conducted.

1. 12-month follow-up comparison

Primary and secondary outcomes will be compared at 12-month follow-up using the statistical approach outlined above.

2. Repeated measures comparison including all timepoints

Primary and secondary outcome measures will be compared at all follow-up timepoints (3, 12 months) using repeated measures analyses, including all participants with data available for at least one of the three follow-up timepoints.

3. Per protocol analysis

Primary and secondary outcomes at 12 months will also be compared using a per protocol analysis ('per protocol' being defined for all interventions as completion of a pre-specified minimum level of usage of the unguided self-help intervention (e.g., complete at least 3 modules of 6 modules in treatment package) and a complier average causal effect (CACE) analysis using instrumental variable regression (Angrist et al., 1996; Dunn et al., 2005), using engagement with the app as the measure of adherence. These analyses will use observed data only; the CACE analysis will include participants on the same basis as the ITT analyses.

4. Imputation of missing data

Patterns of missing outcome data at follow-up will be extensively investigated. Multiple imputation models will be used to impute missing primary and secondary outcome data at all follow-up time points. Results for the between group comparisons based on these imputed data sets will be presented in addition to complete case regression analyses described above. Propensity for missingness associated with baseline characteristics will be investigated; imputation models will include treatment allocation as well as stratification variables, baseline variables, and any variables associated with missingness or included in the models as covariates due to baseline imbalance. Such imputation models are based on the assumption that missing data is 'missing at random', which may not be a valid assumption in this context. Nevertheless, use of imputed data will increase power if there is substantive missing data and is the least likely method to introduce bias.

### 10.4 Subgroup analyses

Primary and secondary analyses will be extended to explore potential subgroup effects by including interaction terms between the intervention allocation and the stratification variables (site, history of depression). Since the trial is powered to detect overall differences between the groups rather than interactions of this kind, the results of these exploratory analyses will be presented using confidence intervals, as well as a global p-value for the interaction between treatment and each variable and interpreted with due caution.

### 10.5 Interim analysis and criteria for the premature termination of the trial

No interim analyses are planned. In order to detect potential harms the study will monitor potential adverse effects. Adverse and serious adverse effects will be reported to TSC and DMEC who will recommend discontinuation of the trial if there is cumulative evidence that the intervention may cause harm. There are no plans to terminate the trial prematurely due to futility.

### 10.6 Other statistical considerations.

Comparisons will be made between all the two arms. No formal p-value adjustment will be made for multiple testing; the results of the ITT observed data analyses will be interpreted first, with the results of the additional analyses interpreted in this light. Interpretation of results will draw focus on confidence intervals rather than emphasising p-values.

Primary analyses will be performed by a statistician who remains blinded to group allocation and will be presented as such to the investigators. The results will be discussed and interpreted prior to the unblinding of group allocations. Additional analyses will then be performed following unmasking.

### 10.7 Mediational analyses

Mediational analyses will test the hypotheses that the unguided i-RFCBT is effective by changing unhelpful habits, increasing self-compassion, and changing cognitive and behavioural skills. Each of these potential mediators of the primary outcome is a continuous variable, assessed via the brief meditator measures across the first 8 weeks post-randomisation. For the continuous outcomes, we will use a structural equation modelling approach to evaluate the indirect (mediation) effect of the intervention via the potential mediators. We will adjust for stratification variables and baseline scores of the outcome variable, and baseline scores of the mediator variable.

For mediation analyses of longitudinal data, assuming ICC =.5, the sample sizes to achieve MCID calculated above can detect small effect sizes for mediators (β=.14) in RCTs (with up to 8 micro-repeated assessments), at power = 0.80.

A series of models will be performed for each outcome, investigating the mediation effect of each mediator variable individually, and the mediation effect of each mediator variable in an overall model combining all mediators. The mediation effect will be reported as the indirect effect of treatment via the specified mediator, with 95% confidence interval, and the proportion of the total intervention effect mediated. Analyses will include the use of instrumental variables to account for effects of unobserved confounding on mediators (Dunn et al., 2005).

## 11 DATA MANAGEMENT

### 11.1 Data collection tools and source document identification

Database management, data curation and sharing will be supported by UNEXE and EXCTU. Efficacy/effectiveness parameters will be directly and automatically entered into an EDC system licenced/programmed by Exeter CTU. At assessment participants will directly complete electronic questionnaires and tasks online into this EDC system and this data will be automatically processed to extract relevant anonymised parameters (from which an individual's identity cannot be detected) and will be stored in the secure database prepared and managed by EXCTU.

An eCRF will be designed and set up for participants to enter data electronically by completing the website assessments designed to capture relevant pseudo-anonymised and de-identified data. Programmed and manual queries on the data completed in the eCRF will be raised centrally by UNEXE and managed by data manager – the EDC will include a reporting system so the trial team can monitor progress in recruitment, follow-up, risk and adverse events in a straightforward manner. This monitoring process of the clinical database will be done in real time throughout the course of the trial. After the

database has been locked, cleaned and findings dissemination and following successful evaluation by the Steering Committee, access to the project data may be granted to other parties, following rules that will be defined in a specific agreement between the partners and third parties. Only data required for the trial will be collected.

### 11.2 Data handling and record keeping

A separate data management plan accompanies this trial protocol.

There is a separate data management plan which accompanies this trial protocol which gives greater detail.

No data will be collected or used without the explicit informed consent of the participants.

During the project, the team will stipulate any conclusive needs within the project regarding participants' data. This may refer to the temporariness of data storage, security of data transfer, relevant consent applications and relevant advertisement of the use of the data. To safeguard the confidentiality of the participants' personal information, such data will be stored in a record that will be kept locked in the institution. Only the researchers will be aware of this personal information. For research purposes each participant will be given a numerical code (to be used in place of a name). The technology should cater for the fact that each participant will be given a unique identification code, rather than a name, and all data will be securely stored and preserved, both electronically and on paper.

Only authorized research personnel will have access to the password protected electronic database. No unauthorized access will be possible. A separate list linking codes with names will be kept in a secure place. The data will be introduced and analysed by computers. As for Internet use and monitoring by means of mobile apps, data protection systems will be designed (using secure passwords, encryption, etc.). The researchers will have access to the database using a password. Also, in order to protect all information, we will follow the AES (Advanced Encryption Standard) strategies for personal password use and data encryption. The study researchers will promise to not reveal data from which personal and health information about the participants could be deduced. The same principles will be taken into consideration in the dissemination of data in the publication of scientific papers and the presentation of research reports at scientific conferences.

Database infrastructure: The project will use a distributed electronic database (managed by UNEXE, Partner 1) during the project that will store all the downloaded cohort data and clinical trial data. Within the clinical trial, UNEXE will be in charge of the set-up and management of the database. The equivalent of anonymised electronic Case Report Form (eCRF) data will be set-up and entered in a data management system, which is fully validated. The eCRF and associated database will be automatically populated from the responses entered by participants via websites and app platform: data will be encrypted and anonymised before downloading from the website or app and then stored securely and converted into an electronic database suitable for analysis. A data manager will be appointed to build and manage the database infrastructure. Data will be routinely backed-up during and after the project to ensure the availability of all the information.

Data Management Plan: The Data Management Plan will describe how the data will be exploited, checked, shared, curated, and preserved. Thus, the procedure for granting access will be detailed and the mechanisms to access the data after the project will be described. The ownership of data generated during the project will be described in the Consortium Agreement.

Data format and types: Standard data formats will be used during the project and will be compliant with Clinical Data Interchange Standards Consortium - Clinical Data Acquisition Standards Harmonisation (CDISC-CDASH) standard. Data types will include Volunteer data: Demographics, information provided by participants on questionnaires and on EC assessment instruments.

Data exploitation: All information will have a digital format that will be handled in accordance with national data protection regulations. A mechanism to request access, mine, exploit, reproduce or disseminate data generated in the framework of this project will be put in place. After successful evaluation by the consortium, access to the project data may be granted to other parties, following rules that will be defined in a specific agreement between the partners and third parties.

### 11.3 Access to Data

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

### 11.4 Archiving

Source documents, and trial-related electronic and other data will be stored safely and in accordance with the requirements of the UKGDPR and Data Protection Act (1998), no longer than legally required (for a minimum of ten years) or as stipulated by the Sponsor's requirements, and the applicable regulations and as per the Clinical Trial Units existing Business Continuity, Disaster Recovery & Archiving Standard Operating Procedures.

Data Access: Post-analysis, the final anonymised dataset will preferentially be stored in Open Research Exeter (ORE), the University of Exeter's open access repository.

Interoperability: Source data will be stored in Microsoft SQL server, formatted to maximise fidelity. This can be transposed and converted during the analysis stage into any format required. For the Open Research Exeter repository XML or CSV with a separate data dictionary is recommended.

Archiving: Items submitted to ORE will be retained indefinitely. ORE content is securely held on University of Exeter servers and regularly backed up according to current best practice. The ORE team will also try to ensure continued readability and accessibility of content, including the migration to new file formats where necessary.

Data archiving is described in further detail within the Data Management Plan.

### 11.5 Authorisation of participating sites

The trial will be conducted and managed directly from the University of Exeter and Exeter CTU – with other institutions only used to advertise the trial to aid recruitment of participants, as such each site may

not need their own site-specific ethics, and there may be no requirement for data transfer between Exeter and the recruitment sites.

# 12 MONITORING, AUDIT & INSPECTION

## Monitoring and vigilance activities

UNEXE will perform a risk assessment and base a monitoring plan on this risk assessment. UNEXE will assign a data manager to this role, who will provide monitoring of recruitment, retention, and adverse events and management of the centralised recruitment and data management systems, and support and evaluate the quality and integrity of study operating procedures and protocol adherence to applicable regulations. Additionally, the trial manager will manage study progress by tracking ethics submissions and approvals, recruitment and enrolment, data completion, and data queries (generation and resolution).

Central vigilance and the reporting of Serious Adverse Events (SAEs) will be provided by UNEXE (Part. 1) following good practice. A l SAE-Form will be available to be completed by the research team as appropriate. Safety and tolerability will be evaluated by recording AEs and SAEs throughout the study.

## Quality assurance procedures for the Clinical Trial

The appropriate design of a clinical trial protocol ensures the safety, rights, and well-being of participating patients. The clinical protocols for the trial will be finalised after being reviewed and approved by the UNEXE ethics board. International Conference on Harmonisation and Good Clinical Practice quality standards and Standard Operating Procedures will be set-up including case documentation, data collection, monitoring, validation, evaluation, archiving and reporting of adverse events, with support from the UNEXE Clinical Trial Unit. This includes finalising the trial protocol and registration of the trial and publication of the trial protocol.

The Sponsor will be responsible for the development of the essential trial documentation delegated to the Exeter CTU and the trial manager (located in the CTU) such as electronic Case Report Form (eCRF) and documents related to monitoring (initiation, monitoring and close-out visit reports). This includes the development of a specific data management plan for the trial, starting with an initial data management plan that provides a generic overview of how to make the data findable, accessible, interoperable, and reusable, including the handling of data during and after the project, which data will be collected, processed and generated, the methodology and standards applied, and plans for data sharing, data curation and data preservation..

UNEXE will have overall responsibility for the monitoring of the delivery of the clinical studies across the internet website, EDC and internet delivered treatment and will therefore employ a trial manager, who will provide monitoring checks and site management, evaluate the quality and integrity of study sites practices and protocol adherence to applicable regulations, and manage the progress by tracking regulatory submissions and approvals, recruitment and enrolment, data entry, data management, data completion, data queries (generation and resolution). This process will be automated through the use of the EDC system as primary point of access to study and to collect data, provide intervention and monitor outcomes. The trial manager at UNEXE will check and coordinate this process.

# 13 ETHICAL AND REGULATORY CONSIDERATIONS

The research activities of this project include: Collection and processing of personal data, including sensitive personal data (i.e. health), and tracking of participant's symptoms and well-being over time; - Intervention programme (the selected participants undergo unguided i-RFCBT).

We note the urgent need to conduct research in young people in order to overcome equipoise and establish the evidence base for potential preventative interventions and treatments.

Key ethical issues are (a) individual autonomy entailing the giving of free and informed consent and respect for privacy and confidentiality of personal data;

(b) the safety and wellbeing of participants.

Before the start of the study, approval will be sought for the study protocol, informed consent forms and other documents from the University of Exeter REC.

To address (a), participation will be free and voluntary; electronically-signed informed consent will be obtained from each participant prior to entering each study; all research data will be pseudonymously recorded using identification numbers rather than contact details (name, email) to assure participant confidentiality in numerical databases. All information collected in this study will be kept confidential, except as required by law. Data will be obtained and stored in line with GDPR requirements, using secure university servers/cloud-based systems.

With respect to (b) there is no known health risk associated with any of the assessments or initiatives proposed. We anticipate that self-help CBT will improve wellbeing. Nonetheless, we will assess for potential harms. Project researchers will be trained in and provided with a protocol to safeguard students, assess and manage risk, including referral to local student MH service, and access to a designated MH clinician to support them. The initial screening process for RCTs will exclude anyone with currently severe psychiatric disorder and those reporting elevated suicidality and automatically signpost these individuals towards appropriate guidance and help, including general information on the presenting symptom, recommended actions to keep themselves safe, advice to seek medical help from GP, direct links to relevant national sources of help, and the option to request that the respective university support services contact the individual.

For participants consented into surveys or studies who report risk (e.g., suicidal thoughts) or significant/worsening symptoms on outcome measures on the screening or follow-up websites, the same automatic messaging re recommended actions and signposting is provided plus participants continue in the study and can contact a site researcher via e-mail or telephone to seek advice. This procedure has been successfully used in prior student studies, received ethical approval, and agreed in partnership with university mental health services and Student Guild welfare representatives. Similar in-person safeguarding procedures will be used to support student partners as necessary.

## 13.1 Research Ethics Committee (REC) review & reports

Ethical considerations have been taken into account from the design of the study, to the conduct and even to the reporting of study results. International Conference on Harmonisation (ICH) has entered ethics into clinical studies, determining sponsor and investigator responsibilities and developed the concept of Good Clinical Practice (GCP), which provides guidance to investigators that can result in a common approach to

clinical trials performed in multiple countries. GCP compliance provides assurance that the reported data are accurate, and that the rights, integrity, and confidentiality of participants are protected.

Standard Operating Procedures (SOP) will be written and reviewed by the consortium according to the ethical standards of the Helsinki Declaration of 1975 on GCP, as revised in 2013 by the ICH.

The investigator will supply all necessary information to the sponsor for submission of the protocols and consent forms to the national competent regulatory (local Ethic Research Committee), to the UNEXE IRB and to the national authorities for the data protection for review and approval and for the registration in clinical databases.

Research will only start after obtaining approval from the local Ethic Research committee and IRB. The local Ethic Research Committee and IRB will only approve a specific research proposal.

Participation will be free and voluntary and electronically-signed informed consent will be obtained from each participant prior to entering the study. Because the project is principally conducted through digital medium (website and apps), information sheets and consent forms will be provided through these medium and participants will be able to signify their consent electronically. All data will be anonymously recorded using specific Case Report Forms (CRFs) to assure participant confidentiality in numerical databases, as required by personal data protection laws. Quality assurance will be assured by the organisation of monitoring (via the EXECTU website) and control of CRFs to evaluate the progress of the study, verify the accuracy and completeness of data and assure that all protocol requirements, applicable local laws and GPC/ICH guidelines are respected. At the end of the study, according to GPC/ICH guidelines, the closure of the study will be checked. All data analyses and CRFs will be archived in Exeter according to the local regulation.

All procedures at the very least comply with international guidelines and with current national legislation. The project will only start after approval of the corresponding local ethical committee.

All information collected in this study will be kept confidential, except as permitted by law. Data obtained for this research study will be accessible only for the researchers directly involved in this study. If any publication or presentations results from this research, the participants will not be identified by name or other potentially identifying information.

This project involves human data collection and processing of personal data. No physical injury, financial, social or legal harm will be directly posed to the participants, and potential psychological risks will not exceed the daily life standard. The PIs at each site and have extensive experience with handling and collection of data of this type for research purposes.

The main ethical issues for the clinical trials are ensuring:

(i) Understanding and voluntary written/electronic informed consent from all participants;

(ii) Participant confidentiality and anonymity;

(iii) The safety and well-being of participants.

The study investigators will conduct the clinical study in adherence to the fundamental ethical principles of respect for human dignity, non-exploitation, non-discrimination and non-instrumentalisation. The following principles will also be adhered to:

- Individual autonomy (entailing the giving of free and informed consent, and respect for privacy and confidentiality of personal data)
- Justice and the principle of beneficence and non-maleficence (namely with regard to the improvement and protection of health)
- Proportionality (including that research methods are necessary to the aims pursued and that no alternative more acceptable methods are available).

Before the start of the trial, approval will be sought from a REC for the trial protocol, informed consent forms and other relevant documents. Ethical approval will be sought from the REC of the University of Exeter.

In either case the following principles will be upheld:

- substantial amendments that require review by REC will not be implemented until the REC grants a favourable opinion for the trial
- all correspondence with the REC will be retained in the Trial Master File/Investigator Site File
- the Chief Investigator will notify the REC of the end of the trial
- if the trial is ended prematurely, the Chief Investigator will notify the REC, including the reasons for the premature termination
- within one year after the end of the trial, the Chief Investigator will submit a final report with the results, including any publications/abstracts, to the REC

### 13.2 Peer review

The project received favourable review from the UKRI Medical Research Council for grant award.

### 13.3 Public and Patient Involvement

**Student Advisory Group (SAG)**

In order the maximise the quality and benefits realised from the project and its outputs, the role of end users will be emphasised and a co-design approach will be adopted by including young persons in decision-making. For this, we are creating a Student Advisory Group, which will advise us on all aspects of the overall project. Roles for the SAG include:

- Help to steer, guide, and shape the project as it unfolds.
- Help the project access the full spectrum of students, to achieve diversity and representation in those who take part.
- Provide representation into project decision-making and governance (Steering committee; Independent Advisory board)
- Develop branding and engagement strategy to maximise student involvement.
- Develop, co-design, and consult on adapting research materials, surveys, interventions and wellbeing tools.

- Help to publicise findings and outputs and to support the dissemination to students and active implementation into universities of evidence-based approaches

The Group consists of undergraduate and postgraduate students at the Universities of Exeter, Cardiff, Oxford, Southampton, Newcastle, and King's College London

The SAG will meet ahead of key decisions making points in the project in order to make the most of this resource.

Students (e.g., via Student Advisory Board) will advise and have input to the wording and content of the information sheet and informed consent form to ensure simple, clear, comprehensive and meaningful for the target population.

### 13.4 Trial management responsibilities

A dedicated trial manager will assist in the day-to-day management of the project, coordinate recruitment and retention, and will be responsible for effective communication and monitoring progress. The trial will be managed by a core research team who will meet weekly. There will be a Cohort Trial Senior Management group, who will meet by teleconference or video-conference on a bi-monthly basis to review progress and set targets. The trial manager will be mentored by an EXCTU senior manager. The trial will be registered with www.controlledtrials.com or other recognised international trial registration sites and assigned an ISRCTN number. Researchers will be trained in Good Clinical Practice. We will comply with the UK Department of Health Research Governance Framework for Health and Social Care. The trial will be conducted to protect the human rights and dignity of participants as reflected in the 1996 version of Helsinki declaration. Trial documents will be retained for a period of 10 years after the completion of the study as detailed in the Patient Information Sheet.

### 13.5 Regulatory Compliance

The trial will not commence until a Favourable REC opinion is obtained.

### 13.6 Protocol compliance

Prospective, planned deviations or waivers to the protocol are not allowed under the UK regulations on Clinical Trials. The trial team will take all efforts to prevent and monitor any deviations so that they will not be used, e.g., it is not acceptable to enrol a participant if they do not meet the eligibility criteria or restrictions specified in the trial protocol

Accidental protocol deviations will be adequately documented on a relevant protocol form and reported to the Chief Investigator, Sponsor, and TSC within 2 working days.

The trial team recognises that deviations from the protocol which are found to frequently recur are not acceptable, will require immediate action and could potentially be classified as a serious breach.

Participants are told who will be excluded from taking part in the trial on all recruitment materials and on the introductory pages of the CTU screener. This is so that they know if they would be excluded before they take part in the screening and can choose not to take part in the assessment, rather than be excluded.

All advertising will also only be targeted at those meeting the relevant criteria. This is possible by setting online adverts to only those of the specified age group and residency and associated with particular universities (e.g., geographic location) promoting recruitment where only this age group study, work or enjoy leisure activities. There will be no recruitment through any NHS services.

Should it be identified that a participant taking part was recruited in error (would have met the exclusion criteria) then this will be recorded as a protocol violation. A log of all protocol violations will be kept and protocol violations will be reported to the chief investigator and the sponsor within one working day.

### 13.7 Notification of Serious Breaches to GCP and/or the protocol

The log of protocol violations and any SAE's will be considered and monitored by both the sponsor and the TSC. If the sponsor and/or the Steering Committee consider that there is any significant danger to the participants of the trial or a reduction in the scientific value of the trial then this will be discussed with the ethics committee within 7 days.

### 13.8 Data protection and patient confidentiality

Data protection

The conduct of the project will comply with the GDPR. Adequate measures to ensure data protection and confidentiality will be duly taken into account by the project team. Local and national rules on data protection will be followed and no personal information of participants will be transferred unless such transfer is essential for the conduct of the trial.

A privacy impact assessment (data protection impact assessment) will be carried out if requested by the funder, ethics committee or sponsor. If one is carried out it will be conducted according to the guidelines of the UK Information Commissioners Office: Conducting privacy impact assessments code of practice, Information Commissioner's Office (ICO), 2014.

https://ico.org.uk/media/fororganisations/documents/1595/pia-code-of-practice.pdf.

Data will be stored in separate databases that are linked by the unique identifier ID to pseudonymize all information collected. The first database contains information related to informed consent and information enabling researchers to directly contact participants. On the screening platform, participants are not asked to provide their name or any contact details until they have been provided with the participant information sheet and privacy policy. At the point of asking participants to consent to take part in the assessment, they are asked for their name, email address and phone number. The second database contains all the baseline and follow up data collected from the EDC system. A third database will store all data collected as part of the project directly from the internet treatment platform. The codes linking contact information with the databases containing outcome will be destroyed as early as is legally required (no earlier than all data being archived) – data (including participant details and consent) may need to be retained and not deleted for a longer period due to future research indicators that may require researchers to contact the individual or actions taken by participant against the research. This approach has proven successful in prior digital interventions for well-being and been approved by multiple institutional and National Health Service research ethics in the UK; adaptations will be made as necessary for specific local ethical requirements.

The site research teams will access to the database that connects the ID number to a person and their full contact details. This is so that they can contact the participant if they report technical difficulties, if any suicide risk is indicated, and to send reminders regarding assessments. Email and text for reminders

will never contain personal or other information about the collected data, but remind participants, in a general manner, about open tasks. Exeter Nurture-U researchers, clinicians and the chief investigator only will be set up with a username and password to access the CTU database that stores the personal data. The site researchers are not given the allocation details so as to maintain blind..

**Digital Information**:

Files containing digital information must be encrypted with password-protection where appropriate and stored on a secure network (not a local 'C') drive. Where local copies are required for processing or transfer preparation, it should be ensured that the target workstation is compliant with all host organisation security policies and that they are followed in use. This is particularly important for laptops/netbooks/portable workstations, especially about encryption and should be confirmed by the host organisation before transferring data.

The relevant university guidelines and policies will be followed (e.g., for the University of Exeter, the University Information Security Policy, and the University Computing Regulations - a copy of the specific University guidelines for portable devices is available here: http://alf.exeter.ac.uk/share/s/GwluvMWoQn-_FPAwNFxS7g. Participants identifiable data must not be stored on home computers, personal laptops, unencrypted memory sticks, CDs, handheld devices, digital cameras or other imaging equipment even if they are password protected. An encrypted memory stick may be used if required.

All data generated will be stored by University of Exeter in encrypted and password-locked files behind a secured firewall operating within a university environment with state-of-the-art safety protection measures, and transmission of information via electronic means will be performed using encrypted data files. The exact process for data storage and encryption for the data processors will be directed by the data controller and outlined in the data management plan.

**Privacy by Design**:

Privacy by design means that each new service or business process that makes use of personal data must take the protection of such data into consideration. An organisation needs to be able to show that they have adequate security in place and that compliance is monitored. In practice this means that privacy must be taken into account during the whole life cycle of the system or process development.

**Participant data:**

Participant confidentiality and welfare will always be maintained as the highest priority. Anyone with access to data, including the investigators, is subject to professional secrecy during and after the trial. Collaborators outside of Exeter will only be given access to de-identified data, and they must sign a declaration stating that they will adhere to UK data protection legislation. We plan to use the standard contract for transfer of personal data.

Anonymised data (health information, socio-demographic information, platform usage information) will not be deleted until the completion of the scientific analysis of the data plus the mandatory period for retaining clinical data (at least ten years in the UK).

**Responsibility:**

The University of Exeter as sponsor of the trial is the data controller. The controller has the responsibility to ensure that the security and access arrangements for the database comply with the Data Protection Act (1998), and that all data processing and locally held personal data are registered with the host institution according to their employer's processes. Because this trial involves the processing of personal information the Information Commissioner's Office (ICO), will be notified accordingly.

Legal data transfer agreements will be written and signed between the data controller and any relevant data processors prior to any participant being recruited. These agreements will be confirmation that the

data processors will adhere to GDPR regulations, which protect and safely store participant personal and outcome data.

A common data protection and privacy policy authorised by the sponsor and the University of Exeter data protection team will be available on the study website. The screening website will also email this policy to consenting participants with the information sheet and consent form or provide it as download.

**Transfer of data to consortium researchers:**

All data transfers must be approved by the Trial Management Team and must be logged and accompanied by a Data Transfer Form signed by the CTU staff member transferring the data, consistent with data protection legislation and the responsibility of University of Exeter as the data controller. Outcome data will be extracted from the database (usually SPSS or STATA format), on a routine basis and prior to per protocol analysis, to be made available to the project statistician in a secured manner (encrypted files via ftps/https servers). University of Exeter will be responsible for collecting all data and analysing it for the trial so it is unlikely that Exeter will be sending data to other sites.

**Data Monitoring:**

Data will be accessed by the trial manager/data manager on the EXCTU data base on a regular basis (typically at least weekly) to check recruitment numbers and data quality and to monitor that all processes are working correctly. Detailed checks will occur early in the project to confirm that all systems are working properly. To download data the trial manager/data manager has to login via user name and password.

**Breach of confidentiality:**

Occasionally records containing personal data that should not have been disclosed, e.g. an e-mail with a data file containing identifiable details may be received by a member of CTU staff or another staff member from an internal or external source. In such situations, the member of staff should contact the person who sent the data and make them aware of the breach of confidentiality. The records received should be either promptly deleted or any identifying details thoroughly erased. All suspected breaches should be investigated, documented in the study file and reported to the Sponsor as appropriate, following an established data breach the UNEXE procedure will be followed.

### 13.9 Financial and other competing interests for the chief investigator, PIs at each site and committee members for the overall trial management

To our knowledge, the chief investigator, PIs at each site and committee members for the overall trial management have no financial and other competing interests for the trial management. At regular intervals (6-monthly), trial management and Trial Steering Committee will be asked to declare if any financial or other competing interests.

### 13.10 Indemnity

The University of Exeter will have insurance cover place to cover the legal liability for any illness or injury to a participant of the trial arising from participating in the trial.

### 13.11 Amendments

Changes to the protocol should only be made via an approved protocol amendment. Protocol amendments must be approved by the sponsor and the local Ethic Research Committee prior to

implementation, except when necessary to eliminate hazards and/or protect the safety, rights, or welfare of subjects.

### 13.12 Post trial care

Medical care is not being provided in this trial so will not be provided after the trial. It is expected that the unguided i-RFCBT intervention will be used for at least one to three-month period following randomisation but it is available for use throughout the full 12 month period of their follow-up.

### 13.13 Access to the final trial dataset

At the end of the trial collaborators will be able to request copies of the anonymised data from Exeter CTU. Who is able to access which data will be decided by the steering group.

# 14 DISSEMINATION POLICY

## 14.1 Dissemination policy

There is an overall dissemination policy for the project, within which there is a specific dissemination policy for the trial results.

Key aspects of the dissemination policy for the trial include:

(i) the Consort Guidelines and checklist are reviewed prior to generating any publications for the trial to ensure they meet the standards required for submission to high quality peer reviewed journals etc. http://www.consort-statement.org/

(ii) Anonymised data arising from the trial is owned by UNEXE as trial lead, lead for trial design, CTU, and trial analysis, and developer of the intervention, managed by UNEXE as the data controller.

(iii) On completion of the trial, the data will be analysed and tabulated and a Final Trial Report prepared and made publicly available on the trial website and via the funder. This will be published before the end of the grant.

(iv) Our publication policy stipulates that all potential publication plans need to be reviewed by the Project Steering Committee before release of data to coordinate activity between partners, determine appropriate authorship and avoid duplication and replication of effort.

(v) Authorship will be determined on standard criteria (i.e., consistent with the criteria for individually named authors or group authorship such as The International Committee of Medical Journal Editors defined authorship criteria for manuscripts submitted for publication http://www.icmje.org/recommendations/browse/roles-and-responsibilities/defining-the-role-of-authors-and-contributors.html#two) and will require contributions with respect to design of the study, development of paradigms and interventions within the study, involvement in delivery of the trial, data analysis and/or writing up of the paper. Seniority of authorship will be determined by relative contribution on these elements – individuals leading on design, analysis and write-up of papers will have lead authorship, with this typically following pre-allocated lead roles for the work packages in the grant in the first instance, unless deferred. All papers will include a detailed statement of the relevant author contributions following a standard template.

(vi) All publications as well as all tools described in this section will acknowledge funding from the UKRI Adolescence, Developing mind and mental health scheme.

(vii) There are plans to notify the participants of the outcome of the trial, through a combination of a specifically designed newsletter, blog, vlog, videos and website, communicated to participants via email and relevant social media on completion of the study.

(viii) It is possible for the participant to specifically request results from their PI and this information be provided after the results had been published.

(ix) The trial protocol, full trial report, anonymised participant level dataset, and statistical code for generating the results will be made publicly available.

## 15 REFERENCES

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# 16 APPENDICES

## Appendix A:
## Risk Assessment and Reporting: automated feedback during assessments

In the assessments we explicitly ask and screen for symptoms of distress, wellbeing and poor mental health (including symptoms of depression, suicidal risk, prior diagnosis by a clinician as self-reported by user of depression, mania or psychosis, and antidepressant use). Whether meeting exclusion criteria at baseline or indicating risk at follow up, participants will be provided with automatic feedback with suggested sources of help such as the recommendation to consult their GP or weblinks or phone numbers for national services.

Pre-screening

In response to recommendations from our ethical review boards we have now added a pre-screening section to our website to allow those with experience of, or symptoms of depression to access help pages linking to sources of support as soon as possible.

In Trial

For those taking part in the trial there is the option for seeking more information from the study team and where risk is indicated a trial clinician may contact them directly.

Each occurrence of elevated symptomatology (PHQ9>20) or risk will be logged by the electronic system and the relevant research officer informed.

We note that the nature of the high level of confidentiality means that we do not have relevant GP or family doctor details for participants, unless these are provided voluntarily in additional communications, and thus of the main management pathways for detecting a clinical presentation, the default response is direct information disclosure to the participant of a potential clinical issue with appropriate advice and signposting. Transmission of the collected information to the GP will not be routinely possible and requesting this information a priori would negate the ethical and recruitment benefits of pseudo-anonymity and confidentiality for participants. Nonetheless, when we alert a student that they are having symptoms consistent with clinical cut-offs the clinician/researcher can offer to contact their primary care doctor on their behalf if they volunteer the necessary contact information.

The third option (“right not to know”) is not deemed appropriate in this context when applied to the individual young person: since the likeliest presentation (elevated symptoms of depression, distress and stress) is treatable. Based on recent recommendations, our default policy is to inform young people of the possibility of them having these conditions and to recommend they seek help. This is to prioritize their welfare.

Preventing abuse of participants and risk analysis

Our risk analysis indicates potential theoretical risks and opportunities for abuse of the research findings and of participants within the study including psychological harms (e.g., distress), invasion of privacy (e.g., intrusion into private affairs, public disclosure of embarrassing private information, publicity that puts the individual in a false light to the public, or appropriation of an individual’s name or picture for personal/ commercial advantage), loss of confidentiality (personal data becoming public through error or thorough deliberate hacking), and social harms (e.g., embarrassment, stigmatization).

The risk analysis indicates that the likelihood of these risks occurring is relatively low although any potential impact for participants would be high, and, as such, we will enact a detailed participant risk register and update it regularly through the project. Multiple steps and processes will be put into place to mitigate and minimise these risks including (a) explaining potential risks in the information sheet; (b) the welfare procedures described above to minimise participant distress; (c) high levels of security and the use of privacy by design protocols for the app and database; (d) a privacy impact assessment; (e)

the emphasis on confidentiality in the project and the separation of collected data from personal identifiers; (f) the use of a code of conduct for all researchers.

In this trial no medical care is provided regardless of the level of risk presented. This is because we are a promotion/prevention trial delivering unguided self-help through a website and so will not have routine contact with GP's or other medical practitioners. Participants are advised of this on the information sheets and sign the section on the consent form to confirm that they understand this.

**Identifying Suicide Risk**

These are 2 ways that that a recruit or participant could indicate risk to the research team either during a screening/follow-up assessment, or in direct contact with a trial researcher by phone, text or email.

1) **EDC Website at Screening**

A recruit may indicate risk on website during the screening assessment in response to questions about suicidality. If the participant scores 1-3 on question 9 of the PHQ9, then further questions to assess risk will automatically be presented:

*PHQ9Q9*

*Over the last two weeks, how often have you been bothered by any of the following problems? Thoughts that you would be better off dead, or of hurting yourself in some way?*

*Those scores would represent the answers several days (1), more than half the days (2) and nearly every day (3)*

The further risk questions which will automatically be asked:

*R1 In the last 2 weeks have you been experiencing regular thoughts about suicide?*

*R2 In the last 2 weeks have you had any intention to hurt or kill yourself?*

*R3 In the last 2 weeks have you made any plans to harm yourself or end your life?*

If score includes PHQ9 -Q9>= 2 and yes to R2 or R3 at screening excluded from trial and signposted to relevant help re suicidality re automatically presented with the following risk page:

**"Your responses to these questions suggest you have been thinking about suicide or about hurting yourself.**

These kinds of thoughts can vary a lot. This may have just been a brief passing thought or reflect a sense of feeling trapped, but without any intention to do anything. These thoughts are relatively common and not that unusual in people who feel stressed. If you would like support with these thoughts, please contact your GP or relevant medical professional.

**If you feel at high risk to yourself or others, please contact your GP immediately.**

**You can contact your GP** using the normal telephone number for your GP practice. If the surgery is not open, you will either be re-directed automatically to the out-of-hours GP service or you will be given

another number to call. You can also **phone 111 to access the NHS 111 service**, which provides access to local NHS healthcare services in England, and is available 24 hours a day, 365 days a year.

However, you may have been thinking about your death a lot, having persistent thoughts about killing yourself, experiencing suicidal intentions and urges, or be making plans to end your life. In any of these cases or if you have any other thoughts of suicide, we strongly recommend that you contact your general practitioner or family doctor **RIGHT AWAY** for advice and tell them how you are feeling

**If you don't think you can stay safe**, please go to the nearest hospital accident and emergency room. If none of these options are available, please contact a family member or a trusted friend, so that you won't be alone right now. It's important to seek out the company of people who can support you and who will help to keep you safe.

Try to commit to a plan of action that does not involve suicide. If you have items that maybe dangerous for you at home, please consider giving them to a trusted friend, neighbour, the police or a pharmacist for safe keeping until you feel stronger. Try to minimise the use of alcohol or illicit drugs, as using these substances are likely to make your recovery harder. It can also be helpful to think about your faith, loved ones, family and pets. It is important to remember that these feelings and urges do pass, and when individuals feel better, they are glad that they did not act on them. There are effective treatments that can help, and there is no need to struggle alone. Talking to people who understand can make it much easier to manage your symptoms so do please call one of the specialist helplines above. There may be reasons for hope that you have yet to consider. Sometimes the smallest reasons for living can get you through a difficult time. Having thoughts of suicide is nothing to be ashamed of and we encourage you to seek help.

Because the study is focused on promoting mental health and preventing poor mental health in the future, rather than treating current difficulties, this study is not suitable for you. The unguided internet treatment has not been designed to help with these difficulties so we are sorry to say that taking part in the study would not be in your best interests at this time. Thank you for your interest.

**We strongly recommend contacting your GP or family doctor as the best person to decide what help you need**.

In addition to your GP or if you don't feel that you can talk to your GP, there are many useful services and useful sources of support.

**IN AN EMERGENCY – SUICIDAL THOUGHTS**

If you are experiencing suicidal thoughts and think that you might be unable to keep yourself safe, visit your nearest Accident and Emergency department or call 999.

**University Based Support**

**GP:** Book an appointment with your GP. They can offer advice or refer you to other more specific services to get help. You can register with an external medical practice if you prefer.

**University specific support:**

- For students at the University of Exeter, there are a wide range of wellbeing and support services - https://www.exeter.ac.uk/students/wellbeing/
- For students at the University of Cardiff, there are a wide range of wellbeing and support services - https://www.cardiff.ac.uk/study/student-life/student-support
- For students at the University of Oxford, there are a wide range of wellbeing and support services - https://www.ox.ac.uk/students/welfare
- For students at the University of Southampton, there are a wide range of wellbeing and support services – https://www.southampton.ac.uk/studentservices/support-wellbeing.page
- For students at Newcastle University, there are a wide range of wellbeing and support services – https://www.ncl.ac.uk/wellbeing/
- For students at King's College London, there are a wide range of wellbeing and support services - https://www.kcl.ac.uk/wellbeing

We hope that you find one or more of the following helpful:

- **Papyrus 0800 068 4141 or text: 07786 209697** offers National support to young people up to age 35 who are feeling suicidal. (Monday-Friday 10:00am-5:00pm and 7:00pm-10:00pm; 2:00pm-5:00pm on weekends, pat@papyrus-uk.org
- The **Samaritans 08457 90 90 90** Freephone (UK and Republic of Ireland): 116 123 (24 hours) offer a confidential service so you can talk about your feelings, you can contact them at www.samaritans.org, Email: jo@samaritans.org
- **SANE** offers support to anyone coping with mental illness, including concerned relatives or friends. The SANE helpline **0845 767 8000** is available 7 days a week from 6.pm-11 pm
- **Maytree** is a registered charity supporting people in suicidal crisis and is open for calls and emails 24 hours a day. **– 020 7263 7070,** maytree@maytree.org.uk
- **Young Minds Crisis Messenger** provides free, 24/7 crisis support across the UK if you are experiencing a mental health crisis. If you need urgent help text YM to 85258. Texts are free from EE, O2, Vodafone, 3, Virgin Mobile, BT Mobile, GiffGaff, Tesco Mobile and Telecom Plus.
- **CALM 0800 58 58 58** (Daily 17:00-midnight) Offers support to young men in the UK who are down or in a crisis, www.thecalmzone.net
- **The Mix**, Freephone: 0808 808 4994 (13:00-23:00 daily), If you're under 25 you can talk to The Mix for free on the phone, by email or on their webchat. You can also use their phone counselling service, or get more information on support services you might need. www.themix.org.uk
- There are a series of NHS self-help guides which can be found here https://web.ntw.nhs.uk/selfhelp/
- There are more guides and online courses here: https://www.cci.health.wa.gov.au/Resources/Looking-After-Yourself

If you would like further advice on these issues from the team, you can contact us by submitting the form below to send an email to the research team.

We note that the research team are not clinicians and cannot provide therapy. However, we can guide you in accessing help, for example, by contacting your GP, which is why we ask for GP details. The team are only available during normal working hours, Monday to Friday and may take 1 or 2 working days to respond.

**FORM TO SUBMIT**

**Name**

**Address**

**Phone number**

**GP Name**

**GP Phone number**

**GP Address**

## 2) Assessment Website at Follow-up (3 months, 12 months)

A recruit may indicate risk on the assessment website in follow-up assessments in response to questions about suicidality. If the participant scores 1-3 on question 9 of the PHQ9, then further questions to assess risk will automatically be presented:

*PHQ9Q9*

*Over the last two weeks, how often have you been bothered by any of the following problems? Thoughts that you would be better off dead, or of hurting yourself in some way?*

*Those scores would represent the answers several days (1), more than half the days (2) and nearly every day (3)*

The further risk questions which will automatically be asked:

*R1 In the last 2 weeks have you been experiencing regular thoughts about suicide?*

*R2 In the last 2 weeks have you had any intention to hurt or kill yourself?*

*R3 In the last 2 weeks have you made any plans to harm yourself or end your life?*

If the recruit answers yes to any of those questions then they would continue in the trial and would be automatically presented with the following risk page:

**"Your responses to these questions suggest you have been thinking about suicide or about hurting yourself.**

These kinds of thoughts can vary a lot. This may have just been a brief passing thought or reflect a sense of feeling trapped, but without any intention to do anything. These thoughts are relatively common and not that unusual in people who feel stressed. If you would like support with these thoughts, please contact your GP or relevant medical professional;

**If you feel at high risk to yourself or others, please contact your GP immediately.**

**You can contact your GP** using the normal telephone number for your GP practice. If the surgery is not open, you will either be re-directed automatically to the out-of-hours GP service or you will be given

another number to call. You can also **phone 111 to access the NHS 111 service**, which provides access to local NHS healthcare services in England, and is available 24 hours a day, 365 days a year.

However, you may have been thinking about your death a lot, having persistent thoughts about killing yourself, experiencing suicidal intentions and urges, or be making plans to end your life. In any of these cases or if you have any other thoughts of suicide, we strongly recommend that you contact your general practitioner or family doctor RIGHT AWAY for advice and tell them how you are feeling

**If you don't think you can stay safe**, please go to the nearest hospital accident and emergency room. If none of these options are available, please contact a family member or a trusted friend, so that you won't be alone right now. It's important to seek out the company of people who can support you and who will help to keep you safe.

Try to commit to a plan of action that does not involve suicide. If you have items that maybe dangerous for you at home, please consider giving them to a trusted friend, neighbour, the police or a pharmacist for safe keeping until you feel stronger. Try to minimise the use of alcohol or illicit drugs, as using these substances are likely to make your recovery harder. It can also be helpful to think about your faith, loved ones, family and pets. It is important to remember that these feelings and urges do pass, and when individuals feel better, they are glad that they did not act on them. There are effective treatments that can help, and there is no need to struggle alone. Talking to people who understand can make it much easier to manage your symptoms so do please call one of the specialist helplines above. There may be reasons for hope that you have yet to consider. Sometimes the smallest reasons for living can get you through a difficult time. Having thoughts of suicide is nothing to be ashamed of and we encourage you to seek help.

**We strongly recommend contacting your GP or family doctor as the best person to decide what help you need.**

In addition to your GP or if you don't feel that you can talk to your GP, there are many useful services and useful sources of support.

**IN AN EMERGENCY – SUICIDAL THOUGHTS**

If you are experiencing suicidal thoughts and think that you might be unable to keep yourself safe, visit your nearest Accident and Emergency department or call 999.

**University Based Support**

**GP:** Book an appointment with your GP. They can offer advice or refer you to other more specific services to get help. You can register with an external medical practice if you prefer.

**University specific support:**

- For students at the University of Exeter, there are a wide range of wellbeing and support services - https://www.exeter.ac.uk/students/wellbeing/
- For students at the University of Cardiff, there are a wide range of wellbeing and support services - https://www.cardiff.ac.uk/study/student-life/student-support
- For students at the University of Oxford, there are a wide range of wellbeing and support services - https://www.ox.ac.uk/students/welfare

- For students at the University of Southampton, there are a wide range of wellbeing and support services – https://www.southampton.ac.uk/studentservices/support-wellbeing.page
- For students at Newcastle University, there are a wide range of wellbeing and support services – https://www.ncl.ac.uk/wellbeing/
- For students at King's College London, there are a wide range of wellbeing and support services - https://www.kcl.ac.uk/wellbeing

We hope that you find one or more of the following helpful:

- **Papyrus 0800 068 4141 or text: 07786 209697** offers National support to young people up to age 35 who are feeling suicidal. (Monday-Friday 10:00am-5:00pm and 7:00pm-10:00pm; 2:00pm-5:00pm on weekends, pat@papyrus-uk.org
- The **Samaritans 08457 90 90 90** Freephone (UK and Republic of Ireland): 116 123 (24 hours),offer a confidential service so you can talk about your feelings, you can contact them at www.samaritans.org, Email: jo@samaritans.org
- **SANE** offers support to anyone coping with mental illness, including concerned relatives or friends. The SANE helpline **0845 767 8000** is available 7 days a week from 6.pm-11 pm
- **Maytree** is a registered charity supporting people in suicidal crisis and is open for calls and emails 24 hours a day. **– 020 7263 7070,** maytree@maytree.org.uk
- **Young Minds Crisis Messenger** provides free, 24/7 crisis support across the UK if you are experiencing a mental health crisis. If you need urgent help text YM to 85258. Texts are free from EE, O2, Vodafone, 3, Virgin Mobile, BT Mobile, GiffGaff, Tesco Mobile and Telecom Plus.
- **CALM 0800 58 58 58** (Daily 17:00-midnight) Offers support to young men in the UK who are down or in a crisis, www.thecalmzone.net
- **The Mix**, Freephone: 0808 808 4994 (13:00-23:00 daily), If you're under 25 you can talk to The Mix for free on the phone, by email or on their webchat. You can also use their phone counselling service, or get more information on support services you might need. www.themix.org.uk

If you would like further advice on these issues from the team, you can contact us by submitting the form below to send an email.

We note that the research team are not clinicians and cannot provide therapy. However, we can guide you in accessing help, for example, by contacting your GP, which is why we ask for GP details. The team are only available during normal working hours, Monday to Friday and may take 1 or 2 working days to respond.

**FORM TO SUBMIT**

**Name**

**Address**

**Phone number**

**GP Name**

**GP Phone number**

**GP Address**

In the event that a participant indicates suicide risk at follow up and this screen is displayed, an automated report/record from the website will be sent to the therapists and chief investigator and logged by them and the trial manager.. The record will show the trial number and the answers to the 3 risk questions (e.g., R1=Y, R2=N, R3=N). This data will monitor frequency of suicidality across the trial arms.

### 3) Participants at screening with current depression (without risk)

If a participant reports current depression at screening, but then does not report current risk then they are ineligible for the prevention trial, but will be eligible for the acute treatment trial.

The screening website will automatically provide them with the following information if they meet criteria for current depression – **it should redirect to the consent page for the acute depression trial**:

**"Your responses to these questions suggest that within the last month, your overall mood has been low for at least 2 weeks and has had a negative effect on your life. It may be that you are currently experiencing an episode of depression or going through a period of stress or loss.**

This means that you are eligible for the Nurture-U trial that is investigating digital cognitive behavioural therapy to treat anxiety and depression. The trial details are explained on subsequent pages [there would be access to relevant information sheet and consent form for the parallel acute depression study].

If you currently are having problems with the symptoms of depression then **we strongly recommend that you talk to your general practitioner, family doctor or a mental health professional** about your difficulties, as he or she may be able to find ways to help you to improve your mood and handle life's difficulties better.

If you have not had a health check recently that may also be worth doing so. If you have a diagnosis of depression, please make sure that you follow your treatment regime and consult with the medical professionals involved in your care.

**You can contact your GP** using the normal telephone number for your GP practice. If the surgery is not open, you will either be re-directed automatically to the out-of-hours GP service or you will be given another number to call. You can also **phone 111 to access the NHS 111 service**, which provides access to local NHS healthcare services in England, and is available 24 hours a day, 365 days a year.

As well as your GP, there are many other services available who are really experienced at helping people with your symptoms:

**University specific support:**

- For students at the University of Exeter, there are a wide range of wellbeing and support services - https://www.exeter.ac.uk/students/wellbeing/
- For students at the University of Cardiff, there are a wide range of wellbeing and support services - https://www.cardiff.ac.uk/study/student-life/student-support
- For students at the University of Oxford, there are a wide range of wellbeing and support services - https://www.ox.ac.uk/students/welfare

- For students at the University of Southampton, there are a wide range of wellbeing and support services – https://www.southampton.ac.uk/studentservices/support-wellbeing.page
- For students at Newcastle University, there are a wide range of wellbeing and support services – https://www.ncl.ac.uk/wellbeing/
- For students at the King's College London, there are a wide range of wellbeing and support services - https://www.kcl.ac.uk/wellbeing

Here are some useful websites that you access directly:

- **Students against depression** is a website by students, for students offering information, guidance and resources to those affected by low mood, depression and suicidal thinking. Alongside clinically-validated information and resources it presents the experiences, strategies and advice of students themselves – after all, who better to speak to their peers about how depression can be overcome? https://www.studentsagainstdepression.org/
- **YoungMinds** are there to make sure all young people get the best possible mental health support and have the resilience to overcome life's difficulties. They provide lots of resources to help with young person's mental health: https://youngminds.org.uk/find-help/
- **Mind** The Mental Health Charity provide information, advice, and support to empower anyone experiencing a mental health problem. They provide information about mental health problems and potential treatments as well as tips for everyday living. https://www.mind.org.uk/
  - **For info about depression:** https://www.mind.org.uk/information-support/types-of-mental-health-problems/depression/#.XGQRn1X7SUk
  - **For apps to help with your mental health and wellbeing:** https://www.mindcharity.co.uk/advice-information/how-to-look-after-your-mental-health/apps-for-wellbeing-and-mental-health/
- **Rethink Mental Illness** Provide expert advice and information to everyone affected by mental health problems, and provide services and groups; including resources specific to young people https://www.rethink.org/living-with-mental-illness/young-people
  - Toolkit for young people with questions or worries about their mental health: https://www.rethink.org/media/1020652/ResourceFinal.pdf

  **There are a series of NHS self-help guides which can be found here** https://web.ntw.nhs.uk/selfhelp/
- **There are more guides and online courses here:** https://www.cci.health.wa.gov.au/Resources/Looking-After-Yourself

**Helplines**

Alternatively, here are helplines you can ring to talk to someone about what you're going through:

- **Papyrus 0800 068 4141 or text: 07786 209697** offers National support to young people up to age 35 who are feeling suicidal. (Monday-Friday 10:00am-5:00pm and 7:00pm-10:00pm; 2:00pm-5:00pm on weekends, pat@papyrus-uk.org

- The **Samaritans 08457 90 90 90** Freephone (UK and Republic of Ireland): 116 123 (24 hours),offer a confidential service so you can talk about your feelings, you can contact them at www.samaritans.org, Email: jo@samaritans.org

- **SANE** offers support to anyone coping with mental illness, including concerned relatives or friends. The SANE helpline **0845 767 8000** is available 7 days a week from 6.pm-11 pm
- **Maytree** is a registered charity supporting people in suicidal crisis and is open for calls and emails 24 hours a day. **– 020 7263 7070,** maytree@maytree.org.uk
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Talking to people who understand can make it much easier to manage your symptoms so **please do call your GP or one of the specialist helplines above**.

### 4) Significant levels of depression at follow-up assessments

**For participants reporting significant levels of depression at any of the follow-up assessments (defined as PHQ-9 score >20),** the follow-up website will automatically provide them with the following information:

**"Your responses to these questions suggest that within the last month, your overall mood has been low for at least 2 weeks and has had a negative effect on your life. It may be that you are currently experiencing an episode of depression or going through a period of stress or loss.**

If you currently are having problems with the symptoms of depression then **we strongly recommend that you talk to your general practitioner, family doctor or a mental health professional** about your difficulties, as he or she may be able to find ways to help you to improve your mood and handle life's difficulties better.

If you have not had a health check recently that may also be worth doing so. If you have a diagnosis of depression, please make sure that you follow your treatment regime and consult with the medical professionals involved in your care.

**You can contact your GP** using the normal telephone number for your GP practice. If the surgery is not open, you will either be re-directed automatically to the out-of-hours GP service or you will be given another number to call. You can also **phone 111 to access the NHS 111 service**, which provides access to local NHS healthcare services in England, and is available 24 hours a day, 365 days a year.

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- **Mind** The Mental Health Charity provide information, advice, and support to empower anyone experiencing a mental health problem. They provide information about mental health problems and potential treatments as well as tips for everyday living. https://www.mind.org.uk/
  - **For info about depression:** https://www.mind.org.uk/information-support/types-of-mental-health-problems/depression/#.XGQRn1X7SUk
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  - Toolkit for young people with questions or worries about their mental health: https://www.rethink.org/media/1020652/ResourceFinal.pdf

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**Helplines**

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Talking to people who understand can make it much easier to manage your symptoms so **please do call your GP or one of the specialist helplines above**.

### 5) Exclusions- Bipolar and Psychosis

If a potential recruit is excluded on the basis of a self-reporting at the screening questionnaire a previous diagnosis of Bipolar disorder or psychosis then would be automatically provided with the following information:

"**You have reported that you have previously received a diagnosis of either bipolar disorder or psychosis.**

Because this study is focused on promoting mental health and preventing poor mental health in the future, rather than treating current difficulties, the current study is not suitable for you at this time. The internet treatment has not been designed to help with these difficulties so we are sorry to say that taking part in the study would not be in your best interests at this time. Thank you for your interest.

**Your GP or relevant medical professional is the best person to decide what help you need.**

**You can contact your GP** using the normal telephone number for your GP practice. If the surgery is not open, you will either be re-directed automatically to the out-of-hours GP service or you will be given another number to call. You can also **phone 111 to access the NHS 111 service**, which provides access to local NHS healthcare services in England, and is available 24 hours a day, 365 days a year.

Alongside your GP, there are other services available to you to provide information and support:

**University specific support:**

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- For students at Newcastle University, there are a wide range of wellbeing and support services – https://www.ncl.ac.uk/wellbeing/
- For students at King's College London, there are a wide range of wellbeing and support services - https://www.kcl.ac.uk/wellbeing

Useful **WEBSITES** that you can access directly below include:

- **YoungMinds** are there to make sure all young people get the best possible mental health support and have the resilience to overcome life's difficulties. They provide lots of resources to help with young person's mental health: https://youngminds.org.uk/find-help/
- **Mind** The Mental Health Charity provide information, advice, and support to empower anyone experiencing a mental health problem. They provide information about mental health problems and potential treatments as well as tips for everyday living. https://www.mind.org.uk/
  - **For bipolar disorder:** https://www.mind.org.uk/information-support/types-of-mental-health-problems/bipolar-disorder/about-bipolar-disorder/?o=1142#.XGQJJVX7SUk
  - **For psychosis:** https://www.mind.org.uk/information-support/types-of-mental-health-problems/psychosis/#.XGQI_lX7SUk
  - **For schizophrenia**: https://www.mind.org.uk/information-support/types-of-mental-health-problems/schizophrenia/about-schizophrenia/?o=6266#.XGQJQlX7SUk
  - **For apps to help with your wellbeing and mental health:** https://www.mindcharity.co.uk/advice-information/how-to-look-after-your-mental-health/apps-for-wellbeing-and-mental-health/
- **BipolarUK** National charity dedicated to supporting individuals with bipolar, their families and carers. Their websites has information leaflets and links to support, including a peer support line https://www.bipolaruk.org/
- **Rethink Mental Illness**. Provide expert advice and information to everyone affected by mental health problems, and provide services and groups; including resources specific to young people https://www.rethink.org/living-with-mental-illness/young-people
  - **Toolkit for young people with questions or worries about their mental health:** https://www.rethink.org/media/1020652/ResourceFinal.pdf
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Alternatively, here are **HELPLINES** you can ring to talk to someone about what how you are feeling

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- The **Samaritans 08457 90 90 90** Freephone (UK and Republic of Ireland): 116 123 (24 hours),offer a confidential service so you can talk about your feelings, you can contact them at www.samaritans.org, Email: jo@samaritans.org
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If you find your symptoms particularly distressing or have thoughts about ending your life then please go to the nearest emergency room, or immediately contact your GP.

Talking to people who understand can make it much easier to manage your symptoms so **please do call your GP or one of the specialist helplines above**.

### 6) Exclusions- substance dependence

If a potential recruit is excluded on the basis of a self-reporting at the screening questionnaire a previous diagnosis of substance dependence then would be automatically provided with the following information:

“You have reported that you have previously received a diagnosis of alcohol or substance disorder. Because this study is focused on treating anxiety and depression, rather than treating alcohol or substance disorder, the current study is not suitable for you at this time. The internet treatment has not been designed to help with these difficulties so we are sorry to say that taking part in the study would not be in your best interests at this time. Thank you for your interest.

Your GP or relevant medical professional is the best person to decide what help you need.

You can contact your GP using the normal telephone number for your GP practice. If the surgery is not open, you will either be re-directed automatically to the out-of-hours GP service or you will be given another number to call. You can also phone 111 to access the NHS 111 service, which provides access to local NHS healthcare services in England, and is available 24 hours a day, 365 days a year.

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- For students at King's College London, there are a wide range of wellbeing and support services - https://www.kcl.ac.uk/wellbeing

Useful WEBSITES that you can access directly below include:

- Alcoholics Anonymous: They offer telephone, online and face-to-face help and advice related to alcohol or a drinking problem.
  https://www.alcoholics-anonymous.org.uk/

  FRANK: For friendly, confidential drugs advice, call FRANK on: 0300 123 6600. Or you can access their website at:
  http://www.talktofrank.com

- YoungMinds are there to make sure all young people get the best possible mental health support and have the resilience to overcome life's difficulties. They provide lots of resources to help with young person's mental health: https://youngminds.org.uk/find-help/
- Mind The Mental Health Charity provide information, advice, and support to empower anyone experiencing a mental health problem. They provide information about mental health problems and potential treatments as well as tips for everyday living. https://www.mind.org.uk/
  - For apps to help with your wellbeing and mental health: https://www.mindcharity.co.uk/advice-information/how-to-look-after-your-mental-health/apps-for-wellbeing-and-mental-health/
- Rethink Mental Illness. Provide expert advice and information to everyone affected by mental health problems, and provide services and groups; including resources specific to young people https://www.rethink.org/living-with-mental-illness/young-people
  - Toolkit for young people with questions or worries about their mental health: https://www.rethink.org/media/1020652/ResourceFinal.pdf
- There are a series of NHS self-help guides which can be found here https://web.ntw.nhs.uk/selfhelp/

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Alternatively, here are HELPLINES you can ring to talk to someone about what how you are feeling

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If you find your symptoms particularly distressing or have thoughts about ending your life then please go to the nearest emergency room, or immediately contact your GP.

Talking to people who understand can make it much easier to manage your symptoms so please do call your GP or one of the specialist helplines above.

### 7) Exclusions- receiving current therapy elsewhere

If potential participants are excluded on the basis of receiving current therapy elsewhere then they would be provided with the following screen:

**“Your responses to these questions indicate you are currently receiving psychological therapy for your mental health.**

Because this trial is focused on promoting mental health and preventing poor mental health in the future, rather than treating current difficulties, and we are testing the effect of the digital treatment, currently receiving psychological therapy means that this study is not suitable for you at this time. However, once you complete your course of psychological therapy, you may be eligible for the study, and if you are still interested, we recommend returning to the trial website and completing the screening questions again to see if you can join the study. Thank you for your interest.

**If you have concerns about your current therapy, your GP or therapist is the best person to talk to.**

**You can contact your GP** using the normal telephone number for your GP practice. If the surgery is not open, you will either be re-directed automatically to the out-of-hours GP service or you will be given another number to call. You can also **phone 111 to access the NHS 111 service**, which provides access to local NHS healthcare services in England, and is available 24 hours a day, 365 days a year.

If you do feel like you need some extra help as well as your GP and current therapy, there are many other services available to get you through this difficult time:

**University specific support:**

- For students at the University of Exeter, there are a wide range of wellbeing and support services - https://www.exeter.ac.uk/students/wellbeing/
- For students at the University of Cardiff, there are a wide range of wellbeing and support services - https://www.cardiff.ac.uk/study/student-life/student-support
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- For students at King's College London, there are a wide range of wellbeing and support services - https://www.kcl.ac.uk/wellbeing

Useful **WEBSITES** that you can access directly below include:

- **Students against depression** is a website by students, for students offering information, guidance and resources to those affected by low mood, depression and suicidal thinking. Alongside clinically-validated information and resources it presents the experiences, strategies and advice of students themselves – after all, who better to speak to their peers about how depression can be overcome? https://www.studentsagainstdepression.org/
- **YoungMinds** are there to make sure all young people get the best possible mental health support and have the resilience to overcome life's difficulties. They provide lots of resources to help with young person's mental health: https://youngminds.org.uk/find-help/
- **Mind** The Mental Health Charity provide information, advice, and support to empower anyone experiencing a mental health problem. They provide information about mental health problems and potential treatments as well as tips for everyday living. https://www.mind.org.uk/
    - **For info about depression:** https://www.mind.org.uk/information-support/types-of-mental-health-problems/depression/#.XGQRn1X7SUk
    - **For apps to help with your mental health and wellbeing:** https://www.mindcharity.co.uk/advice-information/how-to-look-after-your-mental-health/apps-for-wellbeing-and-mental-health/
    - **For info about mindfulness,** a technique you can learn which involves making a special effort to notice what's happening in the present moment. Many people find mindfulness

helps them manage their day-to-day wellbeing. https://www.mind.org.uk/information-support/drugs-and-treatments/mindfulness/#.XGQBhFX7SUk

- **Rethink Mental Illness** Provide expert advice and information to everyone affected by mental health problems, and provide services and groups; including resources specific to young people https://www.rethink.org/living-with-mental-illness/young-people
    - Toolkit for young people with questions or worries about their mental health: https://www.rethink.org/media/1020652/ResourceFinal.pdf
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- The **Samaritans 08457 90 90 90** Freephone (UK and Republic of Ireland): 116 123 (24 hours),offer a confidential service so you can talk about your feelings, you cancontact them at www.samaritans.org, Email: jo@samaritans.org
- **SANE** offers support to anyone coping with mental illness, including concerned relatives or friends. The SANE helpline **0845 767 8000** is available 7 days a week from 6.pm-11 pm
- **Maytree** is a registered charity supporting people in suicidal crisis and is open for calls and emails 24 hours a day. **– 020 7263 7070,** maytree@maytree.org.uk
- **Young Minds Crisis Messenger** provides free, 24/7 crisis support across the UK if you are experiencing a mental health crisis. If you need urgent help text YM to 85258. Texts are free from EE, O2, Vodafone, 3, Virgin Mobile, BT Mobile, GiffGaff, Tesco Mobile and Telecom Plus.
- **CALM 0800 58 58 58** (Daily 17:00-midnight) Offers support to young men in the UK who are down or in a crisis, www.thecalmzone.net
- **The Mix**, Freephone: 0808 808 4994 (13:00-23:00 daily), If you're under 25 you can talk to The Mix for free on the phone, by email or on their webchat. You can also use their phone counselling service, or get more information on support services you might need. www.themix.org.uk

If you find your symptoms particularly distressing or have thoughts about ending your life, go to the nearest emergency room, or **immediately contact your GP.**

### 8) Exclusions- receiving antidepressant medications

If potential participants are excluded on the basis of receiving current antidepressant medication then they would be provided with the following screen:

**“Your responses to these questions indicate you are have recently started or changed medication for anxiety or depression.**

Because this trial is focused on promoting mental health and preventing poor mental health in the future, rather than treating current difficulties, and we are testing the effect of the digital treatment, we need to be able to rule out other possible causes for any improvement such as taking medication for anxiety and depression. We therefore require participants to be on a stable dose of a medication for at least four weeks before entering the study, which means that this study is not suitable for you just now. However, once you have been on the same dose of your medication for at least four weeks, you can return and check your eligibility again. Thank you for your interest.

**If you have concerns about your current medication, your GP is the best person to talk to.**

**You can contact your GP** using the normal telephone number for your GP practice. If the surgery is not open, you will either be re-directed automatically to the out-of-hours GP service or you will be given another number to call. You can also **phone 111 to access the NHS 111 service**, which provides access to local NHS healthcare services in England, and is available 24 hours a day, 365 days a year.

If you do feel like you need some extra help as well as your GP and current therapy, there are many other services available to get you through this difficult time:

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Useful **WEBSITES** that you can access directly below include:

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  - **For info about depression:** https://www.mind.org.uk/information-support/types-of-mental-health-problems/depression/#.XGQRn1X7SUk
  - **For apps to help with your mental health and wellbeing:** https://www.mindcharity.co.uk/advice-information/how-to-look-after-your-mental-health/apps-for-wellbeing-and-mental-health/
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  - Toolkit for young people with questions or worries about their mental health: https://www.rethink.org/media/1020652/ResourceFinal.pdf
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Alternatively, here are **HELPLINES** you can ring to talk to someone about what how you are feeling

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- The **Samaritans 08457 90 90 90** Freephone (UK and Republic of Ireland): 116 123 (24 hours),offer a confidential service so you can talk about your feelings, you can contact them at www.samaritans.org, Email: jo@samaritans.org
- **SANE** offers support to anyone coping with mental illness, including concerned relatives or friends. The SANE helpline **0845 767 8000** is available 7 days a week from 6.pm-11 pm
- **Maytree** is a registered charity supporting people in suicidal crisis and is open for calls and emails 24 hours a day. **– 020 7263 7070,** maytree@maytree.org.uk
- **Young Minds Crisis Messenger** provides free, 24/7 crisis support across the UK if you are experiencing a mental health crisis. If you need urgent help text YM to 85258. Texts are free from EE, O2, Vodafone, 3, Virgin Mobile, BT Mobile, GiffGaff, Tesco Mobile and Telecom Plus.
- **CALM 0800 58 58 58** (Daily 17:00-midnight) Offers support to young men in the UK who are down or in a crisis, www.thecalmzone.net
- **The Mix**, Freephone: 0808 808 4994 (13:00-23:00 daily), If you're under 25 you can talk to The Mix for free on the phone, by email or on their webchat. You can also use their phone counselling service, or get more information on support services you might need. www.themix.org.uk

If you find your symptoms particularly distressing or have thoughts about ending your life, go to the nearest emergency room, or **immediately contact your GP."**

## 9) Exclusions- under the age of 16

If potential participants are excluded on the basis of being under the age of 16 then they would be provided with the following screen:

"This research requires that participants can provide their own informed consent – which in the UK requires you to be aged 16 or over. Because you indicated that you are aged under 16, you are therefore not eligible for the study. Thank you for your interest. We will be recruiting for over a year so if you are over 16 during the next year, you would be able to reapply for the study via our website.

**If you have any concerns about your wellbeing or mental health, your GP is the best person to decide what help you need.**

**You can contact your GP** using the normal telephone number for your GP practice. If the surgery is not open, you will either be re-directed automatically to the out-of-hours GP service or you will be given another number to call. You can also **phone 111 to access the NHS 111 service**, which provides access to local NHS healthcare services in England, and is available 24 hours a day, 365 days a year.

Alongside your GP, there are other services available to you to provide information and support:

**University specific support:**

- For students at the University of Exeter, there are a wide range of wellbeing and support services - https://www.exeter.ac.uk/students/wellbeing/
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Useful **WEBSITES** that you can access directly below include:

- **YoungMinds** are there to make sure all young people get the best possible mental health support and have the resilience to overcome life's difficulties. They provide lots of resources to help with young person's mental health: https://youngminds.org.uk/find-help/
- **Mind** The Mental Health Charity provide information, advice, and support to empower anyone experiencing a mental health problem. They provide information about mental health problems and potential treatments as well as tips for everyday living. https://www.mind.org.uk/
- **For apps to help with your wellbeing and mental health:** https://www.mindcharity.co.uk/advice-information/how-to-look-after-your-mental-health/apps-for-wellbeing-and-mental-health/

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    - **Toolkit for young people with questions or worries about their mental health:** https://www.rethink.org/media/1020652/ResourceFinal.pdf
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Alternatively, here are **HELPLINES** you can ring to talk to someone about what how you are feeling

- **Papyrus 0800 068 4141 or text: 07786 209697** offers National support to young people up to age 35 who are feeling suicidal. (Monday-Friday 10:00am-5:00pm and 7:00pm-10:00pm; 2:00pm-5:00pm on weekends, pat@papyrus-uk.org

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- **CALM 0800 58 58 58** (Daily 17:00-midnight) Offers support to young men in the UK who are down or in a crisis, www.thecalmzone.net
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If you find your symptoms particularly distressing or have thoughts about ending your life then please go to the nearest emergency room, or immediately contact your GP.

Talking to people who understand can make it much easier to manage your symptoms so **please do call your GP or one of the specialist helplines above**."

**10) Exclusions- not a student at a UK university**

If potential participants are excluded on the basis of not being a student at a UK university then they would be provided with the following screen:

"This research is focused on students (undergraduate and postgraduate) at UK universities. Because you do not indicate that you were at a UK university, you are not eligible for this research. Thank you for your interest.

**If you have any concerns about your wellbeing or mental health, your GP is the best person to decide what help you need.**

**You can contact your GP** using the normal telephone number for your GP practice. If the surgery is not open, you will either be re-directed automatically to the out-of-hours GP service or you will be given another number to call. You can also **phone 111 to access the NHS 111 service**, which provides access to local NHS healthcare services in England, and is available 24 hours a day, 365 days a year.

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Useful **WEBSITES** that you can access directly below include:

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    - **Toolkit for young people with questions or worries about their mental health:** https://www.rethink.org/media/1020652/ResourceFinal.pdf
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If you find your symptoms particularly distressing or have thoughts about ending your life then please go to the nearest emergency room, or immediately contact your GP.

Talking to people who understand can make it much easier to manage your symptoms so **please do call your GP or one of the specialist helplines above**."

**11) Message for participants who are eligible for feasibility trial but not from Exeter university:**

"Thank you for completing the NURTURE U trial screener. Based on your answers to the screening questions, it appears that you are currently not particularly stressed, worried, anxious or feeling down – this means that you are currently not eligible for any of our trials at this time because they are focused on helping people experiencing elevated symptoms or stress. We wish you all the best and hope that you continue to feel well.

Have a nice day!"

***12)*** **Message for participants who are eligible for Feasibility/Acute/Rumination but they refuse to consent after completing screening:**

***"***Thank you for completing the Nurture-U trials screener and for reading our information sheet and consent form. You are only able to proceed further into the study if you consent to participate in the study. Because you have not consented to join the study, you are unable to proceed further. If this is a mistake and you do want to take part, please go back and complete the consent form. Thank you for your interest.

**If you have any concerns about your wellbeing or mental health, your GP is the best person to decide what help you need.**

**You can contact your GP** using the normal telephone number for your GP practice. If the surgery is not open, you will either be re-directed automatically to the out-of-hours GP service or you will be given another number to call. You can also **phone 111 to access the NHS 111 service**, which provides access to local NHS healthcare services in England, and is available 24 hours a day, 365 days a year.

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If you find your symptoms particularly distressing or have thoughts about ending your life then please go to the nearest emergency room, or immediately contact your GP.

Talking to people who understand can make it much easier to manage your symptoms so **please do call your GP or one of the specialist helplines above**."

**13) Introduction/welcome information for the Nurture-U trials screening page:**

"Thank you for your interest in taking part in one of the Nurture-U research trials to improve university student mental health.

The Nurture-U project includes several studies to investigate different interventions to help university students including a study of a mobile app to increase confidence and reduce worry, and a study comparing therapist-supported versus self-directed digital cognitive-behavioural therapy for anxiety and depression, to find out what works best for whom. We have a brief online survey before you can proceed to these studies to assess if you are eligible and to then either direct you to the relevant study or to information about why the study is not suitable for you.

We ask you to complete brief online questions about demographics, symptoms and coping styles. These questions should take less than 5 minutes to complete."

**Risk Assessment and Reporting: telephone and email contact**

All researchers and clinicians that have direct contact (by telephone or email) with recruits or participants will be familiar and trained how to use this SOP and will sign the delegation log to say that this has been done. The purpose of the SOP is to script the contact between researcher and participant so that the risk is assessed.

PIs/supervisors/clinicians (e.g., local psychiatrists or clinical psychologists) will also familiarise themselves with this SOP and provide researchers with their contact details in case the researcher needs advice. When clinical academic staff are away on leave, they should ensure appropriate cover is arranged to support researcher with advice on for any risk issues that might arise in their absence. The clinician is available to support and guide the researcher in responding to risk and where requested in communicating and providing guidance to the participant.

**1) Telephone contact**

When conducting telephone interviews in which risk may be disclosed, the interviewer should establish the telephone number and location of the participant at the start of the call, and clarify the boundaries of confidentiality:

'Hi, is that (name) this X from the Nurture-U trial, is now a convenient time to talk?' [or in response to answering a call direct from a participant – at which point we would ask for name and email, so we can identify them]

If yes 'This call is confidential and the only reason I would break that is if I thought you were at risk to yourself or others and it was in your best interests.

We just wanted to give you a call after your message to us in the email you sent / I would like to clarify what you are telling me now on the phone.

Can I just check where you are at the moment? [obtain details of location/address]

*"I see that you've said / you mentioned that…….. (examples: if thoughts of death /"what is the point?" / "it might be better if I did not wake up",*

*"Has this gone as far as thinking about harming yourself or killing yourself?" If yes, or if already stated:*

*'These are common thoughts and can vary a lot in their severity and it's important to make sure you are receiving the right kind of support. So I would now like to ask you some more questions that will explore these feelings in a little more depth."*

***INTENTION***

Have you had any intention to hurt or kill yourself? YES OR NO

**PLANS**

1 Do you know how you would kill yourself? Yes / No

If **yes – ask for and record** details

2 Have you made any actual plans to end your life? Yes / No

If **yes – ask for and record** details

**ACTIONS**

3. Have you made any actual preparations to kill yourself? Yes / No

If **yes – ask for and record** details

4. Have you ever attempted suicide in the past? Yes / No

If **yes – ask for and record** details

3. **PREVENTION**Is there anything stopping you killing or harming yourself at the moment? Yes / No

If **yes – ask for and record** details

4. Do you feel that there is any immediate danger that you will harm or kill yourself? Yes / No

Ask for and record Details:

***If yes to any of questions 1-4***

- [ if yes to 4 only, or yes to 1 only] I can see that things have been very difficult for you, but it seems to me these thoughts about death are not ones you would act on – would this be how you see things? *(if they say yes)* I would advise you to make an appointment to see your GP to talk about these feelings.
- [if any of 1-3] Would you like us to write a letter to your GP letting them know how you are feeling? If yes, please can you give us your permission to do so *(and provide their contact details)*
- [all] I can also email you a list of website and helplines for people that have expertise at helping in just this kind of situation, would that be helpful?

***If yes to 2 and 3 or to 6, request clinical input if not a clinician and say the following***

- I am very concerned about your safety at this moment….

- I am not a clinician but I would like you to talk to one right now. With your permission I am going to call the site clinician/your GP to let them know how you are feeling and to arrange for you to receive immediate help/a call back. Can you provide their contact details?

***In addition, If yes to question 6 [immediate risk]***

- I think its best that you get emergency support at this time. I am going to call your GP/the emergency services and send them to your location.

*Keep the participant on the phone while you call the clinician from another number or email.*

If immediate risk is disclosed the interviewer should not hang up if at all possible.
In case contact is lost, the participant should be informed that the interviewer / supervisor will call them back straight away but that if they are unable to make contact the participant's G.P. or the emergency

services will be informed. Good practice is to call /use a phone line for participants that (a) is mobile so that researcher can contact clinical supervisor if physically proximal (b) have a second line to contact clinical supervisor (e.g., by text) whilst maintaining conversation with participant.

**2) E-mail contact**

In the eventuality that participants send emails to researchers that indicate potential elevated suicide risk (e.g., talking about death, ending it all, seeing no hope, referring to suicide or self-harm, seeing no way out), then further follow-up steps will be taken, including attempts to respond to the participant to clarify the severity of the risk. These emails will provide guidance and signposting information (replicating the information provided on the automated webpage in response to reporting suicidality on the screening/assessment website) and enquire about risk following the questions above (e.g., asking about suicidal ideation, plans, preparation, prevention, means).

An email will be sent to the participant, acknowledging their potential distress and thoughts of death and self-harm, including the following questions:

Self Risk Q1 Are you currently experiencing any thoughts about suicide?

Self Risk Q2 Do you have any intention to hurt or kill yourself?

Self Risk Q3 Have you made any current plans to end your life or harm yourself?

Self Risk Q4 Do you have the means to harm yourself or end your life?

A template email for initial response is as follows, to be adapted to directly respond to details and concerns raised in specific email from the participant:

“Dear ,

Thank you for contacting us.

Your email suggested that you might have been having thoughts about harming or killing yourself. These thoughts can vary a lot from person to person. These may have just been brief passing thoughts or reflect a sense of feeling trapped, but without any intention to do anything. These thoughts are relatively common and not that unusual in people who feel stressed.
On the other hand, you may have been thinking about your death a lot, or you may have thought about killing yourself. You may have even have thought about how you might kill yourself or made a plan to end your life. In any of these cases, we strongly urge you to talk to someone about these thoughts, and in particular your GP or family doctor.

It would be useful to know more about the sort of thoughts you are having at the moment.
Are they just thoughts about death? Or are you having thoughts about killing or harming yourself?
If it is the latter, have you made any actual plans to end your life? Have you made any actual preparations to kill yourself? Is there anything stopping you killing or harming yourself at the moment?
I would appreciate you letting me know the answers to these questions, so I can help you as best I can.

If you are having thoughts of ending your life or harming yourself, I **advise you to contact your general practitioner or family doctor or mental health professional as soon as possible** and tell them how you are feeling. If you don't think you can stay safe, please go to the nearest hospital accident and emergency room or contact one of the suicide hotlines at Befrienders.org or Samaritans.org. If none of these options are available, please contact a family member, a trusted friend, or any other trusted person so that you won't be alone right now.

**Throughout the UK, please contact your GP** using the normal telephone number for your GP practice. If the surgery is not open, you will either be re-directed automatically to the out-of-hours GP service or you will be given another number to call. You can also **phone 111 to access the NHS 111 service**, which provides access to local NHS healthcare services in England, and is available 24 hours a day, 365 days a year. Details for out of hours services and support across the UK can be found in the leaflet on national out-of-hours services which has been attached to this email.

**If you don't think you can stay safe**, please go to the nearest hospital accident and emergency room. If none of these options are available, please contact a family member or a trusted friend, so that you won't be alone right now. If you have already made a plan, as best you can, please try and get rid of the means to harm yourself, whilst keeping yourself safe. It can also be helpful to focus on anything that may stop you from killing or harming yourself at the moment, such as thinking about your faith, loved ones, family and pets. It is important to remember that these feelings and urges do pass, and when individuals feel better, they are glad that they did not act on them. There are effective treatments that can help, and there is no need to struggle alone. Getting help may make it easier to manage your symptoms and to live the kind of life you would like to live.

Best wishes,
Researcher Name”

Similar actions will be taken for email responses as for telephone contacts (see section above). Follow-up emails may be necessary to either further clarify responses to questions, provide further guidance and support, or provide more detailed signposting for help.

**Risk Assessment and Reporting: Risk register**

All risk alerts whether via email or telephone contact will be logged on a risk register/log with any action taken, by whom and when (see below). Site researchers will follow up on risk alerts within 1 working day using the risk assessment and reporting SOP including responding to participants and registering the action taken. This will need to be logged and available at the lead site (Exeter) in an anonymised format.

1) **Action to take after responding to immediate risk:**

   i. Document action taken on the risk register/log and a risk report form (see below).

   ii. Telephone or send letter to GP by post or email documenting information gathered and action taken.

   iii. Seek / offer supervision around support and debriefing as appropriate.

Determine if AE/SAE reporting is necessary (Section 9).

GP letters have been provided to participating sites as part of the document packs reviewed by REC and the SAE reporting form can be found on the EDC and/or in the paper CRF pack.

**Risk Report Form**

Participant Trial Number

| |
|---|
| *Suicide risk information: [note answers to all questions above re yes/no answers and details]*<br>*Intention:*<br><br>*Plans:*<br><br>*Actions:*<br><br>*Prevention:*<br><br>*Prior attempts:*<br><br>*Immediate risk:*<br><br>*Date reported: ___/___/___* |
| *Additional notes / actions taken:*<br><br>*Date action taken: ___/___/___* |

Researcher / assessor: _____ Signed: _____ Date: ___/___/___

Supervisor: _____ Signed: _____ Date: ___/___/___

**Appendix B: Mediator measures**

**A**. PHQ/GAD-4 adapted

**In the past 7 days, how often were you bothered by each of the following problems?**

| | | Not at all | Several days | More than half the days | Nearly every day |
|---|---|---|---|---|---|
| a. | Feeling nervous, anxious, or on edge GADPHQ_1 | ○ | ○ | ○ | ○ |
| b. | Not being able to stop or control your worrying GADPHQ_2 | ○ | ○ | ○ | ○ |
| c. | Little interest or pleasure in doing things GADPHQ_3 | ○ | ○ | ○ | ○ |
| d. | Feeling down, depressed, or hopeless GADPHQ_4 | ○ | ○ | ○ | ○ |

**B. How much stress have you had in your life over the past 7 days?**
StressSev

- ○ Very severe
- ○ Severe
- ○ Moderate
- ○ Mild
- ○ None

**Cognitive and Behavioral Response to Stress Scale (CB-RSS) Miner et al., 2015 adapted**

**1. During the past 7 days in a stressful or upsetting situation:**

**(a) How often did you take a moment to question your interpretation of what was happening when you got upset (e.g., look for a more positive or balanced explanation; weigh up different accounts, try and put things in perspective)??**

| 0 Never | 1 Rarely | 2 Occasionally | 3 Sometimes | 4 Often | 5 Very Often | 6 Always |
|---|---|---|---|---|---|---|
| ○ | ○ | ○ | ○ | ○ | ○ | ○ |

**(b) How helpful was this in making you feel better?**

| 0 Not at all very helpful | 1 Slightly helpful | 2 Somewhat helpful | 3 Moderately helpful | 4 Fairly helpful | 5 Very helpful | 6 Extremely helpful |
|---|---|---|---|---|---|---|
| ○ | ○ | ○ | ○ | ○ | ○ | ○ |

**2. During the past 7 days in a stressful or upsetting situation:**

**(a) How often did you plan and/or do activities you knew you would enjoy?**

| 0 Never | 1 Rarely | 2 Occasionally | 3 Sometimes | 4 Often | 5 Very Often | 6 Always |
|---|---|---|---|---|---|---|
| ○ | ○ | ○ | ○ | ○ | ○ | ○ |

**(b) How helpful was this in making you feel better?**

| 0 Not at all very helpful | 1 Slightly helpful | 2 Somewhat helpful | 3 Moderately helpful | 4 Fairly helpful | 5 Very helpful | 6 Extremely helpful |
|---|---|---|---|---|---|---|
| ○ | ○ | ○ | ○ | ○ | ○ | ○ |

**3. During the past 7 days in a stressful or upsetting situation:**

**(a) How often did you use relaxation or similar techniques to soothe, focus or calm yourself (e.g., meditation, breathing, focusing attention, imagery)?**

| 0 Never | 1 Rarely | 2 Occasionally | 3 Sometimes | 4 Often | 5 Very Often | 6 Always |
|---|---|---|---|---|---|---|
| ○ | ○ | ○ | ○ | ○ | ○ | ○ |

**(b) How helpful was this in making you feel better?**

| 0 Not at all very helpful | 1 Slightly helpful | 2 Somewhat helpful | 3 Moderately helpful | 4 Fairly helpful | 5 Very helpful | 6 Extremely helpful |
|---|---|---|---|---|---|---|
| ○ | ○ | ○ | ○ | ○ | ○ | ○ |

**N. 2-item version of Self-Compassion Scale Short-Form**

**"Please indicate how often you behaved in the stated manner during the past 7 days on a scale from 1 (Almost never) to 5 (Almost always).**

| | 1 Almost never | 2 | 3 | 4 | 5 Almost always |
|---|---|---|---|---|---|
| When I'm going through a very hard time, I give myself the caring and tenderness I need | ○ | ○ | ○ | ○ | ○ |
| When I feel inadequate in some way, I try to remind myself that feelings of inadequacy are shared by most people | ○ | ○ | ○ | ○ | ○ |

**Nurture -U Prevention trial Relevant measures**

**Screening Measures for Rumination prevention trial (screening measures common to all trials)**

| Measure | Thresholds & Decisions | Further information |
|---|---|---|
| **5-item Brooding scale from Ruminative Response scale (see A in appendix for detailed measures below)** | **Above previously established cut-offs for worry and rumination; brood >= (defined as scoring in top quartile in one measure and at least top tercile in other measure). This is 40 on the full measure so needs recalculating for 5-item. For 5-item scale (range 5-20), cut-off is >=10 (Cook et al., 2019; Topper et al., 2017), in ECoWeB study it was >11 for worst tercile, > 12 for worst quartile, we will use this more conservative threshold for Nurture-U** | **Sample needs to have elevated worry and/or rumination for prevention trial** |
| **Short-form Penn State Worry Questionnaire (see B in detailed questionnaires below)** | **Above previously established cut-offs for worry and rumination; PSWQ >= (defined as scoring in top quartile in one measure and at least top tercile in other measure), this is 50 on the full scale, needs recalculating for short-form – based on ECoWeB validation data it is >24 for top tercile and >26 for top quartile** | **Sample needs to have elevated worry and/or rumination for prevention trial** |
| **Self-reported conditional branching questionnaire to ascertain whether current episode of major depression – see adapted form of LIDAS outlined below -focused on meeting DSM-5 criteria for major depression in last month and ever in lifetime (see C in appendix below)** | **Do not currently meet diagnostic criteria for major depression (in the last month, 30 days) – SEE LIDAS BELOW** | **As a prevention study, need to exclude those with current episode of major depression – likely to be eligible for acute treatment trial; Includes contingent questions so will vary in length depending on prior answers – criteria for exclusion is meeting diagnostic criteria for current major depression on LIDAS measures PLUS PHQ9 >=10 [to ensure all participants are relevant for one or more studies]** |
| **PHQ-9 to assess current level of depression (see D in appendix for questionnaires below)** | **Check that not overly-elevated current depression symptoms – exclude if >20 – Option of acute treatment trial; used to distinguish between different trial suitability at screening,** | **Exclusion criteria if >=10– will be eligible for acute treatment trial** |

| | | |
|---|---|---|
| | **secondary outcome (data ported into baseline measures)** | |
| **GAD-7 to assess current level of anxiety symptoms (see E in appendix for questionnaires below)** | **Used to distinguish between different trial suitability at screening, secondary outcome** | |
| **Self-reported check on history of diagnosis for drug/alcohol dependence (see C in appendix of questionnaires below)** | **No history of drug/alcohol/ substance dependence** | **Exclusion criteria** |
| **Self-reported check on history of diagnosis of psychosis ((see C in appendix of questionnaires below)** | **No history of psychosis** | **Exclusion criteria** |
| **Self-reported check on history of diagnosis of bipolar disorder (see C in appendix of questionnaires below)** | **No history of bipolar disorder** | **Exclusion criteria** |
| **Self-reported check on whether receiving psychological treatment or antidepressant medication ((see C in appendix of questionnaires below)** | **Not currently receiving psychological treatment at point of entry into study (or had more than 20 sessions or expecting less than 4)** | **Exclusion criteria** |
| **Question re university of study (drop-down list – with 6 primary universities -Universities of Exeter, Oxford, Cardiff, King's College London, Southampton, Newcastle and other option-with text block to report which institution)** | **To check that University student; a factor for stratification in randomisation** | |
| **Age** | **16 or older** | **Necessary to provide independent informed consent** |
| **Access to PC/smart phone/internet** | | **Necessary for delivery of intervention** |
| **Question about where participant found out about the study** | | **Where did you find out about the Nurture-U project and this intervention study?" Then options for response including:**<br>- **University website**<br>- **Social media post**<br>- **Social media advertising**<br>- **Email**<br>- **Poster** |

| | | |
|---|---|---|
| | | - **Word of mouth – from a friend or peer**<br>- **Nurture-U social event**<br>- **University society**<br>- **Student Union or Student Guild**<br>- **Resilience workshop**<br>- **Within a lecture or seminar**<br>- **Other (with text option to complete)** |

**Baseline measures – pre-randomisation for rumination prevention digital trial**

| Measure | Rationale | Further information |
|---|---|---|
| **WEMWBS (7-item) [see F in appendix below]** | **Secondary outcome – mental wellbeing** | |
| **Demographic including Gender identity (M/F/neither/both); sexual orientation, race/ethnicity; birthplace, educational level, topic of study [see G in appendix below]** | **To explore diversity of sample and representativeness against student body** | **Demographics** |
| **Past history of depression; as ascertained by LIDAS past history [within screener questionnaire for efficiency -see C in appendix below]** | **Prior research finds this as a potential moderator of outcome, increases base risk of incidence of depression, a factor for stratification in randomisation** | **Mental health history** |
| **High current stress severity, recent stressful life events stress reactivity (Perceived Stress Scale) and the post-secondary student stressors index (PSSI) shortened; see in H Appendix** | **Prior research found this as a moderator of outcomes; high stressed students more likely to benefit from intervention** | **Stress** |
| **WSAS (see I in appendix below)** | **Secondary outcome – social and work functioning** | |
| **Brief Resilience Scale (see J in appendix below)** | **Secondary outcome - resilience** | |
| **Academic grades self-report (see K in Appendix below)** | **Secondary outcome to assess impact on academic studies** | |

| | | |
|---|---|---|
| **PHQ9, GAD7, RRS, PSWQ piped through from screener** | | |

**Mediator measures – repeated weekly for 8 weeks post-randomisation, taking less than 5 minutes to complete, 23 items to rate**

| Measure | Rationale | Further information |
|---|---|---|
| **PHQ-2 (see L in appendix below** | **Brief measure of depression** | **2-item scale** |
| **GAD-2 (see L in appendix below)** | **Brief measure of anxiety** | **2-item scale** |
| **Stress**<br><br>**How much stress have you had in your life over the past 7 days? (StressSev).**<br>**Scored as: Very severe (4), severe (3), moderate (2), mild (1), none (0), list with circle to select** | **Single item to assess stress** | **laid out with ratings as choice buttons along horizontal paralleling other questions in this section** |
| **During the past 7 days in a stressful or upsetting situation:**<br>**a) How often did you take a moment to question your interpretation of what was happening when you got upset (e.g., look for a more positive or balanced explanation; weigh up different accounts, try and put things in perspective)?**<br>**0= Never, 1=Rarely, 2=Occasionally, 3=Sometimes, 4=Often, 5= Very often, 6= Always;**<br><br>**(b) How helpful was this in making you feel better?**<br>**0=Not at all helpful, 1 = Slightly helpful, 2=Somewhat helpful, 3=Moderately helpful, 4= Fairly helpful, 5=Very helpful, 6=Extremely helpful, N/A=Didn't do this last week**<br><br>**During the past 7 days in a stressful or upsetting situation:** | **Use of cognitive and behavioural skills, 6-items, these reflect different potential strategies that individuals may use and that may be provided within the intervention** | **Brief questions to capture cognitive and behavioural strategies from Cognitive and Behavioral Response to Stress Scale (CB-RSS) Miner et al., 2015, with addition based on student feedback, see Appendix M for example of questionnaire** |

| | | |
|---|---|---|
| **(a) How often did you plan and/or do activities you knew you would enjoy? 0= Never, 1=Rarely, 2=Occasionally, 3=Sometimes, 4=Often, 5= Very often, 6= Always; (b) How helpful was this in making you feel better? 0=Not at all helpful, 1 = Slightly helpful, 2=Somewhat helpful, 3=Moderately helpful, 4= Fairly helpful, 5=Very helpful, 6=Extremely helpful, N/A=Didn't do this last week**<br><br>**During the past 7 days in a stressful or upsetting situation: (a) How often did you use relaxation or similar techniques to soothe, focus or calm yourself (e.g., meditation, breathing, focusing attention, imagery)?**<br><br>**0= Never, 1=Rarely, 2=Occasionally, 3=Sometimes, 4=Often, 5= Very often, 6= Always; (b) How helpful was this in making you feel better? 0=Not at all helpful, 1 = Slightly helpful, 2=Somewhat helpful, 3=Moderately helpful, 4= Fairly helpful, 5=Very helpful, 6=Extremely helpful, N/A=Didn't do this last week** | | |
| **During the past 7 days worry is something that "I do automatically" "I do without thinking" "I start doing before I realise I'm doing it" Each of 3 items rated on 1 to 7 scale from Strongly** | **Change in habit applied to worry, 3 items – to assess whether rumination/worry becomes more or less of a habit; the intervention focuses on changing habit** | **Adapted items from SRHI index, Gardner et al., 2012, laid out with ratings as choice buttons along horizontal paralleling other questions in this section** |

| | | |
|---|---|---|
| **disagree to Strongly agree [Strongly disagree, Moderately Disagree, Slightly Disagree, Neither Agree or Disagree, Slightly Agree, Moderately Agree, Strongly Agree)** | | |
| **During the past 7 days problem solving is something that<br>"I do automatically"<br>"I do without thinking"<br>"I start doing before I realise I'm doing it"<br>Each of 3 items rated on 1 to 7 scale from Strongly disagree to Strongly agree (Strongly disagree, Moderately Disagree, Slightly Disagree, Neither Agree or Disagree, Slightly Agree, Moderately Agree, Strongly Agree)** | **Change in habit applied to problem-solving, 3 items – to assess whether more helpful responsive becomes more or less of a habit** | **Adapted items from SRHI index, Gardner et al., 2012, laid out with ratings as choice buttons along horizontal paralleling other questions in this section** |
| **Please indicate how often you behaved in the stated manner during the past 7 days on a scale from 1 (Almost never) to 5 (Almost always).<br>"When I'm going through a very hard time, I give myself the caring and tenderness I need";<br>"When I feel inadequate in some way, I try to remind myself that feelings of inadequacy are shared by most people"** | **Self-compassion, 2-items; the intervention includes a self-compassion element** | **Selected items from SCS-SF (Self-Compassion Scale – Short Form), items from Self-kindness and Common humanity scales – see N in appendix for example of shortened questionnaire** |
| **2-items from Brooding questionnaire – "Indicate whether you never, sometimes, often or always thought or did each of the following when you felt sad, down or depressed over the past 7 days.<br>A. Think "Why do I always react this way?"<br>B. Think "Why can't I handle things better?"** | **Rumination, 2-items** | **Adapted from the RRS-B-Brooding 5-item questionnaire,<br>Treynor et al., 2003, see Appendix A for the full questionnaire – this uses two items from it** |

| | | |
|---|---|---|
| **“In the last seven days I feel better prepared to handle situations I could not handle before” rated using a seven-point Likert scale ranging from −3 (“absolutely not true), 0 (“neither nor”) and +3 (“absolutely true”).** | **Self-efficacy/Mastery** | **Laid out as horizontal rating scale underneath the description item** |
| **“In the last seven days, I understand myself and my problems better” rated using a seven-point Likert scale ranging from −3 (“absolutely not true), 0 (“neither nor”) and +3 (“absolutely true”).** | **Problem clarification** | **Laid out as horizontal rating scale underneath the description item** |

**Outcome measures at 3 months and 12 months (12 months primary outcome)**

| Measure | Rationale | Further information |
|---|---|---|
| **Incidence of depression over 3 and 12 months assessed by well-validated questionnaire reflecting structured clinical interview (LIDAS adapted for time-scale – see C adaptation in appendix below)** | **Primary outcome -incidence of depression over 3 and then 12 months** | **Includes contingent questions so will vary in length depending on prior answers** |
| **PHQ-9 (see D in appendix below)** | **Secondary outcome** | |
| **GAD-7 (see E in appendix below)** | **Secondary outcome** | |
| **WEMWBS (see F in appendix below)** | **Secondary outcome – mental wellbeing** | |
| **Measures of stress (see H in appendix below)** | **Secondary outcome, potential moderator of effect** | |
| **WSAS (see I in appendix below)** | **Secondary outcome – social and work functioning** | |
| **5-item Brooding scale (see A in appendix below)** | **Secondary outcome** | **Test whether intervention reduces worry and rumination** |
| **Short-form Penn State Worry Questionnaires (see B in appendix below)** | **Secondary outcome** | **Test whether intervention reduces worry and rumination** |
| **Brief Resilience Scale (see J in appendix below)** | **Secondary outcome** | |
| **Academic grades self-report (see K in Appendix below)** | **Secondary outcome to assess impact on academic studies** | |
| **Use of services /treatment received–incorporating NHS and student services (see O in appendix below)** | **To understand level of treatment sought and received – from list of student, NHS, and other options** | |

**Measures to be given ONLY to intervention arm [i.e., built into final module of internet platform, NOT in assessment system)**

**1. Use and application of intervention:**

**"How many days in the past 3 months did you log on and use the internet therapy"? Response options 0-90**

**"How many days in the past month did you use any of the skills you learned in the internet therapy?" Response option 0-30**

**"On average about how many times per day do you use these skills?" (0+)**

**"In the past month, how helpful were the skills you learnt in the internet treatment?" Response options – very helpful; somewhat; a little; not at all helpful; they made things worse**

**2. Satisfaction with intervention**
**Adapted Client Satisfaction Questionnaire – Internet-based interventions (Bos et al., JMIR 2016)**

**Scored 1= "Does not apply to me" to 4="Does totally apply to me.**

**Replaced "service" with "training" – may adapt to "therapy"**

**1. The online therapy was of high quality**

**2. I received the kind of therapy I wanted**

**3. The therapy has met my needs**

**4. I would recommend this therapy to a friend, if she or he were need of similar help**

**5. I am satisfied with the amount of help I received**

**6. The therapy helped me deal with my problems more effectively**

**7. In an overall general sense I am satisfied with the therapy**

**8. I would come back to this therapy if I were to seek help again**

**Plus**
**How much did this treatment help with the specific problem that led you to therapy?**
**Made things a lot better 1, made things somewhat better 2, made no difference 3, made things somewhat worse 4, made things a lot worse 5**

## APPENDIX C: DETAILED APPENDIX OF MEASURES

### A. 5-item Brooding subscale of Ruminative Response Scale (screen/outcome)

People think and do many different things when they feel sad, blue or depressed. Please read each of the items below and indicate whether you almost never, sometimes, often or almost always think or do each one when you feel sad, down or depressed. Please indicate what you generally do, not what you think you should do.

| | | Almost Never | Sometimes | Often | Almost Always |
|---|---|---|---|---|---|
| 1. | Think “What am I doing to deserve this?” | 1 | 2 | 3 | 4 |
| 2. | Think “Why do I always react this way?” | 1 | 2 | 3 | 4 |
| 3. | Think about a recent situation, wishing it had gone better | 1 | 2 | 3 | 4 |
| 4. | Think “Why do I have problems other people don’t have?” | 1 | 2 | 3 | 4 |
| 5. | Think “Why can’t I handle things better?” | 1 | 2 | 3 | 4 |

**B. Short form Penn State Worry Questionnaire**

PSWQ -S – 8 item measure of tendency towards worry. Used as outcome, assessment of risk (high vs low) and personalisation. EC-Regulation measure.High risk= PSWQ-A: upper quartile (75%, >=26)

Select the answer that best describes how typical or characteristic each item is of you.

| | | not at all typical | | somewhat typical | | very typical |
|---|---|---|---|---|---|---|
| | | 1 | 2 | 3 | 4 | 5 |
| 1. | My worries overwhelm me. | ❑ | ❑ | ❑ | ❑ | ❑ |
| 2. | Many situations make me worry. | ❑ | ❑ | ❑ | ❑ | ❑ |
| 3. | I know I should not worry about things but I just cannot help it. | ❑ | ❑ | ❑ | ❑ | ❑ |
| 4. | When I am under pressure I worry a lot. | ❑ | ❑ | ❑ | ❑ | ❑ |
| 5. | I am always worrying about something. | ❑ | ❑ | ❑ | ❑ | ❑ |
| 6. | As soon as I finish one task, I start to worry about everything else I have to do. | ❑ | ❑ | ❑ | ❑ | ❑ |
| 7. | I have been a worrier all my life. | ❑ | ❑ | ❑ | ❑ | ❑ |
| 8. | I notice that I have been worrying about things. | ❑ | ❑ | ❑ | ❑ | ❑ |

Scored – all items in positive direction, higher score more worry, scored from range of 8-40

**C. Adapted LIDAS to determine if current major depressive episode or history of depression including screening for history of other disorders**

For Screener/baseline:

START SCORE 0 ON current MDE_KEY CRITERIA variable, 0 ON TOTAL SYMPTOMS_CURRENT MDE variable; START SCORE 0 ON past MDE_KEY CRITERIA variable, 0 ON TOTAL SYMPTOMS_PAST MDE variable;

1. Have you ever in your life had a period of at least two weeks when you felt sad, empty, or depressed?

□1 Yes GO TO 1A

□0 No ► go to question 3

-page break-

1A. In the last month, have you had a period of at least two weeks when you felt sad, empty, or depressed?

□1 Yes GO TO 2

□0 No ► go to question 2A

-page break-

2. For the next question, think about the period of two weeks in the past month when these feelings were at their worst. During this period of two weeks, how often did you feel this way?

□1 Almost every day, most of the day ► go to question 5 SCORE +1 ON CURRENT MDE KEY CRITERIA CODE; SCORE+ 1 ON TOTAL SYMPTOMS CURRENT MDE

□0 Less often Go to 2A

-page break-

2A. For the next question, think about the period of two weeks in your life when these feelings were at their worst. During this period of two weeks, how often did you feel this way?

□1 Almost every day, most of the day ► go to question 5C SCORE +1 ON PAST MDE KEY CRITERIA CODE; SCORE+ 1 ON TOTAL SYMPTOMS PAST MDE

□0 Less often Go to 3

-page break-

3. Have you ever had a period of at least two weeks during which you lost interest in most things like hobbies, work, or activities that usually give you pleasure?

□1 Yes GO TO 3A

□0 No ► go to 46 END –,

-page break-

3A. In the past month, have you had a period of at least two weeks during which you lost interest in most things like hobbies, work, or activities that usually give you pleasure?

□1 Yes GO TO 4

□0 No ► go to 4A –,

-page break-

4. For the next question, think about the period of two weeks in the past month when your loss of interest was at its worst. During this period of two weeks, how often did you feel this way?

□1 Almost every day, most of the day ► go to question 7 SCORE +1 ON CURRENT MDE-KEY CRITERIA CODE; SCORE+ 1 ON TOTAL SYMPTOMS CURRENT MDE

□0 Less often ► go to 4A

-page break-

4A. For the next question, think about the period of two weeks in your life when your loss of interest was at its worst. During this period of two weeks, how often did you feel this way?

□1 Almost every day, most of the day ► go to question 25 SCORE +1 ON PAST MDE- KEY CRITERIA CODE; SCORE+ 1 ON TOTAL SYMPTOMS PAST MDE

□0 Less often ► go to 46 END

-page break-

5. During this period in the past month in which you felt sad, empty, or depressed, did you have a period of at least two weeks when you lost interest in most things like hobbies, work, or activities that usually give you pleasure?

□1 Yes GO TO 6

□0 No ► go to question 5A

-page break-

5A. Have you ever had a period of at least two weeks during which you lost interest in most things like hobbies, work, or activities that usually give you pleasure?

□1 Yes GO TO 5B

□0 No ► go to 7 –,

-page break-

5B. For the next question, think about the period of two weeks in your life when your loss of interest was at its worst. During this period of two weeks, how often did you feel this way?

□1 Almost every day, most of the day ► go to question 7 SCORE +1 ON PAST MDE- KEY CRITERIA CODE; SCORE+ 1 ON TOTAL SYMPTOMS PAST MDE

□0 Less often ► go to 7

-page break-

5C. During this period in which you felt sad, empty, or depressed, did you have a period of at least two weeks when you lost interest in most things like hobbies, work, or activities that usually give you pleasure?

□1 Yes GO TO 6C

□0 No ► go to question 6D

-page break-

6. For the next question, think about the period of two weeks in the past month when your loss of interest was at its worst. During this period of two weeks, how often did you feel this way?

□1 Almost every day, most of the daySCORE +1 ON CURRENT MDE - KEY CRITERIA CODE; SCORE+ 1 ON TOTAL SYMPTOMS-CURRENT MDE go to Question 7

□0 Less often go to question 6B

-page break-

6B. For the next question, think about the period of two weeks in your life when your loss of interest was at its worst. During this period of two weeks, how often did you feel this way?

□1 Almost every day, most of the day ► go to question 7 SCORE +1 ON PAST MDE- KEY CRITERIA CODE; SCORE+ 1 ON TOTAL SYMPTOMS PAST MDE

□0 Less often ► go to 7

-page break-

6C. For the next question, think about the period of two weeks in your life when your loss of interest was at its worst. During this period of two weeks, how often did you feel this way?

□1 Almost every day, most of the day ► go to question 6D SCORE +1 ON PAST MDE- KEY CRITERIA CODE; SCORE+ 1 ON TOTAL SYMPTOMS PAST MDE

□0 Less often ► go to 6D

-page break-

6.D. During the past month did you have a period of at least two weeks when you lost interest in most things like hobbies, work, or activities that usually give you pleasure?

□1 Yes GO TO 6E

□0 No ► go to question 25

-page break-

6E. For the next question, think about the period of two weeks in the past month when your loss of interest was at its worst. During this period of two weeks, how often did you feel this way?

□1 Almost every day, most of the day ► go to question 7 SCORE +1 ON CURRENT MDE-KEY CRITERIA CODE; SCORE+ 1 ON TOTAL SYMPTOMS CURRENT MDE

□0 Less often ► go TO 25

-page break-

7. People who have periods in which they feel sad, empty, or depressed or experience a loss of interest, often have other problems at the same time. In the past month, during this period of at least two weeks when you felt sad, empty, or depressed or lose interest in things:

7. … did you lack energy or feel tired more than usual?

□1 Yes SCORE +1 ON TOTAL SYMPTOMS-CURRENT MDE, GO TO 8

□0 No GO TO 8

8. … have less appetite than usual, almost every day?

□1 Yes SCORE + 1 ON TOTAL SYMPTOMS-CURRENT MDE. GO TO 9

□0NO GO TO 9

9. …did you lose weight without trying to, as much as a kilo a week during several weeks?

□1 Yes SCORE + 1 ON TOTAL SYMPTOMS-CURRENT MDE UNLESS SCORED ON 8, GO TO 10

□0 No ► go to question 11

-page break-

10. About how much weight did you lose in these weeks? □□ kg go to question 14

-page break-

During this period of <u>at least two weeks</u> when you felt sad, empty or depressed or experienced a loss of interest in things:

11. … did you have a <u>much larger appetite than usual, and this</u> almost every day for at least two weeks?

□2 Yes SCORE + 1 ON TOTAL SYMPTOMS-CURRENT MDE, GO TO 12

□1 Yes, only because of pregnancy or a growth spurt GO TO 12

□0 No GO TO 12

12. … did your appetite increase so much that you <u>gained weight</u>, as much as a kilo a week during several weeks?

□1 Yes SCORE + 1 ON TOTAL SYMPTOMS-CURRENT MDE UNLESS SCORED ON 11, GO TO 13

□0 No ► go to question 14

-page break-

-page break-

13. About how much weight did you gain in these weeks? □□ kg

During this period of at least two weeks when you felt sad, empty, or depressed or experienced a loss of interest in things:

14. …. Did you have trouble sleeping almost every night, either trouble falling asleep, waking in the middle of the night, or waking up too early?

□1 Yes SCORE + 1 ON TOTAL SYMPTOMS-CURRENT MDE GO TO 15

□0 No ► go to question 15

15. …. Did you wake up at least two hours before you wanted to, every day for at least two weeks?

□1 Yes SCORE + 1 ON TOTAL SYMPTOMS-CURRENT MDE UNLESS SCORED ON 14

□0 No

16. …. Were you sleeping too much almost every day?

□1 Yes SCORE + 1 ON TOTAL SYMPTOMS-CURRENT MDE

□0 No

-page break-

During this period of at least two weeks when you felt sad, empty or depressed or experienced a loss of interest in things:

17. …. Did you talk or move more slowly than is normal for you almost every day, and did other people noticed this?

□2 Yes, I talked or moved more slowly and other people noticed SCORE + 1 ON TOTAL SYMPTOMS-CURRENT MDE

□1 Yes, I talked or moved more slowly but other people did not notice

□0 No

18. …. did you have to be moving all the time, that is, you couldn't sit still and paced up and down or couldn't keep your hands still when sitting, and did other people noticed this?

□2 Yes, I had to be moving all the time and other people noticed SCORE + 1 ON TOTAL SYMPTOMS-CURRENT MDE UNLESS SCORED ON 17

□1 Yes, I had to be moving all the time but other people did not notice

□0 No

-page break-

19. During this period of two weeks, did you have a lot more trouble concentrating than usual?

□1 Yes SCORE + 1 ON TOTAL SYMPTOMS-CURRENT MDE

□0 No

20. During this period, were you unable to make up your mind about things you ordinarily had no trouble deciding about?

□1 Yes SCORE + 1 ON TOTAL SYMPTOMS-CURRENT MDE UNLESS SCORED ON 19

□0 No

21. People sometimes feel down on themselves, no good, or worthless. During this period of two weeks, did you feel guilty or worthless?

□1 Yes SCORE + 1 ON TOTAL SYMPTOMS-CURRENT MDE

□0 No

22. During this period of two weeks, did you think a lot about death – either your own, someone else's, or death in general?

□1 Yes SCORE + 1 ON TOTAL SYMPTOMS-CURRENT MDE

□0 No

-page break-

For the next question, please think about the period in the past month of at least two weeks when you felt sad, empty, or depressed or experienced a loss of interest in things.

23. During this period of at least two weeks did it seriously interfere with your ability to do your job, or take care of your house, family, or yourself?

□1 Yes

□0 No

24. About how long has this period of experiencing these symptoms lasted? You may give an estimate.

_____ Weeks

MEETS CRITERIA FOR CURRENT MDD IF CURRENT-MDE-KEY CRITERIA >=1 AND TOTAL SYMPTOMS-CURRENT MDE >=5

IF MEETS CRITERIA FOR CURRENT MDE, THEN GO TO 42; IF NOT MEET CRITERIA FOR CURRENT MDE, go to 25.

25. People who have periods in which they feel sad, empty, or depressed or experience a loss of interest, often have other problems at the same time. During this period of at least two weeks when you felt sad, empty, or depressed or lose interest in things:

25. … did you lack energy or feel tired more than usual?

□$_1$ Yes SCORE +1 ON TOTAL SYMPTOMS-PAST MDE, GO TO 26

□$_0$ No GO TO 26

26. … have less appetite than usual, almost every day?

□$_1$ Yes SCORE + 1 ON TOTAL SYMPTOMS-PAST MDE. GO TO 27

□$_0$NO GO TO 27

27. …did you lose weight without trying to, as much as a kilo a week during several weeks?

□$_1$ Yes SCORE + 1 ON TOTAL SYMPTOMS-PAST MDE UNLESS SCORED ON 26, GO TO 28

□$_0$ No ► go to question 29

-page break-

28. About how much weight did you lose in these weeks? □□ kg go to question 32

-page break-

During this period of at least two weeks when you felt sad, empty or depressed or experienced a loss of interest in things:

29. … did you have a much larger appetite than usual, and this almost every day for at least two weeks?

□2 Yes SCORE + 1 ON TOTAL SYMPTOMS-PAST MDE, GO TO 30

□1 Yes, only because of pregnancy or a growth spurt GO TO 30

□0 No GO TO 30

30. … did your appetite increase so much that you gained weight, as much as a kilo a week during several weeks?

□1 Yes SCORE + 1 ON TOTAL SYMPTOMS-PAST MDE UNLESS SCORED ON 29, GO TO 31

□0 No ► go to question 32

-page break-

31. About how much weight did you gain in these weeks? □□ kg

During this period of at least two weeks when you felt sad, empty, or depressed or experienced a loss of interest in things:

32. …. Did you have trouble sleeping almost every night, either trouble falling asleep, waking in the middle of the night, or waking up too early?

□1 Yes SCORE + 1 ON TOTAL SYMPTOMS-PAST MDE GO TO 33

□0 No ► go to question 33

33. …. Did you wake up at least two hours before you wanted to, every day for at least two weeks?

□1 Yes SCORE + 1 ON TOTAL SYMPTOMS-PAST MDE UNLESS SCORED ON 32

□0 No

34. …. Were you sleeping too much almost every day?

□1 Yes SCORE + 1 ON TOTAL SYMPTOMS-PAST MDE go to 35

□0 No go to 35

-page break-

During this period of <u>at least two weeks</u> when you felt sad, empty, or depressed or experienced a loss of interest in things:

35. …. Did you talk or move more <u>slowly</u> than is normal for you almost every day, and did other people noticed this?

□2 Yes, I talked or moved more slowly and other people noticed SCORE + 1 ON TOTAL SYMPTOMS-PAST MDE go to 36

□1 Yes, I talked or moved more slowly but other people did not notice go to 36

□0 No go to 36

36. …. did you have to be <u>moving</u> all the time, that is, you couldn't sit still and paced up and down or couldn't keep your hands still when sitting, and did other people noticed this?

□2 Yes, I had to be moving all the time and other people noticed SCORE + 1 ON TOTAL SYMPTOMS-PAST MDE UNLESS SCORED ON 35

□1 Yes, I had to be moving all the time but other people did not notice

□0 No

-page break-

37. During this period of two weeks, did you have a lot more trouble concentrating than usual?

□1 Yes SCORE + 1 ON TOTAL SYMPTOMS-PAST MDE

□0 No

38. During this period, were you unable to make up your mind about things you ordinarily had no trouble deciding about?

□1 Yes SCORE + 1 ON TOTAL SYMPTOMS-PAST MDE UNLESS SCORED ON 37

□0 No

39. People sometimes feel down on themselves, no good, or worthless. During this period of two weeks, did you feel guilty or worthless?

□1 Yes SCORE + 1 ON TOTAL SYMPTOMS-PAST MDE

□0 No

40. During this period of two weeks, did you think a lot about death – either your own, someone else's, or death in general?

□1 Yes SCORE + 1 ON TOTAL SYMPTOMS-PAST MDE

□0 No

-page break-

For the next question, please think about the period of <u>at least two weeks</u> when you felt sad, empty, or depressed or experienced a loss of interest in things.

41. During this period of at least two weeks did it seriously interfere with your ability to do your job, or take care of your house, family, or yourself?

□1 Yes

□0 No

42. About how long did the longest of periods like this last? *You may give an estimate.*

□□□ Weeks

43. How many periods like this have you had in your life in total?

□1 1 (just this one) □2 2 □3 3 □4. 4 □5 5 or more

44. Did you have a period like this in the last 3 months?

□1 Yes □0 No

45. About how old were you the first time you had a period like this? (whether or not you received any help for it)

□□ Years old

Section to check on past history of mental health and other exclusion criteria

46. Have you ever been diagnosed with a mental health disorder or been treated for a mental health disorder by a professional or medical doctor? YES or NO

IF NO, skip to end

-page break-

If YES:

47. Please select the disorders that you have been diagnosed with and/or received treatment by a professional or medical doctor ever in your life. You can select more than one answer.

select from the drop-down menu:

□a An eating disorder
□b ADD/ADHD
□c An anxiety disorder
□d Panic disorder
□e Phobia
□f Post traumatic stress disorder

□g Obsessive compulsive disorder

□h Bipolar disorder (manic depression) links to Bipolar/Psychosis feedback exclusion page

□i Schizophrenia or psychosis links to Bipolar/Psychosis feedback exclusion page

□J Alcohol or substance use disorder – link to substance use feedback exclusion page

□K Current treatment for Anxiety or Depression

If yes to K– goes to question asking – Are you currently receiving psychological treatment for anxiety or depression from a health professional (e.g., cognitive-behavioural therapy, counselling)? Yes or No

If yes, How many sessions received? Number response option

If yes, How many further sessions planned? Number response option

If yes, and sessions received < 20 and sessions planned > = 4 excluded for current treatment but given message can return to trial once treatment completed.

If yes to K, “Are you currently taking any medication for anxiety and/or depression?” If yes, what medication and dose in open text box.

How long have you been taking this dose of medication (weeks)? If > 4 weeks on stable can proceed, if < 4 weeks exclusion but able to return once taking on stable dose for 4 weeks.

□L Past treatment or diagnosis of depression

□M Other, namely: text entry

-page break-

MEETS CRITERIA FOR PAST LIFETIME MDD IF KEY CRITERIA >=1 AND TOTAL SYMPTOMS >=5 OR self-reported diagnosis (46 and 47L)

MEETS CRITERIA FOR CURRENT MDD for exclusion from digital prevention trial IF IF KEY CRITERIA >=1 AND TOTAL SYMPTOMS >=5 AND PHQ-9 total score >=10

48: end of section – no depression

LIDAS adapted for follow-ups – questions adjusted for relevant time-scale, i.e., 3 month or 12 month follow-up

WP 6/7 Lifetime Depression Assessment Self-report (LIDAS) instrument adapted to assess incidence of depression during the past 3 or 12 months, depending on the follow-up period.

START SCORE 0 ON KEY CRITERIA, 0 ON TOTAL SYMPTOMS

1. In the past 3 / 12 months, have you had a period of at least two weeks when you felt sad, empty, or depressed?

□1 Yes GO TO 2

□0 No ► go to question 3

-page break-

2. For the next question, think about the period of two weeks in the past 3 / 12 months when these feelings were at their worst. During this period of two weeks, how often did you feel this way?

□1 Almost every day, most of the day ► go to question 5 SCORE +1 ON KEY CRITERIA CODE; SCORE+ 1 ON TOTAL SYMPTOMS

□0 Less often

-page break-

3. During the past 3 / 12 months, have you had a period of at least two weeks during which you lost interest in most things like hobbies, work, or activities that usually give you pleasure?

□1 Yes GO TO 4

□0 No ► go to end –, 27

-page break-

4. For the next question, think about the period of two weeks in the past 3 / 12 months when your loss of interest was at its worst. During this period of two weeks, how often did you feel this way?

□1 Almost every day, most of the day ► go to question 7 SCORE +1 ON KEY CRITERIA CODE; SCORE+ 1 ON TOTAL SYMPTOMS

□0 Less often ► go to end 27

-page break-

5. During this period in which you felt sad, empty, or depressed, did you have a period of at least two weeks when you lost interest in most things like hobbies, work, or activities that usually give you pleasure?

□1 Yes GO TO 6

□0 No ► go to question 7

-page break-

6. For the next question, think about the period of two weeks in the past 3 / 12 months when your loss of interest was at its worst. During this period of two weeks, how often did you feel this way?

□1 Almost every day, most of the daySCORE +1 ON KEY CRITERIA CODE; SCORE+ 1 ON TOTAL SYMPTOMS

□0 Less often

-page break-

People who have periods in which they feel sad, empty or depressed or experience a loss of interest, often have other problems at the same time. During this period of at least two weeks when you felt sad, empty or depressed or lose interest in things:

7. … did you lack energy or feel tired more than usual?

□1 Yes SCORE +1 ON TOTAL SYMPTOMS, GO TO 8

□0 No GO TO 8

8. … have less appetite than usual, almost every day?

□1 Yes SCORE + 1 ON TOTAL SYMPTOMS. GO TO 9

□0NO GO TO 9

9. …did you lose weight without trying to, as much as a kilo a week during several weeks?

□1 Yes SCORE + 1 ON TOTAL SYMPTOMS UNLESS SCORED ON 8 GO TO 10

□0 No ► go to question 11

-page break-

10. About how much weight did you lose in these weeks? □□ kg go to question 14

-page break-

During this period of at least two weeks when you felt sad, empty, or depressed or experienced a loss of interest in things:

11. … did you have a much larger appetite than usual, and this almost every day for at least two weeks?

□$_2$ Yes SCORE + 1 ON TOTAL SYMPTOMS, GO TO 12

□$_1$ Yes, only because of pregnancy or a growth spurt GO TO 12

□$_0$ No GO TO 14

12. … did your appetite increase so much that you gained weight, as much as a kilo a week during several weeks?

□$_1$ Yes SCORE + 1 ON TOTAL SYMPTOMS UNLESS SCORED ON 11, GO TO 13

□$_0$ No ► go to question 14

-page break-

13. About how much weight did you gain in these weeks? □□ kg

-page break-

During this period of at least two weeks when you felt sad, empty, or depressed or experienced a loss of interest in things:

14. …. Did you have trouble sleeping almost every night, either trouble falling asleep, waking in the middle of the night, or waking up too early?

□$_1$ Yes SCORE + 1 ON TOTAL SYMPTOMS GO TO 15

□$_0$ No ► go to question 15

15. …. Did you wake up at least two hours before you wanted to, every day for at least two weeks?

□1 Yes SCORE + 1 ON TOTAL SYMPTOMS UNLESS SCORED ON 14

□0 No

16. …. Were you sleeping too much almost every day?

□1 Yes SCORE + 1 ON TOTAL SYMPTOMS unless scored on 14 or 15

□0 No

-page break-

During this period of <u>at least two weeks</u> when you felt sad, empty or depressed or experienced a loss of interest in things:

17. …. Did you talk or move more <u>slowly</u> than is normal for you almost every day, and did other people notice this?

□2 Yes, I talked or moved more slowly and other people noticed SCORE + 1 ON TOTAL SYMPTOMS

□1 Yes, I talked or moved more slowly but other people did not notice

□0 No

18. …. did you have to be <u>moving</u> all the time, that is, you couldn't sit still and paced up and down or couldn't keep your hands still when sitting, and did other people notice this?

□2 Yes, I had to be moving all the time and other people noticed SCORE + 1 ON TOTAL SYMPTOMS UNLESS SCORED ON 17

□1 Yes, I had to be moving all the time but other people did not notice

□0 No

-page break-

19. During this period of two weeks, did you have a lot more trouble concentrating than usual?

□1 Yes SCORE + 1 ON TOTAL SYMPTOMS

□0 No

20. During this period, were you unable to make up your mind about things you ordinarily had no trouble deciding about?

□1 Yes SCORE + 1 ON TOTAL SYMPTOMS UNLESS SCORED ON 19

□0 No

21. People sometimes feel down on themselves, no good, or worthless. During this period of two weeks, did you feel guilty or worthless?

□1 Yes SCORE + 1 ON TOTAL SYMPTOMS

□0 No

22. During this period of two weeks, did you think a lot about death – either your own, someone else's, or death in general?

□1 Yes SCORE + 1 ON TOTAL SYMPTOMS

□0 No

-page break-

For the next question, please think about the periods of <u>at least two weeks</u> when you felt sad, empty, or depressed or experienced a loss of interest in things during the past 3 / 12 months.

23. Did any period of at least two weeks seriously interfere with your ability to do your job, or take care of your house, family, or yourself?

□1 Yes

□0 No

24. About how long did the longest of periods like this last during the past 3 / 12 months? *You may give an estimate.*

□□□ Weeks

25. When did this period of feeling sad, empty, or depressed or experiencing a loss of interest in things start? Think about holidays, birthdays, life events to help to be more precise about the time this period started. Was it near the start, middle or end of a month?

DATE – day, Month, year

25. Are you experiencing a period like this at the moment?

□1 Yes □0 No

MEETS CRITERIA FOR INCIDENCE OF DEPRESSION DURING THE FOLLOW-UP IF KEY CRITERIA >=1 AND TOTAL SYMPTOMS >=5

26: end of section – no depression

**D. PHQ9 to assess depression**

Over the last two weeks, how often have you been bothered by the following problems[4]?

| | 0 – Not at all | 1 – Several days | 2 – More than half the days | 3 – Nearly every day |
|---|---|---|---|---|
| Little interest or pleasure in doing things. | ◯ | ◯ | ◯ | ◯ |
| Feeling down, depressed, or hopeless. | ◯ | ◯ | ◯ | ◯ |
| Trouble falling/staying asleep, or sleeping too much. | ◯ | ◯ | ◯ | ◯ |
| Feeling tired or having little energy. | ◯ | ◯ | ◯ | ◯ |
| Poor appetite or overeating. | ◯ | ◯ | ◯ | ◯ |
| Feeling bad about yourself, or that you are a failure, or have let yourself or your family down. | ◯ | ◯ | ◯ | ◯ |
| Trouble concentrating on things, such as reading the newspaper or watching TV. | ◯ | ◯ | ◯ | ◯ |
| Moving or speaking so slowly that other people could have noticed? Or the opposite - being so | ◯ | ◯ | ◯ | ◯ |

| | | | | |
|---|---|---|---|---|
| fidgety or restless that you have been moving around a lot more than usual? | | | | |
| Thoughts that you would be better off dead or of hurting yourself in some way. | ○ | ○ | ○ | ○ |

If answer to question 9 more than 0 then present the 3 risk questions:

R1 In the last 2 weeks have you been experiencing regular thoughts about suicide?

R2 In the last 2 week have you had any intention to hurt or kill yourself?

R3 In the last 2 weeks have you made any plans to hurt or kill yourself? [harm yourself or end your life?]

IF responses 1, 2 or 3, are selected for the above question then an in-the-moment automated message is providing giving advice and signposting including detailing a number of mental health supports specifically for suicidal thoughts or self-harm – to be adapted from risk messages from ECoWeB – To be adapted with student input;

if score includes PHQ9 -Q9>= 2 and yes to R2 and R3 at screening excluded from trial and signposted to relevant help re suicidality

Score for PHQ9 is total from items 1-9 giving a range of 0-27. There is a further question to ask about interference:

If you checked off any problems, how difficult have these problems made it for you to do your work, take care of things at home, or get along with other people?

| 0 | 1 | 2 | 3 |
|---|---|---|---|
| Not difficult at all | Somewhat difficult | Very difficult | Extremely difficult |
| ○ | ○ | ○ | ○ |

**E. GAD7 to assess anxiety**

Over the last two weeks, how often have you been bothered by the following problems?

| | 0 – Not at all | 1 – Several days | 2 – More than half the days | 3 – Nearly every day |
|---|---|---|---|---|
| Feeling nervous, anxious, or on edge | ◯ | ◯ | ◯ | ◯ |
| Not being able to stop or control worrying | ◯ | ◯ | ◯ | ◯ |
| Worrying too much about different things | ◯ | ◯ | ◯ | ◯ |
| Trouble relaxing | ◯ | ◯ | ◯ | ◯ |
| Being so restless that it's hard to sit still | ◯ | ◯ | ◯ | ◯ |
| Becoming easily annoyed or irritable | ◯ | ◯ | ◯ | ◯ |
| Feeling afraid as if something awful might happen | ◯ | ◯ | ◯ | ◯ |

5b. If you checked off any problems, how difficult have these made it for you to do your work, take care of things at home, or get along with other people?

| 0 | 1 | 2 | 3 |
|---|---|---|---|
| Not difficult at all | Somewhat difficult | Very difficult | Extremely difficult |
| ◯ | ◯ | ◯ | ◯ |

**F. Warwick-Edinburgh Mental Wellbeing Scale**

Below are some statements about feelings and thoughts. Please select the box that best describes your experience of each over the last two weeks.

| | 1 - None of the time | 2 - Rarely | 3 - Some of the time | 4 - Often | 5 - All of the time |
|---|---|---|---|---|---|
| I've been feeling optimistic about the future | ◯ | ◯ | ◯ | ◯ | ◯ |
| I've been feeling useful | ◯ | ◯ | ◯ | ◯ | ◯ |
| I've been feeling relaxed | ◯ | ◯ | ◯ | ◯ | ◯ |
| I've been dealing with problems well | ◯ | ◯ | ◯ | ◯ | ◯ |
| I've been thinking clearly | ◯ | ◯ | ◯ | ◯ | ◯ |
| I've been feeling close to other people | ◯ | ◯ | ◯ | ◯ | ◯ |
| I've been able to make up my own mind about things | ◯ | ◯ | ◯ | ◯ | ◯ |

**G. DEMOGRAPHIC QUESTIONS FOR ALL TRIALS – AT BASELINE**

1. What is your current age?

[Dropdown List]

16

17

18

19

20

21

22

23

24

25

26 and above

2a. How would you describe your gender?

Male

Female

Non-binary

Prefer to self-describe as: _____ [free text box]

Prefer not to say

2b. Does your gender match the sex you were assigned at birth?

Yes

No

Prefer not to say

3. How would you describe your sexual orientation?

Heterosexual

Homosexual/Lesbian/Gay

Bisexual

Asexual

I do not use a label

Prefer to self-describe as: _____ [free text box]

Prefer not to say

4. How would you describe your ethnicity?

Please choose ALL that apply:

Arab

Asian or Asian British – Indian

Asian or Asian British – Pakistani

Asian or Asian British – Bangladeshi

Chinese

Other Asian background

Black or Black British – Caribbean

Black or Black British – African

Other Black Background

Gypsy or Traveller

Mixed - White and Black Caribbean

Mixed - White and Black African

Mixed - White and Asian

Other mixed background (please describe):  [free text box]

Other ethnic background (please describe): [free text box]

White

Not known

Prefer not to say

5. Please describe your current student status with the university:

◯ Domestic (UK) student

◯ International student

IF International student is selected:

What is your country of origin?

[Dropdown]

IF ‘Other’ is selected for country of origin then display:

Please name your country of origin:

[Free text box]

What level of degree are you studying?

[dropdown]

Undergraduate

Postgraduate taught

Postgraduate research (MPhil/PhD)

Which subject are you studying?

[Free text box]

Are you studying full-time or part-time?

[dropdown]

Full-time

Part-time

What is the duration of your course?

1 year

2 years

3 years

4 years

5 years

6 years

Which year of your course are you currently in?

Year 1

Year 2

Year 3

Year 4

Year 5

Year 6

Which of the following best describes where you are currently living?

On /near to university campus (e.g. in your term time accommodation)

Away from university campus (e.g. at a parental home or elsewhere)

=IF on/near to campus ASK:

Which of the following describes your current accommodation?

I am living in accommodation arranged via the University

Away from university campus (e.g. at a parental home or elsewhere)

I am living in a privately-rented / owned house or flat (this could be a term-time address, or a permanent address)

Do you have a disability (including physical disability, blind or visual impairment, deaf or hearing impairment, dyslexia) or long-term health condition?

Yes

No

IF yes

[Display logic]

Could you please specify which disability or long-term health condition (Please tell us about all that apply)

[free text box]

8c. Did you ever spend time in care as a child (e.g., foster care, residential care)?

◯ Yes ◯ No

10. Have you ever been diagnosed with any of the following mental health conditions or learning difficulties?

Please choose ALL that apply:

I have never been diagnosed with a mental health condition or learning difficulty

Mood disorder (e.g. Depression, Dysthymia, Bipolar Disorder)

Anxiety disorder (e.g. PTSD, OCD, Panic Disorder, Social Anxiety Disorder, Generalized Anxiety Disorder)

Psychotic disorder (e.g. Schizophrenia, drug-induced psychosis)

Eating disorder (e.g. Bulimia Nervosa, Anorexia Nervosa, Binge Eating Disorder)

Neurodevelopmental disorder (e.g. Autism Spectrum)

Sleep disorder (e.g. Insomnia)

Substance use disorder (e.g. cannabis, alcohol)

Learning difficulty

ADHD

Other (please describe): _____

*If YES to “I have never been diagnosed with a mental health condition or learning difficulty” is not selected

[Display Logic]

What age were your first diagnosed with a mental health condition?

◯ Age 10 or younger

◯ Age 11-15 years

◯ Age 16 – 19 years

◯ Age 20 or older

**H. Measures to assess Stress**

Perceived Stress Scale

Cohen S, Kamarck T, Mermelstein R. Perceived stress scale. Measuring stress: A guide for health and social scientists. 1994;10(2):1-2.

Thinking about stress, please indicate in the last month, how often have you...[10]

| | Never | Almost never | Sometimes | Fairly Often | Very often |
|---|---|---|---|---|---|
| Felt that you were unable to control the important things in your life? | ◯ | ◯ | ◯ | ◯ | ◯ |
| Felt confident about your ability to handle your personal problems? | ◯ | ◯ | ◯ | ◯ | ◯ |
| Felt that things were going your way? | ◯ | ◯ | ◯ | ◯ | ◯ |
| Felt difficulties were piling up so high that you could not overcome them? | ◯ | ◯ | ◯ | ◯ | ◯ |

-page break-

Over this past 3 months / 12 months how would you rate the level of stress you generally felt related to:

| | Not Stressful | Somewhat Stressful | Very Stressful | Extremely Stressful |
|---|---|---|---|---|
| Examinations (mid-terms, finals) | ◯ | ◯ | ◯ | ◯ |
| Managing my academic load | ◯ | ◯ | ◯ | ◯ |
| Maintaining my grades | ◯ | ◯ | ◯ | ◯ |
| Pressure to succeed | ◯ | ◯ | ◯ | ◯ |
| Adjusting to university life | ◯ | ◯ | ◯ | ◯ |
| Managing relationships (family, friends) | ◯ | ◯ | ◯ | ◯ |

| | | | | |
|---|---|---|---|---|
| Social pressures (drinking, going out late, putting socializing before schoolwork) | ○ | ○ | ○ | ○ |
| Financial concerns (loans, debt, bills) | ○ | ○ | ○ | ○ |
| Managing self-care and health (eating healthy, exercising, hobbies) | ○ | ○ | ○ | ○ |

*In the past 3 / 12 months, have you had a relatively major bad experience in some aspect of your life other than the areas above (e.g., someone close to you dying; losing a job; serious illness or injury to yourself or someone close to you)?"*

0 no 1 yes this happened to me once during this period 2 yes this has happened to me twice during the period, 3 yes this has happened to me more than twice

If more than 0, ask to describe in text, and rate how stressful: not stressful, somewhat stressful, very stressful, extremely stressful

**I. Work and Social Adjustment Scale**

W&SAS

Sometimes people have difficulty with certain day-to-day tasks because of stress, emotional difficulties or reduced mental wellbeing. Please look at each section and determine on the scale provided how much difficulty you have carrying out each activity because of stress, emotional difficulties or reduced mental wellbeing.

1. How difficult is WORK (INCLUDING ACADEMIC STUDIES) – if you choose not to have a job, please select N/A (not applicable)

0 1 2 3 4 5
6 7 8 N/A

Not at all | Slightly | Definitely | Markedly | Very severely, I cannot work

2. How difficult is HOME MANAGEMENT – Cleaning, tidying, shopping, cooking, looking after home/children, paying bills etc.

0 1 2 3 4 5
6 7 8

Not at all | Slightly | Definitely | Markedly | Very severely

3. How difficult are SOCIAL LEISURE ACTIVITIES – With other people, e.g. parties, pubs, outings, sport, entertaining etc.

0 1 2 3 4 5
6 7 8

Not at all | Slightly | Definitely | Markedly | Very severely

4. How difficult are PRIVATE LEISURE ACTIVITIES – Done alone e.g. reading, watching TV/films/streaming, music, social media, hobbies, exercise etc.

0 1 2 3 4 5
6 7 8

Not at all | Slightly | Definitely | Markedly | Very severely

5. How difficult are FAMILY AND RELATIONSHIPS – Form and maintain close relationships with others including the people that I live with.

0 1 2 3 4 5
6 7 8

| Not at all | Slightly | Definitely | Markedly | severely | Very |
|---|---|---|---|---|---|

**J. Brief Resilience Scale**

Please indicate the extent to which you agree with each of the following statements by using the following scale: 1 = strongly disagree, 2 = disagree, 3 = neutral, 4 = agree, 5 = strongly agree.

| | 1 – Strongly Disagree | 2 - Disagree | 3 - Neutral | 4 - Agree | 5 – Strongly Agree |
|---|---|---|---|---|---|
| I tend to bounce back quickly after hard times. | ◯ | ◯ | ◯ | ◯ | ◯ |
| I have a hard time making it through stressful events. | ◯ | ◯ | ◯ | ◯ | ◯ |
| It does not take me long to recover from a stressful event. | ◯ | ◯ | ◯ | ◯ | ◯ |
| It is hard for me to snap back when something bad happens. | ◯ | ◯ | ◯ | ◯ | ◯ |
| I usually come through difficult times with little trouble. | ◯ | ◯ | ◯ | ◯ | ◯ |
| I tend to take a long time to get over setbacks in my life. | ◯ | ◯ | ◯ | ◯ | ◯ |

**K. Academic self-report and experience**

Academic grades self-report

1.Does your academic course of study involve regular summative graded assessments and/or exams or is it assessed differently (e.g., thesis and viva)?

Yes, graded assessments and exams

No, other assessment

[if no to Q1 go to Question5

2. What are your average subject grades for the last term/semester? 0-100% percent slider

3. What were your most recent end-term or exam grades for your main (principal) subject? 0-100% slider

4. What grade are you hoping for / aiming for in your main subject?

0-100% percent slider

5. How satisfied are you with your academic progress over the last 3 months? Please rate the following statement:

Overall, I am satisfied with my progress

Response options: Strongly disagree (-2)  Disagree (-1) Neutral (0) Agree  (+1) Strongly Agree (+2)

6. Have you missed any days from your studies because of illness, stress (e.g., including interruption)? Yes or No

If yes, ask “How many days do you estimate that you have missed?” Number response option

7. Have you been less productive because of stress or poor emotional wellbeing (e.g., trying to work but not concentrating well)? Yes or No

If yes, ask “How many days do you estimate that you have been less productive?” Number response option

8. Have you missed any deadlines or failed to turn in any assignments during this last term/semester? Yes or No

If Yes, how many?

**L. PHQ-2 and GAD-2 in combined measure (in mediational analysis)**

In the past 7 days, how often were you bothered by each of the following problems?

| | Not at all | Several days | More than half the days | Nearly every day |
|---|---|---|---|---|
| Feeling nervous, anxious, or on edge GADPHQ_1 | ○ | ○ | ○ | ○ |
| Not being able to stop or control your worrying GADPHQ_2 | ○ | ○ | ○ | ○ |
| Little interest or pleasure in doing things GADPHQ_3 | ○ | ○ | ○ | ○ |
| Feeling down, depressed, or hopeless GADPHQ_4 | ○ | ○ | ○ | ○ |

**M. Cognitive and Behavioral Response to Stress Scale (CB-RSS) Miner et al., 2015 adapted**

1. During the past 7 days in a stressful or upsetting situation:

How often did you take a moment to question your interpretation of what was happening when you got upset (e.g., look for a more positive or balanced explanation; weigh up different accounts, try and put things in perspective)??

| 0 | 1 | 2 | 3 | 4 | 5 | 6 |
|---|---|---|---|---|---|---|
| Never | Rarely | Occasionally | Sometimes | Often | Very Often | Always |
| ◯ | ◯ | ◯ | ◯ | ◯ | ◯ | ◯ |

(b) How helpful was this in making you feel better?

| 0 | 1 | 2 | 3 | 4 | 5 | 6 |
|---|---|---|---|---|---|---|
| Not at all very helpful | Slightly helpful | Somewhat helpful | Moderately helpful | Fairly helpful | Very helpful | Extremely helpful |
| ◯ | ◯ | ◯ | ◯ | ◯ | ◯ | ◯ |

2. During the past 7 days in a stressful or upsetting situation:

How often did you plan and/or do activities you knew you would enjoy?

| 0 | 1 | 2 | 3 | 4 | 5 | 6 |
|---|---|---|---|---|---|---|
| Never | Rarely | Occasionally | Sometimes | Often | Very Often | Always |
| ◯ | ◯ | ◯ | ◯ | ◯ | ◯ | ◯ |

How helpful was this in making you feel better?

| 0 | 1 | 2 | 3 | 4 | 5 | 6 |
|---|---|---|---|---|---|---|
| Not at all very helpful | Slightly helpful | Somewhat helpful | Moderately helpful | Fairly helpful | Very helpful | Extremely helpful |
| ◯ | ◯ | ◯ | ◯ | ◯ | ◯ | ◯ |

3. During the past 7 days in a stressful or upsetting situation:

How often did you use relaxation or similar techniques to soothe, focus or calm yourself (e.g., meditation, breathing, focusing attention, imagery)?

| 0 | 1 | 2 | 3 | 4 | 5 | 6 |
|---|---|---|---|---|---|---|
| Never | Rarely | Occasionally | Sometimes | Often | Very Often | Always |
| ◯ | ◯ | ◯ | ◯ | ◯ | ◯ | ◯ |

How helpful was this in making you feel better?

| 0 | 1 | 2 | 3 | 4 | 5 | 6 |
|---|---|---|---|---|---|---|
| Not at all very helpful | Slightly helpful | Somewhat helpful | Moderately helpful | Fairly helpful | Very helpful | Extremely helpful |
| ◯ | ◯ | ◯ | ◯ | ◯ | ◯ | ◯ |

**N. 2-item version of Self-Compassion Scale Short-Form**

“Please indicate how often you behaved in the stated manner during the past 7 days on a scale from 1 (Almost never) to 5 (Almost always).

| | 1 Almost never | 2 | 3 | 4 | 5 Almost always |
|---|---|---|---|---|---|
| When I’m going through a very hard time, I give myself the caring and tenderness I need | ◯ | ◯ | ◯ | ◯ | ◯ |
| When I feel inadequate in some way, I try to remind myself that feelings of inadequacy are shared by most people | ◯ | ◯ | ◯ | ◯ | ◯ |

**O. Measure of treatment received or services used**

1. Over the last 3/12 months, have you accessed any university provided wellness, counselling, mental health or learning support resources on campus or remotely?

◯ Yes
◯ No

*If NO [Skip Logic to Question 2]

Which College/University based wellbeing and mental health resource(s) did you access?

Select ALL that apply. [from drop down menu]

__ Student Health Centre or a University affiliated GP (doctor)*
__ University Counselling service/Student Wellbeing service course of counselling or therapy*
__ Student urgent or crisis support (e.g., Student Intervention Team)*
__ Academic or Personal Tutor*
__ Welfare Deans*
__ Student Disability Service (University support for disabilities)*
__ Student Occupational Health*
__ International Student Support*
__ Chaplaincy*
__ Peer Support Service (examples include (but are not limited to) Peer Supporters, Nightline, welfare reps / welfare champions, Student Mentor Scheme)*
Residential Support*
__ Student Union / Student Guild (Representatives, Advice services)*
__ Sexual Harassment and Violence Support Service (e.g. Disclosure Response Team)*
__Guild Societies[a]
__Education Welfare team (support with studies, mitigation)*

__Wellbeing groups[a]

__Self-help workbooks[a]

__Digital self-help e.g., online cognitive-behavioural therapy such as Silvercloud, Qwell, Sleepio)[a]

___Online counselling (e.g., Togetherall)[a]

__ Other (please specify):_____

For each element selected, follow-up questions ask (* if a person to see; [a] if a resource used by self):

*How many times have you seen or talked to someone from this service or resource (e.g., doctor, counsellor, therapist, support worker, tutor)? *Number response option*

[a]How many times did you use this resource? *Number response option*

AND

How much did this service or resource help with your specific problems?

Made things a lot better 1, made things somewhat better 2, made no difference 3, made things somewhat worse 4, made things a lot worse 5

How satisfied are you with this service or resource?

Rate how much you agree with the statement - overall I was satisfied with the help received from this source

1 = strongly disagree, 2 = disagree 3 = neutral 4 = agree 5. = strongly agree

2. During the past 3 / 12 months, have you accessed any wellness, counselling, mental-health, self-help or other relevant support services external to the University?

◯ Yes

◯ No

*If YES [Display Logic], if No skip to question 3.

Which Non-College/University based resource(s) did you access to support your mental health?

Select ALL that apply.

__ GP or family doctor*

_. Nurse at GP surgery*

__ NHS IAPT service (e.g., CBT therapist, guided self-help, counselling)*

__ NHS Secondary Care (e.g., Adolescent or Adult Mental Health Team; specialist service e.g., for eating disorders, psychiatrist)*

__ NHS Accident and Emergency[1]

__ Overnight hospital stay[2]

__ Private talking therapy / psychotherapy / counselling*

__ Mental Health Charity Service (for example, but not limited to: Samaritans, Shout, TogetherAll)[a]

__ Religious / Spiritual Guidance or Pastoral Care[b]

__ Alternative therapy[b]

__Support from friends[a]

__Support from family[a]

__Self-help books[a]

___Online self-help e.g., app, website[a]

_Sexual Harassment, Abuse, and Domestic Violence Support Service[b]

__ Other (please specify):_____

For each element selected, follow-up questions ask (matched by superscript):

*How many times have you seen or talked to this medical practitioner (e.g., doctor or psychiatrist) counsellor, nurse, or therapist?

[2]How many nights have you stayed in hospital for a physical health difficulty?

[2]How many nights have you stayed in hospital for a mental health difficulty?

[1]How many times have you attended accident and emergency?

[a]How many times did you use this resource?

[b]How many times have you seen or talked to someone from this service or resource (e.g., religious/spiritual authority, support worker, therapist)?

AND

How much did this service or resource help with your specific problems?

Made things a lot better 1, made things somewhat better 2, made no difference 3, made things somewhat worse 4, made things a lot worse 5

How satisfied are you with this service or resource?

Rate how much you agree with the statement - overall I was satisfied with the help received from this source

1 = strongly disagree, 2 = disagree 3 = neutral 4 = agree 5. = strongly agree

3. In the last 3 /12 months, have you taken any medication for your mental health?

Yes (1)

No (2)

*If Yes, name medication, entry in text box* _____

*Over the past 3 / 12 months,* how many weeks have you been prescribed this medication for your mental health? _____