

1 **ClinicalTrials.gov**

2

3 **Protocol Registration and Results System (PRS)**

4

5 **ClinicalTrials.gov ID: [Not yet assigned]**

6 **Last review date: October 13th, 2023.**

7

8 **Study Identification Unique Protocol ID: 023-005-OMI(CEI-05022)**

9

10

11 **Brief Title:** Improving Lifestyle Behavior by "Joven, Fuerte y Saludable"
12 Multidisciplinary Program. Official Title: Efecto de Una intervención Multidisciplinaria
13 de Estilo de Vida Sobre el Exposoma de Pacientes premenopáusicas Con cáncer
14 de Mama Estadios I-III.

15

16 **Title:** Improving Lifestyle Behavior by "Joven, Fuerte y Saludable" Multidisciplinary
17 Program. Official Title: Efecto de Una intervención Multidisciplinaria de Estilo de Vida
18 Sobre el Exposoma de Pacientes premenopáusicas Con cáncer de Mama Estadios
19 I-III.

20 **Abstract**

21 **Background.** Breast cancer (BC) is the leading cause of cancer-related death and
22 disability in young women. Patients with BC experience physical symptoms and
23 psychosocial distress that adversely affect their quality of life (QoL), physical
24 functioning, and psychological well-being. "Joven & Fuerte" is a navigation program
25 for young women with BC at the National Cancer Institute in Mexico City. The
26 program proposes an hybrid model (face-to-face and virtual) to support patients on
27 aspects such as oncology, nutrition literacy, and psychology with mindfulness.

28 **Methods.** The study was initially planned as a randomized controlled trial to ensure
29 accurate results. However, during the pilot study, it was adapted to meet the specific
30 needs of patients such as oncology consultations and in consideration of living
31 arrangements. Two groups will be compared: one receives hybrid education and the
32 other, a hybrid education and personalized intervention. Patients who agreed for the
33 face-to-face sessions were assigned to the personalized interventions group, and
34 others, to the hybrid education group. The intervention group receives an in-person
35 consultation to evaluate their physical measurements and an interdisciplinary
36 assessment by experts. Patients can ask for virtual assistance through Zoom and
37 WhatsApp in case of any issues during the intervention. In addition, educational
38 materials such as healthy lifestyle guides and videos can be accessed through
39 Facebook and YouTube groups upon request. To ensure the comprehension of the
40 material, follow-up sessions are conducted through phone calls, video calls, or on-
41 site visits. Validated questionnaires will assess lifestyle habits, QoL status, and
42 levels of distress, anxiety, and depression.

43 What is already known on this topic

44

- 45 • Breast cancer and its treatment impacts the lifestyle and quality of life of
patients.
- 46 • Improvement in nutrition, lifestyle, and psychological wellbeing positively
47 impacts the prognosis of breast cancer and quality of life or survivors.

48 What this study adds

49

- 50 • Provides interventions for patients living far from a hospital.
- 51 • Evaluates the health advantages of educational and personalized
interventions.

52 ● Examines how lifestyle changes affect the quality of life, mental health, and
53 physical functioning of patients with breast cancer receiving cancer treatment.

54 How this study might affect research, practice, or policy

55 ● This hybrid approach is both viable and economical for public institutions.
56 ● The findings of this study will reveal the effects of these interventions and their
57 potential benefits to patients.

58 INTRODUCTION

59 Breast cancer (BC) is a leading cause of death in women worldwide, especially in
60 Latin America, where patients often present with advanced stages of aggressive
61 subtypes of BC at a younger age (1). The risk of BC depends on various factors,
62 including hormone replacement therapy history, reproductive history, alcohol or
63 tobacco consumption, physical activity, and dietary habits, that are collectively called
64 exposome (2). Exposome refers to the exposure to environmental influences and
65 biological responses throughout a person's life from the prenatal stage. It can be
66 influenced by the environment, diet, behavior, and endogenous processes (3).

67 External exposome refers to environmental factors such as mental stress, climate,
68 and lifestyle. In contrast, internal exposome are changes within an organism such
69 as increased stress hormones, inflammatory cytokines, and oxidative stress (4).
70 Constant exposure to environmental factors, such as an unhealthy lifestyle, can
71 cause cellular damage and contribute to the growth and evolution of tumors. Once
72 cellular damage occurs, internal exposome promotes changes that create a harmful
73 environment, favoring cancer cells to acquire mechanisms to cope with stress and
74 drugs, leading to a resistance to oncological treatments (5).

75 Obesity is part of the personal exposome and can impact the internal exposome,
76 potentially affecting BC patients. A significant percentage of patients diagnosed with
77 BC (70.9%) are overweight or obese at the time of diagnosis (6). This weight gain
78 usually occurs during systemic treatment, with 25% of patients gaining weight within
79 six months, 32% between 6-12 months, and 20% between 12-18 months after
80 diagnosis (7). Young women with breast cancer (YWBC) also experience and
81 increase in weight since the initiation of oncological treatment and up to the second
82 year of diagnosis (from 39% at baseline to 46% in two years), highlighting the
83 importance of evaluating the implications of weight gain and whether early
84 intervention would help control the risk factors mentioned earlier (8). Obesity may
85 also be associated with worse disease-free and overall survival (9).

86 Weight gain in patients with BC is often associated with several factors, including
87 systemic treatment, diagnosis at a young age, and lifestyle changes resulting from
88 the disease or treatment. However, the primary mechanism underlying weight gain
89 is reduced physical activity (10). The combination of chemotherapy and endocrine
90 therapy is linked to higher weight gain, especially in patients who are premenopausal
91 (a gain of up to 24 kg). In contrast, those who are postmenopausal tend to lose
92 weight (11).

93 BC patients have reported experiencing physical symptoms and psychological
94 distress, which can negatively impact their quality of life (QoL). These symptoms can
95 affect their physical functioning, psychological well-being, and social support levels
96 (12). Particularly, YWBC is a vulnerable population with specific concerns such as
97 fertility, self-image, QoL, sexuality, and personal goals (13) and experience high
98 anxiety and depression (14). Maintaining a healthy lifestyle can improve QoL and
99 lead to better prognoses and lower mortality rates (15). For example, exercise can
100 reduce breast cancer-related death risk by 30% and all-cause death risk by 41%
101 (16). Patients undergoing oncology treatment face various nutritional challenges that
102 differ based on the type and stage of cancer, and the treatments may worsen these
103 challenges. Early nutritional screening and interventions are crucial in the cancer
104 population, as emphasized in the clinical guidelines (ASPEN/ESPEN) (17).

105 The Instituto Nacional de Cancerología (INCAN) in Mexico City offers a program
106 called "Joven & Fuerte" for young women diagnosed with BC. However, the attention
107 was not systematic and it was difficult to measure the benefits of the intervention. So
108 the present study proposes a psychological intervention, side effect management,
109 physical activity, sleep hygiene, and psychological strategies, with onsite and remote
110 interventions to improve patient adherence and ensure timely attention. The study
111 aims to evaluate the impact of early intervention on metabolic control in newly
112 diagnosed BC patients, their QoL, and clinical outcomes.

113 **METHODS**

114 A controlled trial design was adopted in which patients were assigned to two
115 intervention groups according to the nutritional, psychological, or rehabilitation risk
116 at baseline or according to their geographical localization. The first group will receive
117 a hybrid multidisciplinary lifestyle education intervention, whereas the second group
118 will receive an individualized hybrid multidisciplinary lifestyle intervention.

119 For sample size estimation, we used internal statistics from the Mammary Tumor
120 Department at the INCAN, which has an annual average of 109 women diagnosed
121 and treated based on the selection criteria. Considering the effect on metabolic and
122 inflammatory parameters, a study by Dieli-Conwright et al. (18) was followed to

123 identify the difference in the decrease in insulin parameters by 14%. A confidence
124 level of 95% and power of 80% were considered with a control: intervention ratio of
125 1:1. Thus, a sample size of 132 patients was obtained. Considering a probable loss
126 of 10%, 146 patients were invited to participate in the study, with 73 patients per
127 group.

128 **Inclusion criteria**

129 ● Women aged ≥ 18 and <40 years who were diagnosed with stage I-III BC,
130 confirmed by pathology and image at the INCAN
131 ● Candidates for multidisciplinary treatment, including surgery,
132 chemotherapy, and/or hormonal treatments.
133 ● Signed the informed consent form
134 ● Have access to a mobile phone or any electronic device with an active
135 internet connection to receive the program information.

136 **Exclusion criteria**

137 ● Patients with inflammatory cancer
138 ● Those with cardiomyopathy or ventricular dysfunction (NYHA $>II$),
139 arrhythmia secondary to left ventricular ejection alterations that require
140 medication, previous myocardial infarction, or angina pectoris in the last
141 six months
142 ● Receiving treatment for cardiovascular or cerebrovascular disease,
143 inflammatory bowel disease, malabsorption syndrome, rheumatoid
144 arthritis, lupus, thyroid diseases, or Cushing syndrome
145 ● Unable to walk for at least 1 km
146 ● Have cardiovascular, respiratory, or musculoskeletal diseases that
147 impede physical activity
148 ● Pregnant or breastfeeding
149 ● Have psychiatric conditions impeding active participation in this protocol
150 ● Do not understand Spanish

151 **Selection and group assignment of the patients**

152 Patients will be recruited through an active program at the INCAN, where potential
153 candidates will be identified and invited by the navigator at the program "Joven &
154 Fuerte." After they sign the informed consent form (ICF), patients will be assigned
155 into one of the two groups:

156 Group 1: Hybrid multidisciplinary lifestyle education intervention.

157 Group 2: Individualized hybrid multidisciplinary lifestyle interventions.

158 The initial proposal was randomized assignment to each group; however, the pilot
159 study revealed challenges for patients who lived far from the hospital, in other states,
160 or had personal obligations such as family or work. Therefore, the randomization
161 process was adapted to meet the patients' needs. The intervention aims to facilitate
162 patients' adherence and follow-up with healthcare providers. Additionally, patient
163 preferences were considered when assigning them to a group.

164 **Intervention**

165 The individualized hybrid multidisciplinary lifestyle intervention consists of four
166 phases. During the **initial phase**, (1st month), patients undergo psychological,
167 nutritional, and physical evaluations using validated questionnaires. Weekly follow-
168 ups are scheduled to answer any questions and provide educational materials.
169 Psychological intervention for the management of stress, anxiety, or other sleep
170 disorders begins during this phase. Changes in diet and physical activity levels are
171 prepared based on baseline questionnaires and adjusted to their needs and
172 preferences to facilitate adherence to the intervention. Basic nutritional orientation is
173 provided covering topics such as identification of food groups using guides such as
174 "My Plate" (19) from the American Association of Diabetes, how to read nutrition
175 facts labels, and explanation on following a healthy diet, with available food groups
176 in the country.

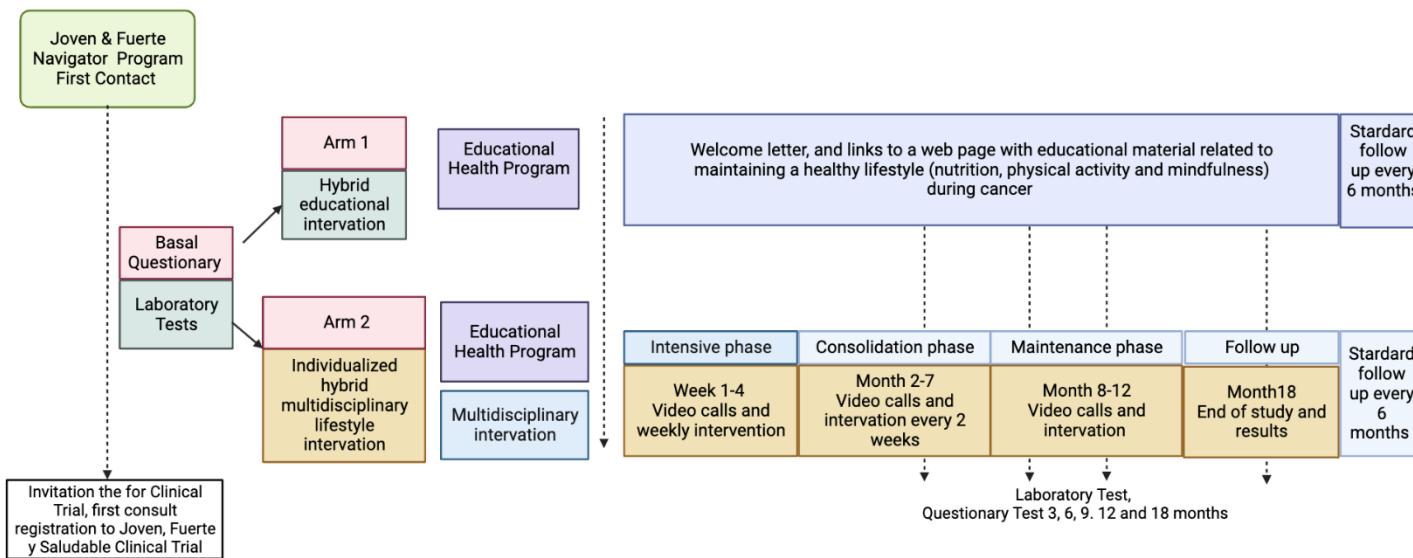
177 In the **consolidation phase**, from second to sixth month, patients undergo follow-
178 ups every two weeks on-site or remotely, depending on the patient's preference.
179 Follow-up was to monitor patients' symptoms and adjust their diet and exercise
180 routines accordingly. Psychological intervention will be tailored to individual needs if
181 a patient experiences symptoms such as nausea, vomiting, diarrhea, or fatigue. This
182 phase aims to help patients become independent and manage their activities without
183 professional help. A personalized diet and exercise plan will be created for each
184 patient, considering their socioeconomic status. The local food groups available to
185 each patient are prescribed. The Avena Health application will monitor water
186 consumption, physical activity, and nutritional adherence if the patient has access.

187 The **maintenance phase**, from seventh to 12th month, the patients will be followed
188 up every two months. Anthropometric measures, blood tests, and questionnaires will
189 be used to assess their progress. The objective of this phase is to reinforce the
190 recommendations of previous phases.

191 The patients undergo check-ins every three months during the follow-up phase,
192 which begins after 12 months. In the medium term, anthropometric measures and

193 questionnaires will be used to evaluate patient adherence to multidisciplinary
194 interventions. Any questions or concerns will be addressed during the checks. See
195 **Figure 1.**

196



Created in BioRender.com

197 Figure 1. Joven, Fuerte y Saludable, Protocol Design.

198 Components of the Multidisciplinary Individualized Intervention

199 Nutritional Intervention

200 Patients will undergo a comprehensive nutritional assessment and receive guidance
201 on maintaining a healthy diet balanced with macronutrients. Assessment of
202 symptoms that affect nutritional or metabolic status; anthropometric indicators such
203 as weight, height, waist circumference, arm circumference, waist-to-hip ratio, and
204 body composition determined by bioelectrical impedance analysis (BIA) will be
205 collected at baseline and follow-up; and biochemical parameters such as blood
206 glucose, insulin, HbA1c, total, low-density lipoprotein-cholesterol, high-density
207 lipoprotein-cholesterol, triglycerides, and c-reactive protein (CRP) will be assessed.
208 Recommendations will be tailored to the individual's needs and budget and any
209 adverse effects related to their cancer treatment, focusing on a healthy, moderately
210 hypocaloric diet (for those who are overweight, obese, or at metabolic risk) or an
211 isocaloric diet for those who are underweight, considering the individualized
212 requirements of energy, protein, carbohydrate, lipids, vitamins, and minerals.
213 Dietetic assessment measures adherence to the diet prescription through a typical

214 feeding model or 24-hour recall. Participants will meet the program nutritionist
215 according to the visit frequency described for each phase.

216 A webpage will be available with weekly modules on nutrition, and patients will be
217 invited to workshops to resolve any obstacles they encounter while implementing
218 recommendations. A virtual class would be offered if someone could not attend the
219 workshop. A workbook with educational information and a diary section will also be
220 provided, allowing patients to share their thoughts on the intervention, challenges
221 they face, and questions.

222 *Physical activity intervention*

223 Patients will be prescribed a customized regimen of dynamic aerobic exercise to
224 improve their physical capacity. A stress test determines maximum effort capacity
225 and identifies contraindications. The rehabilitation team will evaluate the
226 performance status of patients using the Karnofsky Index (a functional scale) and
227 Eastern Cooperative Oncology Group (ECOG). Patients receive personalized
228 treatment based on their diagnoses. In addition, they will receive a digital or physical
229 guide of exercises appropriate for their disease stage. They should perform these
230 exercises 3-5 times weekly for at least 150 minutes, including resistance training and
231 moderate-intensity aerobics. Patients with special needs, such as those with
232 lymphedema, post-surgery, or active treatment, can also undergo various exercises.
233 A healthcare professional trained in oncological rehabilitation will supervise all the
234 exercise sessions.

235 *Psychological intervention*

236 During the diagnosis and treatment of BC, workshops will be held in collaboration
237 with a psychology team to assess the emotional symptoms. Patients will receive
238 videos of relaxation techniques and their anxiety levels will be monitored using a
239 thermometer anxiety tool. Patients who score more than four will complete
240 depressive and anxiety symptom questionnaires (the Patient Health Questionnaire,
241 PHQ-9 and Generalized Anxiety Disorder, GAD-7, respectively) and will be referred
242 for group or individual therapy. The number of therapy sessions will be limited to
243 eight for individual interventions and two for each multidisciplinary intervention
244 phase. The questionnaires will be administered at the beginning and at three, six,
245 nine, and 12 months.

246 Psychological interventions will involve cognitive-behavioral therapy, which will focus
247 on changing cognition and behaviors to reduce symptoms of stress, anxiety, and
248 depression. Treatment will also address the emotional discomfort caused by the
249 diagnosis and treatment and its impact on family and couple dynamics, social and

250 work life, body image, sexuality, and fertility etc. During the sessions, a clinical
251 history will be taken, with which a Clinical Map of Pathogenesis and Goal Scope Map
252 will be generated according to the Nezú and Nezú model (4). This assessment
253 allows the development of a therapy focused on the patient's needs and, to identify
254 intervention strategies for achieving specific goals, such as psychoeducation,
255 relaxation training, cognitive restructuring, problem-solving therapy, behavioral
256 activation, and assertive communication training. Patients can choose between
257 hybrid formats such as Zoom and WhatsApp and onsite sessions with specialists.

258 *Mindfulness + oncologic rehabilitation intervention*

259 The oncological rehabilitation and mindfulness program consists of four modalities:

260 ● Group face-to-face,
261 ● Individuals face-to-face
262 ● Group online, and
263 ● Individual online

264 The program can be applied at different time points during patient treatment: before,
265 after, and after surgery with chemotherapy and/or radiotherapy.

266 Physical exercises include different activity levels for patients to improve their
267 flexibility, range of motion, strength, and recovery capacity; exercises included in the
268 program are aimed at working different parts of the body, combined into different
269 techniques divided into static, moving, breathing, and meditation techniques, and
270 Thai-Chi and Qi Gong, as part of the mindfulness program. The contents of the
271 program are presented in **Table 1**.

272 **Table 1. Mindfulness and oncologic rehabilitation content**

PROGRAM ADMISSION	ONCOLOGIC REHABILITATION	EXERCISES	MOVEMENT TECHNIQUES	STATIC TECHNIQUES	BREATHING TECHNIQUES	MEDITATION TECHNIQUES	EDUCATIONAL MATERIAL
Interview (E)	Flexibility (RFi)	Neck (C)	Expansion and contraction (ECS)	Body scan (on the floor) (EA)	Conscious breathing (RCS)	Static meditation (ME)	Welcome to the program! (BVP)
Initial evaluation (EI)	Range of movement (RRM.ii)	Upper limbs (MS)	Expansion and contraction on the wall (ECP)	Body scan (seated) (ES)	Conscious breathing (5 words) (RCS5)	Static meditation (seated) (MES)	Benefits of oncologic rehabilitation (BFRO)

Questionnaire application (AC)	Strength (Rfza. III)	Lower limbs (MI)	21 movements (21M)	Internal circulation channel (CIC)	Breathing awareness (chest, costal, abdominal) (RAWS)	Lay down meditation (MA)	Benefits of mindfulness (BFAP)
Postural hygiene (HP)	Recovery (RR.IV)	Legs (P)	Tai Chi's 13 movements (13M)		Abdominal breathing (RA)	Walking meditation (MC)	Stress consequences (CSCE)
Integration of the program (IP)		Thorax (T)	5 animals (Qi Gong) (5A)		Breath count (CR)	Moving meditation (MCM)	Cortisol (CZ)
Psychological intervention (IPS)		Hip (H)					Sixth sense (SS)
							Nutrition (NT)

273 *Codes used in this intervention are marked in bold and in parentheses.

274

275 Finally, sessions will be completed by ensuring that the patients are aware of the
 276 importance of how stress impacts health, reminding them that specific at-home
 277 exercise techniques could improve their physical condition.

278 **Educative intervention**

279 *Psychologic and mindfulness educative intervention*

280 Virtual educational intervention was adjusted to STREAM intervention for BC after
 281 adapting it for our population (20). Based on our experience with the Joven & Fuerte
 282 program this intervention will continue for 10 weeks, from the beginning of the
 283 diagnosis, which, is when the patient requires understanding and assimilating their
 284 diagnosis and the life changes that cancer treatments will represent, as well as adapt
 285 to the institution. This intervention intends to manage the emotional stress of this
 286 phase in collaboration with the psychology and mindfulness team.

287 Questionnaires will be administered to evaluate QoL (QLQ-C30 and QLQ-BR23) at
 288 the baseline and at three, six, 12, and 18 months, and healthy lifestyle (WCFR/AICR)
 289 at the beginning and end of the intervention in both groups.

290 While these activities are performed, patients will participate in a mindfulness
291 workshop for 10 weeks, which includes breathing counting techniques (Zazen),
292 guided meditations (five words of self-composure), meditation exercises with static
293 movement (BaDuanJin), conscious walking (Kinjun), body scan, energy
294 concentration work and physical movement (five healing animals), moving
295 meditation (TaiChi), and yoga. All of these techniques are intended to be tools for
296 the patient to deal with the stress she faces during her BC diagnosis.

297 *Healthy lifestyle educative intervention*

298 The healthy lifestyle education intervention was adapted from the Diabetes
299 Prevention Program (DPP)(21) funded by the National Institute of Diabetes and
300 Digestive and Kidney Diseases (NIDDK) and has been used in BC studies, such as
301 SUCCESS (22), MEDEA (23), and PASAPAS (24). This educational material is
302 planned to be given to all intervention groups. Every week, in a hybrid format,
303 patients will receive a WhatsApp or, through the Facebook group, the written
304 information, video, and/or audio of the subjects included in the program. Additionally,
305 patients will receive a manual with a weekly description of the topic to be discussed
306 and the activities they must carry out that week in a way that the patient will have
307 the whole week to carry out her activities; on Friday, a session will be opened both
308 on Zoom or WhatsApp, or in the case of patients who can physically go to the
309 institute in person. The expert will also be available so that the patient can share her
310 doubts and difficulties faced during the week.

311 On **Table 2**, educational subjects reviewed on every intervention phase are
312 described.

313

Intervention phase	Follow-up	Week	Title	Content
Intensive phase: weekly follow-up	1	1	Welcome to the program	Introduction
	2	2	Caloric balance	Caloric restriction
	3	3	Type of fatty acids	Caloric restriction
	4	4	Reducing calories, controlling portions	Caloric restriction

	5	5	Muscular movement	Physical activity
	6	6	Working with your surroundings	Behavioral support
	7	7	Problem-solving	Behavioral support
	8	8	Being active: a way of living	Physical activity
	9	9	Healthy eating	Caloric restriction
	10	10	Healthy eating and breast cancer	Breast cancer and nutrition
	11	11	Preparing a better breakfast, lunch, and dinner	Caloric restriction and behavioral support
	12	12	Progress review	Recap and evaluation
Consolidation phase: two-week follow-up	13	14	Answering negative thoughts	Behavioral support
	14	16	The slope in changing to a healthy lifestyle	Behavioral support
	15	18	Intensifying physical activity	Physical activity
	16	20	10 ways to control hunger	Behavioral support
	17	22	What to eat on holidays	Behavioral support
	18	24	Making balance and celebrating success	Recap and evaluation
	19	28	How to stay motivated	Behavioral support

Maintenance phase: monthly follow-up	20	32	Recovering from excess eating	Behavioral support
	21	36	Weight loss review	Caloric restriction
	22	40	How to adapt to long-lasting success	Behavioral support
	23	44	Preparing for what's yet to come	Recap and evaluation
	24	48	Congratulations! You finished the program!	Recap and evaluation

314 **Table 2. Intervention phases adapted from the diabetes education program (DPP)**

315 *Barriers and facilitators for the multidisciplinary program implementation*

316 As this program is being implemented for the first time and with the aim of enhancing
 317 patient care, the assessment of barriers will be carried out through questionnaires
 318 administered to both program staff and enrolled patients. The purpose is to identify
 319 the barriers faced by each party, thereby enabling the provision of solutions
 320 alongside the interventions. The questionnaire design was based on the CFIR/RE-
 321 AIM framework, a tool used to assess the success of program implementation (25,
 322 26).

323 **Data analysis**

324 Descriptive statistics will be performed for the clinical and demographic data.
 325 Inferential comparisons will be made by calculating the relative risk with 95%
 326 confidence intervals. To compare the effect between groups, a statistical comparison
 327 with the Kolmogorov-Smirnov test will be performed, and depending on the
 328 distribution of data, parametric (normal distribution) or non-parametric (non-normal
 329 distribution) tests will be applied. To evaluate the differences between groups,
 330 Student's T test for related groups or the Mann-Whitney test will be used, while for
 331 the analysis of repeated samples, analysis of variance (ANOVA) will be used for
 332 three or more variables, depending on the nature of the data.

333 Chi-square and Fisher's tests will be used to compare categorical variables, and the
 334 alpha value will be set to 0.05. Bivariate analysis will be performed to identify
 335 differences between groups and associations with survival concerning the measured

336 clinical variables and biomarkers. To analyze the existing correlation with the clinical
337 variables, Pearson or Spearman regression with a 95% confidence interval will be
338 used, depending on the nature of the data distribution. To determine the associations
339 between independent variables, multivariate logistic regression models were used,
340 adjusting for the remaining clinical variables.

341 **Discussion**

342 Although various interventions provide nutritional and physical activity counseling,
343 most of them are focused on patients who have survived cancer and do not include
344 those who have been diagnosed recently. Emotional support is also not taken into
345 account. A recent meta-analysis published by Cochrane reviewed 20 studies and
346 involved 2028 patients with breast cancer who received interventions for weight loss.
347 The results showed that these interventions for survivors of breast cancer with
348 obesity resulted in moderate weight reduction, improved body mass index and waist
349 circumference, and enhanced quality of life through diet and exercise interventions
350 (7). It appears that a multidisciplinary approach could lead to even better results, and
351 probably it has to be since the diagnosis to start a mentality switch since the
352 beginning of the disease.

353 Nutritional interventions in patients with cancer ensure adequate intake of energy
354 and nutrients during oncological treatment, which results in an improved response
355 and reduced toxicity of pharmacological anti-cancer therapies. These health
356 changes reduce the long-term side effects of treatment and promote long-term
357 overall health (27). The Women's Intervention Nutrition Study (WINS) demonstrated
358 the impact of nutritional intervention on the prognosis and survival of BC, with a low-
359 fat diet promoting modest weight loss, improving metabolic biomarkers, and
360 positively affecting disease-free survival (28). According to lifestyle guidelines
361 recommended by the World Cancer Research Fund (WCRF)/American Institute for
362 Cancer Research (AICR), a fiber- and soy-rich diet and limited consumption of fatty
363 acids (especially saturated fatty acids) can improve survival after BC diagnosis (27).

364 According to research by Demark-Wahnefried et al., women undergoing
365 chemotherapy may experience a decrease in energy expenditure due to reduced
366 activity despite same calorie intake (29). The Health, Eating, Activity, and Lifestyle
367 (HEAL) study also found that patients who engaged in less exercise and physical
368 activity had a higher risk of weight gain. Patients who underwent chemotherapy
369 experienced a more significant decrease in exercise time (3.6 hours per week) than
370 those who underwent surgery (1.6 hours per week). Furthermore, a study showed
371 that all patients who underwent chemotherapy experienced amenorrhea; therefore,
372 changes in hormones and menopause could impact metabolism, affecting body

373 composition and the waist-to-hip ratio. This can result in increased estrogen and
374 insulin levels (30).

375 Oncological rehabilitation (OR) and mindfulness stimulate specific neurovascular
376 terminals that activate ATP, improve bloodstream flow, and stimulate the
377 parasympathetic nervous system (PNS), thereby generating serotonin and
378 endorphins, relaxing muscles, improving digestion, and reducing insomnia. It also
379 prevents sarcopenia and stimulates immunoglobulins and the osteomioarticular
380 system (OMAS). Mindfulness provides a profound knowledge of the mind and its
381 discriminative processes, allowing free radicals to be dosed. Through extensive
382 practice, the patient learns how to regulate their attention and manages to focus on
383 the present, which enhances the experience itself and the exercises at hand (31).

384 Psychological treatments for patients with BC indicated that cognitive behavioral and
385 psycho-educational therapies have a significant positive impact. These therapies
386 improved QoL, reduced anxiety and depression, and improved mood. The study
387 found that treatment lasting between six and twelve weeks achieved better
388 psychological results than shorter or longer interventions (32). Relaxation
389 techniques are commonly used in mindfulness programs and psychological
390 interventions to alleviate symptoms of depression, anxiety, stress, and fear of
391 recurrence. Survivors of BC have reported improved sleep quality after practicing
392 these techniques. (33). Cognitive-behavioral approaches have successfully
393 overcome fatigue and improved sleep quality. (34). A randomized trial conducted by
394 Rogers et al. revealed that physical activity positively impacted overall sleep quality
395 compared to usual care in BC patients. (35).

396 Patients with BC have benefitted from virtual psychological interventions. One study
397 called the Web-Based Stress Management for Newly Diagnosed Patients with
398 Cancer (STREAM) developed an online stress management program that
399 significantly improved the QoL for patients in the intervention group (73.2%)
400 compared to the control group (59%). The Hospital Anxiety and Depression scale
401 (HADS) score decreased, mainly due to reduced levels of distress (20). Another
402 study used a web-based psychological intervention called Web-Based Self-
403 Management for Psychological Adjustment After Primary Breast Cancer (BREATH),
404 which resulted in lower levels of distress (84%) and clinical deterioration (16%) for
405 the intervention group (36).

406 **Conclusion**

407 Although there have been several studies on interventions for breast cancer patients,
408 such as those related to nutrition, physical activity, mindfulness, or psychological
409 support, these interventions have typically been conducted separately and focused

410 primarily on survivors. This highlights the necessity for multidisciplinary
411 interventions, as proposed in this study.

412 **Acknowledgments**

413 The authors thank the CAAI (Centro de Apoyo para la Atención Integral) of the
414 Instituto Nacional de Cancerología for the facilities and spaces for the
415 implementation of workshops for the described intervention.

416 **Contributors**

417 Cruz-Ramos: protocol design, principal researcher, and draft preparation. Fajardo-
418 Espinoza: Protocol design, draft preparation, nutritional intervention design, and
419 implementation. Martínez-Palacios: Draft preparation and hybrid educational
420 intervention design. Pérez-Camargo: Nutritonal intervention design and
421 implementation. Cedillo-Compeán: Oncological rehabilitation intervention design
422 and implementation. Rodríguez-Fonseca: Mindfulness specialist, hybrid educational
423 intervention design and implementation. Blandón-Hernández and Labra-Alvarado:
424 Psychological and Mindfulness Intervention Implementation. Gálvez-Hernández and
425 Bejarano-Colina: Psychological intervention design and implementation. Villarreal-
426 Garza: Reviewer and protocol design. Cabrera-Nieto, Barranco-Cortés, González-
427 Pérez, Madariaga-Cobos: Nutritional intervention implementation. Bargalló-Rocha,
428 Matus-Santos, Espinosa-Fernández and Cabrera-Galeana oncological follow-up
429 protocol and patient reference to the program. Mohar-Betancourt: Reviewer and
430 protocol design.

431 **Conflict of interest**

432 The authors declare no conflicts of interest.

433 **Patient consent for publication.** Not required

434 **Ethics approval**

435 The authors declare that this study was conducted according to the Declaration of
436 Helsinki, and all procedures were performed with adequate understanding and
437 written consent from the individuals. The study protocol was approved by the Ethics
438 Committee of Instituto Nacional de Cancerología (023-005-OMI, CEI-025022).

439 **Funding**

440 None. At the time of publication, the project had not received any specific grant from
441 public, commercial, or not-for-profit funding agencies or laboratories.

442 **Data availability statement.**

443 Study results are not available yet.

444

445 1. Amadou A, Torres-Mejía G, Hainaut P, Romieu I. Breast cancer in
446 Latin America: global burden, patterns, and risk factors.

447 2. Bessonneau V, Rudel RA. Mapping the human exposome to uncover
448 the causes of breast cancer. *Int J Environ Res Public Health.* 2020 Jan 1;17(1).

449 3. Fang M, Hu L, Chen D, Guo Y, Liu J, Lan C, et al. Exposome in human
450 health: Utopia or wonderland? Vol. 2, The Innovation. Cell Press; 2021.

451 4. Daiber A, Kröller-Schön S, Frenis K, Oelze M, Kalinovic S, Vujacic-
452 Mirski K, et al. Environmental noise induces the release of stress hormones
453 and inflammatory signaling molecules leading to oxidative stress and vascular
454 dysfunction—Signatures of the internal exposome. Vol. 45, *BioFactors.*
455 Blackwell Publishing Inc.; 2019. p. 495–506.

456 5. Kalita-de Croft P, Sharma S, Sobrevia L, Salomon C. Extracellular
457 vesicle interactions with the external and internal exposome in mediating
458 carcinogenesis. Vol. 87, *Molecular Aspects of Medicine.* Elsevier Ltd; 2022.

459 6. Reynoso Noverón N, Villarreal Garza C, Soto Pérez de Celis E, Arce
460 Salinas C, Matus Santos J, Ramírez Ugalde MT, et al. Clinical and
461 Epidemiological Profile of Breast Cancer in Mexico: Results of the Seguro
462 Popular. 2017.

463 7. Shaikh H, Bradhurst P, Ma LX, Tan SY, Egger SJ, Vardy JL. Body
464 weight management in overweight and obese breast cancer survivors. Vol.
465 2020, *Cochrane Database of Systematic Reviews.* John Wiley and Sons Ltd;
466 2020.

467 8. Villarreal-Garza C, Platas A, Miaja M, Mesa-Chavez F, Garcia-Garcia
468 M, Fonseca A, et al. Patients' satisfaction with a supportive care program for
469 young breast cancer patients in Mexico: Joven & Fuerte supports patients'
470 needs and eases their illness process. *Supportive Care in Cancer.* 2020 Oct
471 1;28(10):4943–51.

472 9. Bustamante-Marin XM, Merlino JL, Devericks E, Carson MS, Hursting
473 SD, Stewart DA. Mechanistic Targets and Nutritionally Relevant Intervention

474 Strategies to Break Obesity–Breast Cancer Links. Vol. 12, *Frontiers in*
475 *Endocrinology*. Frontiers Media S.A.; 2021.

476 10. Ee C, Cave A, Vaddiparthi V, Naidoo D, Boyages J. Factors associated
477 with weight gain after breast cancer: Results from a community-based survey
478 of Australian women. *Breast*. 2023 Jun 1;69:491–8.

479 11. Nyrop KA, Deal AM, Shachar SS, Park J, Choi SK, Lee JT, et al.
480 Weight trajectories in women receiving systemic adjuvant therapy for breast
481 cancer. *Breast Cancer Res Treat*. 2020 Feb 1;179(3):709–20.

482 12. Perry S, Kowalski TL, Chang CH. Quality of life assessment in women
483 with breast cancer: Benefits, acceptability and utilization. Vol. 5, *Health and*
484 *Quality of Life Outcomes*. 2007.

485 13. Villarreal-Garza C, Águila C, Platas A, Lara-Guerra H. Cáncer de
486 mama en mujeres jóvenes en México: necesidades y retos clínicos. *Revista*
487 *de Investigación Clínica*. 2014;66(6):547–88.

488 14. Campbell-Enns H, Woodgate R. The psychosocial experiences of
489 women with breast cancer across the lifespan: a systematic review protocol.
490 *JBI Database System Rev Implement Rep*. 2015 Jan 1;13(1):112–21.

491 15. Montagnese C, Porciello G, Vitale S, Palumbo E, Crispo A, Grimaldi
492 M, et al. Quality of life in women diagnosed with breast cancer after a 12-month
493 treatment of lifestyle modifications. *Nutrients*. 2021 Jan 1;13(1):1–15.

494 16. Ruiz-Vozmediano J, Löhnchen S, Jurado L, Recio R, Rodríguez-
495 Carrillo A, López M, et al. Influence of a Multidisciplinary Program of Diet,
496 Exercise, and Mindfulness on the Quality of Life of Stage IIA–IIB Breast Cancer
497 Survivors. *Integr Cancer Ther*. 2020;19.

498 17. Richards J, Arensberg MB, Thomas S, Kerr KW, Hegazi R, Bastasch
499 M. Impact of early incorporation of nutrition interventions as a component of
500 cancer therapy in adults: A review. Vol. 12, *Nutrients*. MDPI AG; 2020. p. 1–
501 19.

502 18. Dieli-Conwright CM, Wong L, Waliany S, Bernstein L, Salehian B,
503 Mortimer JE. An observational study to examine changes in metabolic
504 syndrome components in patients with breast cancer receiving neoadjuvant or
505 adjuvant chemotherapy. *Cancer*. 2016 Sep 1;122(17):2646–53.

506 19. Snetselaar LG, de Jesus JM, DeSilva DM, Stoody EE. Dietary
507 Guidelines for Americans, 2020-2025: Understanding the Scientific Process,
508 Guidelines, and Key Recommendations. *Nutr Today*. 2021 Nov-
509 Dec;56(6):287-295.

510 20. Urech C, Grossert A, Alder J, Scherer S, Handschin B, Kasenda B, et
511 al. Web-Based Stress Management for Newly Diagnosed Patients With
512 Cancer (STREAM): A Randomized, Wait-List Controlled Intervention Study. *J
513 Clin Oncol* [Internet]. 2018;36:780-8. Available from:
514 <https://doi.org/10.1200/JCO.2017>.

515 21. Fowler S. Diabetes Prevention Program (V8) [Dataset]. NIDDK Central
516 Repository. 2023;

517 22. Hauner D, Rack B, Friedl T, Hepp P, Janni W, Hauner H. Rationale
518 and description of a lifestyle intervention programme to achieve moderate
519 weight loss in women with non-metastatic breast cancer: The lifestyle
520 intervention part of the SUCCESS C Study. *BMJ Nutr Prev Health*. 2020 Dec
521 1;3(2):213-9.

522 23. Di Meglio A, Martin E, Crane TE, Charles C, Barbier A, Raynard B, et
523 al. A phase III randomized trial of weight loss to reduce cancer-related fatigue
524 among overweight and obese breast cancer patients: MEDEA Study design.
525 *Trials*. 2022 Dec 1;23(1).

526 24. Febvey-Combes O, Jobard E, Rossary A, Pialoux V, Foucaut AM,
527 Morelle M, et al. Effects of an Exercise and Nutritional Intervention on
528 Circulating Biomarkers and Metabolomic Profiling During Adjuvant Treatment
529 for Localized Breast Cancer: Results From the PASAPAS Feasibility
530 Randomized Controlled Trial. *Integr Cancer Ther*. 2021;20.

531 1. Amadou A, Torres-Mejía G, Hainaut P, Romieu I. Breast cancer in
532 Latin America: global burden, patterns, and risk factors.

533 2. Bessonneau V, Rudel RA. Mapping the human exposome to uncover
534 the causes of breast cancer. *Int J Environ Res Public Health*. 2020 Jan 1;17(1).

535 3. Fang M, Hu L, Chen D, Guo Y, Liu J, Lan C, et al. Exposome in human
536 health: Utopia or wonderland? Vol. 2, The Innovation. Cell Press; 2021.

537 4. Daiber A, Kröller-Schön S, Frenis K, Oelze M, Kalinovic S, Vujacic-
538 Mirski K, et al. Environmental noise induces the release of stress hormones
539 and inflammatory signaling molecules leading to oxidative stress and vascular

540 dysfunction—Signatures of the internal exposome. Vol. 45, BioFactors.
541 Blackwell Publishing Inc.; 2019. p. 495–506.

542 5. Kalita-de Croft P, Sharma S, Sobrevia L, Salomon C. Extracellular
543 vesicle interactions with the external and internal exposome in mediating
544 carcinogenesis. Vol. 87, Molecular Aspects of Medicine. Elsevier Ltd; 2022.

545 6. Reynoso Noverón N, Villarreal Garza C, Soto Pérez de Celis E, Arce
546 Salinas C, Matus Santos J, Ramírez Ugalde MT, et al. Clinical and
547 Epidemiological Profile of Breast Cancer in Mexico: Results of the Seguro
548 Popular. 2017.

549 7. Shaikh H, Bradhurst P, Ma LX, Tan SY, Egger SJ, Vardy JL. Body
550 weight management in overweight and obese breast cancer survivors. Vol.
551 2020, Cochrane Database of Systematic Reviews. John Wiley and Sons Ltd;
552 2020.

553 8. Villarreal-Garza C, Platas A, Miaja M, Mesa-Chavez F, Garcia-Garcia
554 M, Fonseca A, et al. Patients' satisfaction with a supportive care program for
555 young breast cancer patients in Mexico: Joven & Fuerte supports patients'
556 needs and eases their illness process. *Supportive Care in Cancer*. 2020 Oct
557 1;28(10):4943–51.

558 9. Bustamante-Marin XM, Merlino JL, Devericks E, Carson MS, Hursting
559 SD, Stewart DA. Mechanistic Targets and Nutritionally Relevant Intervention
560 Strategies to Break Obesity–Breast Cancer Links. Vol. 12, *Frontiers in
561 Endocrinology*. Frontiers Media S.A.; 2021.

562 10. Ee C, Cave A, Vaddiparthi V, Naidoo D, Boyages J. Factors associated
563 with weight gain after breast cancer: Results from a community-based survey
564 of Australian women. *Breast*. 2023 Jun 1;69:491–8.

565 11. Nyrop KA, Deal AM, Shachar SS, Park J, Choi SK, Lee JT, et al.
566 Weight trajectories in women receiving systemic adjuvant therapy for breast
567 cancer. *Breast Cancer Res Treat*. 2020 Feb 1;179(3):709–20.

568 12. Perry S, Kowalski TL, Chang CH. Quality of life assessment in women
569 with breast cancer: Benefits, acceptability and utilization. Vol. 5, *Health and
570 Quality of Life Outcomes*. 2007.

571 13. Villarreal-Garza C, Águila C, Platas A, Lara-Guerra H. Cáncer de
572 mama en mujeres jóvenes en México: necesidades y retos clínicos. *Revista
573 de Investigación Clínica*. 2014;66(6):547–88.

574 14. Campbell-Enns H, Woodgate R. The psychosocial experiences of
575 women with breast cancer across the lifespan: a systematic review protocol.
576 JBI Database System Rev Implement Rep. 2015 Jan 1;13(1):112–21.

577 15. Montagnese C, Porciello G, Vitale S, Palumbo E, Crispo A, Grimaldi
578 M, et al. Quality of life in women diagnosed with breast cancer after a 12-month
579 treatment of lifestyle modifications. Nutrients. 2021 Jan 1;13(1):1–15.

580 16. Ruiz-Vozmediano J, Löhnenchen S, Jurado L, Recio R, Rodríguez-
581 Carrillo A, López M, et al. Influence of a Multidisciplinary Program of Diet,
582 Exercise, and Mindfulness on the Quality of Life of Stage IIA–IIB Breast Cancer
583 Survivors. Integr Cancer Ther. 2020;19.

584 17. Richards J, Arensberg MB, Thomas S, Kerr KW, Hegazi R, Bastasch
585 M. Impact of early incorporation of nutrition interventions as a component of
586 cancer therapy in adults: A review. Vol. 12, Nutrients. MDPI AG; 2020. p. 1–
587 19.

588 18. Dieli-Conwright CM, Wong L, Waliany S, Bernstein L, Salehian B,
589 Mortimer JE. An observational study to examine changes in metabolic
590 syndrome components in patients with breast cancer receiving neoadjuvant or
591 adjuvant chemotherapy. Cancer. 2016 Sep 1;122(17):2646–53.

592 19. U.S. Department of Agriculture. <https://www.myplate.gov/>. My Plate.

593 20. Urech C, Grossert A, Alder J, Scherer S, Handschin B, Kasenda B, et
594 al. Web-Based Stress Management for Newly Diagnosed Patients With
595 Cancer (STREAM): A Randomized, Wait-List Controlled Intervention Study. J
596 Clin Oncol [Internet]. 2018;36:780–8. Available from:
597 <https://doi.org/10.1200/JCO.2017>.

598 21. Fowler S. Diabetes Prevention Program (V8) [Dataset]. NIDDK Central
599 Repository. 2023;

600 22. Hauner D, Rack B, Friedl T, Hepp P, Janni W, Hauner H. Rationale
601 and description of a lifestyle intervention programme to achieve moderate
602 weight loss in women with non-metastatic breast cancer: The lifestyle
603 intervention part of the SUCCESS C Study. BMJ Nutr Prev Health. 2020 Dec
604 1;3(2):213–9.

605 23. Di Meglio A, Martin E, Crane TE, Charles C, Barbier A, Raynard B, et
606 al. A phase III randomized trial of weight loss to reduce cancer-related fatigue

607 among overweight and obese breast cancer patients: MEDEA Study design.
608 Trials. 2022 Dec 1;23(1).

609 24. Febvey-Combes O, Jobard E, Rossary A, Pialoux V, Foucaut AM,
610 Morelle M, et al. Effects of an Exercise and Nutritional Intervention on
611 Circulating Biomarkers and Metabolomic Profiling During Adjuvant Treatment
612 for Localized Breast Cancer: Results From the PASAPAS Feasibility
613 Randomized Controlled Trial. Integr Cancer Ther. 2021;20.

614 25. Batsis JA, McClure AC, Weintraub AB, Sette D, Rotenberg S, Stevens
615 CJ, et al. Barriers and facilitators in implementing a pilot, pragmatic,
616 telemedicine-delivered healthy lifestyle program for obesity management in a
617 rural, academic obesity clinic. Implement Sci Commun. 2020 Dec 1;1(1).

618 26. King DK, Shoup JA, Raebel MA, Anderson CB, Wagner NM, Ritzwoller
619 DP, et al. Planning for Implementation Success Using RE-AIM and CFIR
620 Frameworks: A Qualitative Study. Front Public Health. 2020 Mar 3;8.

621 27. De Cicco P, Catani MV, Gasperi V, Sibilano M, Quaglietta M, Savini I.
622 Nutrition and breast cancer: A literature review on prevention, treatment and
623 recurrence. Vol. 11, Nutrients. MDPI AG; 2019.

624 28. Hoy MK, Winters BL, Chlebowski RT, Papoutsakis C, Shapiro A, Lubin
625 MP, et al. Implementing a Low-Fat Eating Plan in the Women's Intervention
626 Nutrition Study. J Am Diet Assoc. 2009 Apr;109(4):688–96.

627 29. Demark-Wahnefried W. Reduced rates of metabolism and decreased
628 physical activity in breast cancer patients receiving adjuvant chemotherapy1 3
629 [Internet]. Vol. 65. 1997. Available from:
630 <https://academic.oup.com/ajcn/article-abstract/65/5/1495/4655500>

631 30. Makari-Judson G, Braun B, Joseph Jerry D, Mertens WC. Weight gain
632 following breast cancer diagnosis: Implication and proposed mechanisms. Vol.
633 5, World Journal of Clinical Oncology. Baishideng Publishing Group Co.,
634 Limited; 2014. p. 272–82.

635 31. Kabat-Zinn J. Mindfulness-based interventions in context: Past,
636 present, and future. Vol. 10, Clinical Psychology: Science and Practice. 2003.
637 p. 144–56.

638 32. Guarino A, Polini C, Forte G, Favieri F, Boncompagni I, Casagrande
639 M. The effectiveness of psychological treatments in women with breast cancer:

640 A systematic review and meta-analysis. Vol. 9, Journal of Clinical Medicine.
641 MDPI; 2020.

642 33. Lengacher CA, Reich RR, Paterson CL, Shelton M, Shivers S,
643 Ramesar S, et al. A Large Randomized Trial: Effects of Mindfulness-Based
644 Stress Reduction (MBSR) for Breast Cancer (BC) Survivors on Salivary
645 Cortisol and IL-6. *Biol Res Nurs.* 2019 Jan 1;21(1):39–49.

646 34. Widiasih R, Ermiati, Jayanti TN, Rais Y. Psychosocial Interventions for
647 Improving the Quality of Life in Breast Cancer Survivors: A Literature Review.
648 In: IOP Conference Series: Earth and Environmental Science. Institute of
649 Physics Publishing; 2019.

650 35. Rogers LQ, Courneya KS, Oster RA, Anton PM, Robbs RS, Forero A,
651 et al. Physical activity and sleep quality in breast cancer survivors: A
652 randomized trial. *Med Sci Sports Exerc.* 2017 Oct 1;49(10):2009–15.

653 36. Van Den Berg SW, Gielissen MFM, Custers JAE, Van Der Graaf WTA,
654 Ottevanger PB, Prins JB. BREATH: Web-based self-management for
655 psychological adjustment after primary breast cancer-results of a multicenter
656 randomized controlled trial. *Journal of Clinical Oncology.* 2015 Sep
657 1;33(25):2763–71.