Effects of Mobile Healthcare Applications on the Lifestyle of Patients With Breast Cancer: A Protocol for a Randomized Clinical Trial

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ABSTRACT

Purpose: Physical activity (PA) in patients with breast cancer is associated with improved quality of life (QoL); however, many breast cancer survivors do not meet the recommended PA level. This study aims to evaluate the effect of digital health interventions using mobile apps to promote PA and QoL in patients with postoperative breast cancer. This study will also identify effective digital intervention methods and perform an economic analysis. The main hypothesis is that the use of mobile healthcare apps will improve health-related quality of life (HRQOL), promote PA, and reduce healthcare costs.

Methods: The Promotion of a better lifestyle (PA) with Precise and Practicable digital healthcare in postoperative CANCER patients through a Multi-Disciplinary Network (P4CancerMDnet) study is examined by a prospective 4-group randomized controlled trial with a concurrent cost–utility evaluation. Patients are randomly assigned to 3 different mobile app intervention groups or control groups in a 1:1:1:1 ratio. The intervention group is encouraged to use the assigned mobile app. The targeted outcomes are HRQOL, metabolic health markers, and quality-adjusted life-years. The outcomes will be measured at the 6- and 12-month follow-ups.

Discussion: This study will contribute towards a better lifestyle and HRQOL through digital healthcare for postoperative breast cancer patients. These findings are expected to provide evidence of the effectiveness of mobile apps for breast cancer survivors.

Trial Registration: Clinical Research Information Service Identifier: KCT0005447

Keywords: Breast Neoplasms; Cost–Utility Analysis; mHealth; Survivorship

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INTRODUCTION

Breast cancer is the most common cancer in women worldwide [1]. In the past few decades, breast cancer mortality has decreased owing to the development of screening and adjuvant therapies [2]. As a result, the number of breast cancer survivors is rapidly increasing, and in 2019, there were more than 3.8 million breast cancer survivors in the United States [3]. Cancer diagnosis and treatment cause significant psychosocial distress and decreased quality of life (QoL) in cancer survivors [4,5]. The National Comprehensive Cancer Network and American Society of Clinical Oncology guidelines recommend distress screening and management in patients [6,7].

Exercise is one of the recommended non-pharmacological interventions for distress management [7]. Increased physical activity (PA) significantly (13%–51%) reduces breast cancer-specific mortality in breast cancer survivors [8,9]. In addition, current evidence indicates that regular participation in PA may alleviate common side effects of adjuvant therapy for breast cancer and improve QoL [10]. Breast cancer survivors should aim for at least 150 minutes of moderate or 75 minutes of vigorous aerobic exercise per week [11]. However, only 32% of breast cancer survivors meet the recommended amount of exercise [12]. Physical inactivity is associated with poor health-related QoL (HRQOL) [13].

The number of cancer survivors with comorbidities has significantly increased over the past 2 decades [14]. Moreover, adjuvant treatment for breast cancer after surgery is related to weight gain and has a negative impact on the metabolic profile, which negatively affects breast cancer prognosis [15]. Several studies have investigated the association between lifestyle and breast cancer prognosis, which is emerging as an important survivorship issue [16]. Risk factors related to diet, PA, and metabolism can be improved by lifestyle modifications.

Mobile healthcare has emerged as a way to improve QoL and modify lifestyles. Mobile health (mHealth) is defined by the World Health Organization’s Global Observatory for eHealth as “medical and public health practice supported by mobile devices, such as mobile phones, patient monitoring devices, personal digital assistants, and other wireless devices” [17]. Recently, the number of mHealth apps has increased with the high utilization of smartphones, and there has been growing interest from users. However, there is insufficient evidence regarding the use of mHealth apps in cancer survivors [18]. Moreover, no studies have examined which mobile app is most effective and economical for breast cancer survivors. Therefore, we designed and initiated a randomized trial for the Promotion of a better lifestyle (PA) with Precise and Practicable digital healthcare in postoperative CANCER patients through a Multi-Disciplinary Network (P4CancerMDnet).

This study aims to evaluate the degree of improvement in QoL and metabolic indicators through exercise, diet, and lifestyle correction in patients who underwent surgery for breast cancer and to identify effective digital interventions. The main hypothesis is that the use of mHealth apps will improve HRQOL, promote PA, and reduce healthcare costs.
METHODS

Study design
P4CancerMDnet is a single-center, 4-group, randomized controlled trial with concurrent cost–utility evaluation. This study (protocol version 2.6 on July 19, 2021) was approved by the Institutional Review Board (IRB) of Asan Medical Center (2020-1015) and was registered in the Clinical Research Information Service of the Republic of Korea (KCT0005447; date of registration, October 6, 2020). Participants will be recruited from an academic medical center in South Korea. Written informed consent will be obtained from all participants by the investigators prior to enrollment. Investigators will generate the allocation sequence using a computer program, enroll participants, and assign them to groups. Patients will be randomly assigned in a 1:1:1:1 ratio to the 3 mobile healthcare intervention groups (groups A, B, or C) or the control group (group D) postoperatively. The enrolled patients will be stratified according to chemotherapy status (neoadjuvant, adjuvant, or no chemotherapy). Randomization will be performed using an Internet-based system. The study design and participant flow are shown in Figure 1. Patients in the intervention group will have access to the mHealth app and receive routine care and follow-ups. Patients in the control group will receive routine care and follow-ups.

Study population
This study enrolled women with stage 0–III breast cancer aged 20–60 years at diagnosis who underwent curative breast cancer surgery. Eligible patients had an Eastern Cooperative Oncology Group performance status of 0. Patients with recurrent or metastatic breast cancer, those with a severe underlying disease such as cardiovascular disease, and those who did not have or could not use a smartphone were excluded. Recruitment began in November 2020 and was completed in September 2021.

Figure 1. Study flowchart.
Intervention

After randomization, patients in the intervention group downloaded the app assigned to their smartphones. The investigator instructed them on how to use the app. We used 3 mHealth apps as a study platform: (1) Noom (Noom, Inc., New York, USA), a paid global mobile app that provides a structured curriculum and personalized feedback using artificial intelligence and human coaches who communicate with users in real time. Users are encouraged to log their daily diet, weight, and exercise into the application and receive personalized feedback. Screenshots from the Noom app (Figure 2) show the main screen and its functions. (2) WalkOn (Swallaby Co., Ltd., Seoul, Korea) is a free mobile app that tracks activities. Users can record their daily step counts and the intensity of walking. This app also provides an activity ranking among users. In this app, we opened the mobile app-based community for this study, where users can view other members’ daily step counts to motivate them and promote health-related activities. Screenshots from the WalkOn app (Figure 3) show the main screens and the ranking system. (3) Second Doctor (Medi Plus Solution Co., Ltd., Seoul, Korea) is a paid mobile app only for patients with cancer. There are separate apps for each cancer type, and these apps are specialized for the health management of cancer patients. When users start to use this app, they are encouraged to enter cancer-related information (surgery information and ongoing treatment), in addition to basic characteristics. Users can log their daily diet, weight, and exercise into the apps. If the user has linked the smart band to the app, the number of steps is automatically recorded in the app. This app provides one-on-one cancer-specific online consultation. Screenshots from the Second Doctor app (Figure 4) show the main screen and functions. By using 3 apps with different features, we can compare the effects of personalized and general feedback (Noom vs. others), paid and free apps (Noom and Second Doctor vs. WalkOn), and a general and cancer-specific app (Second Doctor vs. others).

Figure 2. Screenshots from the Noom app. (A) The main screen where users can record and view daily weight, diet, water intake, target walking steps, and other records from above. (B) Daily diet input screen with calorie information for each meal—calories for breakfast, snack, lunch, snack, dinner, and snack from above. (C) Consultation chat on daily diet with a human coach.
Endpoints and assessments

The study endpoints will be compared between each of the 4 study groups: Noom app group, WalkOn app group, Second Doctor app group, and control group. The primary endpoint is to compare the HRQOL at 6 months. The secondary endpoints are to compare (1) the degree of change in body measurements, such as body weight, body mass index, and waist circumference; (2) the changes in distress level; (3) the level of side effects of antihormonal therapy; and (4) the changes in laboratory test values related to metabolic abnormalities. Outcomes will be measured at enrollment and at the 6- and 12-month follow-up. The 3- and 18-month follow-up periods are optional. Schedules of measures and time of assessment are shown in the format recommended by the Standard Protocol Items: Recommendations for Interventional Trials (SPIRIT) guidelines (Figure 5). We will also evaluate compliance with the use of the app in the intervention group. The SPIRIT checklist is presented in Supplementary Table 1.

HRQOL is measured using the EuroQol five-dimension (EQ-5D), Health-related Quality of Life Instrument with 8 Items, and Fear of Progression Questionnaire – Short Form. The side effects of antihormonal therapy are evaluated using the Menopause Rating Scale questionnaire, and bone mineral density is measured using dual-energy X-ray absorptiometry (DXA). Follow-up DXA after the initial test is performed based on clinical needs. The patient’s level of distress is measured using the Patient Health Questionnaire-9 and a Distress Thermometer. Metabolic health outcomes are measured using body measurements (body weight, body mass index, and waist circumference) and laboratory tests (fasting blood sugar, HbA1c, triglyceride, and high-density lipoprotein-cholesterol levels). In addition, regarding the cost item, we will consider individual patients’ healthcare costs for breast cancer.
The cost-effectiveness of each intervention will be measured by the incremental cost–utility ratio (ICUR), which compares changes in healthcare costs and quality-adjusted life years (QALY) between the intervention and control groups upon completion of patient follow-up. Sensitivity analyses of the ICUR will be conducted by considering variations in costs and utility.

**Data collection**

Clinicopathological data will be collected from electronic medical records when patients are recruited. Data will be collected until 18 months after the last patient enrollment, and each patient will be followed-up every 6 months after baseline data collection. Outcomes related to HRQOL will be collected via self-report, paper-based questionnaires. Logged data from each application will be collected from the intervention groups. Medical data will be collected using an electronic case-report form. Socioeconomic data and healthcare costs will be collected from medical registers after the completion of the follow-up for cost–utility analysis of the intervention. Compliance with mHealth apps will be analyzed by collecting data regarding the access time of each app. Unique identification codes are assigned to each patient to protect patient data. Healthcare cost data will be obtained from the hospital database for claims. All data are stored in a file accessible by a password and can only be used by investigators. Important protocol modifications will be decided by all investigators through online and offline meetings, and will be updated in the Clinical Research Information Service of the Republic of Korea registry with IRB approval. There is no

Figure 4. Screenshots from the Second Doctor app. (A) The main screen where users can record and view daily exercise, diet, blood sugar, blood pressure, time to take medicine, weight with emoticon boxes at the top, and a daily summary of walking step counts, calories burned, sleeping time, and stress level at the bottom. (B) Cancer-specific information input screen for cancer type, surgery information including name of surgery, date of surgery, and date of discharge, chemotherapy, endocrine therapy, and radiotherapy from above. (C) Online consultation screen showing the question waiting to be answered at the top, and the question answered by a nutrition expert and an exercise expert at the bottom.
data monitoring committee because there are no safety concerns caused by this study. Data monitoring will be performed by the investigators.

**Sample size calculation**

This study was powered to detect differences in QoL between the 4 groups at 6 months. In the previous study of QoL in patients with breast cancer, the EQ-5D index of the patients at 6 months was approximately 0.86 (standard deviation [SD], 0.1). Conversely, the EQ-5D index of the healthy control group considering age was 0.95 (SD, 0.08) [19]. Generally, a

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**Figure 5.** Timeline of enrollment and assessments.  
HDL = high-density lipoprotein; BMD = bone mineral density; DXA = dual-energy X-ray absorptiometry; EQ-5D = EuroQol five-dimension; HINT-8 = Health-related Quality of Life Instrument with 8 Items; FoP-Q-SF = Fear of Progression Questionnaire – Short Form; MRS = Menopause Rating Scale; PHQ-9 = Patient Health Questionnaire-9; DT = Distress Thermometer.  
*Follow-up assessments will be performed 6- and 12-month after surgery, and 3- and 18-month follow-ups will be optional depending on the patient.  
†DXA assessment based on clinical needs.
meaningful, minimally important difference for EQ-5D is approximately 0.03–0.07 [20,21]. Therefore, it was assumed that the difference in EQ-5D scores at 6 months was 0.05. The null hypothesis of this study was that there would be no difference in the EQ-5D index between the 4 groups. In this study, the alpha error was corrected by considering 4 clinical trial groups. Assuming a corrected alpha error of 0.008 and power of 0.8, the sample size for each group was calculated to be at least 63 to reject the null hypothesis. Assuming a dropout rate of 20%, the sample size was calculated as 79. Therefore, the final sample size was calculated to be 80 in each group, for a total of 320 participants. Sample size calculations were performed using a website [22].

**Data analyses**

Data analyses will be performed using SPSS version 21.0 (IBM Corp., Armonk, USA). The main aim will be to examine the differences between and within groups and investigate the cost–utility outcome. Descriptive statistics (frequency and percentage) will be applied for categorical variables, and the \( \chi^2 \) test and Fisher’s exact test will be used for comparison. The Student’s \( t \)-test or Mann-Whitney test will be used for continuous variables. The variances of each group will be compared using a one-way repeated-measures analysis of variance for the 4 groups, and the significant difference between the groups will be tested. Data will be analyzed following both intention-to-treat and per-protocol analyses. Multiple imputations will be used for the missing data. For the economic analysis, we will calculate the ICUR by comparing the cost and QALY between the intervention and control groups. Investigators will share the study results through presentations at relevant scientific conferences and publications in peer-reviewed scientific journals.

**DISCUSSION**

Many unmet needs persist, even after treatment for breast cancer [23]. The HRQOL and lifestyle are important components of survivorship care. To improve PA in breast cancer survivors, intervention strategies that can increase PA tailored to the current situation are required. One study suggested that self-management programs have several benefits, including improved knowledge, acquisition of skills, and self-monitoring for cancer survivors [24]. The mHealth app on a personal smartphone could be a way to implement self-management of cancer survivorship care.

Adherence to digital healthcare interventions varies between studies depending on the study subject, intervention method, and duration of intervention. A review of adherence to Internet interventions for anxiety and depression reported lower dropout rates from randomized controlled trials of web interventions compared to the dropout rates from open access websites [25]. In contrast, a randomized study of web-based interventions for PA showed that the interventions were efficacious at 4 months but did not maintain improvements in HRQOL and daily step counts at 12 months [26]. In our previous observational study, we reported a higher overall compliance rate for smartphone apps to collect PA data than for smart bands (data collection rates of smartphone apps vs. smart bands: 88.0% vs. 52.5%) [27]. This suggests that simple activity tracking alone has a limit in encouraging user behavior, and the dropout rate increases in the long-term follow-up.

Therefore, the development of mobile apps using cognitive behavioral therapy principles has increased in the research area [28]. The apps used in this study have functions related to
cognitive behavior. By using 3 apps with different specialized functions, we try to evaluate which one will be the most effective for survivorship care. The Noom (Noom, Inc.) app was considered to provide active assurance through personalized artificial intelligence and human coaches. The WalkOn (Swallaby Co., Ltd.) app was considered to motivate health-related activities through activity ranking and user community. The Second Doctor (Medi Plus Solution Co., Ltd.) app was considered to provide cancer-specific and tailored management for breast cancer through a one-on-one consultation.

In addition to the analysis of clinical outcomes, economic evaluations of mobile healthcare interventions are gradually increasing [29]. However, few studies have combined the clinical outcomes and economic evaluations of the use of apps for cancer survivors. We plan to conduct a cost–utility analysis of the intervention, which may confirm the utility of the app.

Among the growing number of mHealth apps, little is known about which features of mHealth apps are the most effective and how effective they will be. To the best of our knowledge, our study is the first randomized controlled trial to compare the effects of multiple apps combined with an economic evaluation for postoperative breast cancer. The results of this study will provide evidence of the effectiveness of mHealth apps for breast cancer survivors. This study will contribute to a better lifestyle and HRQOL through mHealth apps for patients with postoperative breast cancer.

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SUPPLEMENTARY MATERIAL

Supplementary Table 1
SPIRIT checklist

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REFERENCES

1. Siegel RL, Miller KD, Fuchs HE, Jemal A. Cancer statistics, 2022. CA Cancer J Clin 2022;72:7-33.
PUBMED | CROSSREF
2. Berry DA, Cronin KA, Plevritis SK, Fryback DG, Clarke L, Zelen M, et al. Effect of screening and adjuvant therapy on mortality from breast cancer. N Engl J Med 2005;353:1784-92.
PUBMED | CROSSREF
3. DeSantis CE, Ma J, Gaudet MM, Newman LA, Miller KD, Goding Sauer A, et al. Breast cancer statistics, 2019. CA Cancer J Clin 2019;69:438-51.
PUBMED | CROSSREF
4. Schumacher JR, Palta M, Loconte NK, Trentham-Dietz A, Wirt WP, Heidrich SM, et al. Characterizing the psychological distress response before and after a cancer diagnosis. J Behav Med 2013;36:591-600.
PUBMED | CROSSREF
5. Lidgren M, Wilking N, Jönsson B, Rehnberg C. Health related quality of life in different states of breast cancer. Qual Life Res 2007;16:1073-81.
PUBMED | CROSSREF
6. Riba MB, Donovan KA, Andersen B, Braun I, Breithart WS, Brewer BW, et al. Distress management, version 3.2019, NCCN clinical practice guidelines in oncology. J Natl Compr Canc Netw 2019;17:1229-49.

7. Andersen BL, DeRubeis RJ, Berman BS, Gruman J, Champion VL, Massie MJ, et al. Screening, assessment, and care of anxiety and depressive symptoms in adults with cancer: an American Society of Clinical Oncology guideline adaptation. J Clin Oncol 2014;32:1605-19.

8. Beasley JM, Kwan ML, Chen WY, Weltzien EK, Kroenke CH, Lu W, et al. Meeting the physical activity guidelines and survival after breast cancer: findings from the after breast cancer pooling project. Breast Cancer Res Treat 2012;131:637-43.

9. Friedenreich CM, Neilton HK, Farris MS, Cournaya KS. Physical activity and cancer outcomes: a precision medicine approach. Clin Cancer Res 2016;22:4766-75.

10. Loprinzi PD, Cardinal BJ. Effects of physical activity on common side effects of breast cancer treatment. Breast Cancer 2012;19:4-10.

11. Runowicz CD, Leach CR, Henry NL, Henry KS, Mackey HT, Cowens-Alvarado RL, et al. American Cancer Society/American Society of Clinical Oncology breast cancer survivorship care guideline. CA Cancer J Clin 2016;66:43-73.

12. Murphy DJ, Myers MG Jr, liberman RA, Mersky L, Prouty RA, Portenoy RK, et al. Multimodal pain management in breast cancer: American Society of Clinical Oncology clinical practice guideline update 2009. J Clin Oncol 2009;27:5720-30.

13. Irwin ML, McTiernan A, Bernstein L, Gilliland FD, Baumgartner R, Baumgartner K, et al. Physical activity levels among breast cancer survivors. Med Sci Sports Exerc 2004;36:1484-91.

14. Paxton RJ, Phillips KL, Jones LA, Chang S, Taylor WC, Cournaya KS, et al. Associations among physical activity, body mass index, and health-related quality of life by race/ethnicity in a diverse sample of breast cancer survivors. Cancer 2012;118:4024-31.

15. Jiang C, Deng L, Karr MA, Wen Y, Wang Q, Perimbetti S, et al. Chronic comorbid conditions among adult cancer survivors in the United States: results from the National Health Interview Survey, 2002-2018. Cancer 2022;128:828-38.

16. Arpino G, De Angelis C, Buono G, Colao A, Giuliano M, Malgieri S, et al. Metabolic and anthropometric changes in early breast cancer patients receiving adjuvant therapy. Breast Cancer Res Treat 2015;154:127-32.

17. Milne-Ives M, Lam C, De Cock C, Van Velthoven MH, Meinert E. Mobile apps for health behavior change in physical activity, diet, drug and alcohol use, and mental health: systematic review. JMIR Mhealth Uhealth 2020;8:e17046.

18. Yu J, Son WS, Lee SB, Chung IY, Son BH, Ahn SH, et al. Uneven recovery patterns of compromised health-related quality of life (EQ-5D-3 L) domains for breast cancer survivors: a comparative study. Health Qual Life Outcomes 2018;16:143.

19. Walters SJ, Brazier JE. Comparison of the minimally important difference for two health state utility measures: EQ-5D and SF-6D. Qual Life Res 2005;14:1523-32.

20. Tsiplova K, Pullenayegum E, Cooke T, Xie F. EQ-5D-derived health utilities and minimally important differences for chronic health conditions: 2011 Commonwealth Fund Survey of Sicker Adults in Canada. Qual Life Res 2016;25:3009-16.

21. Brant R. n.d. Power/sample size calculator. https://www.stat.ubc.ca/~rollin/stats/ssize/n2.html. Accessed February 15th, 2022.

22. Cheng KK, Wong WH, Koh C. Unmet needs mediate the relationship between symptoms and quality of life in breast cancer survivors. Support Care Cancer 2016;24:2025-33.
24. Nolte S, Elsworth GR, Sinclair AJ, Osborne RH. The extent and breadth of benefits from participating in chronic disease self-management courses: a national patient-reported outcomes survey. Patient Educ Couns 2007;65:351-60.

PUBMED | CROSSREF

25. Christensen H, Griffiths KM, Farrer L. Adherence in internet interventions for anxiety and depression. J Med Internet Res 2009;11:e13.

PUBMED | CROSSREF

26. Moy ML, Martinez CH, Kadri R, Roman P, Holleman RG, Kim HM, et al. Long-term effects of an internet-mediated pedometer-based walking program for chronic obstructive pulmonary disease: randomized controlled trial. J Med Internet Res 2016;18:e215.

PUBMED | CROSSREF

27. Chung IY, Jung M, Lee SB, Lee JW, Park YR, Cho D, et al. An assessment of physical activity data collected via a smartphone app and a smart band in breast cancer survivors: observational study. J Med Internet Res 2019;21:e13463.

PUBMED | CROSSREF

28. Rathbone AL, Clarry L, Prescott J. Assessing the efficacy of mobile health apps using the basic principles of cognitive behavioral therapy: systematic review. J Med Internet Res 2017;19:e399.

PUBMED | CROSSREF

29. Iribarren SJ, Cato K, Falzon L, Stone PW. What is the economic evidence for mHealth? A systematic review of economic evaluations of mHealth solutions. PLoS One 2017;12:e0170581.

PUBMED | CROSSREF