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Role of eHealth application Oncokompas in supporting self-management of symptoms and health-related quality of life in cancer survivors: a randomised, controlled trial

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Summary

Background Knowledge about the efficacy of behavioural intervention technologies that can be used by cancer survivors independently from a health-care provider is scarce. We aimed to assess the efficacy, reach, and usage of Oncokompas, a web-based eHealth application that supports survivors in self-management by monitoring health-related quality of life (HRQOL) and cancer-generic and tumour-specific symptoms and obtaining tailored feedback with a personalised overview of supportive care options.

Methods In this non-blinded, randomised, controlled trial, we recruited patients treated at 14 hospitals in the Netherlands for head and neck cancer, colorectal cancer, breast cancer, Hodgkin lymphoma, or non-Hodgkin lymphoma. Adult survivors (aged ≥18 years) were recruited through the Netherlands Cancer Registry (NCR) and invited by their treating physician through the Patient Reported Outcomes Following Initial Treatment and Long term Evaluation of Survivorship (PROFILES) registry. Participants were randomly assigned (1:1) by an independent researcher to the intervention group (access to Oncokompas) or control group (access to Oncokompas after 6 months), by use of block randomisation (block length of 68), stratified by tumour type. The primary outcome was patient activation (knowledge, skills, and confidence for self-management), assessed at baseline, post-intervention, and 3-month and 6-month follow-up. Linear mixed models (intention-to-treat) were used to assess group differences over time from baseline to 6-month follow-up. The trial is registered in the Netherlands Trial Register, NTR5774 and is completed.

Findings Between Oct 12, 2016, and May 24, 2018, 625 (21%) of 2953 survivors assessed for eligibility were recruited and randomly assigned to the intervention (320) or control group (305). Median follow-up was 6 months (IQR 6–6). Patient activation was not significantly different between intervention and control group over time (difference at 6-month follow-up 1·7 [95% CI −0·8–4·1], p=0·41).

Interpretation Oncokompas did not improve the amount of knowledge, skills, and confidence for self-management in cancer survivors. This study contributes to the evidence for the development of tailored strategies for development and implementation of behavioural intervention technologies among cancer survivors.

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Introduction

In cancer survivorship care, government policy statements and national guidelines reflect scientific and societal support for an integrated approach to supportive care, which includes rehabilitation, psychosocial care, and lifestyle interventions.[1,2] For optimal referral to supportive care, there are guidelines on patient-reported outcome measures in clinical practice. Behavioural intervention technologies are used to collect and process patient-reported outcome measure data. Most are adjunctive or guided behavioural intervention technologies, and a health-care provider is needed to discuss the results and the supportive care options that best fit the patient's needs.[3] Reviews showed that online self-management interventions can have positive effects on health-related quality of life (HRQOL) and symptom burden in patients with cancer.[3–5] Randomised controlled trials mostly targeted cancer survivors during or shortly after treatment, included cancer-generic symptoms and less often tumour-specific symptoms, and most interventions comprised adjunctive or guided behavioural intervention technologies.[3–7] Knowledge about the efficacy of a fully automated behavioural intervention technology that can be used by cancer survivors independently from a health-care provider is scarce. Therefore, we developed Oncokompas, which supports cancer survivors in

Research in context

Evidence before this study

We searched for systematic reviews and meta-analyses in PubMed and via reference lists of papers published, from July 1, 2014, to July 1, 2019 with the search terms "cancer survivors", "patient reported outcome", "symptom monitoring", "self-management interventions", and "eHealth". Results from reviews on web-based symptom monitoring as well as on self-management interventions suggest that these can be effective to reduce symptom burden and improve health-related quality of life (HRQOL). However, most of the previous studies targeted patients during or shortly after treatment, included most often cancer-generic symptoms but less often tumour-specific symptoms, and most interventions comprised behavioural intervention technologies that were part of routine care, as adjunctive or guided behavioural intervention technologies. Knowledge on the reach and efficacy of a fully automated behavioural intervention technology that can be used by survivors independently from a health-care provider is scarce. Therefore, we developed the eHealth self-management application Oncokompas, which aims to support survivors in self-management by monitoring cancer-generic and tumour-specific symptoms, providing feedback and information on their scores, as well as a personalised overview of supportive care options, with the aim to reduce symptom burden and improve HRQOL. According to participatory design principles, several studies were done to investigate the needs of patients and health-care professionals, and the feasibility of Oncokompas.

Added value of this study

This randomised controlled trial showed that Oncokompas did not significantly improve knowledge, skills, or confidence for self-management or other secondary outcome measures, such as supportive care needs, but seems to reduce symptom burden and improve HRQOL. These findings contribute to developing tailored strategies for development and implementation of eHealth applications among cancer survivors.

Implications of all the available evidence

Considering all available evidence, fully automated behavioural intervention technologies such as Oncokompas could potentially facilitate sustainability of long-term cancer survivorship care; however, this trial did not find a difference in the primary endpoint of patient activation. Further research is needed to identify which components of Oncokompas are fundamental for improving HRQOL and symptoms and whether Oncokompas is cost-effective compared with usual survivorship care. Also, further qualitative research and process evaluations are needed to guide scaling up of behavioural intervention technologies such as Oncokompas, which remains a challenge.

self-management, by monitoring symptoms (cancer-generic and tumour-specific) and HRQOL, providing feedback and information, and a personalised overview of supportive care options, with the aim to reduce symptom burden and improve HRQOL.[8–13] Oncokompas follows a tailored care approach: survivors receive personalised information on their scores; survivors with minor problems are informed about self-help interventions, and survivors with major problems about professional care.

Oncokompas was developed according to a participatory design approach, including survivors, health-care professionals, managerial staff, and insurance companies. Qualitative studies suggested that there was a need for Oncokompas among survivors and health-care providers.[8,10] Quantitative feasibility studies showed that the proportion of participants who used Oncokompas was high (64%), that survivors and health-care professionals were satisfied with the application,[9,11] and that it might lead to improved knowledge, skills and confidence for self-management.[11] A national pilot study on the adoption and implementation of Oncokompas in 65 hospitals showed that the adoption rate was 31%, and within these adopting hospitals, implementation rate was 71%.[12] One of the reasons given for not adopting or implementing Oncokompas was that no information was available on efficacy.

The aim of the present study was to evaluate the reach, usage as intended, and efficacy of Oncokompas to improve knowledge, skills, and confidence for self-management among survivors of head and neck cancer, colorectal cancer, breast cancer, Hodgkin lymphoma, or non-Hodgkin lymphoma. We also explored effects on HRQOL and tumour-specific symptoms, mental adjustment to cancer, supportive care needs, self-efficacy, personal control, and patient–physician interaction.

Methods

Study design and participants

In this randomised controlled trial, cancer survivors were recruited through the Netherlands Cancer Registry, and invited by their (former) treating physician at 14 hospitals through the Patient Reported Outcomes Following Initial Treatment and Long term Evaluation of Survivorship (PROFILES) registry (appendix p2).[14] Inclusion criteria were survivors diagnosed with head and neck cancer, colorectal cancer, breast cancer, Hodgkin lymphoma, or non-Hodgkin lymphoma. These tumour types were chosen to ensure variability regarding age, sex, tumour type prevalence, solid and non-solid tumour types, cancer-related and treatment-related symptoms, and the need for various types of supportive care. Patients had to be aged at least 18 years and be 3 months to 5 years after treatment with curative intent (all treatment modalities). Survivors on endocrine or immunotherapy, or a wait-and-see regimen were included 3 months after previous treatment or diagnosis. Exclusion criteria were no access

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to the internet or no email address, severe cognitive impairment, insufficient mastery of the Dutch language, physical inability to complete a questionnaire, and male breast cancer survivors.[13]

To establish the reach of Oncokompas (defined as the proportion of eligible survivors and the proportion of participating survivors), survivors were first invited in an online or paper-and-pencil survey on supportive care. Eligible survivors were invited to participate in the randomised controlled trial. After the first recruitment phase with sufficient respondents to evaluate the reach, survivors were invited directly to participate in the randomised controlled trial, to speed up recruitment. We needed at least 200 participants to do multivariable logistic regression analyses on eligbility and participation. This deviated from the protocol, which specified that all participants in the randomised controlled trial were recruited via the survey on supportive care.[13]

For more on **EORTC** see https://qol.eortc.org/

Participants in the randomised controlled trial provided informed consent online; for the survey on supportive care, there was the option to send the informed consent form by post. The study protocol was approved by the Medical Ethics Committee of VU University Medical Center (2015.523). The protocol has previously been published.[13]

Randomisation and masking

Participants were randomly assigned (1:1) to the intervention group (direct access to Oncokompas) or wait-list control group (access to Oncokompas after 6 months) using block randomisation. Randomisation was done by a researcher not involved in the study; the allocation sequence was extracted from a database with all included participant numbers. Randomisation was stratified by tumour type, and blocks with a length of 68 were used. Assignment to the trial group and invitation to the intervention was done by a researcher (AvdH). Owing to the nature of the intervention, participants could not be masked.

Procedures

The web-based eHealth application Oncokompas aims to support cancer survivors in self-management by monitoring cancer-generic and tumour-specific symptoms and HRQOL, providing feedback and information on the scores and a personalised overview of supportive care options, with the aim to reduce symptom burden and improve HRQOL. According to the biopsychosocial model,[29] the content of Oncokompas includes various topics in five generic HRQOL domains: physical functioning, psychological functioning, social functioning, lifestyle, and existential issues, and included topics in tumour-specific modules (appendix p 1). Following the chronic care self-management model,[30] Oncokompas consists of three components: Measure, Learn, and Act. It is expected that users improve their knowledge, skills, and confidence for self-management if they use at least the two components Measure and Learn (so, Measure and Learn or Measure, Learn, and Act, for at least one topic). Cancer survivors are informed in Oncokompas that can they can choose which topics they want to address. Automatically generated reminders are sent every 3 months, to encourage repeated use of Oncokompas. A helpdesk is available, which users can contact via email or telephone.

See **Online** for appendix

In the Measure component, survivors can complete patient-reported outcome measures on the topics of choice. Per topic, a patient-reported outcome measure was selected by the project team in collaboration with experts, on the basis of Dutch guidelines and literature searches, for instance, subscales of the European Organisation for Research and Treatment of Cancer (EORTC). Data from the Measure component are processed in real-time and linked to tailored feedback to the survivor in the Learn component. All algorithm calculations are based on available cut-off scores, or are defined on the basis of Dutch practice guidelines, literature searches or consensus by teams of experts. In the Learn component, feedback is provided by means of a 3-colour system: green (no elevated wellbeing risks), orange (elevated wellbeing risks), and red (seriously elevated wellbeing risks). Survivors receive personalised information on the outcomes (eg, on the topic depression, information is provided on symptoms of depression and the proportion of survivors who suffer from depressive symptoms). Special attention is paid to evidence-based associations between outcomes. For example, feedback on the association between depression and fatigue is provided, if a survivor has an orange or a red score on depression as well as on fatigue. The feedback in the Learn component concludes with tailored self-care advice, with tips and tools. In the Act component, survivors are provided with personalised supportive care options, on the basis of their patient-reported outcome measure scores and expressed preferences (eg, preference for individual therapy *vs* group therapy). If a survivor has elevated wellbeing risks (orange score), the feedback includes suggestions for self-help interventions. If a survivor has seriously elevated wellbeing risks, the feedback includes advice to contact a medical specialist or their general practitioner. This advice is evidence-based (when evidence was found in literature), based on guidelines, or consensus recommendations from expert meetings.

Cancer survivors obtain access to Oncokompas via their health-care provider who invites the survivor by submitting an online form within Oncokompas including name, email address, date of birth, treatment phase (before–during–after treatment), and postal code. The Oncokompas system then automatically sends an activation link to the email address of the survivor. Verification of identity happens in real-time by asking survivors to re-enter date of birth, after which registration is completed and they can start the Measure component

as described. Oncokompas is considered to be a medical device and is in compliance with Dutch and European laws and regulations (Medical Device Directive and General Data Protection Regulation). All data are stored safely and encrypted by a hosting company, which is certified for Dutch NEN7510 norms for information security in health care. Code-sharing of the algorithms in Oncokompas is possible after signing a bilateral confidentially agreement. Outcome measures were collected at time of inclusion (baseline), 1 week post-intervention, and after 3 months and 6 months of follow-up. In the intervention group, the first post-intervention questionnaire was sent 1 week after the use of Oncokompas, but not later than 2 weeks after randomisation. In case a participant did not use Oncokompas, the first post-intervention questionnaire was sent 2 weeks after randomisation. In the control group, the first post-intervention questionnaire was sent 2 weeks after randomisation.

The Patient Activation Measure is a patient-reported outcome measure that measures a patient's amount of knowledge, skills, and confidence for self-management. The score ranges from 0 to 100 (higher score indicates higher patient activation).[15] The patient activation measure is a 13-item patient-reported outcome measure in which the respondents are asked to report their level of agreement with various statements on a 4-point Likert scale (ie, strongly disagree, disagree, agree, strongly agree) or to indicate that the item is not applicable. Statements are for instance, "Taking an active role in my own health care is the most important factor in determining my health and ability to function", "I am confident I can tell my health-care provider concerns I have even when he or she does not ask", and "I understand the nature and causes of my health condition(s)". The summary score of the EORTC QLQ-C30 is based on five functional scales (physical, cognitive, emotional, social, and role functioning), three symptom scales (fatigue, nausea–vomiting, and pain) and five single items (dyspnoea, insomnia, appetite loss, constipation, and diarrhoea). The summary score ranges from 0 to 100 (higher score representing better HRQOL).[16] The mental adjustment to cancer scale comprises two summary subscales: summary positive adjustment (scores range 17–68; higher score indicating more positive adjustment) and summary negative adjustment (score range 16–64; higher score indicating more negative adjustment).[17] The Supportive Care Needs Survey Short Form 34 contains 4 domains: physical and daily living, psychological, sexuality, and health system, information, and patient support. Scores range from 0 to 100 (higher score reflecting a higher need).[18] The General Self-Efficacy scale assesses optimistic self-beliefs regarding coping with difficult demands in life; its total score ranges from 10 to 40 (higher score reflecting higher self-efficacy).[19] The Pearlin & Schooler Mastery Scale measures global sense of personal control; its score ranges from 7 to 35 (a higher score reflecting greater mastery).[20] The Perceived Efficacy Patient-Physician Interactions scale measures patients' confidence in interacting with their care provider; its score ranges from 5 to 25 (a higher score reflecting better confidence).[21] Head and neck cancer symptoms were measured by means of the EORTC QLQ-H&N43;[22] colorectal cancer symptoms were measured by means of the EORTC QLQ-CR29;[23] breast cancer symptoms were measured by means of the EORTC QLQ-BR23;[24] and Hodgkin lymphoma and non-Hodgkin lymphoma symptoms were measured by means of the EORTC-QLQ-NHL-HG29 (high grade non-Hodgkin lymphoma), EORTC QLQ-NHL-LG20 (low grade non-Hodgkin lymphoma), and EORTC QLQ-HL27 (Hodgkin lymphoma).[25] All EORTC scales and single items scores range from 0 to 100 (higher scores on symptom scales indicating higher burden of symptoms, and higher scores on functional scales indicating better functioning). Sociodemographic factors and clinical characteristics were measured with a study-specific questionnaire (marital status, education, treatment modality, comorbidities, employment status), or extracted from the NCR (age, sex, tumour type, tumour stage, time since cancer diagnosis). The Functional, Communicative and Critical Health Literacy scale measures health literacy; its score ranges from 1 to 4 (a higher score reflecting better health literacy).[26] The Multidimensional Health Locus of Control scale measures three domains (subscales) of health locus of control: internal health locus of control, powerful others, and chance. Subscale scores range from 6 to 36 points (a higher score indicating stronger self-perceived influence of that domain).[27] The eHealth Impact Questionnaire (Part 1) measures attitudes towards online health information, comfort with sharing health experiences online, and usefulness of sharing health experiences online. Subscale scores range from 0 to 100.[28]

Outcomes

The primary outcome was patient activation (knowledge, skills and confidence for self-management) according to the patient activation measure (range 0–100 [highest scores show highest activation]).[15] Secondary outcomes were HRQOL (including tumour-specific symptoms within the tumour groups), mental adjustment to cancer, supportive care needs, self-efficacy, personal control, and perceived efficacy in patient–physician interaction. Reach (an exploratory outcome) was defined as the proportion of eligible survivors and proportion of participating survivors. Cost-utility outcomes was also prespecified as a secondary outcome and will be reported elsewhere.

Statistical analysis

The hypothesis was that Oncokompas supports cancer survivors to improve their knowledge, skills, and confidence for self-management (patient activation). The study was powered to detect a clinically meaningful

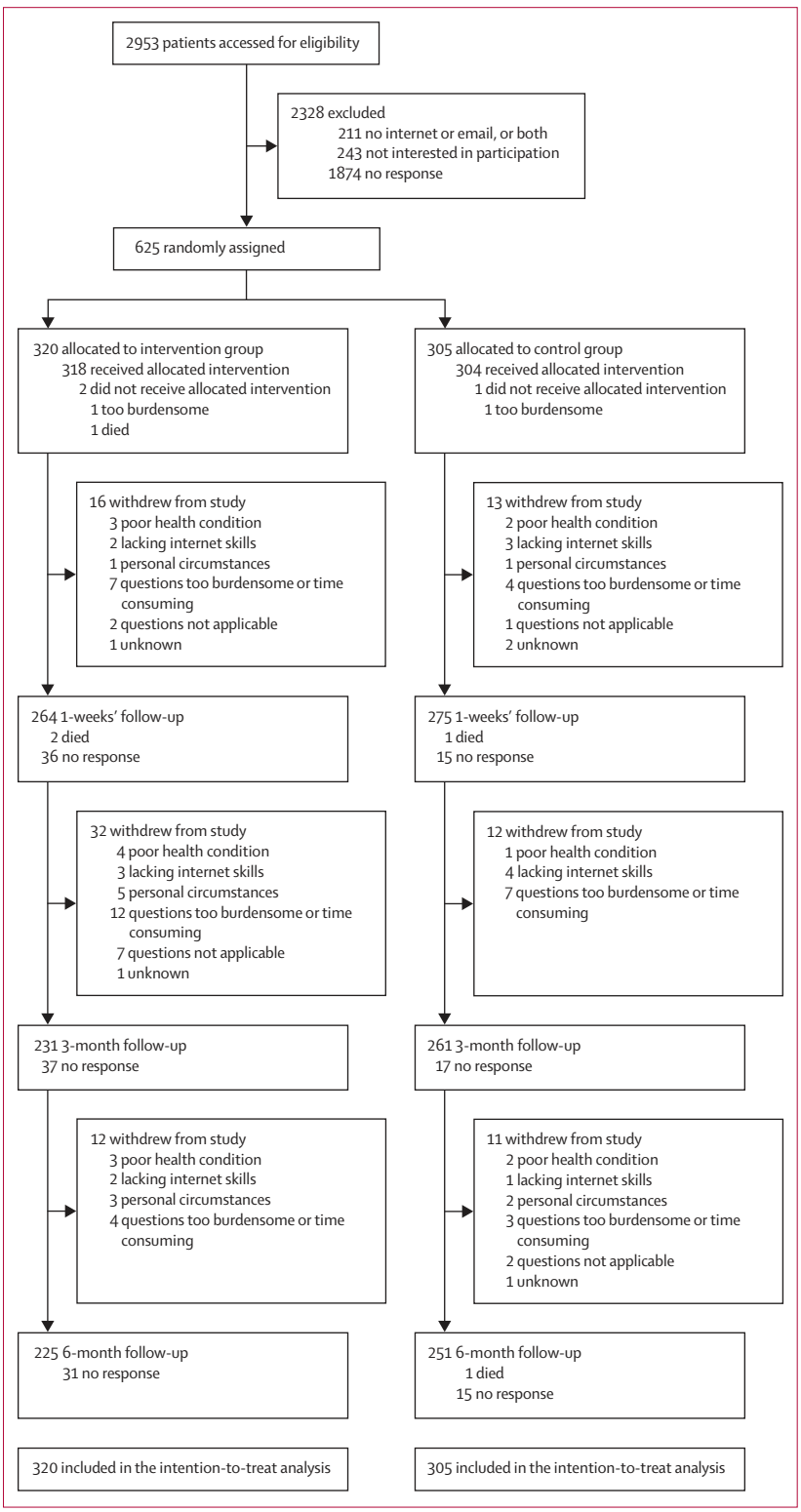

Figure 1: **Trial profile**
Randomisation and sending the invitation for Oncokompas to participants in the intervention group were on the same day. The follow-up measurements were 3 and 6 months after randomisation, for both groups. In the intervention group, first post-intervention questionnaire was sent 1 week after the use of Oncokompas, and in the control group, first post-intervention questionnaire was sent 2 weeks after randomisation.

difference of 0·5 standard units for the intervention group versus control group on the primary outcome measure (patient activation measure score) per tumour type (head and neck cancer, colorectal cancer, breast cancer, Hodgkin lymphoma, or non-Hodgkin lymphoma) at 6-months follow-up. With a power of 80% and α of 0·05, a minimum of 51 participants were needed per study arm. Anticipating drop-out of 25%, we aimed to include 136 participants for each tumour type divided into two arms, and in total 544 participants.

Descriptive statistics were generated for socio-demographic and clinical characteristics and outcome measures. χ^2 tests, independent samples *t* tests or Mann-Whitney *U* tests were used to analyse whether randomisation resulted in similar patient groups as prespecified in the study protocol. $p<0·05$ was deemed to be significant.

The proportion of eligible survivors was calculated as the number of eligible respondents (access to the internet and an email address) divided by the number of respondents of the survey on supportive care. The proportion of participating survivors was calculated as the number of participants who were randomly assigned, divided by the number of eligible respondents.

Multivariable logistic regression analyses were done to identify which sociodemographic, clinical, and psychosocial factors were associated with eligibility and participation in Oncokompas (reach). In case there were missing questions, the scoring manual of the questionnaire was followed on how to deal with missing items.

Linear mixed models were used to compare longitudinal changes in primary and secondary outcomes between both groups over time, according to the intention-to-treat principles. The models included fixed effects for group, time, and the interaction for time*group, and a random intercept for subject. For the primary outcome, linear mixed models analyses were also stratified per tumour type.

Post-hoc analyses were done among outcomes with a significantly different course between intervention and control group over time, to assess at which follow-up measurements the groups were different, with independent samples *t* tests. Cohen's *d* was calculated (effect size) by computing the difference between mean score of the intervention group minus the mean score of the control group divided by the pooled standard deviation. The magnitude of the effect size was classified as large (≥0·80), moderate (0·50–0·79), or small (<0·50). We also assessed engagement post-hoc, which was defined as the proportion of survivors in the intervention group who used Oncokompas as intended. For associations with eligibility, participation and usage, sociodemographic (sex, age, education, marital status, employment status), clinical (tumour type, stage, treatment, time since diagnosis, comorbidity), and psychosocial factors (outcomes on efficacy, locus of

control, and health literacy) were taken into account, and for the associations with participation and engagement also internet-related factors (hours of internet use, cancer-related internet searching, attitude towards eHealth [participation only]). The research committee of the Amsterdam Public Health research institute audited the study. First, univariable logistic regression analyses were done. Due to the large number of possible covariates, variables with a p-value of <0·25 in the univariable logistic regression analyses were selected. With those variables, a multivariable backward selection procedure was performed to identify factors that were independently associated with eligibility for, participation in, and usage of Oncokompas.

All analyses were two-sided and done by means of SPSS (version 25). The trial is registered with the Netherlands Trial Register, NTR5774.

Role of the funding source

The funder of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report. The corresponding author had full access to all of the data and the final responsibility to submit for publication.

Results

2953 cancer survivors were invited to participate between Oct 12, 2016, and May 24, 2018. 625 (21%) of these survivors consented to participate, completed the baseline assessment, and were randomly allocated to the intervention (n=320) or control (n=305) group (figure 1, table 1). Overall, 56% of participants had tumour stage I or II, 76% had no or only one comorbidity, and 57% had survived for more than 2 years after diagnosis (table 1). Baseline scores were in the top 10–30% of the score for HRQOL, negative adjustment to cancer, unmet supportive care needs, self-efficacy, and patient-physician interaction (table 2), as well as on most of the tumour-specific symptoms (table 3). 60 (19%) of 320 participants in the intervention group and 36 participants (12%) of 305 patients in the control group withdrew from the study (figure 1). The median follow-up period was 6 months (IQR 6–6).

The results of the linear mixed-model analyses are shown in table 2. The course of patient activation (primary endpoint) was not significantly different between the intervention group and the control group over time (difference at 6-months follow-up 1·7 [95% CI −0·8 to 4·1; p=0·41]; table 2), nor in the stratified analyses per tumour type (appendix p 3). The course of HRQOL summary score was significantly different between the intervention group and control group over time (p=0·048; difference at 6 months follow-up 2·3 [95% CI 0·0–4·5]; table 2, figure 2A). There were no significant differences between intervention and control group on the course of mental adjustment to cancer, supportive care needs, self-efficacy, personal control, or patient-physician interaction over time (table 2). Effects of Oncokompas on various tumour-specific symptoms are shown in table 3.

	Intervention (n=320)	Control (n=305)
Age, years	65 (56–71)	65 (57–71)
Women	158 (49%)	158 (52%)
Men	162 (51%)	147 (48%)
Education level		
Low	111 (35%)	117 (39%)
Medium	105 (33%)	85 (28%)
High	103 (32%)	100 (33%)
Missing	1 (<1%)	3 (1%)
Health literacy	3·2 (0·5)	3·2 (0·5)
Marital status, partner	265 (83%)	269 (88%)
Employment status, employed	122 (38%)	99 (33%)
Tumour type		
Breast cancer	66 (21%)	72 (24%)
Colorectal cancer	80 (25%)	72 (24%)
Head and neck cancer	99 (31%)	86 (28%)
Lymphoma	75 (23%)	75 (25%)
High grade non-Hodgkin lymphoma	47 (15%)	47 (15%)
Low grade non-Hodgkin lymphoma	20 (63%)	20 (66%)
Hodgkin lymphoma	8 (3%)	8 (3%)
Tumour stage		
Stage I	106 (35%)	104 (36%)
Stage II	73 (24%)	70 (24%)
Stage III	61 (20%)	67 (23%)
Stage IV	64 (21%)	52 (18%)
Missing	16 (5%)	12 (4%)
Treatment		
None or single treatment	137 (43%)	124 (41%)
Multimodal treatment	183 (57%)	181 (59%)
Comorbidities		
None or one comorbidity	249 (78%)	229 (75%)
Multiple comorbidities	71 (22%)	76 (25%)
Time since diagnosis, months	25·0 (16·0–41·0)	29·0 (16·5–41·0)
3–<12	39 (12%)	38 (13%)
12–<24	104 (33%)	85 (28%)
24–60	177 (55%)	182 (60%)

Data are mean (SD), n (%), or median (IQR).

Table 1: **Baseline characteristics**

In head and neck cancer survivors, the course of the symptoms pain in the mouth, social eating, swallowing, coughing, and trismus were significantly different between the intervention group and control group over time. In colorectal cancer survivors, the course of the symptom weight was significantly different between the intervention group and control group over time. In high grade non-Hodgkin lymphoma survivors, the course of the symptom emotional impacts was significantly

	Baseline		1 week post-intervention		3-month follow-up		6-month follow-up			Linear mixed-model analysis (p value)
	n	Mean (SD)	n	Mean (SD)	n	Mean (SD)	n	Mean (SD)	Difference (95% CI)	
Intervention	320	..	264	..	231	..	225	..	..	..
Control	305	..	275	..	261	..	251	..	..	..
Patient activation										
Total score, patient activation measure										
Intervention	292	59·2 (12·5)	245	57·2 (12·2)	217	59·5 (12·7)	209	60·0 (13·7)	1·7 (−0·8 to 4·2)	0·41
Control	277	59·5 (12·6)	251	56·9 (11·4)	241	57·9 (12·5)	234	58·3 (12·7)	..	..
HRQOL										
Summary score QLQ-C30										
Intervention	320	85·3 (14·9)	259	88·4 (12·1)	228	88·7 (13·2)	223	89·3 (12·3)	2·3 (0·0 to 4·5)	0·048
Control	304	85·4 (13·6)	271	86·2 (12·8)	253	86·5 (13·1)	247	87·0 (12·7)	..	..
Mental adjustment to cancer										
Summary positive adjustment*										
Intervention	319	48·8 (6·1)	259	47·8 (6·3)	228	47·9 (6·5)	223	47·8 (7·1)	0·5 (−0·7 to1·8)	0·77
Control	304	47·6 (6·8)	271	47·3 (6·9)	253	47·1 (6·8)	247	47·3 (6·6)	..	..
Summary negative adjustment										
Intervention	320	28·2 (7·0)	259	27·8 (6·7)	228	27·3 (6·7)	223	27·2 (6·8)	−1·1 (−2·4 to 0·1)	1·00
Control	304	29·0 (7·0)	271	29·1 (7·4)	253	28·5 (7·6)	247	28·4 (7·4)	..	..
Supportive care needs										
Physical and daily living										
Intervention	319	22·2 (24·7)	260	18·6 (22·9)	229	17·1 (22·7)	224	17·4 (23·6)	−1·1 (−5·3 to 3·1)	0·50
Control	305	22·6 (23·4)	273	20·8 (22·1)	257	20·0 (22·4)	249	18·6 (22·8)	..	..
Psychological										
Intervention	319	24·1 (24·0)	260	18·8 (21·2)	229	16·4 (19·2)	224	15·5 (19·9)	−5·2 (−9·1 to 1·3)	0·18
Control	305	25·0 (23·1)	273	22·3 (22·4)	257	21·5 (22·1)	249	20·7 (23·1)	..	..
Sexuality										
Intervention	308	15·7 (25·3)	252	11·9 (22·0)	223	12·3 (23·1)	220	11·3 (21·3)	−2·0 (−6·2 to 2·1)	0·35
Control	297	15·9 (26·5)	268	14·6 (24·1)	253	14·6 (24·4)	240	13·4 (23·7)	..	..
Health system, information and patient support										
Intervention	319	20·0 (22·2)	260	14·8 (19·0)	229	12·2 (17·0)	223	12·6 (18·3)	−1·0 (−4·3 to 2·4)	0·41
Control	305	20·4 (21·9)	272	17·1 (19·7)	254	15·0 (18·7)	248	13·5 (18·7)	..	..
Self-efficacy										
Total score, general self-efficacy scale										
Intervention	320	32·1 (5·2)	263	32·1 (4·8)	229	32·1 (5·0)	224	32·0 (5·1)	0·5 (−0·4 to 1·4)	0·31
Control	305	31·6 (5·0)	274	31·0 (4·6)	259	31·2 (4·9)	250	31·5 (4·6)	..	..
Personal control										
Total score, Pearlin and Schooler mastery scale										
Intervention	320	24·3 (4·8)	262	24·6 (4·1)	229	24·6 (4·6)	224	24·5 (4·7)	0·9 (0·0 to 1·7)	0·68
Control	305	24·0 (5·2)	273	23·7 (4·5)	258	23·8 (4·7)	250	23·6 (4·8)	..	..
Perceived efficacy in patient-physician interaction										
Total score, perceived efficacy patient–physician interactions scale										
Intervention	320	20·8 (3·5)	262	20·5 (3·3)	229	20·6 (3·3)	224	21·0 (3·1)	0·4 (−0·1 to 0·9)	0·22
Control	305	20·8 (3·1)	273	20·4 (3·0)	258	20·7 (3·0)	249	20·6 (2·9)	..	..

HRQOL=health-related quality of life. QLQ-C30=quality of life questionnaire core 30 items. *The difference between the intervention and control group at baseline was statistically different.

Table 2: **Mean scores per group per assessment and results of linear mixed-model analyses on the primary and secondary outcomes for the total group**

different between the intervention group and control group over time. No effects on symptoms were found among breast cancer survivors (details can be found in table 3). For post-hoc analyses of effect sizes at each follow-up assessment for significant outcomes, see appendix p 4.

The first 1491 survivors (as prespecified in the protocol) were invited to complete a survey, of whom 655 (44%) responded. Respondents were older (65·6 years *vs* 64·2 years, p=0·028) and had a shorter time since diagnosis (27·9 months *vs* 30·1 months,

	Baseline		1 week post-intervention		3-month follow-up		6-month follow-up			Linear mixed-model analysis (p value)
	n	Mean (SD)	n	Mean (SD)	n	Mean (SD)	n	Mean (SD)	Difference (95% CI)	
Head and neck cancer, EORTC QLQ-H&N43										
Fear of progression										
Intervention	99	15·3 (21·9)	82	12·0 (17·2)	68	8·6 (14·3)	68	9·6 (18·5)	−2·2 (−8·1 to 3·8)	0·51
Control	86	16·7 (20·8)	76	17·1 (20·9)	71	13·8 (18·7)	64	11·7 (15·9)	..	..
Body image										
Intervention	99	9·4 (19·1)	82	9·2 (19·5)	68	6·5 (20·2)	68	7·7 (21·0)	−3·3 (−10·3 to 3·7)	0·62
Control	86	12·5 (20·8)	76	13·6 (19·2)	71	11·3 (18·1)	64	10·9 (19·6)	..	..
Dry mouth and sticky saliva										
Intervention	99	35·2 (28·9)	82	35·2 (27·7)	68	31·1 (28·9)	68	26·0 (26·5)	−3·4 (−12·6 to 5·7)	0·48
Control	86	32·9 (28·5)	76	36·6 (31·5)	71	31·7 (29·2)	64	29·4 (26·7)	..	..
Pain in the mouth										
Intervention	99	14·1 (16·0)	82	14·1 (17·6)	68	9·6 (14·8)	68	7·0 (10·7)	−8·6 (−14·2 to 3·1)	0·010
Control	86	14·5 (18·1)	76	16·8 (18·2)	71	15·7 (18·6)	64	15·6 (19·9)	..	..
Sexuality										
Intervention	83	20·7 (30·4)	70	19·0 (27·7)	60	14·7 (27·3)	58	13·8 (26·5)	−10·7 (−22·8 to 1·4)	0·11
Control	73	25·1 (34·4)	66	30·1 (34·6)	57	24·9 (32·8)	49	24·5 (35·0)	..	..
Problems with senses										
Intervention	99	19·0 (26·5)	82	18·5 (25·7)	68	12·0 (19·7)	68	13·5 (22·0)	−2·7 (−11·2 to 5·9)	0·36
Control	86	17·4 (25·8)	76	17·3 (26·9)	71	16·7 (25·4)	64	16·1 (27·5)	..	..
Problems with shoulder										
Intervention	99	10·3 (20·3)	82	11·2 (19·3)	68	8·6 (18·5)	68	10·3 (20·6)	−3·0 (−10·6 to 4·6)	0·82
Control	86	10·7 (19·8)	76	11·2 (20·6)	71	12·2 (22·4)	64	13·3 (23·6)	..	..
Skin problems										
Intervention	99	10·5 (14·7)	82	8·7 (15·7)	68	4·2 (7·4)	68	6·0 (13·6)	−0·6 (−5·4 to 4·2)	0·51
Control	86	9·0 (17·3)	76	9·1 (15·1)	71	6·6 (11·7)	64	6·6 (14·2)	..	..
Social eating										
Intervention	99	16·3 (27·0)	82	15·8 (24·6)	68	10·7 (24·2)	68	7·6 (17·8)	−9·6 (−18·2 to 1·0)	0·038
Control	86	16·3 (25·9)	76	18·3 (27·6)	71	17·5 (29·2)	64	17·2 (30·0)	..	..
Speech										
Intervention	99	16·0 (23·9)	82	15·1 (25·5)	68	10·9 (22·4)	68	8·5 (15·4)	−6·9 (−13·0 to −0·8)	0·19
Control	86	15·0 (19·8)	76	19·4 (23·1)	71	16·0 (20·7)	64	15·4 (19·9)	..	..
Swallowing										
Intervention	99	15·3 (23·1)	82	13·3 (21·0)	68	10·8 (21·3)	68	7·0 (12·7)	−6·2 (−12·5 to 0·2)	0·045
Control	86	14·1 (22·4)	76	15·9 (24·0)	71	14·4 (22·8)	64	13·2 (22·4)	..	..
Problems with teeth										
Intervention	99	12·8 (20·0)	82	11·0 (17·2)	68	8·2 (14·7)	68	8·5 (14·1)	−5·0 (−12·4 to 2·3)	0·29
Control	86	15·0 (26·4)	76	14·6 (23·9)	71	14·6 (23·2)	64	13·5 (26·1)	..	..
Coughing										
Intervention	99	13·8 (24·7)	82	13·8 (21·6)	68	10·3 (19·3)	68	6·9 (15·8)	−7·2 (−14·2 to −0·2)	0·017
Control	86	11·2 (20·8)	76	17·5 (28·0)	71	16·4 (25·7)	64	14·1 (23·6)	..	..
Swelling in the neck										
Intervention	99	5·4 (14·8)	82	6·9 (20·1)	68	5·4 (18·8)	68	2·9 (11·1)	1·4 (−1·9 to 4·6)	0·97
Control	86	4·7 (15·5)	76	6·1 (17·0)	71	3·8 (13·3)	64	1·6 (7·1)	..	..
Neurological problems										
Intervention	99	12·8 (24·6)	82	14·6 (25·2)	68	11·3 (21·2)	68	8·3 (17·6)	−6·8 (−14·9 to 1·3)	0·24
Control	86	16·7 (29·3)	76	15·8 (28·0)	71	12·7 (24·1)	64	15·1 (27·8)	..	..
Trismus										
Intervention	99	14·8 (27·4)	82	15·9 (27·3)	68	10·3 (22·5)	68	7·8 (20·9)	−11·9 (−21·5 to −2·4)	0·046
Control	86	16·7 (29·7)	76	18·0 (30·0)	71	19·7 (31·7)	64	19·8 (32·9)	..	..

(Table 3 continues on next page)

	Baseline		1 week post-intervention		3-month follow-up		6-month follow-up			Linear mixed-model analysis (p value)
	n	Mean (SD)	n	Mean (SD)	n	Mean (SD)	n	Mean (SD)	Difference (95% CI)	
(Continued from previous page)										
Social contact										
Intervention	99	2·7 (10·3)	82	2·0 (9·6)	68	1·5 (6·9)	68	1·0 (5·7)	−3·7 (−8·1 to 0·7)	0·92
Control	86	5·4 (16·9)	76	6·6 (20·4)	71	6·1 (18·9)	64	4·7 (16·7)	..	..
Weight loss										
Intervention	99	10·8 (24·7)	82	7·3 (18·9)	68	3·9 (15·8)	68	2·9 (13·8)	−1·7 (−7·0 to 3·5)	0·48
Control	86	9·7 (25·0)	76	9·6 (24·2)	71	7·0 (22·5)	64	4·7 (16·7)	..	..
Problems with wound healing										
Intervention	99	6·7 (19·0)	82	3·3 (11·2)	68	3·9 (15·8)	68	1·0 (5·7)	−1·1 (−4·5 to 2·3)	0·12
Control	86	5·0 (17·4)	76	5·7 (16·7)	71	0·9 (7·9)	64	2·1 (13·1)	..	..
Colorectal cancer, EORTC QLQ-CR29										
Urinary frequency										
Intervention	80	27·3 (22·5)	67	20·6 (21·7)	59	27·4 (24·1)	61	21·3 (20·7)	−6·2 (−13·4 to 1·1)	0·39
Control	72	31·7 (23·4)	63	27·8 (20·3)	63	27·8 (21·0)	60	27·5 (19·6)	..	..
Blood and mucus in stool										
Intervention	80	1·7 (6·3)	67	1·0 (4·9)	59	1·4 (5·6)	61	1·1 (4·2)	−2·0 (−4·5 to 0·6)	0·47
Control	72	2·1 (7·4)	63	2·9 (11·0)	63	1·9 (6·8)	60	3·1 (8·9)	..	..
Stool frequency										
Intervention	80	17·1 (22·0)	67	12·4 (17·0)	59	14·4 (19·4)	61	12·0 (17·8)	−6·6 (−13·4 to 0·2)	0·56
Control	71	19·2 (20·4)	63	18·3 (19·8)	63	19·8 (21·1)	60	18·6 (20·1)	..	..
Body image										
Intervention	80	10·1 (15·5)	67	8·6 (13·2)	59	8·3 (13·9)	61	8·2 (12·3)	−8·5 (−14·7 to −2·2)	0·53
Control	72	15·9 (22·1)	63	17·1 (21·7)	63	16·6 (19·7)	60	16·7 (21·3)	..	..
Urinary incontinence										
Intervention	80	10·8 (18·2)	67	9·0 (18·0)	59	10·7 (19·0)	61	12·6 (23·7)	8·2 (1·4 to 14·8)	0·18
Control	72	4·2 (11·1)	63	5·8 (14·1)	63	4·2 (11·2)	60	4·4 (11·4)	..	..
Dysuria										
Intervention	80	0·8 (5·2)	67	0	59	2·3 (8·5)	61	1·1 (8·5)	0·0 (−2·7 to 2·6)	0·32
Control	72	0·5 (3·9)	63	1·1 (5·9)	63	1·1 (5·9)	60	1·1 (6·0)	..	..
Abdominal pain										
Intervention	80	10·8 (20·4)	67	10·0 (20·9)	59	13·0 (21·5)	61	5·5 (16·3)	−6·2 (−13·3 to 0·9)	0·064
Control	72	10·2 (21·4)	63	8·5 (15·8)	63	13·2 (25·1)	60	11·7 (22·8)	..	..
Buttock pain										
Intervention	80	10·4 (19·6)	67	10·4 (22·6)	59	9·0 (20·4)	61	8·2 (20·8)	−0·1 (−7·0 to 6·7)	0·64
Control	72	8·3 (21·5)	63	7·4 (15·2)	63	7·9 (19·6)	60	8·3 (16·9)	..	..
Bloating										
Intervention	80	16·3 (24·3)	67	10·0 (21·7)	59	10·7 (21·8)	61	10·4 (18·8)	−2·4 (−9·6 to 4·8)	0·12
Control	72	13·4 (19·9)	63	14·3 (20·5)	63	16·4 (26·0)	60	12·8 (21·3)	..	..
Dry mouth										
Intervention	80	12·5 (22·1)	67	14·9 (24·8)	59	14·1 (24·9)	61	14·8 (24·0)	−0·8 (−8·7 to 7·1)	0·97
Control	72	12·5 (20·5)	63	13·8 (20·4)	63	13·8 (19·5)	60	15·6 (19·9)	..	..
Hair loss										
Intervention	80	1·3 (6·4)	67	0·5 (4·1)	59	1·1 (6·1)	61	0	−2·8 (−6·4 to 0·9)	0·060
Control	72	0·5 (3·9)	63	2·6 (10·9)	63	0·5 (4·2)	60	2·8 (14·1)	..	..
Taste										
Intervention	80	2·5 (12·7)	67	2·0 (9·8)	59	1·7 (9·6)	61	1·1 (6·0)	−2·8 (−7·0 to 1·4)	0·92
Control	72	6·5 (19·9)	63	5·8 (17·5)	63	5·8 (17·5)	60	3·9 (15·1)	..	..
Anxiety										
Intervention	80	13·3 (18·8)	67	14·4 (18·6)	59	14·7 (19·8)	61	11·5 (18·1)	−8·5 (−16·2 to −0·9)	0·80
Control	72	19·0 (22·9)	63	19·6 (22·9)	63	19·0 (20·5)	60	20·0 (23·9)	..	..

(Table 3 continues on next page)

	Baseline		1 week post-intervention		3-month follow-up		6-month follow-up			Linear mixed-model analysis (p value)
	n	Mean (SD)	n	Mean (SD)	n	Mean (SD)	n	Mean (SD)	Difference (95% CI)	
(Continued from previous page)										
Weight										
Intervention	80	15·4 (22·5)	67	14·4 (21·9)	59	12·4 (18·5)	61	10·4 (17·8)	−10·7 (−18·1 to −3·3)	0·028
Control	72	20·4 (27·2)	63	19·6 (22·1)	63	21·2 (21·8)	60	21·1 (22·9)	..	..
Flatulence										
Intervention	80	31·7 (31·3)	67	27·9 (28·8)	59	26·6 (27·5)	61	25·1 (27·7)	−7·1 (−17·0 to 2·8)	0·13
Control	71	29·6 (23·6)	63	29·6 (20·8)	63	33·3 (27·4)	60	32·2 (27·4)	..	..
Faecal incontinence										
Intervention	80	8·8 (21·0)	67	8·0 (19·3)	59	9·0 (19·4)	61	6·0 (14·3)	−2·9 (−8·6 to 2·8)	0·49
Control	71	8·0 (19·1)	63	10·6 (17·8)	63	11·1 (19·9)	60	8·9 (17·2)	..	..
Sore skin										
Intervention	80	12·9 (24·0)	67	10·9 (21·2)	59	9·6 (20·6)	61	7·7 (19·6)	−1·8 (−8·3 to 4·7)	0·24
Control	71	8·5 (20·9)	63	12·7 (21·1)	63	9·5 (21·9)	60	9·4 (16·3)	..	..
Embarrassment										
Intervention	80	16·3 (27·0)	67	15·4 (27·4)	59	15·8 (25·8)	61	12·0 (22·8)	−4·6 (−13·5 to 4·2)	0·65
Control	71	16·9 (28·7)	63	17·5 (26·7)	63	19·6 (26·5)	60	16·7 (26·4)	..	..
Stoma care problems										
Intervention	10	10·0 (31·6)	10	10·0 (22·5)	8	0	7	0	−2·8 (−10·5 to 5·0)	0·30
Control	14	0	13	5·1 (18·5)	14	2·4 (8·9)	12	2·8 (9·6)	..	..
Sexual interest (men)										
Intervention	45	42·2 (27·0)	41	44·7 (24·3)	35	42·9 (23·7)	34	49·0 (22·1)	0·1 (−10·3 to 10·5)	0·76
Control	46	44·2 (24·4)	47	46·8 (27·5)	48	47·2 (23·7)	47	48·9 (23·9)	..	..
Impotence (men)										
Intervention	45	46·7 (38·5)	37	45·0 (36·2)	35	38·1 (38·0)	34	45·1 (36·6)	1·4 (−14·7 to 17·5)	0·76
Control	46	37·0 (38·6)	44	41·7 (36·7)	47	42·6 (39·1)	45	43·7 (34·7)	..	..
Sexual interest (women)										
Intervention	23	27·5 (23·9)	19	29·8 (21·9)	15	35·6 (19·8)	19	29·8 (21·9)	3·9 (−12·7 to 20·5)	0·49
Control	11	21·2 (16·8)	10	16·7 (17·6)	11	27·3 (20·1)	9	25·9 (14·7)	..	..
Dyspareunia (women)										
Intervention	23	5·8 (16·4)	15	15·6 (24·8)	15	2·2 (8·6)	18	1·9 (7·9)	−5·6 (17·2 to 6·1)	0·26
Control	9	3·7 (11·1)	6	11·1 (17·2)	12	5·6 (13·0)	9	7·4 (14·7)	..	..
Lymphoma (high grade non-Hodgkin), EORTC QLQ-NHL-HG29										
Symptom burden										
Intervention	47	15·2 (17·0)	35	15·2 (18·8)	36	13·5 (19·2)	33	12·7 (17·8)	0·7 (−7·3 to 8·6)	0·33
Control	47	15·3 (16·0)	43	11·8 (11·3)	34	13·7 (19·3)	38	12·0 (15·7)	..	..
Neuropathy										
Intervention	47	23·4 (26·8)	35	22·9 (28·9)	36	22·7 (26·2)	33	16·7 (25·0)	−2·6 (−15·4 to 10·2)	0·30
Control	47	17·4 (25·3)	43	17·1 (23·7)	34	17·6 (28·1)	38	19·3 (28·6)	..	..
Physical condition/fatigue										
Intervention	47	20·1 (23·4)	35	15·2 (19·2)	36	17·2 (24·1)	33	15·2 (22·2)	−4·0 (−14·3 to 6·4)	0·97
Control	47	19·6 (18·7)	43	16·0 (16·7)	34	17·6 (20·9)	38	19·1 (21·4)	..	..
Emotional impacts										
Intervention	47	16·7 (21·2)	35	14·8 (19·0)	36	17·1 (23·1)	33	12·1 (17·9)	−3·2 (−12·4 to 6·0)	0·049
Control	47	20·6 (22·2)	43	17·2 (20·6)	34	13·7 (20·3)	38	15·4 (20·6)	..	..
Worries/fears about health and functioning										
Intervention	47	19·0 (16·7)	35	17·3 (17·7)	36	16·1 (16·3)	33	13·9 (16·1)	−2·6 (−12·0 to 6·7)	0·75
Control	46	17·8 (19·8)	43	15·7 (18·7)	34	18·2 (25·0)	38	16·6 (22·2)	..	..

(Table 3 continues on next page)

	Baseline		1 week post-intervention		3-month follow-up		6-month follow-up			Linear mixed-model analysis (p value)
	n	Mean (SD)	n	Mean (SD)	n	Mean (SD)	n	Mean (SD)	Difference (95% CI)	
(Continued from previous page)										
Breast cancer, EORTC QLQ-BR23										
Body image										
Intervention	66	80·6 (26·9)	55	87·4 (19·6)	45	88·7 (16·5)	45	88·7 (18·6)	0·1 (−7·2 to 7·4)	0·43
Control	72	83·3 (22·6)	65	85·5 (21·9)	62	88·3 (18·1)	62	88·6 (18·9)	..	..
Sexual functioning										
Intervention	62	23·4 (21·2)	47	25·2 (20·8)	39	23·9 (21·9)	38	24·6 (18·1)	−2·6 (−11·1 to 5·8)	0·76
Control	62	23·1 (21·6)	57	24·9 (20·7)	53	25·8 (19·2)	49	27·2 (20·9)	..	..
Sexual enjoyment										
Intervention	35	52·4 (28·3)	28	50·0 (23·1)	22	56·1 (26·0)	24	56·9 (23·0)	−0·3 (−14·1 to 13·4)	0·98
Control	35	57·1 (27·5)	37	55·0 (25·1)	36	57·4 (27·2)	32	57·3 (27·1)	..	..
Future perspective										
Intervention	66	68·7 (27·3)	55	75·2 (23·3)	45	74·8 (20·3)	45	77·8 (23·6)	5·2 (−4·5 to 14·9)	0·40
Control	72	70·4 (26·0)	65	75·9 (25·4)	62	71·0 (26·6)	62	72·6 (26·0)	..	..
Systemic therapy side-effects										
Intervention	66	16·5 (14·1)	55	13·1 (12·3)	45	12·4 (10·8)	45	15·3 (13·7)	0·1 (−4·9 to 5·0)	0·87
Control	71	16·0 (12·3)	65	15·0 (12·2)	62	14·8 (11·0)	62	15·3 (11·9)	..	..
Breast symptoms										
Intervention	66	17·7 (18·2)	55	16·4 (17·7)	45	14·3 (14·2)	45	14·1 (13·0)	−1·0 (−7·4 to 5·4)	0·44
Control	72	18·2 (19·6)	65	16·8 (18·5)	62	19·0 (19·6)	62	15·1 (18·5)	..	..
Arm symptoms										
Intervention	66	19·5 (18·4)	55	18·2 (18·9)	45	18·5 (16·6)	45	16·3 (17·7)	0·5 (−6·9 to 7·9)	0·53
Control	72	16·7 (18·6)	65	17·1 (18·5)	62	18·1 (18·0)	62	15·8 (19·8)	..	..
Upset by hair loss										
Intervention	14	38·1 (38·9)	9	18·5 (24·2)	10	16·7 (23·6)	14	16·7 (28·5)	−3·3 (−21·0 to 15·0)	0·31
Control	16	16·7 (21·1)	12	13·9 (17·2)	13	17·9 (17·3)	15	20·0 (16·9)	..	..

Owing to the small numbers of low-grade non-Hodgkin lymphoma and Hodgkin lymphoma survivors, the linear mixed models analyses were not performed on tumour-specific symptoms for these two types of lymphoma. EORTC=European Organisation for Research and Treatment of Cancer. QLQ=quality of life questionnaire. H&N43=head and neck 43 items. CR29=colorectal cancer 29 items. NHL-HG29=non-Hodgkin lymphoma, high grade, 29 items. BR23=breast cancer 23 items.

Table 3: **Mean scores per group per assessment and results of linear mixed-model analyses on tumour-specific symptoms**

p=0·009) than non-respondents. There were no differences regarding sex, tumour type, or tumour stage. Of the 655 respondents, 211 (32%) were not eligible for participation. Multivariable regression analyses showed that male sex (odds ratio [OR] 0·48, 95% CI 0·26–0·88), younger age (0·94, 0·92–0·97), higher health literacy (2·68, 1·75–4·10), higher positive adjustment (1·05, 1·02–1·09), and lower unmet supportive care needs regarding health system information and supportive care (0·57, 0·35–0·93) were significantly associated with eligibility; also, survivors of colorectal cancer (2·42, 1·27–4·63), breast cancer (2·84, 1·37–5·92), Hodgkin lymphoma, or non-Hodgkin lymphoma (3·50, 1·42–8·59) were more likely to be eligible than were head and neck cancer survivors. The other measured sociodemographic, clinical, and psychosocial characteristics were not significantly associated with eligibility.

Of the 444 eligible survivors invited to participate in the first recruitment phase, 201 (45%) agreed (the reach). Multivariable regression analyses showed that higher education (medium *vs* low OR 1·90, 95% CI 1·16–3·09), unmet supportive care needs for sexual problems (1·64, 1·02–2·63), and a higher belief of control of health by powerful others (ie, medical specialists; 1·06, 1·02–1·11) were significantly associated with participation in the trial. The other measured sociodemographic, clinical, and psychosocial characteristics were not significantly associated with participation. After the first recruitment phase with sufficient respondents to evaluate the reach (n=655), survivors were invited directly to participate in the randomised controlled trial.

Within the intervention group, 248 (78%) of the 320 survivors activated their account, and 167 (52%) used Oncokompas as intended at least once during the 6-month follow-up period. Among intended users, the mean number of logins was 3·84 (SD 2·86). Post-hoc multivariable regression analyses showed that higher education (high *vs* low 95% CI 2·24, 1·26–3·96), having a partner (1·98, 1·07–3·66), and not being employed (0·56, 0·35–0·91) were significantly associated with

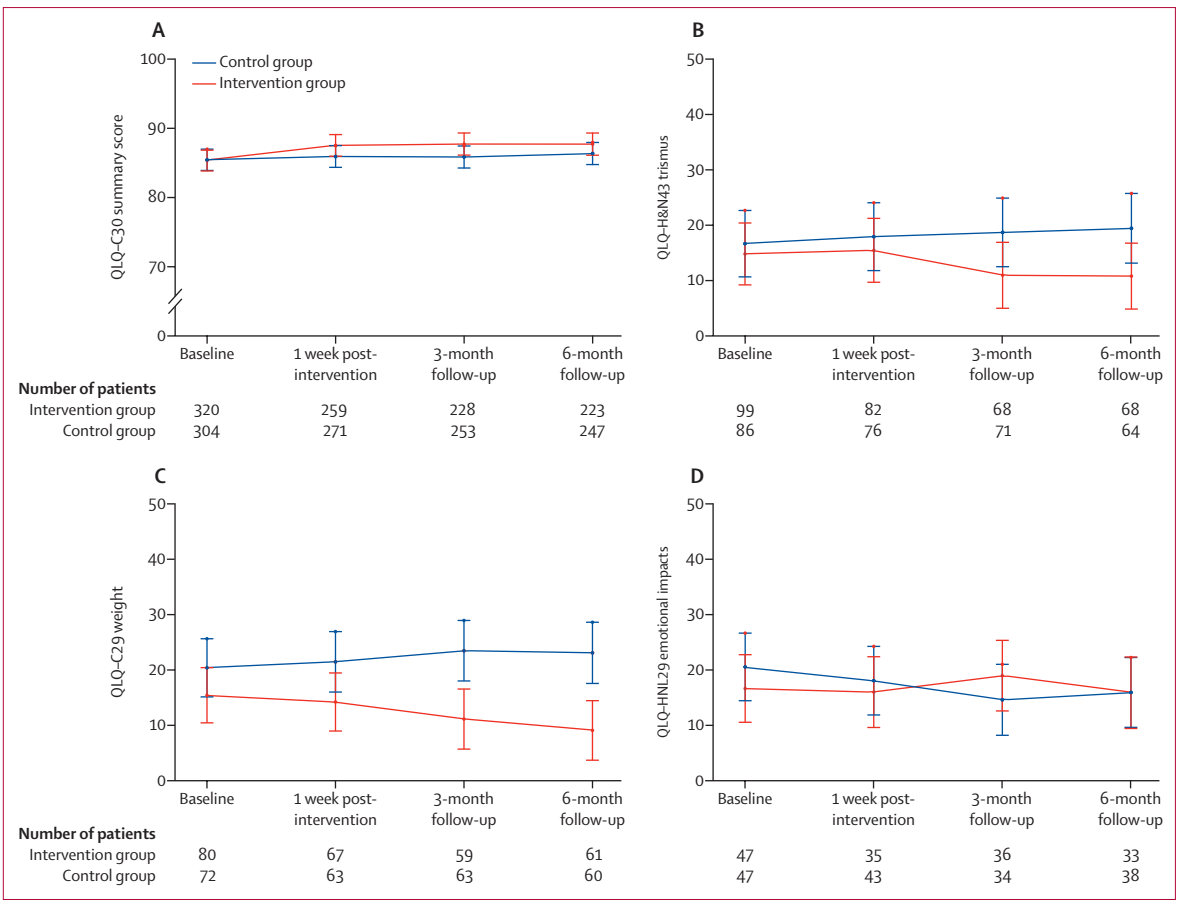

Figure 2: The course of different measures over time

(A) HRQOL summary score (a higher score indicates better HRQOL). (B) Trismus in head and neck cancer survivors (a higher score indicates higher symptom burden). (C) Worries about weight in colorectal cancer survivors (a higher score indicates higher symptom burden). (D) Emotional impact for both groups in high grade non-Hodgkin lymphoma survivors (a higher score indicates higher symptom burden). HRQOL=health-related quality of life. QLQ=quality of life questionnaire. C30=core 30 items. H&N43=head and neck 43 items. CR29=colorectal cancer 29 items. NHL-HG29=non-Hodgkin lymphoma, high grade, 29 items.

usage of Oncokompas as intended. The other measured sociodemographic, and clinical, psychosocial, and internet-related factors were not significantly associated with usage.

Discussion

In this randomised controlled trial, we investigated whether the fully automated behavioural intervention technology Oncokompass could support cancer survivors in self-management. There was no significant effect on the patients' amount of knowledge, skills, and confidence for self-management (patient activation), the primary outcome measure, or the secondary outcome measures mental adjustment to cancer, supportive care needs, self-efficacy, personal control, or perceived efficacy in the patient-physician interaction. Oncokompas did improve secondary outcome measures of HRQOL and tumour-specific symptom burden.

Regarding patient activation, the results did not confirm the findings from a pilot study on Oncokompas among breast cancer survivors, with a pre-test–post-test design, in which an increase of patient activation was found after use of Oncokompas.[11] This might be explained by the study design (with a pre–post-test design, participants are not randomised), or the fact that the time since diagnosis was longer in our randomised controlled trial than the pilot study (median of 27 months *vs* 12 months in the pilot study), and baseline scores of patient activation were higher than they were in the pilot study (mean patient activation measure score of 59·3 in our randomised controlled trial *vs* 55·8 in the pilot study). Since 57% of the randomised controlled trial participants were long-term survivors (ie, more than 2 years after cancer diagnosis), it is possible that they had already obtained sufficient knowledge, skills, and confidence regarding self-management. Offering Oncokompas at an earlier timepoint might therefore be beneficial.

The study population in the randomised trial already performed relatively well (mean scores in the better range of the scales) on most outcome measures when measured at baseline. Despite that, the course of secondary

outcomes HRQOL and several tumour-specific symptoms was better for survivors in the intervention group compared with the control group, albeit that the effect sizes were small. Some effects were found directly post-intervention, and sustained over time (eg, HRQOL), suggesting that providing survivors with tailored information and advice might only improve HRQOL soon after cancer survivors start using the application. Conversely, effects also occurred at 3 months or 6 months follow-up (eg, social eating in head and neck cancer survivors). However, it should be noted that this study was not powered to detect a difference in secondary outcomes such as HRQOL, so these results should be interpreted with caution. It might be that survivors need time to follow-up on the advice provided and use supportive care options and interventions offered through Oncokompas to improve symptoms. It could also be the case that survivors returned to Oncokompas during the follow-up period, and that they chose other topics than the previous time they completed Oncokompas, so that they recieved new information and advice. In practice, repeated use of behavioural intervention technologies such as Oncokompas is recommended, so that users can monitor their scores over time, and compare them with previous sessions. This will allow users to monitor whether symptoms are improving or when new symptoms arise, so that they receive tailored information to their current health status and preferences.

Supporting survivors to maintain or improve HRQOL and minimise symptom burden after treatment is important, but it is difficult to optimally organise long-term cancer survivorship care.[2] This study shows that a fully automated behavioural intervention technology such as Oncokompas that helps to support survivors can potentially improve HRQOL and reduce symptom burden. Most effects were found in head and neck cancer, several in colorectal cancer and non-Hodgkin lymphoma, but no effects were found in breast cancer. This might be explained by the differences in the effect of the cancer itself and the treatment, but also the availability of online information and supportive care between various tumour types.

The advantage of fully automated behavioural intervention technologies is that they can be used at any time and place, and information and content can be tailored to users' specific needs and preferences, as was applied in Oncokompas. A 2019 study of long-term prostate cancer survivors also showed that a self-management intervention with personally tailored information is promising, especially when tailored to the symptom area of choice.[7]

The results of this study should be considered with caution, because of some limitations. The study was done in the Netherlands, and the Dutch health-care system and percentage of households with internet access might not be representative for other countries. Another limitation of this study is that a p value of less than 0·05 was considered as significant, for both primary and secondary outcomes, and that we have tested many secondary outcomes, including HRQOL and tumour-specific symptoms, which might have caused random error, and for which the study was not powered. No corrections for multiple testing were applied because the analyses on secondary outcomes were exploratory, because Oncokompas is a complex intervention with various cancer-generic and tumour-specific topics in multiple HRQOL domains, which leads to several conceptually different hypotheses and statistical tests. Attrition was higher in the intervention group than in the control group, which might have affected the results. Since 52% of survivors in the intervention group used Oncokompas as intended, further qualitative research and use of system data is needed to understand the way users interact with the system and content of Oncokompas, and how this might influence efficacy. The effect size on HRQOL was small and possibly not clinically relevant (mean difference between groups was less than 10 points on a 100-point scale). In the stratified analyses per tumour type, effect sizes on tumour-specific symptoms varied from moderate to large, and only the difference on trismus in head and neck cancer survivors, and weight in colorectal cancer survivors, was clinically relevant (difference of >10 points). Another limitation is that participants had relatively few comorbidities, were often long-term survivors of early stage cancer, and were doing relatively well with respect to most outcome measures. Although it is important to know that this well performing population of cancer survivors still benefitted from Oncokompas, further qualitative research is needed into the reasons some survivors were not reached.

A strength of this study is the large sample size, with survivors from 14 hospitals, and that we included survivors with both more prevalent (breast cancer and colorectal cancer) and less prevalent tumour types (head and neck cancer, Hodgkin lymphoma and non-Hodgkin lymphoma), both men and women, and survivors from 3 months up to 5 years after treatment. Another strength is that we investigated the eligibility for eHealth in general (estimated at 68%) and the reach of a fully automated behavioural intervention technology such as Oncokompas in particular (estimated at 45% of eligible survivors), and also the usage of Oncokompas as intended (estimated at 52%), which were associated with several sociodemographic, clinical, and psychosocial factors. These findings contribute to developing tailored strategies for development and implementation of eHealth applications for cancer survivors. As positive effects were found on tumour-specific symptoms, developing more tumour-specific modules could be explored in future. Another strength is that Oncokompas is a self-management application that survivors can use independently of their health-care provider, in contrast to previous studies,[5] which might facilitate sustainability of long-term survivorship care. Further research will

provide insight into whether Oncokompas is cost-effective compared with usual survivorship care. Further qualitative research and process evaluations are needed to guide upscaling of behavioural intervention technologies such as Oncokompas. This study also raises new questions on which factors contribute to the efficacy of a behavioural intervention technology such as Oncokompas. We will further investigate engagement and the influence of sociodemographic, clinical, and psychosocial factors on the efficacy.

In conclusion, Oncokompas did not improve knowledge, skills, and confidence for self-management or other secondary outcome measures such as supportive care needs. Only secondary outcomes of HRQOL and tumour-specific symptom burden were improved.

Contributors

AvdH, CFvU-K, BIL-W, FJ, CRL, PC, LVvdP-F and IMV-dL contributed to the design of the study. AvdH, CFvU-K, LVvdP-F and IMV-dL coordinated the study. AvdH, CFvU-K, KH, GAPN, JAH, RJBdJ, NLT-V, DWS, KdH, CGS, R-JES, KB, MWMvdB, JFP, MW, JH, RPT, IH, WTvdB, RdB, PJ, SEJE, CRL, JMZ, LVvdP-F, IMV-dL contributed to the data collection. AvdH, BIL-W, FJ, KH, LVvdP-F, and IMV-dL did the data analyses. AvdH, LVvdP-F, and IMV-dL drafted the manuscript. All authors critically revised the manuscript. All authors read and approved the final manuscript.

Declaration of interests

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Data sharing

Data collected for this study, including individual patient data, can be made available on request via the corresponding author up to 15 year after the end of the study taking into account possible legal restrictions (eg, Dutch, EU).

References

1 Alfano CM, Ganz PA, Rowland JH, Hahn EE. Cancer survivorship and cancer rehabilitation: revitalizing the link. *J Clin Oncol* 2012; **30:** 904–06.

2 Lagergren P, Schandl A, Aaronson NK, et al. Cancer survivorship: an integral part of Europe's research agenda. *Mol Oncol* 2019; **13:** 624–35.

3 Warrington L, Absolom K, Conner M, et al. Electronic Systems for Patients to Report and Manage Side Effects of Cancer Treatment: Systematic Review. *J Med Internet Res* 2019; **21:** e10875.

4 Howell D, Harth T, Brown J, Bennett C, Boyko S. Self-management education interventions for patients with cancer: a systematic review. *Support Care Cancer* 2017; **25:** 1323–55.

5 Fridriksdottir N, Gunnarsdottir S, Zoëga S, Ingadottir B, Hafsteinsdottir EJG. Effects of web-based interventions on cancer patients' symptoms: review of randomized trials. *Support Care Cancer* 2018; **26:** 337–51.

6 Berry DL, Hong F, Halpenny B, et al. Electronic self-report assessment for cancer and self-care support: results of a multicenter randomized trial. *J Clin Oncol* 2014; **32:** 199–205.

7 Skolarus TA, Metreger T, Wittmann D, et al. Self-Management in long-term prostate cancer survivors: a randomized, controlled trial. *J Clin Oncol* 2019; **37**: 1326–35.

8 Lubberding S, van Uden-Kraan CF, Te Velde EA, Cuijpers P, Leemans CR, Verdonck-de Leeuw IM. Improving access to supportive cancer care through an eHealth application: a qualitative needs assessment among cancer survivors. *J Clin Nurs* 2015; **24:** 1367–79.

9 Duman-Lubberding S, van Uden-Kraan CF, Jansen F, et al. Feasibility of an eHealth application "OncoKompas" to improve personalized survivorship cancer care. *Support Care Cancer* 2016; **24:** 2163–71.

10 Duman-Lubberding S, van Uden-Kraan CF, Peek N, Cuijpers P, Leemans CR, Verdonck-de Leeuw IM. An eHealth application in head and neck cancer survivorship care: health care professionals' perspectives. *J Med Internet Res* 2015; **17:** e235.

11 Melissant HC, Verdonck-de Leeuw IM, Lissenberg-Witte BI, Konings IR, Cuijpers P, Van Uden-Kraan CF. 'Oncokompas', a web-based self-management application to support patient activation and optimal supportive care: a feasibility study among breast cancer survivors. *Acta Oncol* 2018; **57:** 924–34.

12 Matthijs de Wit L, van Uden-Kraan CF, Lissenberg-Witte BI, et al. Adoption and implementation of a web-based self-management application "Oncokompas" in routine cancer care: a national pilot study. *Support Care Cancer* 2019; **27:** 2911–20.

13 van der Hout A, van Uden-Kraan CF, Witte BI, et al. Efficacy, cost-utility and reach of an eHealth self-management application 'Oncokompas' that helps cancer survivors to obtain optimal supportive care: study protocol for a randomised controlled trial. *Trials* 2017; **18:** 228.

14 van de Poll-Franse LV, Horevoorts N, van Eenbergen M, et al. 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:** 2188–94.

15 Hibbard JH, Mahoney ER, Stockard J, Tusler M. Development and testing of a short form of the patient activation measure. *Health Serv Res* 2005; **40:** 1918–30.

16 Giesinger JM, Kieffer JM, Fayers PM, et al. Replication and validation of higher order models demonstrated that a summary score for the EORTC QLQ-C30 is robust. *J Clin Epidemiol* 2016; **69:** 79–88.

17 Watson M, Homewood J. Mental Adjustment to Cancer Scale: psychometric properties in a large cancer cohort. *Psycho-Oncology* 2008; **17:** 1146–51.

18 Boyes A, Girgis A, Lecathelinais C. Brief assessment of adult cancer patients' perceived needs: development and validation of the 34-item Supportive Care Needs Survey (SCNS-SF34). *J Eval Clin Pract* 2009; **15:** 602–06.

19 Schwarzer R, Bäßler J, Kwiatek P, Schröder K, Zhang JX. The assessment of optimistic self-beliefs: Comparison of the German, Spanish, and Chinese versions of the general self-efficacy scale. *Appl Psychol* 1997; **46:** 69–88.

20 Pearlin LI, Schooler C. The structure of coping. [Erratum]. *J Health Soc Behav* 1978; **19:** 2–21.

21 Maly RC, Frank JC, Marshall GN, DiMatteo MR, Reuben DB. Perceived efficacy in patient-physician interactions (PEPPI): validation of an instrument in older persons. *J Am Geriatr Soc* 1998; **46:** 889–94.

22 Singer S, Amdal CD, Hammerlid E, et al. International validation of the revised European Organisation for Research and Treatment of Cancer Head and Neck Cancer Module, the EORTC QLQ-HN43: Phase IV. *Head Neck* 2019; **41:** 1725–37.

23 Whistance RN, Conroy T, Chie W, et al. Clinical and psychometric validation of the EORTC QLQ-CR29 questionnaire module to assess health-related quality of life in patients with colorectal cancer. *Eur J Cancer* 2009; **45:** 3017–26.

24 Sprangers MA, Groenvold M, Arraras JI, et al. The European Organization for Research and Treatment of Cancer breast cancer-specific quality-of-life questionnaire module: first results from a three-country field study. *J Clin Oncol* 1996; **14:** 2756–68.

25 van de Poll-Franse L, Oerlemans S, Bredart A, et al. International development of four EORTC disease-specific quality of life questionnaires for patients with Hodgkin lymphoma, high- and low-grade non-Hodgkin lymphoma and chronic lymphocytic leukaemia. *Qual Life Res* 2018; **27:** 333–45.

26 Ishikawa H, Takeuchi T, Yano E. Measuring functional, communicative, and critical health literacy among diabetic patients. *Diabetes Care* 2008; **31:** 874–79.

27 Wallston KA, Wallston BS, DeVellis R, Wallston BS, DeVellis R. Development of the Multidimensional Health Locus of Control (MHLC) Scales. *Health Educ Monogr* 1978; **6:** 160–70.

28 Kelly L, Ziebland S, Jenkinson C. Measuring the effects of online health information: scale validation for the e-Health Impact Questionnaire. *Patient Educ Couns* 2015; **98:** 1418–24.
29 Engel GL. The need for a new medical model: a challenge for biomedicine. *Science* 1977; **196**: 129–36.
30 McCorkle R, Ercolano E, Lazenby M, et al. Self-management: enabling and empowering patients living with cancer as a chronic illness. *CA Cancer J Clin* 2011; **61:** 50–62.