Final Report

Randomised controlled trial of 3MDR for Treatment Resistant Post-traumatic Stress Disorder (PTSD) in military veterans

Professor Jonathan I Bisson
Chief Investigator
Professor in Psychiatry
Cardiff University School of Medicine

Professor Robert van Deursen
Professor in Physiotherapy
Cardiff University School of Healthcare Sciences

Professor Ben Hannigan
Professor of Mental Health Nursing
Cardiff University School of Healthcare Sciences

Dr. Neil J Kitchiner
Principal Clinician, Veterans' NHS Wales,
Cardiff and Vale University Health Board

Leigh Abbott
3MDR Laboratory Technician
Cardiff University School of Healthcare Sciences

Kali Barawi
Research Assistant and PhD Student
Cardiff University School of Medicine

Kate Jones
3MDR Laboratory Technician and PhD Student
Cardiff University School of Healthcare Sciences

Tim Pickles
Statistician
Cardiff University School of Medicine

Lt-Col. (Retired) John Skipper
Public representative

Caroline Young
Research Nurse
Cardiff and Vale University Health Board

Acknowledgments

The research team would like to express our sincere gratitude to a number of people and organisations, without whom this study could not have been completed.

We thank Forces in Mind Trust for funding the research costs of the study and helpful feedback during the development of the Executive Summary and Study Report, and Welsh Government, through Health and Care Research Wales, for funding the NHS costs of the study.

We thank Eric Vermetten, Marieke van Gelderen and Mirjam Mink-Nijdam for their input to training, supervision, treatment fidelity checks and general advice and support.

We thank Vanessa Bailey, Clare Crole-Rees, Neil Kitchiner, William Watkins, Dean Whybrow and Victoria Williams for becoming 3MDR therapists and delivering 3MDR treatment so skilfully.

Finally, and most of all, we thank the participants of the study for taking part and joining us in our quest to develop more effective treatments for people with post-traumatic stress disorder.

Contents

Foreword

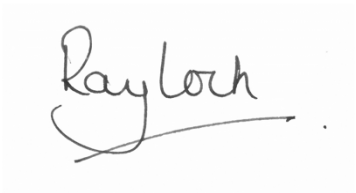
Most members of the Armed Forces make a successful, sustainable and healthy transition into civilian life. But some do not. A number leave the Armed Forces in poor health; indeed, in some cases, their very departure may be caused by that condition. And though the number will be small, individually they represent some of the most vulnerable members of the ex-serving community, and hence those most deserving of the work of Forces in Mind Trust.

It is known that certain experiences during a Service career are more likely to lead to Post-traumatic Stress Disorder, such as close combat, and that of those who do seek help, some prove resistant to the range of available treatments. Again, it is easy to see why this most vulnerable sub-cohort warrants the time, effort and resources that are necessary to identify a way to deliver better mental health.

None of this is easy, nor is it cheap. The report on this Phase 2 trial is the culmination of over 3 years of work, and hundreds of thousands of pounds of investment by Forces in Mind Trust and others. As with all of our work, what matters most is not the research itself, impressive though it undoubtedly is, but the impact it will ultimately have on improving the psychological wellbeing of the ex-Service community.

The test, therefore, is whether a systemic change can be achieved. Specifically, will this innovative and promising intervention, 3MDR, whose efficacy this trial clearly demonstrates, become formally adopted by our National Health Services? And if so, can it then be made available across the United Kingdom?

Having championed this project since 2016, including attending its convincing open day last year, I am confident that a full Randomized Control Trial is feasible, and that its outcome is likely to be a positive one when measured against these criteria. Our collective challenge now is to take these next steps, and to ensure that all ex-Service personnel can, and do, have every opportunity to live successful civilian lives.



Air Vice-Marshal Ray Lock CBE
Chief Executive, Forces in Mind Trust

1: Summary

1.1. Post-traumatic stress disorder (PTSD) is a common and debilitating condition that is estimated to affect over 7% of British military veterans and 17% of those who have deployed in a combat role, compared to 4.4% of the civilian population. Unfortunately, many veterans with PTSD remain symptomatic despite having received evidence-based interventions and there is an urgent need to develop more effective treatments.

1.2. Modular motion-assisted memory desensitisation and reconsolidation (3MDR) is a new treatment for PTSD based on virtual reality exposure therapy and eye movement desensitization and reprocessing (EMDR), embedded in a novel context in which the patient walks on a treadmill whilst interacting with a series of self-selected images that are displayed on a large screen.

1.3. Preliminary results from research conducted by the originators of 3MDR in the Netherlands were promising. We, therefore, decided to explore the potential efficacy of 3MDR further by conducting a randomised controlled trial with nested process evaluation to assess fidelity, adherence and factors that influence outcome.

1.4. Forty-two military veterans living in South Wales who continued to experience service-related PTSD following treatment with trauma-focused psychological therapy took part in the study. Participants completed a baseline assessment and were then randomised to receive 3MDR immediately or after a delay of 14 weeks, with follow-up assessments occurring at 12 and 26 weeks post randomisation. Retention rates were very high; 83% (35 participants) at 12 weeks and 86% (36 participants) at 26 weeks.

1.5. Eleven of the participating veterans and all six of the 3MDR therapists participated in a single qualitative interview, designed to provide greater understanding about 3MDR, the experience of receiving it and of delivering 3MDR, and of being involved in the research trial. Participating veterans were purposively selected to learn from as wide a range of individuals as possible, with different characteristics and experiences.

1.6. PTSD symptom severity was statistically and clinically significantly better for the immediate treatment group (37% average reduction of PTSD symptoms after receipt of 3MDR) than the delayed treatment group (14% average reduction in PTSD symptoms whilst waiting for 3MDR) at the 12-week follow-up point, which shows a 19% greater reduction in PTSD symptoms for the immediate treatment group over the delayed treatment group at that point. The delayed treatment group experienced an average 28% further PTSD symptom reductions following 3MDR and the immediate treatment group maintained their improvement at 26-week follow-up. It is important to note, however, that not all participants improved following 3MDR and some reported increased symptoms. The likely effect size of 3MDR was found to be 0.65, representing a moderate treatment effect despite it being tested in veterans with treatment-resistant PTSD.

1.7. 3MDR was found to be acceptable to most, but not all, participants and to all the therapists delivering the intervention, albeit with recommendations on what could be done to enhance its effect and acceptability. Key findings in this regard included the appropriate assessment and selection of potential candidates for 3MDR, enhanced

preparation in advance of 3MDR, the number of treatment sessions available, support between sessions and greater flexibility with respect to content of later 3MDR sessions.

1.8. This study has shown emerging evidence of 3MDR being effective for treatment resistant PTSD and further research through a pragmatic effectiveness randomised controlled trial is now required to determine its true effectiveness and optimal delivery.

2: Background

2.1. The majority of those who serve in the UK armed forces do well after they leave[1]. Military service, particularly combat experience, can, however, have adverse effects and these are of concern for the armed forces, other government departments, service personnel and veterans, and their families. Successive UK governments have been accused of neglecting veterans, with reports that homelessness[2], imprisonment[3], unemployment and alcoholism are the fate of many[4]. It is estimated that over 7% of British military veterans meet the criteria for PTSD and 17% of those who been have deployed in a combat role[5]. The financial and social impact is considerable[6]. Many veterans with PTSD struggle in their transition to civilian and family life, are unable to work and are in receipt of long-term incapacity benefits[7].

2.2. Only a limited proportion of people with mental health problems seek professional help. Among military populations this is true of veterans as well as serving personnel, albeit to a lesser extent[8]. Engaging veterans in mental health treatment programmes can be challenging due to stigma, perceived weakness in acknowledging emotional difficulties, and military macho cultures[9]. That said, a recent report found that the impact of stigma on help-seeking is not significant, and that other barriers are more important, e.g. failure to recognise having a mental health problem, negative beliefs/experiences of treatment and provision of support[10]. Most studies have found that informal sources of help such as family, friends and clergy are preferred[11, 12].

2.3. In military and veteran populations, recent trials of the first-line trauma-focused interventions Cognitive Processing Therapy (CPT) and Prolonged Exposure (PE) have shown clinically meaningful improvements for many patients with PTSD[13, 14]. However, non-response rates have been high, many patients continue to have symptoms, and trauma-focused interventions only show marginally superior results compared with active control conditions[15].

2.4. There is limited existing research into treatment-resistant PTSD and even more limited significant advances. Emerging work with MDMA-assisted psychotherapy shows promise[16] but is unlikely to be appropriate for all people with treatment-resistant PTSD. Pharmacological augmentation strategies have had modest success[17] but have not achieved the step-change required. The 2018 International Society for Traumatic Stress Studies (ISTSS) prevention and treatment guidelines[18] and the 2018 update of the NICE guidelines for PTSD[19] provide strongest support for trauma-focused psychological treatments, which have a positive albeit often partial and sometimes absent effect. Smaller, yet still positive, effects were found for a range of other therapeutic options including pharmacological and non-trauma focused psychological treatments. In addition, a number of novel treatments were found to have emerging evidence of effect in individuals who had already tried other treatments (e.g. neurofeedback and transcranial magnetic stimulation (TMS)). The current evidence points to a clear need for

improvement in existing PTSD treatments and for the development and testing of novel treatments, including more intense interventions for those who have not responded to less intense interventions.

2.5. Modular motion-assisted memory desensitisation and reconsolidation (3MDR)[20] is a new treatment that aims to reduce cognitive avoidance and augment engagement with therapy. 3MDR is based on known therapeutic principles of virtual reality exposure therapy[21] and eye movement desensitization and reprocessing (EMDR)[22], embedded in a novel context in which the patient walks on a treadmill whilst interacting with a series of self-selected images that are displayed on a large screen. Exposure by virtual reality, enhanced with walking, music and high affect pictures, eliminates cognitive avoidance during exposure and promotes presence. ***This is an important distinction between 3MDR and traditional trauma focused techniques which are sedentary; patients learn how to move through their avoidance by, literally, walking back into their trauma memory.***

2.6. In 3MDR, a dual task is used to facilitate desensitisation and reconsolidation of the emotional content of the traumatic event that is captured on a service-related photograph. This is congruent with working memory theory, which has been used to explain the therapeutic mechanism of EMDR[23]. According to this theory, working memory has limited resources; if a dual task (for example, following a specific object with your eyes) uses some of those resources, less memory will be available for other memory processes, which in turn will make the recollection of memories less vivid and less affect-laden. In 3MDR, the dual task is different from most EMDR treatments. Instead of making eye movements (or alternative bilateral stimulation) alone, numbers need to be called out whilst the patient is also walking, thereby optimally taxing working memory.

2.7. Preliminary results from research conducted by the originators of 3MDR in the Netherlands regarding the efficacy of 3MDR in veterans with treatment resistant, service-related PTSD are promising. A pilot study[20] showed a decrease in PTSD symptoms and no dropouts from the treatment, with the two participants positive about the treatment. No adverse effects were reported and we, therefore, decided to explore the potential efficacy of 3MDR further.

3: Aims and Objectives

3.1. The main aim of the proposed research was to determine whether 3MDR was able to reduce traumatic stress symptoms in British military veterans with treatment-resistant, service-related PTSD, to a significantly greater degree than being on a waiting list for 3MDR.

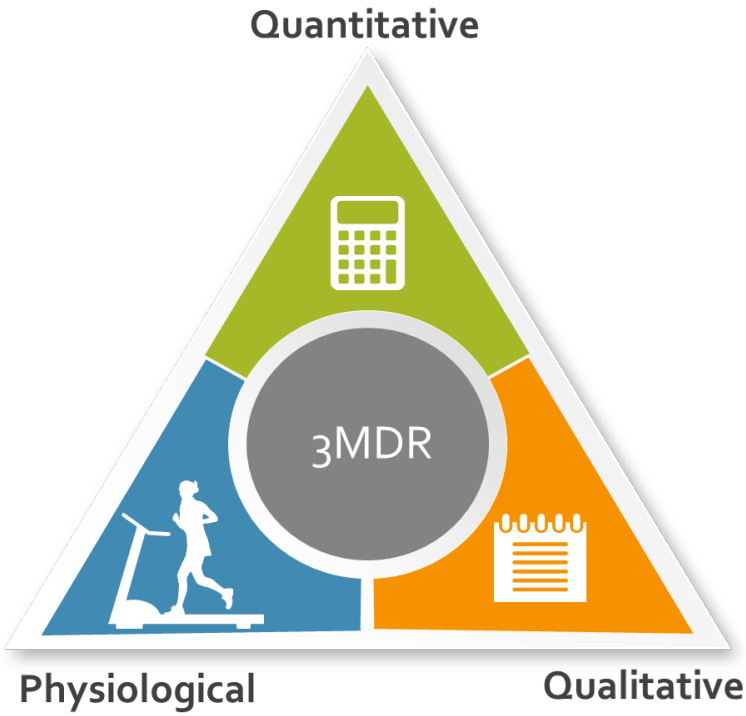
3.2. The main objective was to answer the eight research questions in the table below.

Table 1: Research questions

A.	For British military veterans with treatment-resistant, service-related PTSD, does 3MDR reduce symptoms of PTSD as measured by the CAPS5 to a significantly greater degree than being on a waiting list for 3MDR?
B.	For British military veterans with treatment-resistant, service-related PTSD, what is the impact of 3MDR on quality of life, functioning, symptoms of depression and anxiety, insomnia, alcohol and illicit substance use and perceived social support?
C.	Is 3MDR acceptable to British military veterans with treatment-resistant, service-related PTSD and those delivering the intervention as measured by qualitative semi-structured interviews?
D.	What is the likely effect size of 3MDR?
E.	What factors may impact efficacy and successful roll-out of 3MDR for treatment-resistant, service-related PTSD, if 3MDR is shown to be efficacious? (Mechanism and process evaluation)
F.	What is the behavioural response of the 3MDR sessions in terms of stress and cognitive processing during different dual task phases and how can this guide us in optimal design of the intervention and a Phase III definitive trial? (Mechanism evaluation)
G.	Can examination of the integrity of the study protocol, trial recruitment rate, self-report outcome measures, clinician administered outcome measures, randomisation procedure, treatment integrity and acceptability enhance decision making in planning a Phase III definitive trial?
H.	Is a Phase III definitive RCT indicated and feasible?

4: Methods

Figure 2: 3MDR Paradigm



Study design

4.1. The study was an exploratory, randomised, parallel-group, controlled trial with evaluation to assess fidelity (if the treatment was delivered as planned), adherence (how well participants could comply with the treatment and requirements of the trial) and factors that influence outcome.

Setting, research team and approvals

4.2. The study took place in the Schools of Medicine and Healthcare Sciences at Cardiff University Hospital of Wales. The research team, led by Professor Jonathan Bisson, has internationally recognised expertise in traumatic stress research and treatment, quantitative and qualitative research approaches, movement analysis and research involving military veterans. The study was approved by the South East Wales Research Ethics Committee and Health and Care Research Wales. The study was registered as a randomised controlled trial (Trial Registration Number – ISRCTN80028105).

Sample size

4.3. Although it can be argued a standard power calculation is not appropriate for a Phase II exploratory trial we believed it appropriate to use a power calculation based on a previous study of TFCBT for PTSD[24] to inform our sample size and ensure it was adequate. The calculation suggested that for an 80% chance of detecting a mean 15 point difference on the Clinician Administered PTSD Scale between 3MDR and waiting list at a 0.05 confidence level assuming a standard deviation of 15.18, 17 subjects in each group would be needed. Allowing for a conservative estimate of a 20-25% drop out, it was planned that an extra 4 subjects would be recruited to each arm representing a total proposed sample size of 42.

4.4. For the qualitative study, in order to learn from veterans with a full range of views and experiences maximum variation sampling[25] was used. This was to allow interviews to be held with veterans who had appeared to benefit from 3MDR, along with those who appeared not to have benefited and/or had dropped out of therapy. Based on previous

research[26], we anticipated that interviews would be conducted with around 10 participants, purposively sampled, and all six therapists.

Inclusion/exclusion criteria

4.5. Wide eligibility criteria were used to ensure the results would be applicable to the majority of military veterans with treatment-resistant PTSD. Given the high rate of co-morbidity of PTSD and other conditions such as depression and substance misuse, individuals with co-morbidity were included if they satisfied the other inclusion/exclusion criteria and PTSD was considered the primary diagnosis. This is consistent with NICE guidance and resulted in a pragmatic trial with generalisable findings. The inclusion and exclusion criteria are shown in the table below.

Table 2. Inclusion and exclusion criteria

Inclusion Criteria	Exclusion Criteria
Aged 18 or over	Psychosis
Informed consent	DSM5 severe major depressive episode
Meet DSM5[29] criteria for service-related PTSD	Substance dependence
Treatment-resistance defined as prior receipt of a trauma focused psychological treatment without loss of PTSD diagnosis	Change in psychotropic medication within one month
	Suicidal intent
	Inability to walk at a normal pace for 30-45 minutes on a treadmill

Participants, recruitment and consent

4.6. British military veterans who attended the Veterans' NHS Wales Service and/or Cardiff and Vale Traumatic Stress Service who were considered to be likely to fulfil the inclusion criteria for the study were asked by a clinician involved in their care if they were willing for their details to be passed on to the research team. Veterans who had been discharged from the service and considered likely to fulfil the inclusion criteria for the study were sent a letter from a clinician involved in their care inviting them to consider taking part in the study and to contact the clinician if interested. If clinicians did not hear back from the veteran within two weeks, a follow up letter was sent and if the veteran did not respond they were not contacted again. The clinical team undertook the necessary checks, e.g. to ensure there was no evidence of the veteran having asked not to be contacted about research or being deceased, before sending out letters in order to avoid distress to the veteran and/or their families.

4.7. The research team contacted potential participants and provided them with an information sheet about the study. They were given at least 24 hours to consider this before being asked if they required further information or any questions answered. If potential participants wished to proceed, arrangements were made to enter them into the study.

4.8. Informed consent, that ensured the veteran was fully aware of the demands of the trial and their rights, was always obtained before the initial assessment proceeded. The

member of the research team conducting the assessment checked that the participant had read and understood the information sheet by assessing the following factors:

a. whether the participant had any questions arising from the information sheet and answered any that arose.
b. that the participant understood their participation was voluntary and that they were free to withdraw at any time without giving any reason, without their medical care or legal rights being affected.
c. whether the participant agreed to their GP being informed of their participation in the study.
d. whether the participant agreed to take part in the study.

4.9. The member of the research team who was conducting the assessment then requested that the participant completed the consent form.

4.10. All work was conducted in full compliance with the Data Protection Act and GDPR.

Outcome measures

4.11. The primary outcome was symptoms of PTSD measured by the Clinician Administered PTSD Scale for DSM5 (CAPS5)[27]. The CAPS5 is a 29-item structured interview for assessing PTSD diagnostic status and symptom severity. The CAPS is the gold standard in PTSD assessment and can be used to make a current diagnosis according to symptoms in the past month, a lifetime diagnosis according to symptoms over the course of the individual's life, or to assess symptoms over the past week. Items correspond to the DSM5 criteria for PTSD. Previous versions of the CAPS have excellent reliability and excellent convergent and discriminant validity, diagnostic utility, and sensitivity to clinical change[28].

4.12. Secondary outcome measures were self-report measures that are routinely collected by Increasing Access to Psychological Therapies (IAPT) services in England and veteran services at present (PTSD Checklist[29] for traumatic stress; Work and Social Adjustment Scale[30] for quality of life/functional impairment; Patient Health Questionnaire-9[31] (PHQ-9) for depression; General Anxiety Disorder-7[32] (GAD-7) for anxiety; AUDIT-O[33] for alcohol use) and changes in sleep were measured by the insomnia severity index (ISI)[34]. In addition, the Multidimensional Scale for Perceived Social Support[35] was used to assess perceived social support. Changes in health-related quality of life were measured by the EQ5D-5L[36]. Brief descriptions of the secondary outcome measures are included in Table 3.

Table 3. Secondary outcome measures

PTSD Checklist (PCL-5)	20-item scale which aims to assess self-reported symptoms of PTSD as described in the Diagnostic and Statistical Manual of Mental Disorders (DSM-5). The PCL -5 is based on an earlier version of the PCL, which is widely used and well validated[29]
The Work and Social Adjustment Scale (WSAS)	assesses the impact of a person's mental health difficulties on their ability to function in terms of work, home management, social leisure, private leisure and personal or family relationships. The WSAS is the outcome measure of choice for evaluating improvement in functioning in IAPT services. The

	WSAS has been demonstrated to show good reliability and validity and is sensitive to change[30]
The PHQ-9	reliable and well-validated brief self-report measure of depression[31]. It is the outcome measure of choice for evaluating improvement in depressive symptoms in IAPT services[37]
GAD-7	reliable and well-validated brief self-report measure of anxiety[32]. It is the outcome measure of choice for evaluating improvement in anxiety symptoms in IAPT services[37]
AUDIT-O[33]	10 multiple choice questions on quantity and frequency of alcohol consumption, drinking behaviour and alcohol-related problems or reactions over the preceding 3 months
Insomnia Severity Index (ISI)	7-item self-report questionnaire assessing the nature, severity, and impact of insomnia. It has been shown to be reliable and valid in terms of detecting insomnia and in measuring treatment response in clinical patients[34]
Multidimensional Scale for Perceived Social Support (MSPSS)	12-item Likert scale measuring the subjective assessment of adequacy of social support from family, friends, and partners[38]. The reliability, validity, and factor structure of the MSPSS have been demonstrated with a number of populations[35,39,40]
EQ5D-5L[63]	widely used instrument in health economic analysis and recognised by NICE as an appropriate measure for health related quality of life. The questionnaire provides a simple descriptive profile, which translates to a single utility score for health status. The first part of the instrument identifies the extent of perceived problems – across five levels - in each of five life dimensions: mobility; self-care; usual activities; pain and discomfort; and anxiety and depression. The responses to each of the five questions are used to generate a utility score for self-rated health status on a 0-1 scale, where 0 represents the worst possible health state and 1 the best possible health state. The second part is a visual analogue scale, which allows the responder to indicate their current health status on a 0-100 scale

4.13. Two experienced researchers blind to randomisation conducted the assessments. The initial assessment ensured that the inclusion criteria were satisfied and participants were then asked to monitor their symptoms for two weeks. The baseline assessment of all the outcome measures occurred after this; those who continued to fulfil the inclusion criteria were randomised to one of the two groups: 3MDR or wait list for 14 weeks followed by 3MDR. Follow up occurred 12 and 26 weeks after randomisation. This involved re-administration of all the outcome measures. Following completion of their 3MDR treatment, a purposively selected sample of participants were asked to participate in semi-structured interviews to elicit their experience and views of the programme.

4.14. A statistician used a computer programme to generate randomisation codes on a 1:1 basis with a block size of 6 and no stratification. The codes were sealed in opaque brown envelopes numbered from 1-42. The 3MDR lab researcher (who was blind to their content) opened the envelopes consecutively, advised the participant of the arm they had been allocated to and the date/anticipated date of their first 3MDR session.

Figure 3: 3MDR Intervention

4.15. The 3MDR therapy was delivered weekly over nine weeks (two weeks preparation, six weeks 3MDR and one concluding session) by six experienced psychological therapists, including two military veterans, who work with Veterans' NHS Wales and Cardiff University. The waiting list group received no intervention for 14 weeks post-randomisation and then received 3MDR over nine weeks.

4.16. Training in 3MDR treatment delivery involved two one-day workshops facilitated by the originators of 3MDR and then in-house training sessions involving role-play. Therapists were provided with monthly clinical supervision from the originators via Skype or telephone conference which reduced to bi-monthly supervision as the trial progressed. Dr Neil Kitchiner also facilitated bi-monthly in-house peer clinical supervision via Skype or telephone conference calls. All treatment sessions were video-recorded and one randomly selected session per participant was fidelity rated by the originators of 3MDR.

4.17. Prior to the 3MDR sessions, participants were asked to select and bring 12 pictures (from their personal records or the Internet) that evoked memories of the traumatic event. The therapists guided the participant to limit avoidance during picture selection. Supported by the therapist, the pictures were arranged according to psychological distress (SUD) score and theme. For each session, a maximum of 7 out of the 12 pictures were used and selected based on the SUD score or a particular theme. Pictures could be repeated during a session, particularly if the associated SUD score was high, reducing the number of pictures used for some sessions. Participants also chose two pieces of music. The first for the mental and physical warm-up walk aimed to take the participant back to the time of their traumatic event, e.g. music that reminded them of this period. The second, for the warm-down, aimed to bring the participant back to the here and now and remind them that they are safe now. This was likely to be a more recent piece of music.

4.18. Participants were introduced to the intervention and research setup, and the general procedures to be used were explained. They were asked to wear suitable clothing and footwear and to wear a sensor on the chest, secured with a comfortable belt. A safety harness, connected to the ceiling, was worn to guarantee safety during

treadmill walking. After initial familiarisation with the GRAIL system, participants were asked to walk on the treadmill using "self-paced mode" in a neutral virtual environment. In this mode, preferred walking speed was determined whereby participants familiarise themselves with the system which makes automatic adjustments. Once preferred walking speed was established, participants were asked to walk for 1 minute whilst their heart rate (HR) and step width variability was recorded as a baseline determination of their physiological and motor response. Participants were then requested to walk for 1 minute whilst carrying out a standard dual-task: the Stroop test. The Stroop test involves naming the colour of a sequence of words; the words themselves represent a colour but do not match the colour the words are displayed in. This incompatibility results in increased demands for cognitive processing. HR and step width variability were recorded during the test and, on completion, participants gave a score on the SUD scale.

4.19. In the 3MDR sessions an introduction phase, intervention phase, and final phase were presented. The participant's preferred walking speed was used to start the introduction phase. After each transition the operator, on request, could adjust the walking speed. During the introduction phase, the participant saw a pathway ahead and their chosen music began to play while verbal guidance prepared the participant for the intervention phase. The participant then entered the first tunnel to approach the first picture whilst being guided by instructions on what to do at each stage. As soon as the participant saw their chosen picture, a literal description of this was requested with a brief account of the related memories and feelings. The therapist repeated every feeling so the operator could enter these on the screen. When the participant confirmed there were no more new feelings or memories to be identified, the dual task was started: a red ball moved across the screen from left to right as a distracter stimulus. Whilst focussing on the feelings written on the screen, the participant was asked to track the ball and call out the numbers displayed on it. After 30 seconds, the distracter stimulus was removed, and a SUD score requested and recorded. The tunnel then re-appeared, and the process was repeated for the next and subsequent pictures. After the last picture, the final phase began with the participant's second piece of music, assisting return to the here and now, and positive feedback about what had been achieved, to conclude the session.

4.20. After the 3MDR session, the operator removed the safety harness and HR monitor from the participant. A therapist-led discussion with the participant then occurred in a private room; open questions were used to elicit how the session was for the participant and to discuss the meaning of the re-experiencing to the participant in this setting. The therapist also ensured that the participant was completely returned to the here and now and aimed to enable the participant to attach a positive meaning to the 3MDR session. Participants were asked to write their experiences and reflections down following each session in a diary format.

4.21. Every 3MDR session was recorded and a report summarising the behavioural response to the intervention was produced. HR and step width variability permitted exploration of the stress response and the cognitive demand during the different phases of each 3MDR session. This also informed the process evaluation component of the study which is described below.

4.22. A more detailed 3MDR Treatment Protocol is available on request from the authors and video clips that demonstrate 3MDR can be found via the following links:

https://www.youtube.com/watch?v=j0CklR0P1RI
https://www.youtube.com/watch?v=IUnWe7tfgSQ
https://www.youtube.com/watch?v=bOAbDv-Ai6o

Analyses

4.23. *Quantitative outcome data* - Continuous intention to treat data were analysed, to ensure all randomised participants were considered, by comparing means using ANCOVA with baseline scores as co-variates. Categorical data were analysed using relative risk analyses. Regression analyses were performed to examine which factors were associated with a positive or negative outcome. All analyses were performed at the end of the data collection period using SPSS software for statistical analysis. More detail on the quantitative outcome data is provided in Section 5 of the report.

4.24. *Qualitative data* - Semi-structured interviews were audio-recorded and transcribed verbatim. Transcripts were imported into QSR NVivo 12[41] software for Computer Aided Qualitative Data Analysis (CAQDA). Relevant themes were identified using a process of Inductive Thematic Analysis, as described by Braun and Clarke[42]. Themes were tested for validity through a variety of recognised techniques, including discussion with the

research team to ensure comprehensiveness, exploration of the participants' underlying reasoning, and examination of elements within the data that appeared to contradict emerging thematic patterns (deviant case analysis). More detail on the qualitative data is provided in Section 6 of the report.

4.25. *3MDR session data* - Results from the 3MDR quantitative analysis of how the experience affected the physiology and movement behaviour through the cycle of a 3MDR session were compared with the subjective reports of disturbance (SUD scores) within sessions and with the qualitative data exploring the experience of the intervention. Review meetings involving the research team were held to discuss the quantitative results from selected individuals after they had completed their intervention to inform topics to be explored in the qualitative interviews. The primary outcome measures along with individual diary notes made by participants during the intervention, to document their experience of it in real time, were also used. The lab research assistant and therapists were kept blind to the details of these meetings to avoid introducing bias to the study. Post analysis of the overall results, further meetings were held to compare the quantitative and qualitative results, achieve integration of the data and generate a deeper understanding of the experience of the intervention, its acceptability, and the ultimate effect it had on the subjects. These final meetings were held with the complete research group to ensure that data were optimally compared. More detail on the 3MDR session data is provided in Section 7 of the report.

Patient and Public Involvement

4.26. Patient and public involvement (PPI) has been embedded throughout the development and delivery of this 3MDR study. One of the co-applicants had lived experience of PTSD and has been a key member of the research team throughout the study. The Cardiff University Traumatic Stress Research Group's PPI Group has provided advice on the study, especially with respect to public facing information and documents. The PPI Group played an integral role in the development of our website www.traumaticstressresearch.co.uk, which features the 3MDR study and provides updates on progress and outcomes.

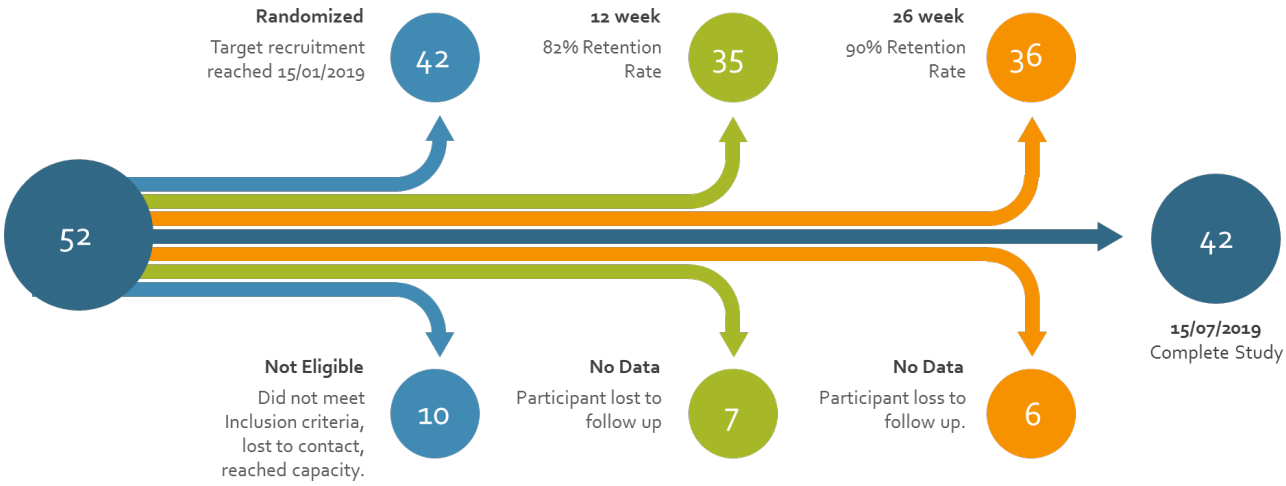
4.27. Meetings during the development of the trial with people with lived experience of PTSD considered views on 3MDR, randomisation and thetreatment of military veterans with treatment resistant PTSD. In order to raise awareness of the trial and to facilitate recruitment to it, members of the research team took part in an especially commissioned short video.

4.28. Members of the PPI Group and participants in the study are now playing key roles in our dissemination work. The 3MDR study's PPI adheres to the recently published National Standards for PPI[43].

5. Quantitative Results

5.1. This section details the analysis for the main quantitative outcome data collected during the 3MDR trial. Figure 4 shows the progression of the 52 military veterans who were referred to the study. Forty-two participants were randomised and the retention rate was 83% at 12 weeks and 86% at 26 weeks.

Figure 4: Participant flow



5.2. All 42 randomised participants were male. The primary traumatic events suffered were: severe human suffering (11, 26.2%); serious injury, harm or death you caused to someone (10, 23.8%); fire or explosion (9, 21.4%); combat or exposure to a war - zone (in the military..) (2, 4.8%); sudden, violent death (homicide, suicide) (2, 4.8%); sudden unexpected death of someone close to you (2, 4.8%); missing data (2, 4.8%); physical assault (1, 2.4%); assault with a weapon (1, 2.4%); sexual assault (rape, attempted rape..) (1, 2.4%); and captivity (kidnapping, abduction etc...) (1, 2.4%).

5.3. Table 5 summarises the demographic characteristics of the participants and allows comparison of those randomised to delayed 3MDR and immediate 3MDR. The average age of participants was 42 and the mean time since their worst traumatic event was over 19 years. The vast majority of participants were White British (95%) and around a third were employed and a third unable to work. Almost half the participants had a co-morbid depressive disorder.

Table 5: Demographics

		Arm						Total	
		Delayed			Immediate				
		N	%/Mean|SD		n	%/Mean|SD		n	%/Mean|SD
Age		21	44.0	12.0	21	40.2	10.1	42	42.1 |11.1
Time since trauma (months)		21	271.4	186.4	21	191.2	145.4	42	231.3|170.1
Ethnic origin	White British	19	90.5		21	100.0		40	95.2
	Any other Mixed/multiple ethnic background	1	4.8		0	0.0		1	2.4
	African	1	4.8		0	0.0		1	2.4
Highest level of qualification	No qualifications	1	5.0		0	0.0		1	2.6
	1-4 GCSEs or equivalent	6	30.0		7	36.8		13	33.3
	5+ GCSEs or equivalent	3	15.0		7	36.8		10	25.6
	Apprenticeship	1	5.0		0	0.0		1	2.6
	2+ A Levels or equivalent	4	20.0		1	5.3		5	12.8
	Degree level or above	5	25.0		4	21.1		9	23.1
	Other qualifications	0	0.0		0	0.0		0	0.0
Current employment status	Employed	10	50.0		4	19.0		14	34.1
	Self-employed or freelance	2	10.0		1	4.8		3	7.3
	Been made redundant	0	0.0		1	4.8		1	2.4
	Homemaker	0	0.0		1	4.8		1	2.4
	Retired	1	5.0		3	14.3		4	9.8
	Volunteering	0	0.0		3	14.3		3	7.3
	Unable to work	7	35.0		8	38.1		15	36.6
Diagnosis of depressive disorder	No	12	57.1		11	52.4		23	54.8
	Yes	9	42.9		10	47.6		19	45.2

5.4. Table 6 provides data on the outcome measures at baseline, 12 weeks and 26 weeks post randomisations. Table 7 demonstrates statistically significant greater improvement for participants in the immediate 3MDR versus delayed 3MDR group at the primary 12 weeks on the CAPS-5, PCL-5, GAD-7 and ISI. There was no significant difference between the groups on WSAS, PHQ-9, EQ-5D-5L, Audit-O and MSPSS.

Table 6: Primary and secondary outcome mean (SD) scores at all time points

		Time point								
		Baseline			Week 12			Week 26		
		n	Mean	SD	n	Mean	SD	n	Mean	SD
CAPS-5	Delayed	21	47.6	7.05	19	40.8	10.80	19	29.5	17.67
	Immediate	21	48.5	8.39	16	30.8	17.09	17	30.8	18.30
	Total	42	48.0	7.67	35	36.3	14.71	36	30.1	17.72
PCL-5	Delayed	21	60.0	9.83	15	59.0	5.98	17	48.2	17.90
	Immediate	21	58.0	7.22	14	46.1	16.57	12	39.4	22.80
	Total	42	59.0	8.58	29	52.8	13.73	29	44.6	20.17
WSAS	Delayed	21	24.7	8.00	15	25.1	7.91	17	17.7	11.56
	Immediate	21	26.6	5.86	14	24.6	9.25	12	18.8	13.17
	Total	42	25.6	6.99	29	24.8	8.43	29	18.2	12.03
PHQ-9	Delayed	21	17.2	5.70	15	17.5	5.67	17	14.3	6.01
	Immediate	21	17.1	5.14	13	14.8	6.14	13	14.1	8.26
	Total	42	17.2	5.36	28	16.3	5.95	30	14.2	6.94
GAD-7	Delayed	21	16.6	4.42	15	15.1	5.13	17	13.3	5.64
	Immediate	21	14.6	3.94	14	10.6	5.40	12	12.3	6.83
	Total	42	15.6	4.25	29	12.9	5.66	29	12.9	6.06
ISI	Delayed	21	20.0	5.19	15	21.7	4.94	17	19.6	6.00
	Immediate	21	19.8	6.43	14	13.4	5.99	12	14.7	9.00
	Total	42	19.9	5.77	29	17.7	6.84	29	17.6	7.65
EQ-5D-5L*	Delayed	20	0.44	0.28	15	0.46	0.26	17	0.51	0.27
	Immediate	21	0.54	0.25	14	0.52	0.33	12	0.47	0.41
	Total	41	0.49	0.27	29	0.49	0.29	29	0.49	0.33
AUDIT-O	Delayed	21	7.9	5.64	15	5.7	5.21	17	8.2	8.56
	Immediate	21	7.3	9.29	14	6.8	9.41	12	5.8	9.50
	Total	42	7.6	7.59	29	6.2	7.41	29	7.2	8.88
MSPSS	Delayed	21	55.3	19.59	15	58.9	19.85	17	55.8	19.20
	Immediate	21	47.0	12.50	14	52.9	14.82	12	54.3	20.89
	Total	42	51.1	16.77	29	56.0	17.56	29	55.2	19.56

*Crosswalk to EQ-5D-3L UK tariff

Table 7: Primary and secondary outcome analyses for differences at Week 12

		Time point						Diff in Means	95% Conf'nce Interval	p-value
		Delay			Immediate					
		n	Mean	SD	n	Mean	SD			
CAPS-5	Baseline	19	47.6	7.34	16	47.0	8.63	**-9.25**	**-16.52 to -1.99**	**0.013**
	Week 12	19	40.8	10.80	16	30.8	17.09			
PCL-5	Baseline	15	59.4	9.42	14	57.3	7.06	**-10.41**	**-18.58 to -2.25**	**0.012**
	Week 12	15	59.0	5.98	14	46.1	16.57			
WSAS	Baseline	15	24.5	8.58	14	26.4	5.65	-1.49	-7.07 to 4.10	0.602
	Week 12	15	25.1	7.91	14	24.6	9.25			
PHQ-9	Baseline	15	16.2	5.47	13	16.8	5.26	-2.96	-6.47 to 0.56	0.099
	Week 12	15	17.5	5.67	13	14.8	6.14			
GAD-7	Baseline	15	15.6	4.69	14	13.9	3.94	**-4.95**	**-8.62 to -1.29**	**0.008**
	Week 12	15	15.1	5.13	14	10.6	5.40			
ISI	Baseline	15	19.3	5.33	14	19.6	6.95	**-6.96**	**-10.07 to -3.86**	**<0.001**
	Week 12	15	21.7	4.94	14	13.4	5.99			
EQ-5D-5L*	Baseline	15	0.46 14	0.264 81	14	0.570 5	0.260 51	-0.04	-0.196 to 0.113	0.600
	Week 12	15	0.46 22	0.257 02	14	0.520 5	0.330 95			
AUDIT-O	Baseline	15	5.4	3.89	14	6.1	9.57	0.19	-1.69 to 2.07	0.843
	Week 12	15	5.7	5.21	14	6.8	9.41			
MSPSS	Baseline	15	56.7	21.71	14	48.1	13.14	-1.23	-11.64 to 9.18	0.817
	Week 12	15	58.9	19.85	14	52.9	14.82			

*Crosswalk to EQ-5D-3L UK tariff
Bold has been used to highlight results that were statistically significant at the α=0.05 level
Model covariates: Baseline version of outcome, Age, Diagnosis of depressive disorder and Time since trauma (in months).
Difference in Means between Randomisation arms: Delay is the reference.

5.5. Table 8 demonstrates the absence of statistically significant differences between the immediate and delayed 3MDR groups at 26-week group with the exception of the ISI (in favour of the immediate treatment group) and the EQ-5D-5L (in favour of the delayed treatment group).

Table 8: Primary and secondary outcome analyses for differences at Week 26

		Time point				
		Delay	Immediate			

		n	Mean	SD	n	Mean	SD	Mean Diff	95% Confidence Interval	P-value
CAPS-5	Baseline	19	48.8	5.63	17	46.9	8.37	-2.71	-13.34 to 7.92	0.62
	Week 26	19	29.5	17.67	17	30.8	18.30			
PCL-5	Baseline	17	61.9	9.74	12	58.5	5.44	-13.28	-27.51 to 0.95	0.07
	Week 26	17	48.2	17.90	12	39.4	22.80			
WSAS	Baseline	17	25.6	8.45	12	26.8	5.65	-2.27	-10.36 to 5.81	0.58
	Week 26	17	17.7	11.56	12	18.8	13.17			
PHQ-9	Baseline	17	17.4	5.82	13	16.7	5.15	-1.21	-5.68 to 3.26	0.60
	Week 26	17	14.3	6.01	13	14.1	8.26			
GAD-7	Baseline	17	16.4	4.84	12	14.8	3.07	0.07	-4.45 to 4.58	0.98
	Week 26	17	13.3	5.64	12	12.3	6.83			
ISI	Baseline	17	20.2	5.54	12	21.4	4.56	**-5.88**	**-10.21 to -1.56**	**0.008**
	Week 26	17	19.6	6.00	12	14.7	9.00			
EQ-5D-5L*	Baseline	17	0.41	0.29	12	0.60	0.27	**-0.24**	**-0.45 to -0.03**	**0.03**
	Week 26	17	0.51	0.27	12	0.47	0.41			
AUDIT-O	Baseline	17	7.5	5.26	12	6.8	10.23	-1.14	-5.66 to 3.39	0.62
	Week 26	17	8.2	8.56	12	5.8	9.50			
MSPSS	Baseline	17	54.2	21.14	12	47.9	13.41	8.29	-4.30 to 20.88	0.20
	Week 26	17	55.8	19.20	12	54.3	20.89			

*Crosswalk to EQ-5D-3L UK tariff
Bold has been used to highlight results that were statistically significant at the α=0.05 level
Model covariates: Baseline version of outcome, Age, Diagnosis of depressive disorder and Time since trauma (in months).
Difference in Means between Randomisation arms: Delay is the reference.

5.6. Table 9 demonstrates the presence of a statistically significant difference between the immediate and delayed 3MDR groups at 12 weeks but not at 26 weeks for CAPS-5 sensitivity analyses with multiple imputation for differences at Week 12 and 26.

Table 9: CAPS-5 sensitivity analyses with multiple imputation for differences at Week 12 and 26

		Difference in Means	95% Confidence Interval	p-value
CAPS-5	Week 12	**-9.065**	**-16.678 to -1.451**	**0.020**
	Week 26	-3.180	-13.985 to 7.625	0.563

Imputed using model covariates: Randomised arm, Baseline CAPS-5, Age, Diagnosis of depressive disorder and Time since trauma (in months). In proportion with the number of cases missing the outcome, 17 imputations are used for Week 12 and 15 imputations are used for Week 26.
Difference in Means between Randomisation arms: Delay is the reference.
Bold has been used to highlight results that were statistically significant at the α=0.05 level

5.7. Figure 5 illustrates the relative reductions in CAPS scores over time between those randomised to immediate 3MDR and those to delayed 3MDR. Figure 6 shows the means and standard deviations of CAPS-5 at each time point for the two randomisation arms. The differences between the two groups can be seen at 12 weeks (when only the immediate treatment group had received 3MDR) along with the close alignment of the two groups at baseline and 26 weeks (when both groups have received 3MDR).

Figure 5: Mean CAPS-5 over time by Randomisation arm

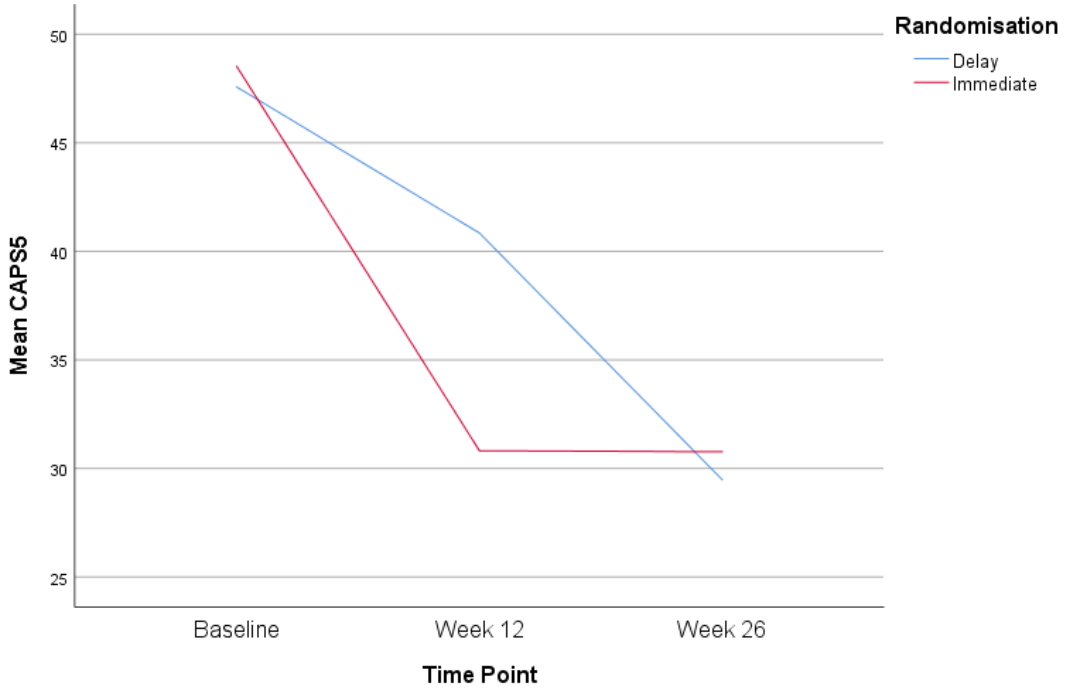
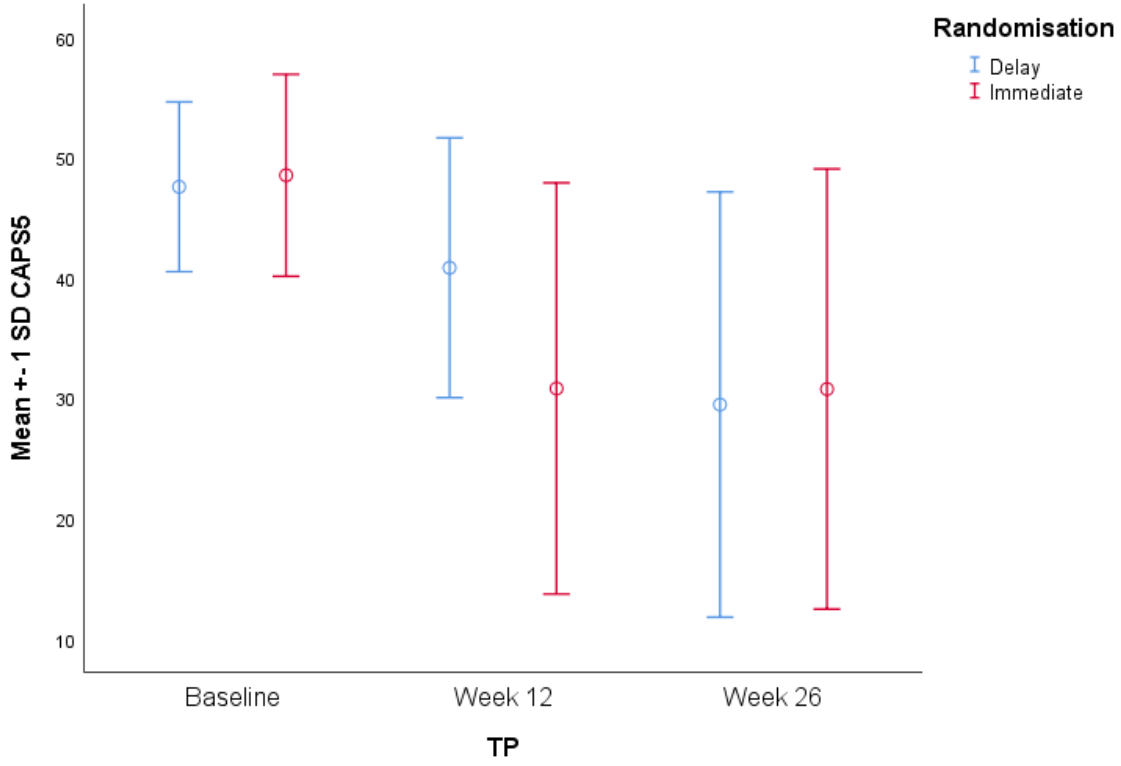


Figure 6: Means and Standard Deviations of CAPS-5 over time by Randomisation arm



5.8. Figures 7 and 8 highlight the different trajectories of CAPS-5 change between individual participants. The variation between individuals can be seen. The majority of participants experienced a reduction in PTSD symptoms between their assessments immediately pre and immediately post when they were due to receive 3MDR. Some appeared to experience no discernible change and some a small increase in symptoms although it should be noted that not all participants attended for their 3MDR sessions as planned. It is also notable that some participants' symptoms continued to reduce after 3MDR ended, some experienced no real change and some experienced an increase in their symptoms.

Figure 7: CAPS-5 individual trajectories for the Delay arm

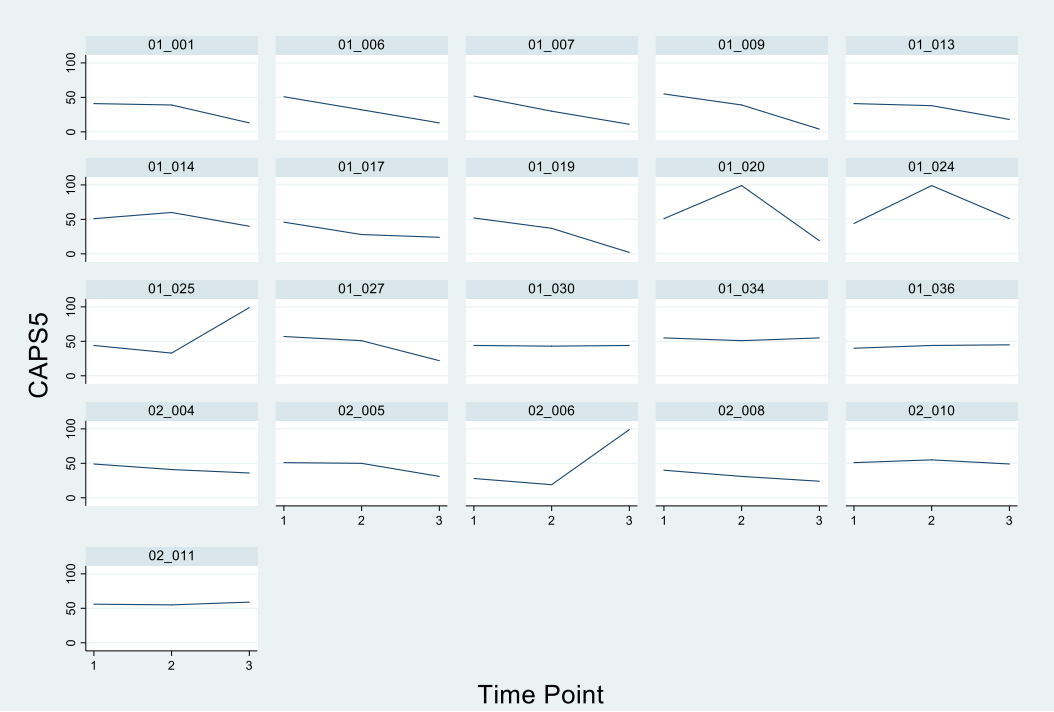
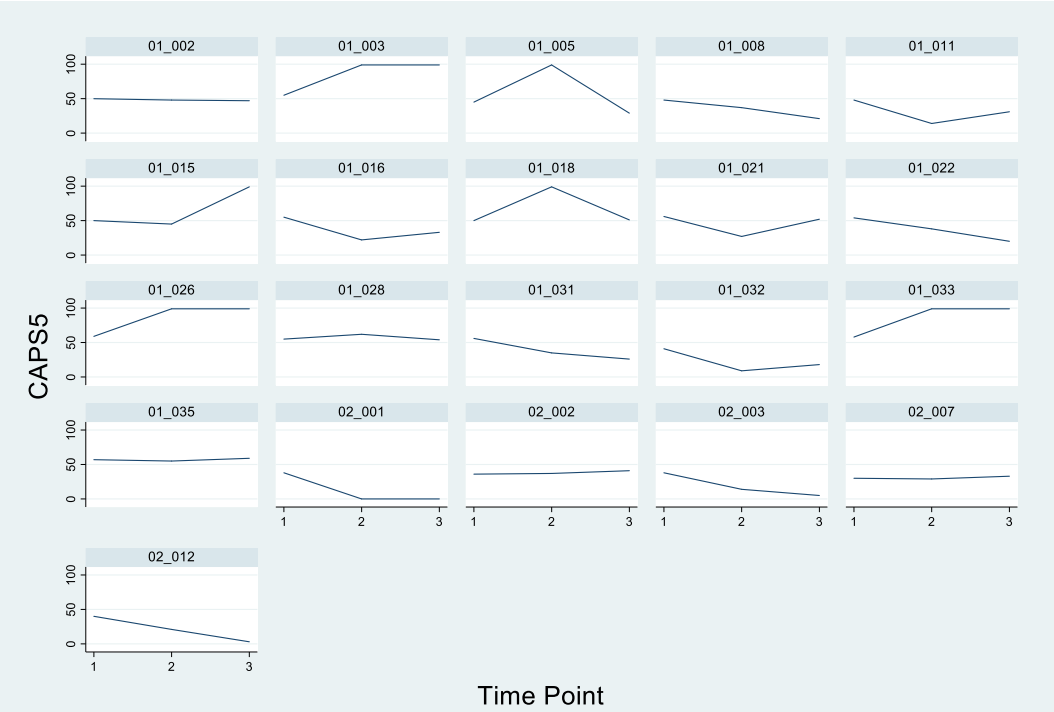


Figure 8: CAPS-5 individual trajectories for the Immediate arm



6. Qualitative Data Generation and Analysis

6.1. An important study objective was to examine the experiences and views of people both receiving, and providing, 3MDR with a view to learning about the therapy's acceptability and feasibility in addition to its clinical outcomes. Data reported on in this part of the project report were generated using one-to-one semi-structured interviews, these being a key method used in the evaluation of complex interventions[44].

Sampling

6.2. Eleven participants who had no further 3MDR therapy sessions planned participated in a single interview, from a total of 14 who received invitations. Participants were purposively selected on an ongoing basis as the trial progressed, via discussions at monthly trial management group meetings not involving members of the team involved in rating the primary quantitative outcome. To learn from as wide a range of veterans as possible, individuals with a range of characteristics and experiences were recruited, with criteria decided at the project's outset.

6.3. Participants were included:

- who, judging by observations in the 3MDR clinic, had accommodated well to the therapy (e.g., participating in all sessions, voicing hope about being helped);
- who, judging by observations in the clinic, had accommodated poorly to the therapy (e.g., missing sessions, voicing anxieties);
- from both the immediate treatment and the waiting list arms of the trial;
- from the treatment lists of all 3MDR-providing therapists;
- across a wide age range;
- with a range of lengths of time since trauma experiences, and of previous experiences of different therapies;
- who had dropped out of treatment.

6.4. Initial invitations to participate in a qualitative interview were sent out following the completion of therapy. Participants who consented to participate following receipt of an information sheet approved by the NHS Research Ethics Committee were interviewed by a researcher who had no involvement in the provision of therapy and no prior relationship with participants. Interviews were conducted between November 2017 and October 2018 on dates, at times and in places convenient for each participant; most were conducted in veterans' homes, with some conducted at NHS or University premises.

6.5. The therapists were invited to take part in a single semi-structured interview once they had completed all their 3MDR treatment sessions. The therapist interviews were conducted by the same researcher, with all taking place in therapists' workplaces. The researcher with responsibility for the management of the 3MDR clinic and for the operation of the equipment during treatment (and who therefore had experience of working with all therapists and of supporting therapy with multiple veterans) was also interviewed. Interviews with therapists and the researcher took place between August 2018 and August 2019.

Interview schedules, audio-recording and transcribing

6.6. Semi-structured interview schedules were developed in advance through whole-team discussion and approved for use by the relevant NHS REC. Interviews were conversational, allowing space to follow lines of discussion as they arose.

6.7. Broadly, veterans were invited to talk about:

- initial thoughts and expectations at the start of therapy, including discussions with family and friends and the selection of images and music;
- first impressions of the clinic and experiences of 3MDR being explained;
- selections of images and music within and across sessions, and experiences and views of therapy sessions over time;
- factors helping continuation with therapy;
- the integration of 3MDR into everyday life;
- discussions (if any) with family or friends about 3MDR experiences;
- the extent to which expectations were, or were not, fulfilled;
- helpful and unhelpful aspects of 3MDR, and views on continuation if available;
- views on recommending 3MDR to others with similar experiences;
- in the case of those who had dropped out, factors hindering continuation;
- how 3MDR might be organised or delivered differently.

6.8. The therapists and the researcher were invited to talk about:

- initial thoughts and expectations at the start of therapy, including expectations regarding effectiveness;
- first impressions of the clinic and experiences of 3MDR being explained;
- preparation and support for becoming a 3MDR therapist, including training and supervision;
- working with veterans to select images and music, and experiences and views of therapy sessions over time;
- attending to veterans during therapy and working with the trial protocol;
- factors helping and/or hindering veterans' continuation with therapy;
- the extent to which expectations were, or were not, fulfilled;
- suggestions for how 3MDR might be organised or delivered differently.

6.9. With each participant's agreement all interviews were digitally audio-recorded, before being transcribed verbatim.

Characteristics of participants

6.10. Tables 10 and 11 below summarise the characteristics of interview participants and the length of each interview conducted. In the case of veterans (Table 10) basic demographic information is included along with information on treatment arm and reasons for selection.

Table 10: Veterans taking part in interviews				
Name*	**Age at interview**	**Arm of study**	**Reason for sampling**	**Length of interview (minutes)**
Dai	67	Waiting list	First veteran into trial, traumas dating from the 1970s	63
Rhys	39	Immediate	First veteran to have 3MDR, traumas from the 2000s	33
Callum	49	Immediate	Trauma not service-related	25
Terry	59	Waiting list	Multiple traumas, developmental and learning problems	94
Gethin	43	Immediate	Reported major benefits before end of scheduled 3MDR sessions, and early discontinuation	35
Chris	45	Waiting list	Strong emotional responses to therapy	47
Duncan	56	Waiting list	Reported unanticipated physical health improvements	31
Berwyn	62	Immediate	Dropped out early	76
Harry	53	Waiting list	Co-existing physical health problems and disabilities, financial issues	53
Charlie	56	Immediate	Discontinued before final treatment session, as could not find photos evoking strong-enough emotions	48
Tony	57	Immediate	Dropped out early	43
*Pseudonyms have been used to preserve anonymity				

Table 11: Therapists and project worker taking part in interviews		
Name*	**Role**	**Length of interview (minutes)**
Mary	Therapist	79
Alan	Therapist	37
Pete	Therapist	80
Julie	Therapist	82
Mark	Therapist	44
Amanda	Therapist	55
Joanne	Project worker	60
*Pseudonyms have been used, and genders changed in some cases to preserve anonymity		

Data management and analysis

6.11. Transcripts were read in full, and all spoken names of people removed and replaced with pseudonyms to help preserve anonymity. Queries from the transcriber over accuracy, and missing segments, were checked against the original audio-recordings and corrected where possible. All accurate and anonymised transcripts were then imported into version 12 of the qualitative data analysis software package NVivo[41] in preparation for analysis.

6.12. The meaningful transformation of qualitative data involves active and engaged interpretation[45], and it is in this sense that analytic ideas or themes never simply 'emerge'[46] With the intention of revealing the fullest range of views and experiences interview data were interrogated for recurring, thematic patterns found across different transcripts as well as for singularities[47], or what Silverman[48] refers to as 'deviant cases'. This process followed the steps described by Braun and Clarke[42], and was conducted by the researcher who had conducted the interviews. It commenced with a process of familiarisation, involving the reading of transcripts and the noting of initial ideas accomplished at the same time as the transcripts were anonymised. Initial codes, created from close readings of the transcripts, were attached to analytically interesting segments of data using NVivo's 'nodes' function. Examples of codes were 'selecting images', 'anticipating first visit to clinic' and 'experience of walking'. Reflecting their shared, broader, meanings codes were then grouped together into candidate themes. These were then reviewed, refined and organised into a final set of named themes and sub-themes using NVivo's hierarchical node function and written up as a report for discussion amongst the research team. A final version was then incorporated into this larger report.

6.13. Findings are presented in three sections. The first reports on an analysis of interview data generated with veterans, and the second on an analysis of interview data generated with therapists and the researcher. The third compares and contrasts, and draws conclusions.

Findings: veterans' interviews

6.14. Findings arising from an analysis of interviews conducted with veterans are organised under four themes: *Motivations and expectations; Preparing, planning and first impressions; Progressing, immersing and incorporating; Reflecting and recommending.*

Motivations and expectations

6.15. Veterans described two main, initial motivations for taking part in the trial: a wish to better manage their troubling experiences of PTSD, and a desire to be part of something which might help others in the future. Dai, who had lived with the consequences of trauma since the 1970s, said how he had '*jumped at the chance*' whilst Rhys, the youngest of the veterans interviewed, said how he was:

> *[…] of a mind that I'm willing to try anything if it's going to improve my life or the lives of my family, because I'm quite aware that I've been under treatment for quite a while now, various types of treatment, and that's why when my therapist said 'look we've got this', I jumped at the chance, like I said I don't really care what it is, if it's going to improve me slightly, you know, then that's what I'm about.* [Rhys, veteran]

6.16. For Berwyn, who dropped out of the study,, part of his early motivation to join was to contribute to efforts to help others in the future:

> *I'm more than happy to take part in trials and experiments, whatever you like to call it, because my thoughts are not for myself but by taking part others might benefit if the whatever you're looking at has got positive outcomes.* [Berwyn, veteran]

Preparing, planning and first impressions

6.17. Having been introduced to 3MDR by their existing therapists, veterans engaged in a variety of strategies to find out more about what the treatment might involve with some discussing potential participation with family and friends. For six of the veterans taking part in post-therapy interviews, material found via internet searching or signposted from the participant information sheet proved useful, and for some this had a high impact. Harry described the immediate appeal of a 3MDR YouTube video clip:

> *[…] it [the YouTube clip] wasn't very long, it was only a few minutes and I was taken aback by it and I thought, 'well this is, from one minute sitting in the classroom, you know, writing things down, to what your thoughts are and then the next when you're on a treadmill and you're walking through a war zone' and I thought you know, instantly I thought, wow, that's for me personally.* [Harry, veteran]

6.18. The prospect of participating in 3MDR also triggered apprehension, and most (but not all) veterans talked with partners, family members, friends, fellow veterans and/or support workers to inform their decisions on taking part. Preparing and planning for therapy then involved the task of selecting images and music for use in 3MDR sessions. Other than for one veteran, selecting music was a less difficult task than choosing images. Some searched through personal collections of photographs they had taken, or which had been shared by friends and former colleagues, whilst others turned to the internet. This essential pre-therapy work was variously done alone, in discussion with partners, or with support from therapists, and was typically described as challenging. Dai's search for images associated with his historic trauma involved seeking out information online in ways he had never done before, with this proving a tough task even with support from his wife:

> *[…] the two incidents, three incidents, that caused most of the problems I managed to get sort of, you look at a specific newspaper and there are other papers you can get onto their websites, you can find then those things that I've never found before. I wouldn't have tracked them down and obviously the one incident, I managed to get quite a bit of information on, pictures and I was quite surprised at what was out there, you know, and it was quite a traumatic experience for me just getting these pictures […].* [Dai, veteran]

6.19. For Berwyn, the work of selecting images without being in the company of a therapist whilst doing so was particularly difficult:

> *I say the big thing that went wrong is I took it [searching for images] very seriously and I spent quite some time selecting images that would trigger me, so, you know, if you're asked to select something that's going to trigger you, what's going to happen? You're going to be triggered, okay?* [Berwyn, veteran]

6.20. Initial visits to the 3MDR clinic, which for numbers of participants meant travelling significant distances and navigating around a large and unfamiliar hospital site, provoked some strong reactions. Dai and Harry described the treadmill and screen set-up as akin to '*NASA*', whilst Gethin likened it to a '*spaceship*'.

Progressing, immersing and incorporating

6.21. Having selected images and music, and having made initial visits to the clinic, all but one of the veterans interviewed progressed to participating in 3MDR therapy sessions with seven of these completing a full course of treatment as per the trial protocol. In order to maximise use of clinic space and time, therapists providing 3MDR were not necessarily known to veterans. Responses to engaging in therapy provided by an unfamiliar therapist varied. For Rhys, learning about 3MDR from a trusted therapist was important; the fact that this same therapist then went on to become his trial therapist he also saw as a benefit. For Charlie, however, learning about 3MDR from a familiar therapist was important, but in his view receiving therapy provided by a new therapist was acceptable because '*you don't judge a book by the cover*'. In Gethin's case, his previously unknown therapist demonstrated his trustworthiness and a lack of familiarity was not perceived as a problem:

> *He made me felt comfortable enough for me to have trust in him, and he's an outstanding bloke. I couldn't ask for a better person to actually do it, do that 3MDR like, and when he stood next to me on the treadmill talking me through these pictures he has that sound, that voice, that reminds me of my father as such, and that's why I trusted him even though when I'm looking at that screen, and he says to me, 'walk into the picture', he's there with me, and if it wasn't for him then I don't think I could, he's a good bloke.* [Gethin, veteran]

6.22. In Berwyn's case, however, the combination of having to travel a long distance to the clinic to meet with an unfamiliar therapist to whom personal, distressing, information would be disclosed proved particularly difficult:

> *[…] if it [the therapy environment] can't be the home then somewhere you're familiar with, and also to have somebody who's known to you. Because I mean the questions you're asking is, you know, 'when was the last time you committed or tried to commit suicide, when was the last time you self-harmed?', well if you've never met anyone before you know, are you going to reveal all?* [Berwyn, veteran]

6.23. Within the group of ten interviewees having therapy, the experience overall proved both powerful and immersive, as these multiple data extracts illustrate:

> *[…] it was quite overwhelming, the whole 3D experience on the treadmill, because you do get sucked into it when you're there and the screen is virtually surrounding you, yeah, you sort of get sucked into the, you're in that picture.* [Callum, veteran]

> *I used to walk out of there and it was like feeling as if you were still there, you were still there, like talking to you now, it's like stepping back 35 years you know and I'm reliving what I'd gone through […].* [Terry, veteran]

> *I think it was a bit of everything, you know, and I couldn't believe how good the walking into the situations, you know, it was like, it was really, once you got used to it, it's like being in the real thing […].* [Duncan, veteran]

6.24. 3MDR required the selection of seven images for each individual therapy session, with a number of approaches to image choice and sequencing being described. Chris described how, across his treatment sessions, he had worked with his therapist to select images he knew would provoke a strong response, and which also helped to tell a specific traumatic story:

> *[…] it worked better with the story because some of the pictures told a story of, like a suicide attack when you're, you know, when you're just in the grass and then you see people and there was a, to me it was not necessarily grading [each individual image for levels of distress] how bad they were but for me I wanted to see a story in front of me, so there were pictures which have different levels of, you know, when I rated them right at the start but the pictures, for me it was important for them to show a story in my thing, which we worked on because I could play it back in my head a bit better as opposed to just random pictures, do you know what I mean, around the thing.* [Chris, veteran]

6.25. Duncan talked of discarding images as they became '*easier*' to view and to describe, Harry described beginning sessions with the most emotionally charged images whilst Rhys spoke of his most laden photographs being used at the end of his individual treatments. Terry specifically negotiated with his therapist for his seven session-specific images to be displayed in random order, as a solution to what he saw as the problem of anticipating and thinking ahead to the next image instead of focusing on what was currently on view.

6.26. Amongst veterans were some who described particularly significant moments or treatment days. With his therapist's help Charlie found an online document, previously unknown to him, which provided essential factual information about his traumatic event and which therefore featured as a key image in his therapy sessions. Duncan gave this vivid account of a process of change:

> *I still believe today that I'd found the answer of what was causing me all the trauma and then it was just a case then of just facing up to it and putting it away, you know. I found that I'd been living, I don't know, living in the past, I hadn't moved on but it wasn't, that, it must have been a habit I would say, of mine, because it was happening all through things, through all my life and then all of a sudden it was like just the penny dropped.* [Duncan, veteran]

6.27. For many, 3MDR was hard work and exerted effects felt long after the conclusion of a session. Harry said how the therapy left him feeling '*mentally drained, really, really drained, exhausted, as though I done a marathon or something*' whilst Rhys said how it took more out of him '*than any other treatment I've ever had*'. Along with two other veterans Rhys described the experience of poor concentration and attention, in his case both immediately after therapy and in the days following. Powerful responses to 3MDR also included, for some, an initial worsening of experiences. Terry's wife was present during parts of his interview, and said how her husband would wake up at night, sweating and with nightmares.

6.28. In the face of 3MDR being an enveloping, demanding and potentially exhausting therapy those who completed their planned treatment spoke of a number of factors helping them along the way. Over half of those interviewed said how they talked with family members, partners, friends and/or support workers about their participation and

for many this made a difference. Around half of the interviewed veterans also spoke of honouring their commitments to taking part being a factor in encouraging them to continue to the end, and for some this linked to the idea of being part of a project which might benefit others. Dai, Chris, Callum and Harry all described themselves as '*determined*' or '*committed*', and for Rhys continuing to the end was connected to having been in the military:

> Interviewer: *Did you ever think about stopping?*
>
> Rhys: *I don't quit anything. I'm still very military-minded, you know, I've always been quite set in my way, I don't like letting people down so once I start something I'll see it through. I mean, don't get me wrong I found it pretty horrendous at times but again I've gone through so much, you know, I know if you just keep pushing through you eventually get to the end, you know, it doesn't mean I wasn't happy to finish the treatment, I was, because it really took a lot out of me, but like I say there was no way I was going to stop.* [Rhys, veteran]

6.29. Practical effort and planning were required by veterans to support their commitments to weekly therapy. Some used public transport, others drove or were driven and amongst those who were in employment flexible working arrangements (sometimes negotiated with sympathetic employers, as in Chris' case) helped.

6.30. Differing explanations were given for discontinuing by the three veterans interviewed who, having commenced therapy, then ended their participation early. Alone amongst the 11 veteran interviewees, Gethin described how his decision (negotiated with his therapist) to end his therapy before reaching his sixth scheduled session was because 'everything' (in his words) had changed for the better, and he could imagine no further benefits accruing:

> *It's like when you look at a tree in the distance, this is how I can explain it, when you look at a tree in the distance without glasses on, it's all blurry and fuzzy and then when you put your glasses on, and look at that tree, it's more detailed, you can picture it, you can clearly picture it, that's what my life is like.* [Gethin, veteran]

6.31. Tony had difficulties finding images associated with two, separate, traumatic events over three decades previously, and said how initially these 'didn't send me right back to where I was so I think the actual feeling when I was given the treatment, I didn't feel that I was there, you know, fully into what I was doing'. Tony's third therapy session, however, was followed by sleep disturbance and significant distress in the context of psychosocial stressors at home. His decision to withdraw, ahead of a re-referral back to his usual trauma therapist, he explained by describing himself as not suitable for 3MDR owing to the length of time since his traumas and their repeated character:

> *I felt I wasn't doing myself justice or the programme, I didn't think it was fair for your team to have me on board giving false, what I would say, readings, because I'm having issues not just the two [specific traumatic events], but, so to me I would say that maybe the treatment is geared towards somebody who's had treatment recently for their trauma rather than someone like myself who's an old dog and had too much you know?* [Tony, veteran]

6.32. Charlie concluded with a single session outstanding as he told his therapist he could not find images evoking strong-enough emotions, whilst Berwyn who dropped out described the challenges of travelling long distances to an unfamiliar clinic environment, having insufficient support during his selection of distressing pictures and not being able to work with images reflecting his particulartrauma.

Reflecting and recommending

6.33. All veteran interviews took place following the completion of final therapy sessions, and provided an opportunity for reflecting back on the experience overall and on offering suggestions for the future. Of the seven interviewed veterans who completed a whole course of therapy as per the trial protocol, five said they would have continued with further 3MDR sessions had they been available. A further veteran, Charlie, despite electing not to have a final session (telling his therapist he no longer had sufficiently evocative images) said he would have been open to additional therapy on the grounds that there should be no prescribed number of treatments in advance. Chris was particularly clear why he would have opted for more therapy, linking this to his sustained exposure to traumatic events over time:

> Interviewer: *Would you have had more if the option had been available?*
>
> Chris: *Absolutely, I think so, I wanted, I wanted as many sessions as it needed to be […] I think more sessions probably would have been useful, I think that I tried, I was to some extent like selecting pictures, I was almost a panic effect, what, I need this one, I need, this happened here and that happened there, this is affecting me.*
>
> *[…]*
>
> *[…] you know like I said, this is not an, it's not like an IED blast and an injured, and stuff, this is six and a half months of exposure to not very nice things and suicide attacks and all sorts of stuff and near misses so there was a lot of things going on.* [Chris, veteran]

6.34. Of the two veterans completing a course of therapy but saying they would not have opted to continue, Rhys said how he would have had more than six sessions had that been part of the initial offer, whilst Duncan spoke (in his words) of having 'had enough'.

6.35. All ten veterans who experienced therapy, including those who declined opportunities to complete the full course of 3MDR on offer, said that they had been helped. Gethin's account of '*everything*' being different is described above in the context of him discontinuing ahead of the end of his available sessions, whilst Dai described being able to '*handle situations a lot more now*'. Callum spoke of being less angry, and both Rhys and Chris talked of improvements in sleeping. Chris described this thus:

> *It was interesting, about session three it was like my brain was being rewired, it's very hard to describe it but there was something happening in my brain and I was feeling, I was feeling better, even though I got a bit upset now but that's, but something was happening in my brain and I was feeling better. It's very hard to put my hands on it but the result is I am sleeping, I am not getting half as upset, and my mood is generally good.* [Chris, veteran]

6.36. Harry said how others were describing him as being '*less on edge*', and Duncan (having previously described a process of change) talked of being a '*happier*' and a '*better*' person having concluded therapy. Charlie spoke of still living with PTSD but of knowing '*a little bit more now about myself, about my character than what I did prior*', whilst Terry described being troubled less by intrusive images. Tony (who discontinued his therapy in the context of a psychosocial crisis) said how:

> *I suppose in one respect it's done some good because I've been able to talk to my family, my wife, my son about what I experienced when I was in [name of place] , talk about maybe my job whereas I've never talked about that before but I had the feeling now I wanted to, to sort of get rid of that you know.* [Tony, veteran]

6.37. Many veterans also said how they would recommend 3MDR to others in a similar situation, but some added caveats about expecting the process to be difficult and not to expect miracle cures. For Charlie, waiting to learn of the longer-term outcomes from therapy was important, whilst Rhys said how he would tell people to expect '*hard work*' and to need '*strength of character*'.

6.38. Offered the opportunity to suggest how the organisation and provision of 3MDR might be changed, veterans volunteered a number of suggestions. Chris spoke of the value of following participants up over a full year, Charlie spoke of the importance of therapy being provided in a '*soft*' environment with '*trees, grass, where they [people having therapy] can, you know, walk*' and Terry recommended more immersive therapy via the use of moving, not static, images. Tony talked of the importance of out-of-hours support. For Berwyn, who made long journeys for his initial assessments but who did not then proceed to therapy, therapist continuity was important as was support in the selection of images and music. He also suggested 3MDR be provided in hospital settings with greater support therefore available.

Findings: therapists' and project worker interviews

6.39. Findings arising from an analysis of interviews conducted with therapists and project workers are also organised under four main themes: *Pushing the boundaries; Theory and practice; Sustaining and supporting; Reflecting and recommending*.

Pushing the boundaries

6.40. Therapists, all of whom were experienced and all bar one of whom worked specifically with veterans in their day-to-day jobs, described excitement at the prospect of joining the trial and of helping push the boundaries of psychological interventions. Mary said:

> *I suppose, what did I expect, to be part of something novel, something incredibly different, something that was the first to be trialled in Britain so I just thought, 'gosh this is going to be very interesting' and yes it's just something that I felt I just want to try this, I want to be part of it, yeah.* [Mary, therapist]

6.41. Alan anticipated 3MDR as an extension of EMDR (Eye Movement Desensitisation and Reprocessing) therapy, and was struck when first visiting the clinic how '*fancy and expensive*' the set-up appeared. Mark was similarly impressed with the equipment on

show, and looked forward to testing a therapy for people for whom existing NICE-recommended therapies had run their course. The opportunity to practise as a '*coach*' and to be part of something beyond the routine appealed to Pete.

6.42. Therapists were open to the potential effectiveness of 3MDR, but also cautious given its experimental nature and the plan to test it with veterans known to be resistant to existing treatments. As preparation ahead of recruiting veterans into the study all therapists took part in a series of dedicated training sessions delivered by the original 3MDR development team: an initial two-day event in October 2016, followed by two single days in December 2016 and March 2017 respectively. Training emphasised practical 3MDR skills, via observing videos and modelling the therapy being provided followed by direct practice with colleagues taking the part of veterans living with trauma.

6.43. Whilst therapists universally appreciated the opportunity to observe, and then practise, 3MDR their views and experiences of how the underpinning theory was presented and then understood were more nuanced. The emphasis on practical skills development and use of the therapy protocol placed a premium on learning about 3MDR's principles through reading recommended papers. Responses to theory reflected, to some degree, therapists' prior orientation and core training. Alan saw 3MDR as sharing a conceptual foundation with EMDR (as described above), as did Amanda. Julie emphasised the importance of being exposed to trauma via walking, and of then cognitively processing during the display of the numbered red balls. For her, having a cognitive behavioural training sensitised her to an expectation that the post-treadmill debriefing component of each session might be a more significant part of therapy than the 3MDR protocol suggested:

> *I remember when they were doing part of, obviously part of the training was to do the debrief after a session which I didn't understand a huge amount really because obviously being sort of like the core piece of therapeutic work that I would do is all this cognitive behavioural therapy so I'd always be quite cognitive in what I know, what's going on all the time. In terms of thinking and impressions and things like that and there was none of that, you know, seriously it felt completely alien really to go into a room with someone after doing something like that and not kind of pursue what, you know in terms of what they were really, what were their thoughts you know, it's up to me to do that but not in the depth you would in the usual CBT session so that felt quite alien really to not delve so much [...].* [Julie, therapist]

6.44. Mark spoke of his training in behavioural psychotherapy and also highlighted the premium 3MDR placed on exposure. For Mark, '*reconsolidating*' was also an important component of 3MDR, which he linked to '*coming back into the room*'. However, Pete (with a primary background in cognitive therapy) talked of wanting to better understand the processes of change triggered by therapy and how the underpinning language and theory of 3MDR was never entirely accommodated within his more cognitive frame of reference:

> *I think they [the original developers of 3MDR] call it 'reconsolidation', there's different kind of language and I think that feels important [...] but actually I think it's those, yeah, I never quite understood the rationale for it if I'm honest, this 'reconsolidation', I think they used it, 'reconsolidation', and it's not a phrase that I've ever used and I can get my head around 'habituation' or I can get my head*

around 'cognitive change' but I never quite knew what they were meaning. [Pete, therapist]

Theory and practice

6.45. Therapists held a range of views on the relative significance of therapeutic continuity, just as did veterans. Mary, who said that as a minimum she needed access to the clinical notes of people she was treating, valued her prior relationship with veterans from her employing health board and speculated on the possible importance of continuity from the perspective of veterans. Julie offered the view that, whilst some veterans might have preferred a familiar therapist (or even, might only have joined the study because of a familiar therapist's recommendation), others might have welcomed the opportunity for a fresh start with someone new. Amanda spoke of the value of the initial pre-therapy assessment as an opportunity to begin building trust between therapist and patient. With regards to not knowing veterans in advance, Alan said how:

> *I thought it would have made more of a difference than it actually did, it didn't make a difference. As long as you can create a very particular relationship with someone, as you can connect with them, it can instil a sense of, I don't know quite what the word to use is, 'we can do this'.* [Alan, therapist]

6.46. Mark suggested that in 3MDR the emphasis on work being done by patients, including the act of walking, meant there was less therapist input than in other therapies resulting in the traditionally understood therapeutic relationship being less important.

6.47. Therapists' experiences of supporting veterans to select images and music, including initial banks of pictures and then the selection and ordering of these at the start of individual sessions, varied. Examples were given of veterans arriving for their first meetings having gathered, entirely as requested, as many as 20 pictures whilst in other cases therapists spoke of selections having to be done together using internet search engines. Across sessions therapists spoke of swapping images out and replacing them with new ones, reflecting veterans' recordings of subjective with Amanda talking of paying particular attention to images which were being avoided. Within sessions, the ordering of images was described as an important, collaborative activity between therapists and veterans with two major considerations typically under consideration: first, the chronology, or narrative, told through the images and, second, how 'hot' or 'cool' each image was. Mark described his way of ordering thus:

> *Yeah, so often I think from my [perspective], it made sense to me and participants to have it chronological so there would be a narrative so it would be where this photo fits with, and, you know, he would often say, 'no it kind of goes that way because that's how it unfolded over my six months', and yes so I very much put the participant in control of where the photos went.* [Mark, therapist]

6.48. For Pete, the idea of exposing veterans to increasingly distressing images within an individual session implied building:

> *[…] on that language of hierarchy, exposure, habituation, all that sort of thing and actually for this, I mean horrific traumas some of them, horrific, and I know all of them really, I think we can do better than that, I do think we can do better than that […].* [Pete, therapist]

6.49. '*Doing better*', for Pete, meant ordering images to reflect storylines:

> *I think quite quickly it became clear that actually doing it thematically or chronologically was easier.* [Pete, therapist]

6.50. Amanda spoke of not being '*overly analytical with them [veterans] about their choice of photographs*', in favour of attending to what happened on the treadmill whilst specific therapist innovations included the idea of closing the very final session with a positive, rather than a negative, picture, this being a practice described by Mary.

6.51. As providers of an intervention being tested in experimental conditions therapists were aware of the importance of adhering to the parameters set by the trial. Joanne, with responsibility for the technology, observed that her and therapists' emphasis on clear organisation and clinic scheduling was important to veterans. Training for therapists involved working with a typed protocol, held on a clipboard, but therapists made efforts to memorise the key components and to develop their expertise in order to become more natural in their provision. Mary, Pete and Mark talked of therapy becoming less manualised and more natural over time, with Mark adding that via supervision with members of the 3MDR originating team, he and others were led to the observation that the treatment protocol is:

> *[…] more of a guideline, a guidance and actually you can go off-piste and delve into your own theoretical background where you're comfortable, and so if you're a very cognitive type therapist which some of us are they would have fallen back on their cognitive therapy protocols that they're familiar with.* [Mark, therapist]

6.52. During therapy sessions, therapists had multiple tasks to perform including communicating with both the technical member of the team operating the clinic's equipment and with each veteran during his time on the treadmill. This was skilled work, requiring accurate physical positioning to the left of the veteran in order to observe, listen and talk but also to avoid casting shadows on the projection screen. Session management required attention also be paid to timing. Well-placed to observe variability between practitioners given that her role involved being present for every 3MDR treatment session, Joanne described differing approaches to therapists' organisation of time and their interactional style.

Sustaining and supporting

6.53. Therapists and Joanne (the technical project team member) spoke of factors sustaining and supporting veterans through courses of treatment, including the clear structure offered by 3MDR and good clinic organisation. Echoing veterans' accounts, therapists also spoke of the importance of positive, helpful relationships even where no prior continuity of care existed. Alan talked of the importance of veterans having hope, and of being able to trust therapists able to stand alongside them in non-judgmental fashion even during the display of deeply distressing images. Consistent, trusting, relationships between veterans and the technical member of the team operating the 3MDR equipment were also seen as crucially important. Partners, families and friends were also talked about, with one example being given of a veteran whose journey to the clinic was always in the company of his father who then remained in the room during each therapy session. Julie observed that people who dropped out, in her experience,

were experiencing psychosocial stressors and that enlisting support from allies outside of sessions might have made a difference:

> *[…] the people who didn't do well, like I said they were, there was stuff going on [at home] and I swear there was something about selection that would have helped. […] the nature of the people who would have gone for that type of therapy wouldn't have been well anyway, they wouldn't have been settled anyway so it's a really hard thing to kind of, you can't really stipulate that they have to, you know, have close networks and people supporting them but I think had there have been some kind of knowledge maybe among family members or close friends who could have supported that person in doing it […].* [Julie, therapist]

6.54. Stressors associated with personal relationships, housing and employment were all seen as factors undermining veterans' capacity to sustain their involvement in the trial along with breaks in the weekly rhythm of therapy.

Reflecting and recommending

6.55. Therapists were able to give examples of veterans they believed had been helped by 3MDR, and all spoke of the therapy's powerful effects. Reflecting on having worked with a veteran she believed had made a speedy recovery, Amanda linked this to this person's specific trauma experience:

> *[…] my best outcome was with somebody who was, it was very clearly a single incident trauma and though they'd had a go at therapy before the trauma itself was a very discrete, very clear single incident trauma and so I do wonder whether this might be beneficial to a wider group of people because of the benefit, I think they only attended for about three sessions or something.* [Amanda, therapist]

Conversely, across the group examples were also given of participants who, in the views of therapists, had not been suitable for 3MDR and/or had not benefited. Recommendations for change were also made, and are detailed directly below.

6.56. Mary gave the case of a veteran she had previously known and treated who, in the context of 3MDR, was able to talk in detail for the first time about historic traumas and to direct the words 'I'm sorry' towards a highly charged image. Pete reflected on the importance of 'self-soothing', or the capacity to self-care, questioning whether all veterans were able to do this in the context of a therapy which sometimes invited disclosure of deeply traumatic events about which participants might feel high levels of guilt and shame. Pete, some of whose patients dropped out, spoke also of the importance of careful assessment, particularly of the reasons for potential participants' avoidance and the possible consequences of overwhelming patients through high levels of exposure.

6.57. Julie's observations on assessment for suitability included the importance of checking on potential participants' social circumstances, and the degree to which support was available, and noted also the difficulties some veterans had faced travelling long distances. Mary said that some veterans' difficulties were particularly complex and more time with them was needed. She also suggested that some veterans' subjective

distress may not have fallen because of secondary gains associated with being a veteran living with PTSD:

> *[…] could be around, secondary gain could be something that's kind of financial, there's a lot of this sort of MoD compensation, there's something in it, benefit to not being well, 'it is my identity, [if] I don't have PTSD, I don't know what I've got or who I am or where I would be'.* [Mary, therapist]

6.58. Mary, along with three other therapists and the member of the project team responsible for the technical operation of the equipment, spoke of how they would have welcomed the opportunity to offer veterans more treatment sessions. She talked of therapist 'flex':

> *I think just, well with this client group, I think if there's multiple trauma, they're treatment resistant, given the opportunity for clinician judgement to be able to extend because not everybody ran with that, I just think it would have given them a little bit more time and then you could perhaps argue, I don't know, lots of things about they've had a lot of time to sort of desensitise that exposure to these particular pictures, I don't know what the sort of final implications and theories of all that would be but I think as a therapist working with this client group with this complexity, knowing that they're treatment resistant, six just felt like I wanted to do, wanted to offer that little bit more.* [Mary, therapist]

6.59. Joanne suggested that the number of images per session was less important than the depth of talk elicited, but that '*there at least needs to be double*' the six treadmill sessions prescribed in the trial protocol. Alan, who also suggested greater flexibility over the number of pictures used in each session, spoke of wanting to spend longer working with some veterans who he could see were starting to be helped. Mark proposed treatment reviews complemented by up to a maximum of 12 sessions:

> *It would be nice to have some flexibility, so six sessions seems, has always to me seemed very short, that active treatment, I would have liked to have had a bit more flexibility so up to 12 but, so if four is enough, great, if six isn't enough let's have another couple, and review. If eight's not enough, okay, we'll do another two, if ten's not enough we've got another two but we do have to finish at twelve.* [Mark, therapist]

6.60. For Julie, however (one of whose additional suggestions was that 3MDR would be a helpful one-off adjunct within an eclectic course of therapy used to help people who are stuck and need to be 'unlocked'), six sessions was long enough to know if therapy was going to help. For Pete, six sessions placed an important boundary around a scarce resource, and for people not benefiting more would have made no difference.

6.67. Therapists and Joanne, the technical project worker, spoke of their empathy for veterans, and spoke of listening to descriptions of (and seeing images associated with) deeply troubling traumas. Opportunities to meet in clinical supervision, including with members of the 3MDR originating team, to share practice, discuss experiences and to both offer and receive support were scheduled but geographical distance meant that some of this activity was mediated via teleconferencing. A particularly valuable exercise for Julie which might have been done more frequently was viewing each other's videos of actually providing 3MDR.

Comparing, contrasting and concluding

6.68. Table 12 summarises findings across both groups of interviewees:

Table 12: Summary of findings	
VETERANS	
THEMES	
MOTIVATIONS AND EXPECTATIONS	• Managing personal experiences of PTSD • Helping others in the future
PREPARING, PLANNING AND FIRST IMPRESSIONS	• Learning about 3MDR and initial reactions • Discussing with family, friends and other veterans • Selecting images and music • Forming initial impressions of the clinic and first experiences
PROGRESSING, IMMERSING AND INCORPORATING	• Experiencing therapeutic continuity and discontinuity • Experiencing 3MDR as immersive and exhausting • Walking as therapy • Working with images • Having new experiences and memories • Noticing attention loss • Managing troubling symptoms • Experiencing psychosocial stressors • Getting support from family and friends • Honouring commitments • Incorporating therapy into day-to-day life
REFLECTING AND RECOMMENDING	• Continuing with 3MDR • Benefiting from therapy • Recommending to others • Suggesting changes
STAFF	
THEMES	
PUSHING THE BOUNDARIES	• Being part of something new • Being open-minded on effectiveness • Learning and practising
THEORY AND PRACTICE	• Understanding theory • Experiencing therapeutic continuity and discontinuity • Supporting images and music selections • Working with narratives and distress • Working with treatment protocols • Attending and communicating •
SUSTAINING AND SUPPORTING	• Organising and structuring

	• Fostering therapeutic alliances • Managing crises and fragmented therapy
REFLECTING AND RECOMMENDING	• Viewing 3MDR as helpful for some but not all • Assessing suitability for therapy • Proposing 'flex' over numbers of sessions • Recommending 3MDR as an adjunct • Having empathy • Participating in supervision

6.69. As Table 12 shows, interview data generated with both veterans and therapists reveal 3MDR to be a complex, powerful, intervention. For those engaging in 3MDR as a therapy it also involves much more than just the time spent on the treadmill. In its totality, it encompasses the initial time spent learning about what 3MDR involves, followed by locating images and music alone or in the company of others. It often includes travelling, and only then engaging in formal sessions including debriefing. It includes being supported by others, where necessary, outside of the clinic. Whilst 3MDR may therefore help some people in an acceptable and feasible manner, it may also not be the right therapy for everyone. Not known is the extent to which veterans' commitments to completing therapy for altruistic reasons might be replicated in civilian populations.

6.70. Therapist views on the importance of psychosocial stability and support outside of the clinic beyond formal treatment sessions may be important considerations in assessing suitability for 3MDR in the future, along with the capacity to self-care. A further observation from therapists related to the suitability of different types of trauma for 3MDR, with one suggestion being that it may be particularly beneficial for people with single-incident traumas. Veterans' descriptions of how challenging it was to select images and music point to the importance of offering specific support at this earliest stage. Therapeutic continuity may be helped by 3MDR being provided by therapists already known to patients, but views on the absolute importance of this were mixed. Trust between therapists and veterans was vitally important, but descriptions by both groups of this being built even where no pre-existing relationships existed suggest that longer term continuity may not be essential. The focus 3MDR has on walking, and its use of visual and auditory stimuli, may place less of a premium on the interpersonal than do other therapies, helping explain some therapists' use of the term 'coaching' to describe the work that they did.

6.71. Both groups of interviewees spoke of the surrounding context for the provision and receipt of 3MDR, including the location of the clinic and travel. Accurate information on parking arrangements and on how to find the clinic are examples of small actions able to make a difference, along with information on how 3MDR treatment sessions can cause a loss of attention and how being accompanied to and from therapy may be advisable. Out of hours support provided by usual NHS mental health services was important for some veterans, particularly those experiencing psychosocial crises, and therapists observed how some people dropping out included those whose personal lives were complex. Knowing that formal out of hours support was needed by some who received 3MDR

means that this need can be anticipated and planned for when 3MDR is provided in the future.

6.72. For therapists, clarity on the theory underpinning 3MDR was important, along with developing expertise in providing the therapy without having to over-rely on a printed protocol. Related to this was knowing how far 3MDR practices might be augmented through drawing on other bodies of skill and knowledge, such as might be deployed in the post-therapy debriefing component of sessions. Agreement on the parameters of practice may be an important consideration in the future, along with guidance relating to the number of treatments available to each participant and the use of images within individual sessions. With some exceptions there was broad agreement across all those interviewed that six sessions may not be enough, and that therapist 'flex' could usefully include making judgments on treatment duration up to a specified maximum. Therapists also spoke of the benefits of having latitude over the sequencing and, potentially, the number of images used in individual sessions. Descriptions of how pictures were ordered with regard to storylines and/or subjective units of distress suggest that further discussion on the boundaries of practice in this area would be valuable to therapists.

Personal Story

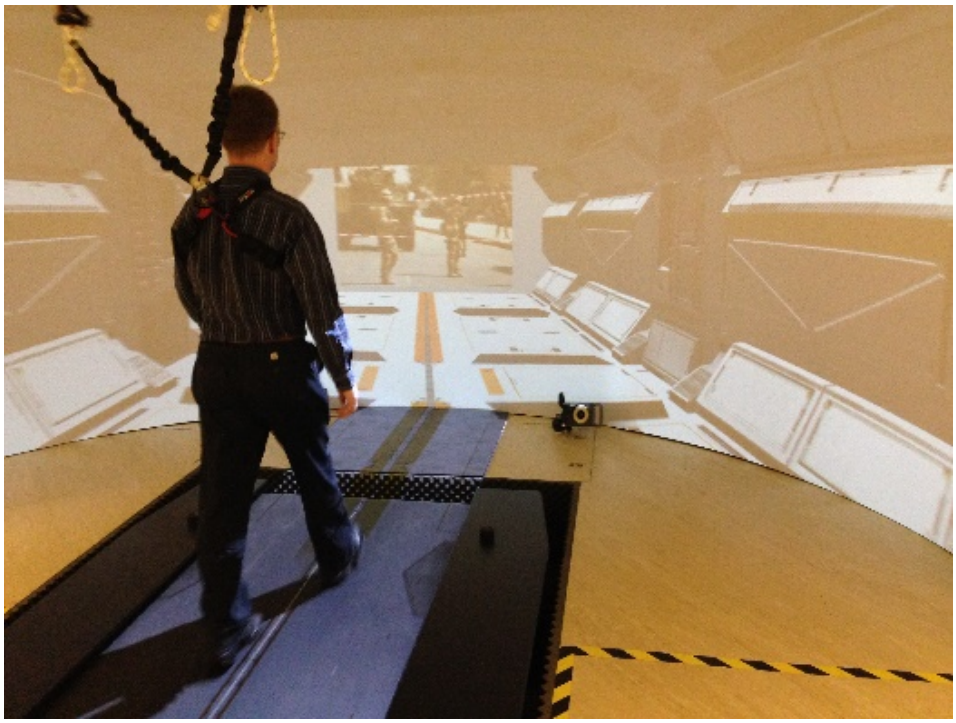
6.73. Matt Neve was a Senior Aircraftman in the RAF until being discharged in 2004. He was introduced to 3MDR by his Veterans NHS Wales therapist having already tried a number of other trauma-focused therapies. He has agreed to share his personal experiences of taking part in this study.
Matt said, “I had done other therapies like EMDR and CBT and they worked to a point. My therapist said, ‘Look, there’s this trial, I think you might be suitable: do you want to give it a go?’ 3MDR sounded ideal: it’s there, it’s in front of your face and you can’t avoid it”.

6.74. Reflecting on having taken part in the trial and having completed a course of 3MDR, Matt went on to say how, “It has helped. It has definitely helped with my daytime symptoms. My night-time issues are still there, unfortunately, but through 3MDR I’ve opened up. I talk a lot more about it, I’ve been more open and I’ve definitely benefited.” He added that: “3MDR is not a cure. It softens the symptoms but doesn’t get rid of them. A big part is accepting that, and learning how to manage.”
6.75. Matt also said how preparation for 3MDR and ongoing support outside of therapy sessions are important: “You need sessions before on grounding, and it’s important to be in the right frame of mind. Having a good support network is important. I started to struggle, and if it wasn’t for my wife, her parents and my therapist I might have stopped.” Matt is now using his experiences in a new role as public and patient member of the 3MDR research team, and is part of a group seeking additional funding to test 3MDR with non-military populations affected by trauma.

7. 3MDR Session Data Results

7.1. The School of Healthcare Sciences at Cardiff University has a Motek Gait Real-time Analysis Interactive Lab (GRAIL) system[49], which was used for implementation of this study. The Motek GRAIL system (Figure 1) uses an instrumented dual-belt treadmill, a motion-capture system and synchronized Virtual Reality (VR) environment, which comprises a 180° projection screen with 4 projectors and a surround sound system. The system is controlled by means of 6 computers in an integrated network using D-flow software. This is a control software suite that provides real-time data streams between many types of integrated hardware.

Figure 9: GRAIL system running the 3MDR protocol



7.2. The 3MDR module for treatment of PTSD was designed to run in D-flow and to record each session by collecting data from the equipment, particularly stepping behaviour, walking speed and distance from the instrumented treadmill. Participants fitted with a Zephyr™ BioHarness™ can be monitored for their physiological responses[50]. At the same time, Heart Rate (HR) and Breathing Rate (BR) were recorded throughout sessions together with information about 3MDR events such as phase transitions; repeated measurements of the score on the subjective units of distress (SUD) scale and the self-reported words used by participants to describe their feelings through all the phases of the session.

7.3. Digital data files were stored on computer and accessible for further analysis using Matlab software[51]; a high-level programming environment to explore and visualise data. This was used to calculate gait parameters through the phases from the treadmill speed and ground reaction force data. Matlab was used to create individual session profiles of the physiological (HR, BR), motor control (walking speed, cadence and step width variability), and SUD data together with the verbal response to the intervention.

Continuous data was obtained during all phases. Summary statistics were extracted to describe changes in these responses over time.

Experimental conditions

7.4. During the introductory 3MDR session, a dual task situation (emotional processing whilst walking) and a multi-task situation (emotional and cognitive processing, i.e. calling out numbers, whilst walking and eye tracking) were used. This was to explore the effect of attentional demand on the amount of short-term memory available for vivid and affect-laden memories. These data facilitated interpretation of observations from the 3MDR therapy sessions. The subsequent sessions were 3MDR therapy sessions up to a maximum of 6 with multiple phases as illustrated in table 12.

Table 12: Phases of 3MDR sessions

Dual task session – visit 1	Therapy session – visit 2 to 7
Warm up (blue zone) without music	Warm up (blue zone) with music
Transition phase (red zone)	Transition phase (red zone)
Tunnel through door 1	Tunnel through door 1
Tunnel through door 2	Tunnel through door 2
At the picture screen standing still	At the picture screen standing still
Neutral words Stroop test	Memories of the scene
Classic Stroop test	Associations of the scene
Emotional Stroop test	Bilateral stimulation phase

7.5. Before stepping onto the treadmill, participants were fitted with the BioHarness around their chest and the safety harness. On the treadmill, the safety harness was connected to ropes secured to the ceiling to protect against falling. During the warm up period, participants got a chance to settle into their stride and get used to the environment. The virtual scene was a blue coloured landscape meant to project calmness. During therapy sessions, self-selected music was played over a high-quality sound around system to take participants back to the time they were affected by their traumatic experiences. Once they were ready and focussed, the music was switched off and the scene transitioned to a red landscape with a road leading to a container-like building.

7.6. As participants arrived at the container-like building, the doors slid open automatically allowing entry into a high-tech looking corridor. At the end of the corridor was a second door which, again, automatically opened when approached. A second corridor was then revealed that led to a picture projected on a wall. This picture was self-selected by the participants and related to their traumatic experiences. Participants were asked to describe the details on the picture as they were walking towards it. Once they were up close, the scene remained static whilst the treadmill continued to run, allowing time to go through the different therapeutic steps.

7.7. First, participants were asked to say how they felt about the picture and the memories it evoked. They were also asked to say how they felt physically. Key words used by the participants were entered onto the screen as a reminder of their responses and to allow them to reflect on them and the feelings associated with them. This process was strongly supported and facilitated by interactions with the therapist to guide their

thoughts in a relevant direction. When the therapist felt that enough time had been spent reflecting on these words and feelings, the screen displayed a ball (bilateral stimulation) moving from left to right and back.

7.8. The participants were requested to track the ball with their eyes for 30 seconds and to call out the random numbers that appeared every time the ball was on the extreme end of its trajectory. After 30 seconds had elapsed the ball disappeared, the picture faded away and the road reappeared leading to another container like building. Participants were asked to rate their experience of the just completed cycle on a scale of 0 to 10 (SUD score) and this was recorded on the computer. The cycle was repeated seven times so that seven different pictures could be processed. Finally, after the seventh cycle, the scene turned blue again for a cool down phase and self-selected music was played, designed to facilitate calming and bring participants back to the present. After a couple of minutes, the treadmill was slowed down to a standstill so that participants could step off and take off the safety harness and BioHarness.

Results

7.9. Table 13 shows that the 3MDR therapy sessions took, on average, just over 1½ hours to complete, during which time this individual walked between 4.8 and 6.0 km (3-4 miles). The average speed of 1 m/s is slower that the average adult walking speed of 1.3-1.4 m/s and, therefore, a very manageable walking speed for most people. The first session was much shorter in duration as it comprised an introduction to the system and a first data collection point, without the influence of any 3MDR effects.

Table 13: Summary table for one participant, showing the total duration and distance walked in each session as well as the average walking speed. Session 1 was the dual task session. Session 2 to 7 were 3MDR therapy sessions.

Parameter	Session 1	Session 2	Session 3	Session 4	Session 5	Session 6	Session 7
Session times (min)	9.3	92.8	95.4	82.5	91.8	95.1	88.7
Session distance walked (m)	535.9	5644.2	6018.2	4790.6	5337.3	5524.4	5152.4
Average walking speed (m/s)	1.00	0.97	1.06	0.97	0.96	0.97	0.96

7.10. Table 14 highlights the lengths of the different phases of a single cycle during a 3MDR session. It can be seen that the duration of some phases was fixed.

Table 14: Duration of phases during a 3MDR cycle

Therapy session – visit 2 to 7
Walking in the red zone to door 1 (± 50 seconds)
Walking in the corridor to door 2 (± 35 seconds)
Walking in the corridor to the picture (± 50 seconds)
Memories of the scene in the picture (variable)
Associations of the scene in the picture (variable)
Bilateral stimulation phase with at the end a SUD score (± 32 seconds)

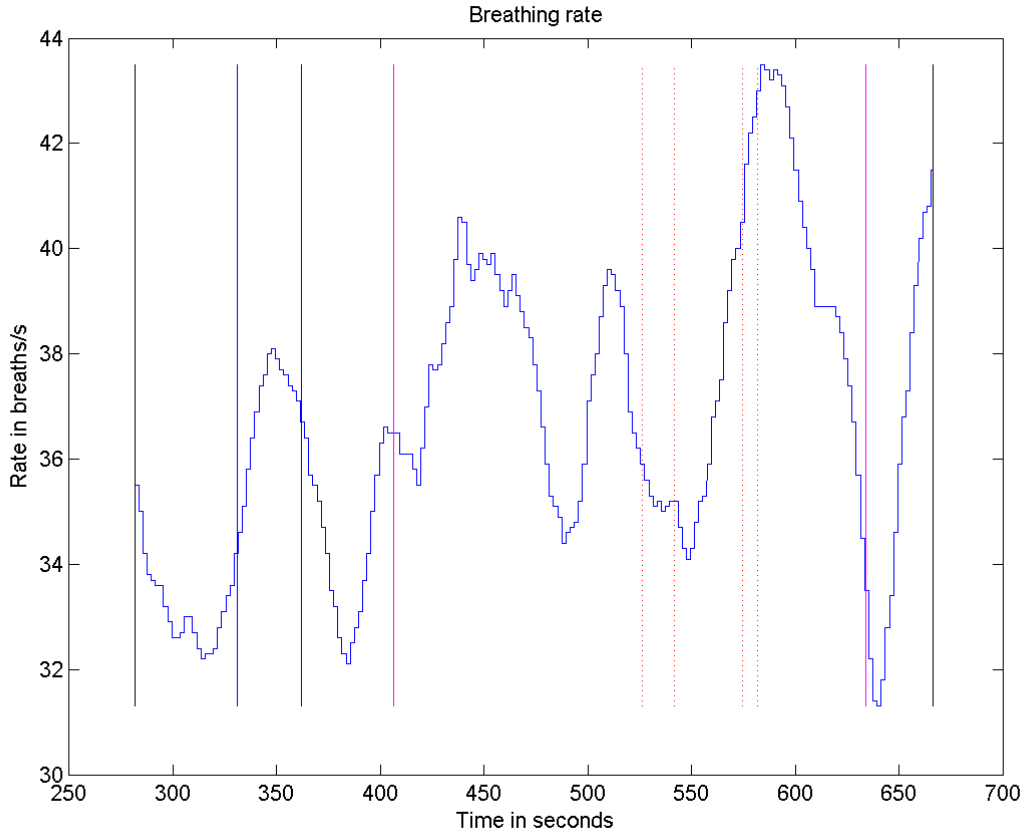
7.11. The time spent in front of the picture to bring up memories and to reflect on the feelings this evoked was variable. Table 15 shows these times for one individual as well as the average walking speed and the time taken during the cool down phase, which also could vary. The overall pattern was one of relative consistency with between 7 and 10 minutes taken for memories and feelings.

Table 15: Summary table for one participant, showing the phase durations and walking speed as an average over each session

Parameter	Session 2	Session 3	Session 4	Session 5	Session 6	Session 7
Memory time (min)	5.9	4.3	3.6	3.9	3.7	4.3
Association time (min)	3.2	5.3	4.1	5.2	5.6	4.2
Walking speed (m/s)	0.97	1.06	0.97	0.97	0.97	0.97
Cooldown time (min)	3.9	4.4	3.9	3.8	3.9	4.0

7.12. As described above, participants were wearing a Bioharness which was able to record heart and breathing rate. An example of the BR trace is shown in Figure 10 and demonstrates the variability in BR during a 3MDR cycle.

Figure 10: Breathing rate trace during one cycle of a 3MDR therapy session



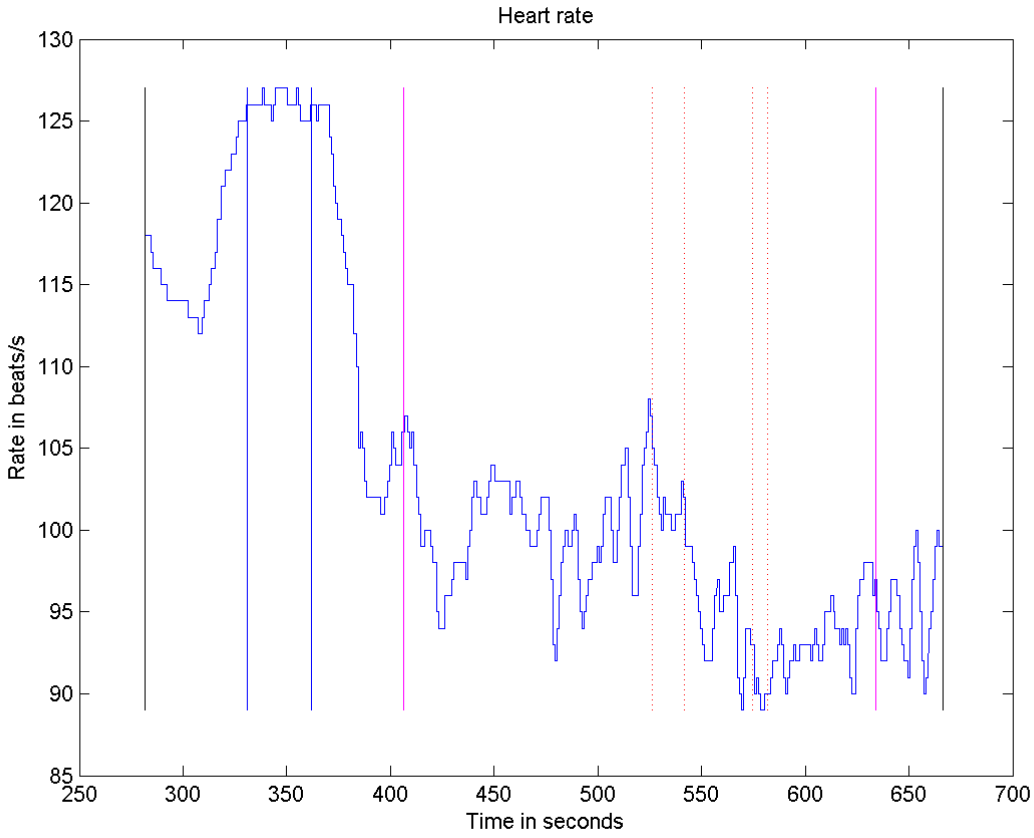
7.13. On the left of Figure 10, the cycle starts at the black vertical line when the road appears leading to the container-like building. The opening of the two doors is indicated

by the two blue vertical lines, the arrival at the picture and coming to a standstill is indicated by the first magenta vertical line. The red dotted lines indicate when the participant gave a word associated with the memory and described his feelings. The second vertical magenta line indicates when the phase started to track the ball and the final black vertical line marks the end of the cycle when the scene opens up to the next one.

7.14. In general, the breathing rate is high throughout the cycle. Normally, breathing rate will be between 12 and 20 and only rise above that with strenuous exercise; a rate of 32-43 should be considered as substantially elevated. Walking on a treadmill at 1 m/s would not be expected to cause such an increase of breathing rate and, therefore, it is reasonable to assume that distress during the session may be causing this response.

7.15. For the same individual and cycle, Figure 11 shows the heart rate that was observed. The figure is set up in the same way as was described for BR. Normally, a maximum heart rate of 100 beats/min would be expected at leisurely walking pace. The HR is slightly elevated at first and then reduces to a normal level a bit later in the cycle. The heart rate can also be seen to have been variable through the different phases of the cycle.

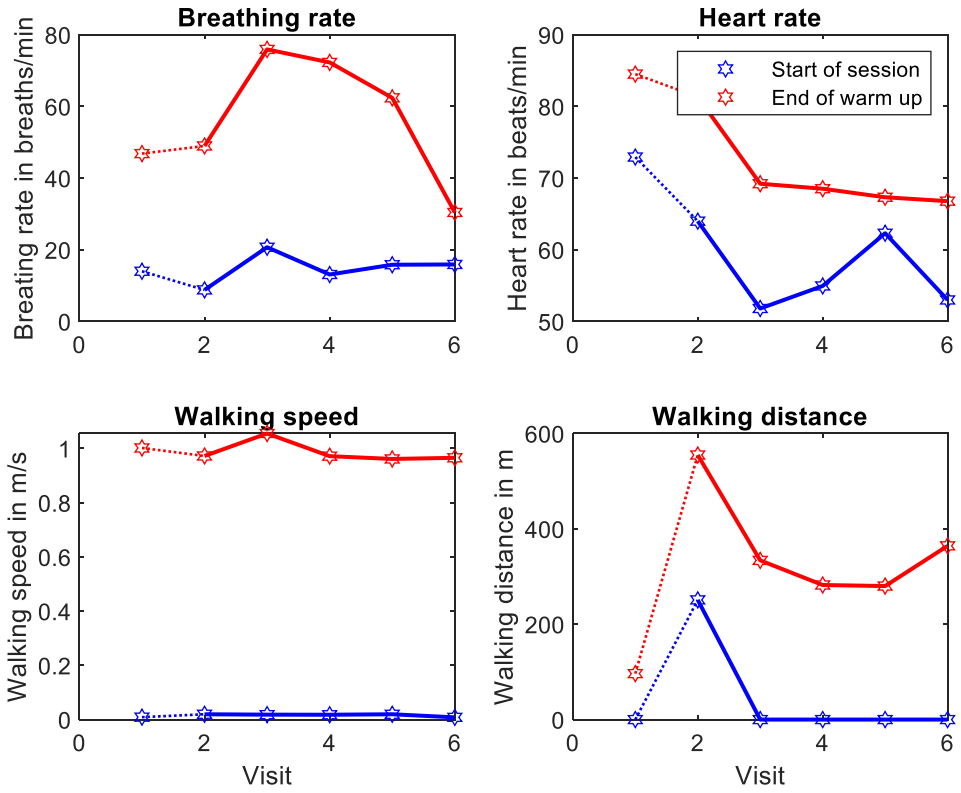
Figure 11: Heart rate trace during one cycle of a 3MDR therapy session



7.16. Because these results are from a single individual during one cycle it is difficult to draw any conclusions from them. To obtain a better understanding of the BR and HR response, these parameters were explored at the very start of a session. Figure 12

provides a summary graph showing results at the start of the warm up phase (blue) when the treadmill had not yet started to move and at the end of the same warm up phase (red) when the participant was walking comfortably at a steady state ready to start with 3MDR. Although these data are from one participant, they are representative of what was observed in most individuals. The Figure shows 6 sessions, with the first representing the dual task session and the remainder are 3MDR therapy sessions.

*Figure 12: BR and HR changes at the start of all 3MDR therapy sessions**



** The anomaly for walking distance in session 2 was caused by repeated start ups of the session. The computer included the distance walked up to that point.*

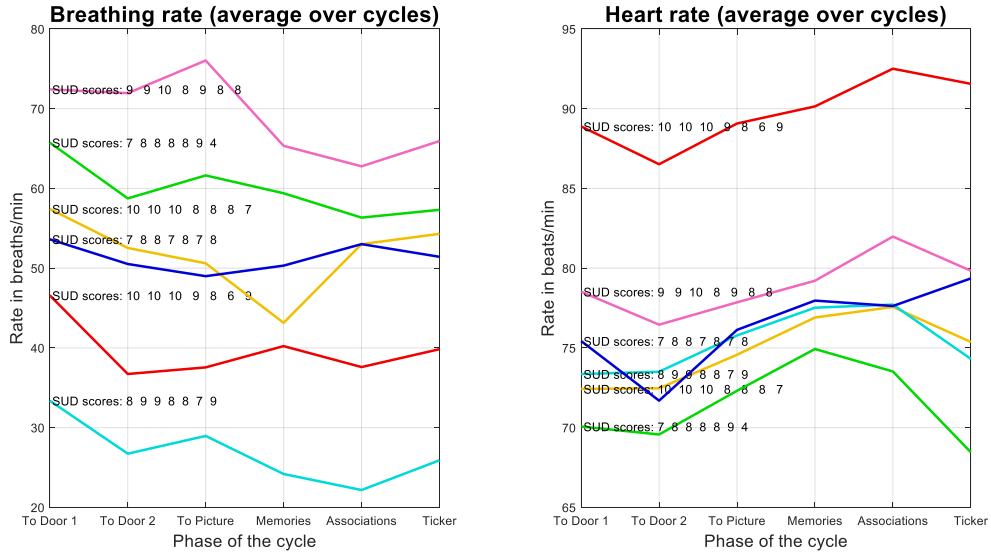
7.17. The walking speed started at 0 m/s and ended at around 1 m/s for all sessions. The warm up walking distance (red) in the first session was short compared to the therapy sessions. The BR was below 20 at first and well above this level by the end of the warm up phase. The HR was between 50 and 70 (blue) at the start and between 70 and 85 at the end of the warm up (red). These results show that the individual had a BR within the normal range before starting the 3MDR sessions which, by the end of the warm up, had increased beyond what would be expected when walking more slowly than the average adult walking speed. This supports the impression that distress from anticipation of the 3MDR session influenced BR although the HR was not obviously affected in the same way for this individual.

7.18. Figure 13 summarises the average changes observed within cycles and between sessions for the same individual. The rate of breathing differs quite clearly between sessions. In all cases it is elevated (above 20) but whilst therapy session 5 (light blue) is relatively close to 20, therapy session 3 (pink) is substantially elevated. There does not

appear to be a clear pattern from session 1 to 6. (It should be noted that it was not expected that BR would reduce consistently over sessions due to changes in the pictures considered.) If a picture was no longer problematic, it could be replaced by a more stress-generating image. Any therapeutic effect would, therefore, not necessarily be demonstrated by the BR graphs which are more indicative that 3MDR effectively evoked a stress response.

7.19. The HR response varied between sessions in a different way to the BR response. First, in all sessions HR was at a normal level but varied to some extent. The highest HR was observed for the 1st (red) therapy session and the lowest HR occurred during the 4th (green) therapy session. Across all sessions, there was no phase where BR was particularly elevated. HR Variability was larger between sessions than between phases. Not shown is the variability between cycles in a session; however, this was relatively small. It seems that BR during a visit remained relatively stable between cycles. With respect to HR, there was a small rise in almost all sessions towards the moment when feelings (associations) were recorded. However, given the fact that this is a single individual it would be wrong to draw conclusions from this pattern.

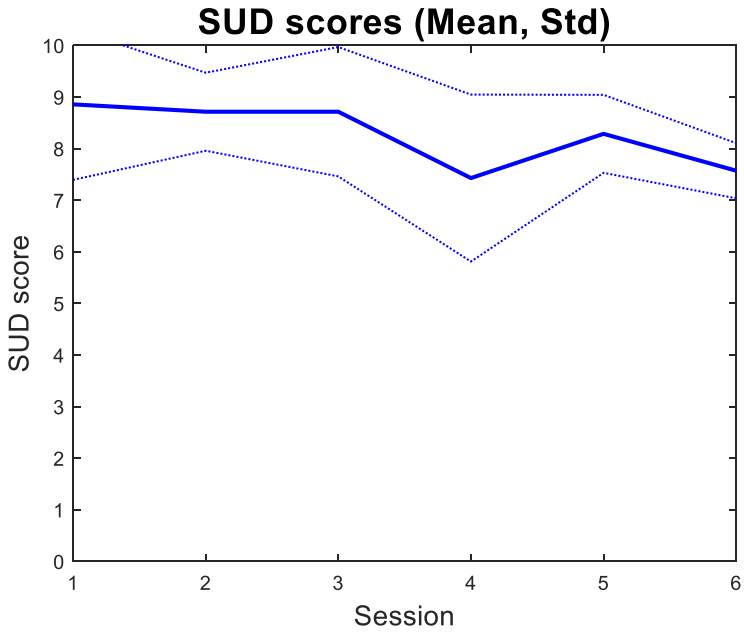
*Figure 13: BR and HR changes during 6 3MDR therapy sessions**



* The average of 7 cycles per session was calculated for each phase of the cycle between the first door opening and the bilateral stimulation phase ending. Each line is a session in the following order: red, orange, pink, green, light blue, dark blue. The SUD scores at the end of each cycle in the session are displayed as a sequence of scores close to start of the relevant line.

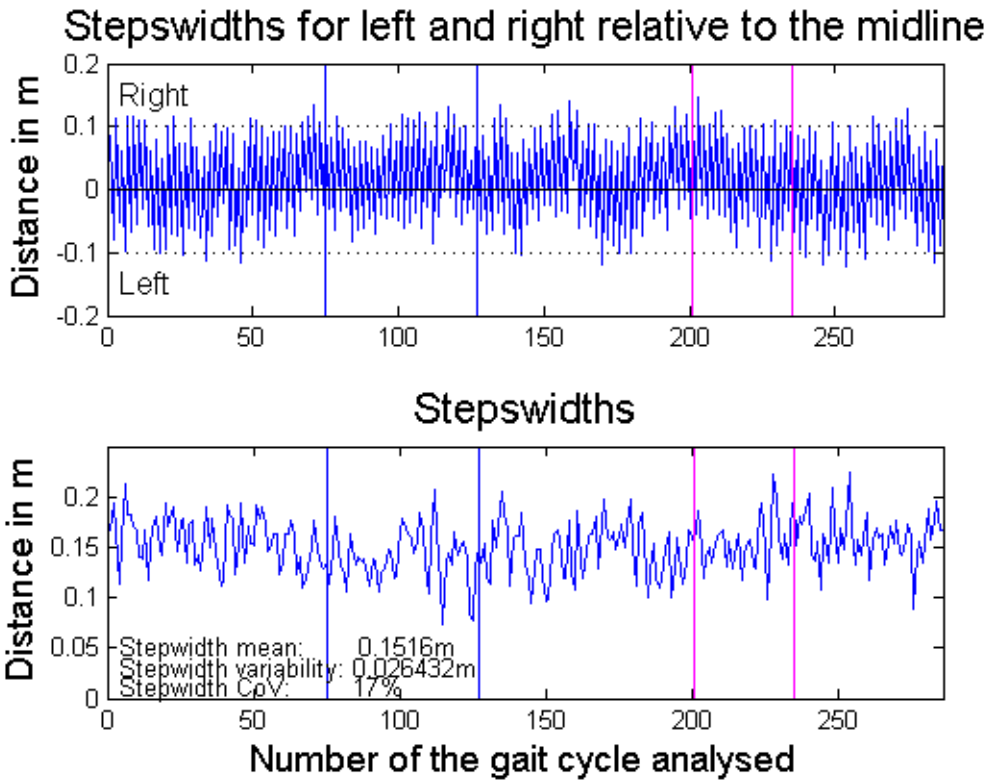
7.20. Figure 13 also shows the SUD scores as a sequence of 7 numbers related to the cycles within a session. For this participant these scores were mostly very high. There does not seem to be an obvious pattern in the SUD scores but they clearly demonstrate that perceived distress was substantial whilst engaging in 3MDR therapy. On closer inspection, Figure 14 does demonstrate a gradual reduction in the SUD score from session 1 to 6 but it is not possible to interpret this as improvement since the pictures were changed between sessions.

Figure 14: The average (with standard deviations) SUD score for 6 therapy sessions



7.21. The force platforms inside the instrumented treadmill permitted analysis of step width variability. Figure 15 illustrates a sequence of foot placements on the treadmill (top) and step width between left and right foot placements during a 3MDR cycle.

Figure 15: Step width variability



7.22. The start of the plot in figure seven is when the scene has just turned to red and the container-like building is being approached. The blue vertical lines indicate when the two doors were opened. Arrival at the picture and start of the bilateral stimulation phase are indicated by the magenta lines. The overall step width was calculated as 0.15 m. The change in variability between phases is the parameter of interest. Processing for this data is time consuming and it will take some time before conclusions can be drawn.

Feelings reported during the association phase

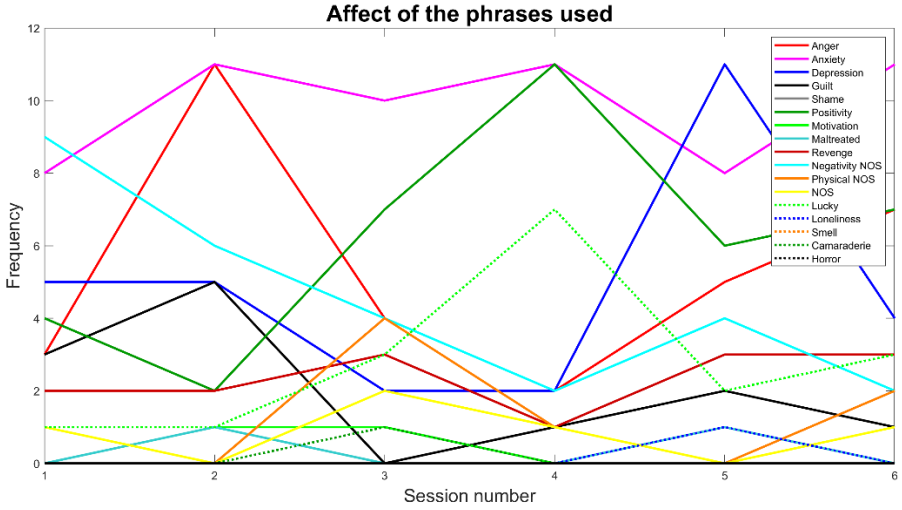
7.23. During the 3MDR sessions, participants described feelings evoked by the pictures. These were at first emotions, but people were also requested to describe what they felt physically and where in their body. The key phrases were typed into the computer so that they could be displayed on the screen in front of them. The words were projected over the picture whilst they were reflecting on the displayed scene. These same phrases were stored into file together with the data from the Bioharness and treadmill and therefore are accessible for further analysis, which is planned.

7.24. Figure 16 gives some idea of the words used by one individual. It should be noted that there was a mix of single words and phrases. Therefore, the word cloud items do not always make clear what they mean. For instance, "chest" on its own does not have obvious meaning but is likely to have been part of a phrase such as "tight chest" when describing a physical experience.

Figure 16: Word cloud for a single individual of the words used during 6 sessions

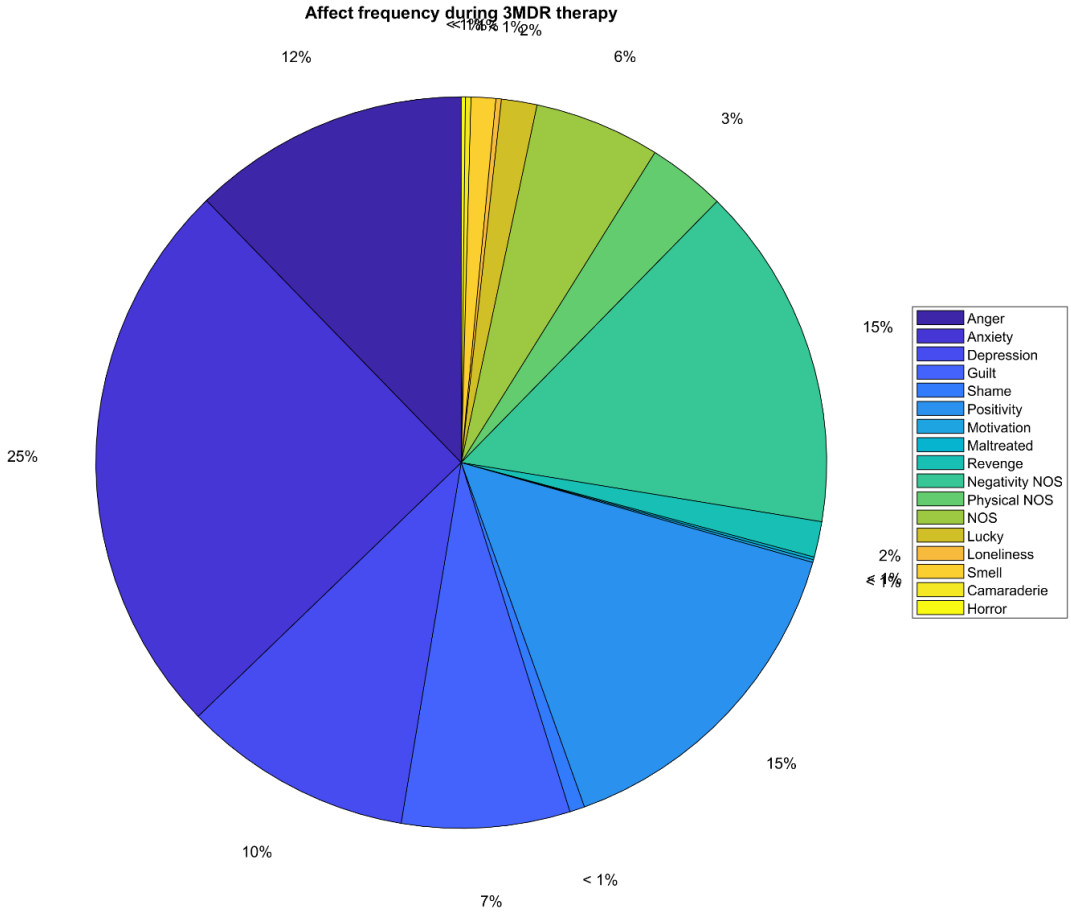
7.25. In our planned further analyses, the phrases used will be extracted to generate a unique list and categorised according to the affect represented, e.g., anger, anxiety, depression and guilt. This will allow analysis of patterns over time. Figure 17 provides an example of this for one individual who attended 6 sessions. The affect of phrases is colour coded with the green line representing positivity, the red line anger, magenta anxiety, and blue depression. A clear pattern is not evident and further analysis is underway.

Figure 17: Frequency of affect expressed over 6 sessions for one participant



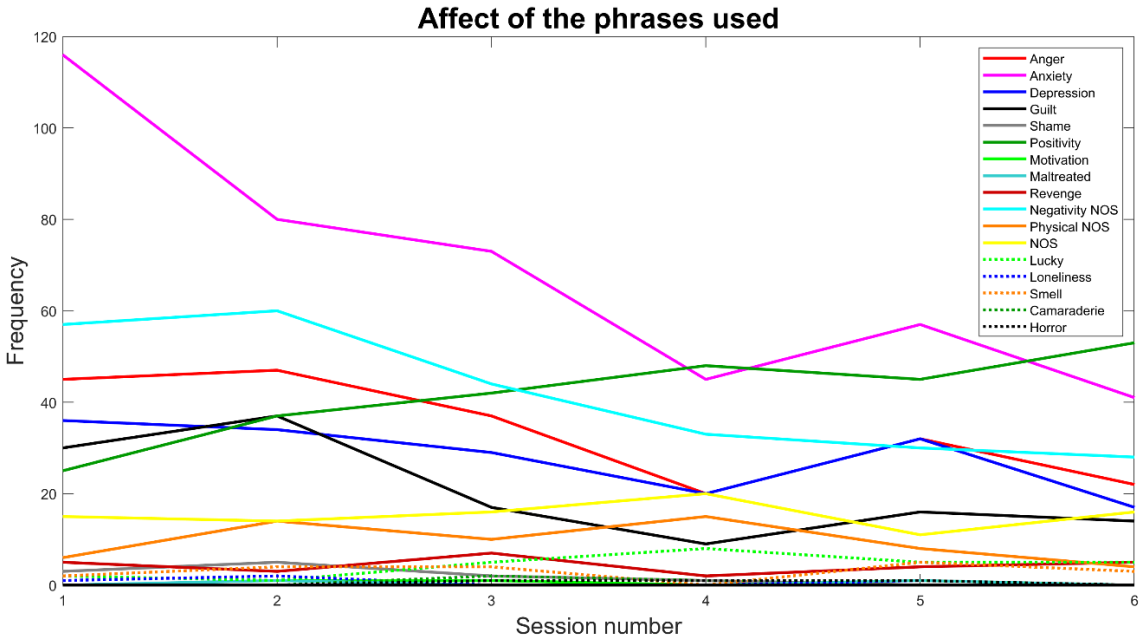
7.26. Figure 18 shows the frequency of different affects expressed during 3MDR treatment. Anxiety was most frequently expressed (25%). Positivity and negativity statements not otherwise specified were made 15% of the time. Anger (12%), depression (10%), and guilt (7%) were also frequently expressed. Other affects occurred less frequently.

Figure 18: Pie chart for affect expression frequency during 3MDR therapy (10 participants)



7.27. Figure 19 shows the change over time in the frequency that an affect was expressed. Anxiety was clearly highest across the group at the start of 3MDR therapy and this gradually declined from the first to the last session. The same seems to apply for anger and negativity, and to some extent depression. On the other hand, positivity was lowest at the start of 3MDR therapy and highest for the last session. These results appear to reflect improvement with 3MDR.

Figure 19: Change in affect frequency expression over sessions (10 participants)



Future data analysis

7.28. The data obtained directly from the 3MDR sessions is a rich source of information but also relatively large and, therefore, data reduction based on prioritisation is essential to be able to make sense of it. The research team has repeatedly reviewed which aspects are of most interest and the results described above include some of these. Bespoke analysis programmes are now in development to extract the results required for further publications and other forms of dissemination.

8. Dissemination and Impact

8.1. The 3MDR trial has already received a great deal of media attention and public and professional awareness has been raised in a variety of ways, including television appearances (including the acclaimed BBCWales documentary 'inside my brain' which featured a large segment on 3MDR), radio interviews, public events, blog posts, presentations, posters and academic publications (see table below).

Team Member(s) / Colleague(s)	Dissemination	Date
Prof Jonathan Bisson	Legion Soldier Magazine	2017
Team	BBC Wales News	19.10.2017
Team	Charlotte Church BBC1 documentary 'Inside My Brain'	01.11.2017
Kali Barawi	Welsh Assemble - Presentation	16.10.2017
Dr Neil Kitchiner	National Centre for Mental Health Podcast	08.09.2017
Kali Barawi & John Skipper	Cardiff University and National Centre for Mental Health Blog post	15.11.2017
Kali Barawi	Health and Care Research Wales Newsletter	24.09.2017
Dr Neil Kitchiner & John Skipper	Cardiff and Vale Health Board commissioned video	19.10.2017
Kali Barawi	Veteran Therapist Meeting - Presentation	02.06.2018 & 10.10.2018
Kali Barawi	Post Graduate Poster Presentation. First Prize Judges choice and First Prize Public choice.	24.01.2018
Kali Barawi	King College London Veterans Conference Poster Presentation. First Prize Public Choice.	15.03.2018
Leigh Abbott & Will Watkins	S4C broadcast of 'Bryn Fôn a PTSD.'	15.02.2018
Team	Darren Miller AM Welsh Conservative Party attended 3MDR lab.	08.02.2018
Team	Vaughan Gethin AM Health Minister, from Welsh Assemble attended 3MDR lab.	25.01.2018
Kali Barawi	DOTHS Conference Poster presentation and oral presentation.	19.06.2018
Kali Barawi	National Centre for Mental Health Public awareness for Mental Health event at the Depot. Hall of Mirrors to demonstrate PTSD symptoms.	20.06.2018
John Skipper	Western Mail and South Wales Echo Interview.	09.07.2018
Kali Barawi	Interview with Belgium Journalist for dissertation on new	26.05.2018

	interventions developed for military veterans.	
Dr Neil Kitchiner & Kali Barawi	Royal College off Psychiatrists Conference.	22.06.2018
Leigh Abbott	Cardiff Institute for Tissue Engineering and Repair presentation.	08.01.2018
Team	Veterans NHS Wales Facebook and Twitter page. 28 shares and reached 2900 people.	Ongoing.
Kali Barawi	Traumatic Stress Research Group Instagram page. 51 followers.	Ongoing
Team	Website Launch: www.traumaticstressresearch.co.uk	19.06.2018
Kali Barawi	Cardiff University Brain Night presentation	15.10.2018
Kali Barawi	I-AM-PHD a national conference for PhD student studying Traumatic stress. Presentation	16.06.2018
Dr Neil Kitchiner and Kali Barawi	Cardiff and Vale Veterans Conference Presentation.	05.10.2018
Dr Neil Kitchiner, John Skipper and Kali Barawi	Cardiff and Vale Within Together conference	11.11.2018
Kali Barawi	33rd Medicine and Dentistry Symposium. Poster and oral presentation. First Prize oral presentation and First Prize Poster presentation.	21.01.2019
Prof Eric Vermetten, Dr Neil Kitchiner and Kali Barawi	Eye Movement Desensitisation and Reconsolidation UK annual Conference, Birmingham.	22.03.2019
Prof Eric Vermetten, Kali Barawi, Marieke Van Gelderen.	Symposium on the development of 3MDR.	14.06.2019
Sam Gibson	Traumatic Stress Research Group blog post.	12.07.2019

8.2. This report represents the first in a series of initiatives to disseminate the results of the 3MDR trial as widely as possible. The aim is to have local, national and international impact through upcoming initiatives and events aimed at a variety of audiences (see table below).

Team Member(s) / Colleague(s)	Dissemination	Date
Kali Barawi	International Society for Traumatic Stress Studies (ISTSS) Conference. Poster presentation.	14.11.2019

Team	ISTSS Conference. Presentation.	14.11.2019
Alice Roberts	Traumatic Stress Research Group blog post.	07.10.2019
Chantelle Wiseman	Traumatic Stress Research Group blog post.	02.09.2019
Team	3MDR Trial Results Launch Event	01.10.2019
Team	3MDR Trial Results Launch Event Media Converge.	01.10.2019
Kali Barawi	The Division of Psychological Medicine and Clinical Neuroscience, newsletter.	01.10.2019
Dr Neil Kitchiner	King's College London Veterans Conference.	12.03.2020

9. Discussion

Main Results

9.1. This study provides quantitative and qualitative evidence that 3MDR is able to reduce traumatic stress symptoms in British military veterans with treatment-resistant, service-related PTSD. The study has addressed and provided useful information with respect to all the research questions asked (see Table 16 below).

Table 16: Research Questions

A.	For British military veterans with treatment-resistant, service-related PTSD, does 3MDR reduce symptoms of PTSD as measured by the CAPS5 to a significantly greater degree than a waiting list?
B.	For British military veterans with treatment-resistant, service-related PTSD, what is the impact of 3MDR on quality of life, functioning, symptoms of depression, symptoms of anxiety, insomnia, alcohol and illicit substance use and perceived social support?
C.	Is 3MDR acceptable to British military veterans with treatment-resistant, service-related PTSD and those delivering the intervention as measured by qualitative semi-structured interviews?
D.	What is the likely effect size of 3MDR?
E.	What factors may impact efficacy and successful roll-out of 3MDR for treatment-resistant, service-related PTSD, if 3MDR is shown to be efficacious? (Mechanism and process evaluation)
F.	What is the behavioural response of the 3MDR sessions in terms of stress and cognitive processing during different dual task phases and how can this guide us in optimal design of the intervention and a Phase III definitive trial? (Mechanism evaluation)
G.	Can examination of the integrity of the study protocol, trial recruitment rate, self-report outcome measures, clinician administered outcome measures, randomisation procedure, treatment integrity and acceptability enhance decision making in planning a Phase III definitive trial?
H.	Is a Phase III definitive RCT indicated and feasible?

9.2. The mean difference in CAPS5 score of 10 between the intervention group and the control group at 12 weeks is likely to be clinically significant and represents a 19% reduction in PTSD compared with the baseline mean scores. It is noteworthy that being on the waitlist also resulted in a mean 6.8-point drop on the CAPS5, suggesting some form of positive impact at the prospect of treatment in individuals with hitherto treatment refractory symptoms. The total reduction pre-post treatment of those receiving 3MDR immediately of 17.7 points on the CAPS5 represented a clearly clinically significant 37% reduction in PTSD symptoms at presentation.

9.3. Participants allocated to delayed treatment also responded well to 3MDR and those who were in the initial treatment group maintained their improvement at 26-week follow-up. The likely effect size of 3MDR was found to be 0.65 representing a moderate treatment effect[52].

9.4. 3MDR also resulted in statistically significantly greater improvements in self-reported symptoms of PTSD (PCL-5), anxiety (GAD-7) and insomnia (ISI). There was, however, no significant difference between the groups on functioning (WSAS), depression (PHQ-9), health-related quality of life (EQ-5D-5L), alcohol misuse (Audit-O) and perceived social support (MSPSS).

9.5. The apparent positive impact of 3MDR on the secondary outcome measures of anxiety and insomnia is consistent with studies of other successful treatments for PTSD[19], suggesting generalisation of positive effects to other groups of symptoms. The absence of effect on alcohol use is perhaps not surprising as those included did not report significant substance misuse problems at baseline. The lack of improvement for functioning, depression, health-related quality of life and increased perceived social support is somewhat disappointing as improvements in these measures are often reported following effective treatment for PTSD[19].

9.6. 3MDR was found to be acceptable to most, but not all, participants and to all the therapists delivering the intervention, albeit with recommendations on what could be done to enhance its effect and to support people during treatment. The study results highlight the fact that 3MDR is not acceptable to all British military veterans with treatment-resistant, service-related PTSD. This is an important finding and further work is underway with data generated from the study to determine those factors associated with better and worse treatment outcomes. These analyses will help with the refinement of selection criteria for 3MDR to ensure that individuals who are unlikely to benefit, or more likely to be adversely affected by it, are not offered 3MDR in future research/clinical practice.

9.7. Rich learning was achieved with respect to the factors that may impact efficacy and successful roll-out of 3MDR for treatment-resistant, service-related PTSD. Key findings in this regard included the appropriate assessment and selection of potential candidates for 3MDR, enhanced preparation in advance of 3MDR, the number of treatment sessions available, support between sessions and greater flexibility with respect to content of later sessions.

9.8. The behavioural response of the 3MDR sessions in terms of stress and cognitive processing during different dual task phases is difficult to interpret with the analyses currently available. Although benefits from receipt of 3MDR were clearly demonstrated, the exact mechanism through which these occurred is not possible to determine. The exposure work involved appeared to be stressful as suggested by the HR and BR responses and qualitative interviews. Habituation seems likely to be at least part of the underlying mechanism to improvement for participants. Reconsolidation after mobilisation of the traumatic memory and cognitive restructuring are other possible mechanisms. The roles played by walking on the treadmill, dual-processing and bilateral stimulation of both hemispheres induced by tracking the ball, key components of 3MDR, are not known but may be very important.

9.9. Key insights to the active ingredients of the 3MDR treatment package were obtained from the qualitative interviews with participants and therapists. A number of participants and therapists felt that more sessions either on the platform or to help integrate/facilitate the platform work would have been beneficial. Several therapists felt that some trauma-focused psychological treatment after the platform session would have resulted in greater improvement for some participants. These findings will be used

to refine the 3MDR treatment protocol and optimally design the intervention for further evaluation. It is likely that an increased maximum number of sessions will be allowed, with a suggested minimum number of platform sessions and then some flexibility regarding the content of further treatment sessions.

9.10. The study protocol worked well for the study overall. It was clear that many of the approaches adopted by the protocol for this study were entirely fit for purpose and would be appropriate to use in a phase III effectiveness study. The approach to identifying and approaching potential participants worked well and take-up by those approached was very high. Involvement of a clinician and regular contact/support provision between sessions proved important; indeed it was felt that support between sessions should be enhanced and formalised more in the future and that it should be available to all participants in a phase III effectiveness study. Regular contact/support between sessions also helped with retention of participants, which was high.

9.11. The trial recruitment rate was steady throughout the study and no difficulties were encountered in recruiting enough participants. The inclusion/exclusion criteria resulted in few individuals being excluded, suggesting that the criteria were pragmatic. Some participants did not, however, benefit from 3MDR suggesting that some changes are required for them to be appropriate for most military veterans with treatment resistant PTSD who are likely to benefit from 3MDR. The self-report and clinician administered outcome measures were well-tolerated by participants and all measures were completed by the majority of individuals at all time points. The only participants with partial data were individuals who had been more difficult to retain, and a pragmatic approach was taken by the raters to complete the primary outcome measure, the CAPS, as a minimum.

9.12. The randomisation procedure worked well although the lack of a full-time trial manager meant that procedures were not always as smooth as they might have been with considerable communication required between the researcher responsible for technological aspects of the 3MDR and the chief investigator to ensure that the raters remained blind to treatment allocation. This points to the potential advantage of having a named trial manager for an effectiveness trial.

9.13. The fidelity ratings provided by the originators of 3MDR supported treatment integrity and the system of making video recordings of sessions and then sharing these through a secure system with fidelity raters worked well. It is appreciated that this may not be as easy for an effectiveness study undertaken in facilities without a Motek GRAIL system, however, attempts should be made to video sessions rather than audiotape sessions, as may be appropriate for more standard psychological treatments of PTSD, given the multi-modular nature of 3MDR.

9.14. The results of the study strongly suggest that a phase III definitive RCT of 3MDR is indicated and feasible.

Results in the context of other research

9.15. Results from the only other early phase randomized controlled trial of 3MDR, conducted by the originators of 3MDR in the Netherlands[53], followed a somewhat different protocol in that “usual care” was allowed for a certain number of sessions and follow-up was at the end of treatment (whenever that was) rather than a specific time post-randomisation. Both these factors would be expected to improve outcomes, yet the

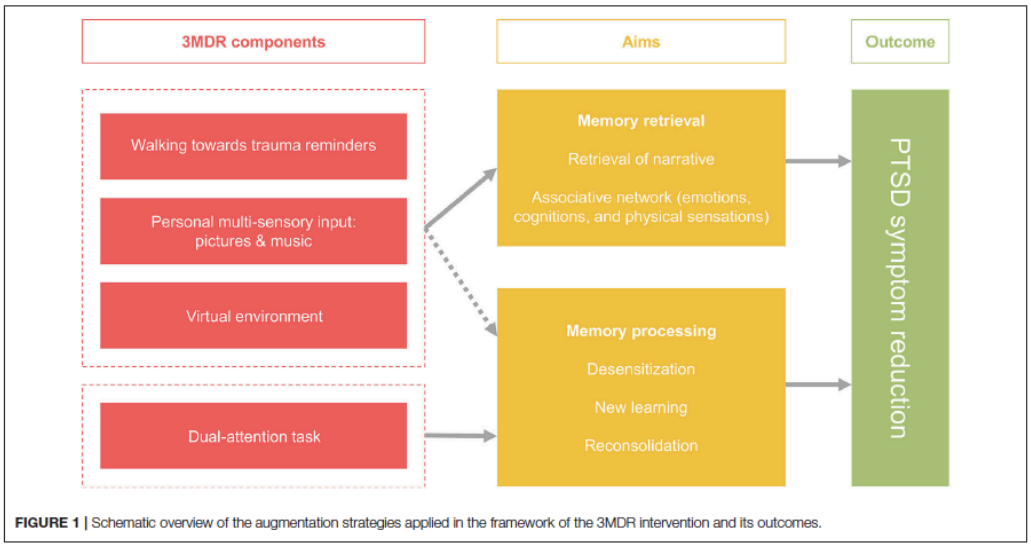
mean CAPS5 point reduction was lower than in this study and the difference at the end of 3MDR platform sessions was not statistically significantly different to the delayed treatment group. 3MDR was, however, statistically significantly better than delayed treatment.

9.16. The Wales and Netherlands trials taken together point to the potential effectiveness of 3MDR and its position as a major candidate for further evaluation. There is an urgent need to identify effective treatments for people with PTSD who do not respond to, or are unable to engage with, current first line treatments. If further work confirmed the results of this study, 3MDR would offer a new treatment option with the potential to treat hitherto untreatable PTSD and reduce the burden of this debilitating condition to individuals, those around them and to society overall. This would result in an additional option of treatment for people with PTSD at a point when, currently, effective active treatment possibilities are often exhausted and the prospects of further recovery low.

9.17. The results of the two RCTs of 3MDR mean that it would have met the criteria for a recommendation of a treatment with emerging evidence if the results had been available to the ISTSS Guidelines Committee at the time the systematic reviews that informed their recommendations were finalised. The effect sizes found places 3MDR on a level with neurofeedback and TMS, as more complicated treatments with emerging evidence of effect in people with likely more treatment-resistant forms of PTSD.

9.18. It is difficult to draw any mechanistic conclusions from the data analysed to date. 3MDR is clearly a complex intervention and it is not known exactly how it works. The results appear to support the combination of elements involved in 3MDR and, in the absence of dismantling studies, Van Gelderen et al's[54] model for 3MDR. The model (see Figure 20) proposes that virtual reality increases presence and attention during treatment to facilitate memory retrieval with the pictures and music personalising the experience. They note the positive effect of physical activity on fear extinction and associative thinking and cognitive theory providing a rationale for decreased avoidance by walking towards cues of the traumatic memories. The bilateral stimulation requiring dual-attention further facilitates new learning and reconsolidation. They also argue that novel elements of the intervention, absent from many standard PTSD treatments, include activation, personalisation and empowerment.

Figure 20: Van Gelderen model for 3MDR (will need permission to reproduce)



Strengths and limitations

9.18. This was a well-designed, RCT that adhered to current methodological recommendations for this type of work. Table 17 assesses risk of bias for the study against the Cochrane Risk of Bias checklist[55]. As can be seen, the overall risk of bias was very low and compares very favourably with the majority of randomised controlled trials of treatments for PTSD.

Table 17: Risk of Bias of Study according to the Cochrane criteria

Risk of Bias	Low, Medium or High Risk
Random sequence generation (selection bias)	This was **low** as the randomisation was generated by a computer programme designed for this purpose.
Allocation concealment (selection bias)	This was **low** as the randomisation codes were sealed in opaque envelopes with each envelope numbered from 1 to 42. The envelopes were opened by a researcher unaware of their content, once a participant had successfully completed a baseline assessment and their eligibility was confirmed.
Blinding of participants and personnel (performance bias)	This was **high** as is true for almost all psychological treatment trials; the participants and therapists could not be blinded to the fact the individuals in the immediate 3MDR group were receiving 3MDR.
Blinding of outcome assessment (detection bias)	This was **low** as the two raters were kept blind to the allocation. Inevitably, the raters did find out which groups a few participants were in due to disclosure by the participant. (Participants were asked not to disclose which group they had been

	randomised to but, not surprisingly, some participants did let slip this information.)
Incomplete outcome data (attrition bias)	This was **low** as the overall retention rate was 82% for the primary outcome point and multiple imputation was used to ensure that the results reported were based on an intention to treat basis.
Selective reporting (reporting bias)	This was **low** as the trial was registered and the protocol adhered to. The reporting is in line with the protocol and adheres to the CONSORT statement (ref).
Other bias	This was **low** as no other risks of bias have been identified.

9.19. The study was designed as a Phase II feasibility trial and, therefore, the number of participants was restricted to 42. A larger sample size would be required for a definitive trial and it is important that the limitations in terms of absolute power are acknowledged when considering the results of this study.

9.20. A major strength of the study was the careful training and supervision of the therapists, along with fidelity checks demonstrating good adherence to the 3MDR treatment protocol. That said, a number of the therapists reported gaining confidence as they treated more participants and it may be that earlier participants could have done better if treated when the therapists had more confidence and experience with the technique.

9.21. Another key strength of the study was the utilisation of both quantitative and qualitative approaches and the ability to cross-reference results from different sources to corroborate or challenge outcomes. The quantitative and qualitative results were very consistent which strengthens the belief that the results are likely to provide a true reflection of the efficacy of 3MDR.

9.22. The significant improvement in members of the delayed treatment group before they received 3MDR does make interpretation more difficult than if there had been no response. It is always difficult to identify a perfect control condition and it may have been that no treatment at all would have provided a better estimate of the absence of treatment at all by removing the anticipation/hope of 3MDR being effective. This was, however, not felt to be ethically optimal for this study and the cross-over design also provided additional information that has been helpful, not least the further improvement post 3MDR in the delayed treatment group.

9.23. A limitation of this report, as opposed to the study, is that a significant amount of data is yet to be fully analysed, in particular data obtained via the GRAIL system during 3MDR platform sessions. Analysis of this data is likely to provide additional insights, particularly with respect to the variety of mechanisms involved in 3MDR treatment to determine which one/combination are linked to what effects.

Clinical Implications

9.24. Due to the preliminary nature of this work, it would be premature to recommend 3MDR for routine clinical practice. If 3MDR were to be shown to be effective for

treatment-resistant PTSD it would be likely to have great appeal to commissioners and practitioners, as it would fill a current gap in service provision. The impact on clinical practice and services would be marked as the potential magnitude of health gain suggested by early phase studies is substantial. If these effects were to be replicated and then successfully implemented in the NHS and beyond, thousands more people with PTSD would recover and the availability of 3MDR would herald a new era in the evidence-based care options available to people with PTSD.

Research Implications

9.25. As would be expected at this stage of 3MDR's development, the research implications are far greater than the clinical implications with the main one being that the results indicate the desirability of a pragmatic phase III effectiveness study of 3MDR.

9.26. This study only included military veterans with PTSD secondary to operational experience. There is no reason to believe that non-military veterans would not benefit from 3MDR, and anecdotal evidence is emerging that 3MDR can help people with treatment resistant PTSD to non-military trauma (Mink-Nijdam, personal communication) but this remains an empirical question and one that needs research to determine it.

9.27. The actual mechanism of 3MDR remains unclear and studies would be required with different designs, including dismantling studies, to shed more light on this. 3MDR is a complex intervention with a number of different elements and it is not possible to say what is and what is not required at present.

9.28. The number of 3MDR sessions requires more scrutiny. The results of this study suggest that more sessions are likely to be needed for some individuals. It is also unclear as to what the nature of additional session should be. It is possible that additional platform sessions and/or integration sessions would be helpful, with a suggestion that some TFPT after the platform sessions could be beneficial for some individuals who are now able to engage with treatment in a way they have not been able to before.

9.29. In addition to considering clinical effectiveness, cost-effectiveness work is also required. 3MDR is an expensive intervention; the equipment is costly and it is resource intensive in terms of therapist time and additional support. Therefore, any effectiveness study should include a health economic evaluation to allow informed choices to be made in the future with respect to funding and adoption by clinical services.

9.30. There is also a need for further process evaluation in future research to further evaluate key issues such as optimal levels of support and the characteristics of people with PTSD most likely to benefit from 3MDR.

10. Conclusion

10.1. Although not suitable for all military veterans with treatment resistant PTSD (specifically PTSD from service-related experiences), 3MDR has been shown to reduce symptoms of PTSD and be well-tolerated by the majority of participants in this study.

10.2. 3MDR has emerging evidence of effectiveness for treatment resistant PTSD. Further research is now required to determine its true effectiveness and optimal delivery.

11. References

1. Iversen A, Nikolaou V, Greenberg N, Unwin C, Hull L, Hotopf M et al. What happens to British veterans when they leave the armed forces?.European Journal of Public Health. 2005;15(2):175-184.

2. Mares A, Rosenheck R. Perceived Relationship Between Military Service and Homelessness Among Homeless Veterans With Mental Illness. The Journal of Nervous and Mental Disease. 2004;192(10):715-719.

3. MacManus D, Fossey M, Watson S, Wessely S. Former Armed Forces personnel in the Criminal Justice System. The Lancet Psychiatry. 2015;2(2):121-122.

4. Fletcher H. (2009). *Armed forces and the criminal justice system*. National Association Probation Officers.

5. Stevelink SAM, Jones M, Hull L, Pernet D, MacCrimmon S, Goodwin L, et al. Mental health outcomes at the end of the British involvement in the Iraq and Afghanistan conflicts: a cohort study. The British Journal of Psychiatry 2018; 1–8. 10.1192/bjp.2018.175

6. http://www.rctcbc.gov.uk/en/relateddocuments/publications/publicrelationsstrategy/armed-forces-community-covenant/package-of-support.pdf

7. Hotopf M, Hull L, Fear N, Browne T, Horn O, Iversen A et al. The health of UK military personnel who deployed to the 2003 Iraq war: a cohort study. The Lancet. 2006;367(9524):1731-1741.

8. Hoge C, Castro C, Messer S, McGurk D, Cotting D, Koffman R. Combat Duty in Iraq and Afghanistan, Mental Health Problems, and Barriers to Care. New England Journal of Medicine. 2004;351(1):13-22.

9. King's Centre for Military Health Research. (2010). *A fifteen year report: What has been achieved by fifteen years of research into the health of the UK Armed Forces?*: Kings College London, University of London.

10. Rafferty L, Stevelink S, Greenberg N, Wessely S. (2019). Stigma and barriers to care in service leavers with mental health problems. https://www.fim-trust.org/wp-content/uploads/2017/11/20171102-FinalReport.pdf

11. Greenberg N, Thomas S, Iversen A, Unwin C, Hull L, Wessely S. Do military peacekeepers want to talk about their experiences? Perceived psychological support of UK military peacekeepers on return from deployment. Journal of Mental Health. 2003;12(6):565-573.

12. Iversen A, van Staden L, Hughes J, Browne T, Greenberg N, Hotopf M et al. Help-seeking and receipt of treatment among UK service personnel. British Journal of Psychiatry. 2010;197(2):149-155.

13. Riddle J, Smith T, Smith B, Corbeil T, Engel C, Wells T et al. Millennium Cohort: The 2001–2003 baseline prevalence of mental disorders in the U.S. military. Journal of Clinical Epidemiology. 2007;60(2):192-201.

14. Monson C, Schnurr P, Resick P, Friedman M, Young-Xu Y, Stevens S. Cognitive processing therapy for veterans with military-related posttraumatic stress disorder. Journal of Consulting and Clinical Psychology. 2006;74(5):898-907.

15. Kitchiner N, Roberts N, Wilcox D, Bisson J. (2012). Systematic review and meta-analyses of psychosocial interventions for veterans of the military. *European Journal of Psychotraumatology, 2012. Available at: http://www.eurojnlofpsychotraumatol.net/index.php/ejpt/article/view/19267>*.

16. Mithoefer MC, Mithoefer AT, Feduccia AA, Jerome L, Wagner M, Wymer M, et al. 3,4-methylenedioxymethamphetamine (MDMA)-assisted psychotherapy for post-traumatic stress disorder in military veterans, firefighters, and police officers: a randomised, double-blind, dose-response, phase 2 clinical trial. *Lancet Psychiatry* 2018; **5**: 486-97.

17. Raskind MA, Peterson K, Williams T, Hoff DJ, Hart K, Holmes H, et al. A trial of prazosin for combat trauma PTSD with nightmares in active-duty soldiers returned from Iraq and Afghanistan. *American Journal of Psychiatry* 2013; **170**: 1003-10.

18. ISTSS (2018). *ISTSS PTSD prevention and treatment guidelines* - https://www.istss.org/treating-trauma/new-istss-prevention-and-treatment-guidelines.aspx

19. NICE (2018). NICE PTSD guidelines. https://www.nice.org.uk/guidance/ng116

20. Vermetten E, Meijer L, van der Wurff P, Mert A. The effect of military motion-assisted memory desensitization and reprocessing treatment on the symptoms of combat-related post-traumatic stress disorder: First preliminary results. *Annual Review of Cybertherapy and Telemedicine* 2013. doi:10.3233/978-1-61499-282-0-125

21. Rothbaum B, Rizzo A, Difede J. Virtual reality exposure therapy for service-related posttraumatic stress disorder. *Annals of the New York Academy of Sciences* 2010; 1208: 126-132.

22. Shapiro F. Eye movement desensitization: A new treatment for post-traumatic stress disorder. *Journal of Behavior Therapy and Experimental Psychiatry* 1989; 20: 211-217.

23. Gunter R, Bodner G. How eye movements affect unpleasant memories: Support for a working-memory account. Behaviour Research and Therapy. 2008;46(8):913-931.

24. Shalev A. Prevention of Posttraumatic Stress Disorder by Early Treatment. Archives of General Psychiatry. 2012;69(2):166.

25. Creswell JW, Plano Clark VL. (2018). Designing and conducting mixed methods research (3rd ed.). London: Sage.

26. Lewis C, Farewell D, Groves V, Kitchiner N, Roberts N, Vick T et al. Internet-based guided self-help for posttraumatic stress disorder (PTSD): Randomized controlled trial. Depression and Anxiety. 2017;34(6):555-565.

27. Blake D, Weathers F, Nagy L, Kaloupek D, Gusman F, Charney D et al. The development of a Clinician-Administered PTSD Scale. Journal of Traumatic Stress. 1995;8(1):75-90.

28. Weathers F, Keane T, Davidson J. Clinician-administered PTSD scale: A review of the first ten years of research. Depression and Anxiety. 2001;13(3):132-156.

29. Ruggiero K, Ben K, Scotti J, Rabalais A. Psychometric properties of the PTSD checklist—civilian version. Journal of Traumatic Stress. 2003;16(5):495-502.

30. Mundt J, Marks I, Shear M, Greist J. The Work and Social Adjustment Scale: a simple measure of impairment in functioning. British Journal of Psychiatry. 2002;180(5):461-464.

31. Kroenke K, Spitzer R, Williams J. The PHQ-9. Journal of General Internal Medicine. 2001;16(9):606-613.

32. Spitzer R, Kroenke K, Williams J, Löwe B. A Brief Measure for Assessing Generalized Anxiety Disorder. Archives of Internal Medicine. 2006;166(10):1092.

33. Saunders J, Aasland O, Babor T, De La Fuente J, Grant M.Development of the Alcohol Use Disorders Identification Test (AUDIT): WHO Collaborative Project on Early Detection of Persons with Harmful Alcohol Consumption-II. Addiction. 1993;88(6):791-804.

34. Morin C, Belleville G, Bélanger L, Ivers H. The Insomnia Severity Index: Psychometric Indicators to Detect Insomnia Cases and Evaluate Treatment Response. Sleep. 2011;34(5):601-608.

35. Dahlem N, Zimet G, Walker R. The Multidimensional Scale of Perceived Social Support: A confirmation study. Journal of Clinical Psychology. 1991;47(6):756-761.

36.EQ5D5L[http://www.euroqol.org/fileadmin/user_upload/Documenten/PDF/Products/Sample_UK__English__EQ-5D-5L.pdf]

37. National IAPT Programme Team. (2011). The IAPT Data Handbook: Guidance on recording and monitoring outcomes to support local evidence-based practice. National IAPT Programme Team: London.

38. Zimet G, Dahlem N, Zimet S, Farley G. The Multidimensional Scale of Perceived Social Support. Journal of Personality Assessment. 1988;52(1):30-41.

39. Cecil H, Stanley M, Carrion P, Swann A. Psychometric properties of the MSPSS and NOS in psychiatric outpatients. Journal of Clinical Psychology. 1995;51(5):593-602.

40. Zimet G, Powell S, Farley G, Werkman S, Berkoff K. Psychometric Characteristics of the Multidimensional Scale of Perceived Social Support. Journal of Personality Assessment. 1990;55(3):610-617.

41. NVivo[computer program]. (2006) Version 10. Doncaster, Victoria, Australia: QSR International Pty Ltd.

42. Braun V, Clarke V. Using thematic analysis in psychology. Qualitative Research in Psychology. 2006;3(2):77-101.

43. NIHR (2019). National Standards for Public Involvement. https://www.invo.org.uk/posttypepublication/national-standards-for-public-involvement/

44. Moore G, Audrey S, Barker M, Bond L, Bonell C, Hardeman W et al. Process evaluation of complex interventions: Medical Research Council guidance. BMJ. 2015;350(mar19 6):h1258-h1258.

45. Coffey A, Beverley H, Paul A. Qualitative Data Analysis: Technologies and Representations. Sociological Research Online. 1996;1(1):1-12.

46. Odell S. Qualitative Data Analysis: A User-Friendly Guide for Social Scientists Ian Dey. London: Routledge, 1993. pp. 285. Behavioural and Cognitive Psychotherapy. 1997;25(1):98-98.

47. Coffey, A. & Atkinson, P. (1996) *Making sense of qualitative data: complementary research strategies,* Sage, London.

48. Silverman, D. (2013) *Doing qualitative research,* Sage, London

49. Ref. http://www.motekmedical.com/products/grail-gait-real-time-analysis-interactive-lab/

50. Ref. http://www.zephyranywhere.com/products/bioharness-3

51. Buck JR, Daniel MM, Singer AC. (2002). Computer explorations in signals and systems using MATLAB. 2nd Edition. Upper Saddle River, NJ: Prentice Hall.

52. Cohen, J. *Statistical power analysis for the behavioral sciences.* Routledge, 1977.

53. Van Gelderen M. Oral presentation at 2019 ESTSS Conference in Rotterdam.

54. Van Gelederen M, Nijdam MJ, Vermetten E. An innovative framework for delivering psychotherapy to patients with treatment-resistant posttraumatic stress disorder: rationale for interactive motion-assisted therapy. *Frontiers in Psychiatry* 2018; https://doi.org/10.3389/fpsyt.2018.00176

55. Higgins, J. P. & Green, S. (Eds.). *Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0*. The Cochrane Collaboration, 2011.

Get in touch

To find out more about our research:

info@ncmh.info

02920 688401

ncmh.info/PTSD

We would once more like to thank our funders Forces in Mind Trust and Health and Care Research Wales.

Finally, and most of all, we thank the participants of this study, for taking part and joining us in our quest to develop more effective treatments for people with post-traumatic stress disorder.

FiMT forces in mind trust SUCCESSFUL SUSTAINABLE TRANSITION

CRONFA GYMUNEDOL COMMUNITY FUND

VETERANS NHS WALES

GIG CYMRU NHS WALES

Ymchwil Iechyd a Gofal Cymru Health and Care Research Wales

Ariennir gan Lywodraeth Cymru Funded by Welsh Government