# REFRESH: Finding New Energy after Cancer

## Feasibility of a Stepped-Care Cognitive Behaviour Therapy Program for Cancer Fatigue Management

Short Title: Feasibility of the REFRESH program

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# CONTENTS

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# BACKGROUND

Cancer-related fatigue (CRF) refers to a distressing, persistent, subjective sense of physical, emotional and/or cognitive tiredness or exhaustion related to cancer and/or cancer treatment that is not proportional to recent activity, and significantly interferes with usual functioning (Bower, et al., 2014).

CRF is reported by approximately 50% of those receiving cancer treatment and is a side effect that can be debilitating years after treatment completion for up to one in three survivors. CRF limits everyday tasks, employment, physical and social activities. Consequently, CRF inhibits functional recovery and treatment adherence, with additional adverse impact on functional cognition (e.g., attention and concentration) and emotional wellbeing including increased depression symptoms. Survivors with CRF report lower quality of life.

Pharmacological treatment for CRF is limited to relieving suffering in advanced disease (Howell et al., 2015) and the need for evidence-based non-pharmacologic treatment is well documented. Cognitive Behaviour Therapy (CBT) is the recommended first line of treatment for persistent cancer fatigue in survivors (Howell et al., 2015). CBT is a longstanding evidence based psychological treatment for a range of psychological symptoms, which focuses on changing unhelpful ways of thinking and modifying learned patterns of unhelpful behaviour. After treatment, the factors which triggered fatigue – cancer and cancer treatment - are no longer actively involved and cognitive and behavioural factors are often maintaining fatigue (Abrahams et al., 2019). Individuals with CRF, in trying to manage the impact of their low energy, often avoid certain physical and social activities. This then exacerbates fatigue symptoms and psychosocial consequences. CBT for CRF targets unhelpful behaviours and thoughts to reduce fatigue severity and fatigue-related disability in cancer survivors (Gielissen, Verhagen, Witjes, & Bleijenberg, 2006).

To date, CBT has not been integrated as an essential part of fatigue management in oncology services due to lack of resources and suitable models of care. As a result, there are currently no structured clinical services that address fatigue in oncology services in Australia. The effectiveness of CBT for CRF has been established in a small number of studies across the Netherlands, Germany, UK and Korea. In a recent systematic review of the effectiveness of psychological interventions for fatigue in cancer survivors, 12 of the 33 studies identified reported on the effects of CBT on CRF (Corbett et al., 2019). Five studies comparing CBT with treatment as usual all reported significant decline over time in fatigue for those who engaged in a CBT program compared to usual care. Further improvements in sleep, quality of life, and mood were also observed. Whilst the content and delivery of the CBT programs varied, most studies included content on psycho-education of CRF, social support, sleep, anxiety and depression, and physical activity.

Whilst the effectiveness of CBT on CRF is now established, the studies often report high treatment dose of up to 26 face-to-face or online sessions with a psychologist. This is typical of standard community delivered CBT which is also resource-intensive, usually involving a series of 2-hour weekly group or individual sessions over 6-12 weeks delivered by a health

professional trained in CBT. This approach can limit translation and reach of interventions to larger patient populations and reduces sustainability of interventions being incorporated into permanent/standardised hospital care. The feasibility of embedding a CBT program for fatigue into "real world" clinical settings (outside of the research context), that considers reach and sustainability has not been established in Australian cancer services.

Stepped-care interventions offer a solution to standard CBT approaches, as they cater for survivors with differing needs using different intensity interventions. Stepped-Care uses low-intensity treatments for patients with lower acuity (e.g., self-management workbook) and 'steps up' to specialist services as clinically required (i.e., dependent on symptom severity and/or response to first line low-intensity treatment). Both self-management and face to face CBT are known to be effective. Therefore, with the same resources as standard CBT, stepped-care can benefit more patients.

We have previously demonstrated the effectiveness of a stepped-care intervention in the Can-Sleep program for individuals with significant sleep disturbance who have received cancer treatment. Can-Sleep involves a self-directed therapeutic intervention using a self-help booklet (step 1), followed up with a CBT group for those still experiencing clinical levels of sleep disturbance (step 2). Approximately 53% of participants required step 2/CBT-Group. The purpose of the current project is to design an Australian-first, evidence-informed stepped-care CBT intervention for cancer survivors targeting fatigue, and test its feasibility.

## AIMS

The overall aim of the project is to evaluate the feasibility of a stepped-care intervention that identifies and treats CRF in adults who have completed treatment for cancer.

Specific project aims:

1. To assess the feasibility and acceptability of a novel stepped-care approach to managing cancer-related fatigue.
    a. Feasibility (e.g., adherence, recruitment and retention rate)
    b. Acceptability (e.g., usefulness of booklet and phone calls/emails, ease of use of booklet, time spent reading booklet)
    c. Satisfaction (e.g., perceived satisfaction with the amount of support received, extent to which program has met needs)
    d. Proportion of people being referred to 'STEP 2'
2. Assessment of processes, procedures and costs associated with implementing REFRESH in a clinical setting.
3. To explore whether participation in the stepped-care intervention shows promise for treatment response: improvements in fatigue, quality of life and emotional wellbeing.

## PROJECT DESIGN

This project will evaluate the 'REFRESH' Program that aims to address problems with persistent fatigue amongst cancer survivors. Available funding is insufficient to achieve

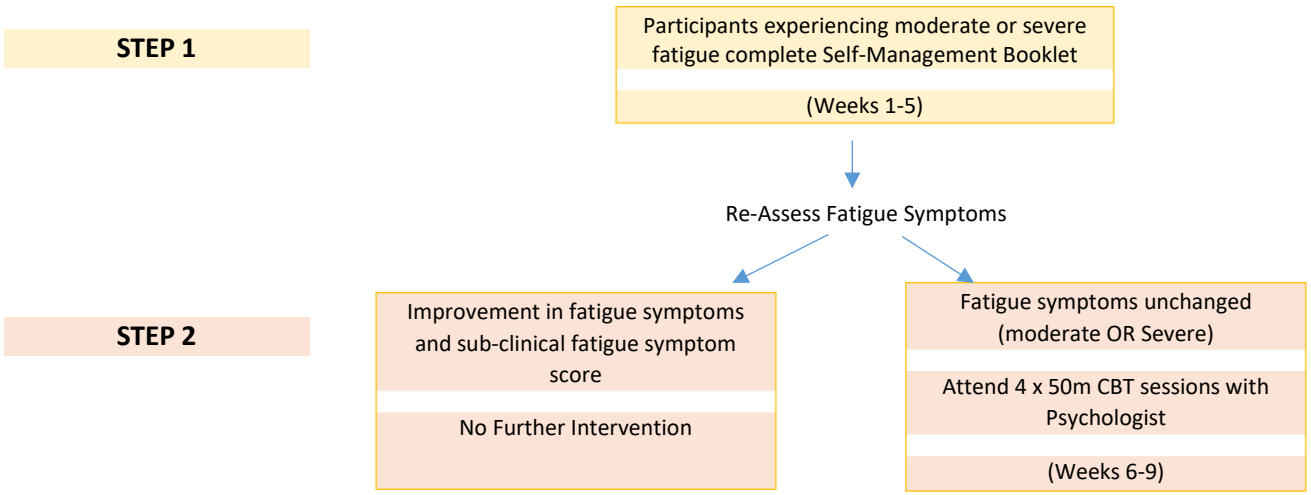
adequate power to evaluate effectiveness of the program on CRF, therefore a non-randomised design with before and after measures will be used.

The REFRESH program is a stepped-care model (Figure 1) of up to 12-weeks duration (including completion of assessments). Participants who are experiencing moderate to severe fatigue are provided with a self-management CBT booklet to assist them with managing symptoms of fatigue and increasing energy (STEP 1). Participants have 5 weeks to work through the booklet independently. Telephone support from a Psychologist at weeks 2 and 5 and email support at weeks 1, 3 and 4 will be provided to support adherence and to address any concerns raised.

At the completion of 5 weeks, participants' fatigue symptoms will again be assessed. Those whose fatigue level does not improve significantly [1] are referred to 4 x 50 minute face-to-face/Telehealth individual or group CBT sessions with a Clinical Psychologist (PI Williams) (STEP 2).

In the Week 2 phone call, participants who have not been able to do the self-management booklet will be encouraged to engage, or fast tracked to STEP 2 for individual support as indicated (e.g., have not started booklet and/or report that they cannot complete the booklet without more support, report fatigue symptoms too distressing and interfering with ability to complete booklet).

**Figure 1: Brief outline of REFRESH Stepped-Care Model**




# METHODS

## *Participants*

Fifty adults who have received cancer treatment will be recruited to the study. This number is in line with our previous studies and is assessed as feasible within the timelines of the study and sufficient for a feasibility study.

[1] Less than 10-point increase on FACIT-F scale

## *Participant Inclusion Criteria*

Each participant must meet the following criteria to participate in the study:

- Aged 18 years or older at the time of recruitment
- Reports moderate to severe fatigue based on a series of screening questions administered on the phone prior to recruitment (see Appendix A).
- Is English speaking and able to read English (the intervention is only available in English)
- Cancer criteria: EITHER
  i. Completed primary treatment for **any cancer** at least 3 months prior (to allow natural recovery)
  **OR**
  ii. Diagnosed with stage III or stage IV **melanoma** AND
    - is receiving maintenance treatment using a single-agent immune checkpoint inhibitor (immunotherapy) or targeted therapy AND
    - has an objective partial or complete tumour response by computed-tomography based imaging, or partial or complete metabolic response by positron emission tomography for a duration greater than 3 months

  **OR**
  iii. Diagnosed with a **haematological cancer** AND
    - a partial or complete response as demonstrated by routine response assessment (ie Imaging or pathology) after at least 3 months treatment with long term therapy OR
    - have previously demonstrated partial or complete response by routine response assessment post intensive treatment and have completed at least 3 months of maintenance therapy or observation OR
    - has not received treatment for a chronic blood cancer due to being below treatment threshold (e.g. indolent disease)

## *Participant exclusion criteria*

- Insufficient English
- At clinical screening interview (see Figure 2) is identified as
    - likely experiencing a significant sleep disorder and would better benefit from our usual care CBT sleep intervention (CAN-Sleep) and/or
    - experiencing psychosis, significant psychological distress or risk of suicide or self-harm
    - not been experiencing *persistent* fatigue (i.e., symptom duration too brief- see Appendix A: clinical screening eligibility checklist)

### *Withdrawal criteria*

We do not expect that participants will be withdrawn by the research team or therapist involved in delivering the intervention. If participants require referral to other practitioners for complementary care (e.g., medication), or care for unrelated morbidity, this will be recorded on the database.

Participants who opt to withdraw from the study will be asked if they consent to continue completing follow-up measures relevant to the highest Step completed and also asked for any existing data to be included in analyses. If consent is not given to the latter, their data will be erased from the database and any records, paper or electronic, will be destroyed at the completion of the study. Participants will be unable to withdraw their data at the completion of the study as their data may have already been used.

## *Procedures*

The study procedure is outlined in detail in Figure 2 (page 11).

### *Recruitment processes*

Potential participants will be identified from the haematology and melanoma late effects clinics, or other specialist clinics at Peter MacCallum Cancer Centre by a member of the nursing, medical or allied health teams. There will also be a REFRESH project information postcard (Appendix B) made available to patients from nursing staff. The REFRESH project information postcard has information about the project and a method for participants to make direct contact with the research team should they be interested in participating.

The research team will gain access to potential/interested participants via two main routes: a) a potential participant will make direct contact with the research team (via the details on the postcard) or b) a member of the PMCC medical or allied health team will identify potential participants; those who have reported to staff that they are struggling with fatigue and/or self-describe their fatigue as orange-red on the fatigue scale lanyard screening tool carried by nursing staff.

A process for recording the consent to share contact details with the research team has been developed. Nursing staff will enter a note into EPIC documenting the following: 'patient x has noted that they are happy to be contacted about the REFRESH study and have consented to having their contact details passed on to a member of the REFRESH study team'. This EPIC note will be cc'd to either Dr Pearson or Dr Williams and will appear in the research study EMR/EPIC inbox, whereby the research team can make contact and commence the study consent and screening process.

After discussions with lead nursing specialists from the haematology and melanoma late effects clinics, we are expecting that the majority of potential participants will be identified via route 2 and there is significant confidence from staff that recruitment sample will be readily achieved.

### *Eligibility Screen*

A member of the research team will contact the participants by phone to explain the project and screen for eligibility using a screening eligibility checklist (see Appendix A.1). Specifically;

- A series of fatigue questions will be administered to assess levels of fatigue, duration and impact of fatigue. These screening questions were chosen to be feasible in usual care.
- Those who are assessed as having **mild fatigue** (report <4 on Q1 and endorse items 2.1-2.3 on the screening eligibility checklist) will be informed that they are not eligible for the research project and will be directed to online cancer-related fatigue resources to prevent fatigue increasing.
- For people that are assessed as having **moderate to severe fatigue** (report >3 on Q1 and endorse items 2.4-3.10 on the screening eligibility checklist), the researcher will complete the remainder of the screening eligibility checklist (Appendix A).

### *Consenting Participants*

- Those meeting full eligibility criteria as described above will be offered follow up care in the REFRESH study. The researcher will explain the study, give opportunity to ask questions and provide a participant information and consent form (PICF) and invite participation in the research project (Appendix C). If preferred by the participant, a hard-copy baseline questionnaire will be sent out with the PICF to reduce delays.
- Participants will provide signed consent in-person or via reply-paid mail, email or SMS photograph to enrol for the study.
- Participants who decline participation will be directed to online cancer-related fatigue resources to prevent fatigue increasing.

## *Administration of Baseline Questionnaire and STEP 1: REFRESH self-management booklet*

- After they consent, participants will be sent a link to complete the online baseline questionnaire (BQ) (or provided a paper copy if preferred) (Appendix A.2).
- On return of the baseline questionnaire, a researcher will provide the participant with a hard copy of the self-management booklet via mail and brief verbal instructions.
- Each participant will be contacted weekly: via email in weeks 1, 3 and 4 (example template in Appendix D) and via telephone at weeks 2 and week 5 to discuss and support their participation, ask any questions and troubleshoot any problems.
- *At the week 2 phone call, if any participant is struggling to engage with the self-management booklet alone (e.g. due to distress, fatigue or other factors) they will receive motivational coaching and may be fast-tracked into STEP 2.*

## *Administration of TIME 1 Questionnaires (following STEP 1)*

- Participants will be asked for their feedback on each Chapter of the self-management booklet as they are working through STEP 1. There are approximately 5 brief questions at the end of each chapter in the booklet. These feedback questions can be removed from the booklet and sent to the research team via email or mail by participants (see TIME 1 Questionnaire PART A (T1Q-A) in Appendix A.3).
- At the completion of the week 5 phone call, participants will be emailed a link to PART B of the TIME 1 online questionnaire (or a paper copy if preferred) (T1Q-B) (see Appendix A.4).
- The FACIT-F score from the T1Q-B will determine eligibility for STEP 2. Participants with a FACIT-F score of 10 or more points higher than baseline will finish their CBT Fatigue treatment, unless they score below 34 (severe). This was established a clinically important improvement (Reddy, Bruera, Pace, Zhang, & Reyes-Gibby, 2007).
- Participants with a FACIT-F score on the T1Q-B questionnaire of less than 10 points higher than baseline and/or below 34 will be offered STEP 2. The decision to be 'stepped up' to STEP 2 will also be made in conjunction with the psychologist's clinical judgement/interview at the week 5 phone-call of STEP 1 (e.g., if questionnaire measures don't appear congruent with clinical observations of further support needs).
- Participants who do not go on to STEP 2 of the program will complete Time 2 Part B Questionnaires (T2Q-B) (see below) 6 weeks after completing the self-management booklet, with the exception of the feasibility, acceptability and satisfaction measures (which will not be applicable as they will have not completed STEP 2).

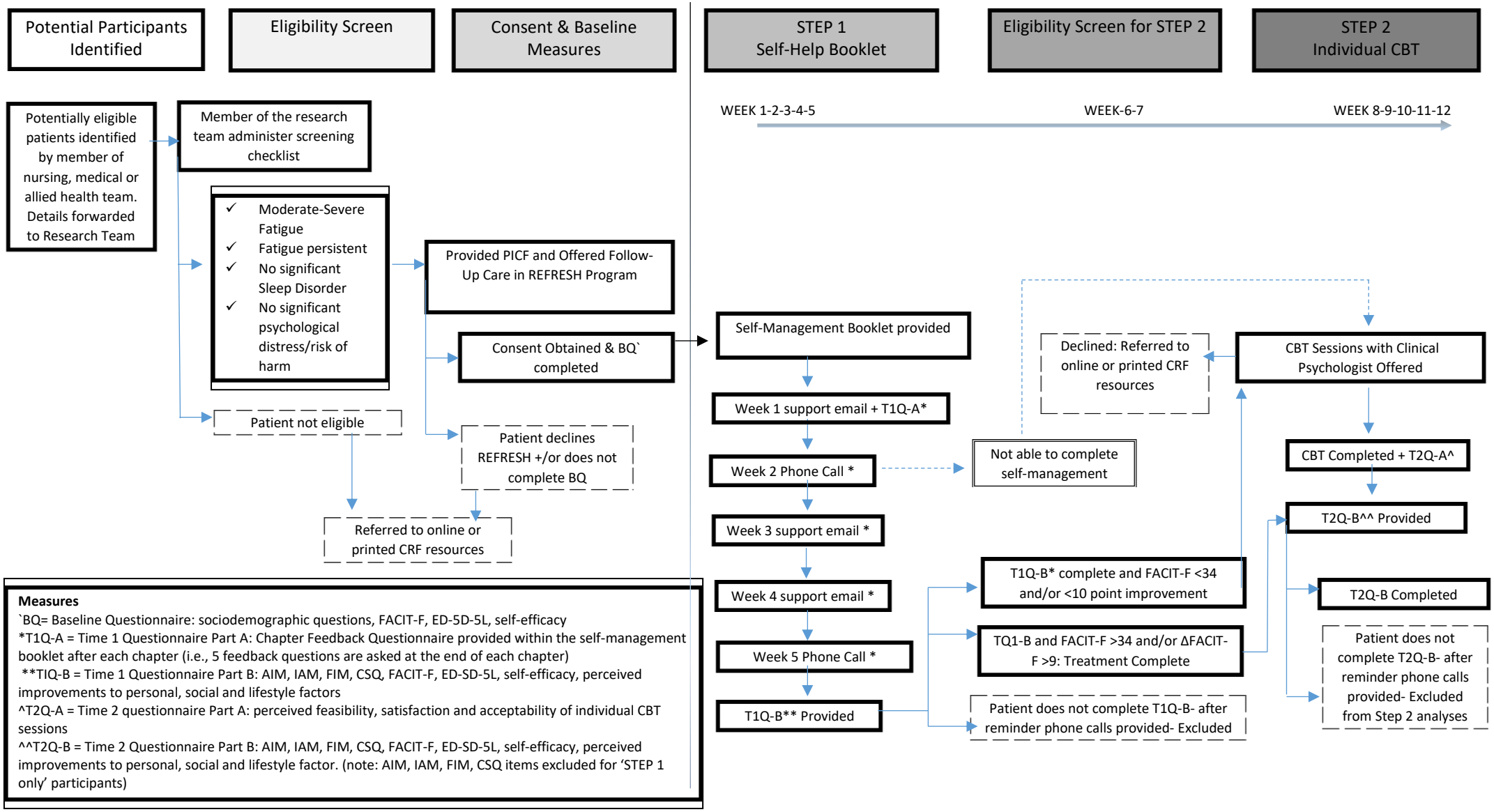
## *Recruitment to STEP 2: Administration of Individual CBT*

- Participants eligible for STEP 2 will be offered up to 4 CBT sessions with a clinical psychologist. These sessions can be delivered one-on-one or in a small group and via face to face or via Telehealth modalities. For Telehealth sessions a secure allied health telehealth platform called CoViu (recommended by the Australian Psychology Association) or the Peter Mac telehealth platform will be utilised.

## *Administration of TIME 2 Questionnaires (following STEP 2)*

- After the participant's last CBT session, PART A of the TIME 2 Questionnaire (T2Q-A) will be administered (either in person or via Telehealth) (Appendix A.5).
- After participants have completed their final CBT session, they will be emailed a link to the second part, PART B, of the TIME 2 questionnaire (T2Q-B) (or provided paper copy if preferred) (Appendix A.6).

**Figure 2: REFRESH Study Process and Measures at each Time Point**



## *Intervention Materials*

### *REFRESH Self-Management Booklet (Intervention STEP 1)*

A REFRESH self-management booklet was developed by the project team based on the following information and expert input:

- Content was informed by literature and previous self-help programs and booklets developed by members of the Clinical Psychology team, utilised in previous research study projects (e.g., CAN-Sleep).
- Internal and external multidisciplinary expert review from a range of clinicians with backgrounds in psychology, nursing, oncology, dietetics, exercise physiology, occupational therapy and social work.
- Consumer review from the PMCC Consumer register. Consumers were adults with experience (either personal or as a carer) in cancer related fatigue.
- Existing literature on the modifiable factors associated with fatigue
- Existing psycho-education and CRF evidence and information on cancer related fatigue
- Booklet design and packaging in consultation with Green Scribble (graphic design and editing currently in progress- the attached version is **NOT** what will be provided to participants).

The self-management booklet includes the following 5 chapters (content closely mirrors the individual CBT sessions (STEP 2) outlined in Table 1):

1. Fatigue Explained: Information and psycho-education about cancer-related fatigue
2. Understanding Feelings: Understanding Emotions and their function in fatigue
3. Helpful Behaviours: Increasing activities, exercise and learning relaxation strategies
4. Adaptive Thinking: Understanding cognitions and changing unhelpful thoughts
5. Moving On: Synthesis of strategies, coping plan for the future

### *CBT Individual/Group Intervention (Intervention STEP 2)*

The CBT intervention will comprise up to 4 x 50 minute sessions with a Clinical Psychologist either face-to-face or via Telehealth (modality at the participant's choice and/or as mandated by COVID-19 restrictions). These sessions may be delivered individually (one-on-one) or via a small group, depending on demand and participant preferences. In previous stepped care studies completed within the PMCC Psychology Department (e.g., Can-Sleep), approximately 50% of those completing STEP 1 progressed to STEP 2. Based on this, with a sample size of 50 we can anticipate 25 individuals meeting eligibility for STEP 2. Depending on how rapidly patients are recruited and work through STEP 1, it may be more feasible to provide STEP 2 sessions via group format. Given this is a feasibility study, the decision to provide individual or group modalities for STEP 2 will be decided at the point of recruitment to STEP 2, depending on numbers and demand. For example, if 2-4 individuals all meet criteria and agree to participate in STEP 2 at the same time, STEP 2 will be offered as a group format, rather than running STEP 2 across 4 separate sessions. If recruitment is slower, we won't hold up running STEP 2 whilst waiting for numbers to

form a group, and these sessions will be offered as individual sessions. Participant preferences for individual versus group will also be considered.

Session length aligns with current scheduling and reimbursements. Each session will be based on the self-management booklet as detailed in Table 1, however tailored to the individual and the maintaining modifiable factors associated specifically with their personal fatigue (e.g., anxiety and inactivity). Note, it is assumed that some knowledge and psycho-education regarding cancer related fatigue and maintaining factors has been achieved from the self-help program, however, if this is not the case, this will be revisited in session 1.

*Table 1: Content of REFRESH CBT-fatigue modules*

| Session | Session Topic | Session Goals & Objectives |
|---|---|---|
| **1** | Understanding Feelings | To understand the impact of emotions on fatigue and strategies to increase pleasant emotions |
| **2** | Helpful Behaviours | To understand the role of behaviours in impacting fatigue. Introduction to relaxation strategies (breathing, muscle relaxation and mindfulness). Mood monitoring, increasing physical activity, pacing and scheduling pleasant and mastery activities for the week ahead as part of behavioural activation. |
| **3** | Adaptive Thinking | To understand the role of cognitions in influencing emotions, behaviour and fatigue. Identifying unhelpful thoughts and 'thinking traps', cognitive restructuring via use of a thought diary. Introduction to worry postponement strategy and coping statements. |
| **4** | Moving On | Summarise skills learnt and identify which are helpful and can be implemented ongoing. Assistance with developing a coping card if this hasn't been done prior. Assistance with identifying additional supports. Assistance with accessing further professional supports if needed. |

## *Evaluation*

Because there is evidence of efficacy of CBT for cancer fatigue (Howell et al., 2015), the evaluation will focus primarily on implementation feasibility of the stepped-care approach.

The evaluation plan uses the Medical Research Council (MRC) framework for conducting and reporting process evaluations (Moore et al., 2015). This means, that rather than focussing on intervention effects (which assume adequate sample size, randomisation etc.) the focus is on understanding *how* interventions work in practice and the mechanisms for behaviour change. Therefore, there is more emphasis on factors such as whether participants read, and were able to use the self-help program booklet, rather than focussing solely on pre-post changes to outcome measures. This approach assists evaluators to decide aspects of the intervention or its context to prioritise for further investigation or clinical implementation.

According to MRC, key functions of process evaluations (Moore, Audrey, & Barker, 2015) will be used as follows:

1. Intervention causal assumptions: CBT for fatigue aims to modify thoughts and behaviours to reduce the impact of fatigue on activity and participation. The causal assumptions for effectiveness of CBT-fatigue relate to reducing fatigue perpetuating factors and focus on symptoms, rather than physical fitness (Hyland et al., 2021; Prinsen et al., 2013).
2. Implementation evaluation:
    a. Implementation processes i.e. program delivery will be evaluated for feasibility, including costs, resources and applicability.
    b. Delivery of the REFRESH program will be monitored for fidelity, dose, adaptations and reach (rate of uptake)
3. Mechanisms of impact: Participant interactions and responses to REFRESH will be assessed using survey methods for acceptability and feasibility. Potential mediators of personal, social and lifestyle factors will be triangulated to indicate characteristics of people who may be more or less suited to the stepped-care CBT approach.
4. Outcomes: Fatigue, self-efficacy and quality of life will be evaluated using validated measures. However, this exploratory study is not sufficiently powered for effectiveness evaluation and these outcomes will be used as preliminary data for a future study of effectiveness and to observe trends.
5. Context: As a mediator for all of the above variables, context is acknowledged but not evaluated. As far as possible this intervention aims to be applicable in a range of settings and this would be the focus of future research.

Therefore, the measures and data collected for the current study will be focussed on the participant and clinical feasibility of REFRESH. Specifically, we will look at participant intervention feasibility, acceptability, satisfaction, clinical feasibility, fidelity and perceived improvements in fatigue and other personal, social and lifestyle factors.

Table 2 presents an overview of the REFRESH program evaluation plan, with details of various measures in the text following. Data collection forms and surveys are provided in Appendix A.

*Table 2: Evaluation Overview and Rationale*

| Implementation Outcomes | Definition | Rationale | Method of evaluation |
|---|---|---|---|
| Intervention **Acceptability** | The perception among users that the program is palatable and satisfactory (Proctor et al., 2011) | Users consider the program acceptable | Online[2] Surveys and Booklet Questionnaire/s – T1Q and TQ2<br>**Abbreviated Acceptability Rating Profile** (AARP)<br>**Client Satisfaction Questionnaire** (CSQ)<br>Recruitment and withdrawal records (spreadsheet) |
| Intervention **Appropriateness** | The perceived fit and relevance of the program to users (Proctor et al., 2011), indicated by proportion of people willing to try and complete the program | Consumers perceive it is worth trying and completing the program | Proportion of eligible participants referred that enrol in and complete the self-help program<br>Recruitment records (spreadsheet)<br>Reasons for not participating (spreadsheet) |
| **Cost** | The resource cost of delivering the program per user | This self-help CBT program is expected to provide therapy at a lower cost compared to face to face, enabling more users to benefit | Booklet cost and records of therapist / administration time per person enrolled (Table 3) |
| **Feasibility** | The extent to which stepped care approach to CBT can be used for cancer fatigue | A majority of participants complete Step 1 in 6 weeks and/or Step 2 in 4 sessions | Phone surveys TQI-A & TQ2-A include number of modules/sessions completed (dose) |
| **Fidelity** | The degree to which the program was implemented as intended (Proctor et al., 2011) | The adherence and deviations to program contacts and stepped care protocol | Field notes maintained by researchers |

[2] Online or paper survey if preferred

| Intervention impact | Definition | Rationale | Method of evaluation |
|---|---|---|---|
| Fatigue | *A distressing, persistent, subjective sense of physical, emotional and/or cognitive tiredness or exhaustion related to cancer and/or cancer treatment (National Comprehensive Cancer Network, 2020)* | The program aims to reduce fatigue | **Functional Assessment of Impact of Chronic Illness Therapy – Fatigue (FACIT-F) subscale** (Cella, Eton, Lai, Peterman, & Merkel, 2002) will be used to determine progression to Step 2 and change in fatigue (online survey T1Q-B and TQ2-B). |
| Self-efficacy | A person's belief in their capacity to do what is necessary to produce specific performance attainments (Bandura, 1977) | Self-efficacy may be a mediator of health behaviour | Online surveys T0Q T1Q-B and T2Q-B.<br>**Perceived self-efficacy for fatigue self-management scale (PSEFSM)** (Hoffman et al., 2011) |
| Health-Related Quality of Life | A multidimensional concept of the influence of health states on the extent to which a person is healthy, comfortable and able to participate in society | A brief appraisal of overall quality of life before and after program | **EuroQual 5 Dimension 5 Level Scale (EQ-5D-5L)** (Rabin & de Charro, 2001) |
| Personal, social and lifestyle factors | Certain modifiable factors can maintain fatigue. The program targets sleep, mood, distress, energy use and engagement in physical, social and leisure activities. | The aim of the CBT intervention is to alter behavioural and cognitive factors that perpetuate fatigue | Online surveys T1Q-B and T2Q-B |

## *Intervention Appropriateness*

Intervention appropriateness for participants will be measured by

a) Retention (proportion of enrolled participants who completed follow-up assessments; proportion of participants who completed each module of step 1; proportion of participants who completed step 2 compared to the proportion of participants who consented to step 2)
b) Adherence to step 1 and step 2 (percentage of sessions attended, reasons for not completing sessions, number of days overdue for completed questionnaires).
c) The Intervention Appropriateness Measure (IAM). The IAM is a 4-item validated measure (Weiner et al., 2017) with items rated on a 5-point Likert scale from 'completely disagree' to 'completely agree' with higher scores indicating greater intervention appropriateness.

## *Intervention Feasibility*

The feasibility of this intervention will be assessed using

a. The Feasibility of Intervention Measure (FIM). The FIM is a 4-item validated measure (Weiner et al., 2017) with items rated on a 5-point Likert scale from 'completely disagree' to 'completely agree' with higher scores indicating greater intervention feasibility (Appendix A.4).
b. Qualitative and quantitative feedback provided in study questionnaires completed after each chapter for STEP 1 and again at the end of STEP 2 of the program where applicable (T1Q-A and T2Q-A). Key indicators will include the number of chapters of the self-management booklet attempted / completed, completion of STEP 1 within 6 weeks and STEP 2 in 4 sessions. Additional details about barriers to completion will be sought.
c. Qualitative field notes maintained by research team.

## *Intervention Acceptability*

Intervention acceptability will be assessed using

a. The Acceptability of Intervention Measure (AIM) will be used to measure acceptability (Appendix A.4). The AIM is a 4-item validated measure (Weiner et al., 2017) with items rated on a 5-point Likert scale from 'completely disagree' to 'completely agree' with higher scores indicating greater intervention acceptability. Intervention acceptability was also measured in the researcher-administered questionnaires (T1Q-A and T2Q-A) designed to elicit participants reports on aspects such as uptake of each module, time spent on each module, completion of module-based activities, perceived helpfulness of modules and barriers to reading modules and completing activities.

b. Intervention satisfaction will be assessed by administering the Client Satisfaction Questionnaire (CSQ) (Attkisson & Zwick, 1982). The CSQ is a well validated 8-item measure of the quality of the intervention, the extent to which the program met participant's needs, perceived increases in skills, and whether participants would recommend the program to others. Total scores range from 8 to 56, with higher scores indicating greater satisfaction. The CSQ will be administered in the T1Q-B and T2Q-B assessments where applicable (appendix A.4 and A.5).
Intervention satisfaction will also be evaluated in part A of the administered questionnaires (T1Q-A and T2Q-A) with open ended items such as "Is there anything you particularly liked or disliked about Chapter 2?" or "Did you find the week 5 phone call helpful?" (see Appendix A.3 and A.5); items designed to elicit participants' own perceptions about their satisfaction with the self-management booklet and the individual CBT sessions (if applicable).
c. Rate of recruitment to / enrolment in program will contribute to evaluation of acceptability. Numbers of referrals received, eligible and enrolled participants, withdrawals and reasons for decline/ withdrawal) will be recorded in a spreadsheet to enable calculation of rates of program uptake, dropouts and factors related to non-participation.

## *Cost of Intervention Delivery (Clinical Feasibility)*

Intervention procedures and costs will be evaluated by documenting and measuring the different activities employed to implement the intervention (e.g., direct and indirect therapy time (includes phone support and notes) x hourly rate), time taken to complete activities x hourly rate of clinician, in addition to costs of materials and program administration time per participant (e.g. screening, scheduling) x AHA hourly rate. (Does not include study related tasks e.g. information and consent). See Table 2.

**Table 2: Clinical Feasibility: Intervention Procedures and Costs**

| Activity | Variables | Data Collected | Cost p/Unit |
|---|---|---|---|
| **Screening** | • Initial screening by existing staff<br>• Stage 2 screening via checklist implementation | • Role of person screening.<br>• Time taken for initial screen | |
| **Intervention Delivery- Self Management** | • Send self-help program booklet<br>• Follow-up phone call at 2 weeks<br>• Follow up phone call at 5 weeks<br>• Emails x 3 | • Time taken to send self-help booklet<br>• Role of person conducting phone calls.<br>• Time taken to conduct phone calls<br>• Time taken to write and send emails | |
| **Screening** | Screen at end of 5 weeks | • Role of person screening<br>• Time taken to re-screen and book step 2 | |
| **Intervention Delivery** | Organise step 2- book in 4 sessions of individual CBT | • Role of person administering CBT<br>• Length of each session<br>• Time taken documenting session | |

## *Fidelity of Program*

Researchers / clinicians will document deviations to screening, program contacts (emails / phone calls) and stepped care protocol and reasons for deviations (if known) via field notes and a clinical note in EPIC for any significant interactions (e.g., a STEP 2 psychology session).

The fidelity of the REFRESH individual CBT sessions will be assessed through a review of each session by the psychologist administering the intervention and a member of the research team.

## *Intervention Impacts (Outcomes)*

The impact of the REFRESH program for participants will be evaluated using an online / paper survey at T0, T1 and T2 (if appropriate). The survey comprises the following sections:

### 1. *Fatigue*

***FACIT-Fatigue*** (Cella et al., 2002)

The key measure of participant impact of the REFRESH program is changes in fatigue measured by the FACIT-F (Appendix A.2). The FACIT-F is a valid tool designed to assess the severity of cancer-related fatigue, with a recall period of 7 days (Cella et al., 2002). FACIT-F is a 13-item scale, with items rated on a 5-point Likert scale from 0 (not at all) to 4 (very much). Score range is 0-52, with the population mean of 43 (Cella et al., 2002). Lower scores on the FACIT-F indicate more fatigue symptoms and impairment. Clinically important change is predicted with an increase of 10 or more points, with 73% sensitivity and 78% specificity (Reddy et al., 2007). A threshold of 34 or 30 is reported to detect severe clinical levels of fatigue (Eek, Ivanescu, Corredoira, Meyers, & Cella, 2021), but a cut off for moderate level is not established. Administration time is 2-5 minutes. A change of 10 greater on the FACIT-F will be considered a clinically significant impact.

### 2. *Self-Efficacy*

***Perceived self-efficacy for fatigue self-management scale (PSEFSM)*** (Hoffman et al., 2011)

Self-efficacy is a concept described as the belief that one can successfully perform the behaviour needed to achieve the goal (Bandura, 1977). There is growing evidence that self-efficacy for self-management is an important mediator of health behaviour (Patel & Ghosh, 2017). This variable is included to help better identify those who can best benefit from the self-management program (Step 1).

The PSEFSM is a valid 6-item instrument developed to measure self-efficacy in CRF management. An 11-point scale (0–10, 10 = very certain) measures confidence in performing fatigue self-management behaviours. Scores of the six items are averaged and

final score ranges from 0-10 with 10 being highest perceived self-efficacy (Hoffman et al., 2011) (Appendix A.2).

### 3. *Quality of Life*

*EuroQual 5 Dimension 5 Level Scale (EQ-5D-5L)* (Rabin & de Charro, 2001)

The EQ-5D-5L is a 5-item measure of Health-Related Quality of Life (HRQoL) (Appendix A.2). There are 5-dimensions; Mobility, Self-Care, Usual Activities, Pain/Discomfort and Anxiety/Depression. Each dimension has 5 levels/response options: no problems, slight problems, moderate problems, severe problems and extreme problems. The patient is asked to indicate his/her health state by ticking the box next to the most appropriate statement in each of the five dimensions. This decision results in a 1-digit number that expresses the level selected for that dimension. The digits for the five dimensions can be combined into a number that describes the patient's health state with a possible range 0-20, with higher scores indicating worse HRQoL.

### 4. *Personal, Social and Lifestyle Factors*

Participants will be asked to rate their perceived post-intervention improvements across a range of personal, social and lifestyle factors (that were modifiable factors targeted in the self-help program booklet and individual CBT sessions). These items will be presented in the online questionnaires (T1Q-B and T2Q-B (Appendix A.4 and A.6).

There are seven items in total (sleep, mood/depression, stress/anxiety/worry, energy, exercise levels, social activity and engagement in hobbies) and participants will be asked to select one of the following response options associated with each item: 'Better', 'Same' or 'Worse' (since starting the program). For participants who select 'Better' on any given item, they will be followed up with an item targeting perceived stage of the program where the change/benefit for that domain was noticed (e.g., sleep started to improve after module 3).

### 5. *Sociodemographic characteristics*

The following sociodemographic characteristics will be collected on enrolment (BQ, Appendix A.2) to gather descriptive information about which participants were drawn to and retained in the study:

- Diagnosis and Treatment details (type and date of diagnosis, treatments undergone)
- Age/date of birth
- Sex (Male, Female, Another term (specify)
- Country of birth, language spoken
- Education status
- Marital status
- Employment status

## *Data Analysis*

Analyses will include all available data and will be performed in R (reference index version 3.6.1 or higher). Responses to PROMs will be scored according to author guidelines. Standard recodes will be applied, as required, for analysis and reporting purposes.

Counts and percentages will be used to summarise missing data, including missing items and forms, for each measure at baseline and post-baseline assessments. Values for missing forms (i.e. PROMs) will not be imputed.

Descriptive statistics will be used to summarise patient demographic and clinical characteristics of all patients enrolled on the study. These will include counts and percentages for nominal and crude-scale ordinal (<10 levels) valued variables; and means and standard deviations or medians and interquartile ranges, as appropriate, for fine-scale (≥10 levels) ordinal and continuous valued variables.

The main feasibility outcomes are acceptability, fidelity and practicability of the stepped-care CBT intervention, including recruitment, retention, adherence and costs. Recruitment data will be summarised using a rate and 95% CI using the Poisson distribution. Adherence and retention data will be summarised using a proportion and 95% CI; this will be estimated using the Wilson method. Descriptive statistics will also be used to summarise acceptability and feasibility.

Changes from baseline at follow-up assessments for fatigue (FACIT-F), self-efficacy (PSEFSM) and Quality of Life (Ed-5D-5L) will be analysed descriptively (means and standard deviations). This will be done separately for patients who participate in Step 1 only and for those who participate in Steps 1 and 2. Effect size estimates (i.e. standardised measures of change from baseline; in this case, mean change divided by the baseline standard deviation), as described by Kazis and colleagues, will be used to characterise the size of observed differences (Kazis, Anderson, & Meenen, 1989)

Free text items from participant questionnaires will be summarised using content analysis, whereby the content of free responses will be coded and grouped, where applicable. It is worth noting that free text items mostly accompany pre-determined response options, so it is not envisaged that all participants will opt to respond to free text items.

# ETHICAL CONSIDERATIONS

This project will be conducted according to the NHMRC national Statement on Ethical Conduct in Human Research (2007 and updates) and the World Medical Association of Helsinki (2013 and updates).

## *Informed Consent*

To ensure that participants do not feel obligated to participate, the study team will ensure invitees that participation is voluntary and that they may stop their involvement in the project at any time. The study team will explain that their decision will not impact on their care or their relationships with hospital staff.

## *Data storage and privacy issues*

A unique study identification number system will be used for all data collection for this project. This system will employ the use of paired tracking numbers, so identifiable participant information (e.g., name, date of birth) and participant contact details (e.g., email and phone number) is kept separate from questionnaire responses. Therefore, participant's personal details cannot be linked with their research involvement and questionnaire responses unless you have access to the paired tracking numbers, which will be stored in an electronic password protected excel spreadsheet that is only accessible by the research team.

All questionnaire responses will be entered into a secure password protected REDCap database. Hardcopy questionnaires and PICF's will be stored in a locked filing cabinet at PMCC Department of Psychology. Only members of the research team will have access to this data, in accordance with the National Statement on ethical Conduct in Human Research 2007 and Australian Code for Responsible Conduct of Research 2018. Five years after publication or dissemination of project outcomes, hard-copy and electronic data will be destroyed.

## *Confidentiality*

It is not expected that participating in this research project will pose any risks of harm to participants. If any disclosures of risks to safety (e.g., suicidal ideation) occur during any stages of the project, standard clinical processes will be followed including safety planning with the participant, and advising a support person of the participant (e.g., trusted family member) and where applicable a member of their treating team. This limit to confidentiality is included in the PICF.

## *Distressed Participants*

It is not envisaged that participating in the REFRESH program will lead to participant distress. Patients that are reporting extreme distress at baseline (e.g., risk of hard, psychotic symptoms) are excluded from the study and will be referred to more appropriate acute psychological intervention. However, in the event that a participant becomes distressed throughout participation in either STEP 1 or STEP 2 of the REFRESH program, a member of the lead project team, all of whom are trained in managing distressed patients, will contact the participant and discuss support options. Participants who disclose or appear to be experiencing distress during support emails or phone calls will also be contacted to discuss support options. For example, a referral to appropriate professional support (e.g., existing hospital or community psychologist patient is already engaged with, Cancer Council Victoria telephone counselling, Employee Assistance Program). Further, participants who report feeling too distressed/unable to engage with the self-help program booklet within two weeks of commencing the program (STEP 1), will be fast tracked to individual support. Weekly contact with participants also ensures the risk of undetected distress is minimal.

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# APPENDICES

Summary of Appendices:

- APPENDIX A (A.1-A.6): PARTICIPANT QUESTIONNAIRES
- APPENDIX B: RECRUITMENT POSTCARD
- APPENDIX C: PARTICIPANT INFORMATION AND CONSENT FORM
- APPENDIX D: EXAMPLE PARTICIPANT EMAIL

# Appendix A Participant Questionnaires

## REFRESH STUDY MEASURES SUMMARY

| Measure Name | Number of items |
|---|---|
| A.1 REFRESH screening checklist (clinician use only) | Total = 18 |
| **A.2: BASELINE QUESTIONNAIRE (BQ)** | **Total = 39** |
| Sociodemographic Items | 15 |
| The Functional Assessment of Chronic Illness Therapy - Fatigue (FACIT-F) | 13 |
| Perceived Self Efficacy for Fatigue Self Management (PSEFSM) | 6 |
| European Quality of Life 5 Dimension 5 Level (EQ-5D-5L) | 5 |
| **A.3: TIME 1 QUESTIONNAIRE PART A (T1Q-A)** | **Total = 30** |
| Booklet Chapter Feedback Questionnaire (self-devised) | 6 (p/chapter) |
| **A.4: TIME 1 QUESTIONNAIRE PART B (T1Q-B)** | **Total = 48** |
| FACIT-F | 13 |
| PSEFSM | 6 |
| EQ-5D-5L | 5 |
| Acceptability of Intervention Measure (AIM) | 4 |
| Intervention Appropriateness Measure (IAM) | 4 |
| Feasibility of Intervention Measure (FIM) | 4 |
| Client Satisfaction Questionnaire (CSQ) | 8 |
| Perceived changes to personal, social and lifestyle factors (self-devised) | 4 |
| **A.5: TIME 2 QUESTIONNAIRE PART A (T2Q-A)** | **Total = 7** |
| Perceived satisfaction with STEP 2 (self-devised) | 7 |
| **A.6: TIME 2 QUESTIONNAIRE PART B (T2Q-B)** | **Total = 48** |
| FACIT-F | 13 |
| PSEFSM | 6 |
| EQ-5D-5L | 5 |
| Acceptability of Intervention Measure (AIM)* | 4 |
| Intervention Appropriateness Measure (IAM)* | 4 |
| Feasibility of Intervention Measure (FIM)* | 4 |
| Client Satisfaction Questionnaire (CSQ)* | 8 |
| Perceived changes to personal, social and lifestyle factors (self-devised) | 4 |

*Applicable for STEP 2 participants only

A FULL COPY OF EACH QUESTIONNAIRE IS PROVIDED IN A SEPARATE ATTACHMENT: 'REFRESH_MEASURES_V3_19.10.21'.

## Appendix B: Recruitment Postcard


**Who can participate?**

- Adults who have completed cancer treatment at least 3 months ago OR are on long-term or maintenance cancer treatment (e.g immunotherapy).
- Experiencing prolonged fatigue that affects everyday activities.

**What support do I get?**

- A self-management booklet with activities and psychological strategies to try, which may assist with your fatigue.
- 4 sessions with a psychologist if required.
- You will also complete 2 or 3 brief questionnaires.

**How do I participate or get more information?**

Ask your nurse to pass your contact details on to us OR contact us directly: Elizabeth Pearson or Lauren Williams on
Phone: **03 8559 5915** OR Email: **refresh@petermac.org**

## Appendix C: Participant Information and Consent Form

Provided as a separate attachment
'REFRESH_PICF_V1_6.8.21'.

# Appendix D: Example Step 1 Email Template

Example REFRESH Step 1 Support Email template (weeks 1, 3 & 4)^

Dear _,

Hello from the REFRESH Team!

It's now been one week *[insert 3 weeks/4 weeks]* since you started your journey in the REFRESH- New Energy after Cancer study.

We hope you have found the REFRESH self-management booklet helpful so far. If you have already worked through Chapter [*insert #*], well done! We hope you have had a chance to try the *[insert name]* activity.

Having trouble/haven't started?

If for some reason, you haven't had a chance to look at the booklet [or *chapter #*] yet, that's also OK. We understand life sometimes gets in the way.

If this is the case, we would encourage you to just focus on the parts of Chapter [*insert #*] that you think are most relevant to you. Irrespective of your progress on Chapter [*insert #*] this week, we encourage you to move on to the next chapter in the coming week.

There is no right or wrong way to use the booklet. We have designed the booklet to flow in order from Chapter 1 to Chapter 5, and this is the approach we would encourage. However, any approach that works for you is OK.

We need your feedback!

Whether or not you have completed Chapter [*insert #*], done parts of Chapter [*insert #*], or are yet to look at Chapter [*insert #*], we would really love your feedback!

At the end of Chapter [*insert #*], there are 5 short questions for you. We have added these questions to help us understand whether people used the booklet, liked the booklet and whether anything got in the way of using it.

Once again, we really appreciate your time and participation.

Questions or Concerns

If you would like further support, we will call you in [x] week/s and can discuss any problems or questions you have then. However, if you have any questions or concerns in the meantime, feel free to reply to this email and we will endeavour to respond as soon as possible.

Kind Regards, the REFRESH team.

*^Email content will be adapted and personalised in line with participant specific progress and project timeline.*