




PAPER

Cocreated internet-based stepped care for individuals with cancer and concurrent symptoms of anxiety and depression: Results from the U-CARE AdultCan randomized controlled trial

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Abstract

Objective: The aim was to evaluate the effects of cocreated internet-based stepped care (iCAN-DO) on anxiety, depression, posttraumatic stress, and health-related quality of life (HRQoL) in individuals with cancer and self-reported anxiety and/or depression symptoms, compared with standard care.

Methods: Clinically recruited individuals with breast, colorectal, or prostate cancer underwent online screening with the Hospital Anxiety and Depression Scale (HADS). Those with anxiety and/or depression symptoms (>7 on any of the HADS subscales) were randomized to iCAN-DO or standard care. iCAN-DO comprised psychoeducation and self-care strategies (step 1) and internet-based cognitive behavioral therapy (iCBT, step 2). Data were collected before randomization and at 1, 4, 7, and 10 months and analyzed with intention-to-treat regression analysis and randomization tests.

Results: Online screening identified 245 (27%) of 909 individuals who reported anxiety and/or depression symptoms. They were randomized to iCAN-DO (n = 124) or standard care (n = 121). Of them 49% completed the 10-month assessment, and in the iCAN-DO group 85% accessed step 1 and 13% underwent iCBT. iCAN-DO decreased the levels of symptoms of depression (−0.54, 95% confidence interval: −1.08 to −0.01, P < .05) and the proportion of individuals with symptoms of

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depression ($P < .01$) at 10 months, compared with standard care, according to HADS. There were no significant effects on anxiety, posttraumatic stress, or HRQoL.

Conclusion: Internet-based stepped care improves symptoms of depression in individuals with cancer. Further studies are needed to gain knowledge on how to optimize and implement internet-based support in oncology care.

KEYWORDS

anxiety, cancer, depression, eHealth, internet, oncology, psycho-oncology, psychosocial intervention, randomized controlled trial, technology-based interventions

1 | BACKGROUND

Individuals diagnosed with cancer are predisposed to long-term negative mood symptoms, such as anxiety and depression.¹ The support needed varies, some may need counseling including psychoeducation and problem-solving while others will manage with peer support only. A few may be in need of psychological treatment, such as cognitive behavioral therapy.¹ Barriers to support exist within the healthcare organization and within the individual, among known barriers are issues with travelling, stigma, or not wanting to be part of a group.² Most of the support provided by healthcare is delivered through scheduled visits to a hospital, which may not be optimal for all.

Internet-based applications containing education and self-management strategies, is a complementary strategy to empower individuals to achieve optimal health during the cancer trajectory. Self-management interventions are recommended to be cocreated with representatives of the target population as well as being based on scientific evidence and theories. However, such approaches are missing in most randomized controlled trials evaluating self-management interventions.³ Internet-based applications can lead to increased knowledge, positive behavioral changes, and improved social support and clinical outcomes in individuals with chronic diseases, but more studies are needed to determine the effects in specific diseases, such as cancer.⁴ Internet-based support targeting individuals with cancer have shown improved health-related quality of life (HRQoL) and decreased distress compared with standard care.^{5,6} However, as participants are often recruited online and through advertisements, results may be subject to selection bias. In addition, many interventions are directed at individuals without self-reported symptoms.⁷ Screening and stepped care models to target interventions at those with self-reported symptoms have been recommended to increase effectiveness.

Internet-based stepped care may be one way to provide support relevant to individual needs and target more resource-intensive treatments to those with persistent symptoms despite an initial, less resource-intensive support. No internet-based stepped care approach has been evaluated in individuals with cancer and concurrent symptoms of anxiety and depression. The aim of the present study was to evaluate the effects of a cocreated, internet-based stepped care intervention (iCAN-DO) on self-reported symptoms of

anxiety and/or depression in individuals with cancer, compared with standard care. Secondary outcomes were HRQoL and posttraumatic stress.

2 | METHODS

The Uppsala University Psychosocial Care Programme (U-CARE)⁸ is a strategic research venture where all studies concern psychosocial problems in connection with physical illness. Within U-CARE, an internet-based infrastructure (the Portal) for delivering and evaluating internet-based interventions and collecting self-reported data has been developed.

2.1 | Design of AdultCan

AdultCan⁹ is a multicenter randomized clinical trial (RCT; clinicaltrials.gov NCT-01620681) within U-CARE, including a 24-month follow-up period. The present article concerns the primary evaluation at 10 months when the stepped care intervention within AdultCan (iCAN-DO) was finalized (see below) and is presented according to the CONSORT criteria.¹⁰ The 24 month follow-up and a health-economic evaluation are planned to be reported later. The AdultCan RCT was approved by the Swedish Ethical Review Authority (Dnr 2012/003).

2.2 | Recruitment, screening, and randomization

The recruitment ran from 2013 to 2016 at four hospitals in mid Sweden. Individuals were eligible if newly diagnosed (<6 months) with breast, colorectal, or prostate cancer, or with a relapse of colorectal cancer, as we strived for a sample representing individuals with various age, gender, and prognosis. Exclusion criteria were inability to understand Swedish, cognitive impairment, Karnofsky performance status <40, expected survival <3 months, or severe depression or suicide risk on the Montgomery-Åsberg Depression Rating Scale (MADRS-S).⁹ Eligible individuals were consecutively recruited by research nurses/assistants in conjunction with a clinical appointment.

All participants provided written informed consent and received login details through automated e-mails. Participants with self-reported symptoms of anxiety and/or depression, that is, >7 p on either Hospital Anxiety and Depression Scale (HADS) subscale,¹¹ were randomly assigned in the Portal, to either iCAN-DO or standard care (SC) (see Supporting Information, Figure S1, Consort diagram). A computer-generated permuted block method (concealed from all research staff) stratified for curative or palliative treatment was used. Participants with scores ≤ 7 p on both HADS subscales were allocated to a longitudinal descriptive study (data to be presented elsewhere).

2.3 | The internet-based stepped care intervention

iCAN-DO was developed in collaboration with cancer care staff and individuals with lived experience of cancer and based on assumptions from psychoeducation, Orem's self-care deficit nursing theory¹² and social cognitive theory. The theories highlight the importance of providing people with knowledge that strengthens their ability and self-efficacy to cope with problems in connection with illness. The development is described in a previous article.¹³ iCAN-DO was delivered through the Portal and all contacts with participants occurred through written messages. Participants choose which modules to work with during step 1 and step 2.

2.3.1 | Step 1

Step 1 was available from randomization throughout the study period and comprised a library, a peer-support section and an "Ask an Expert" feature. The library comprised 16 modules including short psychoeducative lectures (in both audio-visual and text format) regarding diagnosis, treatment, common physical and psychological symptoms, and self-care strategies. Since anxiety and depression in cancer are associated with physical symptoms,¹⁴ both physical and psychological symptoms were addressed. This was recommended by those with lived experience of cancer, who stressed the importance of iCAN-DO being clearly targeted to individuals treated for cancer. The peer-support section comprised a moderated discussion forum covering various themes. "Ask an Expert" meant that participants could pose questions to a nurse and read others' anonymized questions and answers in the FAQ (frequently asked questions).

2.3.2 | Step 2

Participants with remaining symptoms of anxiety and/or depression (HADS >7 on any subscale) after using step 1, was offered a guided 10-week internet-based cognitive behavioral therapy program (iCBT) alongside step 1. iCBT included psychoeducation, self-monitoring, assignments, and weekly guidance by a psychologist through written messages in the Portal. Participants could choose which problems to work with, among 15 modules covering common cancer-related problems but could only undergo iCBT once at 1, 4, or 7 months post-randomization.

2.3.3 | Standard care

Both the iCAN-DO and the SC group had access to standard care, including routine information about the disease and treatment and basic psychosocial support from nurses and physicians. Additional psychosocial support could be obtained through self-referral to a counselor or the hospital church.

2.4 | Data collection

Data were collected at baseline, 1, 4, 7, and 10 months, all patient-reported outcomes were collected in the Portal, see Appendix A in Data S1.

2.4.1 | Medical and sociodemographic background data and perceived benefits

Information about the disease and treatment was obtained from national quality registers. Data on sociodemographics and perceived benefits (eg, knowledge, self-care strategies) of iCAN-DO were obtained through project-specific questions.

2.4.2 | Primary outcomes: Anxiety and depression

The primary outcomes, anxiety and depression were assessed with HADS,¹¹ consisting of the two subscales anxiety (HADS-A) and depression (HADS-D), at all five assessment points. Both scores of the subscales and the HADS classification (≤ 7 : noncase; 8-10: doubtful case; >10 : clinical case) were used. HADS is developed for use in non-psychiatric care and the most commonly used scale when screening for anxiety and depression among individuals with cancer and also recommended within the PROMS-Cancer Core.¹⁵ Anxiety was also assessed with the STAI-S¹⁶ and depression with MADRS-S⁹ and EROS¹⁷ at baseline and 10 months.

2.4.3 | Secondary outcomes: Posttraumatic stress and health-related quality of life

HRQoL was assessed with EORTC QLQ-C30,¹⁸ cancer-related fatigue by FACIT-F¹⁹ and insomnia with ISI²⁰ at all five assessment points and posttraumatic stress with PCL-C²¹ at baseline and 10 months.

2.4.4 | Sample size calculation

A minimal important difference in HADS-A or HADS-D, established using distribution-based (treatment effects as SD units of change scores) and anchor-based (correlation between HADS and patient-reported anchors) methods, has been reported to correspond to a

20% difference/change in points,²² which equal approximately 2 point change in individuals with cancer and concurrently >7 points on the respective HADS subscale, according to our previous study.¹ To obtain 80% power (alpha .05) to detect a 20% mean score difference between groups, 65 participants were needed per group. The goal was to randomize twice this number, as the study was internet-based a large proportion of participants was expected to drop out²³ (see Figure S1).

2.5 | Analytical strategies

The analyses were performed in R version 3.4.2 and SPSS version 25. Composite scores for all outcomes were calculated according to published instructions. Clinically significant differences/changes were assessed using defined minimal clinically important differences²⁴ for each questionnaire. Questionnaires completed at all five assessment points were analyzed with linear mixed models (LMM), fitted using restricted maximum likelihood. Questionnaires completed at baseline and 10 months only were analyzed with multiple linear regression. All models were adjusted for baseline values and level of education. Differences over time regarding HADS classification (noncase, doubtful case, or clinical case) were analyzed using a test allowing repeated measures analyses of category data (randomization test).²⁵ All outcomes were analyzed according to intention-to-treat (ITT). Missing data were imputed using the last rank carried forward method (LRCF).²⁶ Due to a large degree of missing data over time sensitivity analysis were carried out for the primary outcome measure (HADS) in additional populations; *modified ITT*, including those who completed baseline and at least one follow-up assessment (using LRCF) and *complete cases*, that is, those who completed all assessments. A classification of participants according to whether they reported a clinically important decrease or increase (20% according to Puhan et al²²) in HADS-A and HADS-D, from baseline to 10 months was conducted in individuals with complete data, using a responder analysis.

3 | RESULTS

Compared to nonparticipants (n = 1188) participants (n = 909) were younger (mean: 61 vs 68 years, $t = 17.8$, $df = 2.09$, $P = <.01$), had a larger proportion diagnosed with prostate cancer 33% vs 24% and a smaller with colorectal cancer 14% vs 23% ($\chi^2 = 36.55$, $df = 2$, $P = <.01$). The most common reasons for declining participation were “No computer/internet access or lack of computer skills” (42%) and “No time or energy to participate in research” (12%).

3.1 | Result of screening

A total of 245 individuals (27%) reported symptoms of anxiety and/or depression and were randomized to iCAN-DO (n = 124) or SC (n = 121). Forty-four percent in the iCAN-DO group reported

symptoms of both anxiety and depression at baseline, 34% of anxiety only, and 22% of depression only. Corresponding proportions in the SC group are 39%, 49%, and 12%. The SC group reported a higher mean score for anxiety at baseline than those in iCAN-DO (HADS-A 10.2 vs 9.2, $t = 2.6$, $df = 243$, $P = <.01$) but a larger proportion in iCAN-DO reported depression symptoms at baseline than in SC (HADS-D > 7: 81 of 124 vs 62 of 121, $\chi^2 = 7.7$, $df = 2$, $P = .02$). Ten participants (iCAN-DO: n = 4; SC: n = 6) reported severe symptoms of depression or a present risk of suicide according to the MADRS-S. They were contacted by a clinical psychologist by phone to assess the need for referral to psychiatric care; no such measures were needed, and participants remained in the study. A majority, 69%, were included within 4 months from diagnosis and underwent oncological treatment during the study period. There were no statistically significant differences between iCAN-DO and SC at baseline regarding sociodemographic/medical characteristics (see Table S1). However, at 10 months, a larger proportion in iCAN-DO (41%) reported higher education (University/university college >3 years), compared to SC (20%).

3.2 | Utilization and perceived benefits of iCAN-DO

According to self-reports during the study period, no participant was receiving psychosocial support or psychological treatment in addition to iCAN-DO. One hundred and five of 124 participants (85%) used iCAN-DO to some extent. All of them used step 1 (median number of visits per person = 9, range = 1-92). iCBT was offered to 82 (78%) of those who used step 1, due to persistent symptoms of anxiety and/or depression, 16 (20%) accepted and 7 of those (representing individuals with breast, and colorectal cancer) completed at least one module. Most visits (78%) in iCAN-DO were conducted within 4 months after randomization. Visits to the library section were the most common (87%), modules on radiotherapy and fatigue were visited by most, 35% and 31%, respectively. The modules on anxiety and depression was visited by 13% and 19%, respectively. The peer-support section was visited by 65% and “Ask an Expert” by 58% (see Appendix B in Data S1). At 1 month (before start of iCBT), 95 (90%) of the 105 who used iCAN-DO answered project-specific questions about the benefits of iCAN-DO: 90% stated that they used the recommended self-care strategies and 76% perceived an increase in knowledge about the disease and its symptoms since they got access to step 1.

3.3 | Anxiety and depression

3.3.1 | Hospital anxiety and depression scale

Mean depression was statistically but not clinically significantly lower in iCAN-DO compared with SC, 1 to 10 months after randomization (LMM; ITT adjusted mean = -0.54, 95% CI: -1.08 to -0.01, $P = <.05$;

see Table S2). There were no statistically significant differences between iCAN-DO and SC according to modified ITT ($P = .07$) or the complete cases analyses ($P = .50$). However, a clinically meaningful decrease in mean depression ($>20\%$) was seen in all analysis populations within iCAN-DO, but not within SC (see Table S2). A larger proportion in iCAN-DO than in SC changed from doubtful/clinical cases of depression to noncases, according to the HADS classification, during the study period (randomization test, $P = <.01$; see Figure S2). Higher levels of anxiety and/or depression at baseline were associated with higher levels of anxiety and depression over time (data not presented). A larger proportion of participants in iCAN-DO, compared to SC, reported a clinically meaningful decrease (>2 points) in depression (54% vs 35%) and anxiety (52% vs 38%) at 10 months, according to the responder analysis. Also, a smaller proportion in iCAN-DO reported a clinically meaningful increase (>2 points) in depression (8% vs 26%) and anxiety (16% vs 31%) (see Appendix C in Data S1).

3.3.2 | STAI-S, EROS, AND MADRS-S

There were no differences between iCAN-DO and SC regarding anxiety according to STAI-S or in depression according to EROS and MADRS-S (see ITT analysis, Appendix D in Data S1).

3.4 | Health-related quality of life and posttraumatic stress

There were no statistically significant differences between iCAN-DO and SC with regard to HRQoL, including fatigue and insomnia, or posttraumatic stress. However, according to Cocks et al estimates of relevant mean differences of EORTC QLQ-C30 scales, mean changes from baseline to 10 months suggested improvements of likely clinical relevance in role functioning, social functioning, and fatigue²⁷ in iCAN-DO and of subtle relevance in SC. In addition, there were small differences of subtle clinical relevance²⁸ between iCAN-DO and SC at 10 months with regard to social functioning and several QLQ-C30 symptom subscales (see ITT analysis, Appendix E in Data S1).

4 | DISCUSSION

To our knowledge, this is the first RCT reporting effects of internet-based stepped care on long-term self-reported symptoms of depression among clinically recruited individuals with cancer. The key strengths of the present study are the online screening and symptom-based recruitment of participants, the stepped care approach, long-term follow-up, and evidence-based development of iCAN-DO.^{4,13,29} The online screening procedure identified about one of four individuals as experiencing symptoms of anxiety and/or depression, a proportion corresponding well with previous findings.¹ iCAN-DO decreased the levels of depression and the proportion of participants

with symptoms of depression, a pattern consistent in all analyses of HADS. However, iCAN-DO did not decrease symptoms of depression as assessed using MADRS-S. The reason for using MADRS-S was to identify individuals with severe symptoms of depression. However, those identified did not report severe symptoms when contacted. Since MADRS-S was originally designed to detect changes in primary depressive illness during treatment with antidepressants it may not be feasible in an oncology setting and more research is needed to determine the feasibility in this population.

Some previous internet-based psychosocial interventions targeting individuals with cancer have resulted in improved HRQoL, increased social support, and decreased distress.^{3,5,6,30} However, differences in interventions, follow-up periods, participants, and outcome measures make comparisons of studies difficult, indicating a need for a theoretical framework as guidance for the development, testing, and evaluation of future internet-based interventions.^{29,31} The lack of effects in several trials may be due to the inclusion of individuals without self-reported symptoms, that is, not using screening procedures. A few previous internet-based self-management interventions have shown improvements in depression in short-time evaluations that was not maintained over time.³ Thus, our results add important knowledge about the long-term value of internet-based support in a clinical setting. Still, the need to improve effectiveness remains, since depression symptoms were still obvious at study end and as anxiety and HRQoL were not statistically significantly improved.

Only a fraction of participants used iCBT, meaning that the intervention comprised step 1 only (and not stepped care) for the large majority. This is in line with our previous study where only a small proportion of clinically recruited participants reported a need for psychological treatment.¹ In the present study, participants reported using the recommended self-care strategies after getting access to step 1 and stated increased knowledge about the disease and common symptoms. Further, a qualitative study of the participants' experiences of iCAN-DO³² showed that step 1 was seen as a safe and relevant complement to standard healthcare. The low adherence to iCBT corroborated findings from other studies with clinically recruited samples.^{33,34} The fact that the participants did not actively seek support may have affected perseverance and may partly explain the low participation as iCBT requires a high level of engagement and occurred in parallel with cancer treatment. Since iCAN-DO did not target all symptoms, efforts to improve the low-intensity support, and to make iCBT more manageable for those who need psychological treatment is still needed. The qualitative study of participants' experiences of iCAN-DO³² showed that the time set for iCBT and choosing between modules was perceived as stressful and difficult to handle by the participants.³² Thus, it seems important to adjust the program to the user's life situation. A recent RCT investigating iCBT in individuals with cancer³⁵ included fewer, predetermined modules over a longer period of time (16 weeks) and showed positive results for both anxiety and depression at an early follow-up.

Despite anxiety being more prevalent than depression, fewer individuals used the library contents targeting anxiety than those targeting depression. The mechanisms behind anxiety are likely to be

related to the real threat of the illness; symptoms are diffuse and not easily recognized as anxiety, for example, irritability, restlessness, and/or difficulties concentrating or sleeping. Tracking symptoms and providing tailored self-care strategies to relieve them might enhance targeting.^{36,37} However, it is important to recognize that tracking of symptoms may cause increased distress in some individuals,³⁶ who will cope with their cancer by avoiding medical and psychosocial information. Their need for information often appears later in the disease trajectory, suggesting a need for personalized internet-based interventions. One way to achieve more relevant tailoring and guidance could be to integrate internet-based support into standard care.³² Further, it has been previously shown that symptoms of anxiety can increase in the posttreatment period,³⁸ when the fear of cancer recurrence (FCR) may be more present, thus iCAN-DO material could be improved by adding content to target FCR specifically.

5 | CONCLUSION

Cocreated internet-based stepped care improves self-reported symptoms of depression in individuals with cancer. Low-intensity support including contents regarding the diagnosis and treatment, together with psychoeducation and self-care strategies can be recommended for clinical care. Efforts are needed to gain knowledge on how to optimize and implement internet-based support and iCBT in oncology care. Screening and symptom-based recruitment is highly recommended in forthcoming studies.

5.1 | Study limitations

Those who declined participation were older and a larger proportion diagnosed with colorectal cancer, the number of recruited individuals with a relapse of cancer were also few and did not allow for subgroup analysis. Thus, our results may be restricted to a somewhat younger group with more favorable prognosis and should not be generalized to all individuals diagnosed with breast, colorectal, or prostate cancer. Further, many participants were lost to follow-up, limiting the validity of the findings. Retention is a well-known challenge in studies evaluating internet-based interventions, indicating the importance of an ITT analysis in these trials. Challenges include nonusage attrition (program not used) and drop-out attrition (assessments not completed).²³ Drop-out may occur when users are satisfied with no need for further use of the intervention.³⁹ Since 78% of the visits in iCAN-DO took place within 4 months of randomization it may be hypothesized that the interest and needs among participants then decreased, even if they had benefitted from the intervention.

5.1.1 | Clinical implications

The present study suggest that clinical cancer care may use the internet when screening for individuals' supportive needs and providing

information and psychoeducation regarding self-care for symptoms of depression, and probably also for other common symptoms. Co-operation with individuals with lived experience of cancer are of greatest importance to ensure that the support is clinically relevant and targeted to the individual's needs.

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CONFLICT OF INTEREST

The authors declare no conflicts of interest.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request. The data are not publicly available due to privacy or ethical restrictions.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of this article.

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