Protocol for a non-randomised wait-list control of a self-management intervention for people living with Long COVID

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Roles and responsibilities:
Dr Faith Martin – analysis, interpretation, lead the reporting, trial registered under name
Dr Hayley Wright – involved in study design and administration
Dr Cain Clark – lead analysis, guide interpretation, reporting
Dr Anna Lynall – study administration, administration of the intervention
Gabriela Matouskova – study administration, administration of the intervention, safety of participants
Stuart Ennis - administration of the intervention
Prof Andy Turner – study lead, overall responsibility

Trial Sponsor: Coventry University
No co-ordinating centre or other management teams owing to the nature of the trial (using intervention that is already being ran)

Introduction

Background and rationale

Long COVID affects over 2% of the UK population [1]. It is characterised by symptoms lasting at least 12 weeks (3 months) following acute COVID infection and can include a range of symptoms from fatigue and respiratory difficulties, to pain and a loss of sense and smell [2]. People living with Long COVID report significantly depleted quality of life and emotional wellbeing, with many also experiencing depression and anxiety owing to the impact of the condition on their lives [2, 3].

Many of the symptoms of Long COVID have been targeted in other conditions using self-management interventions. For example, a non-condition specific self-management intervention know as the Chronic Disease Self-Management Program, shown excellent evidence of improving health status, including pain, shortness of breath, fatigue, illness intrusiveness, health distress and self-reported health when delivered online to people with chronic diseases of heart or lung, and type 2 diabetes [4]; and improved health distress, activity limitation, self-reported global health, and pain for participants with fibromyalgia and / or arthritis [5]. Generic self-management interventions may be of benefit to people living with any long-term impact of COVID-19.

Peer-delivery may be key. Many people with Long COVID describe feeling unsure of themselves, stigmatised by others, and disbelieved by health care professionals [6, 7]. Peer-delivered interventions offer validation and can provide knowledge and practical symptom management techniques, alongside reduced isolation[8]. Digital interventions must be carefully reviewed to ensure they do not deepen health inequalities, however are vital for people with fatigue (which reduce ability to engage with face-to-face meetings and travel) and with likely repeated restrictions on face-to-face meetings owing to the pandemic[2, 6, 9] . Effective peer-delivered self-management interventions use structured, empirically and theoretically grounded interventions, to supplement the social support provided by peer-led support. The use of trained peers offers a potentially cost-effective approach to supporting the needs of people with Long COVID [10]. Using trained peer-facilitators to deliver self-management interventions can address the sense of isolation and being disbelieved/ not understood that many people with long-term conditions experience [11].

Reviewing the literature, there are very few studies reporting outcomes of interventions to support people with Long COVID. Findings are being reported from studies offering physical exercise to people at various periods following acute COVID, including those who have experienced fatigue after COVID [12]. However, these are narrow in focus and do not provide broad intervention for managing the challenges of Long COVID. A case study of the use of cognitive-behavioural therapy to specifically address anxiety and depression has been published, providing an illustration of the use of this approach [13].

There has been no research to date to evaluate the impact of Long COVID peer-support, nor to evaluate a structured peer-delivered intervention. There is ongoing research seeking to understand what techniques for self-management people with Long COVID use [14]. The challenge that these interventions potentially place some “burden” on the person to remember and direct their own care, learning and using strategies with support has been acknowledged, as particular pertinent to people with Long COVID, many of whom experience fatigue and brain fog [15]. Nevertheless, self-management interventions are recommended in various clinical guidelines [15, 16]. The only published study of outcomes of rehabilitation interventions with a self-management element we could locate reported pre-post data from an intervention ran in routine clinical practice within the National Health Service in England [17]. This seven week “course” provides management advice for various symptoms, including emotional wellbeing. Significant improvements were found in health-related quality of life. This intervention is delivered “live” online by an interdisciplinary clinical team. Digital interventions that people can use “as and when” might be particularly important for Long COVID, owing to the high levels of fatigue and “brain fog”.

Whilst there are funded studies underway to develop interventions [18], Long COVID clinics up and down the UK are faced with patients requiring support and treatment. As such, it is important to rapidly develop and evaluate interventions and support packages. There is then an outstanding need for an evidence-based, digitally delivered, peer-support self-management intervention for people living with Long COVID. Our research will evaluate a digital, peer-facilitated self-management intervention for adults with Long COVID symptoms. Our intervention has been developed from our existing self-management programme “ Hope Programme for people living with cancer, in its digital format, using co-design methods with people with Long COVID [19]. We have conducted a simple

pre-post study of our intervention (in review, available in pre-print), which found a retention rate of 60% and provided initial support for the impact of the intervention through paired comparisons on positive wellbeing and self-efficacy to manage the long term condition [19]. Given the lack of established usual care or another effective intervention, there is no clear rationale for any active comparison group. Wait-list comparison was chosen for pragmatic reasons, as this study is embedded in existing planned provision of the Hope Programme

Objectives

The study seeks to test the following hypotheses: using a non-randomised wait-list control group, there will be improvements in positive mental wellbeing (primary outcome), self-efficacy, fatigue, depression, anxiety and loneliness following an 8-week digital peer-supported self-management intervention, for people living with long COVID.

Trial Design

This study is a pragmatic non-blinded non-randomised wait-list controlled pre-post study. The non-randomisation is partly for practical and ethical purposes. The study relates to an intervention that is already on offer to people in the Coventry Warwickshire and Rugby (CWR) area, owing to the way in which the service is funded. The Live well with HOPE project aims to reduce the negative impact of COVID-19 by empowering people across CWR to self-manage their health and wellbeing, develop social connections and peer-support opportunities. https://www.hopecwr.h4c.org.uk/ [The uptake of the intervention is predicted to be high, owing to its novelty and the high needs amongst people living with Long COVID. Given this, the wait-list control design will not alter people's access to the service. Randomisation to intervention or control group will not be conducted, rather people will be allocated to the intervention until full and the following participants will be allocated to the wait-list, as would occur if the study were not taking place.

Methods: Participants, interventions and outcomes

Study setting

This study will take place in a community setting. Participants from the community will be able to access the intervention. The digital intervention delivery means they will be able to use this at their convenience. All data are collected online. Recruitment is not through any specific "site", rather via advertising. The funding prioritises courses for people living in the local community (Coventry, Warwickshire and Rugby), but the courses will be open to people from across the UK. Residents of Coventry, Warwickshire and Rugby will be given priority access to the Hope Programme.

Eligibility

Participants will be eligible if they are aged 18 years or older and self-defining as living with Long COVID. No eligibility checks will be conducted – self-report will be taken as evidence of person living with Long COVID. Participants must be fluent in English and have access to the necessary technology to take part in the digital intervention.

Interventions

Intervention group: Participants will receive the Hope Programme for Long COVID intervention This intervention was delivered entirely online with new content released each week. The web-based platform has information in written and audio/video formats and interactive exercises (e.g. quizzes, activities to record goals). There is the option to post comments and comment on other's posts. There is a digital social forum area where people can "chat" to one another. This provides significant

opportunity for peer support. The intervention is delivered by clinical exercise specialists from Atrium Health Atrium Health (www.atrium-health.co.uk), a Coventry-based social enterprise providing rehabilitation services.

The content includes an emphasis on pacing, as per guidelines for Long COVID [20]. The intervention can be accessed at the participants' convenience, for as many minutes and on as many occasions as desired. The content is summarised in Table 1.

Table 1: Weekly topics and activities

Session	Core content, in addition to weekly goal setting
Week 1: Introduction: Instilling hope	• Welcome and introductions • The benefits of positive emotions • The power of gratitude • Self-compassion • Personalised goal setting • Video: how to set achievable goals • Dates for live sessions
Week 2: Long COVID Symptoms	• Fatigue management; including the boom and bust cycle; prioritizing, planning, and pacing • What is brain fog, and what can we do to help ourselves? • Forum topics: sharing experiences of managing fatigue and brain fog • Further resources and links to Long COVID information and support
Week 3: Managing stress	• Coping with unhelpful thinking patterns • Understanding and managing stress • Self-compassion and acceptance • Mindfulness for stress management and meditation • Video: how to be kind to yourself • Further resources and links (e.g., videos, podcasts, and websites) to self-compassion, mindfulness, and stress management
Week 4: Communication	• Communication skills and tips for talking with health professionals, your employer and your family • Preparing for difficult conversations • Asking for and accepting help • Compassion for worries • Further resources and links (e.g., videos, podcasts, and websites) to Long COVID support groups
Week 5: Sleep and mindfulness	• How does COVID affect our sleep? • Tips for sleeping better • Tips to aide relaxation • Introduction to Mindfulness, meditation and relaxation
Week 6: Move better, feel better	• Keeping active with Long COVID • Post-exertional malaise • Tips for getting active • Eating well for physical and mental health

	• Managing changes to taste and smell after COVID-19
Week 7: Happiness and strengths	• Long COVID and effects on mood • Happiness and hope • Identifying your character strengths • Understanding how using your strengths can lead to a more fulfilling life • Video: The science of character strengths • Managing setbacks • Tips for authentic happiness; managing setbacks and keeping going
Week 8: Moving forward with Hope	• Hopes and dreams • Doing something for yourself • Planning pleasant activities • Keeping in touch with peers • Review of the programme • Feedback • Staying hopeful

Control group: Those allocated to the wait-list control group will access the intervention after follow-up data collection. It will be made clear to them that their responses on the measures will not be shared in an identifiable format with anyone involved in the intervention delivery and that neither their responses nor their participation in the study have any bearing on their subsequent access to the intervention.

This study will collect data from the delivery of the intervention within the community. As such, there are no criteria for discontinuing or modifying the intervention.

To improve adherence to intervention protocols, participants will receive a £10 gift voucher as thanks on completion of the questionnaires.

Owing to the setting of the study, no restrictions will be placed on the use of additional interventions or access to other care for participants.

Outcomes

Primary outcomes: Positive mental wellbeing measured using the Warwick-Edinburgh Mental Wellbeing Scale (WEMWBS) [21], at baseline and 8 weeks later. Emotional wellbeing is impacted by Long COVID [3], and our patient-public involvement groups have highlighted a desire for this to be the primary outcome measure for our self-management intervention. The measure also correlates highly with measures of mental illbeing, i.e. depression and anxiety scales [22].

Secondary outcome measures:

1. Self-efficacy measured by the Self-Efficacy for Managing Chronic Disease 6 item scale (SEMCD6) [23].
2. Fatigue measured by the Fatigue Severity Scale (FSS) [24]

3. Loneliness measured by the UCLA Loneliness Scale, Version 3 (UCLA3) [25]
4. Depression measured by the Patient Health Questionnaire 9 item scale (PHQ9) [26]. This measure will demonstrate both potential improvements and adverse effects in relation to clinical norms.
5. Anxiety measured by the Generalised Anxiety Disorder 7 item scale (GAD7) [27]. This measure will demonstrate both potential improvements and adverse effects in relation to clinical norms.
6. Long COVID symptoms reported via the COVID-19 Yorkshire Rehabilitation Screening Tool (C19-YRS) [28].
All measured at baseline and 8 weeks later.

Mean scores will be calculated for all outcomes. Classification into "caseness" for the depression and anxiety measures will be conducted, using established norms. This will allow investigation of the proportion of people moving between caseness and non-caseness (or vice versa).

Participant timeline
Participants who have already signed-up to the Hope Programme for Long COVID will be contacted by email to invite them to take part in the study. A link will allow them to view the information sheet, email address to contact with any questions, and complete the consent form. It will be made clear that their participation in the study is an entirely voluntary additional element that will not interfere with their ability to access the intervention. If consenting, participants will receive an email link to take them to the baseline measures to complete online, one week before the intervention starts The participants will then either have access to the intervention for 8 weeks, or be placed on the waiting list. Participants living outside of CWR area knew they were on the waiting list when they completed the baseline measures. At the end of the 8 week period, all participants will be emailed a link to complete post-intervention measures - collected within the two weeks following the end of the intervention.

Sample size

This was a pragmatic trial design. Approximately 50-60 participants from CWR area who sign up for the Hope Programme intervention, being run by H4C in January 2022, will constitute the intervention group. Our experience of running digital interventions has shown that optimum group size for social interaction and peer support is approximately 50-60. Participants from outside of the CWR area will be offered a place on another Hope Programme being run in March 2022. These participants will constitute the control group

Recruitment
Participants will be recruited via community groups and partners, social media, flyers placed in libraries, GP surgeries, long COVID clinics and through community events. Participants enrolled in the intervention will then be invited to take part in the study. This will not be a condition of their continued access to the intervention, rather explained that this is an option in addition. The delivery of this intervention in the community plans to recruit 100-120 participants.

Methods: Assignment of interventions
Allocation to the intervention or wait-list condition will be on a first-come, first-served basis. This is as our study takes place in the context of the real-life delivery of the intervention in the community. As such, there is no sequence generation. Allocation will not be concealed and no blinding will be used. All data will be collected using online questionnaires, without interaction with a researcher.

Methods: Data collection, management and analysis

Data collection methods

Data will be collected at baseline and follow-up at the end of the intervention. All participants enrolled in the study will receive links to online questionnaires to complete, regardless of their engagement with the intervention platform. In addition to the measures listed as outcomes, basic demographic information will be collected (age, gender), and basic information about the impact of Long COVID on life (reduction in working hours). Long COVID symptoms will be assessed using the Covid-19 Yorkshire Rehabilitation Scale (C19-YRS) [28]. If participants do not complete their questionnaires within 7-14 days, they will be sent 3 reminders.

Data management

Data will be collected using Qualtrics, an online survey tool. No data entry will then occur by the research team, as everything will be electronically completed by participants. All completed data will be downloaded into SPSS.

Statistical methods

Descriptive statistics will summarise the characteristics of the participants and their movement through the study. Baseline characteristics and follow-up scores will be summarised.

An intention to treat analysis will take place, using multiple imputation to handle missing data.

A per-protocol (PP) analysis will also to include only those participants who completed all study questionnaires and attended at least 4 sessions of the intervention (in the intervention group), therefore are said to have “completed” the intervention.

Both analyses will compare follow-up scores between the two groups, covarying for the baseline score.

Methods: Monitoring

There are no data monitoring plans. We will be collecting data on an intervention occurring in real-life. The outcomes measures will allow us to examine harms in relation to changes in scores that indicate e.g. worsened depression, anxiety, or mental wellbeing. No interim analysis will be conducted. The intervention will be delivered on a digital platform. This is monitored by trained, lay facilitators. Any evidence of adverse events reported in participants' comments or interactions with the intervention will be shared with the researchers.

Ethics and dissemination

Research ethics approval

Approved 22/12/2021, Coventry University Research Ethics Committee (Priory Street, Coventry, CV1 5FB, UK; ethics.uni@coventry.ac.uk), ref: P106036.

Protocol amendments

The study examines the delivery of an intervention in real-life, as such we anticipate no changes to the intervention nor data collection schedule. Changes to the protocol will be recorded and reflected in the reporting of the results.

Consent or assent

Informed consent will be captured digitally: participants will be sent a link to the information sheet, details of who to contact with any questions, and then the digital consent form.

Confidentiality
Limited personal information is collected. Data will not be shared beyond the research team.

Declarations of interests
AT is the co-inventor of the HOPE Program and founder of Hope For The Community (H4C). GM and AL are the CEO and COO, respectively, of H4C.

Access to data
The research team will have access to the data set. There are no contractual requirements for sharing the data in relation to our funding. Interested researchers can contact the researchers to request access to the data.

Ancillary and post-trial care
This study examines an intervention delivered in real-life. The facilitators routinely provide signposting information for people who may require additional resources, for example signposting people for further mental health support.

Dissemination policy
The trial results will be shared with participants via the company delivering the intervention, using their website and email. We plan to publish results in academic publications. We do not intend to use professional writers.

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