Lymphoma InterVEntion (LIVE) – patient-reported outcome feedback and a web-based self-management intervention for patients with lymphoma: study protocol for a randomised controlled trial

Lindy P. J. Arts1*, Lonneke V. van de Poll-Franse1,2,3, Sanne W. van den Berg4, Judith B. Prins4, Olga Husson4, Floortje Mols1,3, Angelique V. M. Brands-Nijenhuis5, Lidwine Tick6 and Simone Oerlemans1,3

Abstract

Background: Patients with lymphoma are at risk of experiencing adverse physical and psychosocial problems from their cancer and its treatment. Regular screening of these symptoms by the use of patient-reported outcomes (PROs) could increase timely recognition and adequate symptom management. Moreover, self-management interventions intend to enhance knowledge and skills and empower patients to better manage their disease and related problems. The objective of the Lymphoma InterVEntion (LIVE) trial is to examine whether feedback to patients on their PROs and access to a web-based, self-management intervention named Living with lymphoma will increase self-management skills and satisfaction with information, and reduce psychological distress.

Methods/design: The LIVE randomised controlled trial consists of three arms: (1) standard care, (2) PRO feedback, and (3) PRO feedback and the Living with lymphoma intervention. Patients who have been diagnosed with Hodgkin lymphoma, non-Hodgkin lymphoma, including chronic lymphocytic leukaemia, as registered in the Netherlands Cancer Registry in various hospitals will be selected for participation. Patients are invited via their haemato-oncologist 6 to 15 months after diagnosis. The PRO feedback includes a graphical overview of patients’ own symptom and functioning scores and an option to compare their scores with those of other patients with lymphoma and a normative population of the same age and sex. The Living with lymphoma intervention is based on cognitive behavioural therapy components and includes information, assignments, assessments, and videos. Changes in outcomes from baseline to 16 weeks, 12, and 24 months post intervention will be measured. Primary outcomes are self-management skills, satisfaction with information, and psychological distress. Secondary outcomes are health-related quality of life, illness perceptions, fatigue, and health care use.

(Continued on next page)
Discussion/design: The results of the LIVE trial will provide novel insights into whether access to PRO feedback and the Living with lymphoma intervention will be effective in increasing self-management skills and satisfaction with information, and reducing distress. The LIVE trial is embedded in a population-based registry, which provides a unique setting to ascertain information on response, uptake, and characteristics of patients with lymphoma in web-based intervention(s). When effective, PRO feedback and Living with lymphoma could serve as easily and widely accessible interventions for coping with lymphoma.

Trial registration: Netherlands Trial Register, identifier NTR5953. Registered on 14 July 2016.

Keywords: Lymphoma, Intervention, Self-management, Psychological distress, Information provision, Patient-reported outcomes, PRO feedback, Population-based, Randomised controlled trial

Background
Due to advances in treatment, the 20-year prevalence of Hodgkin lymphoma (HL) and non-Hodgkin lymphoma (NHL) in the Netherlands is expected to increase by 5% to 6300 and 32,000 patients in 2020, respectively [1, 2]. As a result of their cancer and its treatment, patients with lymphoma are at risk of experiencing adverse physical and psychosocial problems, such as fatigue, neuropathy, and lymphoma at risk of experiencing adverse physical and psychosocial problems, such as fatigue, neuropathy, and cognitive and emotional problems [3–6]. Patients who report adverse problems have a lower health-related quality of life (HRQoL) and visit their physician more often [7–9]. In addition, up to a quarter of patients with lymphoma experience persistent levels of anxiety, depressive feelings, and fears, also called psychological distress [7, 10].

Patient-reported outcomes (PROs) intend to evaluate the impact of a disease and its treatment from the perspective of the patient [11]. PROs are being increasingly recognised to be important in daily practice [12, 13]. Regular screening of physical and psychosocial symptoms by the use of PROs could increase awareness and recognition of symptoms and can contribute to adequate symptom management [11, 14–17]. Moreover, the greater the resources available for coping with symptoms and stress, the lower the risk for psychological distress [18]. Interventions using cognitive behavioural therapy (CBT) components, such as psychoeducation and coping skills, can reduce persistent psychological distress and physical problems and improve HRQoL [8].

As the number of patients surviving lymphoma continues to grow, interventions need to be easily accessible without increasing the burden on health services. Self-management interventions can be effective in strengthening the role of patients, by increasing patient engagement in care, and limiting the burden on health services [19, 20]. Self-management interventions aim to empower patients to have an active role in the management of their disease and its symptoms and consequences including treatment, physical, and psychosocial and lifestyle changes [21, 22]. Web-based technologies are particularly suitable for self-management interventions since they are easily accessible, can reach a large number of patients [19, 23], and provide more anonymity compared to face-to-face interventions [24]. Therefore, web-based interventions have the potential to eliminate barriers to psychosocial care for patients with cancer. However, it is important that such interventions should be evidence-based and empirically tested [25].

The Lymphoma InterVEntion (LIVE) trial consists of two interventions: (1) feedback to patients on their PROs, and (2) a web-based, self-management intervention named Living with lymphoma. Patients will be randomised to: (1) standard care, (2) standard care plus access to PRO feedback or (3) standard care plus access to PRO feedback and the Living with lymphoma intervention. PRO feedback enables patients to monitor their symptoms and compare them with outcomes among other patients. This may help to either reassure that what they experience is ‘normal’ or may empower them to take action. The Living with lymphoma intervention is based on CBT components and is an adaptation from the evidence-based BREAst cancer e-health (BREATHT) intervention [26]. By using the Living with lymphoma intervention, patients will receive psychoeducation and learn coping skills which they can apply as self-management skills in daily life.

Methods/design
Objectives and hypotheses
The objective of the LIVE trial is to examine whether PRO feedback and the Living with lymphoma intervention will increase self-management skills and satisfaction with information and reduce psychological distress. In concordance with the stress-coping model of Lazarus and Folkman (1984), psychological adjustment after cancer is determined by the balance between stress and resources [18]. Therefore, it is hypothesised that patients with access to PRO feedback and/or the Living with lymphoma intervention will report increased self-management skills and satisfaction with information (greater resources available for coping), and lower levels of psychological distress compared to patients receiving standard care.
Moreover, it is expected that patients with access to both PRO feedback and the *Living with lymphoma* intervention will benefit most.

**Study design**
The LIVE trial is designed as a nonblinded randomised controlled trial with three arms. For an overview of the design of the trial, see Fig. 1. Standard care plus the access to PRO feedback and the *Living with lymphoma* intervention (arm 3) will be compared to standard care plus access to PRO feedback (arm 2) and standard care (arm 1). Patients with lymphoma from various hospitals in the Netherlands will be included and asked to complete questionnaires at four points in time: baseline (T0; 6 to 15 months after diagnosis), after 16 weeks (T1; post intervention), after 12 months (T2), and after 24 months (T3).

**Study population**
All patients who have been diagnosed with HL or NHL, including chronic lymphocytic leukaemia (CLL), as defined by the International Classification of Diseases for Oncology-3 codes (ICD-O-3) [27], in the participating hospitals will be selected for participation via the Netherlands Cancer Registry (NCR). Patients must be aged 18 years or older at the time of diagnosis. Patients who have problems with the Dutch language, patients with severe psychopathology or dementia, and patients in transition to terminal care will be excluded from the study.

**Setting**
The LIVE trial will be conducted within the Patient Reported Outcomes Following Initial treatment and Long-term Evaluation of Survivorship (PROFILES) registry [28]. PROFILES is a tool that enables data collection management; from inviting patients to participation in studies, to collecting PRO data via web-based or mailed questionnaires and linking these data with clinical data. Since this trial is embedded in the population-based PROFILES lymphoma registry, we have access to information on response, uptake, and user characteristics of patients with lymphoma in a web-based intervention.

**Recruitment**
The population-based NCR of the Netherlands Comprehensive Cancer Organisation (IKNL) will be used to
select all patients in the participating hospitals who meet the inclusion criteria. The NCR registers all newly diagnosed cancer patients within 6 months after diagnosis. After excluding deceased patients, the treating haemat Oncologists are asked to verify the patients’ study eligibility. All eligible patients will be invited for participation by their own haemat-oncologist. The haemat-oncologists will provide the eligible patients with an invitation package, including an invitation letter and leaflet to inform them about the study, a postcard, and two Informed Consent Forms (i.e. one for the researchers and one for the patient). The letter explains the study objectives and includes a link and password to a secure website so that patients can complete questionnaires online. If patients prefer paper-and-pencil participation, they can complete the postcard and return it by mail to the study manager. Patients will then receive paper-and-pencil questionnaires and a pre-stamped envelope within 1 week of receipt of the postcard. Patients are informed that paper-and-pencil participation automatically means that they will not be able to participate in the LIVE trial and only participate in the observational PROFILES lymphoma registry, as both PRO feedback and the Living with lymphoma intervention are web-based.

If the questionnaire is not completed within 3 weeks, a reminder will be sent by the treating haemat-oncologists. After obtaining informed consent, the subsequent communication to the patients will be addressed via PROFILES. To guarantee anonymity, questionnaires only contain a study number.

Randomisation
Patients who complete the baseline questionnaire online and consent to participate in the LIVE trial will be automatically randomised in an equal ratio (1:1:1) to one of the three study arms: (1) standard care, (2) standard care plus access to PRO feedback or (3) standard care plus access to PRO feedback and the Living with lymphoma intervention. This randomisation will be performed using block randomisation. The randomisation will be performed by a computer randomisation program which will ensure a balance in sample size across groups over time [29].

Interventions versus standard care
Arm 1: Standard care
For patients randomised to arm 1, the haemat-oncologist provides standard care. Most haemat-oncologists give their patients leaflets regarding the diagnosis and treatment they receive. Most information is given during the initial treatment phase, and some of the haemat-oncologists give additional information during follow-up for ad hoc referrals if needed by the patient. Patients who receive standard care can use information about lymphoma on the Internet, but do not have access to PRO feedback or the Living with lymphoma intervention.

Arm 2: PRO feedback
Patients randomised to arms 2 and 3 have access to PRO feedback, including general HRQoL, physical, emotional, cognitive and social functioning, fatigue, neuropathy (only for patients with high-grade NHL), and anxiety and depressive symptoms.

Patients can compare their scores to mean scores of other patients with lymphoma (same sex and age group) and/or a normative population (same sex and age group) to find out whether their scores are average or not (using a traffic light model). A detailed description of how to interpret the scores is added to assist patients in understanding the graphs. Mean scores of the lymphoma sample are extracted from data of our previous research on HRQoL among 856 patients with lymphoma [30]. The normative population was selected from a reference cohort of 1859 individuals from the general Dutch population (CentERpanel). This cohort is representative for the Dutch-speaking population in the Netherlands [31].

Individual scores will be integrated into graphical displays with coloured bar-charts [32, 33]. The colours of the bar-charts are related to clinically relevant mean differences of the evidence-based guidelines of the EORTC QLQ-C30 [34]. A score that differs less than the minimal medium clinically relevant difference from the mean score is considered ‘average’ (amber). A score that differs as much as or more than the minimal medium clinically relevant difference from the mean score is considered ‘above average’ (green) or ‘below average’ (red). The interpretation of anxiety and depressive symptoms is according to the published scoring algorithm: 0–7 indicating no or mild symptoms (green), 8–10 indicating moderate symptoms (amber), and ≥11 indicating severe symptoms (red) [35]. Patients with a score in the red part of the chart are advised to contact their general practitioner. For an example of PRO feedback, see Fig. 2.

To review the PRO feedback, patients have to click on the ‘feedback’ tab after completing the questionnaire. Patients can decide not to review their PRO feedback as they prefer not to.

Arm 3: PRO feedback plus Living with lymphoma intervention
In addition to PRO feedback, patients randomised to arm 3 get access to the Living with lymphoma intervention. This web-based self-management intervention is an adaptation of the evidence-based BREATHT intervention for breast cancer survivors [26, 36]. The content of the intervention is adapted to warrant its relevance for patients with lymphoma. Symptoms that
are typically common in patients with lymphoma, such as neuropathy, infections, and infertility, have been added.

One key feature of the intervention is the ‘work space’ that includes four phases: (1) ‘looking back,’ (2) ‘emotional processing,’ (3) ‘strengthening,’ and (4) ‘looking ahead.’ For a screenshot of the ‘work space,’ see Fig. 3. The intervention is based on CBT techniques, such as psychoeducation, to enhance patients’ knowledge and skills, for instance by providing tailored advices based on patients’ input. Working ingredients of the four phases include information, assignments, assessments, and videos. The information part provides patients with knowledge on various subjects such as adverse physical and psychological problems, work, sexuality, and lifestyle. Assignments are, for example, writing tasks, social engagement or conversation tasks and aim to increase skill-building [26]. Assessments include tests that could be used by patients as a screening instrument of potential problems and are followed by automated feedback. Videos are clips extracted from recorded interviews with patients with lymphoma.

Another feature of the intervention is the library with background and additional information on subjects from the four phases (e.g. work, sexuality, lifestyle). For a screenshot of the library, see Fig. 4. The library also contains links to additional health care services (e.g. psychologists, physiotherapists, dieticians).

The advised intervention usage is one part per week, with a duration of approximately 1 h. However, it is up to the patients how, and to what extent, they use the intervention. From the BREATH intervention it is known that patients use the website quite diversely [37]. The intervention is fully automated and nonguided and is delivered without the professional support of a therapist. Support for content or technical assistance is available by the study manager.

Study outcome measures
Patient demographics and clinical information will be available from the NCR that routinely collects data on, among other things, patients’ age and sex, date of cancer diagnosis, histological classification, stage, treatment, and comorbidity. Information on marital status, educational
level, and employment status are gathered by self-report using questionnaires.

Primary outcomes

Self-management skills are measured by the Health Education Impact Questionnaire (heiQ™) [38]. The heiQ™ contains 40 items across eight scales: positive and active engagement in life, health-directed activities, skill and technique acquisition, constructive attitudes and approaches, self-monitoring and insight, health service navigation, social integration and support, and emotional distress. Each item will be scored on a four-point Likert scale. The scale scores are obtained by computing the mean of respective items. Higher scores indicate better status or self-management, except for emotional distress, in which higher scores indicate higher distress [38]. The heiQ™ has high construct validity [38]. Five scales of the heiQ™ are validated among patients with cancer [39].

Psychological distress will be assessed by the 14-item Hospital Anxiety and Depression Scale (HADS) [35]. A sum score is obtained by adding the items. Its rating system is based on a four-point format and asks how the patient has felt in the past week. Higher scores indicate higher levels of psychological distress. The HADS has shown good reliability and validity in oncology settings [40, 41].

Satisfaction with information will be measured by an adapted version of the 9-item Information Satisfaction Questionnaire (ISQ) [42]. The ISQ has been widely used to assess overall information satisfaction and the need for involvement in decision-making. The original measure requires patients to categorise themselves into one of three groups: those who would like (1) all available information and to be involved in decisions about their illness, (2) only positive information about the illness, and (3) only limited information and would prefer the doctor to make the decisions. However, Fallowfield suggests that there is a distinction between the desire for information and involvement in decision-making [43]. Therefore, we divided that question into two items, one assessing the desire for information and one assessing the desire for involvement in decision-making. Patients are, furthermore, asked to rate their level of satisfaction with the information that they have received about their illness, treatment, and lifestyle. Each of these questions will be scored on a five-point Likert scale. The English version of the ISQ was translated into Dutch by forward-backward translation procedures. Questions about desire for more or less...
information, helpfulness of information, and the use of the Internet (to search for information) were added to the questionnaire.

**Secondary outcomes**

*Health-related quality of life—general* will be assessed using the Dutch validated European Organisation for Research and Treatment of Cancer (EORTC) Quality of Life Questionnaire (QLQ-C30) [44]. This 30-item questionnaire includes five functional scales, three symptom scales, a global health and quality of life scale, and several single-item symptom measures. All items will be scored on a four-point Likert scale, except for the global health and quality of life scale that is scored on a seven-point linear analogue scale. After linear transformation, all scales and single-item measures range in score from 0 to 100. Higher scores on functional and health and quality of life scales indicate better functioning or HRQoL, whereas higher scores on symptom scales indicate more problems [45].

*Self-efficacy* with regard to symptoms (in this study as a result of lymphoma) will be measured with the Self-efficacy Scale (SE28) [46–48]. This scale consists of seven items, which will be scored on a four-point Likert scale. A higher score reflects a greater sense of control. This scale had previously been used to assess self-efficacy concerning post-cancer fatigue [49].

*Adjustment to cancer* will be assessed using the 40-item Mental Adjustment to Cancer Scale (MAC) [50]. Items are rated on a four-point Likert scale. The summary scales (i.e. summary positive adjustment scale, summary negative adjustment scale) can be used to identify general adjustment styles for cancer. The summary positive adjustment scale includes 17 items and scores range from 17 to 68
Morbid conditions that have developed since diagnosis.

**Covariates**

Comorbidity at the time of survey will be assessed with the adapted Self-administered Comorbidity Questionnaire (SCQ) [56]. Patients will be asked to identify comorbid conditions that have developed since diagnosis.

Illness perceptions will be assessed using the validated Brief Illness Perception Questionnaire (B-IPQ) [52]. This scale has nine items, measuring cognitive representations, emotional representations, and illness comprehensibility. Items are scored on a continuous linear 0–10-point scale. A higher score reflects a more threatening view of the illness. The B-IPQ has been previously cross-culturally adapted into the Dutch Language Version (Brief IPQ-DLV), with acceptable face and content validity [53].

Fatigue will be assessed with the 20-item validated Multidimensional Fatigue Inventory (MFI) [54]. The MFI covers five scales: general fatigue, physical fatigue, reduced activity, reduced motivation, and mental fatigue. Each scale contains four items, with two items formulated in a positive (e.g. ‘I feel fit’) and two formulated in a negative direction (e.g. ‘I feel fatigued’). All items are scored on a five-point Likert scale. The negatively formulated items must be recoded before adding up scores. Higher sum scores correspond to more acute levels of fatigue. The MFI is reliable and valid to assess fatigue in patients with cancer [54].

Health care use will be assessed by single items: ‘How often did you contact a general practitioner in the past 12 months?’; ‘How many of these visits were related to cancer of the consequences of your cancer?’; ‘How often did you visit a medical specialist in the past 12 months?’; ‘How many of these visits were related to cancer or to the consequences of your cancer?’ These questions were asked in a similar way as by Statistics Netherlands [55] (http://statline.cbs.nl/). Three questions are asked about follow-up appointments (whether or not receiving follow-up appointment, the frequency of follow-up appointments, and satisfaction with this frequency). Furthermore, patients are asked whether they visited a psychologist, psychiatrist or social worker and the last question was ‘Did you receive care after the treatment of your cancer?’ To answer this question, patients could either choose ‘No’ or ‘Yes’ and then choose multiple additional care services from a list: sexologist, pastoral care, dietician, physical therapist, oncological rehabilitation, creative therapy, oncology nurse, or contact with other cancer survivors.

Personality will be assessed using the Big Five Inventory (BFI) [57]. The BFI is a 44-item inventory designed to measure the Big Five dimensions: extraversion, agreeableness, conscientiousness, neuroticism, and openness to experience. Items are scored on a five-point Likert scale. Scale scores will be created by averaging the items for each domain. The Dutch BFI has good psychometric quality [58].

Usage statistics

In addition to the standardised questionnaires, technical data on the use of the intervention, such as frequency, duration, and activity, will be evaluated.

Sample size calculation

Sample size calculation was performed using G*Power version 3.1.9.2 for Windows. Based on the three primary outcomes of this trial, effect on patient level is defined as increased self-management skills or satisfaction with information (as measured by the heiQ™ and the ISQ, respectively) or reduced psychological distress (as measured with the HADS). Therefore, effectiveness of LIVE is demonstrated when one of the three effects is statistically significant. Significance level of the sample size calculation was adjusted to $p \leq 0.167$ to keep the overall chance for type-I errors at 5%.

Clinically important differences will be determined with Norman’s sum of implied difference, whereby a difference of approximately 0.5 SD indicates a threshold of discriminant change in quality of life scores of a chronic illness [59]. To detect a clinically important difference with 90% power, a sample size of 222 patients with lymphoma (74 in each group) is needed. This sample size calculation is based on a medium effect size of 0.25 for repeated measures analysis of variance (ANOVA) with two measurements, since at least two measurements are necessary to compare pre-intervention and post-intervention outcomes. We take into account a response rate of 70% as observed in earlier studies (of them 60% are expected to complete the questionnaires online) and a study dropout rate of 25%, based on a systematic review on adherence to Internet interventions for anxiety and depression [60]. This results in 663 patients with lymphoma who need to be invited for participation.

Statistical analyses

All statistical analyses will be performed using Statistical Analyses Software (SAS; version 9.4 for Windows, SAS Institute Inc., Cary NC, USA). Analyses on effectiveness of the intervention will be primarily done according to intention-to-treat methodology. Second, per-protocol analysis will be performed to analyze the efficacy of the...
intervention. All statistical tests will be two-sided and considered significant if \( p < 0.05 \).

Missing outcome data will be assumed to be ‘missing at random’ (MAR), conditional on key predictors of ‘missingness’ (in particular, baseline values of the outcome variables of interest, and study arm).

Patients’ sociodemographic and clinical variables will be compared at baseline between the three study arms using chi-square analyses for categorical variables and ANOVA for continuous variables and will be analysed as covariates.

Repeated measures analysis using generalised estimating equations, which account for the intra-patient dependency of the repeated measures, will be used to analyse the effect of the intervention on the outcome variables. We will investigate differences in effect of the two intervention arms and the arm receiving standard care at the different time points. Differential effects of the intervention arms by age, cancer subtype, and baseline levels of the outcomes of interest will be assessed for the outcome measures by adding terms for the interaction between age, cancer subtype, baseline levels, and care arm to the regression models.

Routinely collected data from the population-based NCR on patient and tumour characteristics will enable us to compare paper-and-pencil respondents with online respondents, as well as respondents with nonrespondents and patients with unverifiable addresses in order to determine the external validity of the results and answer our second study objective.

Discussion

Regular screening of symptoms by the use of PROs and access to resources for coping skills could help to detect and/or manage symptoms that up to a quarter of patients with lymphoma are experiencing.

The results of the LIVE trial will provide novel insights into whether access to PRO feedback and the *Living with lymphoma* intervention will be effective in increasing self-management skills and satisfaction with information, and reducing psychological distress. Since one third of patients will be randomised to solely access to PRO feedback and not to the *Living with lymphoma* intervention, it will be possible to investigate the superiority of access to PRO feedback as well as the superiority of access to PRO feedback and the *Living with lymphoma* intervention compared to standard care.

The LIVE trial is embedded in the population-based PROFILES lymphoma registry, which provides a unique setting to ascertain information on response, uptake, and characteristics of patients with lymphoma in web-based intervention(s). This information is important with respect to the generalisability of results and, moreover, it demonstrates which patient subgroups will benefit most from PRO feedback and the *Living with lymphoma* intervention. Patients will not be selected based on their symptoms or distress level prior to study entry and it is up to patients themselves how, and to what extent, they use the intervention(s). When effective, access to PRO feedback and the *Living with lymphoma* intervention could serve as easily and widely accessible interventions for coping with lymphoma in the Netherlands.

**Trial status**

Recruiting.

**Additional files**

| Additional file 1: | SPIRIT 2013 Checklist: recommended items to address in a clinical trial protocol and related documents. (DOC 120 kb) |
|------------------|-------------------------------------------------------------------------------------------------------------------|
| Additional file 2: | SPIRIT Figure: Schedule of enrolment, interventions, and assessments. (DOC 66.5 kb) |

**Abbreviations**

BREATH: BREAsct cancer e-heath; CBT: Cognitive behavioural therapy; CLL: Chronic lymphocytic leukaemia; HL: Hodgkin lymphoma; HRQoL: Health-related quality of life; ICD-O-3: International Classification of Diseases for Oncology, third edition; IKNL: Netherlands Comprehensive Cancer Center; LIVE: Lymphoma InterVention; MAR: Missing at random; NCR: Netherlands Cancer Registry; NHIL: Non-Hodgkin lymphoma; PRO: Patient-reported outcomes; PROFILES: Patient Reported Outcomes Following Initial treatment and Long-term Evaluation of Survivorship; SAS: Statistical Analyses Software

**Acknowledgements**

The PRO feedback is developed with technical assistance for ICT applications of CentERdata, Tilburg, the Netherlands. The *Living with lymphoma* intervention is developed with technical assistance for ICT applications of Karify B.V., Utrecht, the Netherlands.

**Funding**

This trial is supported by the Jonker-Driessen Foundation, The Hague, the Netherlands. The internal funding reference number is 20011. The study funder had no role in the design of this study or writing the manuscript and will not have any role in the collection, management, analysis, and interpretation of data.

**Availability of data and materials**

Data will be made available for noncommercial scientific research once the main findings of this trial have been published.

**Authors’ contributions**

LA is a PhD student and responsible for patient recruitment, data collection, data analysis, and drafting this manuscript. SO developed the original idea, is co-grant applicator, was a major contributor in writing this manuscript and is also responsible for patient recruitment, and data collection and analysis. LA and SO adapted the intervention content and wrote the feedback content. LvdP is grant applicator, project leader, and supervises the trial. JP and SvdB designed the intervention that was originally developed for breast cancer patients and wrote the intervention content. OH and FM were involved in the development of the original idea and were co-grant applicators. AB and LT are responsible for data collection. All authors read and approved the final manuscript.

**Competing interests**

The authors declare that they have no competing interests.

**Consent for publication**

Not applicable.
Ethical approval and consent to participate
The study protocol has been approved by METC Brabant, Tilburg in the Netherlands (reference number: NL54096.028.15/P1533). The study will be conducted according to the principles of the Declaration of Helsinki (latest version, 2013) and in accordance with the Medical Research Involving Human Subjects Act (WMO) and other guidelines, regulations and acts. Study participation of patients is voluntary and participants can refuse to participate or leave the study at any time, for any reason, without any consequences. Patients can call a study manager, a psychologist or an independent general practitioner for more information about the study. By signing and returning an informed consent form patients consent to participate in the study and agree with linkage of the questionnaire data with the clinical data stored in the NCR.

SPIRIT
This protocol has been written in accordance with the Standard Protocol Items: Recommendations for Interventional Trials (SPIRIT) guidelines [61]. A SPIRIT Checklist (Additional file 1) and a SPIRIT figure (Additional file 2) are provided.

Publisher’s Note
Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Author details
1. Department of Research, Netherlands Comprehensive Cancer Organisation, PO Box 190793501 DB Utrecht, the Netherlands. 2. Division of Psychosocial Research and Epidemiology, Netherlands Cancer Institute, Amsterdam, the Netherlands. 3. CORPS – Center of Research on Psychosomatic Diseases, Department of Medical and Clinical Psychology, Tilburg University, Tilburg, the Netherlands. 4. Department of Medical Psychology, Radboud University Medical Center, Nijmegen, the Netherlands. 5. Department of Internal Medicine, Catharina Hospital Eindhoven, Eindhoven, the Netherlands. 6. Department of Internal Medicine, Máxima Medical Centre, Veldhoven, the Netherlands.

Received: 14 December 2016 Accepted: 11 April 2017
Published online: 28 April 2017

References
1. Meulepas JM, Kiemeney LALM, Benvaart J. Cancer in the Netherlands until 2020: trends and prognoses [Kanker in Nederland tot 2020: trends en prognoses]. In: van Driel F, Knoop L, editors. Signaleringscommissie Kanker van KWF Kankerbestrijding. Amsterdam: Dutch Cancer Society; 2011.
2. Netherlands Comprehensive Cancer Organisation: Dutch Cancer Figures http://www.cijfersoverkanker.nl (2016). Accessed 26 Feb 2016.
3. Oerlemans S, Issa DE, van den Broek EC, Nijziel MR, Coebergh JW, Huijgens PC, Mols F, van de Poll-Franse LV. Health-related quality of life and persistent symptoms in relation to (R-)CHOP14, (R-)CHOP21, and other therapies among patients with diffuse large B-cell lymphoma: results of the population-based PHAROS-registry. Ann Hematol. 2014;93(10):1705–15.
4. Oerlemans S, Issa DE, van den Broek EC, Nijziel MR, Coebergh JW, Mols F, van de Poll-Franse LV. Impact of therapy and disease-related symptoms on health-related quality of life in patients with follicular lymphoma: results of the population-based PHAROS-registry. Eur J Haematol. 2014;93(3):229–37.
5. Ganz PA, Moielpour CM, Paulier DK, Kornblith AB, Ganz PA, McVey S, Press OW, Fisher RI. Health status and quality of life in patients with early-stage Hodgkin’s disease treated on Southwest Oncology Group Study 9133. J Clin Oncol. 2003;21(18):3512–9.
6. Smit SM, Prins JB. Rationale of the RICOVER-70 Study. J Clin Oncol. 2001;19(19):3654–64.
7. Carlson LE, Bultz BD. Benefits of psychosocial oncology care: improved quality of life and medical cost offset. Health Qual Life Outcomes. 2003;1:8.
8. Kroenke K, Theobald D, Wu J, Loza JK, Carpenter JS, Tu W. The association of depression and pain with health-related quality of life, disability, and health care use in cancer patients. J Pain Symptom Manage. 2010;40(3):327–41.
9. Loge JH, Abrahamsen AF, Ekeberg O, Hannisdal E, Kaasa S. Psychological distress after cancer care: a survey of 459 Hodgkin’s disease survivors. Br J Cancer. 1997;76(6):791–6.
10. Greenough J. The applications of PROs in clinical practice: what are they, do they work, and why? Qual Life Res. 2009;18(1):115–23.
11. Ayavian JZ, Jacobsen PB. Enhancing research on cancer survivors. J Clin Oncol. 2006;24(2):5419–53.
12. Ganz PA. Why and how to study the fate of cancer survivors: observations from the clinic and the research laboratory. Eur J Cancer. 2003;39(15):2316–41.
13. Kotronoulas G, Kearney N, Maguire R, Hervier B, Di Domenico D, Croy S, MacGillivray S. What is the value of the routine use of patient-reported outcome measures toward improvement of patient outcomes, processes of care, and health service outcomes in cancer care? A systematic review of controlled trials. J Clin Oncol. 2014;32(16):1480–501.
14. Snyder CF, Blackford AL, Wolof AC, Carducci MA, Herman JM, Wu AW, Board PVSA. Feasibility and value of PatientViewpoint: a system for patient-reported outcomes assessment in clinical practice. Psychon Oncol. 2013;22(4):895–901.
15. Valderas JM, Kocjana A, Espallargues M, Gaytán G, Ferreras CE, Halyard MY, Revicki DA, Symonds T, Parada A, Alonso J. The impact of measuring patient-reported outcomes in clinical practice: a systematic review of the literature. Qual Life Res. 2008;17(2):179–93.
16. Velikova G, Booth L, Smith AB, Brown PM, Lynch P, Brown JM, Selby PJ. Measuring quality of life in routine oncology practice improves communication and patient well-being: a randomized controlled trial. J Clin Oncol. 2004;22(4):714–24.
17. Lazarus RS, Folkman S. Stress, appraisal, and coping. New York: Springer; 1984.
18. Groen WG, Kuijpers W, Oldenburg HS, Wouters MW, Aaronson NK, van Harten WH. Empowerment of cancer survivors through information technology: an integrative review. J Med Int Res. 2015;17(11):e270.
19. Panagioti M, Richardson G, Small N, Murray E, Rogers A, Kennedy A, Newman S, Bower P. Self-management support interventions to reduce health care utilisation without compromising outcomes: a systematic review and meta-analysis. BMC Health Serv Res. 2014;14:356.
20. Barlow J, Wright C, Sheasby J, Turner A, Hainsworth J. Self-management approaches for people with chronic conditions: a review. Patient Educ Couns. 2002;48(2):177–87.
21. McCorrkle R, Ercolano E, Lazenny M, Schullman-Green D, Schilling LS, Lorig K, McCorkle R, Ercolano E, Lazenby M, Schulman-Green D, Schilling LS, Lorig K, Wagner EH. Self-management enabling and empowering patients living with cancer as a chronic illness. CA Cancer J Clin. 2011;61(5):50–62.
22. Samoohoa D, Bruijnevels DJ, Elbers NA, Anema JR, van der Beek AJ. Effectiveness of web-based interventions on patient empowerment: a systematic review and meta-analysis. J Med Internet Res. 2010;12(2):e23.
23. Beatty L, Lambert S. A systematic review of internet-based self-help therapeutic interventions to improve distress and disease-control among adults with chronic health conditions. Clin Psychol Rev. 2013;33(4):609–22.
24. Leary E, Thekdi SM, Shimuyama DM, Munoz RF, Riba M, Dunn LB. Internet interventions for improving psychological well-being in psycho-oncology: review and recommendations. Psychon Oncol. 2012;21(9):1016–25.
25. dan van BERG SW, Gillesien MF, Ottevaerger PB, Prins JB. Rationale of the BREAT cancer e-healTH (BREATHT) multicentre randomised controlled trial: an Internet-based self-management intervention to foster adjustment after curative breast cancer by decreasing distress and increasing empowerment. BMC Cancer. 2012;12:394.
26. Fritz A, Percy C, Jack A, Shanmugaratnam K, Sobin L, Parkin DM, Whelan S. International Classification of Diseases for Oncology. 3rd ed. Geneva: World Health Organisation; 2000.
27. van de Poll-Franse LV, Horevoorts N, van Eenbergen M, Denollet J, Roukema JA, Aaronson NK, Vingerhoets A, Coebergh JW, de Vries J, Essink-Bot ML, Mols P, Profiles Registry Group. The Patient Reported Outcomes Following Initial treatment and Long term Evaluation of Survivorship registry: scope, rationale and design of an infrastructure for the study of physical and psychosocial outcomes in cancer survivorship cohorts. Eur J Cancer. 2011;47(14):2188–94.
28. Kanga M, Ragan BG, Park JH. Issues in outcomes research: an overview of randomization techniques for clinical trials. J Athl Train. 2008;43(2):215–21.
29. Oerlemans S, Husson D, Mols F, Poortmans P, Roedink H, Daniels LA, Creutzberg CL, van de Poll-Franse LV. Perceived information provision and satisfaction among lymphoma and multiple myeloma survivors—results from a Dutch population-based study. Ann Hematol. 2012;91(10):1587–95.
31. van de Poll-Franse LV, Mole F, Gundy CM, Creutzberg CL, Nout RA, Verdonck-de Leeuw IM, Taphoorn MJ, Aaronson NK. Normative data for the EORTC QLQ-C30 and EORTC-sexuality items in the general Dutch population. Eur J Cancer. 2011;47(5):667–75.
32. Brundage M, Feldman-Stewart D, Leis A, Beqaj A, Degner L, Velji K, Zetes-Zanatta L, Tu D, Rivo P, Pater J. Communicating quality of life information to cancer patients: a study of six presentation formats. J Clin Oncol. 2005;23(26):6949–56.
33. Kuijpers W, Giesinger JM, Zabernigg A, Young T, Friend E, Tomaszewska IM, Brundage M, Feldman-Stewart D, Leis A, Bezjak A, Degner L, Velji K, Zetes-Zetesc K. Watson M, Homewood J. Mental Adjustment to Cancer Scale: psychometric properties in a large cancer cohort. Psychooncology. 2008;17(11):1146–51.
34. Cocks K, King MT, Velikova G, Martyn St-James M, Fayers PM, Brown JM.
35. van den Berg SW, Gielissen MF, Custers JA, van der Graaf WT, Ottevanger
36. Kuijpers W, Giesinger JM, Zabernigg A, Young T, Friend E, Tomaszewska IM, Aaronson NK, Holzer B. Patients’ and health professionals’ understanding of and preferences for graphical presentation styles for individual-level EORTC QLQ-C30 scores. Qual Life Res. 2016;25(5):595–604.
37. van den Berg SW, Peters EJ, Kraaijeveld JF, Gielissen MF, Prins JB. Usage of a generic web-based self-management for psychological adjustment after primary breast cancer—Results of a multicenter randomized controlled trial. J Clin Oncol. 2015;33(25):2763–71.
38. van den Berg SW, Peters EJ, Kuijpers W, Gielissen MF, Prins JB. Usage of a generic web-based self-management intervention for breast cancer survivors: substudy analysis of the BREATH trial. J Med Internet Res. 2013;15(8):e170.
39. Osborne RH, Elsworth GR, Whitfield K. The Health Education Impact Questionnaire (heiQ): an outcomes and evaluation measure for patient education and self-management interventions for people with chronic conditions. Patient Educ Couns. 2007;66(2):192–201.
40. Van Mulmert L, Stiers M, Aertgeerts B, Langenhove H, Boonen A, van Den Broek K, Vlaeyen JW, Van Hout BA. Quality of Life Questionnaire Core 30. J Clin Oncol. 2011;29(1):89–96.
41. EORTC QOL Module for chronic lymphocytic leukaemia (CLL), non-Hodgkin’s lymphoma (NHL) and Hodgkin’s lymphoma (HL). http://groups.eortc.be/qol/eortc-qol-module-chronic-lymphocytic-leukaemia-CLL-non-Hodgkin%E2%80%99s-lymphoma-NHL-and-Hodgkin%E2%80%99s-lymphoma.
42. Chan AW, Tetzlaff JM, Gotzsche PC, Altman DG, Mann H, Berlin JA, Dickersin K, Hrobjartsson A, Schulz KF, Parulekar WR, Kleda-Jerik K, Laupacis A, Moher D. SPIRIT 2013 explanation and elaboration: guidance for protocols of clinical trials. BMJ. 2013;346:e7586.
43. Fallowfield L. Desire for information is not the same as a desire to talk about breast cancer. Br Med J. 2001;323(7322):1144.
44. Aaronsen NK, Ahmedzai S, Bergman B, Bullinger M, Cull A, Dose NJ, Filliberti A, Flechtner H, Fleishman SB, de Haes JC, et al. The European Organization for Research and Treatment of Cancer QLQ-C30: a quality-of-life instrument for use in international clinical trials in oncology. J Natl Cancer Inst. 1993;85(5):365–76.
45. van den Berg SW, Gielissen MF, Custers JA, van der Graaf WT, Ottevanger
46. van den Berg SW, Peters EJ, Kuijpers W, Gielissen MF, Prins JB. Usage of a generic web-based self-management intervention for breast cancer survivors: substudy analysis of the BREATH trial. J Med Internet Res. 2013;15(8):e170.