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Efficacy and cost-effectiveness of an online mindfulness program (MindOnLine) to reduce fear of recurrence among people with cancer: study protocol for a randomized controlled trial

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Title

Efficacy and cost-effectiveness of an online mindfulness program (MindOnLine) to reduce fear of recurrence among people with cancer: study protocol for a randomized controlled trial

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35 **Abstract**

36 **Introduction:** Fear of cancer recurrence (FCR) is a common condition among cancer survivors
37 that can lead to significant levels of distress, anxiety and depression. Online mindfulness
38 programs may provide the mechanism to support cancer survivors manage FCR and distress,
39 and improve people's wellbeing over the short, medium and long term. The primary aim of
40 this study is to determine the potential efficacy of MindOnLine, a 9 session mindfulness-based
41 program for survivors of breast, prostate and colorectal cancer. A formal economic program
42 will also be conducted.

43 **Methods and analysis:** A single-blind randomized controlled trial to determine the efficacy
44 and cost-efficacy of a MindOnLine program for cancer survivors. A total of 400 people living
45 with cancer will be recruited via online advertisements on social media platforms, peak
46 consumer advocacy groups, or through outpatient services at healthcare providers across
47 Victoria. People will be randomly allocated to either the MindOnLine program (n=200) or
48 waitlist control (n=200). Participant assessments will occur at baseline, at 9 weeks and 9-month
49 follow up. The primary outcome is change in Fear of Recurrence Index Score total score
50 between baseline and 9 weeks; secondary outcomes include changes in depression and anxiety,
51 quality of life and mindfulness. The economic analysis comprises a cost-consequences analysis
52 where all outcomes will be compared to costs.

53 **Ethics and dissemination:** Ethics approval was obtained from the Peter MacCallum Cancer
54 Centre (20-53) and Deakin University (2020-284). Findings will be disseminated in peer
55 reviewed journals and among key stakeholder organisations including hospitals, cancer and
56 community organisations and Government. If successful the project will be rolled out
57 nationally with a formal implementation plan.

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3 58 **Australian New Zealand Clinical Trials Registry:** 12620000645954p. Registered 06 June
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5 59 2020,

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7
8 60 <https://www.anzctr.org.au/Trial/Registration/TrialReview.aspx?id=379520&isReview=true>

9
10 61 **Keywords:** mindfulness, cancer, fear of cancer recurrence, online; economics of cancer;
11
12 62 supportive care; web-based platforms

13 14 15 16 63 **Article Summary**

17 18 64 **Strengths and limitations of this study**

- 19
20 65 • Development of the intervention through a literature review, findings from a pilot study,
21
22 66 involvement of consumer advocacy groups and Government bodies are the study's strengths.
23
24 67 This will ensure translation of the program into policy and practice if shown to be
25
26 68 efficacious.
- 27
28
29 69 • Involvement of consumer advocacy groups to support recruitment.
- 30
31 70 • This study will employ a single-blind randomized controlled trial to determine the efficacy
32
33 71 and cost-efficacy of MindOnLine.
- 34
35 72 • Advances in social platforms, smartphone technology and web-based programming can
36
37 73 change substantially in a short period and while this may affect the actual online platform
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39 74 used, we do not consider this will influence the program content or delivery mechanisms.
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75 **Introduction**

76 Over one million Australians are cancer survivors, and this population is expected to grow
77 substantially over the next 20 years due to an ageing population and improved community-
78 based screening programs and treatments.[1] A cancer diagnosis can cause people to confront
79 their own mortality, often for the first time,[2] so it may be unsurprising that three quarters of
80 cancer survivors experience fear of cancer recurrence (FCR) and 49% report moderate to high
81 levels of fear,[3] as well as high levels of clinical depression [3]and anxiety.[4]

82
83 FCR is a highly prevalent and persistent condition that can result in significant levels of anxiety
84 and depression across the disease trajectory.[5] It is imperative to address this issue and our
85 recent work into early psychosocial support indicates it may be possible to significantly reduce
86 FCR through an online mindfulness program.[6] Mindfulness is a state of mind in which one
87 pays attention to the present experience in a nonjudgmental, curious, and accepting way. Some
88 studies have shown mindfulness is associated with improved mental health outcomes and
89 management of the emotional consequences of cancer, [7, 8] while other have found no
90 effect.[9]

91
92 Mindfulness-based interventions consist of regular informal and formal mindfulness
93 meditation practices and are supported by educational principles that are person and
94 relationship-centred.[10] Research into the use of mindfulness has mostly evaluated face-to-
95 face programs which are time-intensive, of limited accessibility and costly.[11] Online
96 mindfulness programs represent a potentially cost-effective mechanism to help cancer
97 survivors manage FCR and distress, and improve mental wellbeing over the short, medium
98 and long term.[2] While an online mindfulness-based cognitive therapy (MBCT) intervention
99 was found to be as effective as a face-to-face MBCT in reducing psychological distress and

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2
3 100 FCR in cancer patients [12] there is a lack of robust evidence assessing the effectiveness of a
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5 101 general online mindfulness program for cancer survivors, limiting capacity for implementation
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8 102 and dissemination.[13, 14]
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12 104 The aim of this study is to conduct a randomised controlled trial of *MindOnLine*, an online 9
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14 105 session mindfulness-based intervention, for survivors of breast, prostate and colorectal cancer,
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17 106 to determine the effectiveness and cost-effectiveness of the program.
18

19 107 *Preliminary work*

20
21 108 To inform the development of *MindOnLine*, we undertook a systematic review of
22
23 109 methodologies for internet based mindfulness interventions.[15] This review showed a dearth
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25
26 110 of studies with long-term follow up periods. Our team also conducted an exploratory study on
27
28 111 the knowledge of, attitudes toward and behaviours regarding meditation among patients with
29
30 112 melanoma.[16] Our study of 291 cancer survivors recruited at a single tertiary cancer hospital
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32
33 113 found that a key barrier to engaging with meditation was a lack of knowledge about its practice.
34
35 114 Findings also indicated interest in an online meditation-based intervention once informed about
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37 115 possible benefits of meditation for people with cancer. Those interested in an online
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39 116 meditation-based program reported higher perceived stress, indicating a need for such a
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41
42 117 program.
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46
47 119 We conducted a pilot 6-week RCT [6] to determine the feasibility and acceptability of
48
49 120 *MindOnLine*, The secondary aims were to explore intervention impacts on FCR, worry, and
50
51 121 perceived stress compared to usual care. Overall, 69 melanoma survivors agreed to participate,
52
53 122 and 46 participants were randomised into the intervention group (2:1). Scores on all FCR
54
55 123 Inventory (FCRI) subscales reduced in the intervention group, with the severity subscale
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57 124 decreasing significantly compared to the control group (-2.6, 95% CI=(-4.4, -0.7); p=0.008)
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3 125 after 6 weeks. The total FCRI score also showed a decrease albeit non-significant (-6.2 , 95%
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5 126 $CI=(-13.12, 0.68)$, $p=0.07$). Previous studies have indicated that a 4.1 points decrease on the
6
7
8 127 severity scale is a clinically important change.[17]
9

10 128
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12 129 Based on participant feedback regarding the benefits of mindfulness practice and the
13
14 130 suggestion of a maintenance period to enhance sustainability of the effects, *MindOnLine* was
15
16 131 expanded to a 9-week program with the last 3 weeks revisiting concepts already explored in
17
18 132 the program and supporting regular practice.
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23 133 **Methods and analysis**

24 134 **Aims and Hypotheses**

25
26 135 The aims of this study are to determine the effect of *MindOnLine* on FCR, anxiety and
27
28 136 depression in cancer survivors. The specific aims are:

29
30 137 **Aim 1:** To evaluate the impact of the *MindOnLine* intervention on the primary outcome (FCR),
31
32 138 measured using the FCRI total score [18] at the end of the 9-week intervention period.

33
34 139 **HYPOTHESIS 1:** Participants receiving the intervention will report lower average FCRI total
35
36 140 scores at 9 weeks, compared to the waitlist group.

37
38 141 **Aim 2:** To evaluate the impact of *MindOnLine* on secondary outcomes at nine weeks: 1)
39
40 142 Anxiety and Depression, using the Patient Health Questionnaire (PHQ-9) [19] and Generalised
41
42 143 Anxiety Disorder (GAD-7) Scale; [20] 2) Quality of Life (QoL) measured by AQOL-4D; [21]
43
44 144 and 3) Mindfulness, using Cognitive and Affective Mindfulness Scale-Revised (CAMS-
45
46 145 R). [22] **HYPOTHESIS 2:** Compared to the waitlist group, participants in the intervention group
47
48 146 will report improvement in all of the secondary outcomes at nine weeks.
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50 147 **Aim 3:** To assess if the intervention effects on the primary and secondary outcomes are
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52 148 sustained at the nine-month follow-up. **HYPOTHESIS 3:** Compared to the waitlist group,
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3 149 participants in the intervention group will report sustained improvement in primary and
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5 150 secondary outcomes at nine months.
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8 151 **Aim 4:** To assess, from a health sector and broader societal perspective, the cost-effectiveness
9
10 152 of *MindOnLine*. **HYPOTHESIS 4:** Compared to the waitlist group, *MindOnLine* will be cost-
11
12 153 effective with an incremental cost-effectiveness ratio likely to fall below the commonly used
13
14 154 threshold of \$28,000 - \$50,000/Quality of Life Year (QALY).
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17 155
18 156 **Study Design**

19
20 157 This study is a randomised controlled trial, to test the effectiveness and cost-effectiveness of
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22 158 *MindOnLine* compared to usual care on FCR, anxiety, depression and QoL among people
23
24 159 diagnosed with breast, prostate or colorectal cancer. Overall, 400 patients will be recruited with
25
26 160 200 patients randomly allocated to the intervention group and 200 to the waitlist group (usual
27
28 161 care only). The intervention group will receive usual care and the online mindfulness program.
29
30 162 Primary and secondary outcomes will be collected at baseline, nine weeks and nine months
31
32 163 post randomisation. Nine months corresponds to approximately six months following the end
33
34 164 of the intervention period. Following completion of the study (9 months), participants in the
35
36 165 waitlist group will be offered the *MindOnLine* intervention (Figure 1).
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43 167 **Participants**

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45 168 People with a diagnosis of breast, prostate or colorectal cancer will be recruited via online
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47 169 advertisements on social media platforms, peak consumer advocacy groups for each cancer
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49 170 Breast Cancer Network Australia (BCNA), or Prostate Cancer Foundation Australia (PCFA),
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51 171 Bowel Cancer Australia social media platforms and colorectal cancer support groups, or
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53 172 through outpatient services at healthcare providers across Victoria, see Figure 1.
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173 **Figure 1.** Study flowchart

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(Insert Figure 1 here)

For peer review only

FCRI (Fear of Cancer Recurrence Inventory); GAD-7 (General Anxiety and Distress scale; PHQ-9 (Patient Health Questionnaire); CAMS-R (Cognitive and Affective Mindfulness Scale – Revised); AQoL-4D (Assessment of Quality of Life – 4 Dimensions)

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3 189 Inclusion criteria
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5 190 Adults, aged 18 year of older, living in Australia, who completed active treatment for Stage
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7 191 1-3 breast, prostate or colorectal cancer (CRC), (trastuzumab/similar, and hormone treatment
8
9 192 exempt) within the past 5 years; have internet access and a FCRI severity score ≥ 13 , indicating
10
11 193 clinically significant FCR.[18] Our pilot study showed 74% of participants with melanoma
12
13 194 were identified as having clinically significant FCR.[6]
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19 196 Exclusion criteria
20
21 197 Insufficient English language skills to understand videos presented in English, complete
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23 198 surveys in English or living with advanced cancer (Stage IV or metastatic disease).
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28 200 **Recruitment procedures**

29 201 Multiple methods will be applied to recruit people to the study:

- 30 202 1) online through *MindOnLine* social media pages including Facebook, Instagram, Twitter,
31
32 203 Reddit and LinkedIn
33
34 204 2) sharing recruitment flyers through BCNA and PCFA social media platforms, and Australian
35
36 205 based cancer groups
37
38 206 3) email invitations sent to BCNA and PCFA supporters (and colorectal cancer support groups)
39
40 207 and cancer registries
41
42 208 4) paid Facebook and Instagram advertising
43
44 209 5) through outpatient clinics, chemotherapy and radiotherapy units and rooms of oncologists
45
46 210 and surgeons at cancer treatment centres.
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51 211 Online recruitment procedure

- 52 212 1) The *MindOnLine* social media pages will be shared among social networks and will allow
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54 213 people to post questions about the project. 2) A recruitment flyer will be distributed by BCNA,
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56 214 PCFA, Bowel Cancer Australia and colorectal cancer Facebook support groups using their
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3 215 existing social media platforms. 3) Study invitations will be sent to supporters registered with
4
5 216 BCNA and PCFA who have indicated an interest in learning about research projects. 4) Paid
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7 217 advertisements will run throughout the recruitment period on Facebook, Instagram and Twitter
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9 218 to distribute the project details to a wider audience. The use of paid advertisements in health
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11 219 research is becoming popular and a systematic review has shown this to be an effective
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13 220 recruitment strategy.[23]

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17 221 In all online recruitment methods, people will have access to the recruitment flyer, which will
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19 222 provide a brief overview of the study, the link to the *MindOnLine* registration page and the
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21 223 contact number of the project manager.
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26 225 Health service recruitment procedures

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28 226 If recruitment across social media platforms, advertisements and peak consumer advocacy
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30 227 groups does not generate sufficient participation levels, participating health services
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32 228 oncologists or surgeons involved in the project, will support the recruitment process. The
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34 229 research assistant (RA) at each site will screen patients and confirm eligibility of patients with
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36 230 treating clinicians or with nurses working in the outpatient units. RAs will then contact patients
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38 231 by phone and interested patients will be emailed the study details with a link to the study
39
40 232 webpage and registration page). If there is no response from patients, a message will be left
41
42 233 on their phone. Two further attempts to reach patients will be made (a week apart), and after a
43
44 234 third unsuccessful attempt no further contact will be made. If patients have not enrolled in the
45
46 235 study within two weeks, one follow-up phone call will be made to answer any queries patients
47
48 236 may have about the study and to assist with registration. We have used similar screening and
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50 237 recruitment approaches in previous studies and they were found them to be acceptable and
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52 238 successful.[6] We anticipate a recruitment period of 18-months.
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3 240 Consent and screening
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5 241 Once directed to the *MindOnLine* registration page, participants will be presented with the plain
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7 242 language statement and then asked to provide consent. Potential participants will be asked to
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9 243 provide basic demographic and disease information allowing screening to ensure they meet
10
11 244 study eligibility criteria. Potential participants will also complete the severity subscale of the
12
13 245 FCRI to allow those with scores ≥ 13 to be screening into the study. Those screened into the
14
15 246 study will provide their email address and contact number, and directed to the baseline
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17 247 questionnaires. People who are not eligible will receive an online message thanking them for
18
19 248 their interest in the study and referring them to local support services provided by leading
20
21 249 cancer charities should they require support.
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28 251 **Randomisation**
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30 252 Eligible participants will be allocated to treatment groups using random sequences embedded
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32 253 in the online survey platform Qualtrics, ensuring allocation concealment. Randomisation
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34 254 (using stratified random permuted blocks) will be conducted in blocks of size 2, stratified by
35
36 255 cancer type (breast, prostate, CRC) and age (<60 ; ≥ 60 years old). Participants will be unblinded
37
38 256 to group assignment, while researchers and data analysts will be blinded to the group condition.
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44 258 **Control group**
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46 259 Participants allocated to the waitlist group will receive usual care. Following randomisation,
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48 260 they will receive an email with a list of services they may contact for information and support.
49
50 261 They will be informed that they will be granted access to *MindOnLine* intervention in 9-
51
52 262 month's time.
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264 **Intervention group – MindOnLine program**

265 Participants allocated to the intervention will be provided with the link to *MindOnLine*, which
 266 comprises three main components:

267 (1) an educational component to increase participants' knowledge about the science and
 268 practice of mindfulness and how it may benefit them in everyday life;

269 (2) a formal mindfulness meditation practice to improve awareness and emotion regulation;
 270 and

271 (3) an informal practice to teach participants how to bring mindfulness to daily activities.

272 A new theme is introduced each week, with a new meditation practice which participants will
 273 be encouraged to undertake every day *The MindOnLine* program is detailed in Table 1.

274

275 Table 1- Weekly content of the *MindOnLine* Program

Week	Theme	Meditation	Daily practice
1	Introduction to mindfulness	Breath	Being present with the experience
2	Reducing stress	Body Scan	Notice how the body responds to stress
3	Relating to emotions	Working mindfully with emotions	Noticing the cycle of emotions
4	Self-compassion	Self-compassion	Notice self-criticism
5	Communicating mindfully	Listening/ Sound meditations	Bringing attention back to the conversation
6	Living mindfully	Practising with gentleness and patience	Pause throughout the day
7	Reducing worries	Mindfully working with worries and fears	Notice when caught up overthinking

8	Reducing worries mindfully	Loving Kindness meditation	Notice acts of kindness
9	Maintaining mindfulness	Silence with bells	Notice when distracted from being present

276

277 Each module's theme will be explained through a short 5-10 minute video. At the end of each
 278 week, participants will receive an email with a link to the video introducing the theme for the
 279 upcoming week. The script for the videos will be available for downloading and saving or
 280 printing in a pdf format so that participants can keep a copy for later reference. At the end of
 281 each module, participants will receive an automatically generated email reminding them to
 282 continue daily meditation practice (formal practice) and given specific everyday mindfulness
 283 exercises to apply during daily activities (informal practice).

284

285 To enhance adherence and retention to the 9-week program and deepen their mindfulness
 286 experience, participants will have access to additional program features. The features are
 287 guided by a framework proposed by Abraham and Michie [24] to facilitate behaviour change
 288 in interventions:

289 1) Twice daily reminders to complete mindfulness practice. Adapted from the pilot study,
 290 emails containing a link to a short, guided meditation audio file will be sent to
 291 participants twice daily. These emails will serve as reminders to meditate and will
 292 provide easy access to the meditation practice of the week.

293 2) Progress tracking. Participants will be able to monitor their own mindfulness practice
 294 each day by reviewing how many times they have used each section of the program,
 295 and the duration of use. Embedded usage data tracking systems records each login and
 296 provides real time representation of program use.

1
2
3 297 3) Goal setting. When enrolled in the program, participants will have the opportunity to
4
5
6 298 set goals for their mindfulness practice (Figure 2). Goals are linked to usage data
7
8 299 tracking to provide participants with feedback about whether they are reaching their
9
10 300 goals. Goals may be practice orientated e.g. to practise mindfulness for five minutes
11
12 301 each day, or may be specific to each person's situation e.g. I would like to manage my
13
14 302 worries leading up to my oncologist appointment.

15
16
17 303 4) Reflective journaling. Participants will have the opportunity to journal their experiences
18
19 304 during the mindfulness program by using the "My Journal" functionality (Figure 3).
20
21 305 Each week's content will have a journal section, which will include prompts related to
22
23 306 mindfulness program content, participants will be able to enter and save their responses
24
25 307 within the program for future review. Prompts will be developed specifically for the
26
27 308 study.

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31 309 The mindfulness program can be accessed at any time via direct login to the website or via the
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33 310 hyperlink sent to participants in the daily e-mails.

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37
38 312 Figure 2. My Goal functionality in MindOnLine

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41 313 (Insert Figure 2 here)

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46
47 316 Figure 3. My Journal guided self-reflection practise in MindOnLine

48
49 317 (Insert Figure 3 here)

50
51 318

52 53 54 319 **Data collection**

55
56 320 Table 2 illustrates the overall schedule for trial participants in both groups. All assessments
57
58 321 will be performed online. The questionnaires at baseline, at nine weeks including the

322 satisfaction survey for those in the intervention group and at nine months, will be sent via
 323 Qualtrics through an automatically generated schedule. Participants who do not complete
 324 questionnaires will be followed up by telephone at each data collection point. At baseline,
 325 participants' demographic information (i.e., gender, age, marital status, current employment
 326 status, highest level of education, postcode, type of cancer, date of diagnosis, time since end of
 327 last treatment, type of treatment and previous meditation experience) will be collected.

329 Table 2. Schedule of enrolment, interventions, and assessments
 330

TIMEPOINT	STUDY PERIOD											
	Enrolment	Allocation	Post-allocation									Post-Intervention
			Week 1	Week 2	Week 3	Week 4	Week 5	Week 6	Week 7	Week 8	Week 9	9-months
ENROLMENT:												
Eligibility screen	X											
Informed consent	X											
Allocation		X										
INTERVENTIONS:												
Immediate access to MindOnLine			←—————→									
Waitlist group												
ASSESSMENTS (Both groups):												
Demographic characteristics	X											
FCRI [18]	X									X	X	
GAD-7 [20]	X									X	X	
PHQ-9 [19]	X									X	X	
CAMS-R [22]	X									X	X	
AQoL-AD [21]	X									X	X	
Mindfulness experience	X									X	X	
Resource use	X									X	X	

<i>COVID-19 measures</i>	X										X	X
ASSESSMENTS (Intervention group only):												
<i>Adherence tracking and meditation log</i>			X	X	X	X	X	X	X	X	X	X
<i>Program satisfaction</i>											X	X

331

332 **Outcome measures**

333 Fear of cancer recurrence Inventory (FCRI)

334 The 42-item Fear of Cancer Recurrence Inventory (FCRI) is a multidimensional FCR scale

335 intended for use with all cancer patients. Items were developed on the basis of a cognitive–

336 behavioural formulation of FCR (range:0-168).[18] The FCRI consists of seven domains:

337 triggers, severity, psychological distress, functional impairment, reassurance, insight and

338 coping strategies (scoring range:0-36). It has shown high internal consistency, good construct

339 and criterion validity in adults with different cancer types.[18]

340

341 Anxiety and Depression

342 The *Generalized Anxiety Disorder-7 scale (GAD-7)* [20] is a valid and efficient tool for

343 assessing generalised anxiety symptoms and assessing severity in clinical practice and

344 research. The seven items assess the frequency of core symptoms of generalised anxiety

345 disorder within the past 2 weeks (scoring range:0-21).[20]

346 The *Patient Health Questionnaire-9 (PHQ-9)* [19] parallels the nine diagnostic symptom

347 criteria that define DSM-IV major depressive disorder. At only 9 items (scoring range:0-27),

348 the PHQ-9 is shorter than most depression tools. Unlike most other measures of depression,

349 the PHQ-9 was developed, tested and refined for use with medical patients.[19]

350 The PHQ-9 and GAD-7 are recommended for use among cancer survivors in the American

351 Society of Clinical Oncology Guidelines.[25]

352

1
2
3 353 Mindfulness

4
5 354 Trait mindfulness is measured using the Cognitive and Affective Mindfulness Scale-Revised
6
7 355 (CAMS-R),[22] a 10-item self-report questionnaire. This scale uses everyday language
8
9 356 appropriate for those with little meditation experience and is designed to capture mindfulness
10
11 357 as a general daily experience. The questionnaire comprises four domains of mindfulness
12
13 358 (attention, present-focus, awareness, and acceptance/non-judgment). Participants are asked to
14
15 359 rate on a four-point Likert scale how much they relate to each statement (scoring range:4-40).
16
17
18 360 Compared to other measures of mindfulness, the CAMS-R is unique in that it is related to
19
20 361 psychological distress,[26] which is highly relevant to the current study population.[27]
21
22

23 362

24
25 363 Mindfulness experience

26
27 364 In order to control for access to external mindfulness-based programs particularly in the waitlist
28
29 365 group, all participants will be asked whether they have enrolled in a mindfulness-based
30
31 366 program in the period between surveys and/or used other supportive care services (e.g. peer
32
33 367 support, psychologists, psychotherapy, counsellors, yoga and meditation).
34
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38
39 369 Program satisfaction

40
41 370 Participants in the intervention group will be asked to provide feedback about the *MindOnLine*
42
43 371 program. Quantitative and qualitative data using open ended questions will be collected in
44
45 372 relation to satisfaction with program content, the helpfulness of the program, usability, and
46
47 373 areas for improvement. The satisfaction questionnaire has been adapted from the satisfaction
48
49 374 questionnaire used in the pilot study.[6]
50
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52 375

53
54 376 Economic outcomes

55
56 377 *Assessment of Quality of Life (AQoL 4D)* [21] is a health-related quality of life utility measure.
57
58 378 It is generally used in economic evaluations. The *Resource Use Questionnaire* covers general
59
60

1
2
3 379 health care services usage (self-reported), use of other welfare services, and impacts on work
4
5
6 380 force participation. The questionnaire has been successfully used in cancer psychosocial
7
8 381 intervention studies.[28]
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10 382

11
12 383 Adherence tracking and meditation log

13 384 The software package used to run *MindOnLine* was developed at Deakin University and has
14
15
16 385 inbuilt functionality to collect and clean usage data. Google Analytics has been incorporated
17
18
19 386 into the platform to allow for validation of findings. Both software will track participants'
20
21 387 online activity, including login date/times, navigation patterns, page views and duration, and
22
23 388 features used (video, audio, goals and reflective journaling).
24
25

26 389

27
28 390 Impact of COVID-19

29 391 To control for potential environmental impacts on mental wellbeing outcomes, participants will
30
31
32 392 be asked whether COVID-19 has had an impact on their mental wellbeing in the two weeks
33
34 393 prior to baseline, 9-weeks and 9-month assessments.
35

36 394

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38
39 395 **Sample size calculations**

40 396 Power calculations are conservative, i.e. the detectable differences reported below are possibly
41
42
43 397 larger than the true detectable differences, because they are based on two-group comparison of
44
45 398 change while the main analysis (see Analysis Plan) will adjust for baseline values of the
46
47 399 outcome and for factors used in the stratified randomisation.[29] The statistical software PASS
48
49 400 version 14.0.9 (NCSS, LLC) was used for all calculations ($\alpha=0.05$; two-sided tests).
50

51 401

52
53
54 402 Primary outcome

55 403 Change in FCRI total score between baseline and 9 weeks. The target sample size (200
56
57
58 404 participants per arm) achieves 94% (80%) power to detect a mean difference between arms of
59
60

1
2
3 405 10 points (8 points) change in FCRI score or 80% power to detect a difference of 8 points
4
5 406 [standard deviation (SD): 23.5;[30)]. SD estimate obtained from Butow et al., [30] as their
6
7 407 study included a heterogenous sample of cancer patients while our pilot study only included
8
9 408 patients with melanoma Stage 2-3. The selected effect sizes correspond to Cohen's *d* of 0.43
10
11 409 (moderate/large) and 0.34 (small/moderate) respectively. Currently, there is no definition of a
12
13 410 clinically significant improvement for FCRI score, however, the proposed effect size is
14
15 411 comparable to that described in other studies.[30]
16
17
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21

22 413 Secondary outcomes

23 414 The target sample size (200 participants per arm) achieves 80% power to detect an intervention
24
25 415 effect of size 0.34 (Cohen's *f*, small/moderate) at 9 weeks for any of the outcomes. This effect
26
27 416 size corresponds to mean differences between groups of: a) 1.5 point in PHQ-9 depression
28
29 417 score (SD = 4.5, maximum SD reported in patients with breast, colorectal and prostate
30
31 418 cancer;[31] PHQ-9 minimal clinically important difference (MCID) for cancer patients: 2.6 to
32
33 419 5);[32] b) 1.4 point in GAD-7 anxiety score (SD=4.1, maximum SD reported in patients with
34
35 420 breast, colorectal and prostate cancer;[33] MCID=1.95);[32] and mean differences between
36
37 421 group in change from baseline to 9 weeks of: c) 1.2 points in FCRI severity score (SD=3.6,
38
39 422 pilot study effect: 2.6);[6] d) 1.1 points in CAMS-R score (SD=3.4); e) 2.5 points in Worry
40
41 423 score [SD=7.3]; f) 3.0 points in PSS score [SD=8.9]; the last 3 reflecting moderate Cohen's *d*
42
43 424 effect sizes (<0.35).
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51 426 To meet the sample size needs of our desired statistical power, we will recruit 400 participants.

52
53 427 In our pilot study, six participants (13%) withdrew in the intervention group and none in the
54
55 428 control group. Assuming a conservative 30% attrition rate at nine months, we expect to have
56
57 429 complete data for approximately 280 participants (140 per group).
58
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430

431 **Analysis plan**

432 All statistical analysis will be conducted on an intention-to-treat basis whereby all randomised
433 participants with at least one post-baseline measurement will be analysed by original treatment
434 assignment regardless of adherence. Baseline characteristics will be described using summary
435 measures selected based on variable distribution. The main analysis will adjust for baseline
436 values of the outcome and for factors used in the stratified randomisation.[29]

437

438 *Aims 1 and 2.* The effect of the intervention on each of the outcomes, defined as change from
439 baseline to nine weeks, will be assessed using linear models including group and the
440 stratification factors. *Aim 3.* The effect of the intervention across the three measurement times
441 will be estimated using linear mixed models, including study group, time (categorical: 9 weeks,
442 9 months) interaction group×time and the stratification factors as fixed effects and participant
443 as a random effect. If there is a positive intervention effect on mental health outcomes,
444 exploratory mediation analyses will be conducted to determine whether improvements are
445 mediated by increases in mindfulness.[34] For outcomes where it is a plausible assumption that
446 missing data are completely at random, we will use complete case analysis; if not plausible, we
447 will use multiple imputation. *Subgroup analysis:* We will explore whether age or gender
448 modify the effect of the intervention on FCR, depression and anxiety at 9 weeks.

449

450 *Aim 4.* This study will also comprise a cost-consequences analysis where incremental costs of
451 the intervention will be compared with the full spectrum of outcomes included in the study. A
452 series of cost-effectiveness ratios can be determined which have been shown to be useful for
453 decision-makers. Inclusion of the AQoL 4D will also enable a cost-utility analysis to be
454 undertaken, thereby allowing practical judgements to be made regarding value for money

1
2
3 455 credentials of the intervention. Nevertheless, the economic analysis will be primarily from the
4
5
6 456 perspective of the health care sector and a secondary analysis from the broader societal
7
8 457 perspective will also be undertaken. A detailed costing of the intervention will be undertaken
9
10 458 and the evaluation will first measure and value any change to the use of health care resources
11
12 459 over the period of the study between the two arms of the trial and then compare any additional
13
14 460 costs to the additional outcomes achieved. Standardised economic evaluation techniques will
15
16 461 be used including incremental analysis of mean differences and bootstrapping to determine
17
18 462 confidence intervals along with a net monetary analysis to determine the cost-effectiveness of
19
20 463 the intervention for different value for money threshold criteria. The costs of routine roll-out
21
22 464 will be estimated.
23
24
25

26 465

28 466 *MindOnLine* usage data by the intervention group will be reported using descriptive statistics.

30 467 Linear mixed models, with random intercept and slope for each person, will be fitted to estimate
31
32
33 468 time trends in usage.
34

35 469 **Data management**

37 470 Data will be exported from Qualtrics on a monthly basis and crossed checked during
38
39 471 exportation to ensure accuracy in results. All identifying participant information will be
40
41 472 removed from data sets. Documents containing sensitive information will be saved as password
42
43 473 protected files and stored within the Deakin University One Drive.
44
45

46 474 **Monitoring**

48 475 Data

50 476 The adherence data will be monitored by the program developer. The program developer does
51
52 477 not have any competing interests. Other project data will be monitored by the project steering
53
54 478 committee with regular meetings and progress updates. No interim analysis will be performed
55
56 479 during the trial.
57
58

59 480 **Patient and Public Involvement**

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2
3 481 Representatives from three consumer organisations have been involved in the design and
4
5 482 implementation of the project since its inception. Their contribution has included development
6
7 483 of the intervention and its content, wording on recruitment material, and provided advice on
8
9 484 recruitment strategies. Representatives from each consumer organisation has contributed to
10
11 485 project steering meetings.
12
13
14
15

16 486 **Ethics and Dissemination**

17 487 **Harms**

18 488 In the event that a participant reports distress to the project manager they will be advised to
19
20 489 seek assistance from the regular medical professionals and provided with additional referrals
21
22 490 to lifeline.org.au. Ethics approval was obtained from the Peter MacCallum Cancer Centre
23
24 491 (20-53) and Deakin University (2020-284). Any adverse events will be reported to the ethics
25
26 492 committees.
27
28
29
30

31 493 **Auditing**

32 494 The trial may be audited by the governing Human Research Ethics Committees.
33
34
35

36 495 **Protocol amendments**

37 496 Protocol amendments will be approved by the governing Human Research Ethics Committees.
38
39 497 Any relevant changes will be submitted as a modification to the Australian and New Zealand
40
41 498 Clinical Trial Registry.
42
43

44 499 **Dissemination**

45 500 The findings of this study will be written by study authors and published in peer reviewed
46
47 501 journals project steering committee. Access to full datasets will be made available upon
48
49 502 reasonable request. All identifying participant information will be removed prior to publication.
50
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54 503 **Discussion**

55 504 One of the most significant changes across society is the use of web-based technology. Online
56
57 505 mindfulness-based interventions circumvent problems with traditional face-to-face delivery of
58
59
60

1
2
3 506 the program, impacted by work commitments, caring responsibilities and geographic
4
5 507 isolation.[2]
6
7

8 508

9
10 509 This study will rigorously evaluate the efficacy of a self-directed online mindfulness program
11
12 510 in reducing FCR in breast, prostate and CRC survivors. The study will advance the literature
13
14 511 regarding the benefits of mindfulness for cancer survivors by representing one of few large
15
16 512 well controlled trials of a self-directed mindfulness-based program aimed at reducing FCR.
17
18 513 Including a health economic evaluation of the program adds to the utility of the trial with the
19
20 514 study providing information that budget holders and policy makers need when considering
21
22 515 recommendations and support for supportive care programs. This trial will fill a gap in
23
24 516 knowledge regarding the potential impact of mindfulness in supporting cancer survivors.[7]
25
26 517 Extensive pilot work in identifying the type of program cancer survivors are interested in,
27
28 518 involving consumers in designing the content and length of the program and providing
29
30 519 reminders and practice tips increase the likelihood of participants engaging with the program
31
32 520 and the intervention having a positive impact.
33
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37 521

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39
40 522 The study is being conducted in partnership with health services and cancer advocacy and
41
42 523 community groups who have assisted in the design of the research trial and intervention. As
43
44 524 partners in the study, they will ensure the intervention can be rolled out to cancer survivors if
45
46 525 shown to be effective. In addition to consumer advocacy groups, the study is being conducted
47
48 526 in partnership with government. As we expect the *MindOnLine* intervention to improve health
49
50 527 outcomes, reduce the fear and distress in cancer survivorship and reduce health service and
51
52 528 community costs our partnership with government will ensure that policy makers are informed
53
54 529 of the study's findings particularly cost-effectiveness findings.
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1
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3 531 The study has a number of strengths and weaknesses. Development of the intervention through
4
5 532 a review of the literature, input from consumers and findings from a pilot study and
6
7
8 533 involvement of consumer advocacy groups and government are study strengths ensuring
9
10 534 translation of the program into practice if shown to be effective. Involvement of the consumer
11
12 535 advocacy groups also aid in recruitment. Incorporating an economic evaluation into the study
13
14 536 design is a strength as it will complement clinical findings and support decision-making
15
16
17 537 processes for potential implementation. However, several limitations also need to be
18
19 538 acknowledged. Recruitment through social media platforms means we cannot accurately assess
20
21 539 uptake of the intervention, as we will not be able to identify the number of eligible people
22
23 540 exposed to our recruitment flyers. This may limit our ability to determine reach of the program.
24
25
26 541 However, recording the time taken for recruitment and accessing google analytic data on
27
28 542 internet traffic and page visits may provide some information in this area. Participants will need
29
30 543 access to the internet to participate. While this may mean some people will be excluded from
31
32 544 the study, we believe this will have minimal impact on the study. We envisage that the study
33
34 545 will take approximately 4 years to complete. Advances in social platforms, technology and
35
36 546 app-based programing can change substantially in a short period. While this may affect the
37
38 547 actual online platform used for the program, we do not consider this will influence the program
39
40 548 content or delivery mechanisms. As technology advances will likely increase interest in self-
41
42 549 directed support programs for cancer survivors, it is essential that cancer survivors access
43
44 550 programs with demonstrated effectiveness.
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48

49 **Trial Status**

51 **Protocol Version:** Version 5, dated 18 December 2020

53 Recruitment commenced 12.10.2020, it is anticipated recruitment will be for a duration of 18
54
55 554 months finishing on 12.04.2022.

58 555
59
60

1
2
3 556 **Abbreviations**
4

5 557 AQL-4D Assessment of Quality of Life – 4 Dimensions
6

7 558 BCNA Breast Cancer Network Australia
8

9 559 CAMSR Cognitive and Affective Mindfulness Scale-Revised
10

11 560 CI Confidence interval
12

13 561 CRC Colorectal Cancer
14

15 562 FCR Fear of cancer recurrence
16

17 563 FCRI Fear of Cancer Recurrence Inventory
18

19 564 GAD-7 General Anxiety Disorder scale
20

21 565 MBCT Mindfulness-based cognitive therapy
22

23 566 MCID Minimally clinically important difference
24

25 567 PCFA Prostate Cancer Foundation of Australia
26

27 568 PHQ-9 Patient Health Questionnaire
28

29 569 QALY Quality of Life Years
30

31 570 QoL Quality of Life
32

33 571 RA Research assistant
34

35 572 RCT Randomized controlled trial
36

37 573 SD standard deviation
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3 **693 Declarations**
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6 **694 Author's contributions**
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8
9 695 PML, LR, LO, NH, MJ, AU, RC, DWA, EO, VW, developed the program and study design
10
11 696 with input from all authors; EO designed the web platform and analytics with input from LR,
12
13 697 NH, RC, BS, PML. CM designed the economic component of the study. All authors provided
14
15 698 substantial input into the development of the protocol. PML and NH drafted the manuscript
16
17 699 with contributions from the co-authors. Each of the authors contributed to, read and
18
19 700 approved, the final manuscript.
20
21

22 701 Each of the co-authors is on the steering committee, and will oversee implementation of the
23
24 702 study and data collection.
25
26

27 **703 Funding**
28

29 704 This study is funded by the National Health and Medical Research Council (NHMRC)
30
31 705 Partnership Grant ID APP1179317. The funder supported the cost of undertaking the project.
32
33

34 **706 Competing interests**
35

36 707 The authors declare they have no competing interests.
37
38

39
40
41 **709 Figure Legend/Caption:**
42

43 710 Figure 1. Study flowchart
44
45

46 711

47
48 712 FCRI (Fear of Cancer Recurrence Inventory); GAD-7 (General Anxiety and Distress scale;
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50 713 PHQ-9 (Patient Health Questionnaire); CAMS-R (Cognitive and Affective Mindfulness Scale
51
52 714 – Revised); AQoL-4D (Assessment of Quality of Life – 4 Dimensions)
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57 716 Figure 2. My Goal functionality in MindOnline
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718 Figure 3. My Journal guided self-reflection practise in MindOnLine.

For peer review only

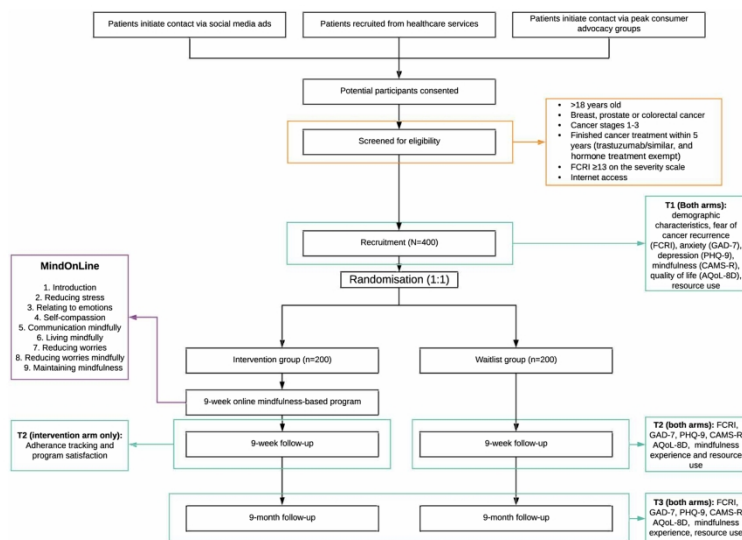


Figure 1. Study flowchart.

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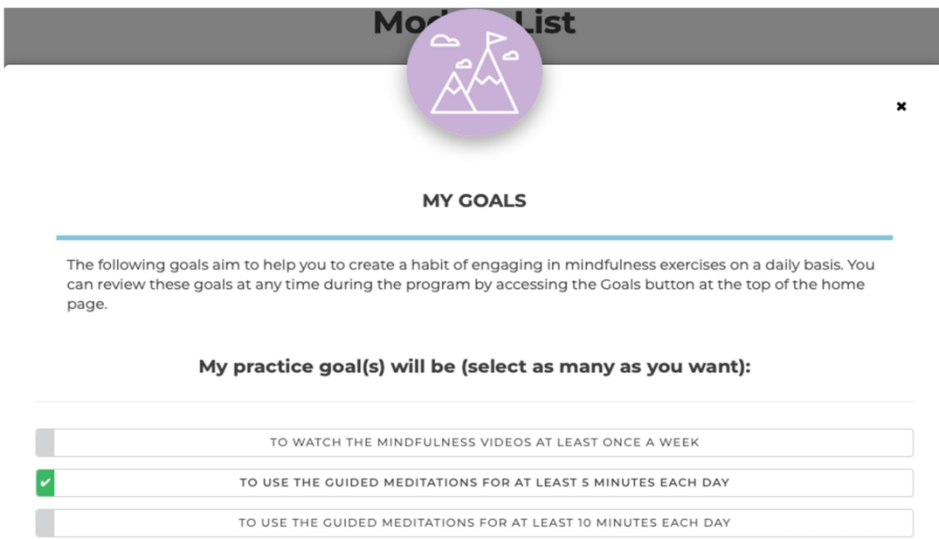


Figure 2. My goal functionality in MondOnline.

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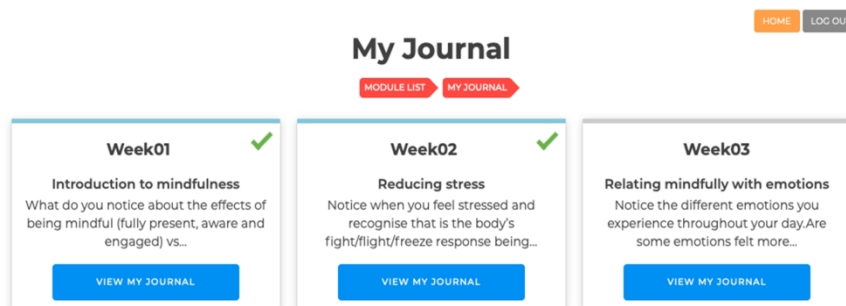


Figure 3. My journal guided self-reflection practice in MindOnline.

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SPIRIT 2013 Checklist: Recommended items to address in a clinical trial protocol and related documents*

Section/item	Item No	Description	Addressed on page number
Administrative information			
Title	1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym	1
Trial registration	2a	Trial identifier and registry name. If not yet registered, name of intended registry	2
	2b	All items from the World Health Organization Trial Registration Data Set	n/a
Protocol version	3	Date and version identifier	2
Funding	4	Sources and types of financial, material, and other support	23
Roles and responsibilities	5a	Names, affiliations, and roles of protocol contributors	1
	5b	Name and contact information for the trial sponsor	1
	5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities	23
	5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee)	23

1 **Introduction**

2

3 Background and 6a Description of research question and justification for undertaking the trial, including summary of relevant 3-5
4 rationale studies (published and unpublished) examining benefits and harms for each intervention
5

6 6b Explanation for choice of comparators 6
7

8 Objectives 7 Specific objectives or hypotheses 5-6
9

10 Trial design 8 Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), 6
11 allocation ratio, and framework (eg, superiority, equivalence, noninferiority, exploratory)
12
13

14 **Methods: Participants, interventions, and outcomes**

15

16 Study setting 9 Description of study settings (eg, community clinic, academic hospital) and list of countries where data will 6, 8
17 be collected. Reference to where list of study sites can be obtained
18

19 Eligibility criteria 10 Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and 8
20 individuals who will perform the interventions (eg, surgeons, psychotherapists)
21

22 Interventions 11a Interventions for each group with sufficient detail to allow replication, including how and when they will be 11-14
23 administered
24

25 11b Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose n/a
26 change in response to harms, participant request, or improving/worsening disease)
27

28 11c Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence 12-13, 16
29 (eg, drug tablet return, laboratory tests)
30

31 11d Relevant concomitant care and interventions that are permitted or prohibited during the trial 16
32

33 Outcomes 12 Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood
34 pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, 15-17
35 median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen
36 efficacy and harm outcomes is strongly recommended
37

38 Participant timeline 13 Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for 14
39 participants. A schematic diagram is highly recommended (see Figure)
40
41
42

1	Sample size	14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations	19
2				
3				
4	Recruitment	15	Strategies for achieving adequate participant enrolment to reach target sample size	9
5				

6 **Methods: Assignment of interventions (for controlled trials)**

7 Allocation:

10	Sequence generation	16a	Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions	10
11				
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16	Allocation concealment mechanism	16b	Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned	10
17				
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20	Implementation	16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions	10
21				
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23				
24	Blinding (masking)	17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how	10
25				
26				
27		17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial	10
28				
29				
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31 **Methods: Data collection, management, and analysis**

33	Data collection methods	18a	Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol	14
34				
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39		18b	Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols	14
40				
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42				

1	Data management	19	Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol	21
2				
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4				
5	Statistical methods	20a	Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol	19
6				
7				
8		20b	Methods for any additional analyses (eg, subgroup and adjusted analyses)	19
9				
10		20c	Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation)	19
11				
12				
13				
14	Methods: Monitoring			
15				
16	Data monitoring	21a	Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed	21
17				
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22		21b	Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial	21
23				
24				
25	Harms	22	Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct	21
26				
27				
28				
29	Auditing	23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor	21
30				
31				
32				
33	Ethics and dissemination			
34				
35	Research ethics approval	24	Plans for seeking research ethics committee/institutional review board (REC/IRB) approval	24
36				
37				
38	Protocol amendments	25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC/IRBs, trial participants, trial registries, journals, regulators)	21
39				
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1	Consent or assent	26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)	10
2				
3				
4		26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable	n/a
5				
6				
7	Confidentiality	27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial	21
8				
9				
10	Declaration of interests	28	Financial and other competing interests for principal investigators for the overall trial and each study site	24
11				
12				
13	Access to data	29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators	21
14				
15				
16	Ancillary and post-trial care	30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation	21
17				
18				
19				
20	Dissemination policy	31a	Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions	21
21				
22				
23				
24		31b	Authorship eligibility guidelines and any intended use of professional writers	21
25				
26		31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code	21
27				
28				
29	Appendices			
30				
31	Informed consent materials	32	Model consent form and other related documentation given to participants and authorised surrogates	attached
32				
33				
34	Biological specimens	33	Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable	n/a
35				
36				

*It is strongly recommended that this checklist be read in conjunction with the SPIRIT 2013 Explanation & Elaboration for important clarification on the items. Amendments to the protocol should be tracked and dated. The SPIRIT checklist is copyrighted by the SPIRIT Group under the Creative Commons [“Attribution-NonCommercial-NoDerivs 3.0 Unported”](https://creativecommons.org/licenses/by-nc-nd/3.0/) license.

BMJ Open

Efficacy and cost-effectiveness of an online mindfulness program (MindOnLine) to reduce fear of recurrence among people with cancer: study protocol for a randomized controlled trial

Journal:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2021-057212.R1
Article Type:	Protocol
Date Submitted by the Author:	30-Nov-2021
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Primary Subject Heading:	Oncology
Secondary Subject Heading:	Communication, Mental health, Public health
Keywords:	ONCOLOGY, Health economics < HEALTH SERVICES ADMINISTRATION & MANAGEMENT, World Wide Web technology < BIOTECHNOLOGY & BIOINFORMATICS



1
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5 **1 Title**

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8 2 Efficacy and cost-effectiveness of an online mindfulness program (MindOnLine) to reduce
9 3 fear of recurrence among people with cancer: study protocol for a randomized controlled trial
10 4

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14 8 Rasmussen B^{1,8}, Whitfield K¹⁰, Ftanou M⁴, Smith AB⁵, Pilatti K¹¹, Sara S¹², Wootten A¹³,
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35 **Abstract**

36 **Introduction:** Fear of cancer recurrence (FCR) is a common condition among cancer survivors
37 that can lead to significant levels of distress, anxiety and depression. Online mindfulness
38 programs may provide the mechanism to support cancer survivors manage FCR and distress,
39 and improve people's wellbeing over the short, medium and long term. The primary aim of
40 this study is to determine the potential efficacy of MindOnLine, a 9 session mindfulness-based
41 program for survivors of breast, prostate and colorectal cancer. A formal economic program
42 will also be conducted.

43 **Methods and analysis:** A single-blind randomized controlled trial to determine the efficacy
44 and cost-efficacy of a MindOnLine program for cancer survivors. A total of 400 people living
45 with cancer will be recruited via online advertisements on social media platforms, peak
46 consumer advocacy groups, or through outpatient services at healthcare providers across
47 Victoria Australia. People will be randomly allocated to either the MindOnLine program
48 (n=200) or waitlist control (n=200). Participant assessments will occur at baseline, at 9 weeks
49 and 9-month follow up. The primary outcome is change in Fear of Recurrence Index Score
50 total score between baseline and 9 weeks; secondary outcomes are changes in depression and
51 anxiety, quality of life and mindfulness. The economic analysis comprises a cost-consequences
52 analysis where all outcomes will be compared to costs.

53 **Ethics and dissemination:** Ethics approval was obtained from the Peter MacCallum Cancer
54 Centre (20-53) and Deakin University (2020-284). All participants will be required to provide
55 written informed consent. Findings will be disseminated in peer reviewed journals and among
56 key stakeholder organisations including hospitals, cancer and community organisations and
57 Government. If successful the project will be rolled out nationally with a formal
58 implementation plan.

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3 59 **Australian New Zealand Clinical Trials Registry:** 12620000645954. Registered 06 June
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5 60 2020,

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7
8 61 <https://www.anzctr.org.au/Trial/Registration/TrialReview.aspx?id=379520&isReview=true>

9
10 62 **Keywords:** mindfulness, cancer, fear of cancer recurrence, online; economics of cancer;
11
12 63 supportive care; web-based platforms

13 14 15 16 64 **Article Summary**

17 18 19 65 **Strengths and limitations of this study**

20 21 66 Strengths

22
23 67 • This study will employ a single-blind randomized controlled trial to determine the efficacy
24
25 68 and cost-efficacy of MindOnLine.

26
27 69 • Advances in social platforms, smartphone technology and web-based programming can
28
29 70 change substantially in a short period and while this may affect the actual online platform
30
31 71 used measures are in place to maintain the same intervention during the study period, so we
32
33 72 do not consider this will influence the program content or delivery mechanisms.

34
35 73 • Involvement of consumer advocacy groups to support recruitment, interpretation of results,
36
37 74 dissemination and translation

38
39 75 • Incorporating an economic evaluation into the study design will complement clinical findings
40
41 76 and support decision-making processes for potential scaling

42 43 44 77 Limitations

45
46 78 • Recruitment primarily through social media platforms means we cannot accurately assess
47
48 79 reach of the intervention, as we will not be able to identify the number of eligible people
49
50 80 exposed to our advertisements

51
52 81 • Participants will need access to the internet which will result in some people unable to take
53
54 82 part in the study.

83 Introduction

84 Over one million Australians are cancer survivors, and this population is expected to grow
85 substantially due to an ageing population and improved community-based screening programs
86 and treatments.[1] A cancer diagnosis can cause people to confront their own mortality, often
87 for the first time,[2] so it may be unsurprising that three quarters of cancer survivors experience
88 fear of cancer recurrence (FCR) and 49% report moderate to high levels of fear,[3] as well as
89 high levels of clinical depression [3] and anxiety.[4]

90
91 FCR is a highly prevalent and persistent condition that can result in significant levels of anxiety
92 and depression across the disease trajectory.[5] It is imperative to address this issue and our
93 recent work into early psychosocial support indicates it may be possible to significantly reduce
94 FCR through an online mindfulness program.[6] Mindfulness is a state of mind in which one
95 pays attention to the present experience in a nonjudgmental, curious, and accepting way. Some
96 studies have shown mindfulness is associated with improved mental health outcomes and
97 management of the emotional consequences of cancer, [7, 8] while other have found no
98 effect.[9]

99
100 Mindfulness-based interventions consist of regular informal and formal mindfulness
101 meditation practices and are supported by educational principles that are person and
102 relationship-centred.[10] Research into the use of mindfulness has mostly evaluated face-to-
103 face programs which are time-intensive, of limited accessibility and costly.[11] Online
104 mindfulness programs represent a potentially cost-effective mechanism to help people with
105 physical health conditions.[12] For cancer survivors, there is evidence that online mindfulness
106 programs may help manage FCR and distress, and improve mental wellbeing over the short,
107 medium and long term.[2]

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2
3 108 There is also some evidence that online mindfulness-based cognitive therapy (MBCT) can
4
5 109 improve psychological outcomes. A recent study compared an online program to face-to-face
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7
8 110 MBCT which showed improved outcomes [13], however, the sample comprised of mainly
9
10 111 breast cancer survivors and it is unclear whether the program would assist with other cancer
11
12 112 types[13]. Although this intervention was found to be as effective as a face-to-face MBCT in
13
14 113 reducing psychological distress and FCR in cancer patients, [13], there is a lack of robust
15
16
17 114 evidence assessing the effectiveness of a general online mindfulness program for cancer
18
19 115 survivors, limiting capacity for implementation and dissemination.[14, 15]
20
21
22 116

23
24 117 The aim of this study is to conduct a randomised controlled trial of *MindOnLine*, an online 9
25
26 118 session mindfulness-based intervention, for survivors of breast, prostate and colorectal cancer,
27
28 119 the most common solid tumours among men and women in Australia, [1] to determine the
29
30 120 effectiveness and cost-effectiveness of the program.
31
32

33 121 *Preliminary work*

34
35 122 To inform the development of *MindOnLine*, we undertook a systematic review of
36
37 123 methodologies for internet based mindfulness interventions.[16] This review showed a dearth
38
39 124 of studies with long-term follow up periods. Our team also conducted an exploratory study on
40
41 125 the knowledge of, attitudes toward and behaviours regarding meditation among patients with
42
43 126 melanoma.[17] Our study of 291 cancer survivors recruited at a single tertiary cancer hospital
44
45 127 found that a key barrier to engaging with meditation was a lack of knowledge about its practice.
46
47 128 Findings also indicated interest in an online meditation-based intervention once informed about
48
49 129 possible benefits of meditation for people with cancer. Those interested in an online
50
51 130 meditation-based program reported higher perceived stress, indicating a need for such a
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53 131 program.
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3 133 MindOnline was initially developed as a 6-week online mindfulness-based intervention and
4
5 134 follows the Framework for mindfulness-based program described by Crane and colleagues.
6
7
8 135 [10] The program promoted awareness and acceptance of thoughts and emotions, and
9
10 136 empowered participants to address their distressing thoughts and emotions in more adaptive
11
12 137 ways. Through this action, participants learn to manage anxious and depressive moods. These
13
14 138 moods are triggered by unhelpful and intrusive thoughts, which are strongly associated with
15
16 139 moderate to high levels of fear of cancer recurrence. [18] A pilot study was conducted to assess
17
18 140 the potential impact of a 6-week mindfulness program and explore whether the intervention
19
20 141 impacted on FCR, worry, and perceived stress compared to usual care. Details of the pilot study
21
22 142 are published elsewhere.[6] Briefly, 69 melanoma survivors agreed to participate, and 46
23
24 143 participants were randomised into the intervention group (2:1). Scores on all FCR Inventory
25
26 144 (FCRI) subscales reduced in the intervention group, with the severity subscale decreasing
27
28 145 significantly compared to the control group (-2.6, 95% CI=(-4.4, -0.7); p=0.008) after 6 weeks.
29
30 146 The total FCRI score also showed a decrease albeit non-significant (-6.2, 95% CI=(-13.12,
31
32 147 0.68), p=0.07). Previous studies have indicated that a 4.1 point decrease on the severity scale
33
34 148 is a clinically important change. [19]
35
36 149 Based on participant feedback from the pilot study [6] regarding the benefits of mindfulness
37
38 150 practice and the suggestion of a maintenance period to enhance sustainability of the effects,
39
40 151 *MindOnLine* was expanded to a 9-week program with the last 3 weeks revisiting concepts
41
42 152 already explored in the program and supporting regular practice. The structure of MindOnLine
43
44 153 reflects the Mindfulness Based Stress Reduction (MBSR) approach by incorporating
45
46 154 characteristics typical of mindfulness-based programs, namely educational component, and
47
48 155 formal and informal mindfulness practices. Keeping in line with Crane et al's., [10] Framework
49
50 156 for adaptation of mindfulness-based programs, MindOnLine adapted the delivery of the
51
52 157 program to an online version to facilitate access and convenience of use.
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158 **Methods and analysis**

159 **Aims and Hypotheses**

160 The aims of this study are to determine the effect of *MindOnLine* on FCR, anxiety and
161 depression in cancer survivors. The specific aims are:

162 **Aim 1:** To evaluate the impact of the *MindOnLine* intervention on the primary outcome (FCR),
163 measured using the FCRI total score [20] at the end of the 9-week intervention period.

164 *HYPOTHESIS 1:* Participants receiving the intervention will report lower average FCRI total
165 scores at 9 weeks, compared to the waitlist group.

166 **Aim 2:** To evaluate the impact of *MindOnLine* on secondary outcomes at nine weeks: 1)
167 Anxiety and Depression, using the Patient Health Questionnaire (PHQ-9)[21]and Generalised
168 Anxiety Disorder (GAD-7) Scale;[22]2) Quality of Life (QoL) measured by AQOL-
169 4D;[23]and 3) Mindfulness, using Cognitive and Affective Mindfulness Scale-Revised
170 (CAMS-R).[24]*HYPOTHESIS 2:* Compared to the waitlist group, participants in the
171 intervention group will report improvement in all of the secondary outcomes at nine weeks.

172 **Aim 3:** To assess To assess if the effect of the intervention on the primary and secondary
173 outcomes, relative to usual care, are sustained at the nine-month follow-up. are sustained at the
174 nine-month follow-up. *HYPOTHESIS 3:* Compared to the waitlist group, participants in the
175 intervention group will report sustained improvement in primary and secondary outcomes at
176 nine months.

177 **Aim 4:** To assess, from a health sector and broader societal perspective, the cost-effectiveness
178 of *MindOnLine*. *HYPOTHESIS 4:* Compared to the waitlist group, *MindOnLine* will be cost-
179 effective with an incremental cost-effectiveness ratio likely to fall below the commonly used
180 threshold of \$28,000 - \$50,000/Quality of Life Year (QALY).

181

182 **Study Design**

183 This study is a randomised controlled trial, to test the effectiveness and cost-effectiveness of
184 MindOnLine compared to usual care on FCR, anxiety, depression and QoL among people
185 diagnosed with breast, prostate or colorectal cancer. Overall, 400 patients will be recruited with
186 200 patients randomly allocated to the intervention group and 200 to the waitlist group (usual
187 care only). The intervention group will receive usual care and the online mindfulness program.
188 Primary and secondary outcomes will be collected at baseline, nine weeks and nine months
189 post randomisation. Nine months corresponds to approximately six months following the end
190 of the intervention period. Following completion of the study (9 months), participants in the
191 waitlist group will be offered the *MindOnLine* intervention (Figure 1).

192

193 **Participants**

194 People with a diagnosis of breast, prostate or colorectal cancer will be recruited via online
195 advertisements on social media platforms, peak consumer advocacy groups for each cancer
196 Breast Cancer Network Australia (BCNA), or Prostate Cancer Foundation Australia (PCFA),
197 Bowel Cancer Australia social media platforms and colorectal cancer support groups, or
198 through outpatient services at healthcare providers across Victoria, see Figure 1.

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2
3 199 **Figure 1.** Study flowchart
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34
35 213 FCRI (Fear of Cancer Recurrence Inventory); GAD-7 (General Anxiety and Distress scale; PHQ-9 (Patient Health Questionnaire); CAMS-R

36
37
38 214 (Cognitive and Affective Mindfulness Scale – Revised); AQoL-4D (Assessment of Quality of Life – 4 Dimensions)
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3 215 **Inclusion criteria**
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5 216 Adults, aged 18 year of older, living in Australia, who completed active treatment for Stage
6
7 217 1-3 breast, prostate or colorectal cancer (CRC), (trastuzumab/similar, and hormone treatment
8
9 218 exempt) within the past 5 years and have no evidence of disease; have internet access and a
10
11 219 FCRI severity score ≥ 13 , indicating clinically significant FCR.[19] Our pilot study showed
12
13 220 74% of participants with melanoma were identified as having clinically significant FCR. [6]
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19 222 **Exclusion criteria**
20

21 223 Insufficient English language skills to understand videos presented in English, complete
22
23 224 surveys in English or living with advanced cancer (Stage IV disease with less than a 12 month
24
25 225 prognosis of survival).
26
27

28 226

29 227 **Recruitment procedures**
30

31 228 Multiple methods will be applied to recruit people to the study:

32
33 229 1) online through *MindOnLine* social media pages including Facebook, Instagram, Twitter,
34
35 230 Reddit and LinkedIn
36

37 231 2) sharing recruitment flyers through BCNA and PCFA social media platforms, and Australian
38
39 232 based cancer groups
40

41
42 233 3) email invitations sent to BCNA and PCFA supporters (and colorectal cancer support groups)
43
44 234 and cancer registries
45

46 235 4) paid Facebook and Instagram advertising
47

48
49 236 5) through outpatient clinics, chemotherapy and radiotherapy units and rooms of oncologists
50
51 237 and surgeons at cancer treatment centres.
52

53
54 238 **Online recruitment procedure**
55

56 239 1) The *MindOnLine* social media pages will be shared among social networks and will allow
57
58 240 people to post questions about the project. 2) A recruitment flyer will be distributed by BCNA,
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3 241 PCFA, Bowel Cancer Australia and colorectal cancer Facebook support groups using their
4
5 242 existing social media platforms. 3) Study invitations will be sent to supporters registered with
6
7 243 BCNA and PCFA who have indicated an interest in learning about research projects. 4) Paid
8
9 244 advertisements will run throughout the recruitment period on Facebook, Instagram and Twitter
10
11 245 to distribute the project details to a wider audience. The use of paid advertisements in health
12
13 246 research is becoming popular and a systematic review has shown this to be an effective
14
15 247 recruitment strategy.[25]

16
17
18 248 In all online recruitment methods, people will have access to the recruitment flyer, which will
19
20 249 provide a brief overview of the study, the link to the *MindOnLine* registration page and the
21
22 250 contact number of the project manager.
23

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26 251

27 28 252 **Health service recruitment procedures**

29
30 253 If recruitment across social media platforms, advertisements and peak consumer advocacy
31
32 254 groups does not generate sufficient participation levels, participating health services
33
34 255 oncologists or surgeons involved in the project, will support the recruitment process. The
35
36 256 research assistant (RA) at each site will screen patients and confirm eligibility of patients with
37
38 257 treating clinicians or with nurses working in the outpatient units. RAs will then contact patients
39
40 258 by phone and interested patients will be emailed the study details with a link to the study
41
42 259 webpage and registration page). If there is no response from patients, a message will be left
43
44 260 on their phone. Two further attempts to reach patients will be made (a week apart), and after a
45
46 261 third unsuccessful attempt no further contact will be made. If patients have not enrolled in the
47
48 262 study within two weeks, one follow-up phone call will be made to answer any queries patients
49
50 263 may have about the study and to assist with registration. We have used similar screening and
51
52 264 recruitment approaches in previous studies and they were found to be acceptable and
53
54 265 successful.[6]We anticipate a recruitment period of 18-months.
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45
6 267 **Consent and screening**

7 268 Once directed to the *MindOnLine* registration page, participants will be presented with the plain
8
9 269 language statement and then asked to provide consent (Supplementary file 1). Potential
10
11 270 participants will be asked to provide basic demographic and disease information allowing
12
13 271 screening to ensure they meet study eligibility criteria. Potential participants will also complete
14
15 272 the severity subscale of the FCRI to allow those with scores ≥ 13 to be screening into the study.
16
17 273 Those screened into the study will provide their email address and contact number, and directed
18
19 274 to the baseline questionnaires. People who are not eligible will receive an online message
20
21 275 thanking them for their interest in the study and referring them to local support services
22
23 276 provided by leading cancer charities should they require support.
24
25
26
27

28 277
2930 278 **Randomisation**

31 279 Eligible participants will be allocated to treatment groups using random sequences embedded
32
33 280 in the online survey platform Qualtrics, ensuring allocation concealment. Randomisation
34
35 281 (using stratified random permuted blocks) will be conducted in blocks of size 2, stratified by
36
37 282 cancer type (breast, prostate, CRC) and age (<60 ; ≥ 60 years old). Participants will be unblinded
38
39 283 to group assignment, while researchers and data analysts will be blinded to the group condition.
40
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46 285 **Waitlist Control group**

47 286 Participants allocated to the waitlist group will receive usual care. Following randomisation,
48
49 287 they will receive an email with a list of services they may contact for information and
50
51 288 support. They will be informed that they will be granted access to *MindOnLine* intervention
52
53 289 in 9-month's time, when intervention participants have completed the final survey.
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290 **Intervention group – MindOnLine program**

291 Participants allocated to the intervention will be provided with the link to *MindOnLine*, which

292 comprises three main components:

293 (1) an educational component to increase participants' knowledge about the science and
294 practice of mindfulness and how it may benefit them in everyday life;

295 (2) a formal mindfulness meditation practice to improve awareness and emotion regulation;

296 and

297 (3) an informal practice to teach participants how to bring mindfulness to daily activities.

298 A new theme is introduced each week, with a new meditation practice which participants will

299 be encouraged to undertake every day *The MindOnLine* program is detailed in Table 1.

300

301 Table 1- Weekly content of the *MindOnLine* Program

Week	Theme	Meditation	Daily practice
1	Introduction to mindfulness	Breath	Being present with the experience
2	Reducing stress	Body Scan	Notice how the body responds to stress
3	Relating to emotions	Working mindfully with emotions	Noticing the cycle of emotions
4	Self-compassion	Self-compassion	Notice self-criticism
5	Communicating mindfully	Listening/ Sound meditations	Bringing attention back to the conversation
6	Living mindfully	Practising with gentleness and patience	Pause throughout the day
7	Reducing worries	Mindfully working with worries and fears	Notice when caught up overthinking

8	Reducing worries mindfully	Loving Kindness meditation	Notice acts of kindness
9	Maintaining mindfulness	Silence with bells	Notice when distracted from being present

302

303 Each module's theme will be explained through a short 5-10 minute video. At the end of each
 304 week, participants will receive an email with a link to the video introducing the theme for the
 305 upcoming week. The transcripts for the videos will be available for downloading and saving or
 306 printing in a pdf format so that participants can keep a copy for later reference. At the end of
 307 each module, participants will receive an automatically generated email reminding them to
 308 continue daily meditation practice (formal practice) and given specific everyday mindfulness
 309 exercises to apply during daily activities (informal practice).

310

311 To enhance adherence and retention to the 9-week program and deepen their mindfulness
 312 experience, participants will have access to additional program features. The features are
 313 guided by a framework proposed by Abraham and Michie [26] to facilitate behaviour change
 314 in interventions:

315 1) Twice daily reminders to complete mindfulness practice. Adapted from the pilot study,
 316 emails containing a link to a short, guided meditation audio file will be sent to
 317 participants twice daily. These emails will serve as reminders to meditate and will
 318 provide easy access to the meditation practice of the week.

319 2) Progress tracking. Participants will be able to monitor their own mindfulness practice
 320 each day by reviewing how many times they have used each section of the program,
 321 and the duration of use. Embedded usage data tracking systems records each login and
 322 provides real time representation of program use.

1
2
3 323 3) Goal setting. When enrolled in the program, participants will have the opportunity to
4
5
6 324 set goals for their mindfulness practice (Figure 2). Goals are linked to usage data
7
8 325 tracking to provide participants with feedback about whether they are reaching their
9
10 326 goals. Goals may be practice orientated e.g. to practise mindfulness for five minutes
11
12 327 each day, or may be specific to each person's situation e.g. I would like to manage my
13
14 328 worries leading up to my oncologist appointment.

15
16
17 329 4) Reflective journaling. Participants will have the opportunity to journal their experiences
18
19 330 during the mindfulness program by using the "My Journal" functionality (Figure 3).
20
21 331 Each week's content will have a journal section, which will include prompts related to
22
23 332 mindfulness program content, participants will be able to enter and save their responses
24
25 333 within the program for future review. Prompts will be developed specifically for the
26
27 334 study.

28
29
30
31 335 The mindfulness program can be accessed at any time via direct login to the website or via the
32
33 336 hyperlink sent to participants in the daily e-mails.

34
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36 337

37
38 338 Figure 2. My Goal functionality in MindOnLine

39
40
41 339 (Insert Figure 2 here)

42
43 340

44
45 341

46
47 342 Figure 3. My Journal guided self-reflection practise in MindOnLine

48
49 343 (Insert Figure 3 here)

50
51 344

52 53 54 345 **Data collection**

55
56 346 Table 2 illustrates the overall schedule for trial participants in both groups. All assessments
57
58 347 will be performed online. The questionnaires at baseline, at nine weeks including the
59
60

348 satisfaction survey for those in the intervention group and at nine months, will be sent via
 349 Qualtrics through an automatically generated schedule. Participants who do not complete
 350 questionnaires will be followed up by telephone at each data collection point. At baseline,
 351 participants' demographic information (i.e., gender, age, marital status, current employment
 352 status, highest level of education, postcode, type of cancer, date of diagnosis, time since end of
 353 last treatment, type of treatment and previous meditation experience) will be collected.

354

355 Table 2. Schedule of enrolment, interventions, and assessments

356

TIMEPOINT	STUDY PERIOD											
	Enrolment	Allocation	Post-allocation									Post-Intervention
			Week 1	Week 2	Week 3	Week 4	Week 5	Week 6	Week 7	Week 8	Week 9	9-months
ENROLMENT:												
Eligibility screen	X											
Informed consent	X											
Allocation		X										
INTERVENTIONS:												
Immediate access to MindOnLine			←—————→									
Waitlist group												
ASSESSMENTS (Both groups):												
Demographic characteristics	X											
FCRI [18]	X									X	X	
GAD-7 [20]	X									X	X	
PHQ-9 [19]	X									X	X	
CAMS-R [22]	X									X	X	
AQoL-AD [21]	X									X	X	
Mindfulness experience	X									X	X	
Resource use	X									X	X	

<i>COVID-19 measures</i>	X										X	X
ASSESSMENTS (Intervention group only):												
<i>Adherence tracking and meditation log</i>			X	X	X	X	X	X	X	X	X	X
<i>Program satisfaction</i>											X	X

357

358 **Outcome measures**359 **Primary outcome**360 **Fear of Cancer Recurrence Inventory (FCRI)**

361 The 42-item Fear of Cancer Recurrence Inventory (FCRI) is a multidimensional FCR scale
 362 intended for use with all cancer patients. Items were developed on the basis of a cognitive–
 363 behavioural formulation of FCR (range:0-168).[19] The FCRI consists of seven domains:
 364 triggers, severity, psychological distress, functional impairment, reassurance, insight and
 365 coping strategies (scoring range:0-36). It has shown high internal consistency, good construct
 366 and criterion validity in adults with different cancer types.[20]

367

368 **Secondary outcomes:**369 **Anxiety and Depression**

370 The *Generalized Anxiety Disorder-7 scale (GAD-7)* [22] is a valid and efficient tool for
 371 assessing generalised anxiety symptoms and assessing severity in clinical practice and
 372 research. The seven items assess the frequency of core symptoms of generalised anxiety
 373 disorder within the past 2 weeks (scoring range:0-21).[22]

374 The *Patient Health Questionnaire-9 (PHQ-9)*[20] parallels the nine diagnostic symptom
 375 criteria that define DSM-IV major depressive disorder. At only 9 items (scoring range:0-27),
 376 the PHQ-9 is shorter than most depression tools. Unlike most other measures of depression,
 377 the PHQ-9 was developed, tested and refined for use with medical patients.[21]

378 The PHQ-9 and GAD-7 are recommended for use among cancer survivors in the American
 379 Society of Clinical Oncology Guidelines. [27]

380

381 Mindfulness

382 Trait mindfulness is measured using the Cognitive and Affective Mindfulness Scale-Revised
383 (CAMS-R), [24] a 10-item self-report questionnaire. This scale uses everyday language
384 appropriate for those with little meditation experience and is designed to capture mindfulness
385 as a general daily experience. The questionnaire comprises four domains of mindfulness
386 (attention, present-focus, awareness, and acceptance/non-judgment). Participants are asked to
387 rate on a four-point Likert scale how much they relate to each statement (scoring range:4-40).
388 Compared to other measures of mindfulness, the CAMS-R is unique in that it is related to
389 psychological distress, [28] which is highly relevant to the current study population.[29]

390

391 Other outcome measures**392 Mindfulness experience**

393 In order to control for access to external mindfulness-based programs particularly in the waitlist
394 group, all participants will be asked whether they have enrolled in a mindfulness-based
395 program in the period between surveys and/or used other supportive care services (e.g. peer
396 support, psychologists, psychotherapy, counsellors, yoga and meditation).

397

398 Program satisfaction

399 Participants in the intervention group will be asked to provide feedback about the *MindOnline*
400 program. Quantitative and qualitative data using open ended questions will be collected in
401 relation to satisfaction with program content, the helpfulness of the program, usability, and
402 areas for improvement. The satisfaction questionnaire has been adapted from the satisfaction
403 questionnaire used in the pilot study.[6]

404

405 **Economic outcomes**

406 *Assessment of Quality of Life (AQoL 4D)* [23] is a health-related quality of life utility measure.

407 It is generally used in economic evaluations. The *Resource Use Questionnaire* covers general
408 health care services usage (self-reported), use of other welfare services, and impacts on work
409 force participation. The questionnaire has been successfully used in cancer psychosocial
410 intervention studies. [30]

411 The surveys will take approximately 20 minutes to complete.

412

413 **Adherence tracking and meditation log**

414 The software package used to run *MindOnLine* was developed at Deakin University and has
415 inbuilt functionality to collect and clean usage data. Google Analytics has been incorporated
416 into the platform to allow for validation of findings. Both software will track participants'
417 online activity, including login date/times, navigation patterns, page views and duration, and
418 features used (video, audio, goals and reflective journaling).

419

420 **Impact of COVID-19**

421 To control for potential environmental impacts on mental wellbeing outcomes, participants will
422 be asked whether COVID-19 has had an impact on their mental wellbeing in the two weeks
423 prior to baseline, 9-weeks and 9-month assessments.

424

425 **Sample size calculations**

426 Power calculations are conservative, i.e. the detectable differences reported below are possibly
427 larger than the true detectable differences, because they are based on two-group comparison of
428 change while the main analysis (see Analysis Plan) will adjust for baseline values of the
429 outcome and for factors used in the stratified randomisation.[31] The statistical software PASS
430 version 14.0.9 (NCSS, LLC) was used for all calculations ($\alpha=0.05$; two-sided tests).

431

432 Primary outcome

433 Change in FCRI total score between baseline and 9 weeks. The target sample size (200
434 participants per arm) achieves 94% (80%) power to detect a mean difference between arms of
435 10 points (8 points) change in FCRI score or 80% power to detect a difference of 8 points
436 [standard deviation (SD): 23.5;[32)]SD estimate obtained from Butow et al., [32]as their study
437 included a heterogenous sample of cancer patients while our pilot study only included patients
438 with melanoma Stage 2-3. The selected effect sizes correspond to Cohen's *d* of 0.43
439 (moderate/large) and 0.34 (small/moderate) respectively. Currently, there is no definition of a
440 clinically significant improvement for FCRI score, however, the proposed effect size is
441 comparable to that described in other studies.[32]

442

443 Secondary outcomes

444 The target sample size (200 participants per arm) achieves 80% power to detect an intervention
445 effect of size 0.34 (Cohen's *f*, small/moderate) at 9 weeks for any of the outcomes. This effect
446 size corresponds to mean differences between groups of: a) 1.5 point in PHQ-9 depression
447 score (SD = 4.5, maximum SD reported in patients with breast, colorectal and prostate
448 cancer;[33] PHQ-9 minimal clinically important difference (MCID) for cancer patients: 2.6 to
449 5);[34] b) 1.4 point in GAD-7 anxiety score (SD=4.1, maximum SD reported in patients with
450 breast, colorectal and prostate cancer;[35] MCID=1.95);[33] and mean differences between
451 group in change from baseline to 9 weeks of: c) 1.2 points in FCRI severity score (SD=3.6,
452 pilot study effect: 2.6);[6] d) 1.1 points in CAMS-R score (SD=3.4); e) 2.5 points in Worry
453 score [SD=7.3]; f) 3.0 points in PSS score [SD=8.9]; the last 3 reflecting moderate Cohen's *d*
454 effect sizes (<0.35).

455

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2
3 456 To meet the sample size needs of our desired statistical power, we will recruit 400 participants.
4
5 457 In our pilot study, six participants (13%) withdrew in the intervention group and none in the
6
7 458 control group. Assuming a conservative 30% attrition rate at nine months, we expect to have
8
9 459 complete data for approximately 280 participants (140 per group).
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460

461 **Analysis plan**

16 462 All statistical analysis will be conducted on an intention-to-treat basis whereby all randomised
17
18 463 participants with at least one post-baseline measurement will be analysed by original treatment
19
20 464 assignment regardless of adherence. Baseline characteristics will be described using summary
21
22 465 measures selected based on variable distribution. The main analysis will adjust for baseline
23
24 466 values of the outcome and for factors used in the stratified randomisation.[31]
25
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467

30 468 *Aims 1 and 2.* The effect of the intervention on each of the outcomes, defined as change from
31
32 469 baseline to nine weeks, will be assessed using linear models including group and the
33
34 470 stratification factors. *Aim 3.* The effect of the intervention across the three measurement times
35
36 471 will be estimated using linear mixed models, including study group, time (categorical: 9 weeks,
37
38 472 9 months) interaction group×time and the stratification factors as fixed effects and participant
39
40 473 as a random effect. If there is a positive intervention effect on mental health outcomes,
41
42 474 exploratory mediation analyses will be conducted to determine whether improvements are
43
44 475 mediated by increases in mindfulness.[36] For outcomes where it is a plausible assumption that
45
46 476 missing data are completely at random, we will use complete case analysis; if not plausible, we
47
48 477 will use multiple imputation. *Subgroup analysis:* We will explore whether age or gender
49
50 478 modify the effect of the intervention on FCR, depression and anxiety at 9 weeks.
51
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3 480 *Aim 4.* This study will also comprise a cost-consequences analysis where incremental costs of
4
5 481 the intervention will be compared with the full spectrum of outcomes included in the study. A
6
7 482 series of cost-effectiveness ratios can be determined which have been shown to be useful for
8
9 483 decision-makers. Inclusion of the AQL 4D will also enable a cost-utility analysis to be
10
11 484 undertaken, thereby allowing practical judgements to be made regarding value for money
12
13 485 credentials of the intervention. Nevertheless, the economic analysis will be primarily from the
14
15 486 perspective of the health care sector and a secondary analysis from the broader societal
16
17 487 perspective will also be undertaken. A detailed costing of the intervention will be undertaken
18
19 488 and the evaluation will first measure and value any change to the use of health care resources
20
21 489 over the period of the study between the two arms of the trial and then compare any additional
22
23 490 costs to the additional outcomes achieved. Standardised economic evaluation techniques will
24
25 491 be used including incremental analysis of mean differences and bootstrapping to determine
26
27 492 confidence intervals along with a net monetary analysis to determine the cost-effectiveness of
28
29 493 the intervention for different value for money threshold criteria. The costs of routine roll-out
30
31 494 will be estimated.
32
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40 496 *MindOnLine* usage data by the intervention group will be reported using descriptive statistics.
41
42 497 Linear mixed models, with random intercept and slope for each person, will be fitted to estimate
43
44 498 time trends in usage.
45
46

47 499 **Data management**

48 500 Data will be exported from Qualtrics on a monthly basis and crossed checked during
49
50 501 exportation to ensure accuracy in results. All identifying participant information will be
51
52 502 removed from data sets. Documents containing sensitive information will be saved as password
53
54 503 protected files and stored within the Deakin University One Drive.
55
56
57

58 504 **Monitoring**

59 505 Data
60

1
2
3 506 The adherence data will be monitored by the program developer. The program developer does
4
5 507 not have any competing interests. Other project data will be monitored by the project steering
6
7 508 committee with regular meetings and progress updates. No interim analysis will be performed
8
9 509 during the trial.

510 **Patient and Public Involvement**

511 Representatives from three consumer organisations have been involved in the design and
512 implementation of the project since its inception. Their contribution has included development
513 of the intervention and its content, wording on recruitment material, and provided advice on
514 recruitment strategies. Representatives from each consumer organisation has contributed to
515 project steering meetings.

516 **Ethics and Dissemination**

517 **Harms**

518 All participants will be required to provide written informed consent. In the event that a
519 participant reports distress to the project manager they will be advised to seek assistance from
520 the regular medical professionals and provided with additional referrals to lifeline.org.au.
521 Ethics approval was obtained from the Peter MacCallum Cancer Centre (20-53) and Deakin
522 University (2020-284). Any adverse events will be reported to the ethics committees.

523

524 **Auditing**

525 The trial may be audited by the governing Human Research Ethics Committees.

526 **Protocol amendments**

527 Protocol amendments will be approved by the governing Human Research Ethics Committees.

528 Any relevant changes will be submitted as a modification to the Australian and New Zealand

529 Clinical Trial Registry.

1
2
3 **530 Dissemination**

4
5 531 The findings of this study will be written by study authors and published in peer reviewed
6
7 532 journals project steering committee. All identifying participant information will be removed
8
9 533 prior to publication.
10

11
12
13 **534 Discussion**

14
15
16 535 One of the most significant changes across society is the use of web-based technology. Online
17
18 536 mindfulness-based interventions circumvent problems with traditional face-to-face delivery of
19
20 537 the program, impacted by work commitments, caring responsibilities, geographic isolation and
21
22 538 pandemics[37, 38].
23
24

25
26 539

27
28 540 This study will rigorously evaluate the efficacy of a self-directed online mindfulness program
29
30 541 in reducing FCR in breast, prostate and CRC survivors. The study will advance the literature
31
32 542 regarding the benefits of mindfulness for cancer survivors by representing one of few large
33
34 543 well controlled trials of a self-directed mindfulness-based program, involving smartphone
35
36 544 technology, aimed at reducing FCR. Including a health economic evaluation of the program
37
38 545 adds to the utility of the trial with the study providing information that budget holders and
39
40 546 policy makers need when considering recommendations and support for supportive care
41
42 547 programs. This trial will fill a gap in knowledge regarding the potential impact of an online
43
44 548 mindfulness program in supporting cancer survivors.[7] Extensive pilot work in identifying the
45
46 549 type of program cancer survivors are interested in, involving consumers in designing the
47
48 550 content and length of the program and providing reminders and practice tips increase the
49
50 551 likelihood of participants engaging with the program and the intervention having a positive
51
52 552 impact.
53
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1
2
3 554 The study is being conducted in partnership with health services and cancer advocacy groups.
4
5 555 As partners in the study, they will ensure the intervention can be rolled out to cancer survivors
6
7 556 if shown to be effective. In addition to consumer advocacy groups, the study is being conducted
8
9
10 557 in partnership with government. As we expect the *MindOnLine* intervention to improve health
11
12 558 outcomes, reduce the fear and distress in cancer survivorship and reduce health service and
13
14 559 community costs our partnership with government will ensure that policy makers are informed
15
16
17 560 of the study's findings particularly cost-effectiveness findings.
18

19 561

20
21 562 The study has a number of strengths and weaknesses. Development of the intervention through
22
23 563 a review of the literature, input from consumers and findings from a pilot study and
24
25 564 involvement of consumer advocacy groups and government are study strengths ensuring
26
27 565 translation of the program into practice if shown to be effective. For example, consumer
28
29 566 advocacy groups have contributed to the design of the intervention program, recruitment of
30
31 567 eligible patients, and will provide advice on the interpretation of results, dissemination and
32
33 568 translation. Incorporating an economic evaluation into the study design is a strength as it will
34
35 569 complement clinical findings and support decision-making processes for potential
36
37 570 implementation.
38
39

40 571

41
42
43
44 572 However, several methodological limitations also need to be acknowledged. Recruitment
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46 573 through social media platforms means we cannot accurately assess uptake of the intervention,
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48 574 as we will not be able to identify the number of eligible people exposed to our advertisements.
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51 575 This may limit our ability to determine reach of the program. However, recording the time
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53 576 taken for recruitment and accessing google analytic data on internet traffic and page visits may
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55 577 provide some information in this area. Participants will need access to the internet to
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57 578 participate. While this may mean some people will be excluded from the study, we believe this
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3 579 will have minimal impact on the study. We envisage that the study will take approximately 4
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5 580 years to complete. Advances in social platforms, technology and app-based programming can
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7 581 change substantially in a short period. While this may affect the actual online platform used for
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9 582 the program, we do not consider this will influence the program content or delivery
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11 583 mechanisms. As technology advances will likely increase interest in self-directed support
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13 584 programs for cancer survivors, it is essential that cancer survivors access programs with
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15 585 demonstrated effectiveness.
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24 587 **Trial Registration** ACTRN12620000645954

25 588 **Protocol Version:** Version 5, dated 18 December 2020

26 589 Recruitment commenced 12.10.2020, it is anticipated recruitment will be for a duration of 18
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28 590 months finishing on 12.04.2022.
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32 592 **Abbreviations**

33 593 AQL-4D Assessment of Quality of Life – 4 Dimensions

34 594 BCNA Breast Cancer Network Australia

35 595 CAMSR Cognitive and Affective Mindfulness Scale-Revised

36 596 CI Confidence interval

37 597 CRC Colorectal Cancer

38 598 FCR Fear of cancer recurrence

39 599 FCRI Fear of Cancer Recurrence Inventory

40 600 GAD-7 General Anxiety Disorder scale

41 601 MBCT Mindfulness-based cognitive therapy

42 602 MCID Minimally clinically important difference

43 603 PCFA Prostate Cancer Foundation of Australia
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3 604 PHQ-9 Patient Health Questionnaire
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5 605 QALY Quality of Life Years
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7 606 QoL Quality of Life
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10 607 RA Research assistant
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12 608 RCT Randomized controlled trial
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14 609 SD standard deviation
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19 **References**
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3 748 **Declarations**
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6 749 **Author's contributions**
7

8 750 PML, LR, LO, NW, MJ, AG, DWA, EO, CM, AU, RC, J P-N, DH, MB, BR, KW, MF, ABS,

9 751 KP, MS, DC and VW contributed to the conception of the program or design of the study.
10

11 752 EO designed the web platform and analytics with input from LR, NW, RC, DWA, AW,
12

13 753 PML. CM designed the economic component of the study. PML, LR, LO, NW, MJ, AG,
14

15 754 DWA, EO, CM, AU, RC, J P-N, DH, MB, BR, KW, MF, ABS, KP, SS, AW, KG, MS, DC,
16

17 755 BP and VW provided substantial input into the development of the protocol or revising it
18

19 756 critically for important intellectual content. PML, LR, NW, LO and VW drafted the
20

21 757 manuscript with contributions from MJ, AG, DWA, EO, CM, AU, RC, J P-N, DH, MB, BR,
22

23 758 KW, MF, ABS, KP, SS, AW, KG, MS, DC, BP.
24

25 759 Each of the authors contributed to, read and approved the final manuscript.
26

27 760 Each of the co-authors, PML, LR, LO, NW, MJ, AG, DWA, EO, CM, AU, RC, J P-N, DH,
28

29 761 MB, BR, KW, MF, ABS, KP, SS, AW, KG, MS, DC, BP and VW, are on the steering
30

31 762 committee, will oversee implementation of the study and data collection and will contribute
32

33 763 to the acquisition, analysis or interpretation of the data.
34

35 764
36

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38

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40

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42

43 768 **Competing interests**
44

45 769 The authors declare they have no competing interests.
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49 771 **Figure Legend/Caption:**
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51 772 Figure 1. Study flowchart
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6 774 FCRI (Fear of Cancer Recurrence Inventory); GAD-7 (General Anxiety and Distress scale;
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8 775 PHQ-9 (Patient Health Questionnaire); CAMS-R (Cognitive and Affective Mindfulness Scale
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10 776 – Revised); AQoL-4D (Assessment of Quality of Life – 4 Dimensions)

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14 778 Figure 2. My Goal functionality in MindOnLine

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19 780 Figure 3. My Journal guided self-reflection practise in MindOnLine.
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For peer review only

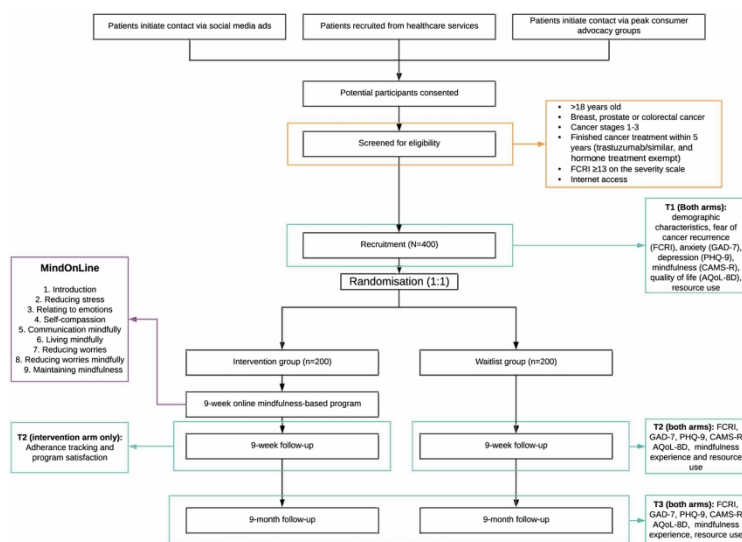


Figure 1. Study flowchart.

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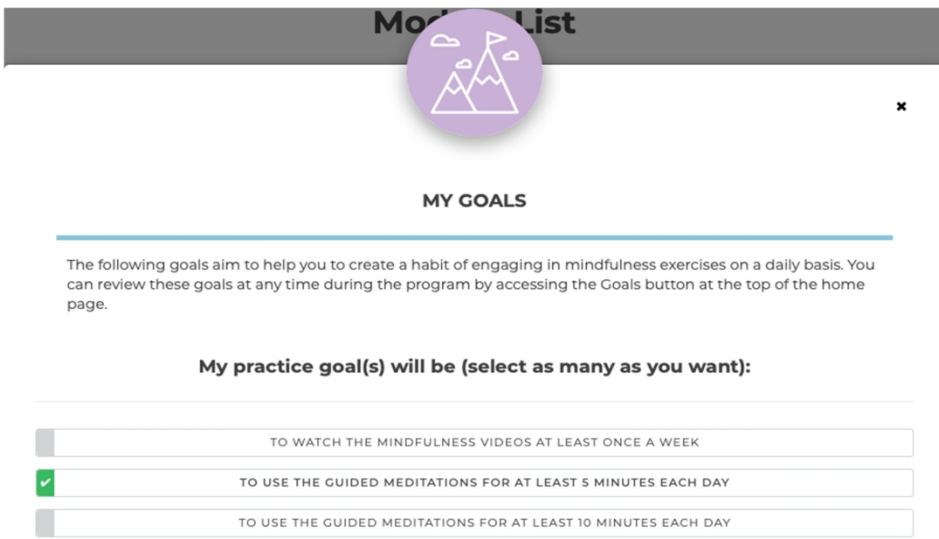


Figure 2. My goal functionality in MondOnLine.

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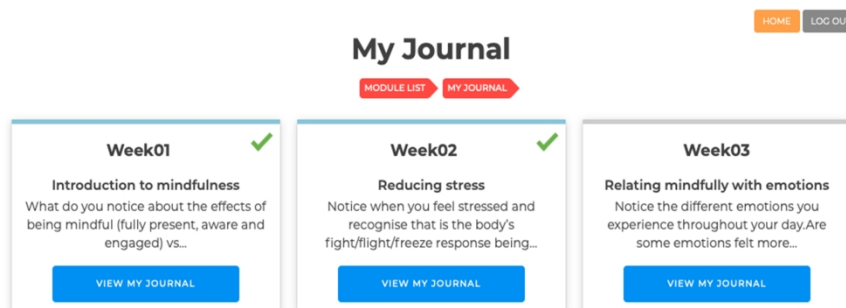


Figure 3. My journal guided self-reflection practice in MindOnline.

308x100mm (400 x 400 DPI)



Peter Mac
Peter MacCallum Cancer Centre
Victoria Australia



Epworth



**Prostate Cancer
Foundation
of Australia**



VICTORIA
State Government

Health
and Human
Services



**Breast
Cancer
Network
Australia**

Participant Information Sheet/Consent Form

Title	MindOnLine: a mindfulness program for people with breast, bowel or prostate cancer.
Short Title	MindOnLine
Principal Investigator	Prof Trish Livingston
Location	Deakin University

Part 1 What does my participation involve?

1 Introduction

You are invited to take part in this research project, because you have received treatment for breast, prostate or bowel cancer. This research project is testing an online mindfulness-based program for people who have completed their treatment.

This Participant Information Sheet/Consent Form tells you about the research project. It explains the procedures involved. Knowing what is involved will help you decide if you want to take part in the research.

Please read this information carefully. Ask questions about anything that you don't understand or want to know more about. Before deciding whether or not to take part, you might want to talk about it with a relative, friend or healthcare worker.

Participation in this research is voluntary. If you don't wish to take part, you don't have to. You will receive the best possible care whether or not you take part.

If you decide you want to take part in the research project, you will be asked to provide consent online. By agreeing you are telling us that you:

- Understand what you have read
- Consent to take part in the research project
- Consent to have the tests and treatments that are described
- Consent to the use of your personal and health information as described.

2 What is the purpose of this research?

Following treatment for cancer, many people feel anxious and scared about the cancer coming back. This is one of the most common fears of cancer survivors, and it can affect people's ability to enjoy life

1 and plan for the future. In some people, this fear can decrease over time, but most people find that they
2 worry at certain times. The mindfulness program aims to help cancer survivors to manage their fears
3 and worries once treatment is completed.
4

5 Research has shown that mindfulness-based programs can help people cope with anxious thoughts
6 about their cancer. The internet allows people to use the program from the comfort of their home, and
7 at their most convenient times. We have tested an online mindfulness program for people who received
8 treatment for melanoma, with promising results. This research is to find out whether mindfulness can
9 help people with breast, prostate or bowel cancer.
10

11 This research is being conducted across healthcare services and cancer organisations and is led by
12 researchers at the School of Nursing and Midwifery at Deakin University.
13
14

15 In this research project we will be testing a mindfulness program among people who meet the following
16 criteria:
17

- 18 - People who are over 18 years of age
- 19 - People who speak English well enough to understand videos and surveys presented in English
- 20 - People who have access to a computer or device to receive the program
- 21 - People who received treatment for breast, bowel or prostate cancer
- 22 - People who finished chemotherapy, radiotherapy or surgery treatment within the last five years
- 23 - People who experience a high level of fear of cancer recurrence.
24

25 You will be asked some questions after providing consent to determine if you meet the eligibility criteria
26 above. To measure your fear of cancer recurrence you will be asked 9 questions about how your
27 thoughts and feelings towards cancer may impact on your everyday living.
28

29 **3 What does participation involve?**

30
31 To participate in this study, each participant will need to have access to a computer, a smartphone, or a
32 similar tablet device, and internet. If you agree to take part in this project you will be allocated to either
33 receive the mindfulness program (intervention group) or stay in your usual care (control group). We
34 need to compare responses from people in these two groups to see if the mindfulness program provides
35 any benefits to cancer survivors. In order to make sure the groups are the same, participants are put
36 into one of the two groups by chance (random).
37
38

39 If you decide to take part in this study, you will need to provide your consent to participate by accessing
40 the following website: <https://mindonline.org.au> Before providing your consent you will be asked a
41 number of questions to make sure you are eligible for the study.
42
43

44 After consenting to take part in the study, you will be asked to complete a survey before being randomly
45 allocated to the intervention or control group. The same survey will be completed again 9 weeks and 9
46 months later. The survey asks you questions about possible fears of the cancer coming back, how
47 stressful and worrisome you perceive your life to be, and the type of thoughts you generally focus on.
48 We will also collect your email address and contact number. Your email and contact number will be used
49 to send you reminders and other information related to the study.
50

51 If you are randomised to the mindfulness program, you will receive an email informing you of your
52 allocation group with instructions on how to access the website. Your participation will involve using the
53 program for 9 weeks. The program is designed to help you understand and experience potential benefits
54 of using mindfulness in your day to day life. You will be invited to:
55

- 56 - Watch short videos at the start of each week. The videos will introduce a new topic about
57 mindfulness.
- 58 - Practice short meditations twice a day. We will help you create a meditation routine by emailing
59 you a direct link to guided meditations at times you will have chosen.
- 60 - Apply mindfulness skills in your day-to-day life.

1
2 If you are assigned to the mindfulness program we will monitor how often the mindfulness program is
3 used. This will be recorded by your study identification number, and no personal information such as
4 your Internet Protocol (IP) address linked to your computer or device will be collected.
5

6 If you are randomised to the control group you will receive an email informing you of your allocation
7 group and you will continue to receive your usual care from your healthcare providers. You will receive
8 emails to ask you to complete the questionnaires at 9 weeks and 9 months. After the 9-month survey
9 you will be able to use the mindfulness program.
10

11
12 We will compare the results between those in the mindfulness program and those who are not, to see if
13 there are any differences in wellbeing between the two groups.
14

15 There are no additional costs associated with participating in this research project, nor will you be paid.
16
17

18 19 **4 Other relevant information about the research project**

20
21 This study will show if the mindfulness program is helpful for people with breast, prostate or colorectal
22 cancer. If successful the program we be made open to the wider population.
23

24 For this study, approximately 400 people will be invited to participate from online and social media
25 advertisements and from healthcare services.
26
27

28 29 **5 Do I have to take part in this research project?**

30
31 Participation in any research project is voluntary. If you do not wish to take part you don't have to. If
32 you decide to take part and later change your mind, you are free to withdraw from the project at any
33 stage.
34

35 Your decision whether to take part or not to take part, or to take part and then withdraw, will not affect
36 your relationship with those treating you or involved in your follow-up care, or your relationship with
37 Deakin University, Breast Cancer Network Australia, or Prostate Cancer Foundation of Australia.
38
39

40 41 **6 What are the possible benefits of taking part?**

42
43 We cannot guarantee or promise that you will receive any benefits from this research; however,
44 possible benefits for the community may include additional support for people who have completed
45 treatment for cancer.
46
47

48 49 **7 What are the possible risks?**

50
51 Some people may feel uncomfortable or upset when answering questions in this survey. If you do not
52 wish to answer a question you may skip it and go to the next question, or you may stop immediately. In
53 the event that you become upset or distressed as a result of your participation, the researcher can
54 arrange for counselling or other appropriate support provided by staff who are not members of the
55 research team. In addition, you may want to contact an external support service such as Lifeline services
56 on 13 11 14, or www.mindhealthconnect.org.au or the Cancer Council 13 11 20 telephone service.
57 If you have any concerns or are unsure whether you should participate in this project, you may wish to
58 speak to your healthcare professional about your feelings.
59
60

8 What if I withdraw from this research project?

If you decide to withdraw, please notify a member of the research team about this decision. This notice will ensure that we can remove you from our records and will mean you will not receive any notices about the project.

If you decide to withdraw from the project, we would like to keep the personal and health information about you that has been collected. This is to help us make sure that the results of the research can be measured properly. If you want to withdraw your data from the study as well, please let them know when you tell them about withdrawing from the study.

9 What happens when the research project ends?

If you wish to obtain a final copy of the research report describing the results of this study, please contact the project manager (Dr Natalie Heynsbergh on 03 9246 8225, or email n.heynsbergh@deakin.edu.au) and she will arrange for a copy to be sent to you after completion of the study in December 2022.

Part 2 How is the research project being conducted?

10 What will happen to information about me?

Any information obtained in connection with this research project that can identify you (e.g. email address) will remain confidential and will only be used for the purpose of this research project. It will only be disclosed with your permission, except as required by law.

All the information you provide will be coded so you cannot be identified by name, and only the research team will have access to the list that can link your name to your data. All identifying information will be stored in password-protected electronic files or in a locked filing cabinet in the office of the research staff, and will be disposed of as confidential waste after five years.

You will not be identified in any report or publication from this study. Information will be provided in such a way that you cannot be identified.

In accordance with relevant Australian and/or Victorian privacy and other relevant laws, you have the right to access the information collected and stored by the researchers about you. You also have the right to request that any information with which you disagree be corrected. Please contact one of the researchers named in the last section below if you would like to access your information.

11 Who is organising and funding the research?

This research project is being managed by Dr Natalie Heynsbergh at Deakin University, and is being funded by a National Health and Medical Research Council (NHMRC) grant.

12 Who has reviewed the research project?

All research in Australia involving humans is reviewed by an independent group of people called a Human Research Ethics Committee (HREC). The ethical aspects of this research project have been

1 approved by the Peter MacCallum Human Research Ethics Committee (Reference number 20/53) and
 2 the Deakin University Human Research Ethics Committee.
 3

4 This project will be carried out according to the *National Statement on Ethical Conduct in Human*
 5 *Research (2007)*. This statement has been developed to protect the interests of people who agree to
 6 participate in human research studies.
 7

10 **13 Further information and who to contact**

11 The person you may need to contact will depend on the nature of your query.
 12

13 If you want any further information concerning this project or if you have any problems which may be
 14 related to your involvement in the project, you can contact:
 15

- 16 • The principal investigator: Prof Patricia Livingston on 03 9244 6609, or email
 17 trish.livingston@deakin.edu.au
 18
- 19 • The project manager: Dr Natalie Heynsbergh on 03 92468225, or email:
 20 n.heynsbergh@deakin.edu.au
 21
 22
 23
 24

25 If you have any complaints about any aspect of the project, the way it is being conducted or any
 26 questions about being a research participant in general, then you may contact:
 27
 28

29 Reviewing HREC name	Peter MacCallum Cancer Centre Ethics Committee
30 Project reference number	20/53
31 HREC Executive Officer	Ethics Coordinator
32 Telephone	03 8559 7540
33 Email	ethics@petermac.org

36 **14 What do I do if I want to participate?**

37 If you would like to participate in this study, please log on to <https://mindonline.org.au>, to answer the
 38 eligibility questions and provide your consent to participate.
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SPIRIT 2013 Checklist: Recommended items to address in a clinical trial protocol and related documents*

Section/item	Item No	Description	Addressed on page number
Administrative information			
Title	1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym	1
Trial registration	2a	Trial identifier and registry name. If not yet registered, name of intended registry	2
	2b	All items from the World Health Organization Trial Registration Data Set	n/a
Protocol version	3	Date and version identifier	2
Funding	4	Sources and types of financial, material, and other support	23
Roles and responsibilities	5a	Names, affiliations, and roles of protocol contributors	1
	5b	Name and contact information for the trial sponsor	1
	5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities	23
	5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee)	23

1 **Introduction**

2

3 Background and 6a Description of research question and justification for undertaking the trial, including summary of relevant 3-5
 4 rationale studies (published and unpublished) examining benefits and harms for each intervention

5

6 6b Explanation for choice of comparators 6

7

8 Objectives 7 Specific objectives or hypotheses 5-6

9

10 Trial design 8 Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), 6
 11 allocation ratio, and framework (eg, superiority, equivalence, noninferiority, exploratory)

12

13

14 **Methods: Participants, interventions, and outcomes**

15

16 Study setting 9 Description of study settings (eg, community clinic, academic hospital) and list of countries where data will 6, 8
 17 be collected. Reference to where list of study sites can be obtained

18

19 Eligibility criteria 10 Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and 8
 20 individuals who will perform the interventions (eg, surgeons, psychotherapists)

21

22 Interventions 11a Interventions for each group with sufficient detail to allow replication, including how and when they will be 11-14
 23 administered

24

25 11b Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose n/a
 26 change in response to harms, participant request, or improving/worsening disease)

27

28 11c Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence 12-13, 16
 29 (eg, drug tablet return, laboratory tests)

30

31 11d Relevant concomitant care and interventions that are permitted or prohibited during the trial 16

32

33

34 Outcomes 12 Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood
 35 pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, 15-17
 36 median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen
 37 efficacy and harm outcomes is strongly recommended

38

39

40 Participant timeline 13 Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for 14
 41 participants. A schematic diagram is highly recommended (see Figure)

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1	Sample size	14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations	19
2				
3				
4	Recruitment	15	Strategies for achieving adequate participant enrolment to reach target sample size	9
5				

6 **Methods: Assignment of interventions (for controlled trials)**

7 Allocation:

8				
9				
10	Sequence	16a	Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions	10
11	generation			
12				
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16	Allocation	16b	Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned	10
17	concealment			
18	mechanism			
19				
20	Implementation	16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions	10
21				
22				
23				
24	Blinding (masking)	17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how	10
25				
26				
27		17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial	10
28				
29				
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31 **Methods: Data collection, management, and analysis**

32				
33	Data collection	18a	Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol	14
34	methods			
35				
36				
37				
38		18b	Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols	14
39				
40				
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42				

1	Data management	19	Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol	21
2				
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4				
5	Statistical methods	20a	Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol	19
6				
7				
8		20b	Methods for any additional analyses (eg, subgroup and adjusted analyses)	19
9				
10		20c	Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation)	19
11				
12				
13				
14	Methods: Monitoring			
15				
16	Data monitoring	21a	Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed	21
17				
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21				
22		21b	Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial	21
23				
24				
25	Harms	22	Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct	21
26				
27				
28				
29	Auditing	23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor	21
30				
31				
32				
33	Ethics and dissemination			
34				
35	Research ethics approval	24	Plans for seeking research ethics committee/institutional review board (REC/IRB) approval	24
36				
37				
38	Protocol amendments	25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC/IRBs, trial participants, trial registries, journals, regulators)	21
39				
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1	Consent or assent	26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)	10
2				
3				
4		26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable	n/a
5				
6				
7	Confidentiality	27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial	21
8				
9				
10	Declaration of interests	28	Financial and other competing interests for principal investigators for the overall trial and each study site	24
11				
12				
13	Access to data	29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators	21
14				
15				
16	Ancillary and post-trial care	30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation	21
17				
18				
19				
20	Dissemination policy	31a	Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions	21
21				
22				
23				
24		31b	Authorship eligibility guidelines and any intended use of professional writers	21
25				
26		31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code	21
27				
28				
29	Appendices			
30				
31	Informed consent materials	32	Model consent form and other related documentation given to participants and authorised surrogates	attached
32				
33				
34	Biological specimens	33	Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable	n/a
35				
36				

*It is strongly recommended that this checklist be read in conjunction with the SPIRIT 2013 Explanation & Elaboration for important clarification on the items. Amendments to the protocol should be tracked and dated. The SPIRIT checklist is copyrighted by the SPIRIT Group under the Creative Commons [“Attribution-NonCommercial-NoDerivs 3.0 Unported”](https://creativecommons.org/licenses/by-nc-nd/3.0/) license.

BMJ Open

Efficacy and cost-effectiveness of an online mindfulness program (MindOnLine) to reduce fear of recurrence among people with cancer: study protocol for a randomized controlled trial

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Date Submitted by the Author:	07-Dec-2021
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Primary Subject Heading :	Oncology
Secondary Subject Heading :	Communication, Mental health, Public health
Keywords :	ONCOLOGY, Health economics < HEALTH SERVICES ADMINISTRATION & MANAGEMENT, World Wide Web technology < BIOTECHNOLOGY & BIOINFORMATICS

SCHOLARONE™
Manuscripts

1
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5 **1 Title**

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7
8 2 Efficacy and cost-effectiveness of an online mindfulness program (MindOnLine) to reduce
9 3 fear of recurrence among people with cancer: study protocol for a randomized controlled trial
10 4

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35 **Abstract**

36 **Introduction:** Fear of cancer recurrence (FCR) is a common condition among cancer survivors
37 that can lead to significant levels of distress, anxiety and depression. Online mindfulness
38 programs may provide the mechanism to support cancer survivors manage FCR and distress,
39 and improve people's wellbeing over the short, medium and long term. The primary aim of
40 this study is to determine the potential efficacy of MindOnLine, a 9 session mindfulness-based
41 program for survivors of breast, prostate and colorectal cancer. A formal economic program
42 will also be conducted.

43 **Methods and analysis:** A single-blind randomized controlled trial to determine the efficacy
44 and cost-efficacy of a MindOnLine program for cancer survivors. A total of 400 people living
45 with cancer will be recruited via online advertisements on social media platforms, peak
46 consumer advocacy groups, or through outpatient services at healthcare providers across
47 Victoria Australia. People will be randomly allocated to either the MindOnLine program
48 (n=200) or waitlist control (n=200). Participant assessments will occur at baseline, at 9 weeks
49 and 9-month follow up. The primary outcome is change in Fear of Recurrence Index Score
50 total score between baseline and 9 weeks; secondary outcomes are changes in depression and
51 anxiety, quality of life and mindfulness. The economic analysis comprises a cost-consequences
52 analysis where all outcomes will be compared to costs.

53 **Ethics and dissemination:** Ethics approval was obtained from the Peter MacCallum Cancer
54 Centre (20-53) and Deakin University (2020-284). All participants will be required to provide
55 written informed consent. Findings will be disseminated in peer reviewed journals and among
56 key stakeholder organisations including hospitals, cancer and community organisations and
57 Government. If successful the project will be rolled out nationally with a formal
58 implementation plan.

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2
3 59 **Australian New Zealand Clinical Trials Registry:** 12620000645954. Registered 06 June
4
5 60 2020,

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7
8 61 <https://www.anzctr.org.au/Trial/Registration/TrialReview.aspx?id=379520&isReview=true>

9
10 62 **Keywords:** mindfulness, cancer, fear of cancer recurrence, online; economics of cancer;
11
12 63 supportive care; web-based platforms

16 64 **Article Summary**

19 65 **Strengths and limitations of this study**

- 21 66 • Strengths of our randomised controlled trial include the assessment of both the efficacy and
22
23 67 cost-effectiveness of the MindOnLine program, and the involvement of consumer advocacy
24
25 68 groups to support recruitment, interpretation of results, dissemination, and translation.
- 26
27 69 • Incorporating an economic evaluation into the study design will complement clinical findings
28
29 70 and support decision-making processes for potential scaling.
- 30
31 71 • Advances in social platforms, smartphone technology and web-based programming can
32
33 72 change substantially in a short period and, while this may affect the actual online platform
34
35 73 used, measures are in place to maintain the same intervention during the study period, so we
36
37 74 do not believe that this will influence the program content or delivery mechanisms.
- 38
39 75 • Recruitment primarily through social media platforms means we cannot accurately assess
40
41 76 reach of the intervention, as we will not be able to identify the number of eligible people
42
43 77 exposed to our advertisements.
- 44
45 78 • Participants will need access to the internet, which will result in some people unable to take
46
47 79 part in the study.

80 Introduction

81 Over one million Australians are cancer survivors, and this population is expected to grow
82 substantially due to an ageing population and improved community-based screening programs
83 and treatments.[1] A cancer diagnosis can cause people to confront their own mortality, often
84 for the first time,[2] so it may be unsurprising that three quarters of cancer survivors experience
85 fear of cancer recurrence (FCR) and 49% report moderate to high levels of fear,[3] as well as
86 high levels of clinical depression [3] and anxiety.[4]

87
88 FCR is a highly prevalent and persistent condition that can result in significant levels of anxiety
89 and depression across the disease trajectory.[5] It is imperative to address this issue and our
90 recent work into early psychosocial support indicates it may be possible to significantly reduce
91 FCR through an online mindfulness program.[6] Mindfulness is a state of mind in which one
92 pays attention to the present experience in a nonjudgmental, curious, and accepting way. Some
93 studies have shown mindfulness is associated with improved mental health outcomes and
94 management of the emotional consequences of cancer, [7, 8] while other have found no
95 effect.[9]

96
97 Mindfulness-based interventions consist of regular informal and formal mindfulness
98 meditation practices and are supported by educational principles that are person and
99 relationship-centred.[10] Research into the use of mindfulness has mostly evaluated face-to-
100 face programs which are time-intensive, of limited accessibility and costly.[11] Online
101 mindfulness programs represent a potentially cost-effective mechanism to help people with
102 physical health conditions.[12] For cancer survivors, there is evidence that online mindfulness
103 programs may help manage FCR and distress, and improve mental wellbeing over the short,
104 medium and long term.[2]

1
2
3 105 There is also some evidence that online mindfulness-based cognitive therapy (MBCT) can
4
5 106 improve psychological outcomes. A recent study compared an online program to face-to-face
6
7 107 MBCT which showed improved outcomes [13], however, the sample comprised of mainly
8
9 108 breast cancer survivors and it is unclear whether the program would assist with other cancer
10
11 109 types[13]. Although this intervention was found to be as effective as a face-to-face MBCT in
12
13 110 reducing psychological distress and FCR in cancer patients, [13], there is a lack of robust
14
15 111 evidence assessing the effectiveness of a general online mindfulness program for cancer
16
17 112 survivors, limiting capacity for implementation and dissemination.[14, 15]
18
19
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24 114 The aim of this study is to conduct a randomised controlled trial of *MindOnLine*, an online 9
25
26 115 session mindfulness-based intervention, for survivors of breast, prostate and colorectal cancer,
27
28 116 the most common solid tumours among men and women in Australia, [1] to determine the
29
30 117 effectiveness and cost-effectiveness of the program.
31
32

33 118 *Preliminary work*

35 119 To inform the development of *MindOnLine*, we undertook a systematic review of
36
37 120 methodologies for internet based mindfulness interventions.[16] This review showed a dearth
38
39 121 of studies with long-term follow up periods. Our team also conducted an exploratory study on
40
41 122 the knowledge of, attitudes toward and behaviours regarding meditation among patients with
42
43 123 melanoma.[17] Our study of 291 cancer survivors recruited at a single tertiary cancer hospital
44
45 124 found that a key barrier to engaging with meditation was a lack of knowledge about its practice.
46
47 125 Findings also indicated interest in an online meditation-based intervention once informed about
48
49 126 possible benefits of meditation for people with cancer. Those interested in an online
50
51 127 meditation-based program reported higher perceived stress, indicating a need for such a
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53 128 program.
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3 130 MindOnline was initially developed as a 6-week online mindfulness-based intervention and
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5 131 follows the Framework for mindfulness-based program described by Crane and colleagues.
6
7 132 [10] The program promoted awareness and acceptance of thoughts and emotions, and
8
9 133 empowered participants to address their distressing thoughts and emotions in more adaptive
10
11 134 ways. Through this action, participants learn to manage anxious and depressive moods. These
12
13 135 moods are triggered by unhelpful and intrusive thoughts, which are strongly associated with
14
15 136 moderate to high levels of fear of cancer recurrence. [18] A pilot study was conducted to assess
16
17 137 the potential impact of a 6-week mindfulness program and explore whether the intervention
18
19 138 impacted on FCR, worry, and perceived stress compared to usual care. Details of the pilot study
20
21 139 are published elsewhere.[6] Briefly, 69 melanoma survivors agreed to participate, and 46
22
23 140 participants were randomised into the intervention group (2:1). Scores on all FCR Inventory
24
25 141 (FCRI) subscales reduced in the intervention group, with the severity subscale decreasing
26
27 142 significantly compared to the control group (-2.6, 95% CI=(-4.4, -0.7); p=0.008) after 6 weeks.
28
29 143 The total FCRI score also showed a decrease albeit non-significant (-6.2, 95% CI=(-13.12,
30
31 144 0.68), p=0.07). Previous studies have indicated that a 4.1 point decrease on the severity scale
32
33 145 is a clinically important change. [19]
34
35 146 Based on participant feedback from the pilot study [6] regarding the benefits of mindfulness
36
37 147 practice and the suggestion of a maintenance period to enhance sustainability of the effects,
38
39 148 *MindOnLine* was expanded to a 9-week program with the last 3 weeks revisiting concepts
40
41 149 already explored in the program and supporting regular practice. The structure of MindOnLine
42
43 150 reflects the Mindfulness Based Stress Reduction (MBSR) approach by incorporating
44
45 151 characteristics typical of mindfulness-based programs, namely educational component, and
46
47 152 formal and informal mindfulness practices. Keeping in line with Crane et al's., [10] Framework
48
49 153 for adaptation of mindfulness-based programs, MindOnLine adapted the delivery of the
50
51 154 program to an online version to facilitate access and convenience of use.
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155 **Methods and analysis**

156 **Aims and Hypotheses**

157 The aims of this study are to determine the effect of *MindOnLine* on FCR, anxiety and
158 depression in cancer survivors. The specific aims are:

159 **Aim 1:** To evaluate the impact of the *MindOnLine* intervention on the primary outcome (FCR),
160 measured using the FCRI total score [20] at the end of the 9-week intervention period.

161 *HYPOTHESIS 1:* Participants receiving the intervention will report lower average FCRI total
162 scores at 9 weeks, compared to the waitlist group.

163 **Aim 2:** To evaluate the impact of *MindOnLine* on secondary outcomes at nine weeks: 1)
164 Anxiety and Depression, using the Patient Health Questionnaire (PHQ-9)[21]and Generalised
165 Anxiety Disorder (GAD-7) Scale;[22]2) Quality of Life (QoL) measured by AQOL-
166 4D;[23]and 3) Mindfulness, using Cognitive and Affective Mindfulness Scale-Revised
167 (CAMS-R).[24]*HYPOTHESIS 2:* Compared to the waitlist group, participants in the
168 intervention group will report improvement in all of the secondary outcomes at nine weeks.

169 **Aim 3:** To assess To assess if the effect of the intervention on the primary and secondary
170 outcomes, relative to usual care, are sustained at the nine-month follow-up. are sustained at the
171 nine-month follow-up. *HYPOTHESIS 3:* Compared to the waitlist group, participants in the
172 intervention group will report sustained improvement in primary and secondary outcomes at
173 nine months.

174 **Aim 4:** To assess, from a health sector and broader societal perspective, the cost-effectiveness
175 of *MindOnLine*. *HYPOTHESIS 4:* Compared to the waitlist group, *MindOnLine* will be cost-
176 effective with an incremental cost-effectiveness ratio likely to fall below the commonly used
177 threshold of \$28,000 - \$50,000/Quality of Life Year (QALY).

178

179 **Study Design**

180 This study is a randomised controlled trial, to test the effectiveness and cost-effectiveness of
181 MindOnLine compared to usual care on FCR, anxiety, depression and QoL among people
182 diagnosed with breast, prostate or colorectal cancer. Overall, 400 patients will be recruited with
183 200 patients randomly allocated to the intervention group and 200 to the waitlist group (usual
184 care only). The intervention group will receive usual care and the online mindfulness program.
185 Primary and secondary outcomes will be collected at baseline, nine weeks and nine months
186 post randomisation. Nine months corresponds to approximately six months following the end
187 of the intervention period. Following completion of the study (9 months), participants in the
188 waitlist group will be offered the *MindOnLine* intervention (Figure 1).

190 **Participants**

191 People with a diagnosis of breast, prostate or colorectal cancer will be recruited via online
192 advertisements on social media platforms, peak consumer advocacy groups for each cancer
193 Breast Cancer Network Australia (BCNA), or Prostate Cancer Foundation Australia (PCFA),
194 Bowel Cancer Australia social media platforms and colorectal cancer support groups, or
195 through outpatient services at healthcare providers across Victoria, see Figure 1.

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3 196 **Figure 1.** Study flowchart
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(Insert Figure 1 here)

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FCRI (Fear of Cancer Recurrence Inventory); GAD-7 (General Anxiety and Distress scale; PHQ-9 (Patient Health Questionnaire); CAMS-R

32 211

(Cognitive and Affective Mindfulness Scale – Revised); AQoL-4D (Assessment of Quality of Life – 4 Dimensions)

1
2
3 212 **Inclusion criteria**
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5 213 Adults, aged 18 year of older, living in Australia, who completed active treatment for Stage
6
7 214 1-3 breast, prostate or colorectal cancer (CRC), (trastuzumab/similar, and hormone treatment
8
9 215 exempt) within the past 5 years and have no evidence of disease; have internet access and a
10
11 216 FCRI severity score ≥ 13 , indicating clinically significant FCR.[19] Our pilot study showed
12
13
14 217 74% of participants with melanoma were identified as having clinically significant FCR. [6]
15

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17 218

18
19 219 **Exclusion criteria**
20

21 220 Insufficient English language skills to understand videos presented in English, complete
22
23 221 surveys in English or living with advanced cancer (Stage IV disease with less than a 12 month
24
25 222 prognosis of survival).
26

27
28 223

29 224 **Recruitment procedures**
30

31 225 Multiple methods will be applied to recruit people to the study:

32
33 226 1) online through *MindOnLine* social media pages including Facebook, Instagram, Twitter,
34

35 227 Reddit and LinkedIn
36

37 228 2) sharing recruitment flyers through BCNA and PCFA social media platforms, and Australian
38

39 229 based cancer groups
40

41
42 230 3) email invitations sent to BCNA and PCFA supporters (and colorectal cancer support groups)
43

44 231 and cancer registries
45

46 232 4) paid Facebook and Instagram advertising
47

48 233 5) through outpatient clinics, chemotherapy and radiotherapy units and rooms of oncologists
49

50 234 and surgeons at cancer treatment centres.
51

52
53 235 **Online recruitment procedure**
54

55 236 1) The *MindOnLine* social media pages will be shared among social networks and will allow
56

57 237 people to post questions about the project. 2) A recruitment flyer will be distributed by BCNA,
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3 238 PCFA, Bowel Cancer Australia and colorectal cancer Facebook support groups using their
4
5 239 existing social media platforms. 3) Study invitations will be sent to supporters registered with
6
7 240 BCNA and PCFA who have indicated an interest in learning about research projects. 4) Paid
8
9 241 advertisements will run throughout the recruitment period on Facebook, Instagram and Twitter
10
11 242 to distribute the project details to a wider audience. The use of paid advertisements in health
12
13 243 research is becoming popular and a systematic review has shown this to be an effective
14
15 244 recruitment strategy.[25]
16
17
18
19 245 In all online recruitment methods, people will have access to the recruitment flyer, which will
20
21 246 provide a brief overview of the study, the link to the *MindOnLine* registration page and the
22
23 247 contact number of the project manager.
24
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29 249 **Health service recruitment procedures**

30 250 If recruitment across social media platforms, advertisements and peak consumer advocacy
31
32 251 groups does not generate sufficient participation levels, participating health services
33
34 252 oncologists or surgeons involved in the project, will support the recruitment process. The
35
36 253 research assistant (RA) at each site will screen patients and confirm eligibility of patients with
37
38 254 treating clinicians or with nurses working in the outpatient units. RAs will then contact patients
39
40 255 by phone and interested patients will be emailed the study details with a link to the study
41
42 256 webpage and registration page). If there is no response from patients, a message will be left
43
44 257 on their phone. Two further attempts to reach patients will be made (a week apart), and after a
45
46 258 third unsuccessful attempt no further contact will be made. If patients have not enrolled in the
47
48 259 study within two weeks, one follow-up phone call will be made to answer any queries patients
49
50 260 may have about the study and to assist with registration. We have used similar screening and
51
52 261 recruitment approaches in previous studies and they were found to be acceptable and
53
54 262 successful.[6]We anticipate a recruitment period of 18-months.
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263

264 Consent and screening

265 Once directed to the *MindOnLine* registration page, participants will be presented with the plain
266 language statement and then asked to provide consent (Supplementary file 1). Potential
267 participants will be asked to provide basic demographic and disease information allowing
268 screening to ensure they meet study eligibility criteria. Potential participants will also complete
269 the severity subscale of the FCRI to allow those with scores ≥ 13 to be screening into the study.
270 Those screened into the study will provide their email address and contact number, and directed
271 to the baseline questionnaires. People who are not eligible will receive an online message
272 thanking them for their interest in the study and referring them to local support services
273 provided by leading cancer charities should they require support.

274

275 Randomisation

276 Eligible participants will be allocated to treatment groups using random sequences embedded
277 in the online survey platform Qualtrics, ensuring allocation concealment. Randomisation
278 (using stratified random permuted blocks) will be conducted in blocks of size 2, stratified by
279 cancer type (breast, prostate, CRC) and age (<60 ; ≥ 60 years old). Participants will be unblinded
280 to group assignment, while researchers and data analysts will be blinded to the group condition.

281

282 Waitlist Control group

283 Participants allocated to the waitlist group will receive usual care. Following randomisation,
284 they will receive an email with a list of services they may contact for information and
285 support. They will be informed that they will be granted access to *MindOnLine* intervention
286 in 9-month's time, when intervention participants have completed the final survey.

287 **Intervention group – MindOnLine program**

288 Participants allocated to the intervention will be provided with the link to *MindOnLine*, which

289 comprises three main components:

290 (1) an educational component to increase participants' knowledge about the science and
291 practice of mindfulness and how it may benefit them in everyday life;

292 (2) a formal mindfulness meditation practice to improve awareness and emotion regulation;

293 and

294 (3) an informal practice to teach participants how to bring mindfulness to daily activities.

295 A new theme is introduced each week, with a new meditation practice which participants will

296 be encouraged to undertake every day *The MindOnLine* program is detailed in Table 1.

297

298 Table 1- Weekly content of the *MindOnLine* Program

Week	Theme	Meditation	Daily practice
1	Introduction to mindfulness	Breath	Being present with the experience
2	Reducing stress	Body Scan	Notice how the body responds to stress
3	Relating to emotions	Working mindfully with emotions	Noticing the cycle of emotions
4	Self-compassion	Self-compassion	Notice self-criticism
5	Communicating mindfully	Listening/ Sound meditations	Bringing attention back to the conversation
6	Living mindfully	Practising with gentleness and patience	Pause throughout the day
7	Reducing worries	Mindfully working with worries and fears	Notice when caught up overthinking

8	Reducing worries mindfully	Loving Kindness meditation	Notice acts of kindness
9	Maintaining mindfulness	Silence with bells	Notice when distracted from being present

299

300 Each module's theme will be explained through a short 5-10 minute video. At the end of each
 301 week, participants will receive an email with a link to the video introducing the theme for the
 302 upcoming week. The transcripts for the videos will be available for downloading and saving or
 303 printing in a pdf format so that participants can keep a copy for later reference. At the end of
 304 each module, participants will receive an automatically generated email reminding them to
 305 continue daily meditation practice (formal practice) and given specific everyday mindfulness
 306 exercises to apply during daily activities (informal practice).

307

308 To enhance adherence and retention to the 9-week program and deepen their mindfulness
 309 experience, participants will have access to additional program features. The features are
 310 guided by a framework proposed by Abraham and Michie [26] to facilitate behaviour change
 311 in interventions:

312 1) Twice daily reminders to complete mindfulness practice. Adapted from the pilot study,
 313 emails containing a link to a short, guided meditation audio file will be sent to
 314 participants twice daily. These emails will serve as reminders to meditate and will
 315 provide easy access to the meditation practice of the week.

316 2) Progress tracking. Participants will be able to monitor their own mindfulness practice
 317 each day by reviewing how many times they have used each section of the program,
 318 and the duration of use. Embedded usage data tracking systems records each login and
 319 provides real time representation of program use.

1
2
3 320 3) Goal setting. When enrolled in the program, participants will have the opportunity to
4
5
6 321 set goals for their mindfulness practice (Figure 2). Goals are linked to usage data
7
8 322 tracking to provide participants with feedback about whether they are reaching their
9
10 323 goals. Goals may be practice orientated e.g. to practise mindfulness for five minutes
11
12 324 each day, or may be specific to each person's situation e.g. I would like to manage my
13
14
15 325 worries leading up to my oncologist appointment.

16
17 326 4) Reflective journaling. Participants will have the opportunity to journal their experiences
18
19 327 during the mindfulness program by using the "My Journal" functionality (Figure 3).
20
21 328 Each week's content will have a journal section, which will include prompts related to
22
23 329 mindfulness program content, participants will be able to enter and save their responses
24
25
26 330 within the program for future review. Prompts will be developed specifically for the
27
28
29 331 study.

30
31 332 The mindfulness program can be accessed at any time via direct login to the website or via the
32
33 333 hyperlink sent to participants in the daily e-mails.

34
35
36 334

37
38 335 Figure 2. My Goal functionality in MindOnLine

39
40
41 336 (Insert Figure 2 here)

42
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46
47 339 Figure 3. My Journal guided self-reflection practise in MindOnLine

48
49
50 340 (Insert Figure 3 here)

51
52 341

53
54
55 342 **Data collection**

56 343 Table 2 illustrates the overall schedule for trial participants in both groups. All assessments
57
58 344 will be performed online. The questionnaires at baseline, at nine weeks including the

345 satisfaction survey for those in the intervention group and at nine months, will be sent via
 346 Qualtrics through an automatically generated schedule. Participants who do not complete
 347 questionnaires will be followed up by telephone at each data collection point. At baseline,
 348 participants' demographic information (i.e., gender, age, marital status, current employment
 349 status, highest level of education, postcode, type of cancer, date of diagnosis, time since end of
 350 last treatment, type of treatment and previous meditation experience) will be collected.

351

352 Table 2. Schedule of enrolment, interventions, and assessments

353

TIMEPOINT	STUDY PERIOD											
	Enrolment	Allocation	Post-allocation									Post-Intervention
			Week 1	Week 2	Week 3	Week 4	Week 5	Week 6	Week 7	Week 8	Week 9	9-months
ENROLMENT:												
Eligibility screen	X											
Informed consent	X											
Allocation		X										
INTERVENTIONS:												
Immediate access to MindOnLine			←—————→									
Waitlist group												
ASSESSMENTS (Both groups):												
Demographic characteristics	X											
FCRI [18]	X									X	X	
GAD-7 [20]	X									X	X	
PHQ-9 [19]	X									X	X	
CAMS-R [22]	X									X	X	
AQoL-AD [21]	X									X	X	
Mindfulness experience	X									X	X	
Resource use	X									X	X	

<i>COVID-19 measures</i>	X										X	X
ASSESSMENTS (Intervention group only):												
<i>Adherence tracking and meditation log</i>			X	X	X	X	X	X	X	X	X	X
<i>Program satisfaction</i>											X	X

354

355 **Outcome measures**356 **Primary outcome**357 **Fear of Cancer Recurrence Inventory (FCRI)**

358 The 42-item Fear of Cancer Recurrence Inventory (FCRI) is a multidimensional FCR scale
 359 intended for use with all cancer patients. Items were developed on the basis of a cognitive–
 360 behavioural formulation of FCR (range:0-168).[19] The FCRI consists of seven domains:
 361 triggers, severity, psychological distress, functional impairment, reassurance, insight and
 362 coping strategies (scoring range:0-36). It has shown high internal consistency, good construct
 363 and criterion validity in adults with different cancer types.[20]

364

365 **Secondary outcomes:**366 **Anxiety and Depression**

367 The *Generalized Anxiety Disorder-7 scale (GAD-7)* [22] is a valid and efficient tool for
 368 assessing generalised anxiety symptoms and assessing severity in clinical practice and
 369 research. The seven items assess the frequency of core symptoms of generalised anxiety
 370 disorder within the past 2 weeks (scoring range:0-21).[22]

371 The *Patient Health Questionnaire-9 (PHQ-9)*[20] parallels the nine diagnostic symptom
 372 criteria that define DSM-IV major depressive disorder. At only 9 items (scoring range:0-27),
 373 the PHQ-9 is shorter than most depression tools. Unlike most other measures of depression,
 374 the PHQ-9 was developed, tested and refined for use with medical patients.[21]

375 The PHQ-9 and GAD-7 are recommended for use among cancer survivors in the American
 376 Society of Clinical Oncology Guidelines. [27]

377

378 Mindfulness

379 Trait mindfulness is measured using the Cognitive and Affective Mindfulness Scale-Revised
380 (CAMS-R), [24] a 10-item self-report questionnaire. This scale uses everyday language
381 appropriate for those with little meditation experience and is designed to capture mindfulness
382 as a general daily experience. The questionnaire comprises four domains of mindfulness
383 (attention, present-focus, awareness, and acceptance/non-judgment). Participants are asked to
384 rate on a four-point Likert scale how much they relate to each statement (scoring range:4-40).
385 Compared to other measures of mindfulness, the CAMS-R is unique in that it is related to
386 psychological distress, [28] which is highly relevant to the current study population.[29]

387

388 Other outcome measures**389 Mindfulness experience**

390 In order to control for access to external mindfulness-based programs particularly in the waitlist
391 group, all participants will be asked whether they have enrolled in a mindfulness-based
392 program in the period between surveys and/or used other supportive care services (e.g. peer
393 support, psychologists, psychotherapy, counsellors, yoga and meditation).

394

395 Program satisfaction

396 Participants in the intervention group will be asked to provide feedback about the *MindOnLine*
397 program. Quantitative and qualitative data using open ended questions will be collected in
398 relation to satisfaction with program content, the helpfulness of the program, usability, and
399 areas for improvement. The satisfaction questionnaire has been adapted from the satisfaction
400 questionnaire used in the pilot study.[6]

401

402 **Economic outcomes**

403 *Assessment of Quality of Life (AQoL 4D)* [23] is a health-related quality of life utility measure.

404 It is generally used in economic evaluations. The *Resource Use Questionnaire* covers general
405 health care services usage (self-reported), use of other welfare services, and impacts on work
406 force participation. The questionnaire has been successfully used in cancer psychosocial
407 intervention studies. [30]

408 The surveys will take approximately 20 minutes to complete.

409

410 **Adherence tracking and meditation log**

411 The software package used to run *MindOnLine* was developed at Deakin University and has
412 inbuilt functionality to collect and clean usage data. Google Analytics has been incorporated
413 into the platform to allow for validation of findings. Both software will track participants'
414 online activity, including login date/times, navigation patterns, page views and duration, and
415 features used (video, audio, goals and reflective journaling).

416

417 **Impact of COVID-19**

418 To control for potential environmental impacts on mental wellbeing outcomes, participants will
419 be asked whether COVID-19 has had an impact on their mental wellbeing in the two weeks
420 prior to baseline, 9-weeks and 9-month assessments.

421

422 **Sample size calculations**

423 Power calculations are conservative, i.e. the detectable differences reported below are possibly
424 larger than the true detectable differences, because they are based on two-group comparison of
425 change while the main analysis (see Analysis Plan) will adjust for baseline values of the
426 outcome and for factors used in the stratified randomisation.[31] The statistical software PASS
427 version 14.0.9 (NCSS, LLC) was used for all calculations ($\alpha=0.05$; two-sided tests).

428

429 Primary outcome

430 Change in FCRI total score between baseline and 9 weeks. The target sample size (200
431 participants per arm) achieves 94% (80%) power to detect a mean difference between arms of
432 10 points (8 points) change in FCRI score or 80% power to detect a difference of 8 points
433 [standard deviation (SD): 23.5;[32]]SD estimate obtained from Butow et al., [32]as their study
434 included a heterogenous sample of cancer patients while our pilot study only included patients
435 with melanoma Stage 2-3. The selected effect sizes correspond to Cohen's *d* of 0.43
436 (moderate/large) and 0.34 (small/moderate) respectively. Currently, there is no definition of a
437 clinically significant improvement for FCRI score, however, the proposed effect size is
438 comparable to that described in other studies.[32]

439

440 Secondary outcomes

441 The target sample size (200 participants per arm) achieves 80% power to detect an intervention
442 effect of size 0.34 (Cohen's *f*, small/moderate) at 9 weeks for any of the outcomes. This effect
443 size corresponds to mean differences between groups of: a) 1.5 point in PHQ-9 depression
444 score (SD = 4.5, maximum SD reported in patients with breast, colorectal and prostate
445 cancer;[33] PHQ-9 minimal clinically important difference (MCID) for cancer patients: 2.6 to
446 5);[34] b) 1.4 point in GAD-7 anxiety score (SD=4.1, maximum SD reported in patients with
447 breast, colorectal and prostate cancer;[35] MCID=1.95);[33] and mean differences between
448 group in change from baseline to 9 weeks of: c) 1.2 points in FCRI severity score (SD=3.6,
449 pilot study effect: 2.6);[6] d) 1.1 points in CAMS-R score (SD=3.4); e) 2.5 points in Worry
450 score [SD=7.3]; f) 3.0 points in PSS score [SD=8.9]; the last 3 reflecting moderate Cohen's *d*
451 effect sizes (<0.35).

452

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3 453 To meet the sample size needs of our desired statistical power, we will recruit 400 participants.
4

5 454 In our pilot study, six participants (13%) withdrew in the intervention group and none in the
6

7
8 455 control group. Assuming a conservative 30% attrition rate at nine months, we expect to have
9

10 456 complete data for approximately 280 participants (140 per group).
11

12 457
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14 15 458 **Analysis plan**

16 459 All statistical analysis will be conducted on an intention-to-treat basis whereby all randomised
17

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19 460 participants with at least one post-baseline measurement will be analysed by original treatment
20

21 461 assignment regardless of adherence. Baseline characteristics will be described using summary
22

23 462 measures selected based on variable distribution. The main analysis will adjust for baseline
24

25 463 values of the outcome and for factors used in the stratified randomisation.[31]
26

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30 465 *Aims 1 and 2.* The effect of the intervention on each of the outcomes, defined as change from
31

32 466 baseline to nine weeks, will be assessed using linear models including group and the
33

34 467 stratification factors. *Aim 3.* The effect of the intervention across the three measurement times
35

36 468 will be estimated using linear mixed models, including study group, time (categorical: 9 weeks,
37

38 469 9 months) interaction group×time and the stratification factors as fixed effects and participant
39

40 470 as a random effect. If there is a positive intervention effect on mental health outcomes,
41

42 471 exploratory mediation analyses will be conducted to determine whether improvements are
43

44 472 mediated by increases in mindfulness.[36] For outcomes where it is a plausible assumption that
45

46 473 missing data are completely at random, we will use complete case analysis; if not plausible, we
47

48
49 474 will use multiple imputation. *Subgroup analysis:* We will explore whether age or gender
50

51 475 modify the effect of the intervention on FCR, depression and anxiety at 9 weeks.
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3 477 *Aim 4.* This study will also comprise a cost-consequences analysis where incremental costs of
4
5 478 the intervention will be compared with the full spectrum of outcomes included in the study. A
6
7 479 series of cost-effectiveness ratios can be determined which have been shown to be useful for
8
9 480 decision-makers. Inclusion of the AQoL 4D will also enable a cost-utility analysis to be
10
11 481 undertaken, thereby allowing practical judgements to be made regarding value for money
12
13 482 credentials of the intervention. Nevertheless, the economic analysis will be primarily from the
14
15 483 perspective of the health care sector and a secondary analysis from the broader societal
16
17 484 perspective will also be undertaken. A detailed costing of the intervention will be undertaken
18
19 485 and the evaluation will first measure and value any change to the use of health care resources
20
21 486 over the period of the study between the two arms of the trial and then compare any additional
22
23 487 costs to the additional outcomes achieved. Standardised economic evaluation techniques will
24
25 488 be used including incremental analysis of mean differences and bootstrapping to determine
26
27 489 confidence intervals along with a net monetary analysis to determine the cost-effectiveness of
28
29 490 the intervention for different value for money threshold criteria. The costs of routine roll-out
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31 491 will be estimated.

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492
493 *MindOnLine* usage data by the intervention group will be reported using descriptive statistics.
494 Linear mixed models, with random intercept and slope for each person, will be fitted to estimate
495 time trends in usage.

496 **Data management**

497 Data will be exported from Qualtrics on a monthly basis and crossed checked during
498 exportation to ensure accuracy in results. All identifying participant information will be
499 removed from data sets. Documents containing sensitive information will be saved as password
500 protected files and stored within the Deakin University One Drive.

501 **Monitoring**

502 Data

1
2
3 503 The adherence data will be monitored by the program developer. The program developer does
4
5 504 not have any competing interests. Other project data will be monitored by the project steering
6
7 505 committee with regular meetings and progress updates. No interim analysis will be performed
8
9 506 during the trial.

12 507 **Patient and Public Involvement**

14 508 Representatives from three consumer organisations have been involved in the design and
15
16 509 implementation of the project since its inception. Their contribution has included development
17
18 510 of the intervention and its content, wording on recruitment material, and provided advice on
19
20 511 recruitment strategies. Representatives from each consumer organisation has contributed to
21
22 512 project steering meetings.

27 513 **Ethics and Dissemination**

30 514 **Harms**

31 515 All participants will be required to provide written informed consent. In the event that a
32
33 516 participant reports distress to the project manager they will be advised to seek assistance from
34
35 517 the regular medical professionals and provided with additional referrals to lifeline.org.au.
36
37 518 Ethics approval was obtained from the Peter MacCallum Cancer Centre (20-53) and Deakin
38
39 519 University (2020-284). Any adverse events will be reported to the ethics committees.
40
41
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43

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46 521 **Auditing**

47 522 The trial may be audited by the governing Human Research Ethics Committees.

49 523 **Protocol amendments**

50 524 Protocol amendments will be approved by the governing Human Research Ethics Committees.

51 525 Any relevant changes will be submitted as a modification to the Australian and New Zealand

52 526 Clinical Trial Registry.

1
2
3 527 **Dissemination**

4
5 528 The findings of this study will be written by study authors and published in peer reviewed
6
7 529 journals project steering committee. All identifying participant information will be removed
8
9 530 prior to publication.
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12
13 531 **Discussion**

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15
16 532 One of the most significant changes across society is the use of web-based technology. Online
17
18 533 mindfulness-based interventions circumvent problems with traditional face-to-face delivery of
19
20 534 the program, impacted by work commitments, caring responsibilities, geographic isolation and
21
22 535 pandemics[37, 38].
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28 537 This study will rigorously evaluate the efficacy of a self-directed online mindfulness program
29
30 538 in reducing FCR in breast, prostate and CRC survivors. The study will advance the literature
31
32 539 regarding the benefits of mindfulness for cancer survivors by representing one of few large
33
34 540 well controlled trials of a self-directed mindfulness-based program, involving smartphone
35
36 541 technology, aimed at reducing FCR. Including a health economic evaluation of the program
37
38 542 adds to the utility of the trial with the study providing information that budget holders and
39
40 543 policy makers need when considering recommendations and support for supportive care
41
42 544 programs. This trial will fill a gap in knowledge regarding the potential impact of an online
43
44 545 mindfulness program in supporting cancer survivors.[7] Extensive pilot work in identifying the
45
46 546 type of program cancer survivors are interested in, involving consumers in designing the
47
48 547 content and length of the program and providing reminders and practice tips increase the
49
50 548 likelihood of participants engaging with the program and the intervention having a positive
51
52 549 impact.
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3 551 The study is being conducted in partnership with health services and cancer advocacy groups.
4
5 552 As partners in the study, they will ensure the intervention can be rolled out to cancer survivors
6
7 553 if shown to be effective. In addition to consumer advocacy groups, the study is being conducted
8
9 554 in partnership with government. As we expect the *MindOnLine* intervention to improve health
10
11 555 outcomes, reduce the fear and distress in cancer survivorship and reduce health service and
12
13 556 community costs our partnership with government will ensure that policy makers are informed
14
15 557 of the study's findings particularly cost-effectiveness findings.
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21 559 The study has a number of strengths and weaknesses. Development of the intervention through
22
23 560 a review of the literature, input from consumers and findings from a pilot study and
24
25 561 involvement of consumer advocacy groups and government are study strengths ensuring
26
27 562 translation of the program into practice if shown to be effective. For example, consumer
28
29 563 advocacy groups have contributed to the design of the intervention program, recruitment of
30
31 564 eligible patients, and will provide advice on the interpretation of results, dissemination and
32
33 565 translation. Incorporating an economic evaluation into the study design is a strength as it will
34
35 566 complement clinical findings and support decision-making processes for potential
36
37 567 implementation.
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44 569 However, several methodological limitations also need to be acknowledged. Recruitment
45
46 570 through social media platforms means we cannot accurately assess uptake of the intervention,
47
48 571 as we will not be able to identify the number of eligible people exposed to our advertisements.
49
50 572 This may limit our ability to determine reach of the program. However, recording the time
51
52 573 taken for recruitment and accessing google analytic data on internet traffic and page visits may
53
54 574 provide some information in this area. Participants will need access to the internet to
55
56 575 participate. While this may mean some people will be excluded from the study, we believe this
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3 576 will have minimal impact on the study. We envisage that the study will take approximately 4
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5 577 years to complete. Advances in social platforms, technology and app-based programming can
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7 578 change substantially in a short period. While this may affect the actual online platform used for
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9 579 the program, we do not consider this will influence the program content or delivery
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11 580 mechanisms. As technology advances will likely increase interest in self-directed support
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13 581 programs for cancer survivors, it is essential that cancer survivors access programs with
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15 582 demonstrated effectiveness.
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21 584 **Trial Registration** ACTRN12620000645954

22 585 **Protocol Version:** Version 5, dated 18 December 2020

23
24 586 Recruitment commenced 12.10.2020, it is anticipated recruitment will be for a duration of 18
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26 587 months finishing on 12.04.2022.
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32 589 **Abbreviations**

33 590 AQL-4D Assessment of Quality of Life – 4 Dimensions

34 591 BCNA Breast Cancer Network Australia

35 592 CAMSR Cognitive and Affective Mindfulness Scale-Revised

36 593 CI Confidence interval

37 594 CRC Colorectal Cancer

38 595 FCR Fear of cancer recurrence

39 596 FCRI Fear of Cancer Recurrence Inventory

40 597 GAD-7 General Anxiety Disorder scale

41 598 MBCT Mindfulness-based cognitive therapy

42 599 MCID Minimally clinically important difference

43 600 PCFA Prostate Cancer Foundation of Australia

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3 601 PHQ-9 Patient Health Questionnaire
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5 602 QALY Quality of Life Years
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7 603 QoL Quality of Life
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9 604 RA Research assistant
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11 605 RCT Randomized controlled trial
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13 606 SD standard deviation
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18 607 **References**
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3 745 **Declarations**
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5

6 746 **Author's contributions**
7

8 747 PML, LR, LO, NW, MJ, AG, DWA, EO, CM, AU, RC, J P-N, DH, MB, BR, KW, MF, ABS,

9 748 KP, MS, DC and VW contributed to the conception of the program or design of the study.
10

11 749 EO designed the web platform and analytics with input from LR, NW, RC, DWA, AW,
12

13 750 PML. CM designed the economic component of the study. PML, LR, LO, NW, MJ, AG,
14

15 751 DWA, EO, CM, AU, RC, J P-N, DH, MB, BR, KW, MF, ABS, KP, SS, AW, KG, MS, DC,
16

17 752 BP and VW provided substantial input into the development of the protocol or revising it
18

19 753 critically for important intellectual content. PML, LR, NW, LO and VW drafted the
20

21 754 manuscript with contributions from MJ, AG, DWA, EO, CM, AU, RC, J P-N, DH, MB, BR,
22

23 755 KW, MF, ABS, KP, SS, AW, KG, MS, DC, BP.
24

25 756 Each of the authors contributed to, read and approved the final manuscript.
26

27 757 Each of the co-authors, PML, LR, LO, NW, MJ, AG, DWA, EO, CM, AU, RC, J P-N, DH,
28

29 758 MB, BR, KW, MF, ABS, KP, SS, AW, KG, MS, DC, BP and VW, are on the steering
30

31 759 committee, will oversee implementation of the study and data collection and will contribute
32

33 760 to the acquisition, analysis or interpretation of the data.
34

35 761
36

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38

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40

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42

43 765 **Competing interests**
44

45 766 The authors declare they have no competing interests.
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49 768 **Figure Legend/Caption:**
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51 769 Figure 1. Study flowchart
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6 771 FCRI (Fear of Cancer Recurrence Inventory); GAD-7 (General Anxiety and Distress scale;
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8 772 PHQ-9 (Patient Health Questionnaire); CAMS-R (Cognitive and Affective Mindfulness Scale
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10 773 – Revised); AQoL-4D (Assessment of Quality of Life – 4 Dimensions)
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12 774
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14
15 775 Figure 2. My Goal functionality in MindOnLine
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19 777 Figure 3. My Journal guided self-reflection practise in MindOnLine.
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Figure 2. My Goal functionality in MindOnLine

Figure 3. My Journal guided self-reflection practise in MindOnLine.

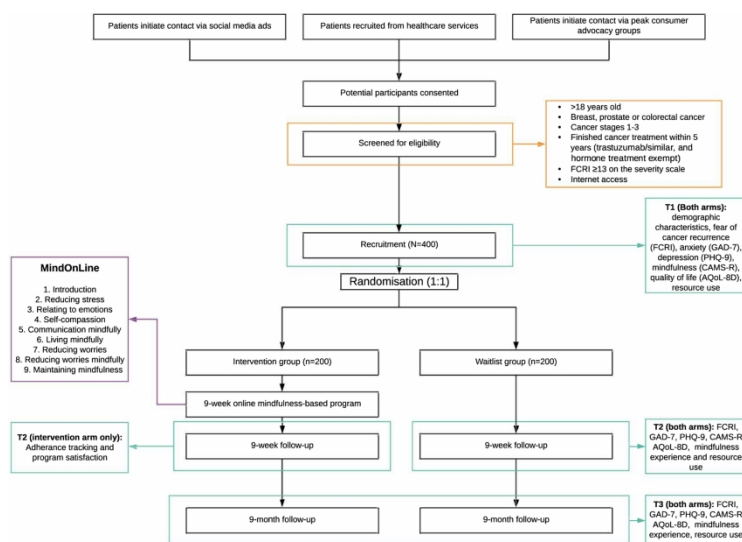


Figure 1. Study flowchart.

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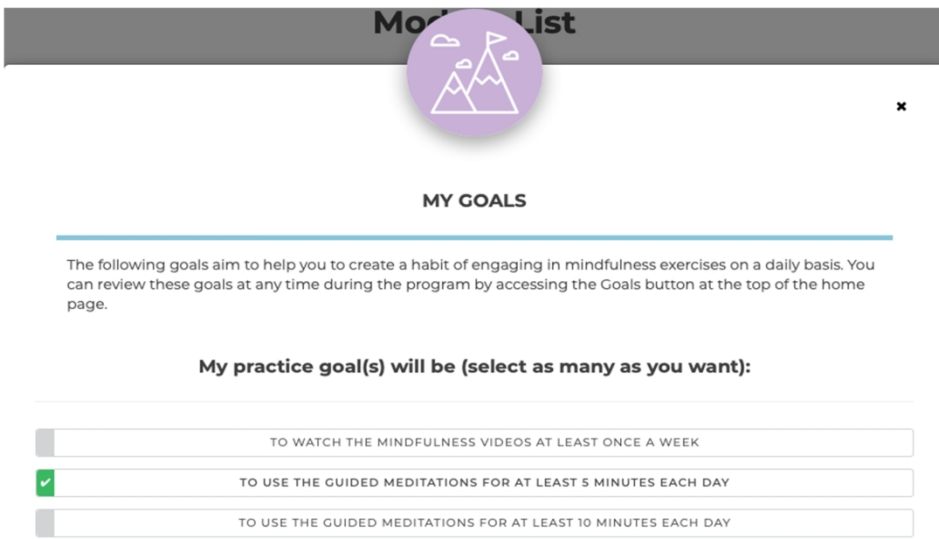


Figure 2. My goal functionality in MondOnLine.

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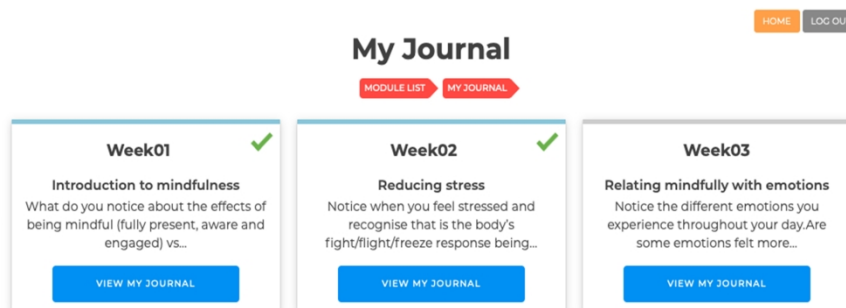


Figure 3. My journal guided self-reflection practice in MindOnline.

308x100mm (400 x 400 DPI)



Peter Mac
Peter MacCallum Cancer Centre
Victoria Australia



Epworth



**Prostate Cancer
Foundation
of Australia**



VICTORIA
State Government

Health
and Human
Services



**Breast
Cancer
Network
Australia**

Participant Information Sheet/Consent Form

Title	MindOnLine: a mindfulness program for people with breast, bowel or prostate cancer.
Short Title	MindOnLine
Principal Investigator	Prof Trish Livingston
Location	Deakin University

Part 1 What does my participation involve?

1 Introduction

You are invited to take part in this research project, because you have received treatment for breast, prostate or bowel cancer. This research project is testing an online mindfulness-based program for people who have completed their treatment.

This Participant Information Sheet/Consent Form tells you about the research project. It explains the procedures involved. Knowing what is involved will help you decide if you want to take part in the research.

Please read this information carefully. Ask questions about anything that you don't understand or want to know more about. Before deciding whether or not to take part, you might want to talk about it with a relative, friend or healthcare worker.

Participation in this research is voluntary. If you don't wish to take part, you don't have to. You will receive the best possible care whether or not you take part.

If you decide you want to take part in the research project, you will be asked to provide consent online. By agreeing you are telling us that you:

- Understand what you have read
- Consent to take part in the research project
- Consent to have the tests and treatments that are described
- Consent to the use of your personal and health information as described.

2 What is the purpose of this research?

Following treatment for cancer, many people feel anxious and scared about the cancer coming back. This is one of the most common fears of cancer survivors, and it can affect people's ability to enjoy life

1 and plan for the future. In some people, this fear can decrease over time, but most people find that they
2 worry at certain times. The mindfulness program aims to help cancer survivors to manage their fears
3 and worries once treatment is completed.
4

5 Research has shown that mindfulness-based programs can help people cope with anxious thoughts
6 about their cancer. The internet allows people to use the program from the comfort of their home, and
7 at their most convenient times. We have tested an online mindfulness program for people who received
8 treatment for melanoma, with promising results. This research is to find out whether mindfulness can
9 help people with breast, prostate or bowel cancer.
10

11 This research is being conducted across healthcare services and cancer organisations and is led by
12 researchers at the School of Nursing and Midwifery at Deakin University.
13
14

15 In this research project we will be testing a mindfulness program among people who meet the following
16 criteria:
17

- 18 - People who are over 18 years of age
- 19 - People who speak English well enough to understand videos and surveys presented in English
- 20 - People who have access to a computer or device to receive the program
- 21 - People who received treatment for breast, bowel or prostate cancer
- 22 - People who finished chemotherapy, radiotherapy or surgery treatment within the last five years
- 23 - People who experience a high level of fear of cancer recurrence.
24

25 You will be asked some questions after providing consent to determine if you meet the eligibility criteria
26 above. To measure your fear of cancer recurrence you will be asked 9 questions about how your
27 thoughts and feelings towards cancer may impact on your everyday living.
28

29 **3 What does participation involve?**

30
31 To participate in this study, each participant will need to have access to a computer, a smartphone, or a
32 similar tablet device, and internet. If you agree to take part in this project you will be allocated to either
33 receive the mindfulness program (intervention group) or stay in your usual care (control group). We
34 need to compare responses from people in these two groups to see if the mindfulness program provides
35 any benefits to cancer survivors. In order to make sure the groups are the same, participants are put
36 into one of the two groups by chance (random).
37
38

39 If you decide to take part in this study, you will need to provide your consent to participate by accessing
40 the following website: <https://mindonline.org.au> Before providing your consent you will be asked a
41 number of questions to make sure you are eligible for the study.
42

43 After consenting to take part in the study, you will be asked to complete a survey before being randomly
44 allocated to the intervention or control group. The same survey will be completed again 9 weeks and 9
45 months later. The survey asks you questions about possible fears of the cancer coming back, how
46 stressful and worrisome you perceive your life to be, and the type of thoughts you generally focus on.
47 We will also collect your email address and contact number. Your email and contact number will be used
48 to send you reminders and other information related to the study.
49

50
51 If you are randomised to the mindfulness program, you will receive an email informing you of your
52 allocation group with instructions on how to access the website. Your participation will involve using the
53 program for 9 weeks. The program is designed to help you understand and experience potential benefits
54 of using mindfulness in your day to day life. You will be invited to:
55

- 56 - Watch short videos at the start of each week. The videos will introduce a new topic about
57 mindfulness.
- 58 - Practice short meditations twice a day. We will help you create a meditation routine by emailing
59 you a direct link to guided meditations at times you will have chosen.
- 60 - Apply mindfulness skills in your day-to-day life.

1
2 If you are assigned to the mindfulness program we will monitor how often the mindfulness program is
3 used. This will be recorded by your study identification number, and no personal information such as
4 your Internet Protocol (IP) address linked to your computer or device will be collected.
5

6 If you are randomised to the control group you will receive an email informing you of your allocation
7 group and you will continue to receive your usual care from your healthcare providers. You will receive
8 emails to ask you to complete the questionnaires at 9 weeks and 9 months. After the 9-month survey
9 you will be able to use the mindfulness program.
10

11
12 We will compare the results between those in the mindfulness program and those who are not, to see if
13 there are any differences in wellbeing between the two groups.
14

15 There are no additional costs associated with participating in this research project, nor will you be paid.
16
17

18 19 **4 Other relevant information about the research project**

20
21 This study will show if the mindfulness program is helpful for people with breast, prostate or colorectal
22 cancer. If successful the program we be made open to the wider population.
23

24 For this study, approximately 400 people will be invited to participate from online and social media
25 advertisements and from healthcare services.
26
27

28 29 **5 Do I have to take part in this research project?**

30
31 Participation in any research project is voluntary. If you do not wish to take part you don't have to. If
32 you decide to take part and later change your mind, you are free to withdraw from the project at any
33 stage.
34

35 Your decision whether to take part or not to take part, or to take part and then withdraw, will not affect
36 your relationship with those treating you or involved in your follow-up care, or your relationship with
37 Deakin University, Breast Cancer Network Australia, or Prostate Cancer Foundation of Australia.
38
39

40 41 **6 What are the possible benefits of taking part?**

42
43 We cannot guarantee or promise that you will receive any benefits from this research; however,
44 possible benefits for the community may include additional support for people who have completed
45 treatment for cancer.
46
47

48 49 **7 What are the possible risks?**

50
51 Some people may feel uncomfortable or upset when answering questions in this survey. If you do not
52 wish to answer a question you may skip it and go to the next question, or you may stop immediately. In
53 the event that you become upset or distressed as a result of your participation, the researcher can
54 arrange for counselling or other appropriate support provided by staff who are not members of the
55 research team. In addition, you may want to contact an external support service such as Lifeline services
56 on 13 11 14, or www.mindhealthconnect.org.au or the Cancer Council 13 11 20 telephone service.
57 If you have any concerns or are unsure whether you should participate in this project, you may wish to
58 speak to your healthcare professional about your feelings.
59
60

8 What if I withdraw from this research project?

If you decide to withdraw, please notify a member of the research team about this decision. This notice will ensure that we can remove you from our records and will mean you will not receive any notices about the project.

If you decide to withdraw from the project, we would like to keep the personal and health information about you that has been collected. This is to help us make sure that the results of the research can be measured properly. If you want to withdraw your data from the study as well, please let them know when you tell them about withdrawing from the study.

9 What happens when the research project ends?

If you wish to obtain a final copy of the research report describing the results of this study, please contact the project manager (Dr Natalie Heynsbergh on 03 9246 8225, or email n.heynsbergh@deakin.edu.au) and she will arrange for a copy to be sent to you after completion of the study in December 2022.

Part 2 How is the research project being conducted?

10 What will happen to information about me?

Any information obtained in connection with this research project that can identify you (e.g. email address) will remain confidential and will only be used for the purpose of this research project. It will only be disclosed with your permission, except as required by law.

All the information you provide will be coded so you cannot be identified by name, and only the research team will have access to the list that can link your name to your data. All identifying information will be stored in password-protected electronic files or in a locked filing cabinet in the office of the research staff, and will be disposed of as confidential waste after five years.

You will not be identified in any report or publication from this study. Information will be provided in such a way that you cannot be identified.

In accordance with relevant Australian and/or Victorian privacy and other relevant laws, you have the right to access the information collected and stored by the researchers about you. You also have the right to request that any information with which you disagree be corrected. Please contact one of the researchers named in the last section below if you would like to access your information.

11 Who is organising and funding the research?

This research project is being managed by Dr Natalie Heynsbergh at Deakin University, and is being funded by a National Health and Medical Research Council (NHMRC) grant.

12 Who has reviewed the research project?

All research in Australia involving humans is reviewed by an independent group of people called a Human Research Ethics Committee (HREC). The ethical aspects of this research project have been

approved by the Peter MacCallum Human Research Ethics Committee (Reference number 20/53) and the Deakin University Human Research Ethics Committee.

This project will be carried out according to the *National Statement on Ethical Conduct in Human Research (2007)*. This statement has been developed to protect the interests of people who agree to participate in human research studies.

13 Further information and who to contact

The person you may need to contact will depend on the nature of your query.

If you want any further information concerning this project or if you have any problems which may be related to your involvement in the project, you can contact:

- The principal investigator: Prof Patricia Livingston on 03 9244 6609, or email trish.livingston@deakin.edu.au
- The project manager: Dr Natalie Heynsbergh on 03 92468225, or email: n.heynsbergh@deakin.edu.au

If you have any complaints about any aspect of the project, the way it is being conducted or any questions about being a research participant in general, then you may contact:

Reviewing HREC name	Peter MacCallum Cancer Centre Ethics Committee
Project reference number	20/53
HREC Executive Officer	Ethics Coordinator
Telephone	03 8559 7540
Email	ethics@petermac.org

14 What do I do if I want to participate?

If you would like to participate in this study, please log on to <https://mindonline.org.au>, to answer the eligibility questions and provide your consent to participate.



SPIRIT 2013 Checklist: Recommended items to address in a clinical trial protocol and related documents*

Section/item	Item No	Description	Addressed on page number
Administrative information			
Title	1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym	1
Trial registration	2a	Trial identifier and registry name. If not yet registered, name of intended registry	2
	2b	All items from the World Health Organization Trial Registration Data Set	n/a
Protocol version	3	Date and version identifier	2
Funding	4	Sources and types of financial, material, and other support	23
Roles and responsibilities	5a	Names, affiliations, and roles of protocol contributors	1
	5b	Name and contact information for the trial sponsor	1
	5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities	23
	5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee)	23

1 **Introduction**

2

3 Background and 6a Description of research question and justification for undertaking the trial, including summary of relevant 3-5
 4 rationale studies (published and unpublished) examining benefits and harms for each intervention

5

6 6b Explanation for choice of comparators 6

7

8 Objectives 7 Specific objectives or hypotheses 5-6

9

10 Trial design 8 Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), 6
 11 allocation ratio, and framework (eg, superiority, equivalence, noninferiority, exploratory)

12

13

14 **Methods: Participants, interventions, and outcomes**

15

16 Study setting 9 Description of study settings (eg, community clinic, academic hospital) and list of countries where data will 6, 8
 17 be collected. Reference to where list of study sites can be obtained

18

19 Eligibility criteria 10 Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and 8
 20 individuals who will perform the interventions (eg, surgeons, psychotherapists)

21

22 Interventions 11a Interventions for each group with sufficient detail to allow replication, including how and when they will be 11-14
 23 administered

24

25 11b Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose n/a
 26 change in response to harms, participant request, or improving/worsening disease)

27

28 11c Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence 12-13, 16
 29 (eg, drug tablet return, laboratory tests)

30

31 11d Relevant concomitant care and interventions that are permitted or prohibited during the trial 16

32

33

34 Outcomes 12 Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood
 35 pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, 15-17
 36 median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen
 37 efficacy and harm outcomes is strongly recommended

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40 Participant timeline 13 Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for 14
 41 participants. A schematic diagram is highly recommended (see Figure)

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1	Sample size	14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations	19
2				
3				
4	Recruitment	15	Strategies for achieving adequate participant enrolment to reach target sample size	9
5				

6 **Methods: Assignment of interventions (for controlled trials)**

7 Allocation:

8				
9				
10	Sequence	16a	Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions	10
11	generation			
12				
13				
14				
15				
16	Allocation	16b	Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned	10
17	concealment			
18	mechanism			
19				
20	Implementation	16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions	10
21				
22				
23				
24	Blinding (masking)	17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how	10
25				
26				
27		17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial	10
28				
29				
30				

31 **Methods: Data collection, management, and analysis**

32				
33	Data collection	18a	Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol	14
34	methods			
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39		18b	Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols	14
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41				
42				

1	Data management	19	Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol	21
2				
3				
4				
5	Statistical methods	20a	Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol	19
6				
7				
8		20b	Methods for any additional analyses (eg, subgroup and adjusted analyses)	19
9				
10		20c	Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation)	19
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14	Methods: Monitoring			
15				
16	Data monitoring	21a	Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed	21
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22		21b	Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial	21
23				
24				
25	Harms	22	Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct	21
26				
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28				
29	Auditing	23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor	21
30				
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33	Ethics and dissemination			
34				
35	Research ethics approval	24	Plans for seeking research ethics committee/institutional review board (REC/IRB) approval	24
36				
37				
38	Protocol amendments	25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC/IRBs, trial participants, trial registries, journals, regulators)	21
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1	Consent or assent	26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)	10
2				
3				
4		26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable	n/a
5				
6				
7	Confidentiality	27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial	21
8				
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10	Declaration of interests	28	Financial and other competing interests for principal investigators for the overall trial and each study site	24
11				
12				
13	Access to data	29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators	21
14				
15				
16	Ancillary and post-trial care	30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation	21
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19				
20	Dissemination policy	31a	Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions	21
21				
22				
23				
24		31b	Authorship eligibility guidelines and any intended use of professional writers	21
25				
26		31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code	21
27				
28				
29	Appendices			
30				
31	Informed consent materials	32	Model consent form and other related documentation given to participants and authorised surrogates	attached
32				
33				
34	Biological specimens	33	Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable	n/a
35				
36				

*It is strongly recommended that this checklist be read in conjunction with the SPIRIT 2013 Explanation & Elaboration for important clarification on the items. Amendments to the protocol should be tracked and dated. The SPIRIT checklist is copyrighted by the SPIRIT Group under the Creative Commons [“Attribution-NonCommercial-NoDerivs 3.0 Unported”](https://creativecommons.org/licenses/by-nc-nd/3.0/) license.