CLINICAL STUDY PROTOCOL

NCT Number: NCT05616676

PROTOCOL NUMBER: P1V-GAINS-IN02

STUDY TITLE: A randomised controlled trial of a brief cognitive task intervention to support NHS staff experiencing intrusive memories of traumatic events from working in the COVID-19 pandemic

Final Protocol Date:	12th February 2024
Sponsor:	P1vital Products Ltd, Manor House, Howbery Park, Wallingford, Oxfordshire, OX10 8BA

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SIGNATURE PAGE

SPONSOR

The signature below constitutes approval of this protocol by the signatory and provides the necessary assurances that this study will be conducted according to all stipulations of the protocol, including all statements regarding regulatory guidelines and confidentiality.

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Protocol Synopsis

Study Title: A randomised controlled trial of a brief cognitive task intervention to support NHS staff experiencing intrusive memories of traumatic events from working in the COVID-19 pandemic.

Short Study Title: A Brief Cognitive Task Intervention for NHS Staff affected by COVID-19 trauma (GAINS-2 Study)

Chief Investigator: Dr Amy Beckenstrom

Study Centre(s): Study will be completed remotely in locations of participant's choosing with internet accessibility

Primary Objective:

- To determine if access to a brief imagery-competing task (intervention) compared to a brief music-listening task (active control) and treatment as usual (TAU), reduces the number of intrusive memories in week 4 (i.e., between-groups comparison), controlling for the number of intrusive memories in the run-in/baseline week.

Secondary Objectives:

- To determine if access to a brief imagery-competing task (intervention) compared to a brief music-listening task (active control) and treatment as usual (TAU), reduces the number of intrusive memories in weeks 12 and 24 (i.e., between-groups comparison), controlling for the number of intrusive memories in the run-in/baseline week.
- To determine if access to a brief imagery-competing task (intervention), compared to a brief music-listening task (active control) and treatment as usual (TAU), reduces the impact of intrusive memories (e.g. disruption to concentration and functioning); clinical symptoms of post-traumatic stress disorder, insomnia, anxiety, and depression; burnout, sickness absence and intention to leave the job; and improves work satisfaction, general functioning and quality of life at 4 weeks, 12 weeks and 24 weeks (i.e., between-groups comparisons).

Exploratory Objectives:

- To assess the number of new traumatic events, the occurrence of adverse events, other treatments received and changes to work.
- To obtain intervention usage data to inform the intervention implementation.
- To assess the acceptability and feasibility of the intervention from participants to inform the intervention implementation.
- To obtain complementary results using alternative statistical methods (e.g. frequentist analysis).

Hypothesis and Brief Rationale:

The primary hypothesis is that participants in the imagery-competing task (intervention) arm, compared to the music-listening task (active control) arm and treatment as usual (TAU) arm, will have fewer intrusive memories in week 4 (between-groups comparison), controlling for the number of intrusive memories in the run-in (baseline) week.

Study Design:

This randomised controlled trial uses a three-arm, parallel-group, design. The study's randomisation method allocates participants using a 2:2:1 (intervention: active control: TAU) overall ratio to the following arms:

1. Intervention = access to a brief imagery-competing task intervention for 24 weeks (first 4 weeks with optional researcher support)
2. Active control = access to a brief music-listening task for 24 weeks (first 4 weeks with optional researcher support)
3. TAU = routine care that participants would otherwise receive if having intrusive memories of traumatic events.

Study Period:

Each participant will be in the study for a total of up to 31 weeks. There will be virtual visits (i.e., audio or video calls between participant and researcher) at screening and on the first day of access to intervention/control. Thereafter contact with the researcher is only for optional qualitative interviews, and to provide support with additional intervention sessions or assist the participant (e.g., with outcome completion) when appropriate. Remote participant assessments (i.e., typically without researcher; online questionnaires only) will take place at Baseline, 4 weeks, 12 weeks and 24 weeks.

Total duration of the study from first participant enrolled to last participant completing the study is expected to last approximately 18 months but will depend on the final number enrolled.

Number of Participants:

The study will enrol up to approximately 150 participants, 60:60:30 per study arm (intervention: active control: treatment as usual).

Main Entry Criteria:

Main Inclusion Criteria:

- Aged 18 or above.
- Able to read, write and speak in English.
- Worked in a clinical role with COVID-19 patients in the NHS during the COVID-19 pandemic.
- Experienced at least one traumatic event related to their clinical work during the COVID-19 pandemic meeting criterion A of the Diagnostic and Statistical Manual of Mental Disorders, 5th edition (DSM-5) criteria for Post-Traumatic Stress Disorder (PTSD): "exposure to actual or threatened death, serious injury, or sexual violence" by "directly experiencing the traumatic event(s)" or "witnessing, in person, the event(s) as it occurred to others".
- Experience intrusive memories of the traumatic event(s).
- Experienced at least three intrusive memories in the week prior to screening.
- Have internet access.
- Willing and able to provide informed consent and complete study procedures.
- Willing and able to be contacted by the research team during the study period.
- Have not taken part in a previous study of this intervention from this research team (e.g., GAINS-01)

Main Exclusion Criteria:

Have fewer than three intrusive memories during the run-in week. We will not exclude those undergoing other treatment for post-traumatic stress disorder (PTSD) or its symptoms, so the study is as inclusive as possible to meet the challenges NHS staff are facing during their work

related to the COVID-19 pandemic.

Study Arms:

1. **Brief imagery-competing task**: the intervention consists of a brief reminder cue to a specific intrusive memory, followed by playing the computer game Tetris® for 20 minutes with instructions to use mental rotation during game play. The intervention is completed by the participant on their smart phone or other internet enabled device delivered on a secure web platform used for clinical self-management of health in general practice (i-spero®). Participants will complete the intervention in an initial guided session with the help of a researcher (by video call), and thereafter use it self-guided (with optional researcher support for the first 4 weeks). As part of the intervention, participants will receive regular reminders (with the option to turn these off if preferred).
2. **Brief music-listening task:** the active control consists of listening to classical music (Mozart) for 20-minutes following an instructional podcast about Mozart. The intervention is completed by the participant on their smart phone or other internet enabled device delivered on a secure web platform used for clinical self-management of health in general practice (i-spero®). Participants will complete the control task in an initial guided session with the help of a researcher (by video call), and thereafter use it self-guided (with optional researcher support for the first 4 weeks). As part of the active control, participants will receive regular reminders (with the option to turn these off if preferred).
3. **TAU**: routine care that participants would otherwise receive if having intrusive memories of traumatic events. This may vary between participants, and include pharmacological treatment, psychotherapy, self-help or no intervention. We will monitor treatments received at follow up assessments.

Outline of Study:

The study is divided into approximately a 1–5-week screening period including one-week run-in period to determine eligibility prior to randomisation, followed by approximately 24 weeks in the study period.

Participants will be recruited through the Intensive Care Society network membership in addition to existing social media followers and targeted advertisements in social media (e.g. Facebook, Instagram, Twitter), using radio, advertising through seminars, social media influencers, via Google, distributing posters & flyers and direct advertising by NHS sites for all NHS staff who have worked.

Those who are interested in taking part in the study will be asked to complete a brief online eligibility questionnaire anonymously, which can be accessed on the study website. Participants will be asked to give online informed consent before completing the questionnaire. Those who meet all the inclusion criteria will be asked to provide their contact details (name, telephone number and email address). A researcher will then arrange a time to contact them by phone or video call to obtain informed consent and go through the study inclusion and exclusion criteria.

After full consent to the study is given, and a participant is enrolled, participants will be asked to complete a daily online intrusive memory diary for a run-in period of one week to record a simple count of the number of intrusive memories they have each day using a secure web-based clinical research system, P1vital® electronic patient reported outcome (ePRO) system. Those meeting the study eligibility criteria will then be sent a link to complete baseline questionnaires using ePRO. After completing baseline questionnaires, participants will be randomised by ePRO to the intervention, active control or TAU arms using a 2:2:1 overall

ratio.

- Participants in the intervention arm will be contacted as soon as possible by a researcher to arrange a video call to go through the imagery-competing task intervention for the first time with researcher support (the single guided intervention session: Day 0). The brief digital intervention is a c. 25-minute session task completed by the participant on their smart phone or other internet enabled device delivered on a secure web platform used for clinical self-management of health in general practice (i-spero®). Participants in this arm will have continuous access to the intervention over the next 24 weeks (Day 1-168) and after the first researcher guided session can use the intervention either on their own (self-guided) or with the option of researcher support (first 4 weeks only). During the first 4 weeks, they will receive regular reminders (with the option to turn these off if preferred).
- Participants in the active control arm will be contacted as soon as possible by a researcher to arrange a video call to go through the music-listening task for the first time with researcher support (the single guided control session: Day 0). The brief digital control is a c.25-minute session task completed by the participant on their smart phone or other internet enabled device delivered on a secure web platform used for clinical self-management of health in general practice (i-spero®). Participants in this arm will have continuous access to the control task over the next 24 weeks (Day 1-168) and after the first researcher guided session can use it either on their own (self-guided) or with the option of researcher support (first 4 weeks only). During the first 4 weeks, they will receive regular reminders (with the option to turn these off if preferred).
- Participants in the TAU arm will be informed that they have been allocated to TAU arm.

Participants in all arms will be asked to complete the primary outcome measure in week 4, 12 and 24 (a simple count of the number of intrusive memories they have each day) using ePRO, and secondary outcome questionnaires using ePRO at 4 weeks (Day 28), 12 weeks (Day 84) and 24 weeks (Day 168). They will also be asked to complete an online feedback questionnaire about their experience of using the intervention at 4 weeks (Day 28) and they may be given the option of completing qualitative interviews with a researcher via audio or video call at 4 weeks (Day 28) and at 12-24 weeks (Day 84-168). These will be completed for participants in the intervention and active control arms.

Endpoints / Outcome Measures

Primary Endpoint:

- Number of intrusive memories of traumatic events recorded by participants in a brief daily online intrusive memory diary for 7 days during week 4 (i.e. from Day 22 to 28 post first intervention/control session/post randomisation in TAU arm). Analysed as between-group comparison controlling for the number of intrusive memories during the run-in (baseline) week.

Secondary Endpoints:

- Number of intrusive memories of traumatic events recorded by participants in a brief daily online intrusive memory diary for 7 days during week 12 (Day 78 to 84) and during week 24 (Day 162 to 168). Analysed as between-group comparison controlling for the number of intrusive memories during the run-in (baseline) week.

- Intrusive memory ratings, PTSD Checklist for DSM-5 (PCL-5), Sleep Condition Indicator (SCI-02), Generalised Anxiety Disorder 2-item version (GAD-2), Patient Health Questionnaire 2-item version (PHQ-2), Scale of Work Engagement and Burnout (SWEBO), number of sick days in the last 4 weeks, Intention To Leave Job, World Health Organization Disability Assessment Schedule (WHODAS 2.0), 5-level EQ-5D (EQ-5D-5L) at 4 weeks, 12 weeks and 24 weeks.

Exploratory Endpoints:

- Changes to health and work at 4, 12 and 24 weeks
- Intervention/control use e.g., number of times used, duration, time of day during the 24 weeks
- Feedback questionnaire at 4 weeks post first intervention/control session
  Optional qualitative interview at 4 weeks, and 12-24 weeks, post first intervention/control session.

Refer to section 5.7 for specific timings of assessments by day.

Statistical Methodology:

Bayesian analyses will be used for statistical inference. Sequential analysis using the Bayesian approach will be used on primary outcome data during the study to determine the final sample size.

Sequential Analysis Ongoing sequential analysis using Bayesian statistical approaches will be used to evaluate efficacy based on the primary outcome (difference in the number of intrusive memories in week 4, controlling for the number of intrusive memories during the run-in week).

End of Study Analysis

Primary Analysis

- Between-groups analysis will be used to test the difference in the number of intrusive memories in week 4 (i.e., from Day 22 to 28) between the intervention, active control and TAU groups. The analyses will control for the number of intrusive memories during the run-in week.

Secondary Analyses

- Between-groups analyses will be used to test the difference in the number of intrusive memories in weeks 12 and 24 between the intervention, active control and

TAU groups. The analysis will control for the number of intrusive memories during the run-in week.

- Between-groups analyses will be used to test for differences in other secondary outcomes at 4 weeks, 12 weeks and 24 weeks between the intervention, active control and TAU groups: intrusive memory ratings; symptoms of post-traumatic stress, insomnia, anxiety and depression; work engagement and burnout, sickness absence, and intention to leave job; and functioning and quality of life.

Exploratory Analyses

Descriptive statistics will be used to summarise:

- the number of ongoing traumatic events
- the occurrence of adverse events
- additional treatments received
- changes to job and hours per week
- usage data for the intervention/active control
- quantitative feedback questionnaire data

Qualitative data (e.g., feedback interview) will be thematically analysed using an inductive thematic, constant comparison approach based on grounded theory (Glaser and Strauss 1967).

References:

Holmes, E. A., James, E. L., Coode-Bate, T., & Deeprose, C. (2009). Can playing the computer game "Tetris" reduce the build-up of flashbacks for trauma? A proposal from cognitive science. PLoS ONE, 4(1), e4153.

Lin, S. T., Yang, P., Lai, C. Y., Su, Y. Y., Yeh, Y. C., Huang, M. F., & Chen, C. C. (2011). Mental Health Implications of Music: Insight from Neuroscientific and Clinical Studies. Harvard Review of Psychiatry, 19(1), 34–46.

Iyadurai, L., Blackwell, S. E., Meiser-Stedman, R., Watson, P.C., Bonsall, M. B., Geddes, J. R., Nobre, A.C., & Holmes, E. A. (2018). Preventing intrusive memories after trauma via a brief intervention involving Tetris computer game play in the emergency department: a proof-of-concept randomized controlled trial. Molecular Psychiatry. 23(3), 674-682.

Kanstrup, M.*, Singh, L.*, Göransson, K., Widoff, J., Taylor, R., Iyadurai, L., Moulds, M. & Holmes, E. A. (2021). Preventing intrusive memories after trauma via a simple cognitive intervention in the hospital emergency department: An explorative randomised controlled pilot trial. *Translational Psychiatry*, *11*(30). https://doi.org/10.1038/s41398-020-01124-6. *co-shared first authorship

Ramineni, V., Millroth. P., Iyadurai, L., Jaki, T., Kingslake, J., Highfield, J., Summers, C., Bonsall, B, M., Holmes, E. A. (2022). Health-care workers experiencing intrusive memories of psychologically traumatic events in the COVID-19 pandemic: Developing a brief digital imagery-competing task intervention using a Bayesian adaptive randomised optimisation trial. Submitted for publication.

List of Abbreviations

AE	Adverse Event
COVID-19	Coronavirus Disease 2019
DSM-5	Diagnostic and Statistical Manual of Mental Disorders, 5th Edition
FDA	Food and Drug Association
GAD-2	Generalised Anxiety Disorder – 2-item questionnaire
GCP	Good Clinical Practice
GP	General Practitioner
ePRO	Electronic Patient Reported Outcomes
EQ-5D-5L	5-level EQ-5D
FTSU	Freedom To Speak Up
ICF	Informed Consent Form
ICU	Intensive Care Unit
IFU	Instructions For Use
ISO	International Organisation for Standardisation
NICE	The National Institute for Health and Care Excellence
NHS	National Health Service
PCL-5	PTSD Checklist for DSM-5
PHQ-2	Patient Health Questionnaire – 2-item version
PI	Principal Investigator
PIS	Participant Information Sheet
PTSD	Post-traumatic Stress Disorder
RCT	Randomised Controlled Trial
REC	Research Ethics Committee
SAE	Serious Adverse Event
SCI	Sleep Condition Indicator
SWEBO	Scale of Work Engagement and Burnout
TAU	Treatment as Usual
WHO	World Health Organization
WHODAS	World Health Organization Disability Assessment Schedule

1.0 Introduction and Rationale

1.1 Background

1.1.1 The mental health impact of covid-19 trauma on health care staff

The mental health of frontline healthcare staff delivering care to COVID-19 patients is a major priority internationally (Holmes et al., 2020), for two reasons:

1. Frontline healthcare staff are at elevated risk of post-traumatic stress disorder (PTSD) and other mental health symptoms due to increased exposure to occupational trauma and require prompt access to effective interventions.
2. Retaining healthcare staff in their jobs and preventing work dropout is necessary for delivering critical care to NHS patients.

During the COVID-19 pandemic, frontline healthcare staff are experiencing extreme exposure to potentially traumatic events, e.g., traumatic, or tragic death of a patient (Adriaenssens et al., 2012; Jonsson & Segesten, 2003; Laposa et al., 2003; Michael & Jenkins, 2001), or heightened risk of infection (Kang et al., 2020; Zhang et al., 2020).

After a trauma, it is common to experience intrusive memories (or sometimes “flashbacks”) of the event. Even before COVID-19, 65% of emergency nurses reported having intrusive memories of work-related traumatic events (Kleim et al., 2015) – emotional, intrusive, and primarily visual memories of the traumatic event that pop suddenly into mind. For some individuals, intrusive memories persist, and become a core symptom of post-traumatic stress disorder (PTSD) (American Psychiatric Association, 2013).

Around 40% of healthcare staff in UK hospitals reported a level of symptoms consistent with a diagnosis of PTSD as of June/July 2020 (Greenberg et al., 2021)- five times higher than in 2015 (Colville et al., 2015). Of this sample of almost 3000 respondents, approximately one quarter report “Repeated, disturbing memories, thoughts of images related to the current pandemic” (i.e., intrusive memories) have been bothersome (scores of 3=moderately to 5=extremely on the PCL-6; (Lang et al., 2012) Greenberg on our Expert Advisory Panel, personal communication (Greenberg, 2021)).

Studies from China report that between 24% and 35% of healthcare workers reported PTSD symptoms during the COVID-19 pandemic (Tan et al., 2020; Lai et al., 2020; Kang et al., 2020).

PTSD has a major impact on an individual’s functioning and incurs great cost for both the individual and society. PTSD symptoms can impair work performance: 27% of healthcare workers who reported PTSD symptoms said they interfered with their work functioning (Laposa & Alden, 2003) and 20% considered changing their job (Laposa, Alden & Fullerton, 2003). Mental health problems are the leading cause of sickness absence in the NHS (NHS Digital, 2020).

A survey of NHS ICU staff found that the period of the pandemic over winter 2020/2021 was associated with not only poorer mental health outcomes but also impaired functioning – raising concerns for patient care and the workforce retention in the long-term (Hall et al. 2022).

1.2 Rationale

1.2.1 Limitation to existing interventions after trauma

Whilst there are effective treatments for PTSD, such as talking therapies like trauma-focused cognitive behavioural therapy (NICE, 2018), uptake in frontline staff is limited by difficulty finding time to attend fixed therapy sessions and mental health stigma. Moreover, we lack evidence-based interventions to target ongoing trauma (as experienced by healthcare staff) as well as sub-clinical symptoms (as many people have symptoms without a diagnosis of a full clinical disorder). We also lack approaches to prevent full-blown PTSD from developing - which is critical to keeping frontline staff working well. We urgently need psychological interventions for healthcare staff that are brief, remotely-delivered (digital), low stigma and scalable. Here, we take a single symptom approach – focusing on intrusive memories.

1.2.2 A mechanism-based intervention to target intrusive memories of trauma

Intrusive memories of trauma may be a potential target for early and preventative interventions post-trauma (Iyadurai et al., 2019). Intrusive memories are centrally linked to other symptoms of the disorder, both at an early and later period post-trauma (Bryant et al, 2017). This has led to the suggestion that targeting intrusive memories may prevent PTSD from developing (McNally, 2017).

Laboratory and clinical studies within Prof Holmes' research group has led to the development of a brief mechanism-driven behavioural intervention to reduce intrusive trauma memories (e.g., Holmes, James, Coode-Bate, & Deeprose, 2009; James et al., 2015).

This brief imagery-competing task intervention consists of a brief reminder cue to orient to the traumatic event, followed by playing the computer game Tetris for 20 minutes with instructions to use mental rotation during game play. The principles of the intervention are informed by the (neuro)science of memory (re)consolidation and cognitive task interference. The hypothesis is that the memory updating process of a traumatic event can be disrupted by engaging in visuospatial demanding tasks, e.g. Tetris, and reduce the frequency of the intrusive memories. However, the ability to voluntarily recall the memories does not appear to be affected in laboratory studies.

1.2.3 Clinical translation and application

The intervention is thought to be effective across different types of traumatic events. A number of pilot and proof-of-concept clinical studies have been

carried out – three randomised controlled trials and three case series studies. An initial randomised controlled trial compared the intervention to usual care in woman who had an emergency caesarean section (traumatic childbirth). The results showed that the frequency of intrusive memories decreased during the following week for the intervention group in comparison to the control group (Horsch et al, 2017). Similar results were found in a randomised controlled study with participants admitted to a UK emergency department after a traumatic motor vehicle accident. Those who received the intervention, compared to an attention-placebo control, reported fewer intrusive memories over the next week (Iyadurai et al., 2018). In a pilot replication trial in a Swedish emergency department, reduction in intrusive memory frequency was maintained (and in fact even greater) at 5 weeks post intervention (Kanstrup, Singh et al., 2021). In all of these trials, feedback from participants indicated that the intervention was acceptable. Finally, the intervention has also been found to reduce intrusive memories in case series studies with patients with chronic PTSD (Kessler et al, 2018), refugees (Kanstrup et al., 2020), and most recently NHS staff exposed to work-related trauma including during the COVID-19 pandemic (Ramineni et al., 2022 submitted for publication).

Our game-based intervention is an 'early intervention' that aims to reduce and prevent the recurrence of intrusive memories during the COVID-19 pandemic. The intervention can be delivered within the timeframes of early prevention (within 1 month after the traumatic event), early preventative treatment (1-3 months after the event), delayed preventative treatment (>3 months after the event), or during ongoing trauma exposure (NICE evidence reviews for PTSD prevention, 2018). Within the NICE evidence reviews for PTSD prevention (2018), the intervention could be considered as 'self-help with or without support'.

The intervention holds particular promise for overcoming some of the challenges of implementing mental health interventions for healthcare staff as it is brief (one guided intervention session of approximately 30 minutes), can be used flexibly in different locations (e.g., on a smartphone during a commute), and is non-stigmatising (involves a digital task including a computer game rather than talking to a trained therapist). Participants can then use it self-guided for additional different intrusive memories they may be experiencing. It can also be delivered following each new traumatic event, and for new intrusive memories as they arise, so is well-suited for healthcare staff facing multiple, repeated or ongoing trauma in their jobs during the pandemic. Participants do not need to talk about the traumatic event in detail, which minimises distress.

We recently developed and tested a guided digital version of this intervention against usual care in a randomised optimisation study with NHS ICU staff who had experienced work-related traumatic events during the Covid-19 pandemic (the GAINS study: REC Reference 21/WA/0173). The study found strong evidence for effect of the intervention, compared to usual care, in reducing the

number of intrusive memories experienced by staff 4 weeks post-intervention (Ramineni, Millroth, Iyadurai, Jaki, Kingslake, Highfield, Summers, Bonsall & Holmes, 2022). There were also beneficial effects on a brief measure of clinical symptoms of PTSD, anxiety and insomnia, work functioning, general functioning, and quality of life at week 4.

Therefore, here we test the intervention:

a) for all NHS staff who worked with COVID-19 patients during the pandemic (not just ICU staff)
b) in a between-subjects design against an active control task as well as usual care (rather than a waitlist design with usual care)
c) with follow up over a longer time period (beyond 4 weeks to 6 months)
d) using a full measure of PTSD (not a brief measure)

For the active control, we will use an alternative brief cognitive task, which includes listening to classical music for 20 minutes rather than playing a computer game for 20 minutes. It will be delivered using the same web platform (i-spero®). We have selected this task to control for some expectation bias as research indicates that listening to classical music is associated with mental health benefits (Lin et al., 2011).

1.2.4 Aims of the current study

The current study aims to test the efficacy of the imagery-competing task intervention against an alternative brief cognitive task (a music-listening task) and TAU for NHS staff with intrusive memories of work-related traumatic events from the pandemic. We test the effect on the number of intrusive memories (primary outcome), and other clinical symptoms, work and general functioning and quality of life (secondary outcomes) at 4, 12 and 24 weeks.

Results of the study will be relevant globally to healthcare staff affected by traumatic events during the COVID-19 pandemic.

1.2.5 Main research questions

1. Can a brief imagery-competing task intervention, relative to a brief music-listening task and TAU, for national health service (NHS) staff who have experienced work-related traumatic events during COVID-19:

a) Reduce the number of intrusive memories in week 4 (primary outcome)?

b) Reduce the number of intrusive memories in week 12 and week 24 (secondary outcomes)?

c) Reduce symptoms of PTSD, anxiety, depression, and insomnia (secondary outcomes)?

d) Improve work functioning, general functioning, and quality of life (secondary outcomes)?

2. Is the intervention feasible and acceptable to NHS staff? (exploratory outcomes)

3. How can we inform implementation of the intervention? (exploratory outcomes)

1.3 Risks and benefits

1.3.1 Benefits

The study holds the following potential benefits to NHS staff who receive the intervention and COVID-19/other patients:

1. Immediate clinical benefit to NHS staff participants, by reducing distressing intrusive memories and other mental health symptoms.

2. Immediate benefit to staff job performance and delivery of care to COVID-19/other patients, by reducing disruption to concentration and work performance caused by intrusive memories.

3. Longer-term/preventative impact on staff participants' mental health, by reducing the persistence of other PTSD symptoms and other mental health symptoms.

4. Longer-term impact on staff sickness absence, burnout and intention to leave the job.

5. Longer-term impact on the delivery of care to COVID-19/other patients, due to improved staff retention.

6. Improvements in terms of general functioning and quality of life for staff participants.

Previous studies show that participants rate the intervention as easy, helpful, minimally distressing/burdensome, and acceptable (Horsch et al, 2017; Iyadurai et al, 2018; Kanstrup, Singh et al, 2021). Moreover, participants reported that the intervention took their mind off the traumatic event (e.g., Iyadurai et al, 2018) and was fun and relaxing (Kanstrup, Singh et al, 2021). Qualitative interviews associated with the previous GAINS study indicate a similar favourable response by NHS ICU staff (REC Reference 21/WA/0173). All participants will be given information on how to seek help for any ongoing mental health concerns at the end of the study, and individuals who are not eligible for the study will be signposted to NHS/Every Mind Matters and other support websites.

For participants allocated to the active control condition, the effect of listening to classical music is likely to be either neutral or associated with mental health benefits (Lin et al., 2011).

1.3.2 Risks and measures to minimise them

The study has no anticipated long-term risks to participants, and no adverse events related to study procedures have been reported by participants in previous trials of the intervention (Horsch et al., 2017; Iyadurai et al., 2018; Kanstrup, Singh et al., 2021; the recent GAINS study REC Reference 21/WA/0173).

However, the study procedures may be associated with the following risks and measures to minimise each risk are also described:

1. Briefly listing image-based intrusive memories of traumatic events and bringing them to mind as part of the intervention (memory reminder) may be unpleasant or distressing for some participants.

This procedure has been tested in several previous studies (Iyadurai et al., 2018; Kanstrup et al, 2020; Kanstrup, Singh et al., 2021; the recent GAINS study REC Reference 21/WA/0173) with no adverse consequences. The procedure is very brief, and participants are only asked to write a few words for each intrusion, before moving on quickly to the next. Participants are only asked to bring to mind the image very briefly, before moving immediately on to playing Tetris. Participants are not required to recall or describe the traumatic event(s) in detail.

2. Some participants may find playing the computer game Tetris difficult or stressful.

Tetris is a simple and popular computer game, and whilst most participants in previous studies have reported finding it fun and distracting, participants occasionally find it difficult or stressful. All participants will be given instructions on how to play Tetris, and in this study the difficulty of the game adapts to the skill of the player. The researcher will be present to help the participant the first time they do the intervention. Many healthcare staff already use computer games for distraction and recreation (BBC News, 2020).

3. Completing outcome measures may be perceived as burdensome by some participants.

We have tried to further minimise participant burden by limiting the number of outcome measures compared to the previous study (the GAINS study REC Reference 21/WA/0173), and wherever possible using shortened versions of measures (e.g., GAD-2 and PHQ-2). We have selected measures with the specific needs and demands of healthcare staff in mind. All outcome measures will be administered online, meaning that participants can complete them at a time and place that suits them.

4. Some staff who do not meet the eligibility criteria may still be experiencing difficulties.

To address this, we will ensure that all potential participants who do not meet the initial screening criteria will be signposted to the NHS/Every Mind Matters and other support website.

The research team includes qualified Clinical Psychologists and Psychiatrists with extensive experience in running clinical research studies in mental health. These include previous studies testing this intervention, trials of other digital mental health interventions, and studies with healthcare staff and students. The study has been designed in line with Good Clinical Practice (GCP) guidance, and all investigators are GCP trained. Dr Lalitha Iyadurai and

Professor Emily Holmes (clinical psychologists) have expertise in treating traumatised individuals and will be involved in the training and monitoring of the study team.

2.0 Study Objectives

2.1 Primary Objective

- To determine if access to a brief imagery-competing task (intervention) compared to a brief music-listening task (active control) and treatment as usual (TAU), reduces the number of intrusive memories in week 4 (i.e., between-groups comparison), controlling for the number of intrusive memories in the run-in/baseline week.

2.2 Secondary Objectives

- To determine if access to a brief imagery-competing task (intervention) compared to a brief music-listening task (active control) and treatment as usual (TAU), reduces the number of intrusive memories in weeks 12 and 24 (i.e., between-groups comparison), controlling for the number of intrusive memories in the run-in/baseline week.
- To determine if access to a brief imagery-competing task (intervention), compared to a brief music-listening task (active control) and treatment as usual (TAU), reduces the impact of intrusive memories (e.g. disruption to concentration and functioning); clinical symptoms of PTSD, insomnia, anxiety, and depression; burnout, sickness absence and intention to leave the job; and improves work satisfaction, general functioning, and quality of life at 4 weeks, 12 weeks, and 24 weeks (i.e., between-groups comparisons).

Exploratory Objectives:

- To assess new traumatic events, adverse events, treatment received and self-reported changes to job or hours worked.
- To obtain intervention usage data to inform the intervention implementation.
- To assess the acceptability and feasibility of the intervention from participants to inform the intervention implementation.
- To obtain complementary results using alternative statistical methods (e.g. frequentist analysis).

3.0 Study Design

3.1 Overview

The study is a randomised controlled trial study of a brief digital imagery-competing task intervention to support NHS staff experiencing intrusive memories of traumatic events from working in the COVID-19 pandemic.

Participants will be randomised to one of three study arms:

Intervention arm = one guided session and access to a brief imagery-competing task intervention (self-guided) for 24 weeks (first 4 weeks with optional researcher support)

Active control arm = one guided session and access to a brief music-listening task

(self-guided) for 24 weeks (first 4 weeks with optional research support)

TAU = routine care that participants would otherwise receive if having intrusive memories of traumatic events for 24 weeks.

The study will enrol up to approximately 150 participants, 60:60:30 per study arm (intervention: active control: TAU) (see sample size calculation, section 11.1).

The study will enrol NHS staff (e.g. doctors, nurses, paramedics and clinical support staff) aged 18 and over who: a) have experienced one or more work-related traumatic events during the COVID-19 pandemic (e.g. a patient death), and b) have intrusive memories of the event(s).

The study is divided into a 1-5 week screening period, randomisation into intervention, active control or TAU arm using a 2:2:1 overall ratio, 24 week in-study period. Each participant will be in the study for a total of up to 31 weeks. All of the study visits will be completed by participants remotely on their smart phone or other internet enabled device.

During the in-study period participants will receive the intervention/active control/TAU for a period of 24 weeks and will collect self-reported questionnaires at Baseline, 4, 12, 24 weeks digitally and remotely.

Optional qualitative interviews will be performed at 4 weeks and 12-24 weeks post intervention/control onset to assess the feasibility and acceptability of the intervention/control (please note: optional qualitative interview will only be conducted for participants allocated to the intervention and control arm)

Total duration of the study from first participant enrolment to last participant completing the study is expected to last approximately 18 months but will depend on the final number enrolled.

The brief imagery-competing task intervention will be delivered on a secure web platform used for clinical self-management of health in general practice (i-spero®).

A secure web-based clinical research system, P1vital® ePRO will be used to:

- Randomise participants and will issue email/text reminders to participants and study researchers when study-related activities are due.
- Collect intrusive memory diary data during the run-in week and at week 4 (Day 22 to 28), week 12 (Day 78 to 84) and week 24 (Day 162 to 168).
- Collect self-reported outcome measurement data at baseline, 4 weeks (Day 28),12 weeks (Day 84) and 24 weeks (Day 168).

The primary comparison will be a between-groups comparison of the number of intrusive memories recorded during week 4 (i.e. from day 22 to 28), controlling for the number of intrusive memories recorded during the run-in week.

3.2 Study design

Participants will be recruited through the Intensive Care Society network membership and existing social media followers. This is supplemented by targeted advertisements in social media (e.g. Facebook, Instagram, Twitter) in addition to

using radio, advertising through seminars, social media influencers, via Google, distributing posters & flyers and direct advertising by NHS sites.

Those who are interested in taking part in the study will be asked to complete a brief online pre-screening eligibility questionnaire anonymously, which can be accessed on the study website. Participants will be asked to give online consent before completing the pre-screening questionnaire. Those who meet all the pre-screening inclusion criteria will be asked to provide their contact details (name, telephone number and email address). They will be given the option to book a meeting with a researcher via the study website. A researcher will then contact them by phone or video call to obtain informed consent and go through the full study inclusion and exclusion criteria.

All participants will be asked to complete a daily online intrusive memory diary for a run-in period of one week where participants will be asked to record a simple count of the number of intrusive memories they have each day followed by an intrusive memory rating at the end of the week using ePRO.

Those meeting the study entry criteria will be sent a link to complete baseline questionnaires using ePRO. After completing the baseline questionnaires participants will be randomised by ePRO to either the intervention, active control or TAU arm using a 2:2:1 overall ratio. After randomisation, participants will be given information explaining what will happen next in the study. This information will differ according to whether they have been allocated to the intervention arm, active control arm or TAU arm.

Participants in intervention and active control arms will be contacted immediately by a researcher to arrange a time (e.g., via video call using Microsoft Teams/Zoom) to go through the intervention or control task for the first time (guided session: Day 0). The intervention and active control both involve brief cognitive tasks completed by the participant on their smart phone or other internet enabled device delivered on a secure web platform used for clinical self-management of health in general practice (i-spero®). Participants in the TAU arm will be contacted to inform them that they should continue to receive any care they would otherwise access.

Participants in intervention and control arms will have continuous access to the intervention and brief music listening task over the next 24 weeks and can use the intervention or control task either on their own or with the option of researcher support for the first 4 weeks.

Participants in all three arms will be asked to complete the primary outcome in week 4 (day 22 to 28), week 12 (Day 78 to 84) and week 24 (Day 162 to 168) (a simple count of the number of intrusive memories they have each day) using ePRO, and secondary outcome questionnaires using ePRO at 4 weeks (Day 28), 12 weeks (Day 84) and 24 weeks (Day 168). Participants in intervention and control arms will also be asked to complete an online feedback questionnaire about their experience

of using the intervention and/or music listening task at 4 weeks, and they may be given the option of completing qualitative interviews with a researcher via audio or video call at 4 weeks and at 12-24 weeks.

Note: Day 0 in the intervention or active control group is defined as the day on which the participant completes the first intervention session and/or control session with researcher support (guided session). Day 0 in the TAU group is defined as the day on which the participant is randomised into the TAU arm.

This randomised control trial uses an adaptive Bayesian design for efficacy evaluation of a brief cognitive task intervention. Recent advances in trial design and methodology offer more efficient alternatives to traditional RCTs to speed up the testing and thus implementation of evidence-based treatments (ACE CONSORT Extension; Dimairo et al. 2020). Adaptive designs enable smaller, more efficient trials without loss of scientific integrity, and allow a trial to be modified on the basis of interim analysis, thereby making optimal use of all data for decision-making.

Sequential analyses at a group level (intervention: active control: TAU) start with a small number of participants (e.g. n=20) and are repeated every approximately 4-10 participants thereafter, up to a maximum of approximately n=150 (in 2:2:1 ratio across intervention, active control and TAU groups, respectively). Prespecified thresholds are used to trigger decision making regarding final sample size (e.g. assessed using Bayes factors which compare different hypotheses). If the intervention is shown to be significantly more effective than controls before reaching the max n=150 participants, then the study may conclude early.

4.0 Study Population

4.1 Inclusion Criteria

Potential participants will be included if they meet the following criteria:

- Aged 18 or above.
- Able to read, write and speak in English.
- Worked in a clinical role with COVID-19 patients in the NHS during the COVID-19 pandemic
- Experienced at least one traumatic event related to their clinical work during the COVID-19 pandemic meeting criterion A of the Diagnostic and Statistical Manual of Mental Disorders, 5th edition (DSM-5) criteria for PTSD: “exposure to actual or threatened death, serious injury, or sexual violence” by "directly experiencing the traumatic event(s)" or "witnessing, in person, the event(s) as it occurred to others”.
- Experience intrusive memories of the traumatic event(s).
- Experienced at least three intrusive memories in the week prior to screening.
- Have internet access.
- Willing and able to provide informed consent and complete study procedures
- Willing and able to be contacted by the research team during the study period.

- Have not taken part in a previous study of this intervention from this research team (e.g. GAINS-01)

4.2 Exclusion Criteria

Have fewer than three intrusive memories during the run-in week. We will not exclude those undergoing other treatment for PTSD or its symptoms, so the study is as inclusive as possible to meet the challenges NHS staff are facing during their work related to the COVID-19 pandemic.

5.0 Study Procedures

Activities taking place during the study are shown in the Time and Events table in Appendix 1.

5.1 Recruitment

Participants will be recruited through the Intensive Care Society network membership and existing social media followers supplemented by targeted advertisements in social media (e.g. Facebook, Instagram, Twitter), using radio, advertising through seminars, social media influencers, via Google, distributing posters & flyers and direct advertising by NHS sites.

The advertisements email will contain a link to the study website, where potential participants will be able to read a summary of the study information including the participant information sheet and watch a video explaining what intrusive memories of traumatic events are. Study web site will also include a link to the pre-screening eligibility questionnaire.

5.2 Pre-Screening

Those who are potentially interested in taking part in the study will be asked to complete an online pre-screening eligibility questionnaire, which can be accessed via the study website. Participants will be asked to give online consent before completing the pre-screening questionnaire. The brief online pre-screening questionnaire is completed anonymously. Those who are not eligible to take part in the study will be sent information signposting them to NHS staff and mental health support websites, such as the NHS Every Mind Matters website. Those who meet all the pre-screening inclusion criteria will be asked to provide their contact details (name, telephone number and email address). They will then be given the option to book a meeting with a researcher via the study website or wait for a researcher to contact them directly. A researcher will send all participants a participant information sheet with full information about the study. The participant information sheet will include: the nature and purpose of the study; the study eligibility criteria; what it will involve for the participant; any risks and benefits involved in taking part; and researcher contact details in case they have any questions. It will be clearly stated that the participant is free to withdraw from the study at any time for any reason, and with no obligation to give the reason for withdrawal. The participant will be allowed as much time as wished to consider the information, and the opportunity to question the Investigator, their GP or other independent parties to decide whether they will

participate in the study. If they are still interested in taking part in the study, a researcher will then arrange a time to contact them by phone or video call to obtain informed consent.

5.3 Informed Consent & Screening (Inclusion Criteria)

Full informed consent will be obtained during a phone or video call. The participant and researcher will complete, sign and date the consent form using a simple electronic signature. Participants will be emailed a copy of the consent form. This will take place before any baseline measures or study specific procedures commence. The consent form will be retained electronically in a secure format. The researcher obtaining informed consent will be GCP trained and authorised to do so by the Principal Investigator. During this meeting, the researcher will also go through the study inclusion criteria with participants, confirm their contact details, and ask what their job role was during the pandemic (if missed, this can be asked any time up to the final endpoint at 24 weeks).

5.4 Screening

5.4.1 Intrusive memory diary

After obtaining informed consent, participants will be asked to complete a daily online intrusive memory diary for a run-in period of one week. Participants will be asked to record a simple count of the number of intrusive memories they have each day. The intrusive memory diary is based on that used in previous studies of the brief behavioural intervention (e.g. Holmes et al., 2009; James et al., 2015; Iyadurai et al., 2018), and adapted for digital delivery using ePRO (used successfully in our study preceding this one, P1V-GAINS-IN01). Participants will be a sent a link to create a personal, password-protected user account to access ePRO. Each day they will receive a reminder (by text/email) to log in and complete their intrusive memory count. Intrusive memories are defined as “mental images from a traumatic event that pop suddenly into your mind when you don’t want them to”. Instructions will include a link to a video explaining what intrusive memories are. Each day, the participant is asked to indicate if they have had any intrusive memories (yes/no) and if so, how many. This type of daily online intrusive memory diary has already been piloted with NHS staff with high (99.4%) completion rates (Ramineni et al., 2023). At the end of the week, they will be asked to rate how accurately they think they completed the diary over the last week (on an 11-point scale from 0 = not at all accurately to 10 = extremely accurately).

After completing the run-in-week diary, participants who meet the eligibility criterion of having 3 or more intrusive memories in the run-in week will be informed that they are eligible to continue to the next stage of the study. Those who are not eligible to take part in the study will be sent information signposting them to NHS staff and mental health support websites, such as the NHS Every Mind Matters website.

5.5 Rescreening

Screening will occur in the 5 weeks prior to Day 0. The study permits the re-screening (after the end of the screening period) of participants who have consented to participate in the study but are not subsequently randomised into the study within 5 weeks for any reason (e.g. the participant had fewer than 3 intrusive memories during the run-in week, but may have more intrusive memories at a later time). The participant will be assigned a new participant identification number, and the screening procedures must be performed again.

5.6 Baseline Assessment

Before randomisation participants will complete the following self-report measures using ePRO.

5.6.1 Demographic information

The following information is collected: age, gender identity, education level, marital status, ethnicity, employment status, number of hours per week currently working, number of years working as a healthcare professional during the pandemic.

5.6.2 Health background

A 2-item questionnaire will be used to assess current/past mental health problems, current treatments/medication for mental health problems.

5.6.3 Checklist of work-related traumatic events

Participants are asked to select from a list the types of traumatic events they have experienced or witnessed during the COVID-19 pandemic, for which they have intrusive memories. The list contains traumatic events previously reported by healthcare professionals in research literature, including a traumatic or tragic death of a patient, increased risk of COVID-19 infection, and severe or unsuccessful resuscitation. They are asked how many work-related traumatic events, and how many non-work-related traumatic events they experienced during the pandemic, and how long ago these events occurred.

5.6.4 Intrusive memory ratings

Participants will be asked to rate 8 items to assess the following characteristics of their intrusive memories over the last week: frequency, distress, disruption to concentration, interference with what they were doing (how much and for how long), duration of interference, impact on work functioning (how much and how) and impact on functioning in other areas of life (how much and how). Two additional items will assess the number of days worked and number of night shifts worked in the last week.

5.6.5 PTSD Checklist for DSM-5 (PCL-5) (Weathers et al., 2013)

This 20-item measure assesses symptoms of PTSD over the last week. Items are rated on a 5-point scale ranging from 0 (''not at all'') to 4 (''extremely''). Scores are summed to give a total severity score (ranging 0 to 80). The measure has sounds internal validity and test-retest reliability.

5.6.6 Sleep Condition Indicator (SCI-02; Espie et al., 2014)

This 2-item scale measures sleep problems against the DSM-5 criteria for insomnia disorder. Item responses are each scored 0-4, with scores from 0 to 2 indicating threshold criteria for insomnia disorder. Total score ranges 0-8, with a higher score indicating better sleep. The SCI-02 is valid, reliable and sensitive to change (Espie et al, 2014; Luik et al, 2019).

5.6.7 Generalized Anxiety Disorder (GAD-2; Kroenke et al., 2007)

This 2-item short-form self-report measure assesses the severity of anxiety symptoms. Items are rated for how often they have bothered the respondent over the last two weeks, from 0 (“not at all”) to 3 (“nearly every day”). The total score ranges 0-6, with a cut-off score of 3 indicating a probable diagnosis of generalised anxiety disorder. The measure has comparable performance to the full 7-item version as a screening tool.

5.6.8 Patient Health Questionnaire (PHQ-2; Kroenke, Spitzer & Williams, 2003)

This 2-item short-form self-report measure assesses symptoms of depression. Items are rated for how often they have bothered the respondent over the last two weeks, from 0 (“not at all”) to 3 (“nearly every day”). The total score ranges 0-6, with a cut-off score of 3 indicating a probable diagnosis of depression. The measure has adequate construct validity with a sensitivity of 83% and a specificity of 92% for detecting major depression.

5.6.9 Scale of work engagement and burnout (SWEBO; Hultell & Gustavsson, 2010)

This 19-item self-report measure assesses work engagement and burnout. The work engagement subscale consists of 10 items assessing three dimensions (vigour, attentiveness, dedication). The burnout subscale also consists of 9 items assessing with three dimensions (exhaustion, disengagement and inattentiveness). Respondents rate how often they have felt each descriptive in the past two weeks, from 1 (not at all) to 4 (all the time). The mean score is calculated for each subscale.

5.6.10 Sickness absence (Revicki et al., 1994)

A single item will assess the number of sick days taken from work during the past 4 weeks.

5.6.11 Intention to leave job (Cohen, 1998)

3 items are used to assess participants’ intention to leave their job e.g. “I think a lot about leaving the job”, each rated from 1 (strongly agree) to 5 (strongly disagree). The total score ranges 3 to 15, with a lower score indicating stronger intention to leave the job.

5.6.12 World Health Organization Disability Assessment Schedule (WHODAS) 2.0

The 12-item, self-report version of the WHODAS 2.0 will be used to assess difficulties in relation to the impact of intrusive memories. Respondents rate how much difficulty they have had in each area in the past 30 days, from 0 (none) to 4

(extreme or cannot do). The measure showed high internal consistency (Cronbach alpha=.83-.92), high 2-week test-retest reliability (intraclass correlation coefficient=.83), adequate construct validity, and was sensitive to change when administered online to individuals with anxiety and stress disorders (Axelsson et al., 2017).

5.6.13 EQ-5D-5L (Herdman et al., 2011)

The 5-level version of the EuroQol-5D (EQ-5D-5L) is a brief measure for assessing general quality of life and health status. Items assess mobility, self-care, usual activities, pain/discomfort, and anxiety/depression each on a 5-point scale. Respondents rate their overall health today from 0 (the worst health you can imagine) to 100 (the best health you can imagine).

5.7 Randomisation

After completing baseline questionnaires, participants will be allocated to either the intervention, active control arm or TAU arm using a 2:2:1 overall ratio. Participants will be randomised using blocked randomisation with random block sizes of multiples of 5. The randomisation program will be incorporated into ePRO to ensure that allocation cannot be influenced by the research team (i.e., randomisation is computerised and automated to ensure allocation concealment). The program will be validated by the independent statistician. Refer to section 7.1.2 of the protocol for more information on the blinding procedures.

After randomisation, participants will be asked to complete the following questionnaire:

5.7.1 Credibility/Expectancy Questionnaire (Devilly & Borkovec, 2000)

This 6-item questionnaire will assess participants' belief that the intervention will help reduce their intrusive memories. Wording is adapted for the current intervention: for example, the word "therapy" is changed to "intervention" and "trauma symptoms" is changed to "intrusive memories".

5.8 Day 0

Day 0 is the date that future visits are scheduled from.

Prior to Day 0 the randomisation status of the participant, which is generated automatically by the randomisation programme (see Section 5.5) is confirmed in ePro by a researcher. Independent of which arm of the study the participant is assigned to (TAU, control, or intervention), the schedule will be the same from the point of Day 0.

For participants on the TAU arm of the study, Day 0 will occur as soon as possible after completion of the Baseline Questionnaires. For the intervention and control arms, Day 0 will be on the same day as the guided session.

5.9 Intervention procedures

Participants allocated to the intervention or active control arms will be contacted to arrange a time to go through the digital intervention/control task with them for the first time (guided session: see below). The investigator team may audio-record the guided intervention sessions using Microsoft Teams/Zoom or an external audio recording device for training and treatment fidelity assessment purposes. They will then have access to the digital intervention/control for 24 weeks. Participants in the TAU arm will contacted to inform them that they can continue to receive any care they would otherwise access.

5.9.1 Imagery-competing task intervention

The brief imagery-competing task intervention is an approx. 25-minute session task (one first session is guided by the researcher, thereafter, can be used self-guided or with support) completed by the participant on their smart phone or other internet-enabled device. It includes briefly bringing to mind an intrusive memory, followed by playing the computer game Tetris for 20 minutes with mental rotation instructions (including instructional videos). The intervention will be delivered on a secure web platform used for clinical self-management of health in general practice (i-spero®). Participants will be a sent a unique registration code to create a personal, password-protected user account to access the intervention. Participants will complete the intervention in an initial guided session with the help of a researcher (by video call), and thereafter use it self-guided (with optional researcher support for the first 4 weeks). As part of the intervention, participants will receive regular reminders (with the option to turn these off if preferred). Use and compliance will be assessed and monitored.

5.9.2 Music-listening task control

The brief music-listening task is an approximately 25-minute session task (the first session is guided by the researcher, thereafter can be used either self-guided or with support) completed by the participant on their smart phone or other internet-enabled device. It includes listening to an instructional podcast to provide information about the composer (Mozart) – approximately matched to timing of the instructional videos in the intervention – followed by listening to a 20-minute piece of music. The task will be delivered on a secure web platform used for clinical self-management of health in general practice (i-spero®). Participants will be a sent a unique registration code to create a personal, password-protected user account to access the intervention. Participants will complete the control task in an initial guided session with the help of a researcher (by video call), and thereafter use it self-guided (with optional researcher support for the first 4 weeks). As part of the active control, participants will receive regular reminders (with the option to turn these off if preferred). Use and compliance will be assessed and monitored.

5.9.3 Intervention accessibility post-trial end date

A version of the digital intervention will be offered to participants who have been allocated to the control arms after the trial's end date (please refer to section 5.12 of the protocol for more information on end of trial definition).

5.10 Follow-up assessment

At 4 weeks, 12 weeks and 24 weeks, participants are additionally asked to complete various measures completed at baseline (see Appendix 2), in addition to the following measure, in ePRO:

5.10.1 Changes to health and work

This 9-item questionnaire assesses the number of any new traumatic events, new treatments received, the occurrence of adverse events, and changes to the job, or changes to the number of hours worked per week since the last assessment.

5.11 Feedback procedures

Participants in the intervention and active control arms will be asked to complete an online feedback questionnaire about their experience of using the intervention at 4 weeks after the first guided session (delivered in i-spero). They may also be given the option of completing qualitative interviews with a researcher at 4 weeks and 12-24 weeks after the first guided session.

5.11.1 Feedback questionnaire

A 12-item questionnaire will assess participants' experience of using the brief cognitive task. The first ten items assess how easy, helpful, distressing, burdensome and acceptable participants found the intervention, how willing they would be to use it in the future, how confident they would be in recommending it to a friend and how much they feel it could be used to support staff within the NHS, each rated from 0 (not at all) to 10 (very). The last two items ask how the brief cognitive task could be improved, for any other comments or suggestions about the intervention, and for the occurrence of any adverse events, all with an open response.

5.11.2 Optional qualitative interview

Participants in intervention and active control arms will be given the option of completing a qualitative interview with a researcher via audio or video call. The semi-structured interview at 4 weeks (qualitative interview A) will consist of questions designed to gain an in-depth understanding of participants' experience of using the brief cognitive task, including acceptability, improvement suggestions, and potential barriers/facilitators to implementation. The semi-structured interview at 12-24 weeks (qualitative interview B) will include questions about pattern of usage, longer-term usage of the intervention and implementation. The interviews will be audio-recorded (using a password-protected digital voice recorder) and will last approximately 30 minutes. The first 10-15 participants in the intervention/active control arms will be invited to take part in the interviews, to maximise the possibility of recruitment in the early stages. This will give insight into recruitment rate (i.e., not all will agree to take part). Once these are completed, a more selective approach using maximum variance sampling will take place according to e.g. gender, age, role, and ethnicity. This

approach was selected to attain data from a wide range of perspectives and experiences.

5.12 In study procedures

5.12.1 Week 1 (D0)

Intervention Arm:

- On Day 0 the participant meets with the researcher (virtual visit) to complete the intervention for the first time with guidance. Following the completion of the first session, participants in this arm will have continued access to the intervention for 24 more weeks (D0-168).

Active Control Arm:

- On Day 0 the participant meets with the researcher (virtual visit) to complete the active control for the first time with guidance. Following the completion of the first session participants in this arm will have continued access to the active control for 24 more weeks (D0-168).

TAU Arm:

- On Day 0 the participants will be contacted by the researcher to be made aware that they can continue to receive any routine care that they would otherwise access for 24 weeks.

5.12.2 Week 1-4 (D0 to D28)

Intervention Arm:

- During days 0 to 28 participants in the intervention arm will have continuous access to the intervention on i-spero®.

Active Control Arm:

- During days 0 to 28 participants in the control arm will have continuous access to the active control on i-spero®.

Week 4 (D22 to D28) *

Intervention Arm:

- All participants in the intervention arm will be asked to complete the online questionnaires at the end of week 4 (D28), including intrusive memory rating, PCL-5 20-item version, GAD-2, PHQ-2, SCI-02, WHODAS 2.0, EQ-5D-5L, number of sick days, Scale of Work Engagement and Burnout (SWEBO) and Intention to leave job on ePRO.
- All participants in the intervention arm will have continuous access to the intervention and during week 4 (D22 to D28) will be asked to complete the daily intrusive memory diary on a daily basis followed by

completion of intrusive memory weekly ratings at the end of week 4 (D28) on ePRO.

- All participants in the intervention arm will be asked to complete a feedback questionnaire at the end of week 4 on i-spero.
- Participants in the intervention arm will be given the option to complete a qualitative interview at the end of Week 4 (+ 21-day window).

Active Control Arm:

- All participants in the control arm will be asked to complete the online questionnaires at the end of week 4 (D28), including intrusive memory rating, PCL-5 20-item version, GAD-2, PHQ-2, SCI-02, WHODAS 2.0, EQ-5D-5L, number of sick days, Scale of Work Engagement and Burnout (SWEBO) and Intention to leave job on ePRO.
- All participants in the control arm will be asked to complete the daily intrusive memory diary during week 4 (D22 to D28) on a daily basis followed by intrusive memory weekly and rating at the end of week 4 (D28) on ePRO.
- All participants in the active control arm will be asked to complete a feedback questionnaire at the end of week 4 on i-spero.
- Participants in the active control arm will be given the option to complete a qualitative interview at the end of week 4 (+21-day window).

TAU Arm:

- All participants in TAU will be asked to complete the online questionnaires at the end of week 4 (D28), including intrusive memory rating, PCL-5 20-item version, GAD-2, PHQ-2, SCI-02, WHODAS 2.0, EQ-5D-5L, number of sick days, Scale of Work Engagement and Burnout (SWEBO) and Intention to leave job on ePRO.
- All participants in the TAU arm will be asked to complete the daily intrusive memory diary during week 4 (D22 to D28) on a daily basis followed by intrusive memory weekly and rating at the end of week 4 (D28) on ePRO.

*In ePRO, each assessment associated with week 4 will expire after +56 days from D28.

5.12.3 Week 5-12 (D29 to D84) †

Intervention Arm:

- All participants in the intervention arm will be asked to complete the online questionnaires at the end of week 12 (D84), including intrusive memory rating, PCL-5 20-item version, GAD-2, PHQ-2, SCI-02, WHODAS 2.0, EQ-5D-5L, number of sick days, Scale of Work Engagement and Burnout (SWEBO) and Intention to leave job on ePRO.

- During days 29 to 84 participants in the intervention arm will have continuous access to the intervention on i-spero®.
- All participants in the intervention arm will have continuous access to the intervention and during week 12 (D78 to D84) will be asked to complete the daily intrusive memory diary daily followed by completion of intrusive memory weekly ratings at the end of week 12 (D84) on ePRO.

Active Control Arm:

- All participants in the active control arm will be asked to complete the online questionnaires at the end of week 12 (D84), including intrusive memory rating, PCL-5 20-item version, GAD-2, PHQ-2, SCI-02, WHODAS 2.0, EQ-5D-5L, number of sick days, Scale of Work Engagement and Burnout (SWEBO) and Intention to leave job on ePRO.
- During days 29 to 84 participants in the active control arm will have continuous access to the active control on i-spero®.
- All participants in the control arm will have continuous access to the music-listening task and during week 12 (D78 to D84) will be asked to complete the daily intrusive memory diary on a daily basis followed by completion of intrusive memory weekly ratings at the end of week 12 (D84) on ePRO.

TAU Arm:

- All participants in the TAU arm will be asked to complete the online questionnaires at the end of week 12 (D84), including intrusive memory rating, PCL-5 20-item version, GAD-2, PHQ-2, SCI-02, WHODAS 2.0, EQ-5D-5L, number of sick days, Scale of Work Engagement and Burnout (SWEBO) and Intention to leave job on ePRO.
- All participants in the TAU arm will be asked to complete the daily intrusive memory diary during week 12 (D78-D84) on a daily basis followed by completion of intrusive memory weekly ratings at the end of week 12 (D84) on ePRO.

† In ePRO, each assessment associated with week 12 will expire 84 days from D84.

5.12.4 Week 13-24 (D85 to D168) ‡

Intervention Arm:

- All participants in the intervention arm will be asked to complete the online questionnaires at the end of week 24 (D168), including intrusive memory rating, PCL-5 20-item version, GAD-2, PHQ-2, SCI-02, WHODAS 2.0, EQ-5D-5L, number of sick days, Scale of Work Engagement and Burnout (SWEBO) and Intention to leave job on ePRO.

- During days 85 to 168 participants in the intervention arm will have continuous access to the intervention on i-spero®.
- All participants in the intervention arm will have continuous access to the intervention and during week 24 (D162-D168) will be asked to complete the daily intrusive memory diary on a daily basis followed by completion of intrusive memory weekly ratings at the end of week 24 (D168) on ePRO.
- Participants in the intervention arm will be given the option to complete a qualitative interview (D85 to D168).

Active Control Arm:

- All participants in the active control arm will be asked to complete the online questionnaires at the end of week 24 (D168), including intrusive memory rating, PCL-5 20-item version, GAD-2, PHQ-2, SCI-02, WHODAS 2.0, EQ-5D-5L, number of sick days, Scale of Work Engagement and Burnout (SWEBO) and Intention to leave job on ePRO.
- During days 85 to 168 participants will have continuous access to the active control task on i-spero®.
- All participants in the active control arm will have continuous access to the active control task and during week 24 (D162 to D168) will be asked to complete the daily intrusive memory diary on a daily basis followed by completion of intrusive memory weekly ratings at the end of week 24 (D168) on ePRO.
- Participants in the active control arm will be given the option to complete a qualitative interview (D85 to D168).

TAU Arm:

- All participants in the TAU arm will be asked to complete the online questionnaires at the end of week 24 (D168), including intrusive memory rating, PCL-5 20-item version, GAD-2, PHQ-2, SCI-02, WHODAS 2.0, EQ-5D-5L, number of sick days, Scale of Work Engagement and Burnout (SWEBO) and Intention to leave job on ePRO.
- All participants in the TAU arm will be asked to complete the daily intrusive memory diary during week 24 (D162 to D168) on a daily basis followed by completion of intrusive memory weekly ratings at the end of week 24 (D168) on ePRO.

‡ In ePRO, each assessment associated with Week 24 will expire 28 days after the date of the individual assessment.

5.13 Definition of End of Trial

The end of the study is defined as the date that the last participant completes their final online assessment (completion of week 24 (D168) endpoint measures).

As described above (section 3.2 Study design), a strength of this adaptive Bayesian design is that interim analyses can guide decision-making about when sufficient evidence has been collected to end this randomised control trial. Prespecified thresholds are used to trigger decision making regarding final sample size (e.g. assessed using Bayes factors which compare different hypotheses). If during interim analyses, there is strong evidence for a negative effect of the intervention based on comparison with TAU arm, the trial may need to be altered or stopped. If there is strong evidence for the effectiveness of the intervention based on comparison with Active Control before reaching n=150, then consideration will be given to stopping the trial early.

5.13.1 Debrief

Following the end of the final outcome assessment (24 weeks post intervention), participants will be sent information by email about the overall study design, how they can access further information about the study once published, and where they can access further mental health information online if needed. They will be given details on how they can contact the research team if they have any questions, concerns, or comments about the study.

5.14 Completion and Discontinuation / Withdrawal

A participant will be considered to have completed the study if they have completed study procedures up to and including the assessment at week 24.

Each participant has the right to withdraw from the study at any time. In addition, the Investigator may discontinue a participant from the study at any time if the Investigator considers it necessary for any reason including:

- Ineligibility (either arising during the study or retrospectively having been overlooked at screening)
- An adverse event that results in participant no longer being able to comply with study procedures.
- Significant protocol deviation
- Withdrawal of consent

In all cases, the reason for withdrawal will be recorded.

5.15 Study Termination

The Sponsor reserves the right to terminate the study at any time. Reasons for the early termination of a study by the Sponsor, may include but are not limited to:

- Failure of the Investigator to comply with the protocol, the Sponsor's procedures, or GCP guidelines;
- Safety concerns;
- Inadequate recruitment of participants.

We note that if the Investigators choose to end the study enrolment before reaching the maximum sample size of approximately n=150, based on strong evidence for an effect of the intervention, this would not be considered as "Study Termination" but would reflect a potential outcome of this Bayesian adaptive study design.

6.0 Trial Intervention

6.1 Description

This brief imagery-competing task intervention consists of a brief reminder cue to the specific intrusive memory, followed by playing the computer game Tetris for 20 minutes with instructions to use mental rotation during game play. The study team will provide a single training session on completing the intervention for the first time (guided session) and can then be self-administered.

Refer to section 5.6.1 for more information about the digital intervention.

The brief digital intervention will be delivered using a secure web platform used for clinical self-management of health in general practice (i-spero®).

The intervention is not a medical device as it does not have a medical purpose.

6.2 Instructions for Use

Instructions for use (IFU) are included within the intervention itself, both digitally (e.g. via videos) and through researcher guidance (virtual visit).

6.3 Manufacturer and Distributor Details

The brief digital intervention on i-spero® is owned and manufactured by P1vital Products Ltd. Tetris® has been licenced for use within i-spero® from The Tetris Company.

6.4 Computer System Validation

ePRO, i-spero®, the brief digital intervention have been validated following a formal computerised system validation methodology which complies with GCP and FDA 21CFR Part 11 and which is a part of ISO 13485-certified Quality Management System and ISO 27001-certified Information Security Management System, and which complies with GCP and FDA 21 CFR Part 11.

6.5 Support and Assistance

In the event that difficulties are experienced with ePRO or i-spero®, researcher or participants should notify P1vital Products Ltd. (telephone number +44 (0)1865522088; email itsupport@p1vital.com).

7.0 Randomisation

7.1.1 Procedure to be followed

Participants who meet the eligibility criterion of having 3 or more intrusive memories in the run-in week will be allocated to either the intervention, active control arm TAU arm using a 2:2:1 overall ratio. Participants will be randomised using blocked randomisation with random block sizes of multiples of 5. A randomisation program will be used to ensure that allocation cannot be influenced by the research team (i.e., randomisation is computerised and automated to ensure allocation concealment). The program will be validated by the independent statistician.

7.1.2 Blinding of Study Intervention

Statisticians will be blinded to allocation, and all assessments are self-report questionnaires administered digitally, eliminating assessor bias (i.e., to ensure blinding of outcome assessment). Participants will be blinded to intervention or active control as both are brief cognitive tasks. Participants in the TAU arm cannot be blinded. Researchers involved in contacting the participants and facilitating the conduct of intervention will not be blinded the remaining principal investigator's delegated study members will also be unblinded during the length of the trial.

8.0 Adverse Event Reporting

8.1 Definitions

8.1.1 Adverse Event (or adverse experience) (AE)

Any untoward medical occurrence, unintended disease or injury, or untoward clinical events experienced by the participant whether or not related to the intervention.

8.1.2 Serious Adverse Event (SAE)

Any adverse event, respectively, that:

- results in death.
- is life-threatening.

  Note: the term "life-threatening" 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;

- requires hospitalisation or prolongation of existing hospitalisation.

  Note: any event that may not be immediately life-threatening or result in death or hospitalisation, but may jeopardise the participant or may require intervention to prevent one of these outcomes;

- results in persistent or significant disability or incapacity

Note: any event that seriously disrupts the ability of the participant to lead a normal life, in other words leads to a persistent or permanent significant change, deterioration, injury or perturbation of the participant's body functions or structure, physical activity and / or quality of life;

- consists of a congenital anomaly or birth defect

Important medical events that may not be immediately life-threatening or result in death or hospitalisation but may jeopardise the patient or may require intervention to prevent one of the other outcomes listed in the definition above should also be considered serious.

8.2 Safety Reporting Procedures

No major risks are expected in association with any part of the study methodology or intervention. The brief behavioural intervention is non-invasive, minimally distressing, and no study-related adverse events have been reported in any previous trials or studies testing the intervention. In this trial, any AE's will be self-reported at 4-week, 12-week and 24-week assessment. If an AE is reported by a participant, this will be reviewed by the Chief Investigator in the first instance, and with a clinical colleague in the research team/Chief Medical Adviser as necessary. If a serious adverse event is identified (i.e. meeting the definition in section 8.1.2 above), this will be reported to the REC if appropriate as per section 8.2.2 below.

As in any study, and unrelated to the study methodology, there may be participants for whom significant risk to themselves or others becomes apparent during the study period, e.g. through spontaneously reporting suicidal intent during contact with the research team or in open-response questionnaire items. In these cases, the research team will encourage the participant to seek help e.g. contact their GP or other relevant healthcare provider. Any such instances will be discussed within the research team and recorded appropriately.

At the end of the study, all participants will be sent information about access to mental health support, such as the NHS/Every Mind Matters website, the Intensive Care Society Wellbeing Hub webpage and advice to contact their GP/occupational health team.

Additionally, if at any point during the study the participant reveals information that may suggest professional malpractice, they will be encouraged by the researcher to report this to their Hospital's Freedom To Speak Up (FTSU) Guardian and/or to follow their Trust Whistleblowing Policy.

8.2.1 All Adverse Events

All AE's will be reported from the time a signed and dated informed consent form is obtained until (participants) completion of the study.

All AE's regardless of seriousness, severity, or presumed relationship to study intervention (if applicable), must be recorded on the paper AE forms designed for this study.

8.2.2 Serious Adverse Events

Research staff must record SAEs that meets the criteria described in section 8.2 on the SAE form and report that to the Chief Investigator immediately (maximum within 24 hours of their knowledge of the event). The initial report of an SAE may be made by telephone, and this must be followed up by written confirmation (by e-mail).

The Chief Investigator will report SAEs immediately to the study Sponsor (maximum within 24 hours of research staff knowledge of the event).

SAE and Incident reporting numbers:

Telephone: 44(0)1865 522 030

Facsimile: +44(0)1865 597 673

Email: admin@p1vital.com

The initial report may be made by telephone and this must be followed up by written confirmation.

Note: P1vital Products Ltd and the Chief Investigator have the same contact details. Safety information will be circulated internally within 24 hours of receipt.

8.2.3 Reporting to Research Ethics Committees and regulatory authorities

An SAE occurring to a research participant should be reported to the main Research Ethics Committee where, in the opinion of the Chief Investigator or Sponsor, the event was:

- Related – that is, it resulted from administration of any of the research procedures or intervention.
- Unexpected – that is, the type of event is not listed in the protocol as an expected occurrence.

The Chief Investigator will report all related, unexpected SAEs to the Research Ethics Committee within 15 days of their becoming aware of the event. The report must be made using the appropriate national/international SAE report forms (e.g. SAE report form for non-Clinical Trials of Medicinal Products, available from the Health Research Authority (HRA) website in the UK).

9.0 Primary and Secondary Endpoints

9.1 Primary Endpoint

- Number of intrusive memories of traumatic events recorded by participants in a brief daily online intrusive memory diary for 7 days during week 4 (i.e. from Day 22 to 28 post first intervention/active control session or post randomisation in TAU arm). Analysed as between-group comparison controlling for the number of intrusive memories during the run-in week.

9.2 Secondary Endpoints

- Number of intrusive memories of traumatic events recorded by participants in a brief daily online intrusive memory diary for 7 days during week 12 (Day 78 to 84) and during week 24 (Day 162 to 168). Analysed as between-group comparison controlling for the number of intrusive memories during the run-in week.

- Intrusive memory ratings, PTSD Checklist for DSM-5 (PCL-5), Sleep Condition Indicator (SCI-02), Generalised Anxiety Disorder 2-item version (GAD-2), Patient Health Questionnaire 2-item version (PHQ-2), Scale of Work Engagement and Burnout (SWEBO), number of sick days in the last 4 weeks, Intention To Leave Job, World Health Organization Disability Assessment Schedule (WHODAS 2.0), 5-level EQ-5D (EQ-5D-5L) at 4 weeks, 12 weeks and 24 weeks.

9.3 Exploratory Endpoints

- Number of new traumatic events
- The occurrence of AE's, treatments received and changes to job and work hours at 4, 12 and 24 weeks
- Intervention/control use e.g., number of times used, duration, time of day during the 24 weeks
- Feedback questionnaire at 4 weeks post first intervention/control session
- Optional qualitative interview at 4 weeks and 12-24 weeks post first intervention/control session.

10.0 Data Handling

10.1 Source Data Collection

Source documents are original documents, data, and records. These include, but are not limited to, informed consent forms, ePRO questionnaire data, i-spero® intervention data, and source document worksheets (including adverse events).

The following data are recorded via the study website:

- Online Pre-Screening Eligibility Questionnaire
- Contact details

The following data will be recorded in the eISF (electronic paper source):

- Participant information sheet/consent form (PIS_ICF)

- Source Document Worksheets (including inclusion/exclusion criteria, job role, contact details, research observations, AE/SAE forms, and questionnaire data that could not be collected via ePRO/i-Spero in exceptional cases).

The following data will be recorded directly into the ePRO system by participants (electronic source):

- Intrusive memory diary
- Intrusive memory rating
- Credibility/Expectancy Questionnaire
- Health background
- Demographics
- Checklist of traumatic events
- PTSD Checklist for DSM-5 (PCL-5
- Generalised Anxiety Disorder (GAD-2)
- Patient Health Questionnaire (PHQ-2)
- Sleep Condition Indicator (SCI-02)
- World Health Organisation Disability Assessment Schedule (WHODAS) 2.0
- EQ-5D-5L (5-LEVEL EuroQol 5D)
- Sickness absence
- Scale of Work Engagement and Burnout (SWEBO)
- Intention To Leave Job
- Changes to health and work

The following data is automatically recorded in the ePRO system (electronic source):

- Randomisation arm
- Inclusion decision

The following data will be recorded directly into the i-spero® system by participants (electronic source).

- Feedback Questionnaire

The following data is automatically recorded in the i-spero® system (electronic source):

- Intervention usage data

The following data will be recorded directly on audio files by a Research Assistant at the University of Nottingham, sent for transcription and anonymised transcripts stored in the study file (electronic source). Following transcription, audio recordings will be deleted.

- Qualitative interviews

The qualitative interviews are recorded using a digital voice recorder; the recordings are immediately transferred to a password protected laptop and are subsequently deleted from the voice recorder. The password protected files are transcribed and anonymised, with the original audio recordings deleted. Anonymised transcripts and interview notes are password protected and stored on OneDrive. Any participant data held by researchers at the University of Nottingham is stored on a password protected spreadsheet on OneDrive. OneDrive encrypts data both in transit and at rest. The service provides several layers of automatic backup and, if required, files

can be recovered. Access to the data stored on OneDrive is via a secure login and will be limited to the research team and relevant regulatory authorities.

10.2 Data Entry / Management

Questionnaire and intervention task data will be collected and stored electronically in the P1vital® ePRO and i-spero® systems. These two systems will be set up, hosted and managed by P1vital Products Ltd, and have been developed, validated and qualified in accordance with regulatory requirements for computerised systems used in clinical research/practice (see further details below). Data will be collected using a unique study-specific ID code for each participant, and the only personal identifiable data collected using these systems will be the participant's first name, email address and mobile phone number, to send them automated emails/texts and reminders about the study procedures. Data will be stored securely on their server until deletion is requested by the research group after the study has terminated and all relevant data has been transferred to the research team. Personal identifiable data will be deleted automatically once a participant completes the study, of if they are not eligible after completing the baseline count of their intrusive memories.

Pseudonymised / deidentified datasets, sent in encrypted files in a .csv/.xlsx file format, will be securely transferred to the research team for statistical analysis. Participants will be identified by an ID code in any database, but their name and any other identifying details will NOT be included in any study data electronic file. During pre-screening, potential participants are asked to complete an anonymous eligibility questionnaire on the study website. Eligible participants will be asked to provide their name, telephone number and/or email address. These data will be deleted as soon as they are no longer needed to contact the participant. Anonymous consent data will be downloaded from the study website. Electronic data will be stored on a secure file server which is firewall and password protected. Study data (including consent forms) will be kept for at least 5 years after final publication/public release, and anonymised data may be archived in an online repository.

Documents containing personal information (e.g. consent form and participant contact details) and audio-recordings will be stored separately from other study data, in restricted-access files on secure file servers, password-protected devices or password-protected online platforms, and only accessible by study staff and authorised personnel. Personal data (except consent forms) will be kept for a maximum of 6 months after the end of the study, after which time it will be destroyed (files will be deleted). If participants give consent to be contacted about future research, their contact details will be held in a password-protected database, until they are no longer required.

Qualitative interview data (audio recordings) will be collected by a Research Assistant at the University of Nottingham and sent for transcription. Anonymised transcripts will be password-protected and sent to a Research Assistant at P1Vital in an encrypted email. These transcripts will then be stored electronically alongside other study data and audio recordings will be immediately deleted.

10.3 P1vital Products Data Security Policies and Procedures

P1vital Products Ltd is fully compliant with the UK Data Protection Act 2018 and UK General Data Protection Regulations (GDPR) and has appropriate data security policies and procedures in place. P1vital Products Ltd are certified to: ISO 27001:2013 Information Security Management System, ISO 13485:2016 Medical Device Quality Management System and Cyber Essentials. The P1vital® ePRO and i-spero® systems are hosted by Amazon Web Services, EU West 1 region (Ireland). The P1vital® ePRO and i-spero® systems administration and support is provided by a third party, Elysium Ltd, who are ISO27001 and ISO9001 certified. P1vital Products Ltd and Elysium Ltd are registered with the Information Commissioners Office, who are responsible for the enforcement of UK data protection.

The P1vital® ePRO and i-spero® systems are only accessible through a secure encrypted web address (https//: web access), via a unique user ID and secure password. All non-study participant users must complete a security access request form to be registered and authorised to use the system. All personal identifiable data is stored in an encrypted form in the application database. The encryption key is only known by 3 system administrators (one primary and two backup personnel) at Elysium Ltd who support the P1vital® ePRO and i-spero® systems. No employees of P1vital Products can access the database or the encryption key.

11.0 Statistical Methods and Data Analysis

This randomised control trial uses an adaptive Bayesian design for efficacy evaluation of a brief cognitive task intervention. Recent advances in trial design and methodology offer more efficient alternatives to traditional RCTs to speed up the testing and thus implementation of evidence-based treatments (ACE CONSORT Extension; Dimairo et al. 2020). Adaptive designs enable smaller, more efficient trials without loss of scientific integrity, and allow a trial to be modified on the basis of interim analysis, thereby making optimal use of all data for decision-making.

A statistical analysis plan will be prepared prior to the first interim analysis, based on the primary outcome (number of intrusive memories at week 4) that will inform decision making regarding final sample size.

11.1 Sample Size

Sequential analyses at a group level (intervention: active control: TAU) start with a small number of participants (e.g. n=20) and are repeated every approximately 4-10 participants thereafter, up to a maximum of approximately n=150 (in 2:2:1 ratio across intervention, active control and TAU groups, respectively). Prespecified thresholds are used to trigger decision making regarding final sample size (e.g. assessed using Bayes factors which compare different hypotheses). If the intervention is shown to be significantly more effective than controls before reaching the max n=150 participants, then the study may conclude early. Our decision for this

maximum sample size has been informed by results from our optimization trial of this brief cognitive task intervention using Bayesian analysis (Ramineni et al., in review), Kanstrup et al. (2021) and James et al. (2015) with effect sizes for no task control of d=0.85, and for positive controls of d=0.57 and d=0.71. Our simulations estimate 90% power (at 0.05 significance) to find strong evidence for the intervention will be reached with maximum sample sizes of 60 for intervention, 60 for active control; and 30 for TAU (total n=150).

11.2 Data Set for Analysis

All analyses will be conducted on an intention to treat (ITT) basis. The ITT is defined as all randomised participants.

11.3 Description of Statistical Methods

A pre-specified analysis plan will be preregistered prior to data analysis (e.g., on the Open Science Framework).

11.3.1 Sequential Analysis

Ongoing sequential analysis using Bayesian statistical approaches (Ramineni et al., in review) will be used to evaluate efficacy based on the primary outcome (difference in the number of intrusive memories in week 4, controlling for the number of intrusive memories during the run-in week and participant). Exploratory data analysis will be used to investigate the distribution of the primary outcome measure. Patterns of missing data will be explored and will be imputed as necessary. In the case where we see excess zeros (i.e., zero inflation) we will explore treating this with the use of an alternative statistical model (e.g., zero inflated Poisson GLM, negative binominal).

11.3.2 End of study Analysis

Bayesian statistical methods will be used to analyse the complete trial data. The sections below (11.3.3 – 11.3.5) give a brief overview of these planned analyses.

Outcome measures will be tested for assumptions of the planned analyses, and where assumptions are violated (e.g., normality of residuals), data will be either transformed or analysed using an alternative model.

Sensitivity analyses will be conducted to examine whether analytical decisions (e.g., the exclusion of outliers, model assumptions, imputation) influences the results.

For exploratory analyses (section 11.3.3 below), a combination of descriptive, qualitative and frequentist analyses will be used.

11.3.3 Analysis of Primary Objective:

A between-groups analysis will be used to test the difference in the number of intrusive memories in week 4 (i.e. from Day 22 to 28) between the intervention, active control and TAU groups. The analysis will control for the number of intrusive memories during the run-in week as a fixed effect and include participant as a random effect.

11.3.4 Analysis of Secondary Objectives:

Bayesian regression modelling will be used to quantify the treatment effect on reducing the number of intrusive memories in week 12 and week 24 and other secondary outcome measures.

Between-groups analyses will be used to test for differences secondary outcomes at week 4, week 12 and week 24 between the intervention, active control and TAU groups for intrusive memory ratings; symptoms of post-traumatic stress, insomnia, anxiety and depression; work engagement and burnout, sickness absence, and intention to leave job; and functioning and quality of life.

For each between group analysis, baseline measure, treatment arm, follow up time, and potential interactions between covariates will be included as fixed effect. Effect of participant will be included as a random effect.

11.3.5 Analysis of Exploratory Objectives:

Quantitative data will be reported using descriptive statistics. Free text comments will be analysed thematically.

Exploratory analyses may also include analysis of the study endpoints using alternative and complementary statistical methods to the main Bayesian analysis (e.g., using traditional frequentist statistics).

Questionnaire and demographic data will be used to guide sampling for the semi-structured interviews.

Qualitative interview data will initially be thematically analysed using an inductive thematic, constant comparison approach based on grounded theory (Glaser and Strauss 1967). Once a thematic analysis has been carried out and key themes identified, data will be explored for suitability in relation to normalisation process theory (or an alternative framework drawn from implementation science, addressing key aspects such as the intervention's design and fit within clinical practice, if more suitable). This will be complemented by the questionnaire data, which will provide quantitative data that includes aspects of normalisation process theory. Normalisation process theory is a sociological theory developed and tested to understand the implementation of new ways of working (including technology) in health care, including depression and in primary care (May et al. 2009). It is likely that we will use normalisation process theory to explore implementation of the intervention. However, using a predetermined analytical framework precludes a more inductive approach and risks the exclusion of relevant insight that is not

discernible through that particular analytical lens. For this reason, choice of analytical framework will be informed by its appropriateness to the data (MacFarlane and O'Reilly de Brun 2012).

Both the questionnaire and interview data will be used to develop an inductive analysis of the value and implementation of the intervention. This type of inductive analysis will further our understanding of how the intervention is used and if changes could be made to enhance its implementation and facilitate its adoption.

12.0 Quality Control and Quality Assurance

Regular monitoring will be performed to verify that the study is conducted, and data are generated, documented and reported in compliance with the protocol, GCP and the applicable regulatory requirements. The Investigator will allow the monitor to carry out study monitoring at regular intervals, depending on the recruitment rate, and at times arranged by mutual agreement.

Quality assurance representatives from the Sponsor or P1vital may visit to carry out an audit of the study in compliance with regulatory guidelines and relevant standard operating procedures.

The Investigator will allow monitors and other persons responsible for audits to:

- meet all members of his / her team involved in the study,
- consult all of the documents relevant to the study,
- directly access source documents to check,
- verify that the study is carried out in compliance with the protocol and local regulatory requirements.

All information dealt with during these visits will be treated as strictly confidential.

13.0 Data Monitoring Committee

An independent data monitoring committee including a psychologist, clinician, statistician, and other appropriate members from the expert advisory panel will be appointed. The Data Monitoring Committee will review trial data and will advise the Sponsor whether changes to the protocol are advisable in light of safety, recruitment and retention of participants and/or sample size.

14.0 Regulatory and Ethical Obligations

14.1 Regulatory Framework

The trial will be conducted in compliance with the principles of the Declaration of Helsinki (1996 – the author should confirm which version is preferred by the sponsor at the time of writing), the principles of GCP and in accordance with all applicable national and international regulatory requirements, including but not limited to the

Research Governance Framework and the Medicines for Human Use (Clinical Trial) Regulations 2004, and any subsequent amendments.

14.2 Approvals

The study protocol, informed consent form, participant information sheet and any proposed advertising material will be submitted to an appropriate Research Ethics Committee (REC) for written approval. Any subsequent updates to these documents will also be sent to the REC for their approval prior to use in the study.

14.3 Study Reports

Annual progress reports and a final report at conclusion of the study will be submitted to the Research Ethics Committee within the required timelines.

14.4 Participant Confidentiality

The study researchers will ensure that the participants' anonymity is maintained. The participants will be identified by a study participant number on the P1vital® ePRO and i-spero® systems. Only the participant consent form and contact details form will include the participant's name, and these will be stored separately from other study data. All documents will be stored securely and only accessible by study staff and authorised personnel. The study will comply with the UK Data Protection Act 2018 and UK General Data Protection Regulations (GDPR) which requires data to be anonymised as soon as it is practical to do so.

15.0 Expenses, Benefits

Participants will be offered a £15 online voucher after week 4 for completion of the primary outcome and £15 online voucher at the end of the study for completion of the follow up questionnaires.

16.0 Financial Aspects

The study is funded by Wellcome Trust discretionary project grant award (223016/Z/21/Z) in mental health and the Sponsor.

17.0 Use of Information and Publication

All information, including but not limited to scientific research data, generated as a result of this study, are considered confidential and remain the sole property of P1vital Products Ltd and its academic and pharmaceutical company collaborators. The results of the primary, secondary and exploratory analysis will be reported in a Study Report generated by P1vital Products Ltd (or delegate).

Any anonymised data collected from the intervention use after participants have completed the trial, will only be used to optimise the intervention, and will not be considered research data.

Study results will be also published in peer-reviewed journals and presented at scientific conferences. Study subject identifiers will not be used in any publications.

18.0 References

1. Adriaenssens, J., De Gucht, V., & Maes, S. (2012). The impact of traumatic events on emergency room nurses: Findings from a questionnaire survey. International journal of nursing studies, 49(11), 1411-1422.
2. American Psychiatric Association. (2013). Diagnostic and statistical manual of mental disorders (5th ed.). Arlington, VA: American Psychiatric Association.
3. Axelsson, E., Lindsäter, E., Ljótsson, B., Andersson, E., & Hedman-Lagerlöf, E. (2017). The 12-item Self-Report World Health Organization Disability Assessment Schedule (WHODAS) 2.0 Administered Via the Internet to Individuals With Anxiety and Stress Disorders: A Psychometric Investigation Based on Data From Two Clinical Trials. JMIR mental health, 4(4), e58. https://doi.org/10.2196/mental.7497.
4. Baddeley, A. D., & Andrade, J. (2000). Working memory and the vividness of imagery. Journal of Experimental Psychology-General, 129(1), 126-145.
5. BBC News (April 2020). Coronavirus: NHS workers get free video games. Accessed at https://www.bbc.co.uk/news/newsbeat-52470542 on 07/10/2020.
6. Blanchard, E. B., Hickling, E. J., Mitnick, N., Taylor, A. E., Loos, W. R., & Buckley, T. C. (1995). The impact of severity of physical injury and perception of life threat in the development of post-traumatic stress disorder in motor vehicle accident victims. Behav Res Ther, 33(5), 529-534.
7. Bovin, M. J., Marx, B. P., Weathers, F. W., Gallagher, M. W., Rodriguez, P., Schnurr, P. P., & Keane, T. M. (2015). Psychometric properties of the PTSD Checklist for Diagnostic and Statistical Manual of Mental Disorders-Fifth Edition (PCL-5) in Veterans. Psychological Assessment, 28, 1379-1391. doi:10.1037/pas0000254.
8. Brunet, A., Weiss, D. S., Metzler, T. J., Best, S. R., Neylan, T. C., Rogers, C., Marmar, C. R. (2001). The Peritraumatic Distress Inventory: A Proposed Measure of PTSD Criterion A2. American Journal of Psychiatry, 158, 1480-1485.
9. Bryant, R. A., Creamer, M., O'Donnell, M., Forbes, D., McFarlane, A. C., Silove, D., & Hadzi-Pavlovic, D. (2017). Acute and chronic posttraumatic stress symptoms in the emergence of posttraumatic stress disorder: A network analysis. JAMA Psychiatry, 74, 135–142.
10. Bryant RA, Mastrodomenico J, Felmingham KL, et al. Treatment of Acute Stress Disorder: A Randomized Controlled Trial. Arch Gen Psychiatry. 2008;65(6):659–667. doi:10.1001/archpsyc.65.6.659
11. Cohen, A. (1998). An examination of the relationship between work commitment and work outcomes among hospital nurses. Scandinavian Journal of Management, 14 (1–2), 1-17.
12. Colville, G., Hammond, J. & Perkins-Porras, L. Post-traumatic stress symptoms in intensive care staff working in adult and paediatric settings. Crit. Care **19,** P531 (2015).
13. Devilly, G. J., & Borkovec, T. D. (2000). Psychometric properties of the credibility / expectancy questionnaire. Journal of Behavior Therapy and Experimental Psychiatry, 31 (2), 73-86.

14. Dimairo, M., Pallmann, P., Wason, J., Todd, S., Jaki, T., Julious, S. A., Mander, A. P., Weir, C. J., Koenig, F., Walton, M. K., Nicholl, J. P., Coates, E., Biggs, K., Hamasaki, T., Proschan, M. A., Scott, J. A., Ando, Y., Hind, D., Altman, D. G., & ACE Consensus Group (2020). The adaptive designs CONSORT extension (ACE) statement: a checklist with explanation and elaboration guideline for reporting randomised trials that use an adaptive design. Trials 21, 528.
15. Espie CA, Kyle SD, Hames P, et al. The Sleep Condition Indicator: a clinical screening tool to evaluate insomnia disorder. BMJ Open 2014;4:e004183. doi:10.1136/bmjopen-2013-004183.
16. Greenberg, N., Weston, D., Hall, C., Caulfield, T., Williamson, V. & Fong, K. Mental health of staff working in intensive care during COVID-19. Occup. Med. (2021). doi:10.1093/occmed/kqaa220.
17. Greenberg, N. Intrusion symptoms in UK healthcare staff, personal communication. (2021).
18. Hagino, A., Hamada, C., Yoshimura, I., Ohashi, Y., Sakamoto, J., & Nakazato, H. (2004).Statistical comparison of random allocation methods in cancer clinical trials. Controlled Clinical Trials, 25(6), 572–584.
19. Hall, C. E., Milward, J., Spoiala, C., Bhogal, J. K., Weston, D., Potts, H. W., Caulfield, T., Toolan, M., Kanga, K., El-Sheikha, S., Fong, K., & Greenberg, N. (2022). The mental health of staff working on intensive care units over the COVID-19 winter surge of 2020 in England: a cross sectional survey. British Journal of Anaesthesia, 128(6), 971–979.
20. Herdman, M., Gudex, C., Lloyd, A. et al. (2011). Development and preliminary testing of the new five-level version of EQ-5D (EQ-5D-5L). Quality of Life Research, 20, 1727–1736. doi:10.1007/s11136-011-9903-x.
21. Holmes, E. A., James, E. L., Coode-Bate, T., & Deeprose, C. (2009). Can playing the computer game "Tetris" reduce the build-up of flashbacks for trauma? A proposal from cognitive science. PLoS ONE, 4(1), e4153.
22. Holmes, E. A., James, E. L., Kilford, E. J., & Deeprose, C. (2010). Key steps in developing a cognitive vaccine against traumatic flashbacks: visuospatial Tetris versus verbal Pub Quiz. PLoS ONE, 5(11), e13706.
23. Holmes, E. A., Ghaderi, A., Eriksson, E., Lauri, K. O., Kukacka, O. M., Mamish, M., James, E. L., & Visser, R. M. (2017). 'I Can't Concentrate': A Feasibility Study with Young Refugees in Sweden on Developing Science-Driven Interventions for Intrusive Memories Related to Trauma. Behavioural and Cognitive Psychotherapy, 45(2), 97–109.
24. Holmes, E. A., O'Connor, R. C., Perry, V. H., Tracey, I., Wessely, S., Arseneault, L., Ballard, C., Christensen, H., Cohen Silver, R., Everall, Ford, T., John, A., Kabir, T., King, K. Madan, I, Michie, S., Przybylski, A. K., Shafran, R., Sweeney, A., Worthman, C. M., Yardley, L., Cowan, K., Cope, C., Hotopf, M., & Bullmore, E. (2020). Multidisciplinary research priorities for the COVID-19 pandemic: a call for action for mental health science. The Lancet Psychiatry, 7(6), 547-560.
25. Horsch, A., Vial, Y., Favrod, C., Morisod Harari, M., Blackwell, S., Watson, P., Iyadurai, L., Bonsall, M & Holmes, E. (2017). Reducing intrusive traumatic memories after

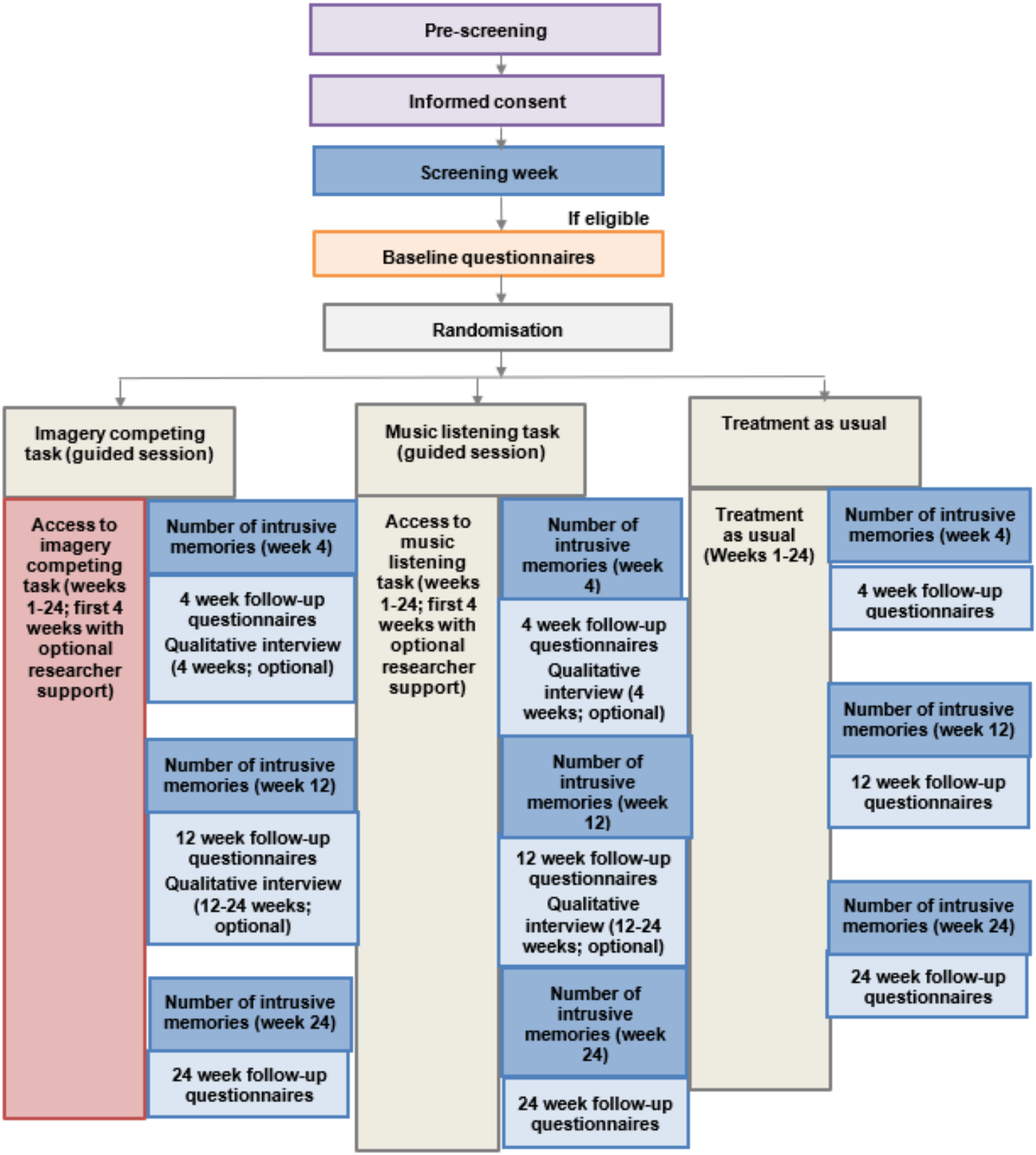
emergency cesarean section: A proof-of-principle randomized controlled study. Behavior Research and Therapy. 94, 36-47. doi: 10.1016/j.brat.2017.03.018

26. Hultell, D., & Gustavsson, J. P. (2010). A psychometric evaluation of the Scale of Work Engagement and Burnout (SWEBO). Work, 37 (3), 261-274.
27. Iyadurai, L., Blackwell, S. E., Meiser-Stedman, R., Watson, P.C., Bonsall, M. B., Geddes, J. R., Nobre, A.C., & Holmes, E. A. (2018). Preventing intrusive memories after trauma via a brief intervention involving Tetris computer game play in the emergency department: a proof-of-concept randomized controlled trial. Molecular Psychiatry. 23(3), 674-682.
28. Iyadurai, L., Visser, R. M., Lau-Zhu, A., Porcheret, K., Horsch, A., Holmes, E. A., & James, E. L. (2019). Intrusive memories of trauma: a target for research bridging cognitive science and its clinical application. Clinical Psychology Review, 69, 67-82.
29. James, E. L., Bonsall, M. B., Hoppitt, L., Tunbridge, E. M., Geddes, J. R., Milton, A. L., & Holmes, E. A. (2015). Computer Game Play Reduces Intrusive Memories of Experimental Trauma via Reconsolidation-Update Mechanisms. Psychological Science, 26(8), 1201–1215.
30. Jonsson, A., Segesten, K., & Mattsson, B. (2003). Post-traumatic stress among Swedish ambulance personnel. Emergency Medicine Journal, 20(1), 79-84.
31. Kang, L., Ma, S., Chen, M., Yang, J., Wang, Y., Li, R., ... & Hu, S. (2020). Impact on mental health and perceptions of psychological care among medical and nursing staff in Wuhan during the 2019 novel coronavirus disease outbreak: A cross-sectional study. Brain, Behavior, and Immunity. https://doi.org/10.1016/j.bbi.2020.03.028.
32. Kanstrup, M.*, Singh, L.*, Göransson, K., Widoff, J., Taylor, R., Iyadurai, L., Moulds, M. & Holmes, E. A. (2021). Preventing intrusive memories after trauma via a simple cognitive intervention in the hospital emergency department: An explorative randomised controlled pilot trial. Translational Psychiatry, 11(30). https://doi.org/10.1038/s41398-020-01124-6. *co-shared first authorship
33. Kanstrup, M, Kontio, E, Geranmayeh, A, Olofsdotter Lauri, K, Moulds, ML, Holmes, EA. (2020). A single case series using visuospatial task interference to reduce the number of visual intrusive memories of trauma with refugees. Clinical Psychology and Psychotherapy, 1– 15. doi: 10.1002/cpp.2489.
34. Kessler, H., Holmes, E. A., Blackwell, S.E., Schmidt, A-C., Schweer, J. M., Bücker, A., Herpertz, S., Axmacher, N., & Kehyayan, A. (2018). Reducing Intrusive Memories of Trauma Using a Visuospatial Interference Intervention with Inpatients with Posttraumatic Stress Disorder (PTSD). Journal of Consulting and Clinical Psychology, 86(12), 1076-1090.
35. Kleim, B., Bingisser, M. B., Westphal, M., & Bingisser, R. (2015). Frozen moments: flashback memories of critical incidents in emergency personnel. Brain and Behavior, 5(7), e00325.
36. Knaak, S., Mantler, E., & Szeto, A. (2017). Mental illness-related stigma in healthcare: Barriers to access and care and evidence-based solutions. Healthcare Management Forum, 30(2), 111–116.
37. Kroenke K, Spitzer RL, Williams JB. The Patient Health Questionnaire-2: Validity of a Two-Item Depression Screener. Medical Care. 2003;41:1284-92.

38. Kroenke K, Spitzer RL, Williams JB, Monahan PO, Löwe B. Anxiety disorders in primary care: prevalence, impairment, comorbidity, and detection. Ann Intern Med. 2007;146:317-25.
39. Lai, J., Ma, S., Wang, Y., Cai, Z., Hu, J., Wei, N., ... & Tan, H. (2020). Factors associated with mental health outcomes among health care workers exposed to coronavirus disease 2019. JAMA Network Open, 3(3), e203976-e203976.
40. Lang, A. J., Wilkins, K., Roy-Byrne, P. P., Golinelli, D., Chavira, D., Sherbourne, C., Rose, R. D., Bystritsky, A., Sullivan, G., Craske, M. G. & Stein, M. B. Abbreviated PTSD Checklist (PCL) as a Guide to Clinical Response. Gen. Hosp. Psychiatry 34, 332–338 (2012).
41. Laposa, J. M., & Alden, L. E. (2003). Posttraumatic stress disorder in the emergency room: exploration of a cognitive model. Behaviour Research and Therapy, 41(1), 49-65.
42. Laposa, J. M., Alden, L. E., & Fullerton, L. M. (2003). Work stress and posttraumatic stress disorder in ED nurses/personnel (CE). Journal of Emergency Nursing, 29(1), 23-28.
43. Lin, S. T., Yang, P., Lai, C. Y., Su, Y. Y., Yeh, Y. C., Huang, M. F., & Chen, C. C. (2011). Mental Health Implications of Music: Insight from Neuroscientific and Clinical Studies. Harvard Review of Psychiatry, 19(1), 34–46. https://doi.org/10.3109/10673229.2011.549769
44. Luik AI, Machado PF, Siriwardena N, Espie CA. Screening for insomnia in primary care: using a two-item version of the Sleep Condition Indicator. British Journal of General Practice 2019; 69 (679): 79-80. DOI: https://doi.org/10.3399/bjgp19X701045
45. Marmar CR, McCaslin SE, Metzler TJ, Best S, Weiss DS, Fagan J, Liberman A, Pole N, Otte C, Yehuda R, Mohr D, Neylan T. Predictors of posttraumatic stress in police and other first responders. Ann N Y Acad Sci. 2006 Jul;1071:1-18. doi: 10.1196/annals.1364.001. PMID: 16891557.
46. McNally, R. J. (2017). Networks and nosology in posttraumatic stress disorder. JAMA Psychiatry, 74, 124–125.
47. Michael, R., & Jenkins, H. J. (2001). Work-related trauma the experiences of perioperative nurses. Collegian, 8(1), 19-25.
48. National Institute for Health Care Excellence. (2018). Post-Traumatic Stress Disorder: Nice Guideline [Ng116]. NICE. https://www.nice.org.uk/guidance/NG116
49. National Institute for Health Care Excellence. (2018). Post-Traumatic Stress Disorder: evidence reviews for Psychological, psychosocial and other non-pharmacological interventions for the prevention of PTSD in adults. NICE.
50. NHS Digital (Sept, 2020). Retrieved from https://digital.nhs.uk/data-and-information/publications/statistical/nhs-sickness-absence-rates/may-2020-provisional on 27th September, 2020.
51. Price M, Szafranski DD, van Stolk-Cooke K, Gros DF. Investigation of abbreviated 4 and 8 item versions of the PTSD Checklist 5. Psychiatry Research. 2016;239:124-130. doi:10.1016/j.psychres.2016.03.014
52. Ramineni, V., Millroth. P., Iyadurai, L., Jaki, T., Kingslake, L., Highfield, J., Summers, C., Bonsall, B, M., Holmes, E. A. (2023). Treating intrusive memories after trauma in healthcare workers: a Bayesian adaptive randomised trial developing an imagery-competing task intervention. Mol Psychiatry (2023). https://doi.org/10.1038/s41380-023-02062-7

53. Revicki, D. A., Irwin, D., Reblando, J., & Simon, G. E. (1994). The accuracy of self-reported disability days. Medical care, 32(4), 401-404.
54. Schönbrodt, F. D., & Wagenmakers, E.-J. (2018). Bayes factor design analysis: Planning for compelling evidence. Psychon. Bull. Rev., 25(1), 128–142.
55. Stallard, N., Hampson, L., Benda, N., Brannath, W., Burnett, T., Friede, T., Kimani, P. K., Koenig, F., Krisam, J., Mozgunov, P., Posch, M., Wason, J., Wassmer, G., Whitehead, J., Faye Williamson, S., Zohar, S., & Jaki, T. (2020). Efficient adaptive designs for clinical trials of interventions for COVID-19. http://arxiv.org/abs/2005.13309.
56. Tan, B. Y., Chew, N. W., Lee, G. K., Jing, M., Goh, Y., Yeo, L. L., ... & Shanmugam, G. N. (2020). Psychological impact of the COVID-19 pandemic on health care workers in Singapore. Annals of Internal Medicine, 1-4. https://doi.org/10.7326/M20-1083.
57. Weathers, F.W., Litz, B.T., Keane, T.M., Palmieri, P.A., Marx, B.P., & Schnurr, P.P. (2013). The PTSD Checklist for DSM-5 (PCL-5). Scale available from the National Center for PTSD at www.ptsd.va.gov.
58. Weathers, F. W., Blake, D. D., Schnurr, P. P., Kaloupek, D. G., Marx, B. P., & Keane, T. M. (2013). The Life Events Checklist for DSM-5 (LEC-5) – Standard. [Measurement instrument]. Available from https://www.ptsd.va.gov/.
59. World Health Organization. (2010). Measuring Health and Disability: Manual for WHO Disability Assessment Schedule (WHODAS 2.0). Geneva, World Health Organization. (WHODAS 2.0 12-item version www.who.int/classifications/icf/WHODAS2.0_12itemsSELF.pdf, accessed 15/09/20.
60. World Health Organization. Problem Management Plus (PM+): Individual psychological help for adults impaired by distress in communities exposed to adversity. (Generic field-trial version 1.1). Geneva, WHO, 2018.
61. Zhang, W. R., Wang, K., Yin, L., Zhao, W. F., Xue, Q., Peng, M., ... & Chang, H. (2020). Mental health and psychosocial problems of medical health workers during the COVID-19 epidemic in China. Psychotherapy and Psychosomatics, 1-9. https://doi.org/10.1159/000507639

APPENDIX 1: STUDY FLOW CHART



APPENDIX 2: TIME OF EVENTS SCHEDULE

Visit Name	Consent Meeting	Screening	Baseline	Intervention Meeting	Week 4	Week 12	Week 24
Day	**Before Screening**	**Day -35**	**Between Screening and Intervention**	**Day 0**	**D22**	**D78**	**D162**
Visit Windows		**+ 35 days**		**N/A**	**+56 days**	**+84 days[3]**	**+28 days[4]**
Consent form (PIS_ICF)	X						
Eligibility check	X						
ePro Registration	X						
Intrusive memory diary (daily for seven days ending on day indicated)		X			X	X	X
Intrusive Memory Diary Weekly		X			X	X	X
Inclusion decision		X					
Demographics			X				
Health background			X				
Checklist of work-related traumatic events			X				
Intrusive memory ratings			X		X	X	X
PTSD Checklist for DSM-5 (PCL-5)			X		X	X	X
Sleep Condition Indicator (SCI-02)			X		X	X	X
Generalized Anxiety Disorder (GAD-2)			X		X	X	X
Patient Health Questionnaire (PHQ-2)			X		X	X	X
Scale of Work Engagement and Burnout (SWEBO)			X		X	X	X
Sickness absence			X		X	X	X
Intention to leave job (ITL)			X		X	X	X
WHODAS 2.0			X		X	X	X
EQ- 5D-5L (5-level EuroQol 5D)			X		X	X	X
Randomised in ePro			X				
Book intervention meeting[5]			X				
Credibility/Expectancy Questionnaire (CEQ)				X[6]			
First guided intervention				X[5]			
Intrusive memory diary (daily for seven days ending on day indicated)					X	X	X
Changes to health and work					X	X	X
Feedback questionnaire					X		
Qualitative interview A (optional)					X[1]		
Qualitative interview B (optional)						X[2]	

[1] Completed within 21-day window if contacted by research team.
[2] Completed within 28-day window of D168 if contacted by research team.

[3] In ePRO, each assessment associated with week 4 will expire +56 days after D28; each assessment associated with week 12 will expire +84 days after D84.

[4] In ePRO, each assessment associated with week 24 will expire +28 days from the date of the individual assessment.

[5] Intervention and control arms only

6 CEQ: For intervention and control arms – is done immediately before first guided session; For TAU – as soon as possible following randomisation, task is activated in ePro by researcher