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A randomised pilot feasibility study of eye movement desensitisation and reprocessing recent traumatic episode protocol, to improve psychological recovery following intensive care admission for COVID-19

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Abstract

Background: Approximately 50% of intensive care survivors experience persistent psychological symptoms. Eye-movement desensitisation and reprocessing (EMDR) is a widely recommended trauma-focussed psychological therapy, which has not been investigated systematically in a cohort of intensive care survivors: We therefore conducted a randomised pilot feasibility study of EMDR, using the Recent Traumatic Episode Protocol (R-TEP), to prevent psychological distress in intensive care survivors. Findings will determine whether it would be possible to conduct a fully-powered clinical effectiveness trial and inform trial design.

Method: We aimed to recruit 26 patients who had been admitted to intensive care for over 24 h with COVID-19 infection. Consenting participants were randomised (1:1) to receive either usual care plus remotely delivered EMDR R-TEP or usual care alone (controls). The primary outcome was feasibility. We also report factors related to safety and symptom changes in post-traumatic stress disorder, (PTSD) anxiety and depression.

Results: We approached 51 eligible patients, with 26 (51%) providing consent. Intervention adherence (sessions offered/ sessions completed) was 83%, and 23/26 participants completed all study procedures. There were no attributable adverse events. Between baseline and 6-month follow-up, mean change in PTSD score was −8 (SD = 10.5) in the intervention group versus +0.75 (SD = 15.2) in controls (p = 0.126). There were no significant changes to anxiety or depression.

Conclusion: Remotely delivered EMDR R-TEP met pre-determined feasibility and safety objectives. Whilst we achieved group separation in PTSD symptom change, we have identified a number of protocol refinements that would improve the design of a fully powered, multi-centre randomised controlled trial, consistent with currently recommended rehabilitation clinical pathways.

Trial registration: ClinicalTrials.gov: NCT04455360.

Introduction

Intensive care survivors frequently experience a range of health sequelae, widely referred to as 'Post Intensive Care Syndrome'.[1] In addition to physical and cognitive impairment, meta-analyses show that 20%–25% experience symptoms of post-traumatic stress disorder (PTSD), in the year following hospital discharge,[2,3] and the prevalence of anxiety and depressive symptoms is 32%–40%[4] and 28%–30%, respectively.[5] These symptoms frequently co-exist[6] and are associated with reduced quality of life,[4,5,7] increased healthcare use,[8] delayed or no return to work[9] and unhealthy coping behaviours.[10] The survivorship phase is frequently overlooked by healthcare providers, and psychological services are widely lacking.[11]

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During the severe acute respiratory syndrome coronavirus two (SARS CoV-2) pandemic, admission illness severity was higher than in previously documented populations.[12] Intensive care services were stretched by unprecedented demand, acute staff shortages and high levels of personal protective equipment.[13] Data from previous infective outbreaks,[14] suggest that clinicians may witness an increased incidence of post-ICU psychopathology, following the pandemic.[15]

Research into attenuating strategies, such as patient diaries,[16] follow-up clinics[17] and nurse-led psychological care[18] has provided mixed evidence of benefit. More recently, calls have grown for collaboration with our colleagues in mental health.[19,20] Eye movement desensitisation and reprocessing (EMDR) is a trauma-focussed psychotherapy believed to reduce distress by facilitating recall, processing and integration of traumatic memories within a positive emotional and cognitive framework.[21] Meta-analyses report reductions in post-traumatic, anxiety and depressive symptoms following a range of traumatic events, including life-threatening medical events.[22,23] International organisations recommend EMDR as an effective and cost-effective treatment for PTSD.[24,25] EMDR reduces post-traumatic symptoms in patients with co-morbid psychotic, depressive, anxiety and substance misuse disorders [26]; an important consideration given the association between pre-existing psychiatric diagnosis and post-intensive care psychopathology.[27] In 2018, Hulme[28] reported reductions in PTSD symptom severity, following EMDR therapy, in a non-randomised pilot study of 10 ICU-survivors. Two recent case studies describe positive treatment effect following ICU admission.[29,30]

The Recent Traumatic Episode Protocol, (R-TEP)[31] is an EMDR intervention, adapted for early delivery, that allows for processing of fragmented, traumatic memories; frequently reported by ICU survivors and associated with post-ICU PTSD development.[32] EMDR R-TEP has reduced PTSD symptoms following missile attacks,[33,34] and life-threatening medical events.[35,36] The aforementioned, case study[30] described a positive treatment response to EMDR R-TEP, following ICU admission.

A number of systematic reviews report uncertainty regarding the timing of psychological interventions, to prevent or ameliorate traumatic stress symptoms. An International Society of Traumatic Stress Studies (ISTSS) review, concluded that there is no strong evidence for early, preventative intervention irrespective of symptomology.[37] Reviews focussing on life-threatening medical events[38] and ICU-survivorship specifically,[39,40] could not identify optimal timing of preventative interventions. Moreover, none of the reviewed studies investigated a protocolised, trauma-focussed psychological therapy aimed at prevention of downstream post-ICU mental health morbidity.

Given the pervasiveness of post-ICU PTSD, paucity of robust evidence and partial support for preventative interventions, we identified both timing of intervention and pre-screening for symptoms, as key uncertainties in our study programme. We therefore elected to investigate delivery of an early EMDR R-TEP intervention, offered to all survivors, to prevent development of PTSD, symptom entrenchment and to avoid excessive suffering.

This study investigated the feasibility of conducting a randomised controlled trial of online EMDR R-TEP with a cohort of intensive care survivors. Through the inclusion of a control group (CG) who received usual care, we aimed to gather preliminary evidence of possible clinical effectiveness. Findings will inform the development and delivery of a subsequent, fully-powered randomised controlled trial (RCT), in a broader cohort of intensive care survivors, which may inform psychological care pathways for this underserved population.

Method

Trial design

COVEMERALD was an investigator-initiated, single-centre, pilot feasibility study. Registered on ClinicalTrials.gov (NCT04455360), in advance of beginning the trial: London-Fulham Research Ethics Committee granted ethical approval on 24th August 2020 (Reference: 20/HRA/3633). At the time of this study, only COVID-19 related research would be considered by UK Health Research Authority. The full study protocol has been published elsewhere.[41] The study was conducted according to Medical Research Council (MRC) guidance on developing complex interventions[42] and is reported according to Consolidated Standards of Reporting Trials (CONSORT) extension to randomised pilot and feasibility trials.[43] All study activity was undertaken at University Hospital Southampton (UHS) National Health Service Foundation Trust (NHS FT), a large regional centre servicing a population of 1.9 million in central southern United Kingdom.

Patients

Patients were eligible to enrol in the study if they had been admitted to intensive care for at least 24 h following a positive COVID-19 test (polymerase chain reaction), were aged 18 years or over, had capacity to provide informed consent, and had been discharged from hospital for less than 3 months. Patients were excluded if they had cognitive impairment, a pre-existing diagnosis of psychosis, suffered acute brain injury or were not expected to survive beyond hospital discharge. Initial inclusion criteria included 24 h of mechanical ventilation, but this was removed on the advice of our patient and public involvement (PPI) group, following reports of distress associated with non-invasive positive pressure ventilation.

Recruitment occurred between October 2020 and April 2021. Consecutive patients were screened for eligibility, following hospital-discharge. The Chief Investigator telephoned potential participants once eligibility criteria were confirmed. Patient information sheets were posted or e-mailed, and a follow-up phone call arranged. If the patient expressed a desire to participate in the study, research staff documented the conversation and recorded

consent in writing. Consenting participants were emailed a link to complete a demographic questionnaire and baseline assessments on an electronic data management system, ALEA Clinical™. All trial procedures were completed remotely due to ongoing COVID-19 restrictions.

Randomisation and treatment

We assigned participants in a 1:1 ratio to receive either usual care (control group CG) or usual care plus online EMDR (Intervention) using computer generated random permutation (ALEA Clinical™): no stratification factors were applied. A brief description of usual care is provided in Supplemental File: Usual care description. Following consent, the study team provided contact details of participants in the intervention arm to the Intensive Psychological Therapies Service (IPTS) at Dorset Healthcare University NHS FT: all sessions took place via Zoom™ videoconferencing platform. The EMDR R-TEP intervention is described in detail according to the Template for Intervention Description and Replication Checklist[44] (see Supplemental File: TIDieR Checklist). Briefly, the sessions consisted of eight phases: history taking; preparation with attention to safety and containment; assessment of points of disturbance (using 0–10 scale of Subjective Units of Distress [SUD] 0=no distress, 10=highest anxiety/distress ever felt); focussed processing and desensitisation with bilateral stimulation; installation of positive cognition with bilateral stimulation; episode body scan; episode closure; re-evaluation of SUD and validity of positive cognition. Each session lasted between 60 and 90 min. Additional sessions were offered if SUD scores were ≥2 on re-evaluation. Up to eight sessions of EMDR were offered. If no points of disturbance were identified (SUD ≤1), sessions were discontinued. Participant flow through the study is shown in Figure 1: Participant flow diagram.

Outcome measures and data collection

Our primary aim was to assess the feasibility of delivering online EMDR to adult survivors of COVID-19 related critical illness. Feasibility objectives were selected from MRC and National Institute for Health and Care Research guidance[45] and pre-published[41]: (i) recruitment rate >30% of patients approached; (ii) intervention session adherence >75%, calculated from sessions completed as a proportion of sessions offered; (iii) protocol adherence >75% of all participants, based upon deviations and violations; (iv) trial completion of >75% of study activities completed; and (v) review of serious events attributable to trial procedures. These were not defined as progression criteria but would inform refinement of study design.

We recorded baseline demographic data, ICU-admission history and medical history; comorbidities, intensive care bed days, length of hospital inpatient stay, total benzodiazepine use, total days of ventilation, (intubated and non-invasive positive pressure ventilation) and illness severity using the Acute Physiology and Chronic Health Evaluation (APACHE) II score. Secondary clinical outcomes were assessed by comparing change in self-reported symptoms from baseline to follow-up (6-month post-hospital discharge), between the control (CG) and intervention groups. The Post-traumatic Stress Disorder Checklist-Civilian version (PCL-C); is a 17 question, patient-reported outcome measure, widely-used and validated in populations including intensive care survivors.[6,46,47] Participants report frequency of experiencing PTSD symptoms, giving a total score between 17 and 85. PCL-C has estimated sensitivity and specificity for PTSD caseness, in primary care populations of 28–30,[48] with an estimated minimal clinically important difference (MCID) in the range of 5.7–10.2 (midpoint of 7.9) based upon comparison with clinician assessment.[49]

Anxiety and depressive symptoms were measured by the Hospital Anxiety and Depression Scale (HADS)[50]; HADS was the most frequently used assessment tool in a meta-analysis of post-ICU depressive symptoms[51] and was used in the UK's largest study of post-ICU mental health outcomes.[6] Scores can be reported separately for anxiety and depression sub-scales, with ≥8[52] defining caseness for each. HADS MCID, for both subscales, is estimated between 1.7[53] and 2[54] points.

PTSD is associated with a range of sequelae, which will be of interest in the main trial and future research workstreams. The following exploratory outcomes were measured in order to explore uncertainty around follow-up rates, questionnaire response rate and time needed to clean and analyse the data; Quality of life was measured using EuroQol Five Dimension-Five level scale (EQ-5D-5L)[55]; We used the Brief Resilience Scale (BRS)[56] to assess resilience. Emerging research is exploring whether bolstering resilience, may offer innovative techniques in ameliorating PTSD symptoms.[57] We used the Council of Nutrition Appetite Questionnaire (CNAQ)[58] to measure appetite and predicted weight change, as PTSD is independently associated with both weight gain and loss.[59] We originally intended to assess cognitive function, physical activity, functional disability and report episodes of delirium in ICU: however, lack of researcher time meant we were unable to perform remote cognition testing, our PPI group recommended removal of functional disability assessment due to participant burden, COVID restrictions denied the opportunity to use physical activity monitors, and delirium episodes had been recorded in the ICU notes only rarely, due to necessary adaptation of clinical practices. Full details and definitions of outcome variables are available in Supplemental File: Table S1. Patient reported outcomes were completed online. All other data were collected by research staff and stored securely, using ALEA Clinical™.

Statistical analysis

This was a feasibility trial in which the effectiveness of EMDR was not evaluated, so a formal power calculation is not appropriate. Sample size was based upon recommendations for feasibility studies,[60] and previously-reported ICU recovery feasibility studies of complex interventions.[61]
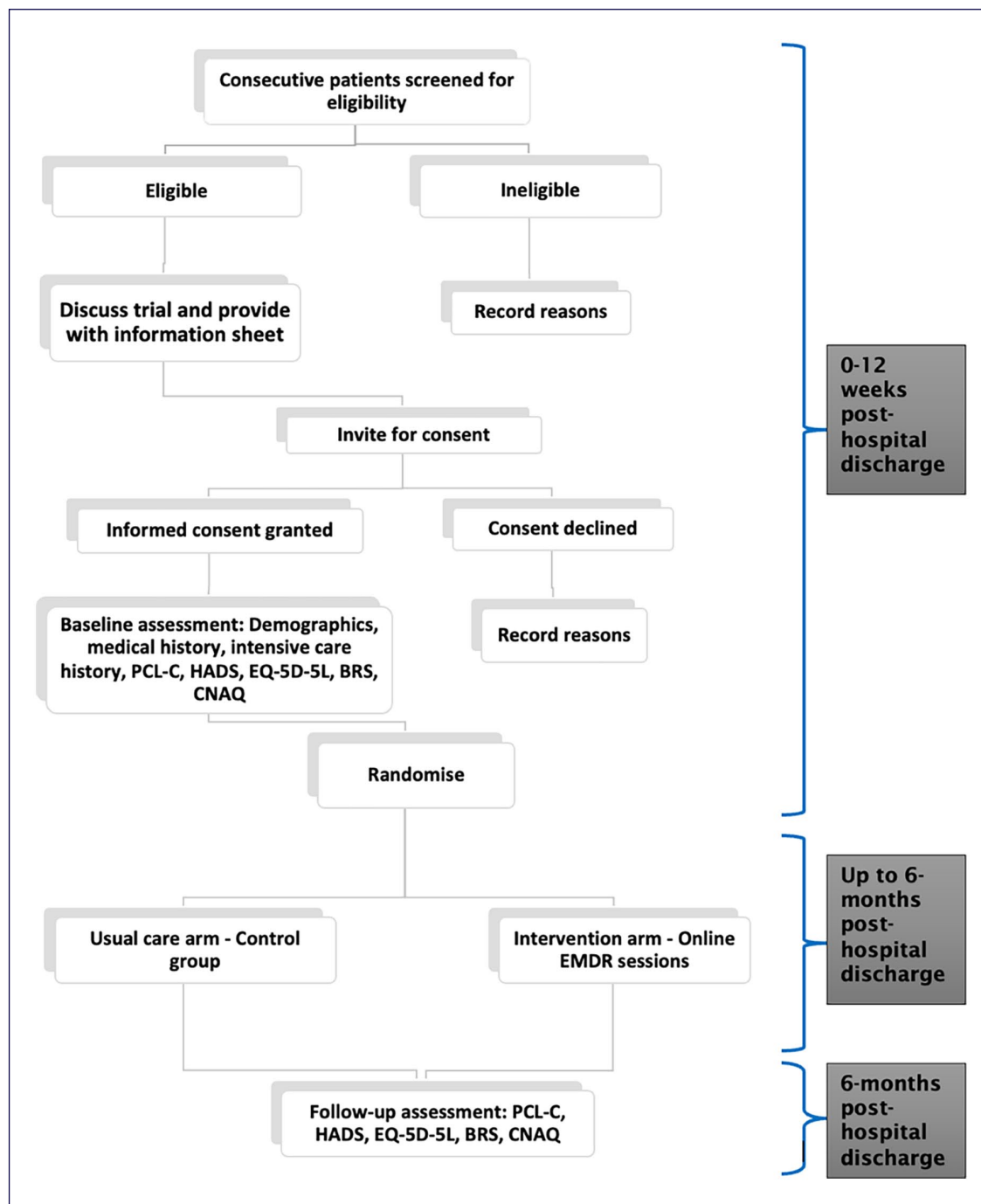
Figure 1. Participant flow diagram.

Twenty-six consenting participants ensured a comprehensive evaluation of feasibility, with 13 randomised to CG and 13 to EMDR. The study statistician was blind to group allocation and downloaded data from ALEA™ to IBM SPSS™ to perform statistical analyses of clinical outcomes. Demographics and baseline characteristics were compared using the Pearson Chi-Square test, or the Fisher's exact test, if nominal, or the Student's t test, or Mann–Whitney U test, if quantitative. Demographic data are reported as numbers (percentage), mean (standard deviation (SD)) and median (inter-quartile range (IQR)) where appropriate. Clinical outcome data are reported as change from Baseline to Follow-up. These data were assessed for normal distribution using the Shapiro-Wilk test.[62] Normally distributed

variables are reported as mean (SD). Non-normally distributed variables are reported as median (IQR). Where appropriate, variables are reported as number (percentage) of the study population.

Results

Feasibility

Seventy-five consecutive, discharged patients were screened for inclusion between October 2020 and April 2021. Nine did not meet inclusion criteria. We could not find contact details for 10 patients and five were missed due to lack of research time for the CI. Fifty-one eligible

patients were approached, with 26(51%) consenting to participation over the 7-month recruitment period. Thirteen participants were allocated to the CG, and 13 to the intervention group. Recruitment, randomisation, retention and trial completion data are shown in Figure 2: Study flowchart (CONSORT) diagram. Sixteen (62%) males and 10 (38%) females were recruited, matching the proportion of patients admitted with severe COVID-19. Demographic and clinical characteristics are summarised in Table 1. There were no significant differences between groups in age, gender, ethnicity, BMI, admission severity (APACHEII), median ICU and hospital length of stay (LOS). Benzodiazepine use was higher in the EMDR R-TEP group (46%) versus CG (23%), although this was not statistically significant.

One participant allocated to intervention did not undertake any EMDR sessions and did not give a reason: the 12 remaining participants attended 34 of 41 arranged sessions, giving an intervention session adherence of 83%. Five sessions were missed due to physical ill health, one due to denial of psychological disturbance, and one due to confusion over appointment date. Mean session attendance was 3.25 per participant. Five participants needed only one session as their Baseline SUD was 1/10. One patient from each group did not complete the 6-month follow-up assessments. One declined but gave no reason and one could not be contacted. Twenty-three participants (88%) completed all study procedures. There were no protocol deviations and no reported adverse events.

Secondary outcomes

The mean Baseline PCL-C score for the whole intervention group was 29.2 although 48.7 in the seven participants who required more than one session. Clinical outcomes are summarised in Table 2. Mean PCL-C score decreased by eight points (Standard deviation (SD) 10.49) in the intervention group but increased by 0.75 (SD 15.17) in the CG ($p=0.126$). There was wide variability in response among participants in the intervention group: 9 reported a reduction in PCL-C scores, (from −3 to −29), one participant reported no change, and one reported an increase of 10 points (a combat veteran with previously reported PTSD diagnosis). In the CG, three of 12 participants reported a reduced PCL-C score (ranging from −5 to −37), three reported no change, six reported increased PCL-C scores (from +3 to +24).

Mean change in overall HADS scores was comparable between groups, with a reduction of 0.91 (SD 4.21) in intervention group and a reduction of 0.42 (SD 6.63) in the CG ($p=0.835$). Mean HADS-Anxiety scores decreased by 0.45 (SD 2.30) in the intervention group and 0.83 (SD 4.02) in the CG ($p=0.787$); median HADS-Depression scores fell by 2 (Inter Quartile Range (IQR) −3,1) in the intervention but increased by 1 (IQR −1.5,2) in the CG ($p=0.263$). Median change in resilience score was −0.17 (IQR −0.03,0.50) in the intervention group, and 0 (IQR −0.33,0.17) in the CG ($p=0.658$). Mean change in CNAQ was 1.6 (SD 3.95) in intervention group and

1.5 (SD 2.54) in the CG ($p=0.943$). Mean EQ-5D-5L scores declined by 0.04 (SD 0.14) in the intervention group and −0.02 (SD 0.15) in the CG ($p=0.657$): mean change in EQ-5D-5L visual analogue score was 11.2 (SD 13.10) in the intervention group and 10.33 (SD 15.33) in the CG ($p=0.889$).

Discussion

To our knowledge COVEMERALD is the first investigation of a protocolised EMDR intervention, following an intensive care admission. We exceeded our pre-published feasibility thresholds and safely delivered online EMDR R-TEP to a cohort of intensive care survivors. We report findings that will inform design changes, and improve the chances of delivering a future fully-powered effectiveness RCT. Our clinical findings indicate that such an investigation of EMDR is warranted, in a broader cohort of intensive care survivors.

The primary outcome of this study was feasibility. We met recruitment target in 7 month, with a mean of 3.7 participants per month, during a period of unprecedented clinical pressure. We were able to recruit 51% of eligible patients approached, exceeding our published target of 30%. To achieve our recruitment target (n=26) we screened 75 patients. Accounting for exclusions, missed patients and trial decliners, 35% of screened patients consented to trial participation. Meaningful comparison of recruitment rates, are difficult due to the novelty of this intervention in this cohort. However, a review of publicly funded trials in the UK noted that the median recruitment rate was 0.98 participants per centre per month, with 50% of RCTs failing to meet recruitment targets.[63]

Consecutive patients were approached for COVEMERALD participation and the demographic characteristics of the study sample were largely representative of the wider patient population: however, the self-declared ethnicity of study participants (96% white) indicates an under-representation of other ethnic groups, based on ICU patient populations. Between September 2020 and April 2021, 28% of patients admitted to UK intensive care units with COVID-19, were of black, Asian, mixed or other ethnicity[12]: 23% of patients admitted to our unit during the recruitment period were black, Asian, mixed or other ethnicity yet in this study >90% of participants were white. Furthermore, 14% of patients who we approached declined participation in our online intervention study, due to lack of digital access. Widely recognised as a social determinant of health[64] and exacerbated by the COVID-19 requirement for social distancing, the digital divide presents an increasing risk of exacerbating health inequality.[65] Recently the UK National Institute for Health and Care Research (NIHR) has published guidance for ensuring inclusivity in research,[66] which will inform the approach to recruitment in future studies.

A key uncertainty of our trial was whether EMDR R-TEP, delivered early (within 3 month of hospital discharge), could work as a protective intervention against development of persistent post-traumatic stress symptoms,
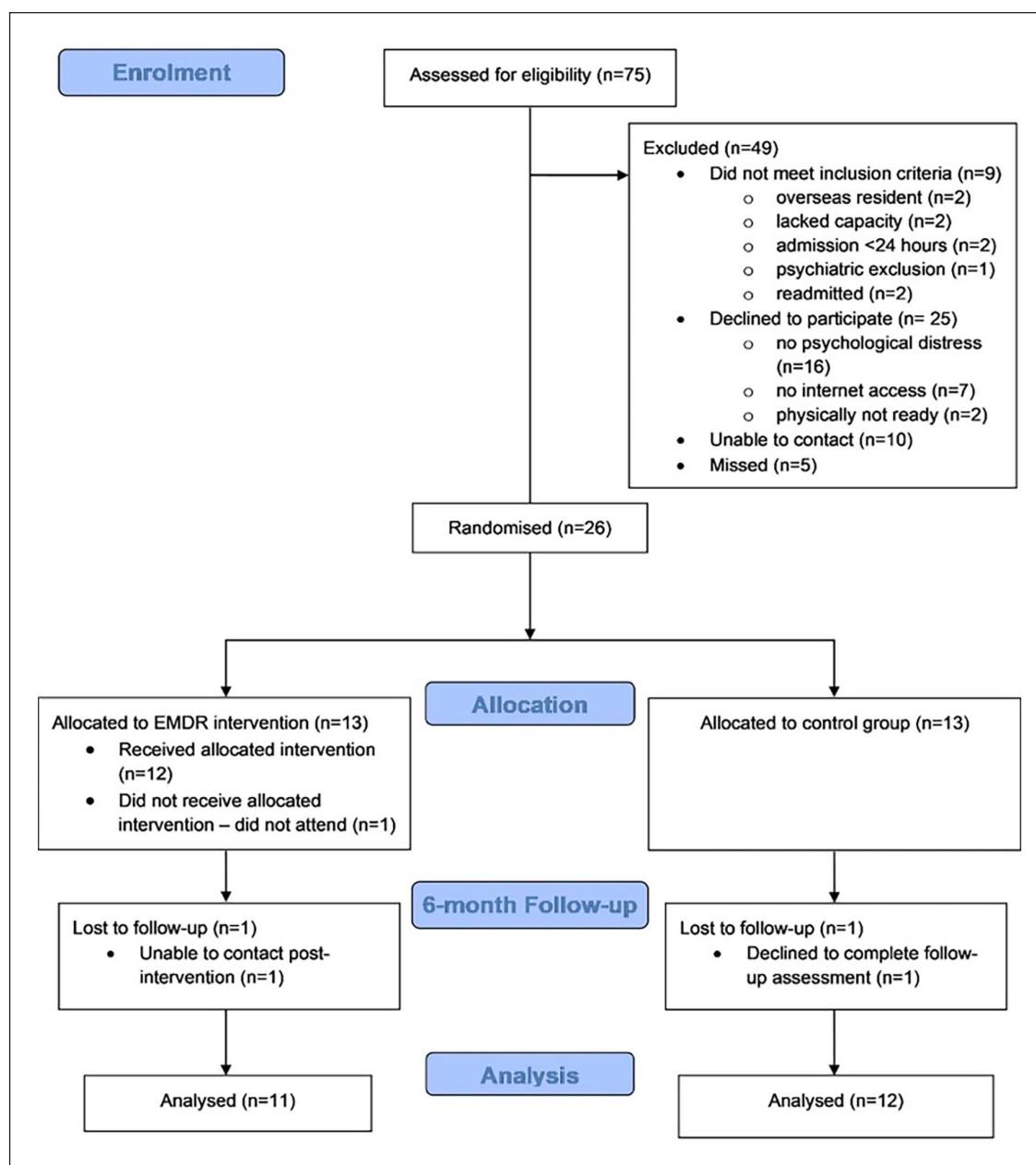
Figure 2. Study flowchart (CONSORT diagram).

irrespective of symptomology at the time of recruitment. Eligible patients most frequently cited lack of psychological distress as the main reason for trial decline. Moreover, of the 12 participants who received the intervention, five patients only had one session, due to no psychological distress. Our cohort was too small to undertake meaningful sub-group analysis, comparing symptom resolution between those above and below clinical cut-offs. We believe our findings assert that future studies should focus on screening for PTSD symptoms before offering EMDR, consistent with international treatment guidance.[24,25,67]

Screening for psychological symptoms at 3 month is further supported by our experience of intervention session adherence: although 34 of 41 (83%) organised sessions were completed suggesting that participants found the intervention acceptable, five of these seven missed sessions were due to physical illness in the early

rehabilitation phase. To promote RCT scalability and clinical implementation, we propose aligning the psychological screening with the 3-month post-hospital discharge follow-up visit, recommended in ICU rehabilitation clinical pathways.[68] A recently published survey reported increasing provision of UK follow-up services, yet highlighted important gaps, most commonly in psychological support.[11] Our work supports the author's conclusion that improving the evidence base will be key to expanding service delivery and impacting upon patient-centred outcomes.

The known relationship between EMDR intervention fidelity and treatment effect size[69] has important implications for future studies of clinical effectiveness. The COVEMERALD EMDR R-TEP intervention was performed by a Consultant clinical psychologist and two trained, experienced psychological therapists. An EMDR

Table 1. Demographic and clinical characteristics at baseline.

Variables	All (N = 26)	Control (N = 13)	EMDR (N = 13)	p-value
Age, mean (SD), years	58.0 (15.3)	58.3 (16.5)	57.7 (14.8)	0.923
Gender, male n (%)	16 (61.5)	8 (61.5)	8 (61.5)	1.00
BMI	32.7 (6.82)	32.5 (6.70)	32.9 (7.21)	0.885
Ethnicity n (%)				0.593
White (British)	23 (88.5)	11 (84.6)	12 (92.3)	
White (Other)	2 (7.7)	1 (7.7)	1 (7.7)	
Unknown	1 (3.8)	1 (7.7)	0 (0.0)	
Medical history n (%)				
Anxiety	1 (3.8)	0 (0.0)	1 (7.7)	0.308
Bipolar	1 (3.8)	0 (0.0)	1 (7.7)	0.308
Cancer	1 (3.8)	1 (7.7)	0 (0.0)	0.308
Cardiovascular	4 (15.4)	4 (30.8)	0 (0.0)	0.030
Depression	1 (3.8)	1 (7.7)	0 (0.0)	0.308
Endocrine	5 (19.2)	2 (15.4)	3 (23.1)	0.619
Gastrointestinal	3 (11.5)	1 (7.7)	2 (15.4)	0.539
Musculoskeletal	3 (11.5)	2 (15.4)	1 (7.7)	0.539
Neurological	1 (3.8)	1 (7.7)	0 (0.0)	0.308
PTSD	1 (3.8)	0 (0.0)	1 (7.7)	0.308
Renal	1 (3.8)	0 (0.0)	1 (7.7)	0.308
Respiratory	4 (15.4)	3 (23.1)	1 (7.7)	0.277
APACHE II score^	11 (7.13)	11 (8.12)	11 (7.13)	0.757
ICU LoS^	8 (5.18)	6 (5.18)	9 (7.17)	0.719
Hospital LoS^	16 (10.30)	13 (10.30)	9 (7.17)	0.976
Total ventilation days^	6 (4.15)	6 (4.19)	5 (3.13)	0.881
Benzodiazepine use n (%)	9 (34.6)	3 (23.1)	6 (46.2)	0.216

SD: standard deviation; IQR: inter-quartile range; BMI: body mass index; PTSD: post-traumatic stress disorder; APACHE: acute physiology and chronic health evaluation; ICU: intensive care unit; LoS: length of stay. Data are presented as mean (SD), ^median (IQR) or n (%).

Table 2. Change from baseline to 6-month in clinical outcomes in intervention and control groups.

Questionnaire	Control (N = 12)	Intervention (N = 11)	p-value
PCL-C	0.75 (15.17)	−8.00 (10.49)	0.126
HADS overall	−0.42 (6.63)	−0.91 (4.21)	0.835
HADS anxiety	−0.83 (4.02)	−0.45 (2.30)	0.787
HADS depression*	1.00 (−1.50, 2.00)	−2.00 (−3.00, 1.00)	0.263
BRS*	0.00 (−0.33, 0.17)	−0.17 (−0.33, 0.50)	0.658
CNAQ	1.50 (2.54)	1.6 (3.95)	0.943
EQ-5D-5L score	−0.02 (0.15)	−0.04 (0.14)	0.657
EQ-5D-5L VAS	10.33 (15.33)	11.2 (13.10)	0.889

PCL-C: post traumatic stress disorder checklist: Civilian; HADS: hospital anxiety and depression scale; BRS: brief resilience scale; CNAQ: council of nutrition and appetite questionnaire; EQ-5D-5L: EuroQol 5 dimensions-5 levels; VAS: visual analogue scale.
Data are presented as mean (Standard Deviation) and p-value reported from t-test, or *median (Inter Quartile Range) and p-value reported from Wilcoxon rank-sum test.

consultant offered clinical supervision: however, we could not formally check intervention fidelity due to time and resource constraints. Future studies should consider using an EMDR fidelity rating scale,[70,71] to ensure validity and enable replication, and provide an account of possible relationships between intervention fidelity and treatment effect size, including individual dose-response variability. Moreover, there are fewer EMDR R-TEP practitioners than those trained in standard protocol EMDR. Careful consideration should be given to which EMDR protocol is most useful and scalable in this context.

There were no protocol deviations or safety incidents, consistent with systematic reviews of EMDR, including those studies in survivors of life-threatening medical events.[72] COVEMERALD exceeded the reported mean completion rate (75%) of seven other studies investigating psychological interventions for ICU survivors[39]

Clinical outcomes

Our study was not powered to detect efficacy of the intervention compared to usual practice. The reported values do match findings from a systematic review of studies of

EMDR in survivors of other life-threatening medical events[72] and show a trend towards symptom reduction in PTSD (−8) and depressive symptoms (−2). These are in the ranges defined as MCID of 5.7–10.2[49] and −2[53] respectively, however, clinical relevance should not be ascribed to these results, given the study design limitations. We do, however, believe these results support the case for further investigations of EMDR for symptom reduction in survivors of critical illness.

This trial was conducted during an ongoing global pandemic, with recognised adverse effect on population mental health. To adequately explore interaction between our patient cohort, contextual and cultural factors, we recommend that future researchers adopt a mixed-methods approach, in larger samples. This would enhance understanding of when, how and under which circumstances EMDR is effective and may offer insight into the wide treatment response variability.

Limitations

The study has a number of design limitations which may affect generalisability, many of which have been outlined in the discussion; this was a small, single-centre study, with inadequate representation of under-served populations, failure to address digital exclusion and lack of intervention fidelity checks. Moreover, there is a high risk of bias associated with non-blinded clinical outcome measures. Our follow-up period was limited to 6 month due to lack of funding. Given the uncertain mental health trajectory following ICU discharge, future studies should report clinical outcomes up to a minimum of 12 month post-discharge, preferably longer. Our study was undertaken during a period of unprecedented clinical pressure, using a patient population limited to sufferers of COVID-19. Rapid changes to the UK's research rules meant that we were limited to undertaking research in this cohort. While this may limit generalisability of our study, emerging evidence suggests that post-discharge challenges faced by COVID patients are comparable to those in wider ICU-survivor cohorts.[73] However, this study does need to be repeated in a more representative cohort of ICU-survivors. Remaining uncertainties require refinement of trial design, before proceeding to a definitive RCT of clinical effectiveness.

Conclusion

This study met feasibility and safety targets. However, fundamental design changes will need to be applied before progression to an adequately powered, multi-centre RCT of clinical effectiveness. A future trial of EMDR for intensive care survivors should consider a larger number of simultaneously recruiting sites, and adopting strategies to ensure representative inclusion of under-served ethnic, socio-economic and digitally-excluded populations. We recommend psychological screening of participants, consistent with recommended ICU clinical rehabilitation pathways. The EMDR intervention should be fidelity-checked, and offered online or face-to-face. To support scalability and rapid translation of findings, the RCT should be embedded within established clinical referral pathways. A mixed-methods approach, should be adopted, in order to capture the complexity of interaction between the intervention, outcome, context, culture and mechanisms of change.

Authors' contributions

AB conceived and designed the study, acquired and interpreted the data, and led manuscript preparation, under the supervision of NP, DSB, RC and MPWG. HG acquired and interpreted the data, designed and formatted the tables. SR conceived and designed the study and led intervention delivery and supervision. ES developed the EMDR R-TEP intervention, trained the psychological therapists and participated in study design. NP provided intellectual input and critical revision of the manuscript. DSB contributed to study design, intellectual input and critical revision of the manuscript. MPWG designed the study, provided intellectual input and critical revision of the manuscript. RC conceived and designed the study, acquired and interpreted the data, provided intellectual input and critical revision of the manuscript. All authors contributed to, edited and approved the final manuscript.

Availability of data and materials

Datasets used in preparation of this manuscript can be accessed from the corresponding author on reasonable request.

Consent for publication

Individual's data is not included in this manuscript, therefore consent for publication is not required.

Declaration of conflicting interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Ethics approval and consent to participate

London-Fulham Research Ethics Committee, United Kingdom granted ethical approval on 24th August 2020. (Reference: 20/HRA/3633). The full study protocol has been published elsewhere(41). Due to the ongoing requirement to maintain social distancing during the pandemic, verbal consent was obtained and documented during telephone consultation between participants and research staff. Consent forms were posted to all participants.

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