Effectiveness of an online support program to help female cancer patients manage their health and illness: Protocol for a randomized controlled trial

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1. Introduction

For patients diagnosed with cancer, coping with the experience and keeping themselves in good health requires that they successfully manage various health-related issues. Information and communications technology (ICT) is being proactively introduced into the healthcare
management of cancer patients. Several systematic reviews have corroborated the positive effects of e-health–based self-management [1], web-based interventions in managing symptoms [2], and mobile phone apps for cancer-related information needs [3]. In response to such a context, we have developed an online support program designed to maintain or improve the quality of life in female cancer patients by empowering them to manage their own health. To verify the effectiveness of our program, we have planned a randomized controlled trial.

1.1. Theoretical basis of the online support program

This study protocol and the online support program were developed from within the context of self-regulation theory, in which goals form an important part of human behavior and energize and direct one’s activities [4]. Many patients diagnosed with cancer struggle with how they should manage their health and life, because their real life is filled with experiences that threaten their goals, standards, and reference values for health. According to self-regulation theory, however, if one is adequately aware of a discrepancy between existing goals and reality, one can take self-regulatory actions in a variety of ways to reduce that discrepancy.

Our online support program consists of three different apps: a monitoring app, a confirmation app, and a writing app. These apps are designed to stimulate cancer patients to find and set their own health-related goals and adapt their behavior to achieve those goals through providing opportunities to monitor health conditions (monitoring app), assess their own understanding of the disease and its treatment (confirmation app), and address mental health issues (writing app). When cancer patients use these apps, they may develop a clearer awareness about discrepancies between their own reality and their goals, standards, and reference values related to their health and illness. At that time, if they want to maintain or improve health-related quality of life (HR-QOL), their desire for reducing discrepancies can elicit self-regulatory actions.

In our program, patient-reported outcomes (PROs) about HR-QOL are collected electronically as patients monitor their health using the monitoring app. Quality of life is a term that represents “an overall sense of well-being, including aspects of happiness and satisfaction with life as a whole” [5], and the HR-QOL concept covers aspects of overall quality of life that affect physical and mental health [5]. PROs refer to “health experiences and evaluations that are assessed by patient report, such as symptoms, assessments of functioning, well-being, health perceptions, and satisfaction with care” [6]. In this study we will measure PROs by using three different HR-QOL scales incorporated in the monitoring app: the Ferrans and Powers Quality of Life Index (QLI) [7,8], the M.D. Anderson Symptom Inventory (MDASI) [9], and the Hospital Anxiety and Depression Scale (HADS) [10,11]. The validity and effectiveness of measuring PROs via electronic media (ePROs) with HR-QOL scales in clinical cancer settings is supported by the results of several studies [12–15]. In our current program, patients can use the monitoring app to compare their current and previous HR-QOL ePROs to track their health progress. Such comparisons seem to work in favor of setting and striving for realistic goals with respect to their health without having too high expectations.

Meanwhile, cancer patients’ understanding of their disease and treatment has a high impact on their goals, standards, and values regarding their health and illness. We think that if using the confirmation app can promote a correct understanding of their disease and treatment and adequate preparation for their illness, it will function effectively to improve HR-QOL by increasing self-regulation to reduce the discrepancies between their goals and reality.

The third component—the writing app—is used to provide an expressive writing intervention, which is one type of expressive psychotherapy. The effectiveness of expressive writing interventions was first tested in 1986 [16,17], and their effectiveness in terms of both psychological and biological health has been subsequently supported by many studies, including a meta-analysis [18]. Patients are asked to write down their deepest thoughts and feelings about a stressful event, and such reflection on the cancer experience is expected to reactivate patients’ self-regulatory actions to manage their disturbed mood and ruminations.

1.2. Theoretical framework of this study

The apps constituting our online support program currently only target patients who have breast cancer, colon cancer, uterine cancer, ovarian cancer, and thyroid cancer. These cancers are particularly common among Japanese women; for example, according to 2016–2018 data [19], breast cancer and colon cancer rank the first and second in incidence/morbidity among Japanese women, and the incidence rate of thyroid cancer in women is 2.7 times that in men. Since there is a wide range of cancer types and treatments, the scope of cancers covered by the confirmation app is restricted to those that are most typical among Japanese women. The age range of the target population is broadly set from 18 to 75 years old; this is based on a study of Japanese breast cancer patients that found that acceptability of using tablet computers to record ePROs was not necessarily age dependent [20].

Because of the several types of cancers in the targeted patients, it is necessary to take into consideration the influence that variations in recovery course, experience, and environmental characteristics have on patients’ HR-QOL. For example, in one study of breast cancer patients, several factors such as older age, economic burden, and higher levels of depression were found to be predictive of the trajectory of their HR-QOL [21]. Therefore, we have chosen to conduct a randomized controlled trial (RCT) to control the influence of such factors.

1.2.1. Study hypothesis

The study hypothesis is that female cancer patients who use all three of the apps composing this online support program will better maintain and improve their HR-QOL measured at 6 months after their first health monitoring compared with those who only monitor their health. We are assuming that compared to the ePROs measured before patients undergo cancer treatment (baselines), the ePROs at 1 month after the first health monitoring will be lower, and that the ePROs at 3 months after the first health monitoring will be higher than those at 1 month after the first health monitoring. It is said that the existential plight that results from being diagnosed with cancer diminishes after the first 100 days [22]. Therefore, the discrepancy that patients notice between their goals and the reality of having cancer might also decrease around that time which will have the effect of reducing their self-regulatory behaviors. However, we thought that if patients who had experienced using the confirmation app to think about their disease and treatment could use the writing app to reactivate their self-regulation activities, they might begin to take more action to improve their HR-QOL. And we expect these reactivated self-regulation activities to continue for 3 months. Meanwhile, we thought that the ePROs of patients who use only the monitoring app (the control group) would probably not improve by 6 months after the first health monitoring compared to those who use all three apps. Additionally, the type of cancer is predicted to make a difference in the average scores of ePROs measured at each time point but to make no difference in the longitudinal recuperative process with respect to HR-QOL.

2. Materials and methods

2.1. Design

The aim of this RCT is to test the effectiveness of intervention using the three apps of the online support program, adopting HR-QOL scores as an indicator to assess the outcome of the intervention. The study is designed as an open, randomized parallel-group trial, with a longitudinal data-collecting method. Patients assigned to the experimental group...
will use all three apps: the monitoring app, confirmation app, and writing app. Patients assigned to the control group will use only the monitoring app. Additionally, stratified permuted block randomization will be adopted, with the stratification factor being the type of cancer: breast, colon, uterine (two sites: corpus of the uterus and endocervix), ovarian, and thyroid.

2.2. Sampling and participants

This study’s subjects are to be female cancer patients receiving treatment at the National Cancer Center Hospital East (NCCHE) in Japan. Participants will be recruited at the outpatient units until the target sample size is achieved. The planned sample size was set to a total of 210 subjects in two groups, and the sampling period is slated to last 1 year.

2.2.1. Inclusion criteria

Patients will be included if they meet the following criteria: (a) have a diagnosis of cancer (breast cancer, colon cancer, uterine cancer, ovarian cancer, or thyroid cancer) and have had their medical condition and treatment courses explained by their physician; (b) are receiving treatment for the first time in the NCCHE; (c) are waiting to be treated in hospital or in an outpatient setting; (d) are from 18 to 75 years old at the time of obtaining informed consent; (e) can go through the online support program using a tablet computer, personal computer, or smartphone in an outpatient setting or in their homes; and (f) are required to receive treatment at either the Department of Breast Surgery, Department of Medical Oncology, Department of Gynecology, Department of Gastrointestinal Oncology, or Department of Head and Neck Medical Oncology.

2.2.2. Exclusion criteria

To ensure safety and efficacy, patients will be excluded if (a) the physician or nurse in charge determines that there is a high possibility of a detrimental health effect occurring if the patient participates in the online support program; (b) the physician or nurse in charge determines that the patient is mentally unstable and will have difficulty participating in the online support program; or (c) a physician in charge or a nurse in charge knows that the patient needs to receive hospital treatment for at least 1 month or longer.

2.2.3. Withdrawal of participants

A participant will be regarded as withdrawn from the study if (a) the clinical diagnosis of cancer is reversed by subsequent histopathological diagnosis; (b) the participant requests to be withdrawn or withdraws consent; (c) hospitalization for more than 1 month is required; (d) the physician or nurse in charge judges that it is appropriate that participation be withdrawn; or (e) the participant discontinues and does not resume using the apps.

2.3. Procedures

A member of this research team will obtain informed consent from each participant after careful explanation of the study, by both oral and written means. The participants will then be registered for this clinical study through the Electronic Data Capture (EDC) system and be randomly allocated to one of two groups: the experimental group or the control group.

The flowchart of participation and the participant flow through study in this longitudinal study is shown in Figs. 1 and 2, respectively. Participants will access the apps for this online support program via a dedicated URL. After completion of registration and before initiation of treatment, participants of both groups will use the monitoring app for health monitoring; the ePROs generated at that time become the baseline of each group. Subsequently, the confirmation app will be used by participants in the experimental group to assess their understanding of

| Time point | t₁ | t₂ | t₃ | t₄ |
|------------|----|----|----|----|
| Enrolment  | X  | X  | X  | X  |
| Interventions | Monitoring app | X  | X  | X  | X  |
|             | Confirmation app | X  |    |    |    |
|             | Writing app      | X  |    |    |    |
| Assessments/evaluations | Background information | X  | X  |    |    |
|             | Endpoints/outcomes | X  | X  | X  | X  |
|             | Healthcare satisfaction | X  |    |    | X  |
|             | Program evaluation |    |    |    | X  |

* Time point: t₁ = baseline; t₂ = 1 month later; t₃ = 3 months later; t₄ = 6 months later.

Fig. 1. Flowchart of participation.
their diagnosis and treatment and their readiness. In addition to the first health monitoring (baseline), participants of both groups will use the monitoring app another three times (four times in all): 1 month later, 3 months later, and 6 months later. After their third health monitoring, participants of the experimental group will use the writing app to address mental health issues. Additionally, participants of both groups will answer a questionnaire at the beginning of the study and again at the end to assess their satisfaction with respect to healthcare, and they will answer an additional questionnaire at the end evaluating their satisfaction with the program. Participants will receive an email reminder shortly before each app needs to be run.

2.3.1. Data storage/management

Both the EDC and online support program systems will be login controlled (ID and password authentication) for each user. Two research members authorized to access the clinical information will anonymize participants’ personal information at the time of case registration. Therefore, names and other identifiable information will not be stored on the online sites. After the RCT is completed, the electronic data will be downloaded onto a portable hard drive in the form of CSV files, and the Principal Investigator will securely store them in a locked filing cabinet for 10 years. Personally identifiable information such as written informed consent will be securely stored in the NCCHC Ladies Center for 10 years.

2.3.2. Ethical considerations and declarations

Approval was obtained in March 2022 from the institutional review board (IRB) of the university hospital with which the Principal Investigator is affiliated (Ethics Committee University of Tsukuba Hospital, R03-243), and implementation of the study was then approved by the IRB of NCCHC, the hospital in which recruitment of study subjects is to be conducted. This study protocol complies with the Japanese government’s Ethical Guidelines for Medical and Biological Research Involving Human Subjects, which came into effect in March 2021 [23], and is conducted so as to protect the participants’ rights in terms of privacy and confidentiality. The ethical guidelines used have been repeatedly revised to comply with the Act on the Protection of Personal Information in Japan. This clinical trial is registered in the Japan Registry of Clinical Trials (Registration Number: JRCT1030210638).

2.4. Support program and apps

2.4.1. Monitoring app

The monitoring app incorporates Japanese-language versions of three different HR-QOL scales (QLI, MDASI, and HADS) that have been proven to be of high reliability and validity [7–11]. Users of the monitoring app answer the questions of these HR-QOL scales and receive a personalized HR-QOL report in the form of average scores and visual line plots representing changes in their HR-QOL scores over time. The app is set up so that users must answer all of the questions required for one scale before opening the next scale.

The QLI consists of two parts that respectively measure satisfaction with and importance of various aspects of daily life using a 1–6 scale across 33 paired items [24]. Once the QLI questions are answered, users are provided, in the form of average scores, with information about their own subjective well-being and overall QOL (total QLI score) and QOL in four domains (subscale scores): health and functioning, psychological and spiritual, social and economic, and family. The possible range of final QLI scores is from 0 to 30, with a lower score indicating a worse QOL. Studies have shown that the Japanese version of the QLI is culturally appropriate [7] and has sufficient reliability and validity to be able to evaluate the impact of cancer and treatment in research and clinical practice [8].

The MDASI consists of two parts that respectively assess the extent of symptoms experienced during the last 24 h and how much those symptoms interfere with various aspects of the patient’s life [25]. Users get to know outcomes of their own assessment through answering questions of a 6-item symptom scale and a 13-item interference scale. Each question of both scales is measured using a 0–10 scale, with higher scores indicating more severe symptoms and interference. The reliability and validity of the Japanese version of the MDASI have been verified [9], and it has been applied to a wide range of research on cancer treatment and clinical practice.

The HADS consists of 14 questions that measure depression and anxiety in patients treated in a clinical setting [26]. Through answering the questions, users can detect their own state of anxiety and depression as either ‘negative’, ‘doubtful’, or ‘definite’, with cutoff points of both scores within the total range of 0–21 for each state. It has been verified that the Japanese version of the HADS is a sensitive and specific screening tool to detect psychological distress in Japanese cancer patients [10,11].

2.4.2. Confirmation app

By answering each online question, users of the confirmation app are able to assess their comprehension of their disease and treatment and their readiness to receive treatment. The confirmation app provides users with an opportunity to think of the impact of the disease and the treatment on themselves and their significant others, life with the illness, and the rest of their life, and to ascertain whether they want to consult someone else (doctor, nurse, other health professional, or family) to help them understand aspects of their disease and treatment that they do not fully comprehend.

The composition of questions used to assess comprehension and readiness was framed around those on the website from the National Cancer Center Japan [19], which offers a ‘cancer information providing service’ for the general population. A nursing representative on this research team prepared a draft version of questions for the confirmation app. Physicians on the research team who conduct diagnosis and treatment and explain those aspects to patients then adjusted the draft questions to better fit their clinical practice, and nurses of the research team added improvements to the content and form of the questions to better fit the patients’ health care needs. The Principal Investigator made the final decision on the contents of the app.

2.4.3. Writing app

The writing app provides the expressive writing intervention. The
format of this intervention follows that of Pennebaker’s guidebook [27],
taking into consideration findings from studies that tested the effects of
expressive writing interventions on Asian breast cancer patients
[28–31]. After the health monitoring at 3 months—a point by which the
impact of a cancer diagnosis generally seems to have become less
intense—users of the writing app are asked to recall a shocking episode
or emotionally stirring story. For 3 days a week over 3 weeks, they write
or type for 20 min a day their account of that stressful event to express
their deepest thoughts and feelings. Their writing is stored on the
dedicated server so that users can go back over it at any time they
choose.

2.5. Evaluation indicators

For each subject in this study, ID code, birth month, date of first visit,
provisional name of the disease, treatment planning, medical history,
departments providing medical care, group allocation (experimental
group or control group), and information on their pathological diag-
nosis, staging, functional disorders, treatment status, and departments
providing medical care will be collected through the EDC system. In
formation on subjects’ education, cohabitant(s), and occupation will be
collected from participants’ responses in the online support program.
The ePROs that are collected through the apps will be used as outcome
measures of this trial.

2.5.1. Primary endpoint

The primary endpoint will be the difference between total QLI scores
measured at baseline and those measured 6 months later.

2.5.2. Secondary endpoints

The indicators used as the secondary endpoints will be: (a) the total
QLI scores measured at baseline, 1 month later, and 3 months later; and
(b) four QLI subscale scores (health/functioning, social/economic,
psychological/spiritual, family), two MDASI subscale scores (symptoms,
symptom-related interference), and two HADS subscale scores (anxiety,
depression) measured at baseline, 1 month later, 3 months later, and 6
months later.

2.5.3. Other indicators

Other indicators will be (a) nominal variables drawn from partici-
pants’ responses to questions in the confirmation app, (b) descriptions
stored when participants engage in expressive writing, (c) level of
satisfaction with healthcare, and (d) evaluation of the functioning of
each app of the online support program.

2.6. Statistical analyses

2.6.1. Sample size

Based on previously published data [8,32–35], we assume that the
mean difference between the experimental and control groups will be 2
points in the QLI scale and the standard deviation will be 5 points in the
QLI scale. The possible range of total QLI score is from 0 to 30. A sample
size of 100 subjects per treatment group will be required to detect a
difference of this magnitude with 80% power for the primary analysis. In
consideration of differences between our study and the previous study
[8] in the methods of handling missing data, the planned sample size is
conservatively set to 105 subjects per group.

2.6.2. Analyses

Three statistical data sets will be used in the analyses: (a) a full
analysis set (FAS) including all subjects who used the apps at least twice
and underwent assessment of the primary endpoint after randomization;
(b) a per-protocol set (PPS) including all subjects without violations of the
eligibility criteria (selection and exclusion criteria) and who used the
apps at the prescribed frequency; and (c) a safety analysis set (SAS)
including all subjects who were randomized. The efficacy analysis will
be performed with the FAS and PPS. The safety analysis will be performed
with the SAS.

To evaluate the mean treatment effect, we will conduct a mixed
model for repeated measures (MMRM analysis [36]) to detect changes in
the total QLI score from baseline to 6 months. The MMRM analysis
model will include the fixed effects of group, time point (1 month later, 3
months later, and 6 months later), group × time interaction, and base-
line measurements. As the primary statistical test, a t-test for the dif-
erence of the adjusted means of the total QLI score between the groups
at 6 months will be conducted. For the secondary analysis, a subgroup
analysis will be conducted by each cancer type. Furthermore, we will
evaluate the demographics of the patients and use this data to provide
descriptive characteristics of the population. We will evaluate whether
any differences in the baseline characteristics between the two groups is
found by a two-sample t-test or Fisher’s exact test after calculating the
mean, standard deviation, and frequency of each baseline characteristic.
The safety assessment will calculate the frequencies and rates of adverse
events. The difference between groups will be analyzed by using Fisher’s
exact test. We will use Stata 16 (StataCorp LP, College Station, TX, USA)
and SAS version 9.4 (SAS Institute Inc., Cary, NC, USA) to conduct the
statistical analyses. Results will be deemed significant at P < 0.05, and
statistical tests will be conducted for two-tailed hypotheses.

3. Discussion

A study of Japanese cancer patients found that simply providing
them with the opportunity to measure their HR-QOL using an electronic
device and providing them a report of their own ePRO was insufficient to
improve or maintain their HR-QOL [20]. In this study, we regard the
confirmation app and writing app as necessary to support the function of
the monitoring app, which provides patients the opportunity to assess
the state that their own health condition is in. The writing app is ex-
pected to give patients the opportunity to process suppressed thoughts
and to address illness-related tasks and cope with them.

3.1. Limitations

With regard to the effectiveness of patients conducting a dialogue
with physicians and nurses about the ePRO profiles elicited through
these apps, although this matter is beyond the scope of the intervention
of our online support program and this study protocol, it has been re-
ported that a physician’s communication style with patients holds the
key to the key to the benefit of assessing HR-QOL using an electronic tool
when patients initiate discussions with the physician about their HR-QOL
profile [37]. Future studies will be needed to identify what approaches
patients need to take to make most efficient use of their own
ePRO profiles.

3.2. Conclusions

If our study’s hypothesis is correct, female cancer patients who use
all three apps will have better HR-QOL than those who use only the
monitoring app. Because our program is based on self-regulation theory,
it is important that the program works in an efficient way to help female
cancer patients find and set goals relevant to their experience of health
and illness and change their behavior to meet their goals through using
each app. That is, it is expected that the experimental group will find it
easier to find and set goals and to refer to those goals to improve their
health-related behaviors than will the control group.

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Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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