CLINICAL STUDY PROTOCOL

Finding My Way UK: Adaptation and Replication Testing of the Benefits of Online Psychological Support for Cancer Survivors

IRAS Number: 288469

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Sponsor: The University of Chester

Project Funder: North West Cancer Research

PROTOCOL APPROVAL/KEY TRIAL CONTACTS

Protocol Title: Finding My Way UK: Adaptation and Replication Testing of the Benefits of Online Psychological Support for Cancer Survivors

Short Title Finding My Way UK

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FUNDING AND SUPPORT IN KIND

FUNDER	FINANCIAL AND NON-FINANCIAL SUPPORT GIVEN
North West Cancer Research	Funding the study in full

ROLE AND RESPONSIBILITIES OF SPONSOR, FUNDER, TRIAL MANAGEMENT COMMITTEES/GROUPS & INDIVIDUALS

Sponsor

The University of Chester

Funder

North West Cancer Research

Trial Steering Committee

The trial steering committee will monitor the ongoing progress of the study and feedback to the research team as appropriate. The trial steering committee will provide final approval for all major study documents, including trial protocol, any necessary amendments, intervention content, and resulting publications. The Trial Steering Committee is chaired by the Chief Investigator.

Data Monitoring (and ethics) Committee

There is no formal data monitoring committee.

Project Management Group

The project management group will ensure all practical details of the trial are progressing and working well and that everyone within the trial understands them.

The group will include representatives from the current research team, the research team responsible for the original Australian intervention, and a patient representative.

The Chief Investigator is a member of the project management group.

Responsibilities

The trial will be designed by the Chief Investigator and Trial Coordinator in consultation with the Trial Steering Group. Clinical Research Network staff will be responsible for patient identification and approach. The research team will manage all aspects of data collection and intervention delivery. The data analysis will be managed by the research team in consultation with a statistician. The interpretation of the results will be agreed between the steering group and the research team. The dissemination of the results will be managed by the research team. The final clinical study report will be generated by the research team with approval from the steering group and sponsor.

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GLOSSARY OF TERMS AND ABBREVIATIONS

Term	Definition
CompACT	Comprehensive assessment of Acceptance and Commitment Therapy processes
CRN	Clinical Research Network
DASS-21	Depression, Anxiety, and Stress Scales (21-item version)
FMW	Finding My Way
LCTC	Liverpool Clinical Trials Centre
MOS	Medical Outcomes Study
PIC	The Psychological Impact of Cancer Scale
QLQ-C30	The European Organisation for Research and Treatment of Cancer Core Quality of Life Questionnaire (version 3.0)
REC	Research Ethics Committee
UK	United Kingdom

1. STUDY SYNOPSIS

Name of Sponsor	North West Cancer Research
Name of Investigational Product:	Finding My Way: An online cognitive behavioural therapy-based psychological intervention for cancer survivors
Title of Study:	Finding My Way UK: Adaptation and Replication Testing of the Benefits of Online Psychological Support for Cancer Survivors
Medical Condition Under Investigation:	Cancer (Of all sites)
Study centres	Multi-centre study in England
Protocol Number:	
Study Design:	Randomised, investigator-blind, waitlist-controlled study to determine the efficacy of an online cognitive behavioural therapy-based intervention in improving psychological outcomes in cancer survivors
Planned Sample Size:	294 participants in total (in order to achieve 147 participants per study arm)
Trial Subjects Selection Criteria:	*Inclusion criteria:* The subject must satisfy the following criteria for entry into the study: • Been diagnosed with cancer in the past six months • Have received anti-cancer treatment with curative intent • Aged 16 years or over • Sufficiently proficient in English to provide informed consent and use the online programme • Able to access the internet • Currently have (or willing to set up) an active email address *Exclusion criteria:* Patients will be excluded from the study if any of the following applies: • Severe comorbidity considered by the screening nurse to interfere with the individual's ability to complete the requirements of the study or provide informed consent (e.g., intellectual disability or neurological impairment).
Study Objectives:	*Primary* • To determine whether the UK-adapted Finding My Way programme reduces cancer-specific distress. *Secondary* • To determine the effects of the UK-adapted Finding My Way programme on anxiety, depression, and general stress. • To determine the effects of the UK-adapted Finding My Way programme on quality of life.

	• To determine the effects of the UK-adapted Finding My Way programme on psychological adjustment to cancer. • To determine the effects of the UK-adapted Finding My Way programme programme on health service utilisation. • To determine whether social support, vulnerability to distress, and motivation to seek information moderate the effects of the UK-adapted Finding My Way programme programme on primary and secondary study endpoints. • To determine whether psychological flexibility mediates the effect of the UK-adapted Finding My Way programme on cancer-specific distress. We will also conduct exploratory analyses testing the potential moderating effects of clinical and demographic variables on primary and secondary study endpoints.
Investigational product	A six-week online programme of cancer-specific cognitive-behavioural therapy modules, plus one additional booster module
Comparator	Waitlist control: This information group will initially receive an information pack informing them of resources already available to cancer survivors in the UK. After the 6-month follow-up questionnaire has been completed, they will then be granted access to the Finding My Way programme.
Maximum Duration of Treatment	The Finding My Way programme includes 6 weeks of content, plus an additional booster module presented one month after initial treatment completion. Participants will continue to be able to access website content for an additional 4 months after the final participant has completed all study-related activities.
Procedures:	*Patient Identification and Approach* Clinical Research Network staff at participating sites will screen clinical data to identify patients who meet all inclusion criteria and no exclusion criteria for the study. Where the next scheduled appointment is over 6 weeks into the future, staff will conduct patient approach via telephone. Where eligible patients have an appointment scheduled within the next 6 weeks, Clinical Research Network staff will introduce the study either in person at a scheduled hospital appointment or via a telephone conversation. Though face-to-face discussion is preferred for patients who have an appointment scheduled within the next 6 weeks, CRN staff may use their own discretion in choosing the best approach method for each patient. Approached patients will be provided with a hard-copy information pack about the clinical trial and given the opportunity to ask questions about the study. *Informed Consent and Baseline Assessment* Information packs provided to participants will contain the link for an online survey. This online survey will present the Participant Information Sheet and allow participants to provide informed consent online via an e-consent form. After providing informed consent, participants will receive access to a baseline

	questionnaire assessing demographic characteristics, baseline cancer-specific distress, anxiety, depression, and general stress, quality of life, psychological adjustment to cancer, health service utilisation, social support, vulnerability to distress, motivation to seek information, and psychological flexibility. A member of the research team will then send the participants an email confirming receipt of their informed consent form and outlining the next stages of the study. The same member of the research team will add the participants' details to the Contact Details database and securely send a copy of the participants' e-consent form to the recruiting site. A staff member from the Clinical Research Network will subsequently log that participants' participation in the study in their patient records. If consent has not been confirmed two weeks after a patient has expressed interest in the study, a staff member from the Clinical Research Network will follow up with that patient to remind them of the study. Staff members from the Clinical Research Network will send a log of screening and patient approach activities undertaken to the research team on a fortnightly basis. This log will not contain personally identifiable information relating to patients who have not consented to take part in the study. A member of the research team will update a database of recruitment uptake data accordingly. *Randomisation* Prior to the beginning of the study, the LCTC will create the randomisation code for the study and set up a randomisation portal to be used by the research team. This system will be set up such that each participant in the study will be randomised to either the active intervention arm of the study or the waitlist control arm in a 1:1 ratio. Following the receipt of each participant's baseline questionnaire, an unblinded member of the research team will conduct randomisation for that participant and log their group allocation in a password-protected randomisation key. For participants in the intervention arm of the study, an unblinded member of the research team will then match each participant with a random username and temporary password combination. An unblinded member of the research team will then activate this participant's account, which will trigger an automatic welcome email to be sent to the participant. The welcome email will contain the participant's username and temporary password, as well as instructions for accessing the FMW website. This member of the research team will also email the participant directly to inform them of their group allocation and to explain the next steps in the study. For participants in the waitlist-control arm, the unblinded research

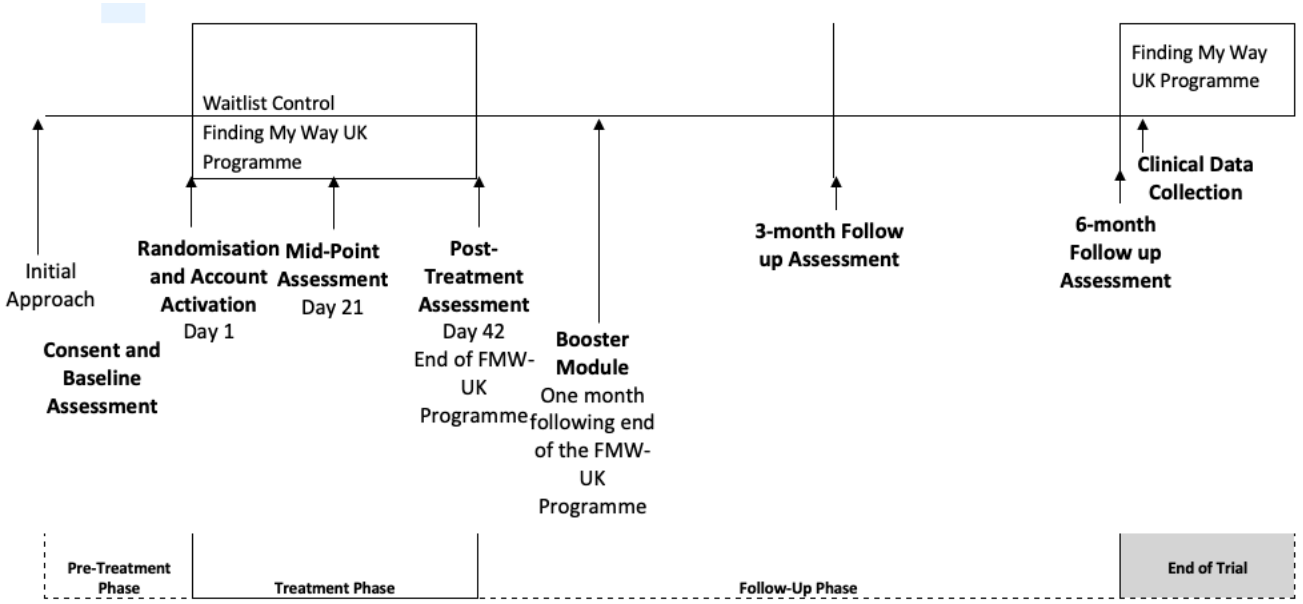
	team member will subsequently email the participant to inform them of their allocation to the waitlist-control condition and provide them with an information pack about existing support and cancer survivorship services in the UK. An unblinded member of the research team will check for new participant log-ins each week and provide a text or phone call reminder if the participant has not logged into the website by Week 2. The mid-point assessment, post-treatment assessment, 3-month follow-up assessment and 6-month assessment will be scheduled from the date of being informed of treatment allocation. *Finding My Way UK Programme* The first time that a participant logs in to the Finding My Way (FMW) website, the website will open on a welcome page, which will immediately play a video describing an overview of the FMW programme and website functionality. Participants will be able to decide the order in which they complete each of the 6 programme modules. Participants will have the opportunity to change this order at any point in the programme, provided that the module being changed has not already been released to the participant. If participants do not change the order of module release, the modules will be released in a standard order decided in advance by the research team. At the beginning of each week, a new cognitive-behavioural therapy-based module will be made available to participants in the active treatment arm, in the order that participants requested. Participants will receive an email reminder about the new available module at this time. Module 1 of FMW focuses on orientation to the treatment team, information about complementary therapies, and decision-making. Module 2 focuses on managing physical symptoms and cognitive changes through activity monitoring, relaxation, and meditation. Module 3 focuses on emotion regulation and stress management. Module 4 focuses on issues around cancer and identity. Module 5 focuses on managing relationships with family and friends. Module 6 focuses on transitioning to life after cancer. *Mid-point assessment* At the end of the third week after being informed of their allocation to the waitlist-control or intervention group, the research team will send all participants a series of questionnaires assessing cancer-specific distress; anxiety, depression, and general stress; quality of life; psychological adjustment to cancer; health service utilisation; and psychological flexibility. *Compliance Assessment* An unblinded member of the research team will check each week for new logins to participants' sixth and final module. Once each

	participant has commenced their sixth module, this member of the research team will send them a survey containing the Self-Help Compliance Scale to complete. *Post-treatment assessment* At the end of the sixth week after being informed of their allocation to the waitlist-control or intervention group, the research team will send all participants a series of questionnaires assessing cancer-specific distress; anxiety, depression, and general stress; quality of life; psychological adjustment to cancer; health service utilisation; and psychological flexibility. *Booster Module* One month after completing the six-week FMW-UK programme, participants in the intervention arm will be given access to an additional booster module. Participants will be notified of this booster module via email. *3-month follow-up assessment* Three months after receiving the link to the post-treatment assessment, participants will be sent questionnaires assessing cancer-specific distress; anxiety, depression, and general stress; quality of life, psychological adjustment to cancer, health service utilisation, and psychological flexibility. *6-month follow-up assessment and debrief* Six months after receiving the link to the post-treatment assessment, participants will be sent questionnaires assessing cancer-specific distress; anxiety, depression, and general stress; quality of life, psychological adjustment to cancer, health service utilisation, and psychological flexibility. After the participant completes the 6-month follow-up assessment, a member of the research team will debrief the participant. Where a participant has not completed the 6-month follow-up assessment, they will instead be debriefed one month from the date on which they were sent the 6-month follow-up questionnaire pack. *Clinical Data Collection* At the time point when each participant receives access to the 6-month follow-up assessment, a member of the research team will contact the referring Clinical Research Network staff member to request the following clinical data: Date of diagnosis; primary or recurrent cancer; whether the participant was treated with curative or palliative intent; the treatment approach adopted for the participant (surgery, chemotherapy, radiotherapy, or watch-and-wait); date of the end of active treatment (if treatment has ended at this point); the date of any recurrence or relapse (if applicable); date of death (if applicable); whether the participant

	received referral to a mental health care professional since their diagnosis of cancer; the number of days of inpatient care since study enrolment and types of healthcare professionals seen during these stays; the number of outpatient visits since study enrolment and types of healthcare professionals seen during these visits; and any diagnosis tests conducted since study enrolment. The Clinical Research Network staff member will extract these data from the participant's medical records and send these data securely to the research team. *Qualitative data collection* Following participant debriefing for the quantitative component of the clinical trial, we will purposively recruit 20-30 trial participants in the intervention arm representing a range of ages, genders, cancer types, and degree of website engagement to take part in qualitative interviews assessing the acceptability, and intervention factors that affect the acceptability, of the Finding My Way online programme. Participants will be given the option to either complete the qualitative interview in-person or via a telephone or video call.
Primary Endpoint:	Cancer-specific distress
Secondary Endpoints:	• Anxiety, depression, and stress • Quality of life • Psychological adjustment to cancer • Health service utilisation
Analyses:	We will purposively recruit 20-30 participants (stratified by age, gender, cancer type, and website engagement) to take part in semi-structured interviews two-to-four weeks after trial completion. Semi-structured interviews allow flexibility in the focus of interviews for each participant, and in-depth probing of the individual experience of research participation, website usage, and suggested intervention improvements. These will be audio recorded, transcribed, and analysed using thematic analysis. The analytic plan matches the Australian FMW randomised controlled trial we are replicating (Beatty et al., 2019). Data analyses are powered to undertake Mixed Model Repeated Measures analyses to examine intervention effects on change from baseline to follow-up for each outcome (intention-to-treat analysis). Two models will be run for each outcome: (i) unadjusted, accounting for co-variance of baseline measures of outcomes; and (ii) fully adjusted, controlling for all potential confounding variables assessed. Sensitivity analyses will evaluate the effects of missing data. Cohen's *d* effect sizes reflect intervention effects, and clinically significant changes will be assessed using Reliable Change Indices.
Ongoing Trials	Not applicable.

1.1. Trial Schedule

1.2. Trial Flow Chart



1.3. Schedule of Events

Procedures	**Screening**	**Initial Approach**	**Informed Consent and Baseline Assessment**	**Start of FMW-UK**	**Mid-point Assessment**	**Beginning of 6th module**	**End of FMW-UK**	**One Month After End of FMW-**	**3-Month Follow Up**	**6-Month Follow Up**	**Clinical Data Collection**	**Ppt approach for Qualitative Sub-Study**	**Informed Consent for Qualitative Sub-Study**	**Qualitative Data Collection**
Clinical data screened for Inclusion/exclusion Criteria	X													
Participant Information Pack Provided		X												
Informed Consent			X											
Randomisation														
Demographic Characteristics			X											
Post-Traumatic Stress Scale			X		X		X		X	X				
Depression, Anxiety, and Stress Scales (21-item version)			X		X		X		X	X				
The QLQ-C30			X		X		X		X	X				
The PIC			X		X		X		X	X				
The UK Cancer Costs Questionnaire			X		X		X		X	X				
The MOS Social Support Survey			X											
Difficulties in Emotion Regulation Scale			X											
The Miller Behavioural Style Scale – Short Form			X											

CompACT			X		X		X		X	X				
Self-Help Compliance Scale						X								
New module provided each week for 6 weeks				X										
Booster module provided								X						
CRN Nurses send clinical data to research team											X			
After completion of the 6-month follow-up questionnaire												X	X	X

STUDY PROTOCOL

Randomised, investigator-blind, waitlist-controlled study to determine the efficacy of an online cognitive behavioural therapy-based intervention in improving psychological outcomes in UK cancer survivors.

2. BACKGROUND

The physical, financial, and existential challenges of living with cancer pose significant threats to psychological wellbeing (Carrera et al., 2018; Mehnert et al., 2018; Vehling & Kissane, 2018), with approximately one in two cancer patients reporting significant levels of psychological distress (Carlson et al., 2019; Mehnert et al., 2018). Aside from the detrimental impact of this distress on quality of life (Huang et al., 2017), high levels of psychological distress are also associated with greater death rates in leukaemia and cancer of the colorectum, prostate, pancreas, and oesophagus after controlling for age, sex, education, socioeconomic status, body mass index, smoking, and alcohol intake (Batty et al., 2017). Furthermore, psychological distress does not immediately resolve following the successful conclusion of treatment.

Cognitive-behavioural therapy interventions are currently considered the gold-standard treatment in managing distress and improving psychological outcomes in cancer populations (Hulbert-Williams et al., 2018). However, the current evidence base for interventions in psychosocial oncology is limited by the large proportion of feasibility studies with small samples sizes and relatively few fully-powered randomised controlled trials (Hulbert-Williams et al., 2018). Further research is, therefore, required in order to determine the optimal means by which to support the psychological needs of cancer patients and cancer survivors.

A systematic review has highlighted that one of the top barriers to accessing psychosocial support identified by cancer patients is difficulty with transport to the health service delivery centre (Dilworth et al., 2014). In order to overcome this barrier, recent research has increasingly investigated the feasibility and efficacy of online psychosocial interventions for cancer patients (Bártolo et al., 2019). Digital psychosocial interventions confer many potential benefits, including greater convenience, reduced burden on cancer patients and carers, and reduced resource use, as compared to traditional face-to-face interventions (Andersson & Titov, 2014). However, most existing online psychosocial interventions for cancer patients are associated with only trend-level benefits, with a need identified for interactive treatment components in order to mitigate the lack of face-to-face interaction (Bártolo et al., 2019).

One psychosocial intervention for cancer patients with early promising results is the Finding My Way programme, developed by Beatty and colleagues for the Australian healthcare setting (Beatty et al., 2019). Finding My Way is an online Cognitive Behavioural Therapy-based intervention specifically tailored to the needs of cancer patients. The Finding My Way programme is composed of six modules, which address the following topics:

1) Starting treatment: This module provides guidance on working with the medical team, including assertive communication and decision making.

2) Coping with physical symptoms and side effects: This module provides information about fatigue, pain, and insomnia and provides activity pacing worksheets and relaxation audio-tracks.
3) Coping with emotional distress: This module covers depression, anxiety, anger and stress and includes both cognitive restructuring worksheets and mindfulness audio-tracks.
4) Body image, identity, and sexuality: This module includes psychosexual worksheets and therapeutic writing activities.
5) Your family and friends: This module provides further guidance on assertive communication and needs assessment worksheets.
6) Completing treatment: This module includes self-management strategies to facilitate healthy lifestyles.

One new module is made available to participants each week, such that the Finding My Way Programme runs over a total of six weeks. The programme also includes one booster module summarizing key programme strategies, including sign-posting to material in the first six modules and some additional text and video content related to survivorship, which is made available to participants one month after the completion of the main six-week programme.

A randomised, controlled trial of 191 Australian cancer patients found that the Finding My Way programme produced statistically significant improvements in emotional functioning at 3-month follow-up and short-term reductions in health service utilization, as compared to an attention control condition (Beatty et al., 2019). Significant differences were not found between the groups in terms of reductions in psychological distress, although this may be partially due to the fact that participants in the active control condition were provided access to an information-only version of Finding My Way, which may have acted as a low-intensity active treatment (Beatty et al., 2019).

3. RATIONALE

Early evidence suggests that the Finding My Way programme is effective in improving emotional functioning in Australian cancer patients. However, future research using an inactive control condition is required to ascertain the efficacy of Finding My Way in reducing distress in cancer populations. Additionally, several components of the Finding My Way programme are Australia-specific, including signposting to Australian resources and video interviews discussing the experiences of Australian cancer patients. The Finding My Way programme, therefore, also requires adaptation before it would be suitable for implementation in the UK. The current study therefore seeks to test the efficacy of a UK-adapted version of the Finding My Way programme.

3.1. Assessment and Management of Risk

Finding My Way (FMW) is an online cognitive-behavioural therapy intervention which carries minimal risk. The version of FMW which will be implemented in the current study is a close adaptation of the original Australian FMW intervention. A recent randomised controlled trial of the Australian Finding My Way programme in 191 cancer patients did not identify any adverse effects associated with the intervention (Beatty et al., 2019).

Nevertheless, we recognise that some of the modules may bring up challenging material related to emotional distress, psychosexual needs, and relationship concerns. We will, therefore, signpost participants to a range of relevant resources, including 24-hour crisis hotlines within the Participant Information Sheet, on the welcome page when they first log in to the FMW website, and within the specific modules that cover challenging material, including the booster module. The participant can navigate back to this web page of resources at any point during the FMW programme. Within the Participant Information Sheet, we will also encourage participants to speak to their GP and clinical care team regarding any mental health concerns that arise, or that they become aware of, during the study.

The FMW programme also includes modules on communicating needs to family, friends, and the participant's treatment team, thus supporting the activation of existing clinical and social supports in light of any distress the participant may experience whilst completing the FMW programme.

4. OBJECTIVES AND OUTCOME MEASURES/ENDPOINTS

4.1. Primary Objective

The primary objective of the study is to determine whether the FMW programme reduces cancer-specific distress.

4.2. Secondary Objectives

Secondary objectives of the study including determining the effects of the FMW programme on anxiety, depression, and general stress, determining the effects of the FMW programme on quality of life, determining the effects of the FMW programme on psychological adjustment to cancer, determining the effects of the FMW programme on health service utilisation, determining whether social support, vulnerability to distress, and motivation to seek information moderate the effects of the FMW programme on primary and secondary study endpoints, and determining whether psychological flexibility mediates the effect of the FMW Programme on cancer-specific distress. We will also conduct exploratory analyses testing the potential moderating effects of clinical and demographic variables on primary and secondary endpoints.

4.3. Primary Endpoint

Cancer-specific distress, as measured by the Post-Traumatic Stress Scale (Foa et al., 1993).

4.4. Secondary Endpoints

Secondary endpoints of the study include depression, anxiety, and stress, as measured by the Depression, Anxiety, and Stress Scales – 21 item version (DASS-21) (Lovibond & Lovibond, 1996); quality of life, as measured by the The European Organisation for Research and Treatment of Cancer Core Quality of Life Questionnaire (version 3.0) (QLQ-C30) (Aaronson et al., 1993); psychological adjustment to cancer, as measured by the Psychological Impact of

Cancer (PIC) Scale (Hulbert-Williams et al., 2019); and health service utilisation, as measured by the UK Cancer Costs Questionnaire.

5. STUDY DESIGN

Patient Identification and Approach

Clinical Research Network staff at participating sites will screen clinical data to identify patients who meet all inclusion criteria and no exclusion criteria for the study. Where the next scheduled appointment is over 6 weeks into the future, staff will conduct patient approach over the telephone. Where eligible patients have an appointment scheduled within the next 6 weeks, Clinical Research Network staff will introduce the study either in person at a scheduled hospital appointment or via a telephone conversation. Though face-to-face discussion is preferred for patients who have an appointment scheduled within the next 6 weeks, CRN staff may use their own discretion in choosing the best approach method for each patient. Approached patients will be provided with a hard-copy information pack about the clinical trial and given the opportunity to ask questions about the study.

Informed Consent and Baseline Assessment

Information packs provided to participants will contain the link for an online survey. This online survey will present the Participant Information Sheet and allow participants to provide informed consent online via an e-consent form. Based on our assessment that this study poses minimal risk to participants, we have deemed that a simple electronic signature, consisting of typewritten initials, a typewritten name and date of birth is a sufficient indication of informed consent, as per the Health Research Authority's joint statement on seeking consent by electronic methods (https://www.hra.nhs.uk/media/documents/hra-mhra-econsent-statement-sept-18.pdf). Participants will be asked whether they would prefer to complete study questionnaires online or in hard-copy (pen-and-paper) form. Participants will also be asked whether they would prefer to receive study reminders via text or phone call. After submitting their e-consent form, participants will be provided with access to the baseline questionnaire assessing demographic characteristics, baseline cancer-specific distress, anxiety, depression, and general stress, quality of life, psychological adjustment to cancer, health service utilisation, social support, vulnerability to distress, motivation to seek information, and psychological flexibility. For all questionnaires in this study, participants will either be directed to complete this questionnaire online or the research team will post a paper questionnaire pack to them, including a pre-paid return envelope, as per the preference indicated by the participant in their consent form. Participants will be given the option to complete questionnaires in more than one sitting in order to reduce participants' burden. Where a participant has submitted their completed e-consent form but not completed the baseline questionnaire, a member of the study team will send the participant a reminder to complete the baseline questionnaire one week after the e-consent form has been received.

A member of the research team will then send the participant an email confirming receipt of their informed consent form and outlining the next stages of the study. The same member of the research team will add each participant's details to the Contact Details database and securely send a copy of each participant's consent form and information regarding the

handling of adverse events to the recruiting site. A staff member from the Clinical Research Network will subsequently log that participant's participation in the study in their patient records.

If consent has not been confirmed two weeks after a patient has expressed interest in the study, a staff member from the Clinical Research Network will follow up with that patient to remind them of the study.

Staff members from the Clinical Research Network will send a log of screening and patient approach activities undertaken to the research team on a fortnightly basis. This log will not contain personally identifiable information relating to patients who have not consented to take part in the study. A member of the research team will update a database of recruitment uptake data accordingly.

Randomisation

Prior to the beginning of the study, the LCTC will create the randomisation code for the study and set up a randomisation portal to be used by the research team. This system will be set up such that each participant in the study will be randomised to either the active intervention arm of the study or the waitlist control arm in a 1:1 ratio. Following the receipt of each participant's baseline questionnaire, an unblinded member of the research team will conduct randomisation for that participant and log their group allocation in a password-protected randomisation key. For participants in the intervention arm of the study, an unblinded member of the research team will then match each participant with a random username and temporary password combination. An unblinded member of the research team will then activate this participant's account, which will trigger an automatic welcome email to be sent to the participant. The welcome email will contain the participant's username and temporary password, as well as instructions for accessing the FMW website. This member of the research team will also email the participant directly to inform them of their group allocation and to explain the next steps in the study. For participants in the waitlist-control arm, the unblinded research team member will subsequently email the participant to inform them of their allocation to the waitlist-control condition and provide them with an information pack about existing support and cancer survivorship services in the UK. An unblinded member of the research team will check for new participant log-ins each week and provide a text or phone call reminder if the participant has not logged into the website by Week 2. The mid-point assessment, post-treatment assessment, 3-month follow-up assessment and 6-month assessment will be scheduled from the date of being informed of treatment allocation.

Finding My Way UK Programme

The first time that a participant logs in to the FMW website, the website will open on a welcome page, which will immediately play a video describing an overview of the FMW programme and website functionality. Participants will be able to decide the order in which they complete each of the 6 programme modules. Participants will have the opportunity to change this order at any point in the programme, provided that the module being changed has not already been released to the participant. If participants do not change the order of

module release, the modules will be released in a standard order decided in advance by the research team.

At the beginning of each week, a new cognitive-behavioural therapy-based module will be made available to participants in the active treatment arm, in the order that participants requested. Participants will receive an email reminder about the new available module at this time. Participants in the intervention group will receive an additional text or phone call reminder (depending on their stated communication preference) if they haven't logged in one week after account activation, and an additional phone call reminder if they haven't logged in two weeks after account activation. Module 1 of FMW focuses on orientation to the treatment team, information about complementary therapies, and decision-making. Module 2 focuses on managing physical symptoms and cognitive changes through activity monitoring, relaxation, and meditation. Module 3 focuses on emotion regulation and stress management. Module 4 focuses on issues around cancer and identity. Module 5 focuses on managing relationships with family and friends. Module 6 focuses on transitioning to life after cancer.

Mid-point assessment

At the end of the third week after being informed of their allocation to the waitlist-control or intervention group, the research team will send participants questionnaires assessing cancer-specific distress; anxiety, depression, and general stress; quality of life; psychological adjustment to cancer; health service utilisation; and psychological flexibility. Participants will receive a text or phone call reminder (depending on their stated communication preference) if they have not completed this survey after one week. Participants will receive an additional phone call reminder if they have not completed the survey after two weeks. The research assistant will offer participants the option to complete the survey via telephone at this time, if they prefer. If participants choose to complete the mid-point assessment via telephone, the research assistant will complete the Qualtrics survey for them, according to the participant's telephone responses.

Compliance Assessment

An unblinded member of the research team will check each week for new logins to participants' sixth and final module. Once each participant has commenced their sixth module, this member of the research team will send them a survey containing the Self-Help Compliance Scale to complete. Participants will receive a text or phone call reminder (depending on their stated communication preference) if they have not completed this survey after one week. Participants will receive an additional phone call reminder if they have not completed the survey after two weeks. The research assistant will offer participants the option to complete the survey via telephone at this time, if they prefer. If participants choose to complete the compliance assessment via telephone, the research assistant will complete the Qualtrics survey for them, according to the participant's telephone responses.

Post-treatment assessment

At the end of the sixth week after being informed of their allocation to the waitlist-control or intervention group, the research team will send all participants a series of questionnaires assessing cancer-specific distress; anxiety, depression, and general stress; quality of life;

psychological adjustment to cancer; health service utilisation; and psychological flexibility. A member of the research team will follow up with a text or phone call reminder (depending on the participant's stated communication preference) after one week if the participant has not completed the survey at this time. Participants will receive an additional phone call reminder if they have not completed the survey after two weeks. The research assistant will offer participants the option to complete the survey via telephone at this time, if they prefer. If participants choose to complete the post-treatment assessment via telephone, the research assistant will complete the Qualtrics survey for them, according to the participant's telephone responses.

Booster Module

One month after completing the six-week FMW programme, participants in the intervention arm will be provided access to an additional booster module. This booster module summarises key programme strategies, sign-posts participants to content in the first six modules that may be useful to them at this stage, and includes some additional text and video content related to life after cancer. Participants will be notified of this booster module via email. An unblinded member of the research team will send a text or phone call reminder (depending on the participant's stated communication preference) after one week if the participant has not logged into the FMW programme by this time.

3-month follow-up assessment

Three months after receiving the link to the post-treatment assessment, participants will be sent a series of questionnaires assessing cancer-specific distress; anxiety, depression, and general stress; quality of life, psychological adjustment to cancer, health service utilisation, and psychological flexibility. A member of the research team will follow up with a text or phone call reminder after one week (depending on the participant's stated communication preference) if the participant has not completed the survey at this time. Participants will receive an additional phone call reminder if they have not completed the survey after two weeks. The research assistant will offer participants the option to complete the survey via telephone at this time, if they prefer. If participants choose to complete the 3-month follow-up assessment via telephone, the research assistant will complete the Qualtrics survey for them, according to the participant's telephone responses.

6-month follow-up assessment and debrief

Six months after receiving the link the post-treatment assessment, participants will be sent a series of questionnaires assessing cancer-specific distress; anxiety, depression, and general stress; quality of life, psychological adjustment to cancer, health service utilisation, and psychological flexibility. A member of the research team will follow up with a text or phone call reminder after one week (depending on the participant's stated communication preference) if the participant has not completed the survey at this time. Participants will receive an additional phone call reminder if they have not completed the survey after two weeks. The research assistant will offer participants the option to complete the survey via telephone at this time, if they prefer. If participants choose to complete the 6-month follow-up assessment via telephone, the research assistant will complete the Qualtrics survey for them, according to the participant's telephone responses. After the participant completes the

6-month follow-up assessment, a member of the research team will debrief the participant. Where a participant has not completed the 6-month follow-up assessment, they will instead be debriefed one month from the date on which they were sent the 6-month follow-up questionnaire pack. An unblinded of the research team will activate the account of participants in the waitlist-control arm at this time. Participants in the waitlist-control arm will then proceed through the intervention modules in exactly the same manner as described above for participants in the intervention arm.

Clinical Data Collection

At the time point when each participant receives access to the 6-month follow-up assessment, a member of the research team will contact the referring Clinical Research Network staff member to request the following clinical data:

- Date of diagnosis;
- Primary or recurrent cancer;
- Whether the participant was treated with curative or palliative intent;
- The treatment approach adopted for the participant (surgery, chemotherapy, radiotherapy, or watch-and-wait);
- Date of the end of active treatment (if treatment has ended at this point);
- The date of any recurrence or relapse (if applicable);
- Date of death (if applicable);
- Whether the participant received referral to a mental health care professional since their diagnosis of cancer;
- The number of days of inpatient care since study enrolment, and types of healthcare professionals seen during these stays;
- The number of outpatient visits since study enrolment, and types of healthcare professionals seen during these visits; and
- Any diagnosis tests conducted since study enrolment.

The Clinical Research Network staff member will complete a standardised Clinical Data Extraction Form containing fields for the above points of information. The Clinical Research Network staff member will then send this form securely to the research team via an encrypted email attachment or an encrypted email. A member of the research team will then add these data to a Clinical Data database. A member of the research team will follow up with the Clinical Research Network if these data have not been received two weeks after the data request.

Qualitative data collection

Following participant debriefing for the quantitative component of the clinical trial, we will purposively recruit 20-30 trial participants in the intervention arm of the study representing a range of ages, gender, cancer types, and degree of website engagement to take part in qualitative interviews assessing the acceptability, and intervention factors that affect the acceptability, of the FMW online programme. An unblinded member of the research team will call participants in the intervention arm after they have been debriefed for the quantitative component of the clinical trial to verbally explain the qualitative component of the study and seek expressions of interest. If the participant does not answer the phone, the

unblinded member of the research team will not leave a voicemail, but will attempt to reach them via telephone two more times. If the unblinded member has not been able to reach them via telephone after three attempts, the research assistant will email the participant instead to gauge their interest in the qualitative sub-study.

An unblinded member of the research team will subsequently email the Participant Information Sheet and consent form for the qualitative interview to participants who have expressed an interest in participating in this component of the study. If the participant does not respond within two weeks, the same member of the research team will follow up with an email prompt. This unblinded member of the research team will coordinate the qualitative interview, answer any additional questions the participant may have and collect the participant's completed consent form. Participants will be given the option to either complete the qualitative interview in-person (either at the University or in their own home) or via a telephone or video call. The researcher conducting the qualitative interview will not be made aware of the participant's name or participant number, and will thus remain blinded for the purposes of subsequent data analysis. This interview will be audio-recorded for later transcription. The unblinded member of the research team will subsequently debrief the participant. Any participant travel expenses will be reimbursed.

6. STUDY SETTING

Participants will be recruited from hospitals in Northwest England and North Wales. The data collection and intervention delivery will occur entirely remotely, so participants may complete the study from any place they have internet or telephone access.

7. ELIGIBILITY CRITERIA

Participants will be recruited from hospitals and clinics in the United Kingdom.

7.1. Inclusion Criteria

For inclusion in the study, subjects must satisfy all of the following criteria:

- Been diagnosed with cancer in the past six months
- Have received anti-cancer treatment with curative intent
- Aged 16 years or over
- Sufficiently proficient in English to provide informed consent and use the online programme
- Able to access the internet
- Currently have (or willing to set up) an active email address

7.2. Exclusion Criteria

Subjects for whom any of the following criteria apply are not eligible for inclusion in the study:

- Severe comorbidity considered by the screening nurse to interfere with the individual's ability to complete the requirements of the study or provide informed consent (e.g., intellectual disability or neurological impairment).

8. TRIAL PROCEDURES

8.1. Recruitment

8.1.1. Screening

Clinical research network (CRN) staff will review patients' clinical information to determine eligibility. CRN staff will be provided with a standardised screening log by the study team. CRN staff will complete this standardised screening log for each fortnight period from the point of the Sponsor Green Light at each site. CRN nurses completing this form are instructed to redact information in the first two columns to ensure anonymity before sharing with the study team; the unredacted version should be retained at the clinical site for the remaining information to be completed (if applicable) following consent being received.

8.1.2. Patient Identification and Approach

Where the next scheduled appointment is over 6 weeks into the future, staff will conduct patient approach over the telephone. Where eligible patients have an appointment scheduled within the next 6 weeks, Clinical Research Network staff will introduce the study either in person at a scheduled hospital appointment or via a telephone conversation. Though face-to-face discussion is preferred for patients who have an appointment scheduled within the next 6 weeks, CRN staff may use their own discretion in choosing the best approach method for each patient. Approached patients will be provided with a hard-copy information pack about the clinical trial and given the opportunity to ask questions about the study. Participants who have been approached entirely via telephone will have this information pack posted to them. For any questions which Clinical Research Network staff are unclear about, participants will be directed to contact the Trial Coordinator.

8.2. Consent

The informed consent process will consist of participants being provided with a written Participant Information Sheet containing details about the clinical trial and being provided with a verbal description of the clinical trial by Clinical Research Network staff. The participant will also have the opportunity to ask questions about the trial to members of the Clinical Research Network staff directly, and they will be provided with contact details for the research team for any further queries they would like to discuss.

Participants' information packs will contain the URL for an online survey, which they will be directed to complete if they would like to proceed with study participation. The first page of this survey will again display the Participant Information Sheet. Provided that the participant is happy to proceed with the study, they will provide informed consent to take part in the study through via an e-consent form. Based on our assessment that this study poses minimal

risk to participants, we have deemed that a simple electronic signature, consisting of a tickbox (next to which they type their initials) and a typewritten name and date of birth is a sufficient indication of informed consent, as per the Health Research Authority's joint statement on seeking consent by electronic methods (https://www.hra.nhs.uk/media/documents/hra-mhra-econsent-statement-sept-18.pdf).

Both the informed consent discussion and the Participant Information Sheet will include explanations of the following:

- That the trial involves research;
- The purpose of the trial;
- The trial treatment(s) and the probability for random assignment to each treatment;
- The trial procedures to be followed;
- The participant's responsibilities;
- Those aspects of the trial that are experimental;
- The reasonably foreseeable risks or inconveniences to the participant;
- The reasonably expected benefits of the study;
- The alternative procedure(s) or course(s) of treatment that may be available to the participant, and their important potential benefits and risks;
- The anticipated prorated payment, if any, to the participant for participating in the trial;
- The anticipated expenses, if any, to the participant for participating in the trial;
- That the patient's participation in the trial is voluntary and that the patient may refuse to participate or withdraw from the trial, at any time, without penalty or loss of benefits to which the participant is otherwise entitled;
- That the monitor(s), the auditor(s), the REC and the regulatory authority(ies) will be granted direct access to the participant's data, without violating the confidentiality of the subject, to the extent permitted by the applicable laws and regulations and that, by signing a written informed consent form, the participant or participant's legally acceptable representative is authorizing such access;
- That records identifying the participant will be kept confidential and, to the extent permitted by the applicable laws and/or regulations, will not be made publicly available. If the results of the trial are published, the participant's identity will remain confidential;
- That the participant or participant's legally acceptable representative will be informed in a timely manner if information becomes available that may be relevant to the participant's willingness to continue participation in the trial;
- The person(s) to contact for further information regarding the trial and the rights of trial subjects, and whom to contact in the event of trial-related injury;
- The foreseeable circumstances and/or reasons under which the patient's participation in the trial may be terminated;
- The expected duration of the patient's participation in the trial;
- The data protection requirements for the trial and open access arrangements for data sharing;
- The approximate number of participants involved in the trial.

Following completion of the informed consent form, a member of the research team will store the consent form securely and send a copy of the survey output of the e-consent form to the recruiting site for inclusion in the participant's clinical notes.

Should any participant lose capacity after previously providing informed consent to take part in the study, the participant will be withdrawn from the study, but data captured up to that point will be retained. Specific consent will be sought to collect clinical data posthumously in the event of participant death.

8.2.1. Additional consent provisions for collection and use of participants' data and biological specimens in ancillary studies

No additional consent will be sought.

8.3. Participant Numbering

Each participant number will consist of one prefix corresponding to the hospital from which they were recruited, an additional prefix corresponding to the clinical group within that hospital from which they were recruited, and an additional number corresponding to the order in which each participant was recruited within each given clinical group. For example, the first participant recruited from hospital 4, clinical group 2, will be labelled '040201', the second participant from this clinical group will be labelled '040202', etc.

8.4. Randomisation Scheme

This study is a parallel randomised controlled trial (RCT), with equal numbers of participants randomised to the intervention and control arms. Permuted block randomisation to active treatment versus waitlist control groups will be conducted on a 1:1 ratio.

8.5. Blinding

The study will be single-blind, such that the Chief Investigator, Trial Co-ordinator and team members involved with data analysis will not know the treatment to which a particular subject has been randomised. The randomisation scheme will be set up by the Liverpool Clinical Trials Centre. Two members of the research will be deliberately unblinded so that they can conduct randomisation using this system.

8.6. Unblinding

The investigator reserves the right to conduct unblinding in exceptional circumstances where a participant's health or safety is reasonably believed to be compromised by continued investigator blinding to the participant's allocated treatment arm.

8.7. Evaluations

8.7.1. Screening

CRN staff will refer to patients' clinical data to confirm that all inclusion criteria and no exclusion criteria are met. The CRN staff member will verbally clarify with the patient if any of these criteria are not included or unclear in the available clinical data.

8.7.2. Baseline Assessment

For the baseline assessment, participants will be sent a link to a survey containing the following questionnaires: demographic characteristics (including age, sex, ethnicity, employment status, education, relationship status, marital status, household income, and residence in England or Wales), the Post-Traumatic Stress Scale (Foa et al., 1993), the DASS-21 (Lovibond & Lovibond, 1996), the QLQ-C30 (Aaronson et al., 1993), the PIC (Hulbert-Williams et al., 2019), the UK Cancer Costs Questionnaire, the MOS Social Support Survey (Sherbourne & Stewart, 1991), the Difficulties in Emotion Regulation Scale (Gratz & Roemer, 2003), the Miller Behavioural Style Scale – Short Form (Miller, 1987; Steptoe, 1989), and the CompACT (Francis et al., 2016).

8.7.3. Mid-Point Assessment

For the mid-point assessment participants will be sent a link to a survey containing the following questionnaires: the Post-Traumatic Stress Scale (Foa et al., 1993), the DASS-21 (Lovibond & Lovibond, 1996), the QLQ-C30 (Aaronson et al., 1993), the PIC (Hulbert-Williams et al., 2019), the UK Cancer Costs Questionnaire, and the CompACT (Francis et al., 2016).

8.7.4. Compliance Assessment

An unblinded member of the research team will check each week for new logins to participants' sixth and final module. Once each participant has commenced their sixth module, this member of the research team will email them a survey containing the Self-Help Compliance Scale (Thiels et al., 2001) to complete.

8.7.5. Post-Treatment Assessment

For the post-treatment assessment participants will be sent a link to a survey containing the following questionnaires: the Post-Traumatic Stress Scale (Foa et al., 1993), the DASS-21 (Lovibond & Lovibond, 1996), the QLQ-C30 (Aaronson et al., 1993), the PIC (Hulbert-Williams et al., 2019), the UK Cancer Costs Questionnaire, and the CompACT (Francis et al., 2016).

8.7.6. 3-Month Follow Up

For the 3-month follow-up assessment participants will be sent a link to a survey containing the following questionnaires: the Post-Traumatic Stress Scale (Foa et al., 1993), the DASS-21 (Lovibond & Lovibond, 1996), the QLQ-C30 (Aaronson et al., 1993), the PIC (Hulbert-Williams et al., 2019), the UK Cancer Costs Questionnaire, and the CompACT (Francis et al., 2016).

8.7.7. 6-Month Follow-Up

For the 6-month follow-up assessment participants will be sent a link to a survey containing the following questionnaires: the Post-Traumatic Stress Scale (Foa et al., 1993), the DASS-21 (Lovibond & Lovibond, 1996), the QLQ-C30 (Aaronson et al., 1993), the PIC (Hulbert-Williams et al., 2019), the UK Cancer Costs Questionnaire, and the CompACT (Francis et al., 2016).

8.7.8. Clinical Data Collection

The following clinical data will be extracted from participants' medical records:

- Date of diagnosis;
- Primary or recurrent cancer;
- Whether the participant was treated with curative or palliative intent;
- The treatment approach adopted for the participant (surgery, chemotherapy, radiotherapy, or watch-and-wait);
- Date of the end of active treatment (if treatment has ended at this point);
- The date of any recurrence or relapse (if applicable);
- Date of death (if applicable);
- Whether the participant received referral to a mental health care professional since their diagnosis of cancer;
- The number of days of inpatient care since study enrolment, and types of healthcare professionals seen during these stays;
- The number of outpatient visits since study enrolment, and types of healthcare professionals seen during these visits; and
- Any diagnosis tests conducted since study enrolment.

8.7.9. Qualitative Interviews

Following participant debriefing for the quantitative component of the clinical trial, we will invite 20-30 trial participants to take part in qualitative interviews assessing the acceptability, and intervention factors affecting the acceptability, of the FMW online programme. Our qualitative interview topic guide is presented in Appendix W.

8.8. Procedures and Assessments

8.8.1. Demographic Characteristics

We will ask participants to self-report the following demographic characteristics: age, gender, sexual identity, employment, education, marital status, and household income.

8.8.2. Post-Traumatic Stress Scale

The Post-Traumatic Stress Scale (Foa et al., 1993) is a 17-item measure of cancer-specific distress. Participants respond on a 4-point Likert scale, where responses are anchored from 0 (Not at all or only one time) to 3 (5 or more times per week / almost always). The Post-Traumatic Stress Scale is associated with excellent internal consistency reliability (α = .91) (Foa et al., 1993). The post-traumatic stress scale has good concurrent validity, including

strong positive correlations with other measures of trauma-related intrusion and avoidance, anxiety, and depression (Foa et al., 1993).

8.8.3. DASS-21

The Depression, Anxiety, and Stress Scales, 21-item version (DASS-21) (Lovibond & Lovibond, 1996) is a short measure of negative emotions experienced over the course of the past week for the individual. Each item is presented as a 4-point Likert scale, anchored as 0 ("Did not apply to me at all"), 1 ("Applied to me some degree, or some of the time"), 2 ("Applied to me to a considerable degree or a good part of the time"), and 3 ("Applied to me very much or most of the time"). The total score for each subscale of the 21-item DASS-21 is calculated by summing participants' responses to the items for each subscale and multiplying this sum by two. Higher scores for each subscale therefore indicate greater levels of depression, anxiety, and stress, respectively. The depression scale of the DASS-21 is associated with excellent internal consistency reliability (α = .91) (Lovibond & Lovibond, 1995). The anxiety scale and the stress scale of the DASS-21 are both associated with good internal consistency reliability (α = .81 and α = .89, respectively) (Lovibond & Lovibond, 1995). The DASS-21 has good concurrent validity, including strong, positive correlations with other measures of depressive symptoms and anxiety (P. F. Lovibond & Lovibond, 1995).

8.8.4. QLQ-C30

The QLQ-C30 (Aaronson et al., 1993) is a 30-item quality of life assessment for cancer patients, which yields a global quality of life score and five functional subscale scores associated with physical, emotional, social, role, and cognitive quality of life domains. The global score for the QLQ-C30 is associated with good internal consistency reliability (α = .86) (Aaronson et al., 1993). The QLQ-C30 is associated with good concurrent validity, with global quality of life and the role functioning and physical functioning scales significantly positively correlated with performance status throughout treatment (Aaronson et al., 1993). The QLQ-C30 score can be converted into an indication of QUALYs to be used in health economic analysis.

8.8.5. The PIC

The PIC (Hulbert-Williams et al., 2019) is a 12-item self-report measure of psychological adjustment to cancer. Each item is presented on a 4-point Likert scale anchored from "Definitely does not apply" to "Definitely does apply". The PIC yields four subscale scores: Cognitive Distress, Cognitive Avoidance, Emotional Distress, and Fighting Spirit. For the purposes of the current study, we will only analyse the Cognitive Distress, Cognitive Avoidance, and Emotional Distress subscales. All subscales are associated with at least fair internal consistency reliability (α > .623) and good concurrent validity with longer measures of psychological adjustment to cancer (Hulbert-Williams et al., 2019).

8.8.6. The UK Cancer Costs Questionnaire

The UK Cancer Costs Questionnaire is a modular self-report measure of resource use by people with cancer and people with a previous diagnosis of cancer. The UK Cancer Costs Questionnaire assesses employment status, family support provided, government benefits, and support provided by other organisations over the previous three months. The UK Cancer Costs Questionnaire prioritises brevity in order to minimise the burden of data collection for participants.

8.8.7. The MOS Social Support Survey

The MOS Social Support survey (Sherbourne & Stewart, 1991) is a 20-item self-report measure of social support. Each item is presented as a 5-point Likert scale anchored from 1 (none of the time) to 5 (all of the time). The MOS Social Support Survey yields four subscale scores: emotional/informational support, tangible support, affectionate support, and positive social interactions. Each subscale is associated with excellent internal consistency reliability ($\alpha > .91$) (Sherbourne & Stewart, 1991). The MOS Social Support Survey is associated with good convergent validity with measures of family ties, family functioning, and mental health and good divergent validity with measures of purely physical health (Sherbourne & Stewart, 1991).

8.8.8. The Difficulties in Emotion Regulation Scale

The Difficulties in Emotion Regulation Scale (Gratz & Roemer, 2003) is a 36-item self-report measure of six dimensions of emotion regulation difficulties: lack of awareness of emotional responses, lack of clarity of emotional responses, non-acceptance of emotional responses, limited access to emotion regulation strategies perceived as effective, difficulties controlling impulses when experiencing negative emotions, and difficulties engaging in goal-directed behaviours when experiencing negative emotions. Each item is presented as a 5-point Likert scale anchored from 1 (almost never) to 5 (almost always). The global difficulties in emotional regulation scale is associated with excellent internal consistency reliability ($\alpha = .93$) and each subscale is associated with good internal consistency reliability ($\alpha > .80$) (Gratz & Roemer, 2003). The difficulties in emotion regulation scale is associated with good construct validity and predictive validity (Gratz & Roemer, 2003).

8.8.9. The Miller Behavioural Style Scale

The Miller Behavioural Style Scale – Short Form (Miller, 1987; Steptoe, 1989) is a self-report measure of information seeking preferences. The scale identifies individual preferences for seeking threat-related cues (monitors) versus seeking distraction to minimise exposure to threat-related cues (blunters). The scale prompts participants to imagine two stressful scenarios, each of which is followed by eight statements that describe different ways of coping with the stressor. Participants are asked to select all statements that apply to them. The Miller Behavioural Style Scale is associated with good test-retest reliability over a 4-month period ($r = 0.72$ for the monitoring subscale and $r = 0.75$ for the blunting subscale) (Miller, 1987). The Miller Behavioural Style Scale is associated with high construct validity, as

indicated by high correspondence with information-seeking behaviour in a stress-inducing laboratory task (Miller, 1987).

8.8.10. The CompACT

The CompACT (Francis et al., 2016) is a 23-item self-report measure of psychological flexibility. Each item is presented as a 7-point Likert scale anchored from 0 (strongly disagree) to 6 (strongly agree). The CompACT is associated with adequate internal consistency reliability (average inter-item correlation, r = 0.34) (Francis et al., 2016). The CompACT is associated good convergent validity with another measure of Acceptance and Commitment Therapy processes and good discriminant validity with a measure of Social Desirability (Francis et al., 2016).

8.8.11. The Self-Help Compliance Scale

The Self-Help Compliance Scale (Thiels et al., 2001) is a brief measure assessing engagement with self-guided psychological interventions. The scale consists of 3 items presented on a 5-point Likert-type scale assessing the amount of information participants read, the number of suggestions and worksheets participants completed, and how much time participants spent using the programme. The questionnaire also includes one open question asking participants what other psychological treatment they have received during the programme.

8.9. Withdrawal Criteria

Other than death or other unforeseen loss of capacity to consent, there are no criteria which will cause the investigator to withdraw any participant from the clinical trial. Participants will be informed that they do not have to complete any online modules they do not wish to, and that they can withdraw themselves from the clinical trial at any time. Participants can skip questions within the self-report measures, but this may mean we can't include them in the analysis. Instructions for addressing missing data differ among the psychometric measures and our decision to exclude any participant from an analysis will therefore depend on which item responses are missing.

8.10. End of Trial

Our recruitment target is 294 participants, although we may over-recruit by up to 30% in order to mitigate the effects of missing data and to allow for at least minimal recruitment of less common cancer types. We will stop recruitment on 28th February 2022. The trial will end after the last participant has completed all study activities.

9. INTERVENTION UNDER INVESTIGATION

9.1. The UK-Adapted Finding My Way Programme

Finding My Way is an online Cognitive Behavioural Therapy-based intervention specifically tailored to the needs of cancer patients. The Finding My Way programme is composed of six modules, which address the following topics:

1) Starting treatment: This module provides guidance on working with the medical team, including assertive communication and decision making.
2) Coping with physical symptoms and side effects: This module provides information about fatigue, pain, and insomnia and provides activity pacing worksheets and relaxation audio-tracks.
3) Coping with emotional distress: This module covers depression, anxiety, anger and stress and includes both cognitive restructuring worksheets and mindfulness audio-tracks.
4) Body image, identity, and sexuality: This module includes psychosexual worksheets and therapeutic writing activities.
5) Your family and friends: This module provides further guidance on assertive communication and needs assessment worksheets.
6) Completing treatment: This module includes self-management strategies to facilitate healthy lifestyles.

One new module is made available to participants each week, such that the Finding My Way Programme runs over a total of six weeks. The programme also includes one booster module summarizing key strategies, which is made available to participants one month after the completion of the main six-week programme. The full intervention content is listed in Appendix X.

Finding My Way UK will run in the same format as the original Australian Finding My Way programme, including the same modules presented in the same time-order. The version of the Finding My Way programme implemented in the current study will include minor adaptations for the UK context (including signposting to UK-relevant resources and video interviews with British cancer survivors).

The original Australian Finding My Way programme can be found at the following link: www.findingmyway.org.au. Access to the programme is free, but users are required to first register an account. The UK version will have restricted access during this trial and account registration will be limited only to trial participants.

9.2. Assessment of Compliance with Finding My Way UK Programme

Compliance with the Finding My Way intervention will be measured via the following website use indicators:

a) The number of logins to the website;
b) Total amount of time logged in;
c) Number of intervention modules completed;
d) Number of worksheets completed; and
e) Responses to the Self-Help Compliance Scale.

10. ADVERSE EVENTS

10.1. Procedures for Eliciting Reports of and Recording and Reporting Adverse Events

We recognise that some of the modules may bring up challenging material related to emotional distress, psychosexual needs, and relationship concerns. We will, therefore, signpost participants to a range of relevant resources, including 24-hour crisis hotlines, within the Participant Information Sheet, on the welcome page when they first log in to the Finding My Way UK website, and within the specific modules that cover challenging material, including the booster module. The participant can navigate back to this web page of resources at any point during the Finding My Way UK programme. Within the Participant Information Sheet, we will also encourage participants to speak to their GP and clinical care team regarding any mental health concerns that arise, or that they become aware of, during the study.

Within the Participant Information Sheet, we will also ask participants to contact the research team if any of the material causes distress. The research team will note this finding down in a database of adverse events and inform the sponsor of all new adverse events recorded in the study. Each time the research team informs the recruiting site of a newly-received consent form, the research team will also send additional material specifying that the clinical team should inform the research team of any distress the participant mentions that has arisen from intervention content. We will request that each clinical team also asks the participant to report these adverse events to the research team directly.

11. STATISTICAL AND DATA ANALYSIS

11.1. Sample Size Calculation

Calculations are based on the primary outcome of change in cancer distress between the two patient groups. The original FMW randomised clinical trial sample size calculation used a standardised effect size of 0.35 and standard deviation of 4 units, which equates to an absolute change in cancer distress scores of 1.4 units. This study observed a larger than expected standard deviation and we propose a sample size based on a conservative estimate of the residual standard deviation of 7 units accordingly (but keeping the clinically relevant difference at the aforementioned 1.4 units). Correlation between successive measurements on the same patient are assumed to be high and a conservative r=0.7 is used. Sample size calculations are performed assuming a paired t-test using a derived standard deviation about the change in the primary outcome of 5.42. Assuming a patient attrition of 20% and a two-sided alpha=0.05, then 294 patients (147 per study arm) are required for statistical power of 80%.

11.2. Statistical Methodology

11.2.1. Analysis sets

All quantitative analyses will be conducted using the intention-to-treat analysis set.

11.2.2. Null and Alternative Hypothesis

The null hypothesis is that there will be no differences between the active treatment and waitlist control groups on any of the primary or secondary endpoints of the study, while the alternative hypothesis is that there will be differences between the participant groups on these endpoints.

11.2.3. Efficacy Analyses

The analytic plan matches the Australian FMW RCT exactly (Beatty et al., 2019). Data analyses are powered to undertake Mixed Model Repeated Measures analyses to examine intervention effects on change from baseline to follow-up for each outcome (intention-to-treat analysis). Two models will be run for each outcome: (i) unadjusted, accounting for co-variance of baseline measures of outcomes; and (ii) fully adjusted, controlling for all potential confounding variables assessed. Sensitivity analyses will evaluate the effects of missing data. Cohen's *d* effect sizes reflect intervention effects, and clinically significant changes will be assessed using Reliable Change Indices.

11.2.4. Health Economic Analyses

The healthcare utilisation outcome will be summarised descriptively for activity counts and cumulative costs. Generalised linear models will be used to adjust for the same confounding variables as the efficacy analysis.

11.3. Significance and Confidence Level

p-values < 0.05 will be considered significant. All confidence intervals will be at the 95% level.

11.4. Qualitative Data Analyses

Qualitative interviews will be analysed using thematic analysis (Braun & Clarke, 2006).

11.5. Criteria for Terminating the Study

No interim analysis is planned. The study will be terminated prematurely only on the grounds of exceptional, unforeseen safety concerns or exceptional, unforeseen recruitment issues.

11.6. Procedure for Accounting for Missing, Unused or Spurious Data

We will conduct data cleaning to ensure that all data values are possible and plausible. Errant data entries will be deleted from the final analysis data set and missing data will be handled as specified for the psychometric measure from which there is a missing response.

11.7. Procedure for Reporting Deviations from the Statistical Plan

In the event that a deviation from the statistical analysis plan becomes necessary or desirable, the reasons for doing so will be set out in the clinical study report.

12. DATA HANDLING

12.1. Data Collection Tools and Source Document Identification

12.1.1. Clinical data collection

Clinical Research Network staff will screen participants' medical records for the clinical data described in Section 8.7.8. Clinical Research Network staff will send these data to the research team securely via an encrypted email or encrypted email attachment.

12.1.2. The web based data collection system

We will collect study data for the online surveys using Qualtrics. Qualtrics is a secure online survey system. The research team will be able to export all study data into an encrypted master database and a separate encrypted contact details database.

12.2. Data handling and Record Keeping

The Sponsor will ensure that all data is processed in accordance with UK Data Protection Law. Once all data have been entered, verified, and validated in the master database, the database will be locked.

12.3. Access to Data

Direct access to source data will be granted to authorised representatives from the Sponsor, auditors, the REC, and the regulatory authorities to permit trial-related monitoring, audits and inspections.

12.4. Archiving

The research team agrees to retain a copy of the protocol, documentation, approvals and all other documents related to the study, including data, for 10 years after the end of the study.

13. ADMINISTRATIVE MATTERS

13.1. Responsibilities of the Investigator

- To ensure that he/she has sufficient time to conduct and complete the study, and has adequate staff and appropriate facilities which are available for the duration of the study and to ensure that other studies do not divert essential subjects or facilities away from the study at hand.
- To submit an up-to-date curriculum vitae for themselves and sub-investigators, and other credentials to the sponsor and, where required, to REC and relevant competent authorities.
- Demonstrate a potential for recruiting the required number of suitable subjects within the agreed recruitment period.
- Conduct the study in accordance with the relevant, current protocol and only make changes after notifying the sponsor, except when protect of the safety, rights, or welfare of the subjects is paramount.

- Record any deviations from the protocol.
- Comply with guidance on Good Clinical Practice.
- Personally conduct or supervise the described investigation.
- Ensure that the requirements relating to obtaining informed consent and ethics review and approval have been met.
- Follow the trial's randomisation procedure and ensure the treatment code is broken only in accordance with the protocol.
- Maintain adequate and accurate records and make these available for inspection by the sponsor [and/or its designee] or any agency authorised by law.
- Ensure that a REC, compliant with local regulations, will be responsible for the initial and continuing review and approval of the clinical investigation.
- Promptly report to the REC all changes in the research activity and all unanticipated problems involving risks to human subjects or others.
- Comply with all other requirements regarding the obligations of clinical investigators and all other pertinent requirements'
- Ensure that all associates, colleagues, and employees assisting in the conduct of the study are appropriately qualified and informed about their obligations in meeting the above commitments.
- Maintain a list of appropriately qualified persons to whom the investigator has delegated significant trial-related duties.
- Inform the sponsor of any changes to staff or facilities.

13.2. Monitoring by Sponsor or Their Representative

The research team will provide the sponsor with copies of the annual reports submitted to the relevant ethical approval bodies.

14. ETHICAL AND REGULATORY CONSIDERATIONS

This study will be conducted according to Good Clinical Practice guidelines, local regulatory requirements and the 2013 Declaration of Helsinki.

14.1. Ethics Approval

This protocol will be submitted to the appropriate REC and their written, unconditional approval obtained and submitted to the sponsor before commencement of the study.

Verification of the ethics committee's unconditional approval of the protocol, participant information sheet and informed consent document will be transmitted to Sponsor prior to the commencement of the study.

The written, unconditional approval from the ethics committee must refer to the study by exact protocol title and number, identify the documents reviewed and state the date of review. Any amendment to the protocol must be approved in the same way.

The ethics committee must be informed by the investigators of all subsequent protocol amendments and of serious or unexpected adverse experiences occurring during the study which are likely to affect the safety of the subjects or the conduct of the study. Approval for such changes must be transmitted in writing to Sponsor via the investigators.

All correspondence with the REC will be retained in the study documentation.

14.2. Peer Review

The initial grant application for this clinical trial underwent a peer review process consisting of independent, external patient and expert reviewers recruited by North West Cancer Research, who approved the study's design. A Trial Steering Group consisting of oncologists, health economists, and psychologists from multiple academic institutions in the UK and Australia, as well as patient, caregiver, and healthcare professional representatives, maintain oversight of the clinical trial on an ongoing basis. The study has also been reviewed by the Ethics Committee for the Department of Psychology at the University of Chester.

14.3. Protocol Compliance

Prospective, planned deviations or waivers to the protocol are not allowed under the UK regulations on Clinical Trials and must not be used (e.g., it is not acceptable to enrol a subject if they do not meet the eligibility criteria or restrictions specified in the trial protocol).

Accidental protocol deviations can happen at any time. They must be adequately documented on the relevant forms and reported to the Sponsor.

14.4. Notification of Serious Breaches to GCP and/or the Protocol

A “serious breach” is a breach which is likely to effect to a significant degree:

(a) the safety or physical or mental integrity of the subjects of the trial; or
(b) the scientific value of the trial

The sponsor must be notified immediately of any case where the above definition applies during the trial conduct phase.

All protocol breaches will be documented and reported in the final study report.

14.5. Data Protection and Patient Confidentiality

All investigators and trial site staff must comply with the requirements of the Data Protection Act 2018 with regards to the collection, storage, processing and disclosure of personal information and will uphold the Act’s core principles.

The Chief Investigator will act as custodian for the research data. All data will be kept completely confidential and will be anonymised and will only be considered in relation to the

project. All audio-recordings made will be suitably anonymised, securely stored in password protected computers and made accessible only to the investigators.

14.6. Financial and Other Competing Interests for the Chief Investigator, Investigators at Each Site and Committee Members for Overall Trial Management

This information will be collected for all participants and retained in the Trial Master File.

14.7. Indemnity

The sponsor will provide Public Liability, Professional Indemnity, and Clinical Trials insurance cover.

14.8. Amendments

Protocol amendments must be made only with the prior approval of Sponsor. Agreement from the Investigator must be obtained for all protocol amendments and amendments to the informed consent document.

The REC must be informed of all amendments and give approval for any amendments.

Any amendment/modification to the protocol will be adhered to by the participating centre (or all participating centres) and will apply to all subjects following its approval.

This will be communicated by the Trial Coordinator and checked for implementation as relevant.

Tracking of the amendment history will be retained in the Trial Master File.

14.9. Post-Trial Care

Participants will be referred to their regular treatment team for any concerns about their physical or mental health following the completion of the randomised controlled trial.

15. DISSEMINATION POLICY

15.1. Dissemination Policy

The clinical trial data will be published in relevant peer-reviewed journals as a joint effort of the trial Steering Group without undue delay following the completion of the study.

15.2. Authorship Eligibility Guidelines and any Intended use of Professional Writers

The Chief Investigator will be the lead author on the primary efficacy publication resulting from the study. The trial coordinator will be the lead author of the publication containing the results of qualitative data analyses. All steering group members will have the opportunity to contribute to all publications arising from the current study and will be granted authorship based on these contributions.

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