Web-based self-management for cancer survivors

Efficacy, cost-utility and reach of Oncokompas

Anja van der Hout

Web-based selfmanagement for cancer survivors

Efficacy, cost-utility and reach of Oncokompas

Anja van der Hout

The research presented in this thesis was performed at the Faculty of Behavioural and Movement Sciences, department of Clinical-, Neuro- and Developmental Psychology of the Vrije Universiteit Amsterdam, within the Amsterdam Public Health insitute (APH) and Cancer Center Amsterdam (CCA). The research described in this thesis was funded by the Alpe d'HuZes/KWF Fund, grant number: VU 2014-7202.

Financial support for printing of this thesis was kindly provided by The Knowledge Institute of Medical Specialists.

Cover: Anja van der Hout

Layout: Anja van der Hout

Printed by: Ipskamp Printing

ISBN: 978-94-6421-203-7

VRIJE UNIVERSITEIT

WEB-BASED SELF-MANAGEMENT FOR CANCER SURVIVORS

EFFICACY, COST-UTILITY AND REACH OF ONCOKOMPAS

ACADEMISCH PROEFSCHRIFT

ter verkrijging van de graad Doctor
aan de Vrije Universiteit Amsterdam,
op gezag van de rector magnificus
prof.dr. V. Subramaniam,
in het openbaar te verdedigen
ten overstaan van de promotiecommissie
van de Faculteit der Gedrags- en Bewegingswetenschappen
op dinsdag 2 maart 2021 om 13.45 uur
in de aula van de universiteit,
De Boelelaan 1105

door

Anja van der Hout

geboren te Naaldwijk

promotoren:	prof.dr. I.M. Verdonck-de Leeuw
	prof.dr. L.V. van de Poll-Franse
copromotor:	dr. C.F. van Uden-Kraan

leescommissie:	prof.dr. H. Riper (voorzitter)
	prof.dr. S. Siesling
	prof.dr. N.H. Chavannes
	prof.dr. H.W.M. van Laarhoven
	prof.dr. J.E. Bosmans
	dr. M.M.H. Lahr

TABLE OF CONTENTS

1

General Introduction

Over the past decades, the number of cancer patients who survive cancer has increased, due to the introduction of screening programs, improved methods for early detection, new drugs and introduction of multimodal treatment.[1–3] In this thesis, the European Organisation of Research and Treatment of Cancer (EORTC) definition of a cancer survivor was used: 'a cancer survivor is an individual who has completed his or her primary treatment for cancer and is currently disease-free'.[2]

Cancer is nowadays often seen as a chronic illness, as cancer survivors often live for many years after their initial diagnosis.[4,5] Given the growing numbers of cancer survivors, and their individual needs and preferences, it is difficult to tailor supportive care to the individual, and make it available at acceptable costs.[6,7] Web-based self-management interventions can be used to tailor supportive care to the individual, are available at relatively low costs and therefore have the potential to contribute to sustainable cancer survivorship care.[8,9] The web-based self-management application Oncokompas was developed to support cancer survivors in self-management by monitoring health-related quality of life (HRQOL) and cancer-generic and tumour-specific symptoms, obtaining tailored feedback and a personalised overview of supportive care options.[10–13]

Cancer survivorship

In the Netherlands, over 117,000 people are diagnosed with cancer annually, and 65% of them are alive 5 years after their diagnosis. It is estimated that more than 777,000 people are living with or after cancer in 2019.[14] Treatment options for cancer are diverse and tailored to the individual patient, based on tumour type and stage, age and other patient characteristics. Cancer treatment often involves surgery, chemotherapy, radiotherapy, immunotherapy, endocrine therapy, or targeted therapy, given as a single treatment, or given in combination as multimodal treatment. Each tumour type and treatment has its own symptoms and side effects, also depending on individual characteristics.[15,16] Cancer survivors often experience physical and psychological symptoms and functional limitations, and also social and existential concerns and lifestyle issues, related to cancer and the treatment of cancer.[7,17–19] Some of these symptoms occur during or short after treatment (short-term effects), and can persist over time (long-term effects). Other symptoms may not be apparent until years after treatment, so-called late effects. Both short and long-term as well as late effects are likely to have an impact on HRQOL and medical care consumption.[2,19,20]

Symptoms and HRQOL are typically measured by patient reported outcome measures (PROMs). PROMs are used in research to evaluate new interventions or treatments, and in clinical practice to

tailor and adapt treatment to the individual, and to evaluate the quality of care.[21–23] Aggregated PROM data can also be used for informing patients and healthcare professionals for medical decision making, for instance the type of treatment. There is growing evidence from randomised controlled trials (RCTs) that incorporating PROMs in the routine care of cancer patients during treatment can help identify psychological and physical problems, monitor them over time, facilitate patient-doctor communication and engage patients in decision-making.[21,24–26] Collecting PROMs during cancer follow-up is suggested to be useful for an overview of patient's symptoms and problems, and possibly leads to improvements in symptom management.[27,28] Studies have shown that PROMs more accurately capture patients' experience of symptoms and other problems than assessments of symptoms by healthcare professionals.[22,27,29,30] Therefore, PROMs can be used to identify cancer survivors' symptoms and needs, and tailor supportive care to the individual.

Supportive care

Supportive care includes the prevention and management of the adverse effects of cancer and its treatment, and the management of psychological symptoms, social functioning, and existential and lifestyle issues related to cancer recurrence.[31–34] Supportive care is increasingly seen as an integral part of quality cancer treatment.[17,35] Supportive care needs are diverse, and will vary from person to person, and within the same person over time.[35,36] Needs can relate to coping with changes in physical and daily functioning, or psychological, social and spiritual problems, related to cancer or its treatment. Examples of supportive care options are a physical therapist for problems with physical functioning, a psychologist for depressive symptoms, therapy by a sexologist for sexual problems, online cognitive behavioural therapy to reduce fatigue, self-help interventions for smoking cessation, or peer support groups on existential questions. Also, access to evidence-based information is seen as an important part of supportive care.[37]

Although there is evidence that supportive care is effective, referral rates are low, and many cancer survivors have unmet needs.[38–42] Many cancer survivors find it difficult to find and obtain supportive care applicable to their situation and needs, or are not aware of supportive care options.[43,44] On the other hand, healthcare providers find it difficult to identify cancer survivors' symptoms and supportive care needs, and are often not aware either of available supportive care services.[12,45] To improve accessibility to optimal supportive care, cancer survivors are expected to adopt an active role in managing their own care.[46–48]

Self-management

Self-management is defined by McCorkle et al. as 'those tasks that individuals undertake to deal with the medical, role, and emotional management of their health condition(s)'.[49] The goal of self-management is to empower patients to achieve optimal health and well-being, while living with a chronic disease.[49,50] Self-management interventions can be used to equip patients with skills to actively participate and take responsibility in the management of their chronic condition in order to optimally function.[51,52] Activated patients, i.e. patients with knowledge, skills, and confidence for self-management, are more likely to have better health outcomes and lower healthcare service utilization.[53,54] Also, a higher level of patient activation is likely to be associated with lower medical costs.[55]

Self-management interventions, such as exercise programs, self-help interventions, or behavioural interventions can improve empowerment and self-efficacy.[56,57] Reviews have shown that self-management of chronic disease has the potential to have moderate, but clinically relevant improvements in self-efficacy, health behaviours, health status and quality of life.[58]

There are different possibilities to deliver self-management interventions, such as individual or group interventions supported by a healthcare professional. Self-management interventions are also very suitable for online delivery in web-based interventions because they can be tailored to the individual user, using algorithms to select content and support, tailored to the needs and preferences of the user. Other advantages of web-based interventions are that they can be used when most needed, i.e. 24 hours per day, there is no need to wait for an appointment with a healthcare professional, these interventions are available in rural areas or for people with reduced mobility, and answers can be given anonymously. Web-based self-management interventions can have positive effects on HRQOL and symptom burden in cancer patients and survivors.[59–63]

eHealth interventions

Delivering online health information, web-based self-management interventions can be classified as eHealth interventions. eHealth refers to information and communication technology that is used for supporting healthcare and promoting a sense of well-being.[64,65] Within the broad field of eHealth, behavioural intervention technologies (BITs) are a subset of eHealth interventions that uses technology features to support behaviour change related to physical, behavioural and mental

health.[66,67] BITs can be delivered or supported by a healthcare professional, to extend the reach of the therapist, e.g. a psychotherapy session delivered via videoconferencing or telephone, but they can also be fully automated, with content delivered using primarily machine-powered systems. Adjunctive or guided BITs need a healthcare professional to discuss results or guide them through the intervention, while fully automated BITs can be used independently from a healthcare professional. Although it is hypothesized that fully automated BITs support cancer survivors in their self-management and improve their quality of life, little is known about the feasibility, reach, and effectiveness of such interventions.

Oncokompas

The web-based self-management application 'Oncokompas' was developed with the aim to support cancer survivors in self-management by monitoring HRQOL and cancer-generic and tumour-specific symptoms, providing feedback and information on their personal scores, as well as a personalized overview of supportive care options. Oncokompas is an eHealth intervention, which can be classified as a fully automated BIT, as it can be used without the help of a healthcare professional. Oncokompas is based on the Chronic Care Model (CCM). CCM is designed to improve health outcomes for people with chronic conditions, by changing the daily care from acute and reactive to proactive, planned and population-based.[49,68–70] The CCM highlights the importance of self-management support; i.e. giving patients the knowledge, confidence and skills for self-management of their condition.[68,70]

Oncokompas contains topics on cancer-generic HRQOL issues and symptoms, clustered in multiple domains. In the biopsychosocial model formulated by Engel, it is stated that biological factors, as well as psychological and social factors play a role in disease and management of disease.[71,72] Following this biopsychosocial model, Oncokompas contains domains on physical, psychological and social functioning. These three domains are supplemented with domains on lifestyle and existential questions, as many cancer survivors have problems related to obtaining a healthy lifestyle, and have existential questions.[33,34] Besides cancer-generic topics in these five domains, covering problems such as fatigue, fear of recurrence, relationships, and smoking cessation, tumour-specific modules were developed, covering problems related to (the treatment of) a specific tumour type. These modules were developed for head and neck cancer, with topics such as swallowing and speech, for colorectal cancer, with topics such as diarrhoea and stoma-related problems, for breast cancer, with

topics such as menopausal symptoms and lymphedema,[73] and for survivors of lymphoma, with topics such as neuropathy and stem cell transplantation. A complete overview of topics within the cancer-generic domains, and tumour-specific modules are shown in **Figure 1**. Oncokompas consists of three components: Measure, Learn and Act. Based on patient reported outcome measures (PROMs) (Measure), users get tailored information (Learn), and a personalised overview of supportive care options (Act).

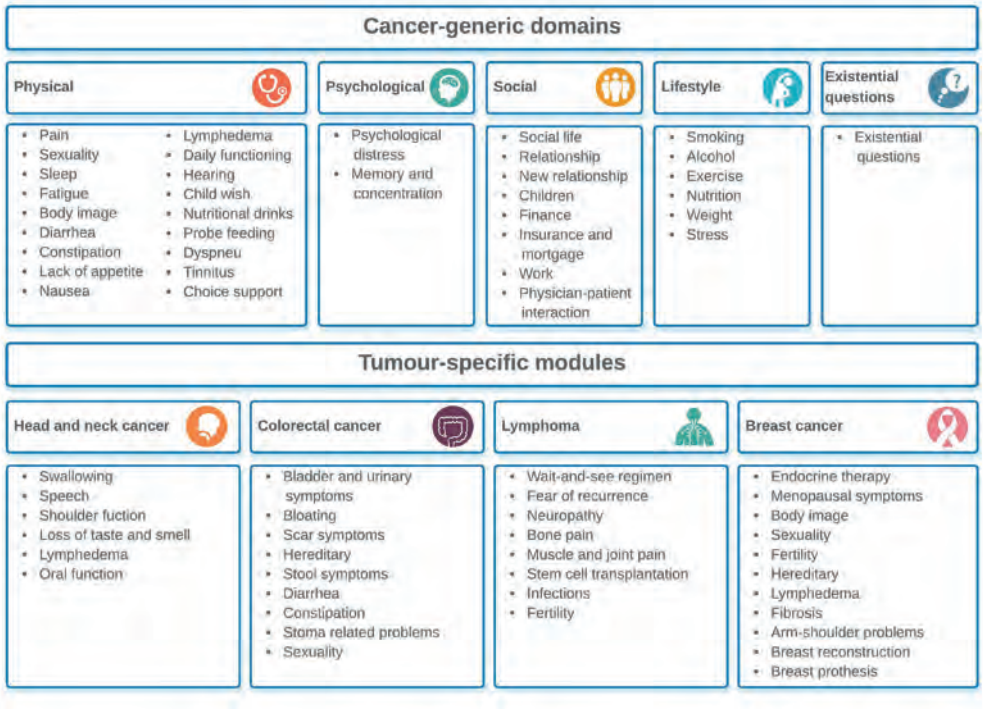


Figure 1 – Overview of topics within generic domains and tumour-specific modules in Oncokompas, as used in the studies in this thesis

The development of the eHealth application Oncokompas started in 2011 at the department of Otolaryngology – Head & Neck Surgery of the VU University Medical Center in Amsterdam. Participatory design principles were followed, to ensure sustainable usage and an application that fits the needs of cancer survivors and healthcare professionals.[64] Relevant stakeholders, such as cancer patients, cancer survivors, and healthcare professionals were involved in the development process.

First, the needs among head and neck cancer survivors and healthcare professionals were explored. A qualitative study was performed among 30 cancer survivors of head and neck and breast cancer, to gain insight in supportive care. Cancer survivors mentioned that they felt unprepared for the post-treatment period, their symptoms often remained unknown to healthcare providers, and the referral to supportive care was suboptimal. Most cancer survivors were positive to an eHealth application that monitors HRQOL and gives a personalised overview of supportive care options, and they mentioned that it could be a valuable addition to follow-up cancer care.[10] A qualitative study among 11 healthcare professionals involved in head and neck cancer care was performed to gain insight in the perspectives of healthcare professionals towards follow-up care and an eHealth application. Several barriers for optimal supportive care were mentioned, including difficulties in detecting symptoms and supportive care needs, and lack of time to encourage cancer survivors to obtain supportive care.[12] Based on this, a prototype of Oncokompas was developed, and its usability was tested among patients and healthcare professionals by means of cognitive walkthroughs. Healthcare professionals emphasized the importance of tailoring care, but they considered the navigation structure of Oncokompas to be complex.[74]

Among 18 head and neck cancer patients, system quality (ease of use), content quality (usefulness and relevance), and service quality (the process of care provided) was evaluated.[64] Some participants had doubts about the added value of Oncokompas in follow-up cancer care, but found it potentially useful when symptoms were present. Many found the insight into supportive care options valuable, and a stimulant to self-manage their health. Based on these findings, the prototype of Oncokompas was adapted and built into a full application, with cancer-generic and head and neck cancer specific topics.

With this version, a feasibility study was conducted among head and neck cancer survivors. A pre-post-test study was performed, in which the reach and usage of Oncokompas was evaluated. Of the 106 head and neck cancer survivors who were invited, 68 (64%) participated. The self-reported use of Oncokompas was 91% among the cancer survivors who completed the post-test. Most participants were satisfied with Oncokompas in general, and 76% evaluated Oncokompas as user-friendly.[11]

Another tumour-specific module was developed, for breast cancer survivors. A pilot study was performed to evaluate the feasibility of Oncokompas and the breast cancer module, in which pre- and post-test differences on patient activation were explored, and usage was evaluated. Of the

101 breast cancer survivors who were invited, 76 (75%) participated. Based on log-data, the usage rate was 75%. The mean satisfaction score with Oncokompas was 6.9, and with the breast cancer module 7.6, on a scale from 0 to 10. After using Oncokompas, the level of patient activation was significantly better than before.[73]

It was concluded that Oncokompas is feasible and fits the user's needs. The next step was to evaluate the impact of Oncokompas in clinical practice. For the evaluation of Oncokompas, the RE-AIM framework was used, which is an evaluation model that conceptualises the impact of an intervention as a function of the factors: reach, efficacy, adoption, implementation, and maintenance (RE-AIM).[75] Because evidence on the cost-utility is also important with respect to the adoption and implementation of newly developed interventions in cancer survivorship care, also the cost-utility of Oncokompas was evaluated. This thesis will focus on the efficacy, cost-utility, and reach of Oncokompas.

AIM AND OUTLINE

The overall aim of this thesis was to investigate the web-based self-management application Oncokompas among cancer survivors, in terms of efficacy, cost-utility, and reach. The research questions addressed in this thesis are:

1. Is Oncokompas effective compared to usual cancer survivorship care?
    a) *What is the effect on cancer survivors' knowledge, skills and confidence for self-management (patient activation)?*
    b) *What is the effect on HRQOL and symptoms, self-efficacy, personal control, supportive care needs, mental adjustment to cancer and perceived efficacy in patient-physician interaction?*
    c) *What are moderating factors of the observed effects of Oncokompas?*
2. Is Oncokompas cost-effective compared to usual cancer survivorship care?
3. Who is reached by web-based self-management interventions, i.e. which factors are associated with eligibility for and participation in Oncokompas?

An RCT was conducted among cancer survivors of head and neck, colorectal, breast cancer and (non-) Hodgkin lymphoma, up to 5 years after diagnosis. Participants were randomised into the intervention group, in which they had access to Oncokompas, or the wait-list control group, in which they had access to Oncokompas after 6 months. A visual overview of Oncokompas is presented in the **Intermezzo**, and the protocol of this RCT is described in **Chapter 2**.

In the first recruitment phase, the reach of Oncokompas was explored, i.e. the number of cancer survivors eligible for Oncokompas, and the number of cancer survivors willing to participate in Oncokompas were explored, as well as factors associated with eligibility and participation. In **Chapter 3**, the results of the efficacy and reach of the eHealth self-management application Oncokompas are described. In **Chapter 4**, moderating factors of the efficacy of Oncokompas are explored, to obtain insight in whether Oncokompas is especially effective in particular subgroups of cancer survivors. In **Chapter 5** the results of the cost-utility of Oncokompas compared to usual cancer survivorship care are described. In **Chapter 6** reasons for not reaching and using Oncokompas are explored, as well as the use and evaluation of Oncokompas.

An overview of the main findings of the studies and a general discussion is provided in **Chapter 7**. Furthermore, strengths and limitations, clinical implications and future perspectives for research and practice of web-based self-management among cancer survivors are discussed, and this chapter ends with the conclusion.

REFERENCES

1. Siegel RL, Miller KD, Jemal A. Cancer statistics, 2019. CA Cancer J Clin 2019; 69: 7–34.
2. Moser EC, Meunier F. Cancer survivorship: A positive side-effect of more successful cancer treatment. Eur J Cancer, Suppl 2014; 12: 1–4.
3. Malvezzi M, Bertuccio P, Rosso T, et al. European cancer mortality predictions for the year 2015: Does lung cancer have the highest death rate in EU women? Ann Oncol 2015; 26: 779–86.
4. Naus MJ, Ishler MD, Parrott CE, Kovacs SA. Cancer survivor adaptation model: Conceptualizing cancer as a chronic illness. J Clin Psychol 2009; 65: 1350–9.
5. Pizzoli SFM, Renzi C, Arnaboldi P, Russell-Edu W, Pravettoni G. From life-threatening to chronic disease: Is this the case of cancers? A systematic review. Cogent Psychol 2019; 6: 1–17.
6. Mayer DK, Alfano CM. Personalized Risk-Stratified Cancer Follow-Up Care: Its Potential for Healthier Survivors, Happier Clinicians, and Lower Costs. J. Natl. Cancer Inst. 2019; 111: 442–8.
7. Lagergren P, Schandl A, Aaronson NK, et al. Cancer survivorship: an integral part of Europe's research agenda. Mol Oncol 2019; 13: 624–35.
8. Murray E. Web-based interventions for behavior change and self-management: Potential, pitfalls, and progress. J Med Internet Res 2012; 14: 1(2):e3.
9. Bashshur RL, Shannon G, Krupinski EA, Grigsby J. Sustaining and Realizing the Promise of Telemedicine. Telemed e-Health 2013; 19: 339–45.
10. 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.
11. 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.
12. Duman-Lubberding S, Van Uden-Kraan CF, Peek N, Cuijpers P, Leemans CR, Verdonck-DeLeeuw IM. An eHealth application in head and neck cancer survivorship care: Health care professionals' perspectives. J Med Internet Res 2015; 17: e235.
13. Duman-Lubberding S, van Uden-Kraan CF, Jansen F, et al. Durable usage of patient-reported outcome measures in clinical practice to monitor health-related quality of life in head and neck cancer patients. Support Care Cancer 2017; 25: 3775–83.
14. Integraal Kankercentrum Nederland (IKNL). Cijfers over kanker. https://www.cijfersoverkanker.nl (accessed May 22, 2020).
15. Burkett VS, Cleeland CS. Symptom burden in cancer survivorship. J Cancer Surviv 2007; 1: 167–75.
16. Harrington CB, Hansen JA, Moskowitz M, Todd BL, Feuerstein M. It's not over when it's over: Long-term symptoms in cancer survivors-a systematic review. Int. J. Psychiatry Med. 2010; 40: 163–81.
17. Aaronson NK, Mattioli V, Minton O, et al. Beyond treatment - Psychosocial and behavioural issues in cancer survivorship research and practice. Eur J Cancer Suppl 2014; 12: 54–64.
18. Given CW, Given BA. Symptom management and psychosocial outcomes following cancer. Semin Oncol 2013; 40: 774–83.
19. Stein KD, Syrjala KL, Andrykowski MA. Physical and psychological long-term and late effects of cancer. Cancer 2008; 112: 2577–92.
20. Rowland JH, Bellizzi KM. Cancer survivorship issues: Life after treatment and implications for an aging population. J. Clin. Oncol. 2014; 32: 2662–8.

21. Basch E, Abernethy AP. Supporting clinical practice decisions with real-time patient-reported outcomes. J. Clin. Oncol. 2011; 29: 954–6.

22. Snyder CF, Blackford AL, Aaronson NK, et al. Can patient-reported outcome measures identify cancer patients' most bothersome issues? J Clin Oncol 2011; 29: 1216–20.

23. Black N, Burke L, Forrest CB, et al. Patient-reported outcomes: pathways to better health, better services, and better societies. Qual Life Res 2016; 25: 1103–12.

24. Velikova G, Booth L, Smith AB, et al. Measuring quality of life in routine oncology practice improves communication and patient well-being: A randomized controlled trial. J Clin Oncol 2004; 22: 714–24.

25. Takeuchi EE, Keding A, Awad N, et al. Impact of patient-reported outcomes in oncology: A longitudinal analysis of patient-physician communication. J Clin Oncol 2011; 29: 2910–7.

26. Warrington L, Absolom K, Velikova G. Integrated care pathways for cancer survivors - A role for patient-reported outcome measures and health informatics. Acta Oncol (Madr) 2015; 54: 600–8.

27. Riis CL, Bechmann T, Jensen PT, Coulter A, Steffensen KD. Are patient-reported outcomes useful in post-treatment follow-up care for women with early breast cancer? A scoping review. Patient Relat Outcome Meas 2019; Volume 10: 117–27.

28. Kotronoulas G, Kearney N, Maguire R, et al. 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: 1480–501.

29. Berry DL, Blumenstein BA, Halpenny B, et al. Enhancing patient-provider communication with the electronic self-report assessment for cancer: A randomized trial. J Clin Oncol 2011; 29: 1029–35.

30. Gordon BBE, Chen RC. Patient-reported outcomes in cancer survivorship. Acta Oncol (Madr) 2017; 56: 166–73.

31. Surbone A, Baider L, Weitzman TS, Brames MJ, Rittenberg CN, Johnson J. Psychosocial care for patients and their families is integral to supportive care in cancer: MASCC position statement. Support Care Cancer 2009; 18: 255–63.

32. Hui D, De La Cruz M, Mori M, et al. Concepts and definitions for 'supportive care,' 'best supportive care,' 'palliative care,' and 'hospice care' in the published literature, dictionaries, and textbooks. Support. Care Cancer. 2013; 21: 659–85.

33. Jordan K, Aapro M, Kaasa S, et al. European Society for Medical Oncology (ESMO) position paper on supportive and palliative care. Ann Oncol 2018; 29: 36–43.

34. Olver I, Keefe D, Herrstedt J, Warr D, Roila F, Ripamonti CI. Supportive care in cancer—a MASCC perspective. Support Care Cancer 2020; : 1–9.

35. Fitch MI. Supportive care framework. Can Oncol Nurs J 2008; 18: 6–14.

36. Aziz NM. Cancer survivorship research: State of knowledge, challenges and opportunities. Acta Oncol (Madr) 2007; 46: 417–32.

37. Harrison JD, Young JM, Price MA, Butow PN, Solomon MJ. What are the unmet supportive care needs of people with cancer? A systematic review. Support Care Cancer 2009; 17: 1117–28.

38. Speck RM, Courneya KS, Mâsse LC, Duval S, Schmitz KH. An update of controlled physical activity trials in cancer survivors: A systematic review and meta-analysis. J Cancer Surviv 2010; 4: 87–100.

39. Hart SL, Hoyt MA, Diefenbach M, et al. Meta-analysis of efficacy of interventions for elevated depressive symptoms in adults diagnosed with cancer. J Natl Cancer Inst 2012; 104: 990–1004.

40. Mewes JC, Steuten LMG, IJzerman MJ, van Harten WH. Effectiveness of Multidimensional Cancer Survivor Rehabilitation and Cost-Effectiveness of Cancer Rehabilitation in General: A Systematic Review. Oncologist 2012; 17: 1581–93.

41. Boyes AW, Girgis A, D'Este C, Zucca AC. Prevalence and correlates of cancer survivors' supportive care needs 6 months after diagnosis: a population-based cross-sectional study. BMC Cancer 2012; 12: 150.

42. Shakeel S, Tung J, Rahal R, Finley C. Evaluation of Factors Associated With Unmet Needs in Adult Cancer Survivors in Canada. JAMA Netw open 2020; 3: e200506.

43. Eakin EG, Strycker LA. Awareness and barriers to use of cancer support and information resources by HMO patients with breast, prostate, or colon cancer: Patient and provider perspectives. Psychooncology 2001; 10: 103–13.

44. Walsh J, Young JM, Harrison JD, et al. What is important in cancer care coordination? A qualitative investigation. Eur J Cancer Care (Engl) 2011; 20: 220–7.

45. Fennell KM, Bamford L, Olver I, Wilson CJ. Good training, systems and funding, not good luck: What hematologists and oncologists believe would make it easier for them to refer their cancer patients to psychosocial care. Transl Behav Med 2019; 9: 139–46.

46. Jansen F, van Uden-Kraan CF, van Zwieten V, Witte BI, Verdonck-de Leeuw IM. Cancer survivors' perceived need for supportive care and their attitude towards self-management and eHealth. Support Care Cancer 2015; 23: 1679–88.

47. Greene J, Hibbard JH, Sacks R, Overton V, Parrotta CD. When patient activation levels change, health outcomes and costs change, too. Health Aff 2015; 34: 431–7.

48. 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.

49. 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.

50. Cuthbert CA, Farragher JF, Hemmelgarn BR, Ding Q, McKinnon GP, Cheung WY. Self-management interventions for cancer survivors: A systematic review and evaluation of intervention content and theories. Psychooncology 2019; 28: 2119–40.

51. Jonkman NH, Schuurmans MJ, Jaarsma T, Shortridge-Baggett LM, Hoes AW, Trappenburg JCA. Self-management interventions: Proposal and validation of a new operational definition. J. Clin. Epidemiol. 2016; 80: 34–42.

52. Lorig KR, Holman HR. Self-management education: History, definition, outcomes, and mechanisms. Ann. Behav. Med. 2003; 26: 1–7.

53. Remmers C, Hibbard J, Mosen DM, Wagenfield M, Hoye RE, Jones C. Is Patient Activation Associated With Future Health Outcomes and Healthcare Utilization Among Patients With Diabetes? J Ambul Care Manage 2009; 32: 320–7.

54. Hibbard JH, Mahoney ER, Stock R, Tusler M. Do increases in patient activation result in improved self-management behaviors? Health Serv Res 2007; 42: 1443–63.

55. Jansen F, Coupé VMH, Eerenstein SEJ, Leemans CR, Verdonck-de Leeuw IM. Costs from a healthcare and societal perspective among cancer patients after total laryngectomy: are they related to patient activation? Support Care Cancer 2018; 26: 1221–31.

56. Cimprich B, Janz NK, Northouse L, Wren PA, Given B, Given CW. Taking charge: A self-management program for women following breast cancer treatment. Psychooncology 2005; 14: 704–17.

57. Kuijpers W, Groen WG, Aaronson NK, Van Harten WH. A systematic review of web-based interventions for patient empowerment and physical activity in chronic diseases: Relevance for cancer survivors. J Med Internet Res 2013; 15: e37.

58. Allegrante JP, Wells MT, Peterson JC. Interventions to Support Behavioral Self-Management of Chronic Diseases. Annu Rev Public Health 2019; 40: 127–46.

59. 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.

60. 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.

61. 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.

62. 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.

63. 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.

64. van Gemert-Pijnen JEWC, Nijland N, van Limburg M, et al. A holistic framework to improve the uptake and impact of eHealth technologies. J Med Internet Res 2011; 13: e111.

65. Eysenbach G. What is e-health? J Med Internet Res 2001; 3: 1–5.

66. Mohr DC, Burns MN, Schueller SM, Clarke G, Klinkman M. Behavioral Intervention Technologies: Evidence review and recommendations for future research in mental health. Gen Hosp Psychiatry 2013; 35: 332–8.

67. Mohr DC, Schueller SM, Montague E, Burns MN, Rashidi P. The behavioral intervention technology model: An integrated conceptual and technological framework for ehealth and mhealth interventions. J Med Internet Res 2014; 16: e146.

68. Wagner EH. Chronic disease management: what will it take to improve care for chronic illness? Eff Clin Pract 1998; 1: 2–4.

69. Coleman K, Austin BT, Brach C, Wagner EH. Evidence on the Chronic Care Model in the new millennium. Health Aff 2009; 28: 75–85.

70. Gee PM, Greenwood DA, Paterniti DA, Ward D, Miller LMS. The eHealth enhanced chronic care model: A theory derivation approach. J Med Internet Res 2015; 17: e86.

71. Engel GL. The need for a new medical model: A challenge for biomedicine. Science (80-) 1977; 196: 129–36.

72. Epstein R, Borrell-Carrio F, Suchman A. The Biopsychosocial Model 25 Years Later: Principles, Practice, and Scientific Inquiry. Ann Fam Med 2004; 2: 576–82.

73. 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 (Madr) 2018; 57: 924–34.

74. Duman-Lubberding S. Intermezzo Oncokompas. In: Online Patient Reported Outcome Measures To Facilitate Supportive Care in Head and Neck Cancer Patients. 2018.

75. Glasgow RE, Vogt TM, Boles SM. Evaluating the public health impact of health promotion interventions: The RE-AIM framework. Am J Public Health 1999; 89: 1322–7.

Overview of Oncokompas

The web-based self-management application Oncokompas was developed with the aim to support cancer survivors in self-management by monitoring health-related quality of life (HRQOL) and cancer-generic and tumour-specific symptoms, providing feedback and information on their personal scores, as well as a personalized overview of supportive care options.

Oncokompas consists of three components: Measure, Learn and Act. Based on patient reported outcome measures (PROMs) (Measure), users get tailored information on multiple quality of life domains (Learn), and a personalised overview of supportive care options (Act).

Users log in at the Oncokompas website, and first complete a short questionnaire on e.g. marital status, treatment type, time since treatment (before, during or after treatment), to determine which topics are relevant. An overview with relevant topics is provided from which users can choose which topics they want to complete (**Figure 1**).

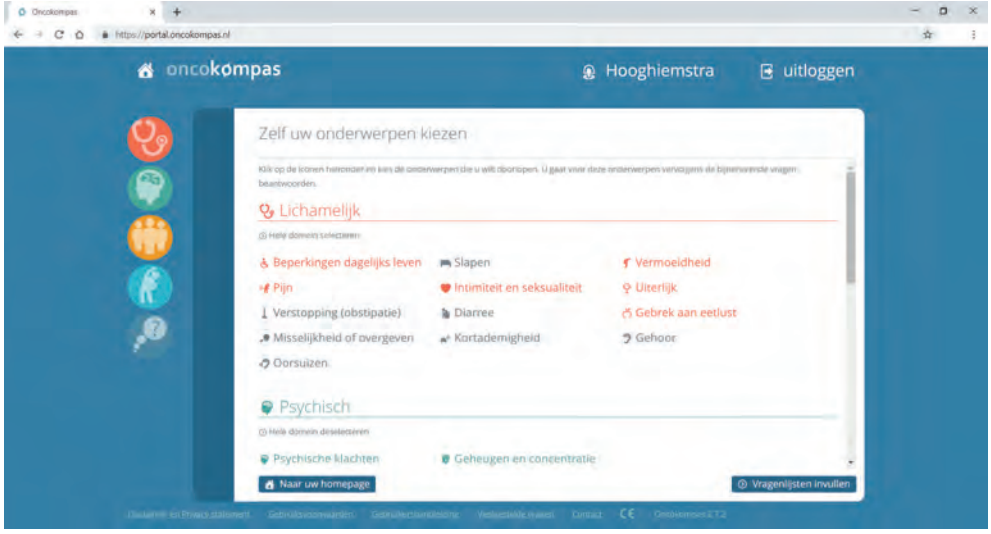


Figure 1 – Overview of topics from which users can select topics of their choice

Measure

In the component 'Measure', users complete PROMs for each of the selected topics (**Figure 2a** and **2b**). Oncokompas is a dynamic system, i.e. based on users' answers, follow-up questions or more in-depth questions are presented when necessary. Data from the Measure component is processed in real-time. Algorithm calculations are based on available cut-off scores, or are defined based on Dutch practice guidelines or consensus by teams of experts.

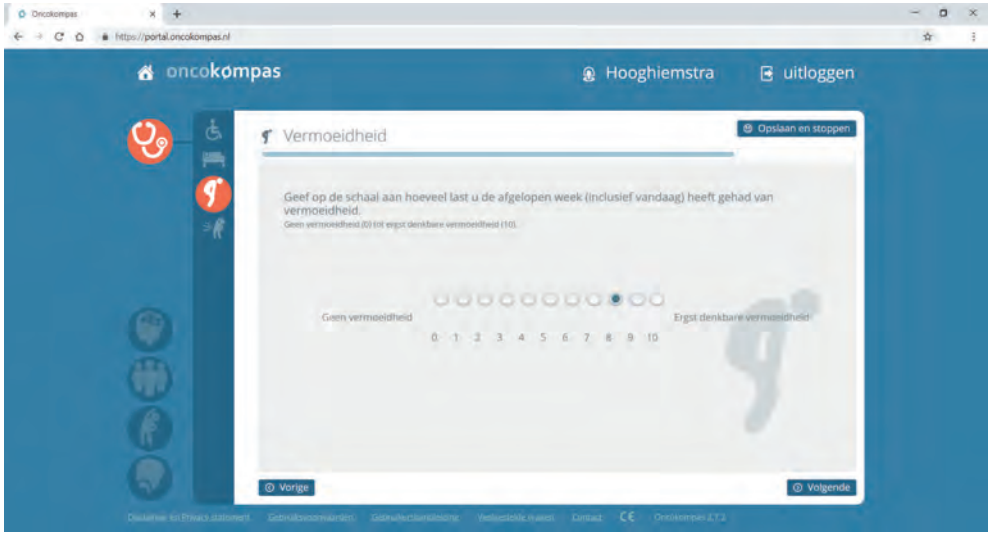


Figure 2a – Question in the component Measure, on the topic fatigue

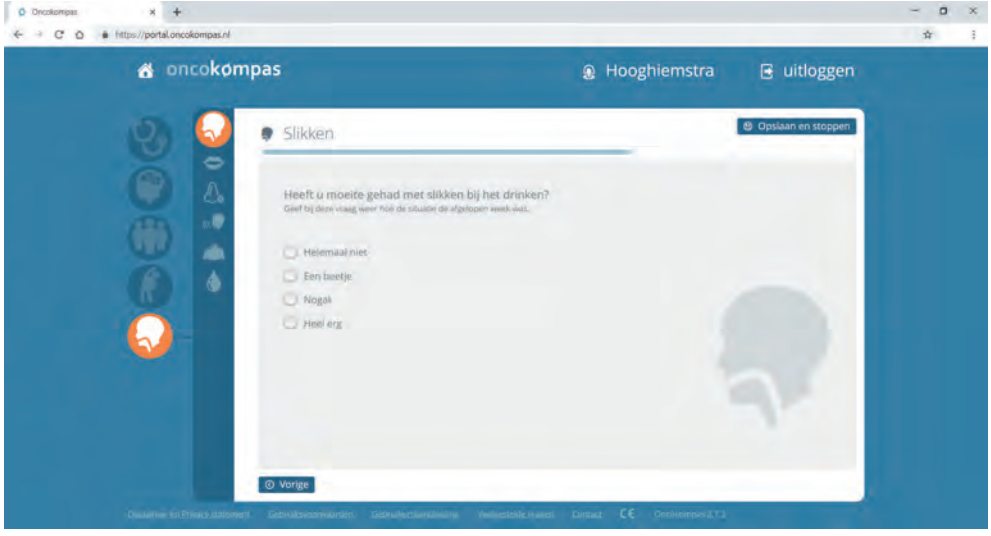


Figure 2b – Question in the component Measure, on the topic swallowing

Learn

In the Learn component, users obtain an overview of their PROM scores (**Figure 3a** and **3b**). Feedback is provided by means of a 3-colour system: green (no elevated well-being risks), orange (elevated well-being risks), and red (seriously elevated well-being risks) scores.

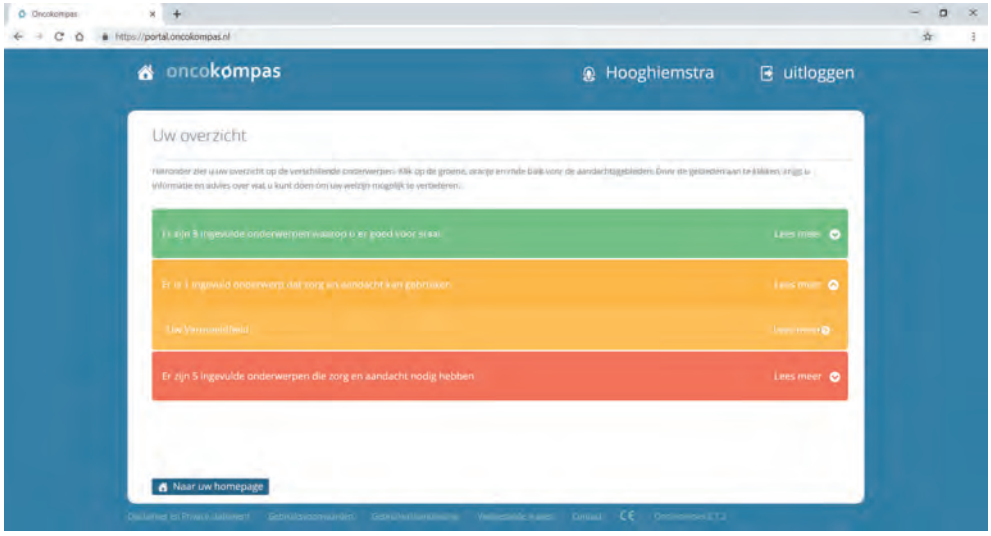


Figure 3a – Overview of well-being scores in the component Learn, with an elevated well-being risk on one topic

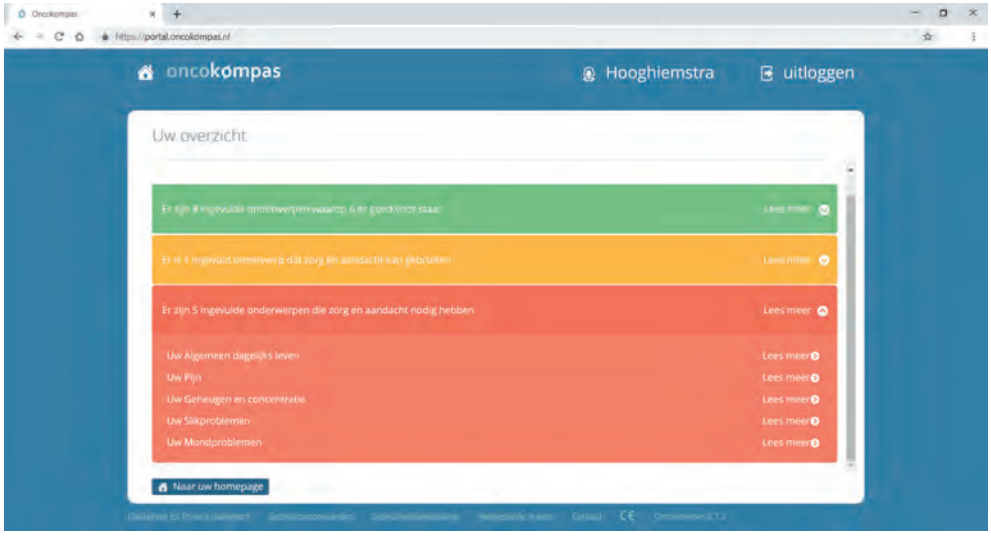


Figure 3b – Overview of well-being scores in the component Learn, with seriously elevated well-being risks on five topics

Users receive personalised information based on their PROM scores, and background information on the topic (**Figure 4a** and **4b**).

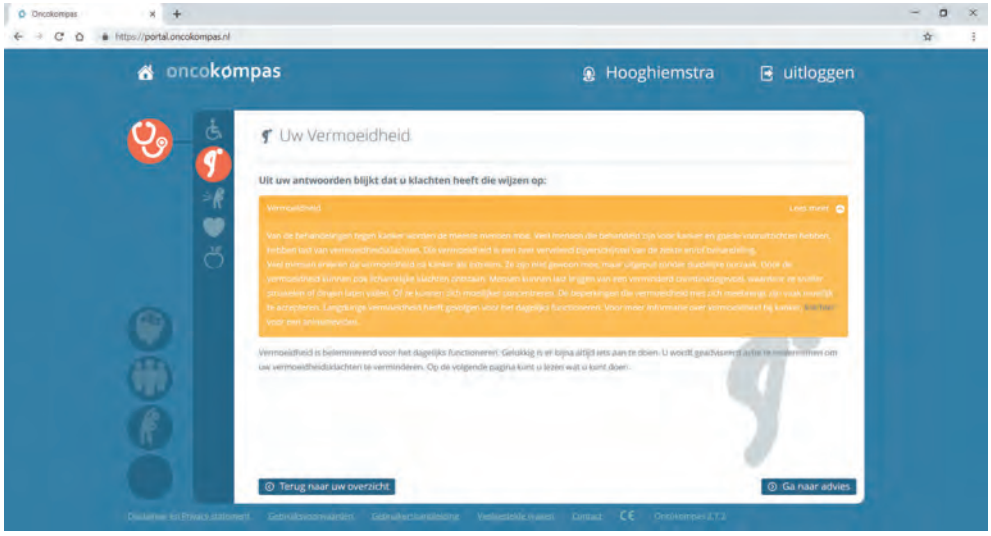


Figure 4a – Page with information in the component Learn, on the topic fatigue, with an orange score

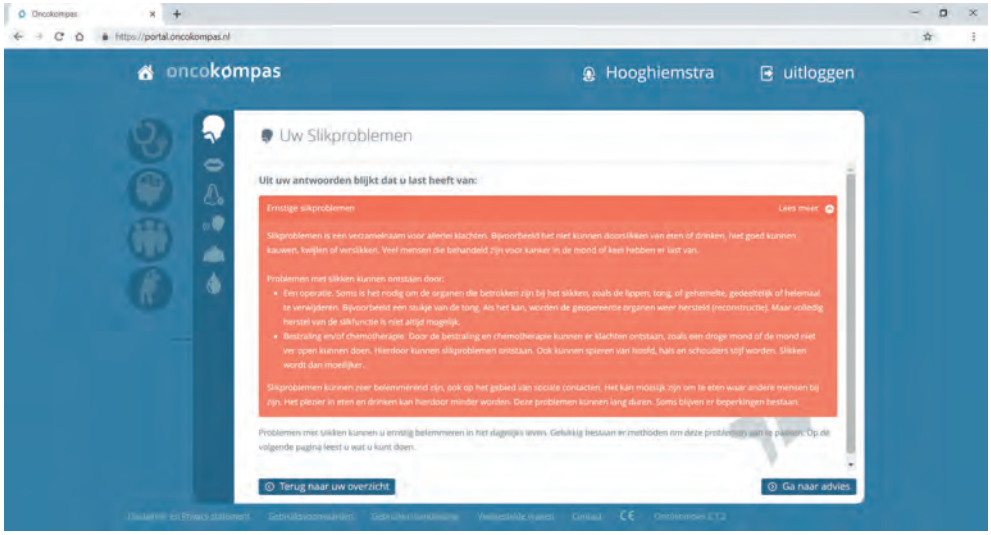


Figure 4b – Page with information in the component Learn, on the topic swallowing, with a red score

In case of (seriously) elevated well-being risks (orange or red scores), also self-care advice (**Figure 5a**) and tips and links to other sources of information are provided (**Figure 5b**), to support users in improving symptom burden themselves.

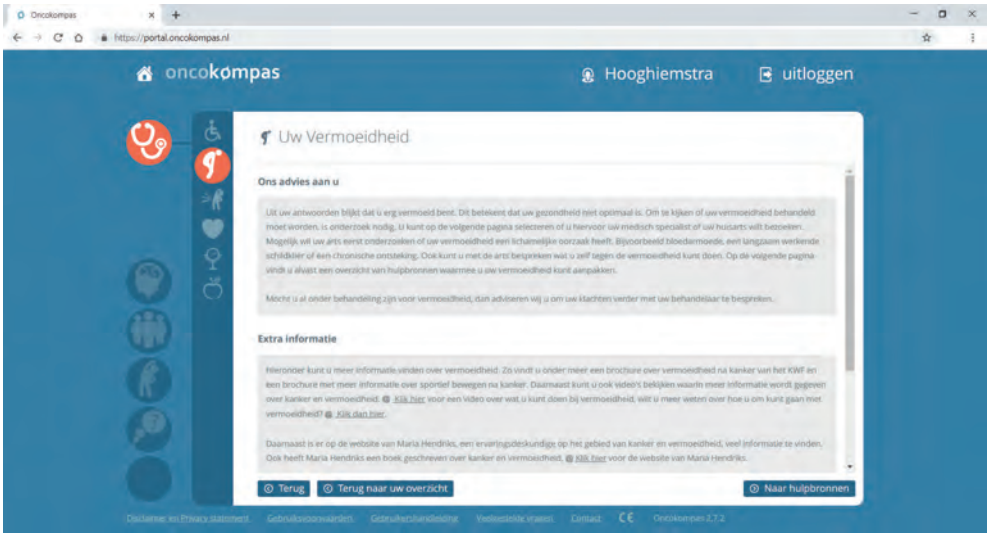


Figure 5a – Page with advice in the component Learn, on the topic fatigue

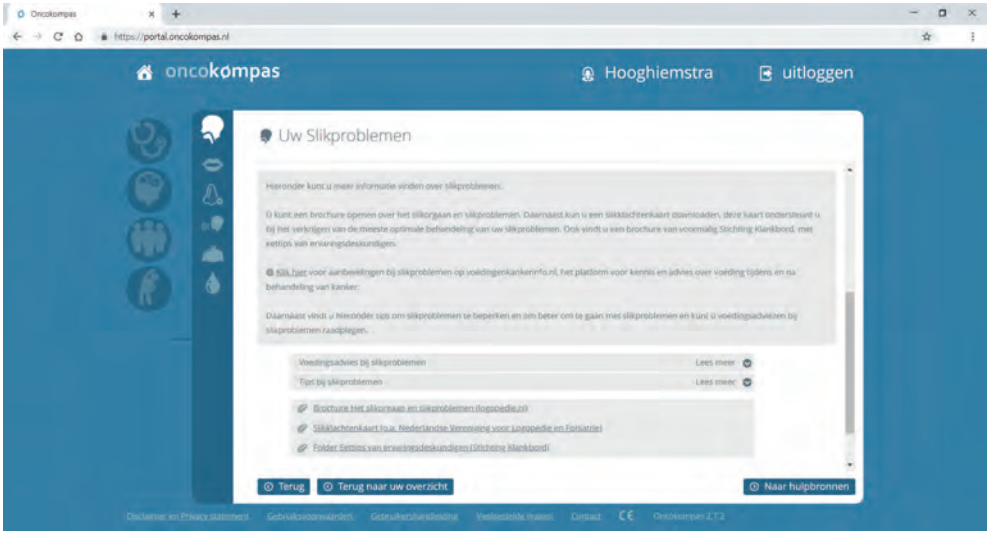


Figure 5b – Page with tips and links to other sources, in the component Learn, on the topic swallowing

Act

In the Act component, users obtain a personalised overview of supportive care options, tailored to their well-being risk and preferences (**Figure 6a**). If the user has an orange score, self-help or low-intensive interventions are suggested, while contact with a medical specialist or their general practitioner, or more intensive interventions are advised if the user has a red score. Users can select the supportive care options in which they are interested (**Figure 6b**).

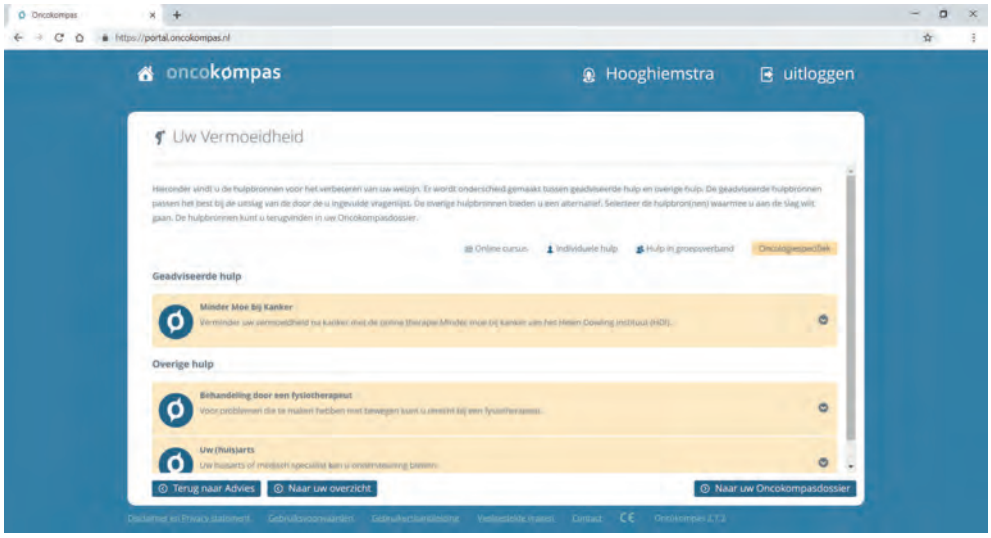


Figure 6a – Overview of supportive care options in the component Act

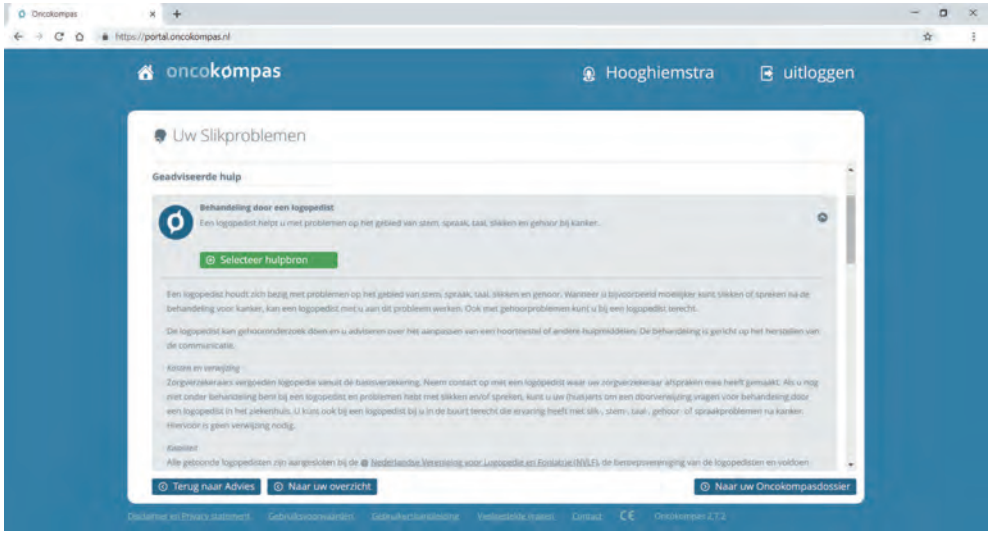


Figure 6b – Selection of supportive care option in the component Act

Users can access Oncokompas at any time, from any place, and Oncokompas can be used multiple times. When users login again, they can see the overview of PROMS scores of their previous visit, and read the corresponding information in the components Learn and Act again, or they can complete Oncokompas once again, and start with the component Measure again. When used repeatedly, users can see an overview of their scores over time (**Figure 7**). Repeated use is encouraged by sending reminders by e-mail every two months.

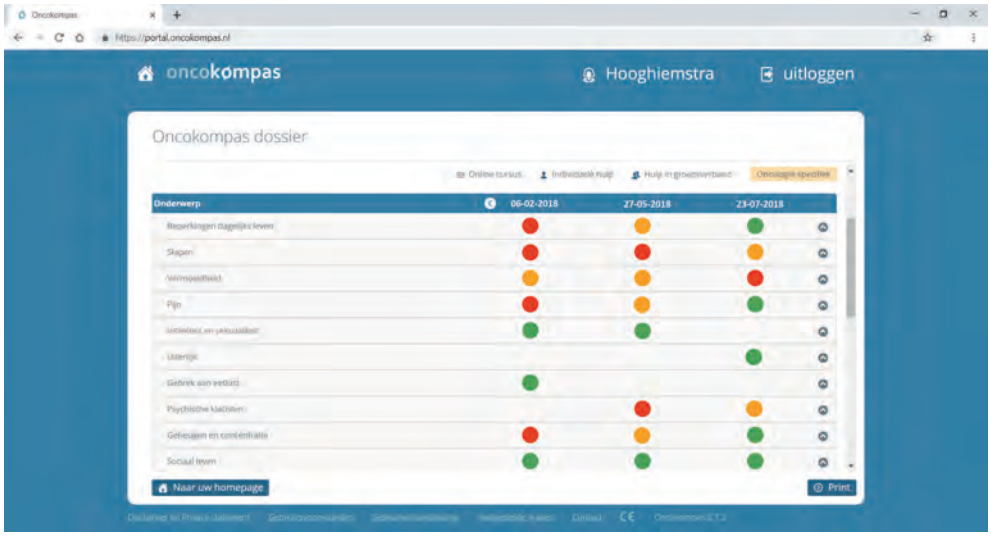


Figure 7 – Overview of scores over time


2

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

A. (Anja) van der Hout, C.F. (Nelly) van Uden-Kraan, B.I. (Birgit) Witte, V.M.H. (Veerle) Coupé, F. (Femke) Jansen, C.R. (René) Leemans, P. (Pim) Cuijpers, L.V. (Lonneke) van de Poll-Franse, I.M. (Irma) Verdonck-de Leeuw

Trials (2017) 18: 228

ABSTRACT

Background: Cancer survivors have to deal with a wide range of physical symptoms, psychological, social and existential concerns, and lifestyle issues related to cancer and its treatment. Therefore, it is essential that they have access to optimal supportive care services. The eHealth self-management application Oncokompas was developed to support cancer survivors with where they need to turn to for advice and guidance, as well as to increase their knowledge on the availability of optimal support. A randomised controlled trial will be conducted to assess the efficacy, cost-utility and reach of Oncokompas as an eHealth self-management application compared with care as usual among cancer survivors.

Methods/design: Adult cancer survivors diagnosed with breast, colorectal or head and neck cancer or lymphoma who are at 3 months to 5 years since curative treatment will be included. In total, 544 cancer survivors will be randomly assigned to the intervention group or a wait-list control group. The primary outcome measure is patient activation. Secondary outcome measures include self-efficacy, personal control, perceived patient-physician interaction, need for supportive care, mental adjustment to cancer and health-related quality of life. Furthermore, cost-utility outcomes will be assessed. Reach is defined as the percentage of cancer survivors who get access to Oncokompas within the context of this trial. Questionnaires will be administered at baseline, post-intervention and at 3- and 6-month follow-up.

Discussion: In this study, we will evaluate the efficacy and cost-utility of Oncokompas among cancer survivors, as well as the reach of Oncokompas. These are essential first steps in the translation of research into practice and contribute to sustainable adoption, implementation, and maintenance of an evidence-based Oncokompas.

BACKGROUND

Cancer survivors have to deal with a wide range of physical symptoms, psychological, social and existential concerns, and lifestyle issues related to their cancer and its treatment. These problems can negatively affect health-related quality of life (HRQOL), may interfere with return to work and often result in higher medical care use.[1,2] Therefore, it is essential that cancer survivors have access to optimal supportive care services. Supportive care for cancer survivors includes management of physical and psychological symptoms, social functioning, and existential and lifestyle issues related to cancer recurrence. Supportive care (e.g. physiotherapy, psychological support, support in the relationship with partner or children, support with existential questions or self-help interventions targeting a healthy lifestyle) is increasingly recognised as an integral part of quality cancer treatment.[1,2] Although there is evidence that supportive care is effective,[3–5] referral rates are low, and many cancer survivors have unmet needs[6,7] related to, for example, fatigue, anxiety, depression or sexuality issues.

To improve accessibility to optimal supportive care services, cancer survivors are expected to adopt an active role in managing their own care.[8] Several studies have shown that self-management strategies ranging from educational interventions, exercise programs and (online) self-help interventions targeting psychological distress are beneficial for cancer survivors in terms of patient activation and self-efficacy.[9–11] Patient activation can be described as an individual's knowledge, skill, and confidence for managing their health and healthcare.[12] Less activated people are more likely than highly activated patients to have unmet medical needs and to delay seeking medical care. As patients' activation levels increase, they gain a greater sense of control over their health and feel empowered to take action.[13]

There is growing interest in eHealth among patients, healthcare providers, healthcare assurance companies and policy-makers as a means to improve self-management.[1] To support cancer survivors in where they need to turn for advice and guidance, as well as increasing their knowledge on optimal support, the eHealth self-management application Oncokompas was developed. With Oncokompas, cancer survivors can monitor their quality of life by means of patient reported outcome measures (PROMs), which is followed by automatically generated tailored feedback and personalised advice on supportive care services.[14]

To ensure sustainable usage of Oncokompas, participatory design principles were followed,[15]

meaning that cancer survivors and healthcare professionals were involved in each step of the development process.[14,16,17] This approach resulted in an eHealth application which fits the needs of patients and healthcare professionals. See the Methods section for more information on Oncokompas and its development process. The aim of the present study is to assess the efficacy and cost-utility of Oncokompas as an eHealth self-management application among cancer survivors, as well as the reach of Oncokompas within the context of this trial.

METHODS/DESIGN

This study is a randomised controlled trial (RCT) evaluating the efficacy and cost-utility of the eHealth application Oncokompas among cancer survivors, as well as the reach of Oncokompas. We closely followed the Standard Protocol Items: Recommendations for Interventional Trials (SPIRIT) checklist.[18,19] Cancer survivors will be randomised into the intervention group (whose members will obtain access to the intervention) or a waitlist control group (whose members will obtain access to the intervention after a 6-month waiting period). The study is subdivided into two parts: part 1 concerns the reach and part 2 the efficacy and cost-utility of Oncokompas. The first part comprises the baseline assessment, and the second part comprises the post-intervention and follow-up assessments.

Intervention

Oncokompas is an eHealth self-management application that supports cancer survivors in finding and obtaining optimal supportive care, adjusted to their personal health status and preferences. Oncokompas consists of three components: 'Measure,' 'Learn,' and 'Act'. In the Measure component, cancer survivors can independently complete PROMs targeting the following quality-of-life domains: physical, psychological, and social functioning, healthy lifestyle, and existential issues. Tumour-specific modules are available for patients with breast cancer, colorectal cancer, head and neck cancer, and lymphoma. Specific PROMs were selected by the project team in collaboration with teams of experts and on the basis of Dutch practical guidelines (from the Netherlands Comprehensive Cancer Organisation [IKNL]) and literature searches. Data derived from the Measure component are processed in real time and linked to tailored feedback to the cancer 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 and/or consensus of teams of experts. In the Learn component, feedback is provided to the participant on the level of topics (e.g. depression, fatigue)

by means of a three-color system: green (no elevated well-being risks), orange (elevated well-being risks) and red (seriously elevated well-being risks). Cancer survivors receive personalised information on the outcomes; for example, on the topic of depression, information is provided on the symptoms of depression and the proportion of cancer survivors who experience 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 participant has an orange or a red score on depression as well as fatigue. The feedback in the Learn component concludes with comprehensive self-care advice with tips and tools. All of this advice is tailored to the individual cancer survivor. In the Act component, cancer survivors are provided with personalised supportive care options based on their PROM scores and expressed preferences (e.g. preference for individual therapy versus group therapy). If a participant has elevated well-being risks (orange score), the feedback includes suggestions for self-help interventions. If a participant has seriously elevated well-being risks, the feedback includes advice to contact the participant's own medical specialist or general practitioner.[14,17]

Several studies were conducted to optimally fit Oncokompas to patients' and care providers' preferences. Cancer survivors and healthcare professionals were involved in each step of the development process. A needs assessment was conducted among cancer survivors and healthcare professionals (step 1).[16] Usability was tested by cancer survivors in two iterative cycles, and healthcare professionals participated in cognitive walk-throughs (step 2).[17] Cancer survivors participated in a multi-centre pilot study to assess feasibility (step 3).[14] Oncokompas was optimised on the basis of the feasibility testing results.

Study population

Part 1: inclusion and exclusion criteria

Inclusion criteria are cancer survivors diagnosed with breast, colorectal, or head and neck cancer or lymphoma; being aged ≥18 years (no upper limit); and having finished treatment with curative intent for 3 months to 5 years (all treatment modalities). Cancer survivors who have not yet completed endocrine therapy or immunotherapy for their breast cancer will be included 3 months to 5 years after their primary treatment. Exclusion criteria are male cancer survivors diagnosed with breast cancer and/or individuals with severe cognitive impairment, insufficient mastery of the Dutch language, and physical inability to complete a questionnaire.

Part 2: additional exclusion criterion

In addition to the inclusion and exclusion criteria of part 1, participants are excluded for part 2 if they do not have access to the Internet, do not use the Internet or do not have access to an email address.

Study design

The study is introduced to eligible cancer survivors as a baseline study (part 1) and a follow-up study (part 2). Study information is given and informed consent is requested for both parts separately. Cancer survivors who fulfil the inclusion criteria and not the exclusion criteria for the first part are asked to participate in the baseline study. Baseline assessment (T0) will take place after the first informed consent form is signed. After completion of the baseline assessment, participants who fulfil the inclusion criteria and not the exclusion criteria for the second part are asked to participate in the follow-up study. After the second informed consent is given, participants will be randomly allocated to one of the two study arms. Follow-up assessments will take place post-intervention (T1) and at 3-month (T2) and 6-month (T3) follow-up. In the intervention group, T1 assessment takes place 1 week after completion of Oncokompas or 2 weeks after inclusion when Oncokompas is not completed. In the control group, T1 assessment takes place 2 weeks after inclusion. Participants allocated to the control group obtain access to Oncokompas after completion of the T3 assessment. A flowchart of the RCT is shown in **Figure 1**, and the schedule of enrolment, interventions and assessments (according to SPIRIT guidelines) is provided in **Figure 2**.

Inclusion procedures

We will recruit cancer survivors through the Netherlands Cancer Registry (NCR), which is hosted by the IKNL. The NCR registers all newly diagnosed cancer patients within 6 months after diagnosis. Data collection will be performed using the registry of Patient Reported Outcomes Following Initial treatment and Long term Evaluation of Survivorship (PROFILES). PROFILES is a registry for the study of the physical and psychosocial impact of cancer and its treatment using a dynamic, growing, population-based cohort of both short- and long-term cancer survivors. PROFILES contains a large web-based component and is linked directly to clinical data from the NCR.[20]

Part 1

A random sample of 1088 cancer survivors will be drawn from the NCR. This number is based on a power calculation (see 'Sample size' subheading) and an expected drop-out rate of 50%

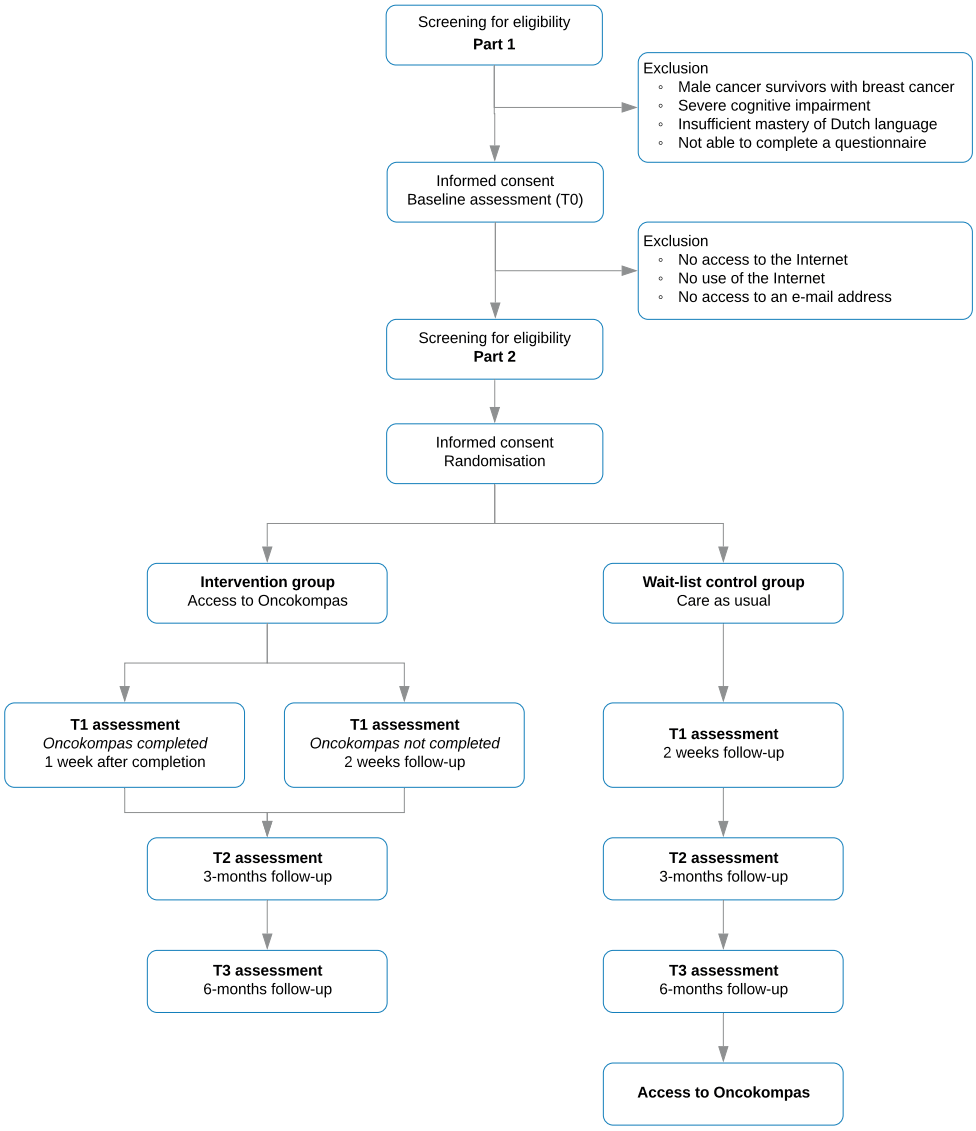


Figure 1 – Flowchart of the randomised controlled trial

between parts 1 and 2. The selection of cancer survivors will be stratified by tumour type (breast, colorectal, and head and neck cancer or lymphoma) and time after finishing treatment (<6 months, 6–12 months, 12–24 months or 24–60 months after treatment). After excluding recently deceased cancer survivors, the (former) treating physicians are asked to verify the cancer survivors' study eligibility (e.g. excluding cancer survivors with serious cognitive impairment or who are in transition to terminal care). Cancer survivors are invited to participate in the baseline study via a letter from their

	STUDY PERIOD						
	Enrolment part 1	Enrolment part 2	Allocation	Post-allocation			Close-out
TIMEPOINT	*T0*			*T1*	*T2*	*T3*	
ENROLMENT:							
Eligibility screen part 1	X						
Informed consent part 1	X						
Eligibility screen part 2		X					
Informed consent part 2		X					
Allocation			X				
INTERVENTIONS:							
Access to Oncokompas (intervention group)			←	—	—	—	→
Care as usual (control group)			←	—	—	—	
Access to Oncokompas (control group)							← →
ASSESSMENTS:							
Primary outcome measure	X			X	X	X	
Associations of Reach	X						
Secondary outcome measures	X			X	X	X	
Cost-utility measures	X				X	X	

Figure 2 – Standard Protocol Items: Recommendations for Interventional Trials (SPIRIT) schedule of enrolment, interventions and assessments

(former) treating physician. The letter includes a link to a secure website as well as a login name and password. Interested cancer survivors can log in and provide informed consent for the first part of the study and complete the baseline questionnaire. If a cancer survivor does not have access to Internet or prefers written rather than digital communication, an informed consent form and a paper-and-pencil questionnaire are sent by postal mail. Non-respondents will be sent a reminder letter and a paper-and-pencil questionnaire within 4 weeks. If they do not respond to this reminder, they will be contacted by telephone within 2 weeks.

Part 2

Cancer survivors who complete the baseline questionnaire will be invited to participate in the follow-up study. An email with information about the follow-up study and Oncokompas will be sent. Interested cancer survivors can provide informed consent for the second part of the study and complete the follow-up questionnaires on the same secure website where the baseline questionnaire resides. Cancer survivors who are not interested in participating in the study are asked about their reasons for non-participation. Non-respondents will be sent a reminder by email within 2 weeks. If they do not respond to this reminder, they will be contacted by telephone within 2 weeks.

Randomisation

Cancer survivors who meet the inclusion criteria and give informed consent for the second part of the study are randomly allocated in a 1:1 ratio to either the intervention group (access to Oncokompas) or the wait-list control group (access to Oncokompas after a 6-month waiting period). Randomisation to either the intervention or the control group will be performed by a researcher not involved in the study using block randomisation. The blocks will have a length of 68. The researcher will determine all possible balanced combinations of assignment within the block (i.e. equal number for all groups within the block). Randomisation will be stratified by tumour type (breast, colorectal, and head and neck cancer or lymphoma). It is expected that this variable has prognostic relevance and therefore needs to be distributed evenly across both groups. The allocation sequence will be generated by PROFILES and will be made available by a data download from the PROFILES database. The researcher (AvdH) will assign participants either to the intervention group and invite participants to engage with Oncokompas by email or to the control group and place participants on the waiting list, where the participants' email address is blocked from Oncokompas for 6 months.

Outcome assessment

The primary outcome measure to assess efficacy of Oncokompas is patient activation. Secondary outcome measures include self-efficacy, personal control, perceived patient-physician interaction, mental adjustment to cancer, need for supportive care and HRQOL. Furthermore, cost-utility outcomes will be assessed. Reach is defined as the percentage of cancer survivors who get access to Oncokompas within the context of this RCT. To obtain insight into possible factors associated with reach, we will obtain data on socio-demographic and clinical characteristics, health literacy, health locus of control (HLC), Internet use, attitude towards eHealth and the outcome measures on efficacy.

Primary and secondary outcome measures to measure efficacy are collected at baseline, post-intervention and at 3- and 6-month follow-up. Cost-utility outcomes are collected at baseline and at 3- and 6-month follow-up. Outcome measures to investigate associations of reach are collected at baseline. An overview of the outcome measures is presented in **Table 1**.

Table 1 – Study outcome measures and instruments

Outcome measure	Instrument
Efficacy [a]	
Primary outcome measure	
Patient activation	Patient Activation Measure (PAM)
Secondary outcome measures	
Self-efficacy	General Self-Efficacy Scale (GSE)
Personal control	Pearlin & Schooler Mastery Scale (PMS)
Perceived patient-physician interaction	Perceived Patient-Physician Interaction (PEPPI-5)
Need for supportive care	Supportive Care Needs Survey Short-Form 34 (SCNS-SF34)
	Head & Neck Cancer specific module (SCNS-HNC)
Mental adjustment to cancer	Mental Adjustment to Cancer Scale (MAC)
Health-related quality of life	EORTC QLQ-C30
Tumour-specific symptoms	EORTC QLQ-BR23
	EORTC QLQ-CR29
	EORTC QLQ-H&N43
	EORTC QLQ-HL27
	EORTC QLQ-NHL-LG20
	EORTC QLQ-NHL-HG29
Cost-utility [b]	
Quality-adjusted life years	EuroQol 5 Dimensions (EQ-5D)
Medical costs	iMTA Medical Consumption Questionnaire (iMCQ)
Productivity costs	iMTA Productivity Cost Questionnaire (iPCQ)
Reach [c]	
Health literacy	Functional, communicative and critical health literacy scales (FCCHL)
Health locus of control	Multidimensional Health Locus of Control (MHLC)
Internet use	Adapted version of questionnaire from Van de Poll-Franse & Van Eenbergen
Attitude towards eHealth	e-Health Impact Questionnaire (eHIQ)
Socio-demographic characteristics	Study-specific questionnaire
Clinical characteristics	Study-specific questionnaire

[a] Assessment at T0, T1, T2, and T3, [b] Assessment at T0, T2, and T3, [c] Assessment at T0

Efficacy

Primary outcome measure

The primary outcome measure is patient activation. The Patient Activation Measure is a 13-item PROM on self-reported knowledge, skills, and confidence in self-management of one's health or chronic condition. Participants are asked to report their level of agreement with various statements on a 4-point Likert scale (i.e. strongly disagree, disagree, agree, strongly agree) or to indicate that the item is not applicable. A total score can be calculated by calculating a mean score of all the applicable items (items which were answered on the 4-point scale), which is transformed to a standardised activation score ranging from 0 to 100.[21]

Secondary outcome measures

Self-efficacy: The General Self-Efficacy Scale (GSE) is designed to assess optimistic self-beliefs regarding coping with a variety of difficult demands in life. The GSE consists of ten items scored on a 4-point Likert scale ranging from 1 (not at all true) to 4 (exactly true). The scores of the ten items are summed to give a total score. A higher score reflects a higher generalised sense of self-efficacy.[22]

Personal control: The Pearlin Mastery Scale (PMS) measures global sense of personal control. It consists of seven items, and individuals respond to a 5-point Likert scale about the extent to which they agree (5 = strongly agree) or disagree (1 = strongly disagree) with the various statements. A PMS score ranges from 7 to 35, with a higher score reflecting greater mastery.[23]

Perceived patient-physician interaction: The five-item Perceived Efficacy in Patient-Physician Interactions measures patients' confidence in interacting with their main care provider using the short five-item version of the scale. Participants can indicate on a 5-point know which questions to ask or are able to make the most out of their care provider visit.[24,25]

Need for supportive care: The 34-item Short Form Supportive Care Needs Survey (SCNS-SF34) measures the need and level of need for supportive care in the last month on the basis of 34 items using a 5-point, two-level response scale. The first response scale consists of two broad categories of need: 'no need' and 'a need'. The 'no need' scale is further subdivided into 'not applicable' for issues that are not a problem to the patient and 'satisfied' for issues on which a patient needs support, but the support is satisfactory. The 'need' category has three subcategories indicating the level of need for additional care: 'low need,' 'moderate need' and 'high need'.[26,27]

In conjunction with SCNS-SF34, a tumour-specific module for patients with head and neck cancer can be used. The SCNS-HNC measures the need for supportive care concerning 11 HNC-specific issues using the same response scale as the SCNS-SF34.[28]

Mental adjustment to cancer: Cognitive and behavioural responses to cancer diagnosis and treatment are determined using the Mental Adjustment to Cancer scale (MAC). The MAC comprises five subscales: Fighting Spirit, Helplessness/Hopelessness, Anxious Preoccupation, Fatalism and Avoidance. The 40 items are rated on a 4-point Likert scale ranging from 1 for 'definitely does not apply to me' to 4 for 'definitely applies to me'. A higher score represents a higher endorsement of the adjustment response.[29]

Health-related quality of life: The 30-item core European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ-C30) is a cancer-specific quality-of-life questionnaire developed for repeated assessments within clinical trials. It was developed in a cross-cultural setting and is a valid and reliable instrument for quality-of-life assessments in various cancer populations. It contains five functional scales (physical, cognitive, emotional, social and role), a global quality-of-life scale, three symptom scales (pain, fatigue and nausea/vomiting) and six single items (dyspnoea, insomnia, loss of appetite, constipation, diarrhoea and financial difficulties). All scales and single items range in score from 0 to 100. A higher score on one of the functioning scales or the global quality-of-life scale represents a better quality of life, whereas a higher score on the symptom scales or the single items indicates a higher level of symptoms.[30,31]

In conjunction with the EORTC QLQ-C30, tumour-specific modules can be used. EORTC QLQ-BR23 is a module meant to be used among patients with breast cancer, varying in stage of disease and treatment. It consists of four functional scales (body image, sexual functioning, sexual enjoyment and future perspective), three symptom scales (systemic therapy side effects, breast symptoms and arm symptoms) and one symptom item (distress caused by hair loss).[32]

EORTC QLQ-CR29 is a module meant to be used among patients with colorectal cancer. It includes two functional scales (body image and future health perspective) and five symptom scales (micturition problems, gastrointestinal problems, defecation problems, sexual problems and chemotherapy-related problems).[33]

EORTC QLQ-H&N43 is a module meant to be used among patients with head and neck cancer. It contains 13 symptom scales (pain, swallowing, senses, speech, social eating, social contact, physical contact, skin, shoulder, body image, teeth, dry mouth and sticky saliva, and anxiety) and 6 symptom items (trismus, cough, lymphedema, wound healing, neurological problems and weight).[34]

EORTC QLQ-HL27, EORTC QLQ-NHL-LG20 and EORTC-QLQ-NHL-HG29 are modules meant to be used with patients with Hodgkin's lymphoma, low-grade non-Hodgkin's lymphoma, and high-grade non-Hodgkin's lymphoma, respectively. All modules have four multi-item scales, but they differ in the number of items per scale: symptom burden due to disease and/or treatment (4–7 items), physical condition/fatigue (4 or 5 items), emotional impact (4–6 items), and worries/fears health and functioning (8–11 items), with an extra item scale on neuropathy (2 items) for EORTC QLQ-NHL-HG29. For all scales, a higher score reflects worse or more symptoms/problems.

Cost-utility

A cost-utility analysis will be conducted; that is, the difference in total 6-month costs between the two arms will be compared with the difference in quality-adjusted life-years (QALYs) based on the 5-dimension EuroQol questionnaire (EQ-5D). The EQ-5D consists of five items measuring problems in five dimensions of quality of life (mobility, self-care, usual activities, pain/discomfort, and anxiety/depression). Participants can answer that they have no problems, some problems or extreme problems.[35] The resulting profile of answers (1 of 243 possibilities) can be transformed to a value given by the general public: the EQ-5D index using the Dutch index tariff.[36] Furthermore, a visual analogue scale is included, which represents the participant's judgment of his or her own health state on a scale from 0 (worst health state) to 100 (best health state).

Direct medical costs (healthcare and medication use), direct non-medical costs (travelling costs and help received from family or friends) and indirect non-medical costs (productivity losses) in the previous 3 months will be measured using an adapted version of the Institute for Medical Technology Assessment Medical Consumption Questionnaire (iMCQ)[37] and Institute for Medical Technology Assessment Productivity Cost Questionnaire (iPCQ)[38] of the Institute for Medical Technology Assessment (iMTA) of Erasmus University Rotterdam (Rotterdam, The Netherlands). In addition, a case report form on healthcare use in the hospital during the study period, including medical specialist visits, day treatment and hospital admission, will be completed using the hospital information system.

Reach

Reach is defined as the percentage of cancer survivors who get access to Oncokompas within the context of this RCT. More precisely, reach is the percentage of cancer survivors who are willing to participate in the second part of the study and thereby get access to Oncokompas (directly or after 6 months). For the numerator, cancer survivors who are willing to participate in the second part of the study and give their informed consent will be counted. For the denominator, all eligible cancer survivors who are invited to participate in the first part of the study will be counted.

Participants who complete the baseline questionnaire will be asked to participate in the follow-up study. To obtain insight into reasons for non-participation, participants not interested in the follow-up study will be asked to indicate their reasons for non-participation in the second part of the study (e.g. no interest in scientific research or no interest in the eHealth self-management application Oncokompas) by means of multiple-choice questions.

To obtain insight into possible factors associated with reach, we will obtain data on socio-demographic and clinical characteristics, health literacy, HLC, Internet use, attitude towards eHealth, and the outcome measures on efficacy.

Socio-demographic and clinical characteristics: A study-specific questionnaire comprises questions about socio-demographics (age, marital status, family situation, education level) and clinical characteristics (co-morbidities). Clinical characteristics, including information on cancer type (breast, colorectal, head and neck cancer or lymphoma), cancer stage (TNM classification), cancer treatment and time since diagnosis, will be extracted from the NCR.

Health literacy: The validated Dutch translation of the self-report Functional, Communicative and Critical Health Literacy scales will be used to measure health literacy. The 14-item questionnaire asks for information on how often participants have had problems with health information and the extent to which they extracted, communicated and analysed health information. The answers are scored on a 4-point Likert scale ranging from 1 = 'never' to 4 = 'often' for functional health literacy and 1 = 'easy' to 4 = 'rather difficult' for communicative and critical health literacy.[39,40]

Health locus of control: HLC is measured with the Multidimensional Health Locus of Control (MHLC) scale form B. The MHLC scale comprises 18 diagnostic statements describing three dimensions of

HLC: internal, powerful others and chance. The subscales 'powerful others' and 'chance' represent external HLC. People with high external HLC scores are presumed to have generalised expectancies that factors such as fate, luck, chance or powerful others will determine their health outcomes, whilst people with high internal HLC scores are presumed to hold the belief that someone becomes healthy or unwell as a result of their own behaviour. Each of the three subscales contains six items measured on a 6-point Likert scale ranging from 1 = 'strongly disagree' to 6= 'strongly agree'. The scores of each subscale range from 6 to 36 points; the higher the score, the stronger the self-perceived influence of a given factor.[41–43]

Internet use: Internet use will be measured with an adapted version of the questionnaire developed by van de Poll-Franse and van Eenbergen.[44] It comprises three broad applications of Internet use (content, communication and community), of which only the application of 'content' will be used in this study, with ten multiple-choice items about the content of Internet use and content of Internet searches.

Attitude towards eHealth: General attitudes towards using the Internet to access health information will be measured using part 1 of the e-Health Impact Questionnaire, which consists of two subscales: attitudes towards online health information (five items) and attitudes towards sharing health experiences online (six items). All items have a 5-point response category ranging from 'strongly disagree' to 'strongly agree'. Each scale will be transformed to a 0 to 100 metric, where 0 represents a low perceived value and 100 a high perceived benefit of using the Internet in relation to health.[45]

Sample size

To demonstrate presence of an effect between T3 and T0 of at least 0.5 standard units as statistically significant in a one-tailed test at $\alpha = 0.05$ and a power of $(1 - \beta) = 0.80$, a minimum of 51 participants per arm in each condition will be required at follow-up. Anticipating a drop-out rate of 25% between T0 and T3, 68 participants per condition arm per tumour type need to be included at T0. The total study cohort thus comprises 544 cancer survivors representing 136 cancer survivors per tumour type (breast, colorectal, and head and neck cancer or lymphoma).

Statistical analyses

Descriptive statistics will be generated for all sociodemographic and clinical characteristics and outcome measures. χ^2 tests, independent samples t tests (in case of normality of the measure) and

Mann-Whitney U tests (in case of non-normality of the measure) will be used to analyse whether randomisation resulted in comparable groups. A p-value of <0.05 will be considered significant. Analyses will be performed using IBM SPSS Statistics version 22 (IBM, Armonk, NY, USA) and Stata version 12.1 (StataCorp, College Station, TX, USA) software.

To investigate the efficacy of Oncokompas, linear mixed models will be used to compare longitudinal changes in outcome measures for efficacy in both groups over time (intention-to-treat analyses). Independent samples t tests will be used to measure differences between the intervention and control groups at follow-up assessments. Cohen's d will be calculated as a measure of effect size (ES) for intervention group versus control group.[46] Cohen's d is computed as the difference between two means, divided by the pooled SD. The magnitude of the ES is classified as large (≥0.80), moderate (0.50–0.79) or small (<0.50).[47]

To investigate associations of the reach of Oncokompas within this RCT, χ^2 tests, independent samples t tests and Mann-Whitney U tests will be used to analyse whether there are differences between participants and non-participants in the follow-up study (part 2) regarding baseline characteristics (part 1).

Cost-utility analyses

An incremental cost-utility ratio (ICUR) will be calculated to measure the cost per gained QALY. The ICUR will be calculated by dividing the incremental costs by the incremental QALYs using the formula: $ICUR = (Costs_{intervention} - Costs_{control})/(QALY_{intervention} - QALY_{control})$. Total costs will be calculated using a societal perspective, including intervention costs, direct medical costs, direct non-medical costs and indirect non-medical costs. Direct medical and non-medical costs will be calculated by multiplying resource use by integral cost prices as presented in the Dutch Health Care Insurance Board (CVZ) guidelines on cost studies.[48] Indirect non-medical costs will be calculated using the friction cost approach as recommended in the CVZ guidelines.[48] The utility scores linked to the various health states of the EQ-5D[36] will be used to calculate QALYs by weighing the length of time spent in a particular health condition by the utility. Missing data on direct medical, direct non-medical and indirect non-medical costs measured using the cost questionnaire, and utilities measured using the EQ-5D will be imputed using multiple imputation. Because follow-up of the study is less than 1 year, neither costs nor effects will be discounted.

The uncertainty surrounding the ICUR will be assessed using bootstrapping with 5000 replications and projected on a cost-utility plane. In addition, cost-utility acceptability curves will be presented and sensitivity analyses will be performed, focusing on uncertainty around the most important cost parameters. The analysis will be conducted in accordance with the intention-to-treat principle.

DISCUSSION

In the proposed study, we will assess the efficacy and cost-utility of the eHealth self-management application Oncokompas among cancer survivors compared with care as usual, as well as the reach of Oncokompas within this trial. There is a growing need for interventions that meet cancer survivors' supportive care needs in a personalised manner because referral rates to supportive care are low, whereas many have unmet needs.[6,7] eHealth is proposed to be useful to improve access to and quality of care[49] and has a cost-saving potential.[50] The benefit of eHealth compared with care as usual is that eHealth may improve accessibility of supportive care without consulting healthcare professionals, who have a tendency to inadequately refer cancer survivors to supportive care.[51,52] An eHealth self-management application such as Oncokompas, which monitors cancer survivors' quality of life, provides personalised advice and referral for supportive care services, could be a solution to meet cancer survivors' individual supportive care needs by improving patient activation and self-efficacy.[16] Cancer survivors with high levels of activation understand their role in the care process, are more likely to engage in positive health behaviours, and are more likely to manage their health conditions more effectively. Less activated cancer survivors are more likely to have unmet needs.[13]

By conducting this RCT, we will provide evidence on the efficacy of Oncokompas. In this way, we hope to establish whether access to an eHealth self-management application is effective in improving patient activation compared with care as usual. Secondary analyses will be conducted to investigate possible moderators that may influence the effect in order to gain knowledge on subgroups of cancer survivors who benefit the most from an eHealth self-management application such as Oncokompas. Also, mediation analyses will be conducted to elucidate whether the effect on patient activation is a direct effect of using Oncokompas or whether the effect is mediated by, for instance, improvement of mental adjustment to cancer.

Effects of self-management and eHealth interventions are often measured with so-called soft or patient-oriented outcome measures, because these types of interventions do not have pre-eminent outcomes like medical interventions.[53] Effects on patient-oriented outcome measures are relevant for patients themselves, but the clinical relevance of these effects is often unknown. In this study, efficacy is based on patient-oriented outcome measures; therefore, the (direct or indirect) effects of the use of Oncokompas on clinical outcomes will remain unknown.

It is argued that costs are often a major factor in determining whether a new intervention that is proven to be effective will be adopted, implemented or maintained.[54] Also, there is a need to explore whether it is possible to control healthcare costs while maintaining the quality of care.[55] Activated cancer survivors are expected to have better health outcomes and less healthcare use.[56] Because it is the aim of Oncokompas to improve self-management, it is expected that cancer survivors using Oncokompas will have less total costs (i.e. medical and non-medical costs) from a societal perspective compared with care as usual.

By investigating the representativeness and characteristics of cancer survivors who are willing to use Oncokompas in a study setting, we expect to be able to better reach the target population in the future. Usually, little is known about who is reached by eHealth interventions, whereas detailed information on non-participants is often not available or cannot be collected owing to ethical considerations.[54] Therefore, a two-step inclusion method was chosen for this RCT because in this way baseline characteristics (part 1) are available for non-participants in the follow-up study (part 2).

In this study, we are evaluating the efficacy, cost-utility and reach of Oncokompas among cancer survivors compared with care as usual. These are the first steps in the translation of research into practice[54] and might improve sustainable adoption, implementation and maintenance of an evidence-based Oncokompas.

REFERENCES

1. Aaronson NK, Mattioli V, Minton O, et al. Beyond treatment - Psychosocial and behavioural issues in cancer survivorship research and practice. Eur J Cancer Suppl 2014; 12: 54–64.

2. Fitch MI. Supportive care framework. Can Oncol Nurs J 2008; 18: 6–14.

3. Speck RM, Courneya KS, Mâsse LC, Duval S, Schmitz KH. An update of controlled physical activity trials in cancer survivors: A systematic review and meta-analysis. J Cancer Surviv 2010; 4: 87–100.

4. Hart SL, Hoyt MA, Diefenbach M, et al. Meta-analysis of efficacy of interventions for elevated depressive symptoms in adults diagnosed with cancer. J Natl Cancer Inst 2012; 104: 990–1004.

5. Mewes JC, Steuten LMG, IJzerman MJ, van Harten WH. Effectiveness of Multidimensional Cancer Survivor Rehabilitation and Cost-Effectiveness of Cancer Rehabilitation in General: A Systematic Review. Oncologist 2012; 17: 1581–93.

6. Boyes AW, Girgis A, D'Este C, Zucca AC. Prevalence and correlates of cancer survivors' supportive care needs 6 months after diagnosis: a population-based cross-sectional study. BMC Cancer 2012; 12: 150.

7. Harrison JD, Young JM, Price MA, Butow PN, Solomon MJ. What are the unmet supportive care needs of people with cancer? A systematic review. Support Care Cancer 2009; 17: 1117–28.

8. Jansen F, van Uden-Kraan CF, van Zwieten V, Witte BI, Verdonck-de Leeuw IM. Cancer survivors' perceived need for supportive care and their attitude towards self-management and eHealth. Support Care Cancer 2015; 23: 1679–88.

9. Cimprich B, Janz NK, Northouse L, Wren PA, Given B, Given CW. Taking charge: A self-management program for women following breast cancer treatment. Psychooncology 2005; 14: 704–17.

10. 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.

11. Kuijpers W, Groen WG, Aaronson NK, Van Harten WH. A systematic review of web-based interventions for patient empowerment and physical activity in chronic diseases: Relevance for cancer survivors. J Med Internet Res 2013; 15: e37.

12. 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.

13. Williams GC, McGregor H, Zeldman A, Freedman ZR, Deci EL, Elder D. Promoting glycemic control through diabetes self-management: Evaluating a patient activation intervention. Patient Educ Couns 2005; 56: 28–34.

14. 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.

15. van Gemert-Pijnen JEWC, Nijland N, van Limburg M, et al. A holistic framework to improve the uptake and impact of eHealth technologies. J Med Internet Res 2011; 13: e111.

16. 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.

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

18. Chan AW, Tetzlaff JM, Altman DG, et al. SPIRIT 2013 statement: Defining standard protocol items for clinical trials. Ann Intern Med 2013; 158: 200–7.

19. Chan AW, Tetzlaff JM, Gøtzsche PC, et al. SPIRIT 2013 explanation and elaboration: guidance for

protocols of clinical trials. BMJ 2013; 346: e7586–e7586.

20. van De Poll-Franse L V., Horevoorts N, Eenbergen M Van, 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.

21. Rademakers J, Nijman J, Van Der Hoek L, Heijmans M, Rijken M. Measuring patient activation in the Netherlands: Translation and validation of the American short form Patient Activation Measure (PAM13). BMC Public Health 2012; 12: 577.

22. Schwarzer, R., Jerusalem M. Generalized Self-Efficacy scale. In J. Weinman, S. Wright, & M. Johnston. Meas Heal Psychol A user's portfolio Causal Control beliefs 1995; : 35–7.

23. Pearlin LI, Schooler C. The Structure of Coping: Erratum. J Health Soc Behav 1978; 19: 237.

24. 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.

25. ten Klooster PM, Oostveen JCM, Zandbelt LC, et al. Further validation of the 5-item Perceived Efficacy in Patient-Physician Interactions (PEPPI-5) scale in patients with osteoarthritis. Patient Educ Couns 2012; 87: 125–30.

26. 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: 602–6.

27. Boyes A, Mcelduff P, Boyes A, Zucca A, Girgis A. Supportive Care Needs Survey : A guide to administration, scoring and analysis Prepared by. 2014.

28. Jansen F, Witte BI, van Uden-Kraan CF, Braspenning AM, Leemans CR, Verdonck-de Leeuw IM. The need for supportive care among head and neck cancer patients: psychometric assessment of the Dutch version of the Supportive Care Needs Survey Short-Form (SCNS-SF34) and the newly developed head and neck cancer module (SCNS-HNC). Support Care Cancer 2016; 24: 4639–49.

29. Watson M, Homewood J. Mental Adjustment to Cancer Scale©: Psychometric properties in a large cancer cohort. Psychooncology 2008; 17: 1146–51.

30. Aaronson NK, Aaronson NK, Ahmedzai S, 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: 365–76.

31. Fayers P, Bottomley A. Quality of life research within the EORTC—the EORTC QLQ-C30. Eur J Cancer 2002; 38: 125–33.

32. McLachlan SA, Devins GM, Goodwin PJ. Validation of the European Organization for Research and Treatment of Cancer quality of life questionnaire (QLQ-C30) as a measure of psychosocial function in breast cancer patients. Eur J Cancer 1998; 34: 510–7.

33. 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.

34. Singer S, Araújo C, Arraras JI, et al. Measuring quality of life in patients with head and neck cancer: Update of the EORTC QLQ-H&N Module, Phase III. Head Neck 2015; 37: 1358–67.

35. Brooks R. EuroQol: the current state of play. Health Policy 1996; 37: 53–72.

36. Lamers LM, Stalmeier PFM, McDonnell J, Krabbe PFM, Busschbach JJ Van. Measuring the quality of life in economic evaluations: the Dutch EQ-5D tariff. Ned Tijdschr Geneeskd 2005; 149: 5.

37. Bouwmans C, Hakkaart-van Roijen L, Koopmanschap M, Krol M, Severens H, Brouwer W. Handleiding iMTA Medical Cost Questionnaire (iMCQ). 2013.

38. Bouwmans C, Hakkaart-van Roijen L, Koopmanschap M, Krol M, Severens H, Brouwer W. Handleiding iMTA Productivity Cost Questionnaire (iPCQ). 2013.

39. Ishikawa H, Takeuchi T, Yano E. Measuring functional, communicative, and critical health literacy among diabetic patients. Diabetes Care 2008; 31: 874–9.

40. van der Vaart R, Drossaert CHC, Taal E, et al. Validation of the Dutch functional, communicative and critical health literacy scales. Patient Educ Couns 2012; 89: 82–8.

41. Wallston KA, Wallston BS, DeVellis R, et al. Development of the Multidimensional Health Locus of Control (MHLC) Scales. Heal Educ Behav 1978; 6: 160–70.

42. Halfens R, Philipsen H. Een gezondheidsspecifieke beheersingsoriëntatieschaal. Betrouwbaarheid en validiteit van de MHLC. T Soc Gezondheidsz 1988; 66: 399.

43. Shneerson C, Taskila T, Greenfield S, Gale N. A survey investigating the associations between self-management practices and quality of life in cancer survivors. Support Care Cancer 2015; 23: 2655–62.

44. van De Poll-Franse L V., Van Eenbergen MCHJ. Internet use by cancer survivors: Current use and future wishes. Support Care Cancer 2008; 16: 1189–95.

45. 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.

46. Cohen J. Statistical Power Analysis. Curr Dir Psychol Sci 1992; 1: 98–101.

47. Cohen J. Statistical power analysis for the behavioral sciences, 2nd edn. Lawrence Erlbaum Associates, 1988.

48. Hakkaart-van Roijen L, Tan SS, Bouwmans-Frijters CAM. Guidelines for pharmacoeconomic research in the Netherlands [in Dutch]. The Hague, 2011.

49. Eysenbach G. What is e-health? J Med Internet Res 2001; 3: 1–5.

50. Bergmo TS. How to measure costs and benefits of ehealth interventions: An overview of methods and frameworks. J Med Internet Res 2015; 17: e254.

51. Steginga SK, Campbell A, Ferguson M, et al. Socio-demographic, psychosocial and attitudinal predictors of help seeking after cancer diagnosis. Psychooncology 2008; 17: 997–1005.

52. Verdonck-de Leeuw IM, de Bree R, Keizer AL, et al. Computerized prospective screening for high levels of emotional distress in head and neck cancer patients and referral rate to psychosocial care. Oral Oncol 2009; 45: e129–33.

53. Baker TB, Gustafson DH, Shaw B, et al. Relevance of CONSORT reporting criteria for research on eHealth interventions. Patient Educ Couns 2010; 81: S77–86.

54. Glasgow RE, Vogt TM, Boles SM. Evaluating the public health impact of health promotion interventions: The RE-AIM framework. Am J Public Health 1999; 89: 1322–7.

55. Owens DK, Qaseem A, Chou R, Shekelle P. Clinical Guidelines Committee of the American College of Physicians. High-value, cost-conscious health care: concepts for clinicians to evaluate the benefits, harms, and costs of medical interventions. Ann Intern Med 2011; 154: 174–80.

56. Hibbard JH, Mahoney ER, Stock R, Tusler M. Do increases in patient activation result in improved self-management behaviors? Health Serv Res 2007; 42: 1443–63.


3

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

A. (Anja) van der Hout, C.F. (Nelly) van Uden-Kraan, K. (Karen) Holtmaat, F. (Femke) Jansen, B.I. (Birgit) Lissenberg-Witte, G.A.P. (Grard) Nieuwenhuijzen, J.A. (José) Hardillo, R.J. (Robert) Baatenburg de Jong, N.L. (Nicolette) Tiren-Verbeet, D.W. (Dirkje) Sommeijer, K. (Koen) de Heer, C.G. (Cees) Schaar, R.J.E. (Robert-Jan) Sedee, K. (Koop) Bosscha, M.W.M. (Michiel) van den Brekel , J.F. (Marije) Petersen , M. (Matthijs) Westerman, J. (Jimmie) Honings, R.P. (Robert) Takes, I. (Ilse) Houtenbos, W.T. (Wim) van den Broek, R. (Remco) de Bree, P. (Patricia) Jansen, S.E.J. (Simone) Eerenstein, C.R. (René) Leemans, J.M. (Josée) Zijlstra, P. (Pim) Cuijpers, L.V. (Lonneke) van de Poll-Franse, I.M. (Irma) Verdonck-de Leeuw

The Lancet Oncology (2020) 21: 80–94

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 cancer survivors 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.

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.

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 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, the 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.[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. Cancer survivors 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 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 eligibility 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]

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,[15] 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 (**Supplementary Figure 1**). Following the chronic care self-management model,[16] 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 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.

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) (for more on EORTC see https://qol.eortc.org/). 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 well-being risks), orange (elevated well-being risks), and red (seriously elevated well-being risks). Survivors receive personalised information on the outcomes (e.g. 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 (e.g. preference for individual therapy vs group therapy). If a survivor has elevated well-being risks (orange score), the feedback includes suggestions for self-help interventions. If a survivor has seriously elevated well-being 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).[17] 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 (i.e. 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).[18] 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).[19] 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).[20] 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).[21] The Pearlin & Schooler Mastery Scale measures global sense of personal control; its score ranges from 7 to 35 (a

higher score reflecting greater mastery).[22] 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).[23] Head and neck cancer symptoms were measured by means of the EORTC QLQ-H&N43;[24] colorectal cancer symptoms were measured by means of the EORTC QLQ-CR29;[25] breast cancer symptoms were measured by means of the EORTC QLQ-BR23;[26] 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).[27] 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).[28] 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).[29] 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.[30]

Outcomes

The primary outcome was patient activation (knowledge, skills and confidence for self-management) according to the patient activation measure (range 0 to 100 [highest scores show highest activation]).[17] 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 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 sociodemographic 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 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 model 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.

RESULTS

2953 cancer survivors were invited to participate between October 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 cancer survivors 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**),

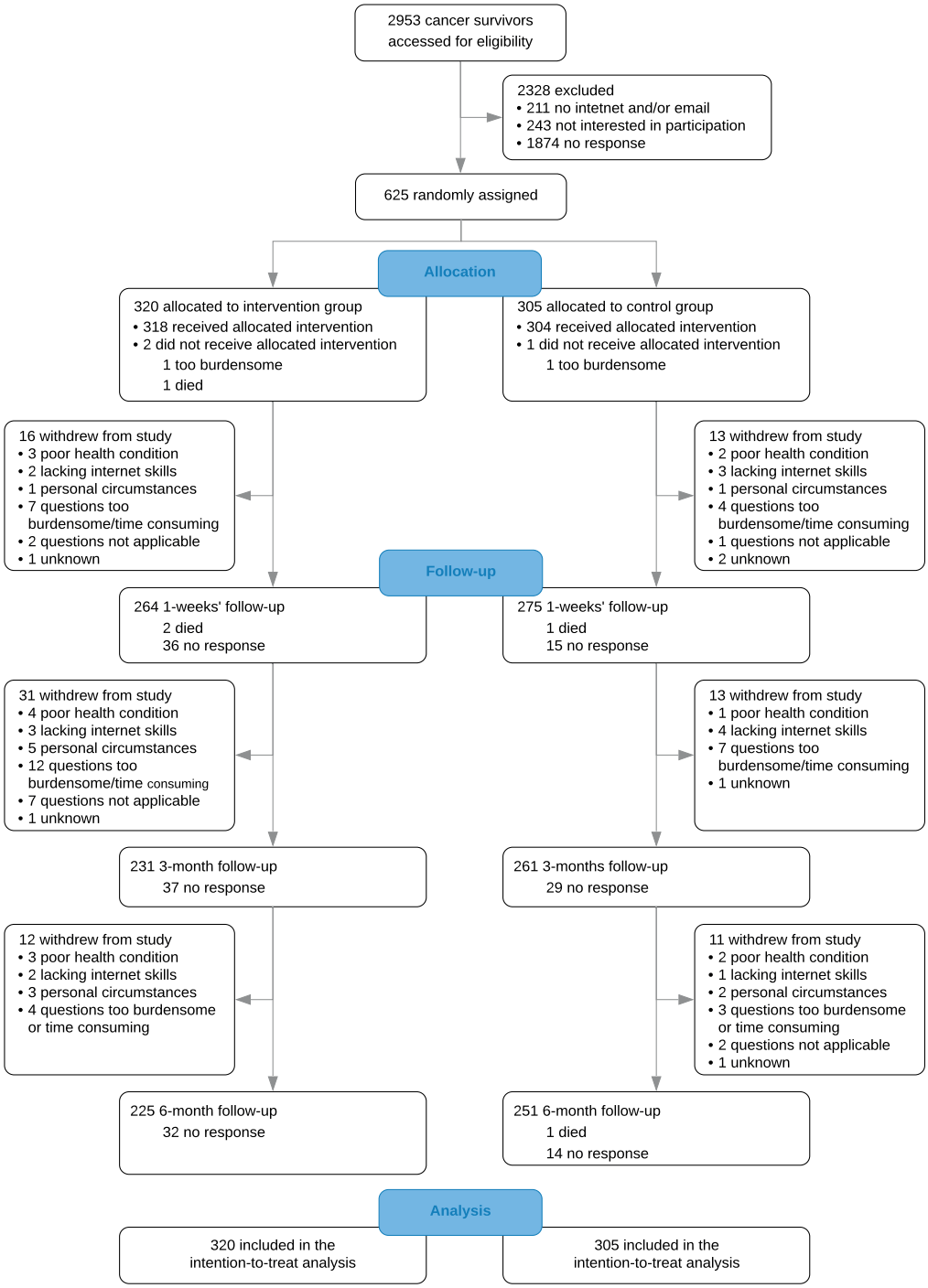


Figure 1 – Trial profile *

** 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 randomization.*

nor in the stratified analyses per tumour type (**Supplementary Table 1**). 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**. 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 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 **Supplementary Table 2**.

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, 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.

Table 1 – Baseline characteristics

	Intervention group (n = 320)	**Control group** (n = 305)
Socio-demographic factors		
Age, years	63.2 (11.2)	63.7 (10.1)
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%)
Unknown	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%)
Clinical factors		
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%)
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	25.0 (16.0-41.0)	29.0 (16.5-41.0)
3-<12 months (n, %)	39 (12%)	38 (13%)
12-<24 months	104 (33%)	85 (28%)
24-60 months	177 (55%)	182 (60%)

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

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 (i.e. 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.

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.

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 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 Oncokompas could support cancer survivors in self-management. There was no significant effect on the cancer survivors' 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.

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

		Baseline			1-week post-intervention			3-months follow-up			6- months follow-up			LMM
		n	Mean	SD	n	Mean	SD	n	Mean	SD	n	Mean	SD	p-value
Intervention group		320			264			231			225			
Control group		305			275			261			251			
Patient activation														
Total score PAM	I	292	59.2	12.5	245	57.2	12.2	217	59.5	12.7	209	60.0	13.7	0.41
	C	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	I	320	85.3	14.9	259	88.4	12.1	228	88.7	13.2	223	89.3	12.3	**0.048**
	C	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*	I	319	48.8	6.1	259	47.8	6.3	228	47.9	6.5	223	47.8	7.1	0.77
	C	304	47.6	6.8	271	47.3	6.9	253	47.1	6.8	247	47.3	6.6	
Summary Negative Adjustment	I	320	28.2	7.0	259	27.8	6.7	228	27.3	6.7	223	27.2	6.8	1.00
	C	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	I	319	22.3	24.7	260	18.6	22.9	229	17.1	22.7	224	17.4	23.6	0.50
	C	305	22.6	23.4	273	20.8	22.1	257	20.0	22.4	249	18.6	22.8	
Psychological	I	319	24.2	23.9	260	18.8	21.2	229	16.4	19.2	224	15.5	19.9	0.18
	C	305	25.0	23.1	273	22.3	22.4	257	21.5	22.1	249	20.7	23.1	
Sexuality	I	308	16.0	25.7	252	11.9	22.0	223	12.3	23.1	220	11.3	21.2	0.35
	C	297	15.9	26.5	268	14.6	24.1	253	14.6	24.4	240	13.4	23.7	
Health system/ information	I	319	20.1	22.3	260	14.8	19.0	229	12.2	17.0	223	12.6	18.3	0.41
	C	305	20.4	21.9	273	17.1	19.7	254	15.0	18.7	248	13.5	18.7	

Table 2 – continued

		Baseline			1-week post-intervention			3-months follow-up			6- months follow-up			LMM
		n	Mean	SD	n	Mean	SD	n	Mean	SD	n	Mean	SD	p-value
Self-efficacy														
	I	*320*	*32.1*	*5.2*	*263*	*32.1*	*4.8*	*229*	*32.1*	5.0	224	32.0	*5.1*	0.31
	C	*305*	*31.6*	*5.0*	*274*	*31.0*	*4.6*	*259*	*31.2*	4.9	250	31.5	4.6	
Personal control														
	I	320	24.3	4.8	262	24.6	4.1	229	24.6	4.6	224	24.5	4.7	0.68
	C	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														
	I	320	20.8	3.5	262	20.5	3.3	229	20.6	3.3	224	21.0	3.1	0.22
	C	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, LMM = Linear mixed model analysis
**The difference between the intervention and control group at baseline was statistically different*

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

		Baseline			1-week post-intervention			3-months follow-up			6- months follow-up			LMM
		n	Mean	SD	n	Mean	SD	n	Mean	SD	n	Mean	SD	p-value
Head and neck cancer, EORTC QLQ-H&N43														
Fear of progression	I	99	15..3	21.9	82	12.0	17.2	68	8.6	14.3	68	9.6	18.5	0.51
	C	86	16.7	20.8	76	17.1	20.9	71	13.8	18.7	64	11.7	15.9	
Body image	I	99	9.4	19.1	82	9.2	19.5	68	6.5	20.2	68	7.7	21.0	0.62
	C	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	I	99	35.2	28.9	82	35.2	27.7	68	31.1	28.9	68	26.0	26.5	0.48
	C	86	32.9	24.5	76	36.6	31.5	71	31.7	29.2	64	29.4	26.7	

Table 3 – continued

		Baseline			1-week post-intervention			3-months follow-up			6- months follow-up			LMM
		n	Mean	SD	n	Mean	SD	n	Mean	SD	n	Mean	SD	p-value
Pain in the mouth	I	99	14.1	16.0	82	14.1	17.6	68	9.6	14.8	68	7.0	10.7	**0.010**
	C	86	14.5	18.1	76	16.8	18.2	71	15.7	18.6	64	15.6	19.9	
Sexuality	I	83	20.7	30.4	70	19.0	27.7	60	14.7	27.3	58	13.8	26.5	0.11
	C	73	25.1	34.4	66	30.1	34.6	57	24.9	32.8	49	24.5	35.0	
Problems with senses	I	99	19.0	16.5	82	18.5	25.7	68	12.0	19.7	68	13.5	22.0	0.36
	C	86	17.4	25.8	76	17.3	26.9	71	16.7	15.4	64	16.1	27.5	
Problems with shoulder	I	99	10.3	20.3	82	11.2	19.3	68	8.6	18.5	68	10.3	20.6	0.82
	C	86	10.7	19.8	76	11.2	20.6	71	12.2	22.4	64	13.3	23.6	
Skin problems	I	99	10.5	14.7	82	8.7	15.7	68	4.2	7.4	68	6.0	13.6	0.51
	C	86	9.0	17.3	76	9.1	15.1	71	6.6	11.7	64	6.6	14.2	
Social eating	I	99	16.3	27.0	82	15.8	24.6	68	10.7	24.2	68	7.6	17.8	**0.038**
	C	86	16.3	25.9	76	18.3	27.6	71	17.5	29.2	64	17.2	30.0	
Speech	I	99	15.0	19.8	82	19.4	23.1	68	16.0	20.7	68	15.4	19.9	0.19
	C	86	16.0	23.9	76	15.1	25.5	71	10.9	22.4	64	8.5	15.4	
Swallowing	I	99	15.3	23.1	76	13.3	21.0	71	10.8	21.3	64	7.0	12.7	**0.045**
	C	86	14.1	22.4	82	15.9	24.0	68	14.4	22.8	68	13.2	22.4	
Problems with teeth	I	99	12.8	20.0	82	11.0	17.2	68	8.2	14.7	68	8.5	14.1	0.29
	C	86	15.0	26.4	76	14.6	23.9	71	14.6	23.2	64	13.5	26.1	
Coughing	I	99	13.8	24.7	82	13.8	21.6	68	10.3	19.3	68	6.9	15.8	**0.017**
	C	86	11.2	20.8	76	17.5	28.0	71	16.4	25.7	64	14.0	23.6	
Swelling in the neck	I	99	5.4	14.8	82	6.9	20.1	68	5.4	18.8	68	2.9	11.1	0.97
	C	86	4.7	15.5	76	6.1	17.0	71	3.8	13.3	64	1.6	7.1	

Table 3 – continued

		Baseline			1-week post-intervention			3-months follow-up			6- months follow-up			LMM
		n	Mean	SD	n	Mean	SD	n	Mean	SD	n	Mean	SD	p-value
Neurological problems	I	99	12.8	24.6	82	14.6	25.2	68	11.3	21.2	68	8.3	17.6	0.24
	C	86	16.7	29.3	76	15.8	28.0	71	12.7	24.1	64	15.1	27.8	
Trismus	I	99	14.8	27.4	82	15.9	27.3	68	10.3	22.5	68	7.8	20.9	**0.046**
	C	86	16.7	29.7	76	18.0	30.0	71	19.7	31.7	64	19.8	32.9	
Social contact	I	99	2.7	10.3	82	2.0	9.6	68	1.5	6.9	68	1.0	5.7	0.92
	C	86	5.4	16.9	76	6.6	20.4	71	6.1	18.9	64	4.7	16.7	
Weight loss	I	99	10.8	24.7	82	7.3	18.9	68	3.9	15.8	68	2.9	13.8	0.48
	C	86	9.7	25.0	76	9.6	24.2	71	7.0	22.5	64	4.7	16.7	
Problems with wound healing	I	99	6.7	19.0	82	3.3	11.2	68	3.9	15.8	68	1.0	5.7	0.12
	C	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	I	80	27.3	22.5	67	20.6	21.7	59	27.4	24.1	61	21.3	20.7	0.39
	C	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	I	80	1.7	6.3	67	1.0	4.9	59	1.4	5.6	61	1.1	4.2	0.47
	C	72	2.1	7.4	63	2.9	11.0	63	1.9	6.8	60	3.1	8.9	
Stool frequency	I	80	17.1	22.0	67	12.1	17.0	59	14.4	19.4	61	12.0	17.8	0.56
	C	71	19.2	20.4	63	18.3	19.8	63	19.8	21.1	60	18.6	20.1	
Body image	I	80	10.1	15.5	67	8.6	13.2	59	8.3	13.9	61	8.2	12.3	0.53
	C	72	15.9	22.1	63	17.1	21.7	63	16.6	19.7	60	16.7	21.3	
Urinary incontinence	I	80	10.8	18.2	67	9.0	18.0	59	10.7	19.0	61	12.6	23.7	0.18
	C	72	4.2	11.1	63	5.8	14.1	63	4.2	11.2	60	4.4	11.4	

Table 3 – continued

		Baseline			1-week post-intervention			3-months follow-up			6- months follow-up			LMM
		n	Mean	SD	n	Mean	SD	n	Mean	SD	n	Mean	SD	p-value
Dysuria	I	80	0.8	5.2	67	0	0	63	1.1	5.9	61	1.1	8.5	0.32
	C	72	0.5	3.9	63	1.1	5.9	59	2.3	8.5	60	1.1	6.0	
Abdominal pain	I	80	10.8	20.4	67	10.0	20.9	59	13.0	21.5	61	5.5	16.3	**0.064**
	C	72	10.2	21.4	63	8.5	15.8	63	13.2	25.1	60	11.7	16.3	
Buttock pain	I	80	10.4	19.6	67	10.4	22.6	59	9.0	20.4	61	8.2	20.8	0.64
	C	72	8.3	21.5	63	7.4	15.2	63	7.9	19.6	60	8.3	16.9	
Bloating	I	80	16.3	24.3	67	10.0	21.7	59	10.7	21.8	61	10.4	18.8	0.12
	C	72	13.4	19.9	63	14.3	20.5	63	16.4	26.0	60	12.8	21.3	
Dry mouth	I	80	12.5	22.1	67	14.9	24.8	59	14.1	24.9	61	14.8	24.0	0.97
	C	72	12.5	20.5	63	13.8	20.4	63	13.8	19.5	60	15.6	19.9	
Hair loss	I	80	1.25	6.4	67	0.5	4.1	59	1.1	6.1	61	0	0	**0.060**
	C	72	0.5	3.9	63	2.6	10.9	63	0.5	4.2	50	2.8	14.1	
Taste	I	80	2.5	12.7	67	2.0	9.8	59	1.7	9.6	61	1.1	6.0	0.92
	C	72	6.5	19.9	63	5.8	17.5	63	5.8	17.5	60	3.9	15.1	
Anxiety	I	80	13.3	18.8	67	14.4	18.6	59	14.7	19.8	61	11.5	18.1	0.80
	C	72	19.0	22.9	63	19.6	22.9	63	19.0	20.5	60	20.0	23.9	
Weight	I	80	15.4	22.5	67	14.4	21.9	59	12.4	18.5	61	10.4	17.8	**0.028**
	C	72	20.4	27.2	63	19.6	22.1	63	21.2	21.8	60	21.1	22.9	
Flatulence	I	80	31.7	31.3	67	27.9	28.8	59	26.6	27.5	61	25.1	27.7	0.13
	C	71	29.6	23.6	63	29.6	20.8	63	33.3	27.4	60	32.2	27.4	
Faecal incontinence	I	80	8.8	21.0	67	8.0	19.3	59	9.0	19.4	61	6.0	14.3	0.49
	C	71	8.0	19.1	63	10.6	17.8	63	11.1	19.6	60	8.9	17.2	

Table 3 – continued

		Baseline			1-week post-intervention			3-months follow-up			6- months follow-up			LMM
		n	Mean	SD	n	Mean	SD	n	Mean	SD	n	Mean	SD	p-value
Sore skin	I	80	12.9	24.0	67	10.9	21.2	59	9.6	20.6	61	7.7	19.6	0.24
	C	71	8.5	20.9	63	12.7	21.1	63	9.5	21.9	12	9.4	16.3	
Embarrassment	I	80	16.3	27.0	67	15.4	27.4	59	15.8	25.8	61	12.0	22.8	0.65
	C	71	16.9	28.7	63	17.5	26.7	14	19.6	26.5	60	16.7	26.4	
Stoma care problems	I	10	10.0	31.6	10	10.0	22.5	8	0	-	7	0	-	0.30
	C	14	0	-	13	5.1	18.5	14	2.4	8.9	12	2.8	9.6	
Sexual interest (men)	I	48	47.9	34.3	44	50.8	32.5	38	50.0	33.6	37	55.9	31.5	0.76
	C	50	51.3	33.8	51	53.6	35.3	50	50.7	28.8	49	52.4	28.9	
Impotence (men)	I	45	46.7	38.5	37	45.0	36.2	35	38.1	38.0	34	45.1	36.6	0.76
	C	46	37.0	38.6	44	41.7	36.7	47	42.6	39.1	45	43.7	34.7	
Sexual interest (women)	I	28	46.4	46.6	23	47.8	44.8	21	63.5	48.2	24	51.4	47.1	0.49
	C	13	38.5	44.8	12	36.1	48.1	13	43.6	43.9	11	45.5	45.4	
Dyspareunia (women)	I	23	5.8	16.4	15	15.6	24.8	15	2.2	8.6	18	1.9	7.9	0.26
	C	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														
Neuropathy	I	47	23.4	26.8	35	22.9	28.9	36	22.7	26.2	33	16.7	25.0	0.30
	C	47	17.4	25.3	43	17.1	23.7	34	17.6	28.1	38	19.3	28.6	
Physical condition/ Fatigue	I	47	20.1	23.4	35	15.2	19.2	36	17.2	24.1	33	15.2	22.2	0.97
	C	47	19.6	18.7	43	16.0	16.7	34	17.6	20.9	38	19.1	21.4	
Emotional impact	I	47	16.7	21.2	35	14.8	19.0	36	17.1	23.1	33	12.1	17.9	**0.049**
	C	47	20.6	22.2	43	17.2	20.6	34	13.7	20.3	38	15.4	20.6	

Table 3 – continued

		Baseline			1-week post-intervention			3-months follow-up			6- months follow-up			LMM
		n	Mean	SD	n	Mean	SD	n	Mean	SD	n	Mean	SD	p-value
Worries/fears health and functioning	I	47	19.0	16.7	35	17.3	17.7	36	16.1	16.3	33	13.9	16.7	0.75
	C	46	17.8	19.8	43	15.7	18.7	34	18.2	25.0	38	16.6	22.2	
Breast cancer, EORTC QLQ-BR23														
Body image	I	66	80.6	26.9	55	87.4	19.6	45	88.7	16.5	45	88.7	18.6	0.43
	C	72	83.3	22.6	65	85.5	21.9	62	88.3	18.1	62	88.6	18.9	
Sexual functioning	I	62	23.4	21.2	47	25.2	20.8	39	23.9	21.9	38	24.6	18.1	0.76
	C	62	23.1	21.6	57	24.9	20.7	53	25.8	19.2	49	27.2	20.9	
Sexual enjoyment	I	35	52.4	28.3	25	50.0	23.1	22	56.1	26.0	24	56.9	23.0	0.98
	C	35	57.1	27.5	37	55.0	25.1	36	57.4	27.2	32	57.3	27.1	
Future perspective	I	66	68.7	27.3	55	75.2	23.3	45	74.8	20.3	45	77.8	23.6	0.40
	C	72	70.4	26.0	65	75.9	25.4	62	71.0	26.6	62	72.6	26.0	
Systemic therapy side effects	I	66	16.5	14.1	55	13.1	12.3	45	12.4	10.8	45	15.3	13.7	0.87
	C	71	16.0	12.3	65	15.0	12.2	62	14.8	11.0	62	15.3	11.9	
Breast symptoms	I	66	17.7	18.2	55	16.4	17.7	45	14.3	14.2	45	14.1	13.0	0.44
	C	72	18.2	19.6	65	16.8	18.5	62	19.0	19.6	62	15.1	18.5	
Arm symptoms	I	66	19.5	18.4	55	18.2	18.9	45	18.5	16.6	45	16.3	17.7	0.53
	C	72	16.7	18.6	65	17.1	18.5	62	18.1	18.0	62	15.8	19.8	
Upset by hair loss	I	14	38.1	38.9	9	18.5	24.2	10	16.7	23.6	14	16.7	28.5	0.31
	C	16	16.7	21.1	12	13.9	17.2	13	17.9	17.3	15	20.0	16.9	

LMM = Linear mixed model analysis. 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. Owing to the small numbers of low-grade non-Hodgkin lymphoma and Hodgkin lymphoma survivors, the linear mixed model analyses were not performed on tumour-specific symptoms for these two types of lymphoma.

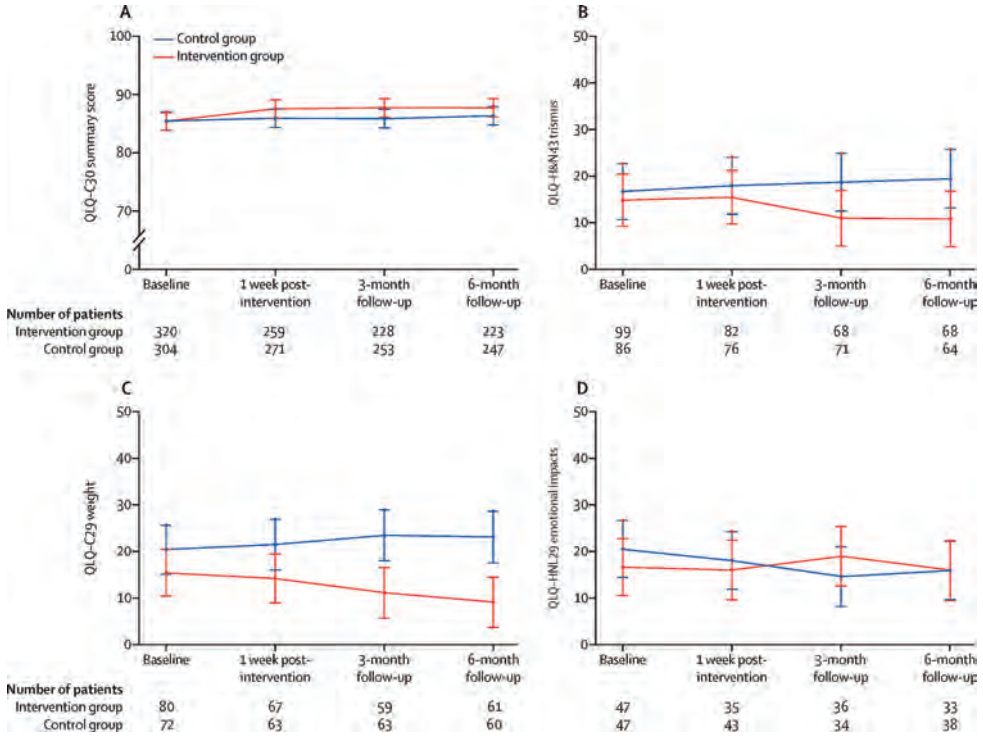


Figure 2 – The course of different measures over time.

*(A) HRQOL summary score (a higher score indicates better HRQOL). (B) Trismus in head and neck cancer survivors (a higher score indicated higher symptom burden). (C) Worries about weight in colorectal cancer survivors (a higher score indicated higher symptom burden). (D) Emotional impact for both groups in high grade non-Hodgkin lymphoma survivors (a higher score indicated 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. **

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 (i.e. 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 time point 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 (e.g. 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 (e.g. 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 received 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.

REFERENCES

1. Alfano CM, Ganz PA, Rowland JH, Hahn EE. Cancer Survivorship and Cancer Rehabilitation: Revitalizing the Link. J Clin Oncol 2012; 30: 904–6.
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-DeLeeuw 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 (Madr) 2018; 57: 924–34.
12. de Wit LM, 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 L V., Horevoorts N, Eenbergen M Van, 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. Engel GL. The need for a new medical model: a challenge for biomedicine. Science (80-) 1977; 196: 129 LP – 136.
16. 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.
17. 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.
18. 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.

19. Watson M, Homewood J. Mental Adjustment to Cancer Scale©: Psychometric properties in a large cancer cohort. Psychooncology 2008; 17: 1146–51.

20. 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: 602–6.

21. 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.

22. Pearlin LI, Schooler C. The Structure of Coping: Erratum. J Health Soc Behav 1978; 19: 237.

23. 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.

24. 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.

25. 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.

26. 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.

27. 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.

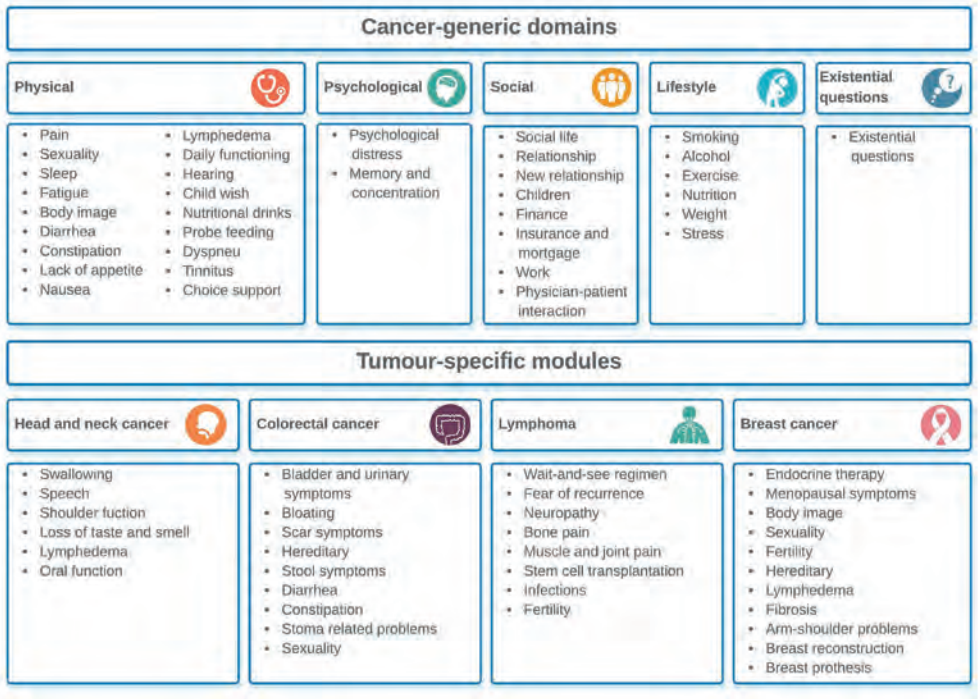
28. Ishikawa H, Takeuchi T, Yano E. Measuring functional, communicative, and critical health literacy among diabetic patients. Diabetes Care 2008; 31: 874–9.

29. Wallston KA, Wallston BS, DeVellis R, et al. Development of the Multidimensional Health Locus of Control (MHLC) Scales. Heal Educ Behav 1978; 6: 160–70.

30. 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: 1418–2

* From van der Hout et al (2020): https://doi.org/10.1016/S1470-2045(19)30675-8

SUPPLEMENTARY MATERIAL



Supplementary Figure 1 – Overview of topics within generic domains and tumour-specific modules in Oncokompas

Supplementary Table 1 – Mean scores per group per assessment and results of linear mixed model analyses on the primary outcome stratified per tumour type

	Baseline		**1-week post-intervention**		**3-month follow-up**		**6-month follow-up**			**LMM**
	n	Mean (SD)	n	Mean (SD)	n	Mean (SD)	n	Mean (SD)	Difference (95% CI)	(p value)
Head and neck cancer										
Total score, patient activation measure										
Intervention	93	58.6 (12.9)	77	56.4 (12.5)	67	59.0 (13.5)	65	59.5 (13.4)	0.9 (−4.1 to 5.8)	0.79
Control	73	60.0 (12.5)	69	55.9 (12.3)	66	57.5 (13.4)	60	58.6 (14.4)		
Colorectal cancer										
Total score, patient activation measure										
Intervention	68	58.3 (12.2)	62	55.1 (11.7)	57	59.1 (13.0)	55	59.5 (15.4)	−0.9 (−6.2 to 4.3)	0.40
Control	67	61.9 (12.0)	62	59.4 (10.9)	59	59.7 (12.5)	58	60.5 (12.7)		
Lymphoma										
Total score, patient activation measure										
Intervention	69	58.4 (11.4)	53	56.2 (9.5)	49	58.9 (10.6)	45	58.6 (11.3)	−0.3 (−5.0 to 4.4)	0.99
Control	67	59.4 (12.9)	59	57.5 (11.0)	54	59.5 (12.0)	60	58.9 (12.5)		
Breast cancer										
Total score, patient activation measure										
Intervention	62	61.8 (13.2)	53	61.6 (13.8)	44	61.5 (13.3)	44	62.8 (14.1)	7.8 (2.9 to 12.6)	0.91
Control	70	56.7 (12.5)	61	54.9 (11.1)	62	55.3 (11.6)	56	55.1 (10.3)		

LMM = Linear mixed model analysis.

Supplementary Table 2 – Results of post-hoc analyses on effect sizes (difference in means between groups divided by pooled standard deviation) and independent sample t tests for differences per follow-up assessment for significant different outcomes in linear mixed model analyses

	1-week post-intervention			3-month follow-up			6-month follow-up		
	Effect size	95% CI	t test (p value)	Effect size	95% CI	t test (p value)	Effect size	95% CI	t test (p value)
Total group, EORTC QLQ-C30									
Summary score	0.18	0.01 to 0.35	**0.041**	0.17	−0.01 to 0.35	0.067	0.18	0.00 to 0.36	0.051
Head and neck cancer, EORTC QLQ-H&N43									
Pain in the mouth	0.15	−0.18 to 0.48	0.35	0.36	0.03 to 0.69	**0.032**	0.80	0.44 to 1.15	**0.003**
Social eating	0.10	−0.23 to 0.42	0.54	0.25	−0.08 to 0.58	0.14	0.39	0.05 to 0.73	**0.029**
Swallowing	0.11	−0.21 to 0.44	0.47	0.16	−0.17 to 0.49	0.33	0.34	0.00 to 0.69	0.057
Coughing	0.15	−0.16 to 0.46	0.35	0.27	−0.07 to 0.60	0.11	0.36	0.01 to 0.70	**0.043**
Trismus	0.07	−0.25 to 0.40	0.64	0.34	0.01 to 0.67	**0.044**	0.44	0.09 to 0.78	**0.015**
Colorectal cancer, EORTC QLQ-CR29									
Weight	0.24	−0.11 to 0.58	0.19	0.43	0.07 to 0.79	**0.019**	0.52	0.16 to 0.88	**0.005**
Lymphoma (high grade non-Hodgkin), EORTC QLQ-NHL-HG29									
Emotional impacts	0.12	−0.33 to 0.57	0.59	−0.18	−0.65 to 0.29	0.52	0.17	−0.30 to 0.64	0.48

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.

The eHealth self-management application 'Oncokompas' that supports cancer survivors to improve health-related quality of life and reduce symptoms: which groups benefit most?

A. (Anja) van der Hout, K. (Karen) Holtmaat, F. (Femke) Jansen, B.I. (Birgit) Lissenberg-Witte, C.F. (Nelly) van Uden-Kraan, G.A.P. (Grard) Nieuwenhuijzen, J.A. (José) Hardillo, R.J. (Robert) Baatenburg de Jong, N.L. (Nicolette) Tiren-Verbeet, D.W. (Dirkje) Sommeijer, K. (Koen) de Heer, C.G. (Cees) Schaar, R.J.E. (Robert-Jan) Sedee, K. (Koop) Bosscha, M.W.M. (Michiel) van den Brekel, J.F. (Marije) Petersen, M. (Matthijs) Westerman, J. (Jimmie) Honings, R.P. (Robert) Takes, I. (Ilse) Houtenbos, W.T. (Wim) van den Broek, R. (Remco) de Bree, P. (Patricia) Jansen, S.E.J. (Simone) Eerenstein, C.R. (René) Leemans, J.M. (Josée) Zijlstra, P. (Pim) Cuijpers, L.V. (Lonneke) van de Poll-Franse, I.M. (Irma) Verdonck-de Leeuw

Accepted for publication in Acta Oncologica

SUMMARY

Background: Oncokompas is a web-based self-management application that supports cancer survivors to monitor their health-related quality of life (HRQOL) and symptoms, and to obtain personalized feedback and tailored options for supportive care. In a large randomised controlled trial among survivors of head and neck cancer, colorectal cancer, and breast cancer and (non-) Hodgkin lymphoma, Oncokompas proved to improve HRQOL, and to reduce several tumour-specific symptoms. Effect sizes were however small, and no effect was observed on the primary outcome patient activation. Therefore, this study aims to explore which subgroups of cancer survivors may especially benefit from Oncokompas.

Methods: Cancer survivors (n = 625) were randomly assigned to the intervention group (access to Oncokompas, n = 320) or control group (6 months waiting list, n = 305). Outcome measures were HRQOL, tumour-specific symptoms, and patient activation. Potential moderators included socio-demographic (sex, age, marital status, education, employment), clinical (tumour type, stage, time since diagnosis, treatment modality, comorbidities), and personal factors (self-efficacy, personal control, health literacy, internet use), and patient activation, mental adjustment to cancer, HRQOL, symptoms, and need for supportive care, measured at baseline. Linear mixed models were performed to investigate potential moderators.

Results: The intervention effect on HRQOL was the largest among cancer survivors with low to moderate self-efficacy, and among those with high personal control and those with high health literacy scores. Cancer survivors with higher baseline symptom scores benefitted more on head and neck (pain in the mouth, social eating, swallowing, coughing, trismus), and colorectal cancer (weight) specific symptoms.

Discussion: Oncokompas seems most effective in reducing symptoms in head and neck cancer and colorectal cancer survivors who report a higher burden of tumour-specific symptoms. Oncokompas seems most effective in improving HRQOL in cancer survivors with lower self-efficacy, and in cancer survivors with higher personal control, and higher health literacy.

INTRODUCTION

eHealth self-management interventions may have positive effects on health-related quality of life (HRQOL) and symptom burden among cancer survivors, but effect sizes vary considerably.[1–4] It is likely that some cancer survivors may benefit more from eHealth interventions than others, but knowledge of possible moderators is scarce.[5–8] Oncokompas is a web-based self-management application that supports cancer survivors to monitor their HRQOL and cancer-generic and tumour-specific symptoms, and can be used without help from a healthcare professional. Oncokompas provides personalized feedback and information based on scores from patient reported outcome measures (PROMs), and a tailored overview of supportive care options. A tailored care approach is followed i.e.,: in case of minor problems information and self-help interventions are proposed, and in case of major problems, professional care is proposed.[9,10]

In a previous paper we reported on the efficacy of Oncokompas in a large randomised controlled trial (RCT) among 625 cancer survivors. We showed that Oncokompas had no significant effect on the primary outcome measure patient activation (i.e., knowledge, skills, and confidence for self-management)[11] in the total group, nor in tumour-specific subgroups of head and neck cancer, colorectal cancer, breast cancer, or (non-)Hodgkin lymphoma.[12] However, a significant beneficial effect was found on HRQOL in the total group and several tumour-specific symptoms in survivors of head and neck cancer, colorectal cancer, and non-Hodgkin lymphoma.[12] Effect sizes on HRQOL were small (0.17 to 0.18) and the effect sizes on symptoms that were significantly different varied from -0.18 to 0.80 up from 1 week to 6 months follow-up.[12]

Investigating the effect of potential moderating variables is important to understand the generalizability of research findings in subgroups.[13,14] However, moderating variables of eHealth interventions are not often investigated. In previous RCTs and systematic reviews, several potential moderating factors were explored on the effect of psychosocial interventions among cancer patients. A systematic review showed that cancer patients with lower quality of life, interpersonal relationships and sense of control benefitted more from psychosocial interventions than those who already had adequate resources.[8] An individual patient-data meta-analysis showed that psychosocial interventions significantly improved HRQOL with small effect sizes after treatment, while the intervention effects were larger among younger patients.[5]

Intervention effects are mostly in favour of those with a higher education level, higher literacy, and those with higher symptom burden or lower quality of life.[5,15,16] It is expected that in eHealth interventions for cancer survivors clinical factors such as tumour type and stage, type of cancer treatment, and time since treatment, can moderate the effect of the intervention, since symptoms and needs might differ across these subgroups and decrease over time.[17,18] Also, it could be expected that survivors with a higher need for supportive care benefit more from interventions such as Oncokompas.

The aim of this study was to investigate potential moderating factors, including socio-demographic, clinical, and personal factors, HRQOL, symptoms, and need for supportive care on the efficacy of Oncokompas on HRQOL, symptoms and patient activation. For clinical practice, it is interesting to know which subgroups of cancer survivors are most likely to benefit from an eHealth self-management application such as Oncokompas in terms of HRQOL and symptoms, and patient activation. This knowledge can be used to further tailor eHealth self-management interventions for optimal cancer survivorship care.

MATERIAL AND METHODS

Study design and population

This study entailed secondary analyses of a randomised controlled trial (RCT) on the efficacy of Oncokompas compared to usual cancer survivorship care. Detailed descriptions of study procedures and primary results can be found elsewhere.[12,19] In short, adult cancer survivors who were treated with curative intent for head and neck cancer, colorectal cancer, or breast cancer, or lymphoma (high- and low-grade non-Hodgkin lymphoma, and Hodgkin lymphoma) 3 months to 5 years previously, were asked to participate in the RCT by their (former) treating physician. Exclusion criteria were: no access to the Internet or no email address, severe cognitive impairment, insufficient mastery of the Dutch language, physical inability to complete a questionnaire, and breast cancer survivors with male sex. Survivors were recruited from 14 hospitals in the Netherlands between October 12, 2016 and May 24, 2018. After providing written (online) informed consent and completing the baseline assessment, participants were randomised into the intervention group (direct access to Oncokompas) or control group (access to Oncokompas after a waiting period of 6 months) in a 1:1 allocation ratio, stratified per tumour type. Follow-up assessments were 1-week post-intervention and at 3- and 6-months follow-up. The study protocol was approved by the Medical Ethics Committee of the VU University

Medical Center (2015.523) and the trial was registered in the Netherlands Trial Register (NTR5774).

Intervention

A detailed description of the intervention has been published previously.[12,19] In short, Oncokompas is an eHealth self-management application that supports cancer survivors to monitor their HRQOL and cancer-generic and tumour-specific symptoms. The main goal is to obtain personalized feedback and information on their scores and a tailored overview of supportive care options. Oncokompas includes various topics in five generic HRQOL domains, which are relevant for survivors of all tumour types: physical, psychological and social functioning, lifestyle, and existential issues, according to the biopsychosocial model.[20] Besides, various tumour-specific topics are addressed in tumour-specific modules targeting head and neck cancer, colorectal cancer, breast cancer and (non-)Hodgkin lymphoma survivors. Oncokompas consists of three components: 'Measure', 'Learn', and 'Act'. In the 'Measure' component, cancer survivors can complete PROMs on the topic(s) of choice. Data from the 'Measure' component are processed in real-time and linked to feedback in the 'Learn' component. In the 'Learn' component feedback is provided to the cancer survivor by means of a 3-colour system: green (no elevated well-being risks), orange (elevated well-being risks), and red (seriously elevated well-being risks). Cancer survivors receive personalized information on the outcomes, and comprehensive self-care advice. In the 'Act' component, cancer survivors are provided with tailored supportive care options, based on their PROM-scores and expressed preferences (e.g. preference for individual therapy versus group therapy). If a user has elevated well-being risks (orange score), the feedback includes suggestions for self-help interventions. If an user has seriously elevated well-being risks, the feedback includes an advice to contact their medical specialist or general practitioner.[12,19,21]

Outcome measurement

Data on the outcome measures HRQOL, symptoms, and patient activation were collected at time of inclusion (baseline (T0)), 1-week post-intervention (T1), and after 3-months (T2) and 6-months (T3) follow-up.

HRQOL was measured with the EORTC QLQ-C30 summary score (SumSC). The SumSC is based on the five functional scales (physical, cognitive, emotional, social, and role functioning), three symptom scales (fatigue and nausea/vomiting, and pain) and five single items (dyspnoea, insomnia, appetite loss, constipation, diarrhoea) of the QLQ-C30. The SumSC ranges from 0 to 100, with a higher score representing better HRQOL.[22]

Tumour-specific symptoms were measured with the EORTC tumour-specific questionnaires. In the present study, those subscales were used on which Oncokompas had a beneficial effect in the RCT[12]: pain in the mouth, social eating, swallowing, coughing and trismus in head and neck cancer survivors (EORTC QLQ-H&N43),[23] weight in colorectal cancer survivors (EORTC QLQ-CR29),[24] and emotional impact in high grade non-Hodgkin lymphoma survivors (EORTC-QLQ-NHL-HG29).[25] All EORTC scales and single items scores range from 0 to 100 (higher score indicating higher burden of symptoms). Only these subscales were chosen to limit the amount of analyses.

Patient activation was measured with the Patient Activation Measure (PAM), which measures a participants' level of knowledge, skills and confidence for self-management. The PAM score ranges from 0 to 100, with a higher score indicating a higher level of patient activation.[11]

Potential moderators

Potential moderators for the effect on HRQOL and patient activation included socio-demographic, clinical and personal characteristics, and patient activation, mental adjustment to cancer, HRQOL, and need for supportive care, measured at baseline. Potential moderators regarding symptoms included socio-demographic and clinical characteristics, and the baseline score of that symptom.

Socio-demographic characteristics included sex (male, female), age (years), marital status (no partner, partner), education level (low, medium, high), and employment status (employed, not employed), and were measured with a study-specific questionnaire.

Clinical characteristics included tumour type (head and neck cancer, colorectal cancer, breast cancer, or lymphoma), tumour stage (low stage (I or II), high stage (III or IV)), time since diagnosis (categorized into 3 to 12 months, 12 to 24 months, and 24 to 60 months), treatment (none/single treatment, multimodal treatment), and comorbidities (none/one comorbidity, two or more comorbidities). These characteristics were retrieved from the Dutch Cancer Registry, or measured with a study-specific questionnaire.[19]

Personal factors included self-efficacy (General Self-Efficacy (GSE) scale[26]), personal control (Pearlin and Schooler Mastery (PSM) scale[27]), health literacy (Functional, Communicative and Critical Health Literacy scale, summary score[28]), health locus of control (Multidimensional Health Locus of Control scale, with internal, powerful others, and chance subscales[29]), and internet use (<7 hours per week, >7 hours per week).

Other potential moderators were patient activation (Patient Activation Measure[11]), mental adjustment to cancer (Mental Adjustment to Cancer scale, with summary positive adjustment and summary negative adjustment subscales[30]), HRQOL (EORTC QLQ-C30 summary score[22]), and need for supportive care (Supportive Care Needs Survey 34-items short form, with physical and daily living, psychological, sexuality, and health system, information and patient support subscales, of which scores were dichotomized into no unmet needs and unmet needs[31,32]). Tumour-specific symptoms for head and neck, colorectal and high-grade non-Hodgkin lymphoma were measured with the EORTC tumour-specific questionnaires QLQ-H&N43, QLQ-CR29, and QLQ-NHL-HG29, respectively.[24,25,33]

Statistical analyses

Descriptive statistics were generated for socio-demographic and clinical characteristics. Statistical analyses were performed using the IBM SPSS Statistics version 26 (IBM Corp. Armonk, NY, USA).

To explore moderating factors on the efficacy of Oncokompas compared to care as usual on HRQOL, symptoms and patient activation, from baseline to 6-months follow-up, exploratory linear mixed model (LMM) analyses were performed. The LMM included fixed effects for group (intervention or control), time, their two-way interaction, the potential moderator, and the two- and three-way interactions with group and time, and a random intercept for subject. A significant three-way interaction effect (group*time*moderator) was considered as an indication of a difference in intervention effect on the outcome, between (groups with) different scores on the moderator. A p-value of <0.05 was considered to be statistically significant, and all analyses were conducted according to the intention-to-treat principle.

To interpret the results of a dichotomous moderator variable, post-hoc linear mixed model analyses were performed stratified for each subgroup of the moderator. To interpret the results of a continuous moderator variable, estimated marginal means were calculated for multiple values of the moderator, and data visualisation was performed to interpret the direction of the intervention effect.

RESULTS

In total, 625 cancer survivors were randomised into the intervention (n = 320) or control group (n = 305). Mean age was 63 years (standard deviation (sd) 11), 51% was female, 85% had a partner,

and 35% was employed at baseline (**Table 1**). Furthermore, 30% was diagnosed with head and neck cancer, 24% with colorectal cancer, 24% with (non-)Hodgkin lymphoma, and with 22% breast cancer. The median time since diagnosis was of 27 months (interquartile range (IQR) 16–43). The baseline score of HRQOL (SumSC) was 85.4 (sd 14.3), and the baseline score of patient activation (PAM) was 59.3 (sd 12.5). Socio-demographic and clinical characteristics of participants are summarized in **Table 1**. Details of the participant flow and dropout have been published previously.[12]

Regarding the effect of Oncokompas on HRQOL, self-efficacy moderated this effect (measurement*group*self-efficacy, F(3,1487)=2.903, p=0.034) (**Table 2**). Data visualisation suggested that survivors with low GSE scores (low self-efficacy) benefitted most from Oncokompas, whereas the intervention effect became smaller when GSE scores were higher, and the intervention effect almost disappeared in survivors with high GSE scores (high self-efficacy) (**Supplementary Figure 1**).

Personal control also moderated the effect of Oncokompas on HRQOL (measurement*group* personal control, F(3,1481)=3.478, p=0.015). Data visualisation suggested that among survivors with low to moderate PSM scores (lower sense of personal control) there was no intervention effect, whereas survivors with high PSM scores (high sense of personal control) benefitted most from Oncokompas, via earlier improvement in HRQOL (**Supplementary Figure 2**).

Also, health literacy moderated the effect of Oncokompas on HRQOL (measurement*group* health literacy, F(3,1478)=2.869, p=0.035). Data visualisation suggested that there is no intervention effect among survivors with low to moderate health literacy, whereas survivors with high health literacy benefit most from Oncokompas, via earlier improvement in HRQOL (**Supplementary Figure 3**).

Regarding the effect of Oncokompas on the investigated symptoms, the baseline score of that tumour-specific symptoms moderated the effect (**Table 3**). Data visualisation suggested that all survivors with some degree of symptom burden at baseline benefitted from Oncokompas, and the intervention effect became larger when the burden of symptoms was higher (e.g. pain in the mouth in **Supplementary Figure 4**). In head and neck cancer survivors this was the case for pain in the mouth, social eating, swallowing, coughing, and trismus. In colorectal cancer survivors, this was the case for weight. Among non-Hodgkin lymphoma survivors, the baseline score did not moderate the effect of Oncokompas on emotional impacts.

Table 1 – Baseline characteristics of participants

	Intervention group (n = 320)	**Control group** (n = 305)
Socio-demographic factors		
Age, years	63.2 (11.2)	63.7 (10.1)
Sex (women)	158 (49%)	158 (52%)
Education level a		
Low	111 (35%)	117 (39%)
Medium	105 (33%)	85 (28%)
High	103 (32%)	100 (33%)
Health literacy	3.2 (0.5)	3.2 (0.5)
Marital status (partner)	265 (83%)	269 (88%)
Employment status (employed)	122 (38%)	99 (33%)
Clinical factors		
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%)
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/single treatment	137 (43%)	124 (41%)
Multimodal treatment	183 (57%)	181 (59%)
Comorbidities		
None/one comorbidity	249 (78%)	229 (75%)
Multiple comorbidities	71 (22%)	76 (25%)
Time since diagnosis	25.0 (16.0-41.0)	29.0 (16.5-41.0)
3-12 months	39 (12%)	38 (13%)
12-24 months	104 (33%)	85 (28%)
24-60 months	177 (55%)	182 (60%)
Personal factors		
HRQOL	85.3 (14.9)	85.4 (13.6)
Patient activation	59.2 (12.5)	59.5 (12.6)

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

Furthermore, among head and neck cancer survivors, Oncokompas was effective to reduce pain in the mouth in women (F(3,154)=5.107, p=0.002, but not in men (F(3,269)=0.441, p=0.72). Oncokompas was effective to improve social eating in HNC survivors without a partner (F(3,70)=3.547, p=0.019), but not in those with a partner (F3,352)=2.055, p=0.11). Oncokompas was effective to improve trismus in head and neck cancer survivors without a partner (F(3,71)=3.613, p=0.017), but not in those with a partner (F(3,354)=0.797, p=0.50). Age also moderated the effect on trismus. Data visualisation suggested that the intervention effect became larger with increasing age.

Regarding patient activation, none of the investigated factors significantly moderated the effect of Oncokompas (**Table 2**).

DISCUSSION

This study aimed to explore which subgroups of cancer survivors may especially benefit from the eHealth self-management application Oncokompas in terms of HRQOL, symptoms, and patient activation. The effect of Oncokompas on HRQOL seems to last longer among cancer survivors with low to moderate self-efficacy, survivors with higher personal control, and those with higher health literacy. In reducing symptoms, Oncokompas was more effective in head and neck and colorectal cancer survivors with higher symptom burden. Among head and neck cancer survivors, Oncokompas was more effective in females (on pain in the mouth), in survivors without a partner (on problems with social eating and trismus), and in older survivors (on trismus). With respect to patient activation, no specific subgroups were found who might benefit more from Oncokompas than others.

Although we aimed to develop a usable web-based application suitable for many cancer survivors, by tailoring information, limiting the amount of text, and making it accessible for low-literate people, health literacy still was found to moderate the effect of HRQOL, in favour of survivors with higher health literacy. Health literacy is known to be an important factor in eHealth interventions,[34] and found to be positively associated with HRQOL.[16,35,36] Adaptations are needed to improve the efficacy among those with lower health literacy, for instance by adding multimedia components, such as videos, podcasts, or infographics, or gamification elements.[37] However, it might be that despite these adaptations this group might benefit more from other types of interventions, e.g. face-to-face or group interventions.

Table 2 – Potential moderators of the effect of Oncokompas on patient activation and HRQOL compared to care as usual

	HRQOL		Patient activation	
Potential Moderator	F (2,df) three-way interaction	P value three-way interaction	F (2,df) three-way interaction	P value three-way interaction
Socio-demographic factors				
Sex (men, women)	1.214 (1476)	0.30	0.036 (1414)	0.99
Age (years)	0.647 (1486)	0.59	0.442 (1430)	0.72
Marital status (no partner, partner)	1.160 (1481)	0.32	0.591 (1417)	0.62
Education level (low, medium, high)	1.699 (1457)	0.12	1.261 (1399)	0.27
Employment status (not employed, employed)	1.468 (1478)	0.22	0.614 (1418)	0.61
Clinical factors				
Tumour type (head and neck, colorectal, breast cancer, lymphoma)	1.780 (1465)	0.067	0.299 (1402)	0.98
Tumour stage (I or II vs III or IV)	0.961 (1398)	0.41	1.031 (1340)	0.38
Time since diagnosis (3-12, 12-24, 24-60 months)	1.633 (1473)	0.13	0.262 (1407)	0.95
Treatment (0/1, ≥2 treatments)	0.177 (1474)	0.91	0.576 (1417)	0.63
Comorbidities (0/1, ≥2 comorbidities)	0.960 (1478)	0.41	0.217 (1410)	0.88
Personal factors				
Self-efficacy	2.903 (1487)	**0.034**	0.487 (1435)	0.69
Personal control	3.478 (1481)	**0.015**	1.620 (1431)	0.18
Health literacy	2.869 (1478)	**0.035**	0.847 (1434)	0.47
Health locus of control				
Internal	0.736 (1475)	0.53	1.085 (1429)	0.35
Powerful others	1.359 (1476)	0.25	1.066 (1430)	0.36
Chance	0.762 (1481)	0.52	0.107 (1430)	0.96
Internet use (<7, >7 hours/week)	1.960 (1470)	0.12	0.851 (1411)	0.47
Patient activation	2.124 (1353)	0.095	0.278 (1460)	0.84
Mental adjustment to cancer				
Positive adjustment	1.192 (1475)	0.31	0.498 (1428)	0.68
Negative adjustment	0.699 (1498)	0.55	0.540 (1442)	0.66
Unmet supportive care needs				
Physical and daily living	1.010 (1479)	0.39	0.756 (1413)	0.52
Psychological	0.237 (1479)	0.87	1.259 (1418)	0.29
Sexual	1.474 (1439)	0.22	0.376 (1372)	0.77
Health system, information and patient support	0.228 (1478)	0.88	0.416 (1417)	0.74
Health-related quality of life	0.903 (1617)	0.44	0.267 (1423)	0.85

Table 3 – Potential moderators of the effect of Oncokompas on tumour-specific symptoms, compared to care as usual

Potential Moderator	HNC Pain in the mouth		HNC Social eating		HNC Swallowing		HNC Coughing		HNC Trismus		CRC Weight		NHL-HG Emotional impacts	
	F (2,df)	P value	F (2,df)	P value	F (2,df)	P value	F (2,df)	P value	F (2,df)	P value	F (2,df)	P value	F (2,df)	P value
Socio-demographic factors														
Sex (men, women)	2.701 (422)	**0.045**	0.204 (423)	0.89	0.498 (420)	0.68	1.127 (424)	0.34	0.817 (425)	0.49	1.338 (364)	0.26	0.419 (208)	0.74
Age (years)	0.800 (424)	0.49	0.684 (424)	0.56	0.231 (421)	0.88	0.215 (427)	0.89	3.033 (426)	**0.029**	1.897 (364)	0.13	0.908 (210)	0.44
Marital status (no partner, partner)	1.930 (426)	0.12	2.952 (423)	**0.032**	1.260 (422)	0.29	0.255 (427)	0.86	3.097 (427)	**0.027**	1.046 (358)	0.37	0.715 (209)	0.54
Education level (low, medium, high)	0.310 (410)	0.93	0.736 (410)	0.62	0.708 (408)	0.64	1.626 (411)	0.14	0.986 (412)	0.43	1.105 (356)	0.36	0.887 (202)	0.51
Employment status (not employed, employed)	0.241 (424)	0.87	0.245 (423)	0.87	0.106 (420)	0.96	0.082 (426)	0.97	1.112 (426)	0.34	0.810 (362)	0.49	0.771 (208)	0.51
Clinical factors														
Tumour stage (I or II, III or IV)	1.109 (419)	0.35	0.680 (419)	0.57	0.685 (417)	0.56	1.001 (422)	0.39	0.136 (422)	0.94	1.476 (358)	0.22	0.793 (190)	0.50
Time since diagnosis (months)	1.043 (423)	0.40	0.438 (419)	0.85	0.398 (417)	0.88	0.956 (425)	0.46	0.339 (423)	0.92	0.731 (356)	0.63	0.811 (201)	0.56
Treatment (0/1, ≥2)	0.307 (423)	0.82	0.630 (422)	0.60	0.246 (420)	0.86	0.324 (424)	0.81	1.305 (425)	0.27	1.662 (364)	0.18	0.567 (207)	0.64
Comorbidities (0/1, ≥2)	0.689 (425)	0.56	0.470 (423)	0.70	0.707 (421)	0.55	0.611 (429)	0.61	0.397 (426)	0.76	0.166 (363)	0.92	0.346 (208)	0.79
Baseline score symptom (continuous)	5.685 (463)	**<0.001**	8.151 (456)	**<0.001**	2.982 (465)	**0.031**	3.703 (482)	**0.012**	4.118 (458)	**0.007**	3.303 (396)	**0.020**	2.560 (232)	0.056

Interestingly, Oncokompas seems more effective in cancer survivors with low to moderate self-efficacy. Self-efficacy is a concept that influences how people think, feel, motivate themselves, and act.[38] Our finding suggests that a low-intensive intervention such as Oncokompas provides help or tools to people with lower motivation or lower self-esteem to act. Moderating effects of self-efficacy were also found with an intervention on treatment information in breast cancer support groups; however, the effect on the outcome emotional well-being was in favour of women with higher self-efficacy.[39] On the other hand, the intervention effect of a psychoeducational intervention for men with prostate cancer has been shown in another study to be in favour of those with lower levels of prostate-specific self-efficacy.[40]

Furthermore, the intervention effect was also in favour of those with high personal control. Personal control, or mastery, refers to the degree to which controlling factors that influence life situations can be perceived, and it has been found important for HRQOL and well-being.[27,41] The improvements in HRQOL that were found in this group, suggest that fully-automated self-management interventions, can provide support to those with high feelings of mastery, to enhance their sense of mastery over their HRQOL and symptoms.

The intervention effect in favour of those with lower self-efficacy and higher personal control seems to be contrary. Examining the study population in the current study, persons with lower self-efficacy were not the same persons as those with higher personal control. It could be that cancer survivors with lower self-efficacy need a push to take action, and with Oncokompas, they have the tools to improve HRQOL. The effect among cancer survivors with higher personal control might be because they feel in control with Oncokompas, which leads to an earlier improvement in HRQOL. However, because the interaction effects were small, it could be that these findings were found by chance. Moderating effects of mastery and self-efficacy on the effects of eHealth interventions are not often investigated among cancer survivors. Further research is needed to confirm whether the identified moderating factors are moderating factors of eHealth interventions in general, or whether these factors especially moderate the effect of fully-automated self-management interventions.

Remarkably, baseline HRQOL did not moderate the effect on HRQOL, but baseline symptoms did moderate the effect on symptoms. This suggests that improvement of HRQOL is possible for every cancer survivor, regardless of having a low or high HRQOL at the start of the intervention, and

the benefit of Oncokompas might be through reducing symptom burden. Evidence on moderating effects of baseline values of HRQOL is inconsistent.[5,42]

As we demonstrated previously, Oncokompas was not effective in improving patient activation.[12] The current analyses showed there are also no subgroups for which patient activation was improved, so it might be that there is truly no effect of Oncokompas on survivors' skills, knowledge and confidence for self-management. This may be explained by the fact that the study population comprises cancer survivors who had access to the internet, and who were doing relatively well in terms of HRQOL, patient-physician interaction, adjustment to cancer, and unmet supportive care needs. Another explanation may be that most were long-term survivors (>2 years after diagnosis), who might already found the information and support they need to build their skills and confidence to manage cancer-related concerns.[12,17]

The strengths of this study is the large sample size, with participants from 14 hospitals across the Netherlands, and includes various categories of moderators. However, the results of this study should be considered with caution, because of some limitations. This study is was not powered to perform secondary exploratory analyses and detect moderating factors. Therefore, it is possible that important moderating factors were not identified, because of a lack of power. Also, with many potential moderators, and multiple outcome measures, many separate models were analysed in the total group. As a result, the observed effects might have been found by chance. Because the analyses were only exploratory, and there is no consensus on how to apply corrections for multiple testing,[43] and no corrections for multiple testing have been made. Further research is needed to confirm the moderating effects that were found, and to enhance the understanding of how and under what circumstances eHealth interventions lead to beneficial effects.

This study provides valuable information on improving the efficacy of future eHealth self-management interventions targeting cancer survivors. Cancer survivors with low to moderate self-efficacy, those with higher personal control, and those with higher health literacy showed larger HRQOL benefits of Oncokompas. Furthermore, Oncokompas is especially effective to improve tumour-specific symptoms among survivors of head and neck cancer and colorectal cancer with higher symptom burden. Targeting these subgroups of survivors might lead to improvements in the intervention effect of eHealth self-management interventions.

REFERENCES

1. 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.

2. 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.

3. 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.

4. Cuthbert CA, Farragher JF, Hemmelgarn BR, Ding Q, McKinnon GP, Cheung WY. Self-management interventions for cancer survivors: A systematic review and evaluation of intervention content and theories. Psychooncology 2019; 28: 2119–40.

5. Kalter J, Verdonck-de Leeuw IM, Sweegers MG, et al. Effects and moderators of psychosocial interventions on quality of life, and emotional and social function in patients with cancer: An individual patient data meta-analysis of 22 RCTs. Psychooncology. 2018; 27: 1150–61.

6. Kim SH, Kim K, Mayer DK. Self-management intervention for adult cancer survivors after treatment: A systematic review and meta-Analysis. Oncol. Nurs. Forum. 2017; 44: 719–28.

7. McAlpine H, Joubert L, Martin-Sanchez F, Merolli M, Drummond KJ. A systematic review of types and efficacy of online interventions for cancer patients. Patient Educ. Couns. 2015; 98: 283–95.

8. Tamagawa R, Garland S, Vaska M, Carlson LE. Who benefits from psychosocial interventions in oncology? A systematic review of psychological moderators of treatment outcome. J Behav Med 2012; 35: 658–73.

9. Krebber AMH, Jansen F, Witte BI, et al. Stepped care targeting psychological distress in head and neck cancer and lung cancer patients: A randomized, controlled trial. Ann Oncol 2016; 27: 1754–60.

10. Singer S, Danker H, Roick J, et al. Effects of stepped psychooncological care on referral to psychosocial services and emotional well-being in cancer patients: A cluster-randomized phase III trial. Psychooncology 2017; 26: 1675–83.

11. 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.

12. van der Hout A, van Uden-Kraan CF, Holtmaat K, et al. Role of eHealth application Oncokompas in supporting self-management of symptoms and health-related quality of life in cancer survivors: a randomised, controlled trial. Lancet Oncol 2020; 21: 80–94.

13. MacKinnon DP. Integrating mediators and moderators in research design. Res Soc Work Pract 2011; 21: 675–81.

14. Kraemer HC, Wilson GT, Fairburn CG, Agras WS. Mediators and moderators of treatment effects in randomized clinical trials. Arch. Gen. Psychiatry. 2002; 59: 877–83.

15. Willems RA, Mesters I, Lechner L, Kanera IM, Bolman CAW. Long-term effectiveness and moderators of a web-based tailored intervention for cancer survivors on social and emotional functioning, depression, and fatigue: randomized controlled trial. J Cancer Surviv 2017; 11: 691–703.

16. Pelikan JM, Ganahl K, Roethlin F. Health literacy as a determinant, mediator and/or moderator of health: empirical models using the European Health Literacy Survey dataset. Glob Health Promot 2018; 25: 57–66.

17. Girgis A. The role of self-management in cancer survivorship care. Lancet Oncol 2020; 21: 8–9.

18. Harrington CB, Hansen JA, Moskowitz M, Todd BL, Feuerstein M. It's not over when it's over: Long-term symptoms in cancer survivors-a systematic review. Int. J. Psychiatry Med. 2010; 40: 163–81.

19. 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.

20. Engel GL. The need for a new medical model: A challenge for biomedicine. Science (80-) 1977; 196: 129–36.

21. Duman-Lubberding S, Van Uden-Kraan CF, Peek N, Cuijpers P, Leemans CR, Verdonck-DeLeeuw IM. An eHealth application in head and neck cancer survivorship care: Health care professionals' perspectives. J Med Internet Res 2015; 17: e235.

22. 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.

23. 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.

24. 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.

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. 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.

27. Pearlin LI, Schooler C. The Structure of Coping: Erratum. J Health Soc Behav 1978; 19: 237.

28. van der Vaart R, Drossaert CHC, Taal E, et al. Validation of the Dutch functional, communicative and critical health literacy scales. Patient Educ Couns 2012; 89: 82–8.

29. Wallston KA, Wallston BS, DeVellis R, et al. Development of the Multidimensional Health Locus of Control (MHLC) Scales. Heal Educ Behav 1978; 6: 160–70.

30. Watson M, Homewood J. Mental Adjustment to Cancer Scale©: Psychometric properties in a large cancer cohort. Psychooncology 2008; 17: 1146–51.

31. 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: 602–6.

32. Jansen F, Witte BI, van Uden-Kraan CF, Braspenning AM, Leemans CR, Verdonck-de Leeuw IM. The need for supportive care among head and neck cancer patients: psychometric assessment of the Dutch version of the Supportive Care Needs Survey Short-Form (SCNS-SF34) and the newly developed head and neck cancer module (SCNS-HNC). Support Care Cancer 2016; 24: 4639–49.

33. Singer S, Araújo C, Arraras JI, et al. Measuring quality of life in patients with head and neck cancer: Update of the EORTC QLQ-H&N Module, Phase III. Head Neck 2015; 37: 1358–67.

34. Kim H, Xie B. Health literacy in the eHealth era: A systematic review of the literature. Patient Educ. Couns. 2017; 100: 1073–82.

35. Zheng M, Jin H, Shi N, et al. The relationship between health literacy and quality of life: A systematic review and meta-analysis. Health Qual. Life Outcomes. 2018; 16: 201.

36. Husson O, Mols F, Fransen MP, Van De Poll-Franse L V., Ezendam NPMM. Low subjective health literacy is associated with adverse health behaviors and worse health-related quality of life among colorectal cancer survivors: Results from the profiles registry. Psychooncology 2015; 24: 478–86.

37. Sardi L, Idri A, Fernández-Alemán JL. A systematic review of gamification in e-Health. J Biomed Inform 2017; 71: 31–48.

38. Zulkosky K. Self-Efficacy: A Concept Analysis. Nurs Forum 2009; 44: 93–102.

39. Namkoong K, Shah D V., Han JY, et al. Expression and reception of treatment information in breast cancer support groups: How health self-efficacy moderates effects on emotional well-being. Patient Educ Couns 2010; 81: S41–7.

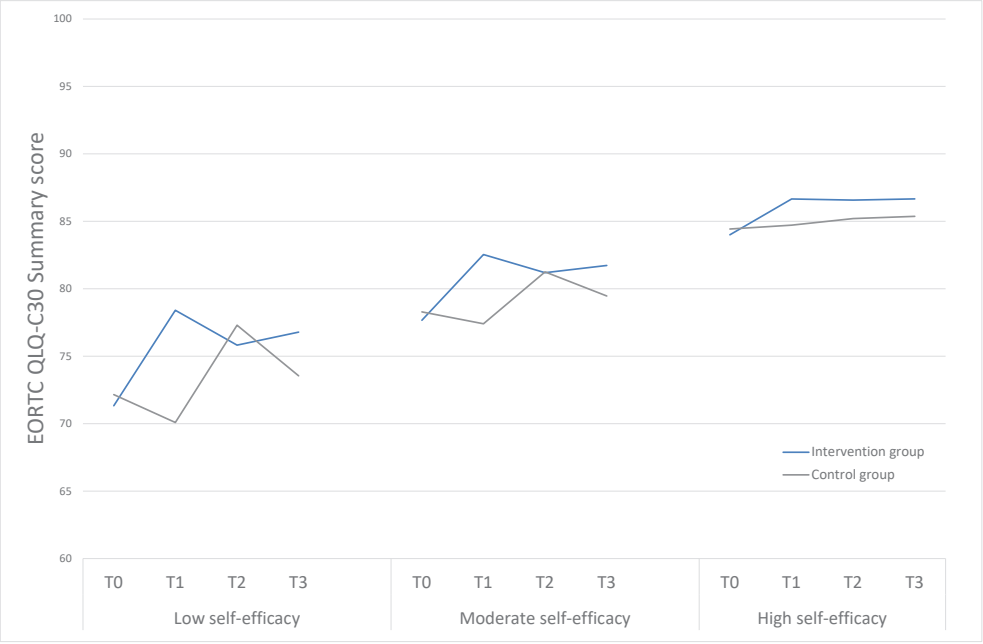
40. Helgeson VS, Lepore SJ, Eton DT. Moderators of the benefits of psychoeducational interventions for men with prostate cancer. Heal Psychol 2006; 25: 348–54.

41. Eklund M, Erlandsson LK, Hagell P. Psychometric properties of a Swedish version of the Pearlin Mastery Scale in people with mental illness and healthy people. Nord J Psychiatry 2012; 66: 380–8.

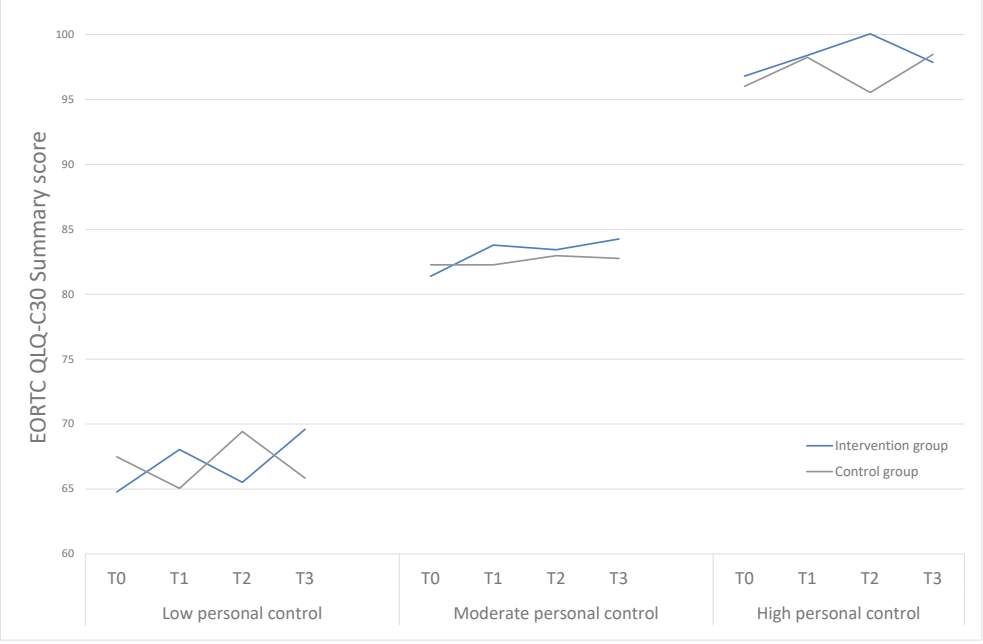
42. Jansen F, Cnossen IC, Eerenstein SEJ, et al. Effectiveness and cost-utility of a guided self-help exercise program for patients treated with total laryngectomy: Protocol of a multi-center randomized controlled trial. BMC Cancer 2016; 16: 580.

43. Gelman A, Hill J, Yajima M. Why We (Usually) Don't Have to Worry About Multiple Comparisons. J Res Educ Eff 2012; 5: 189–211.

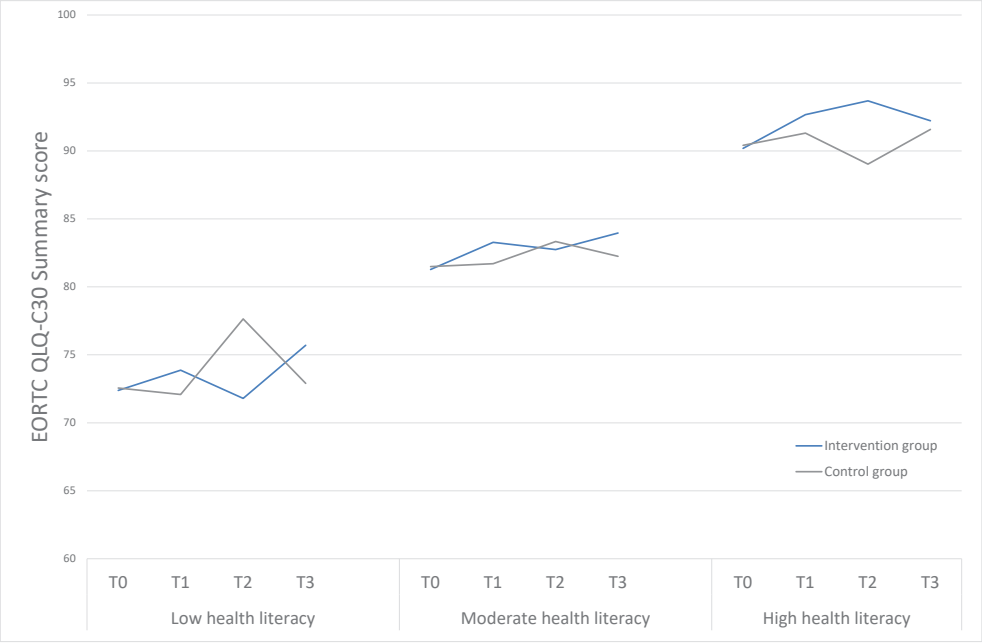
SUPPLEMENTARY MATERIAL



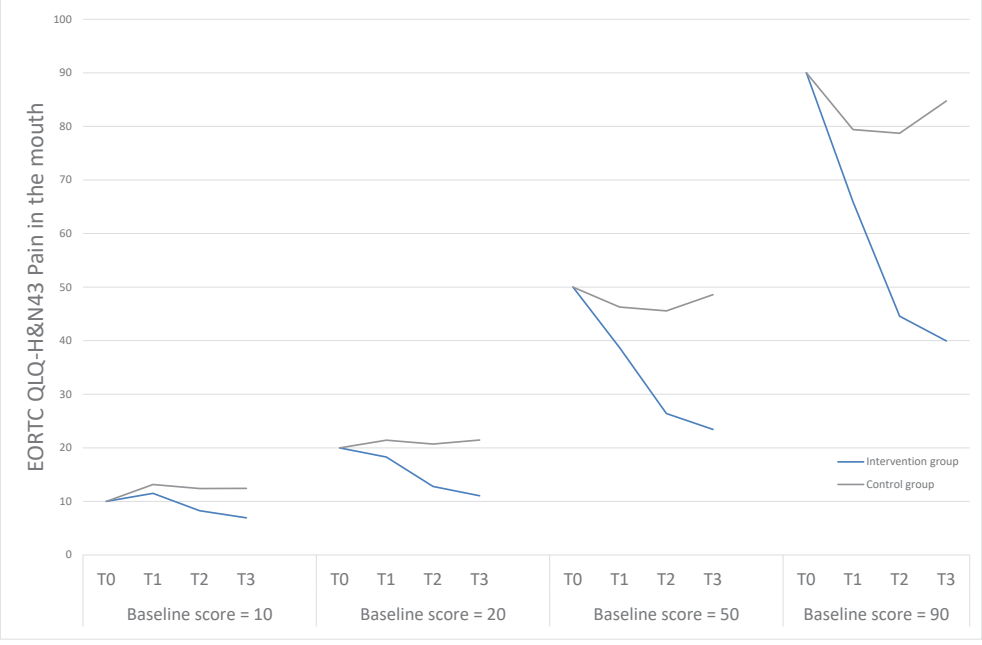
Supplementary Figure 1 – Moderating effect of self-efficacy on HRQOL (higher score indicates better HRQOL)



Supplementary Figure 2 – Moderating effect of personal control on HRQOL (higher score indicates better HRQOL)



Supplementary Figure 3 – Moderating effect of health literacy on HRQOL (higher score indicates better HRQOL)



Supplementary Figure 4 – Moderating effect of baseline score on symptom score pain in the mouth (a higher score indicates higher symptom burden)

5

Cost-utility of an eHealth application 'Oncokompas' that supports cancer survivors in self-management: results of a randomised controlled trial

A. (Anja) van der Hout, F. (Femke) Jansen, C.F. (Nelly) van Uden-Kraan, V.M. (Veerle) Coupé, K. (Karen) Holtmaat, G.A.P. (Grard) Nieuwenhuijzen, J.A. (José) Hardillo, R.J. (Robert) Baatenburg de Jong, N.L. (Nicolette) Tiren-Verbeet, D.W. (Dirkje) Sommeijer, K. (Koen) de Heer, C.G. (Cees) Schaar, R.J.E. (Robert-Jan) Sedee, K. (Koop) Bosscha, M.W.M. (Michiel) van den Brekel, J.F. (Marije) Petersen, M. (Matthijs) Westerman, J. (Jimmie) Honings, R.P. (Robert) Takes, I. (Ilse) Houtenbos, W.T. (Wim) van den Broek, R. (Remco) de Bree, P. (Patricia) Jansen, S.E.J. (Simone) Eerenstein, C.R. (René) Leemans, J.M. (Josée) Zijlstra, P. (Pim) Cuijpers, L.V. (Lonneke) van de Poll-Franse, I.M. (Irma) Verdonck-de Leeuw

Journal of Cancer Survivorship (2020): 1–10

ABSTRACT

Purpose: The eHealth self-management application 'Oncokompas' was developed to support cancer survivors in monitoring health-related quality of life (HRQOL) and symptoms, and obtaining personalized feedback and options for supportive care. The aim of this study was to assess the cost-utility of Oncokompas compared with care as usual (CAU) among cancer survivors.

Methods: Survivors were randomly allocated to the intervention or control group. Direct (non-) medical, indirect non-medical costs, and HRQOL were measured at 3- and 6-month follow-up, using iMTA Medical Consumption and Productivity Costs and the EuroQol-5D questionnaires. Mean cumulative costs and quality-adjusted life-years (QALYs) were compared between both groups.

Results: In total, 625 survivors were randomised into intervention (n = 320) or control group (n = 305). Base case analysis showed that incremental costs from a societal perspective were −€163 (95% CI, −665 to 326), and incremental QALYs were 0.0017 (95% CI, −0.0121 to 0.0155) in the intervention group compared with those in the control group. The probability that, compared with CAU, Oncokompas is more effective was 60%, less costly 73%, and both more effective and less costly 47%. Sensitivity analyses showed that incremental costs vary between −€40 and €69, and incremental QALYs vary between −0.0023 and −0.0057.

Conclusion: Oncokompas is likely to be equally effective on utilities, and not more expensive than CAU, and will therefore contribute to sustainable cancer survivorship care in a (cost-)effective manner.

Implications for cancer survivors: Oncokompas seems to improve HRQOL and reduces the burden of several tumour-specific symptoms, while costs from a societal perspective are similar to CAU.

INTRODUCTION

Cancer survivorship care includes physical rehabilitation, psychosocial care, lifestyle interventions, existential issues, and the (self-)management of survivors' health and healthcare. It is, however, challenging to organise cancer survivorship care, because it is difficult to align individual needs and preferences with existing care options, and also to make cancer survivorship care available at acceptable costs.[1,2]

Data from patient reported outcome measures (PROMs) can be used for optimal referral to supportive care in clinical practice. Behavioural intervention technologies (BITs) are currently often used to collect and process PROM data.[3] Also, eHealth self-management applications can support cancer survivors to self-manage their symptoms and health- related quality of life (HRQOL).[4–8] However, not much is known yet on the cost-effectiveness or cost-utility of eHealth self-management applications and BITs among cancer survivors.

We developed Oncokompas, a fully automated BIT that supports cancer survivors by monitoring their HRQOL and symptoms; obtaining tailored feedback and advice on their physical, psychological and social functioning, lifestyle, and existential questions; and receiving a personalized overview of recommended supportive care services.[9–13] Oncokompas can be used by cancer survivors independently from a healthcare provider and follows a tailored care approach: all cancer survivors receive tailored information, advice, and tips; survivors with minor symptoms are referred to self-help interventions while survivors with major symptoms are primarily referred to professional care. Recently, we showed that Oncokompas has small, but significant effects on improving HRQOL and reducing the burden of several tumour-specific symptoms among cancer survivors.[14]

During studies on the feasibility and implementation of Oncokompas,[10,13,15] we observed that an important barrier among healthcare professionals and healthcare insurance companies to adopt and implement eHealth applications like Oncokompas was related to the uncertainty about costs and reimbursement. Also, it is important to know whether these applications may have a positive influence on costs from a societal perspective, including for example costs of absence from work, and costs of informal care. The aim of the present study was to evaluate the cost-utility of Oncokompas compared with care as usual (CAU) among cancer survivors, from a societal and healthcare perspective.

METHODS

Study design and participants

A randomised controlled trial was carried out among survivors of head and neck cancer, colorectal cancer, breast cancer, and lymphoma (including high- and low-grade non-Hodgkin lymphoma and Hodgkin lymphoma). These tumour types were chosen to ensure variability regarding age, sex, prevalent and less prevalent tumour types, solid and non-solid tumour types, cancer- and treatment-related symptoms, and the need for various types of supportive care. Other inclusion criteria were the following: age ≥18 years (no upper limit) and 3 months to 5 years after treatment with curative intent (all treatment modalities). Survivors who were still receiving endocrine therapy or immunotherapy, or had a wait-and-see regimen, were included 3 months after their previous treatment or diagnosis, respectively. Exclusion criteria were the following: no access 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.[14,16]

The study protocol was approved by the Medical Ethics Committee of the VU University Medical Center (2015.523), published previously,[16] and registered in the Netherlands Trial Register (NTR5774). All participants provided (online) written informed consent.

Randomisation and masking

Cancer survivors who gave their informed consent were randomly allocated to the intervention group (direct access to Oncokompas) or CAU wait-list control group (access to Oncokompas after 6 months), in a 1:1 ratio. Randomisation was stratified by tumour type, and blocks with a length of 68 were used. Due to the nature of the intervention, participants could not be blinded for the allocated arm.

Procedures

Participants were recruited through The Netherlands Cancer Registry (NCR) in 14 hospitals across The Netherlands and invited by their (former) treating physician. Data collection was performed using the Patient Reported Outcomes Following Initial Treatment and Long term Evaluation of Survivorship (PROFILES) registry.[17]

Intervention

Oncokompas supports cancer survivors in self-management, by monitoring (cancer-generic and tumour-specific) symptoms and HRQOL, providing feedback and information on their scores and a personalized overview of supportive care options, with the aim to reduce symptom burden and improve HRQOL.[10,12,16] In three steps, (1) Measure, (2) Learn, and (3) Act, users are guided through the application. In the component 'Measure', patient reported outcome measures (PROMs) are completed on several domains, in 'Learn', data from the PROMs are processed in real-time, and with algorithms linked to tailored information and advice. In 'Act', an overview of healthcare options is given, based on PROMs, survivors' expressed preferences, and the severity of symptoms. In case of elevated well-being risks, self-help options are offered, and in case of seriously elevated well-being risks, professional healthcare options are offered. Oncokompas comprises generic modules for all cancer survivors, targeting physical, psychological, and social functioning, lifestyle, and existential questions. Furthermore, tumour-specific modules are available for cancer survivors diagnosed with head and neck cancer, colorectal cancer, breast cancer, and (non-)Hodgkin lymphoma, covering problems related to the specific type of cancer. A cancer survivor can choose which topics he or she wants to address. Oncokompas was developed according to a participatory design approach, including all relevant stakeholders in each step of the development.[9,12] A detailed description of Oncokompas can be found elsewhere.[10,12,14,16]

Outcomes

The economic evaluation was conducted from a societal perspective, including direct medical costs (costs of healthcare resource use and medication), direct non-medical costs (traveling to and parking at healthcare services, costs of informal care, support groups), indirect non-medical costs (costs due to absence from paid work or loss of productivity from paid work), and intervention costs. All outcome measures were collected at baseline (time of inclusion), and at a 3-month and 6-month follow-up assessment. Since the follow-up of the study was 6 months, neither costs nor effects were discounted.

Direct medical and direct non-medical costs were measured with the Institute for Medical Technology Assessment (iMTA) Medical Consumption Questionnaire (iMCQ).[18] The iMCQ measures the use of healthcare (e.g., number of visits to medical specialists, hospital admissions), other facilities (e.g., hours of informal care use, participation in support groups), and medication (e.g., painkillers, antihypertensive medication, endocrine therapy) in the past 3 months. Direct medical and direct non-

medical costs were calculated as units of resource use multiplied by the integral cost price per unit.[19,20] Direct non-medical costs of traveling to healthcare services were calculated as units of resource use multiplied by the average distance to the location, multiplied by the price per kilometre. All prices were adjusted to 2017 prices using the consumer price index.

Indirect non-medical costs were measured with the iMTA Productivity Costs Questionnaire (iPCQ).[21] Productivity losses through absence from paid work (absenteeism) and through the reduced quality of performed paid work (presenteeism) were measured in the last 3 months. Productivity losses due to absenteeism were calculated as the number of days absent from work, and presenteeism as the number of days with less productivity multiplied by the estimated amount of lost quality of performed work on an 11-point scale. Absenteeism and presenteeism costs were calculated as productivity losses multiplied by the price of productivity costs per hour of paid work, using the friction cost approach for absenteeism, with a friction period of 85 days.[20] The price of one hour paid work was €36.38, irrespective of sex and age.

Health-related quality of life was measured with the EuroQol-5 Dimension (EQ-5D). The utility score was obtained using the Dutch index tariff.[22]

Intervention costs of Oncokompas were calculated using a top-down approach. Costs for running Oncokompas (ICT, product and data management, content updating, implementation, and marketing) are estimated at €450,000 annually. When reaching 18,000 cancer survivors per year (16% of all newly diagnosed cancer patients in the Netherlands),[14,23] the intervention costs are estimated at €25 per user.

Statistical analysis

Analyses were performed using SPSS version 25 (IBM, Armonk, NY) and STATA version 14 (STATA, College Station, TX). Descriptive statistics, Chi-square tests, and independent samples t tests were used to describe and compare baseline characteristics between the intervention and control group. To provide information on types of costs included in the analyses and their relative importance at each time point, data of complete cases (participants who completed baseline and both follow-up measurements) were used.

To test the cost-utility of Oncokompas compared with CAU, a base case intention-to-treat cost-utility analysis was performed, including all participants, with imputed data for missing time points, and estimated intervention costs of €25 per Oncokompas user. The robustness of this finding was tested by four additional sensitivity analyses in which the base case analysis:

1. Was adjusted for baseline EQ-5D scores and baseline total costs,
2. Included varying intervention costs of Oncokompas (range, €15 to €100 per user),
3. Was performed among survivors with complete data at all time-points,
4. Was performed from a healthcare perspective, including only direct medical costs and intervention costs.

In case data was missing on item level (e.g. a patient reported to have visited a general practitioner, but did not report the number of visits), assumptions were made based on means per allocation group and time point. In case data was missing on questionnaire level, missing data was imputed as total costs or utility score per time point per allocation group, using multiple imputations (predictive mean matching) by chained equations. Backward multivariable linear and logistic regression analyses were performed to investigate which variables (socio-demographic, clinical, and psychosocial variables at baseline) were associated with missing data, total costs, or utility scores. A description of these variables is listed in the Appendix. Variables that were found to be associated with missing data (EORTC QLQ-C30 summary score[24]), total costs (age, comorbidities, time since diagnosis, EORTC QLQ-C30 summary score), and utility scores (age, comorbidities, marital status, tumour stage, positive adjustment (subscale of the Mental Adjustment to Cancer (MAC) scale[25]), and employment status), and variables that differed statistically significant between intervention and control group at baseline (positive adjustment (MAC)) were included in the multiple imputation model. Ten imputed datasets were created and analysed separately, and the results of the 10 analyses were pooled, using Rubin's (1987) rules.

The total cumulative costs per cancer survivor were calculated by summing costs measured with the iMCQ and iPCQ at 3- and 6-month follow-up and intervention costs in the intervention group. Quality-adjusted life years (QALYs) were calculated as the EQ-5D utility scores per time point, multiplied by the corresponding time period (i.e. 3 months).

To obtain costs per QALY gained, an incremental cost-utility ratio (ICUR) was calculated as the incremental costs divided by incremental effects, with the following formula: (mean $costs_{intervention}$ – mean $costs_{control}$) / (mean $QALYs_{intervention}$ – mean $QALYs_{control}$). Uncertainty around the ICUR was assessed using bootstrapping with 5000 replications and was projected on a cost-utility plane.

RESULTS

In 14 participating hospitals throughout the Netherlands, 2953 cancer survivors were invited to participate between October 12, 2016, and May 24, 2018. In total, 625 (21%) survivors consented to participate, completed the baseline questionnaire at study inclusion, and were randomly allocated to the intervention (n = 320) or control (n = 305) group. Of them, respectively 205 (64%) and 240 (79%) completed both follow-up questionnaires and were complete cases. **Figure 1** shows the Consolidated Standard of Reporting Trials (CONSORT) diagram of the study inclusion. There were no statistically significant differences in baseline socio-demographic and clinical characteristics between the intervention and control groups (**Table 1**).

The mean EQ-5D score of survivors at baseline was 0.89 (sd 0.15) in the intervention group and 0.87 (sd 0.17) in the control group (p = 0.11). The mean total costs in the previous 3 months at baseline in the intervention group were €1,013 (sd 1760), compared with €1,158 (sd 1936) in the control group (p = 0.33). The mean costs for survivors with complete data per time point per group are presented in **Supplementary Table 1**.

Cost-utility analyses

The results of the cost-utility analyses are shown in **Table 2** and **Figure 2**. In the base case analysis, QALYs gained were similar in the intervention group compared with those in the control group (incremental effects, 0.0017; 95% CI, −0.0121 to 0.0155). The mean total costs in the intervention group were slightly, but non-significantly, lower than the mean total costs in the control group (incremental costs, −€163; 95% CI, −€665 to €326). Of the bootstrapped cost-utility pairs, 47% fell into the southeast quadrant, indicating that Oncokompas was more effective and less costly compared with CAU. The probability that the cumulative QALYs were higher in the intervention group compared with those in the control group was 60%, and the probability that Oncokompas was less costly compared with CAU was 73% (**Figure 2**).

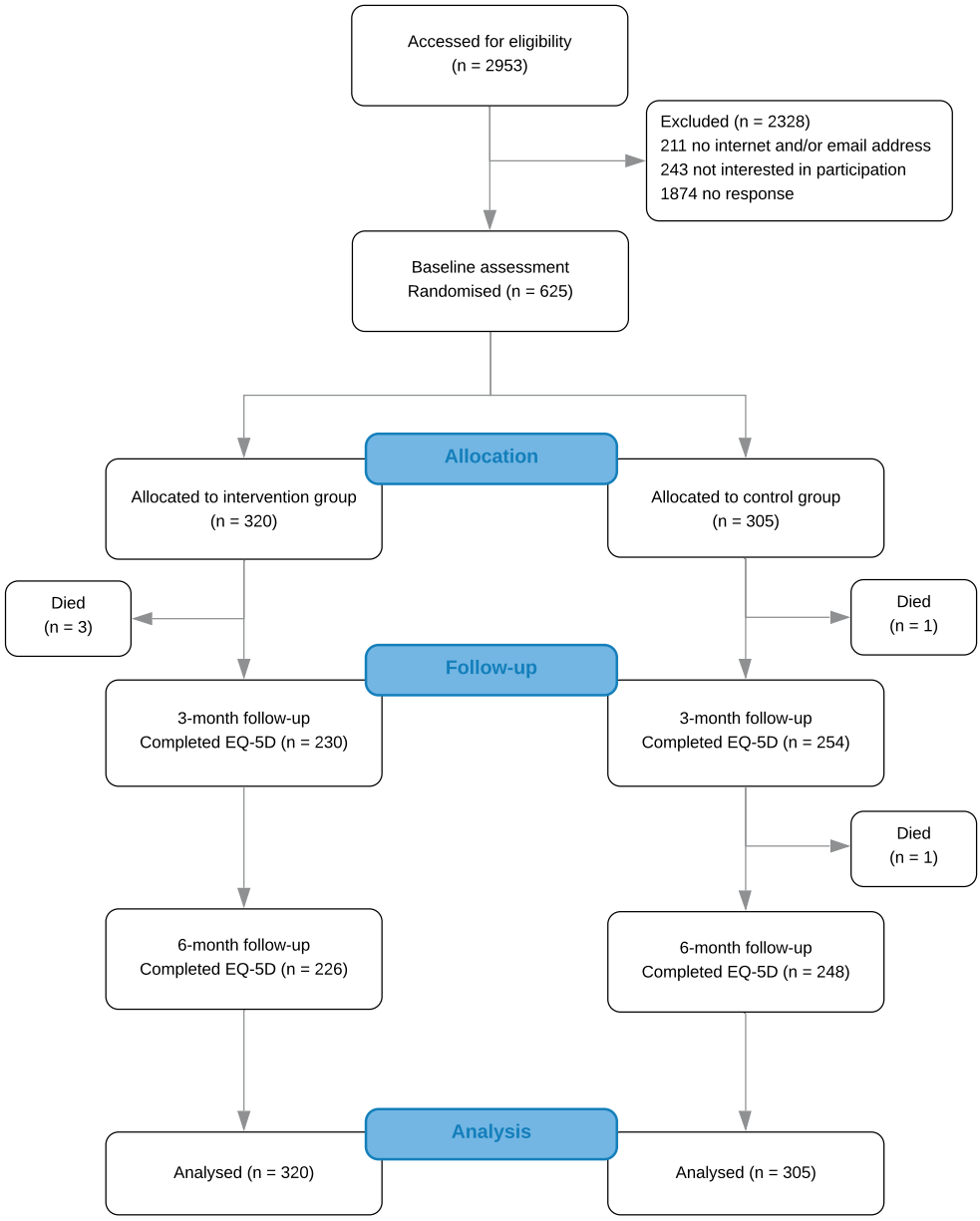


Figure 1 – CONSORT flow diagram

Table 1 – Baseline characteristics

Characteristic	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%)
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%)
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 (16–41)	29.0 (17–41)
3 – <12 months	39 (12%)	38 (13%)
12 – <24 months	104 (33%)	85 (28%)
24 – 60 months	177 (55%)	182 (60%)
Treatment (n, %)		
None or single treatment	137 (43%)	124 (41%)
Multimodal treatment	183 (57%)	181 (59%)
EORTC QLQ-C30 summary score	85.3 (14.9)	85.4 (13.6)

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

To assess the robustness of this finding, four additional sensitivity analyses were performed as shown in **Table 2**.

1. When the base case analysis was corrected for baseline EQ-5D utility scores and costs, the probability that in the intervention group QALYs were higher was 13% (incremental effect, −0.0057), and the probability that costs were lower was 51% (incremental costs, €2), compared with the control group. Because of these results, the subsequent sensitivity analyses were also corrected for baseline EQ-5D and costs.

2. Analyses with intervention costs of €15 and €100 showed that the probability that in the intervention group the QALYs were higher was 13% (incremental effects, −0.0057), and the probability that costs were lower were 52% and 39% (incremental costs, −€8 and €77) respectively, compared with the control group.

3. Analyses on the complete cases showed that the probability that in the intervention group QALYs were higher was 30% (incremental effect, −0.0023), and the probability that costs were lower was 41% (incremental costs, €68), compared with the control group.

4. Analyses with only direct medical costs taken into account showed that the probability that in the intervention group the QALYs were higher was 20% (incremental effect, −0.0043), and the probability that costs were lower was 57% (incremental costs, −€40), compared with the control group.

DISCUSSION

This study investigated the cost-utility of a fully automated BIT 'Oncokompas' among cancer survivors, compared with CAU. In the base case analysis, QALYs were similar and costs were non-significantly lower in the intervention group (−€163), compared with those in the control group. When the base case analysis was corrected for baseline EQ-5D utility scores and costs, QALYs were non-significantly lower in the intervention group and costs were similar compared with those in the control group.

The finding that Oncokompas is more or less equally effective in terms of utilities and costs as CAU confirms our earlier research on the efficacy of Oncokompas.[14] That study showed that Oncokompas has a small positive effect on HRQOL, when measured with a cancer-generic questionnaire (EORTC

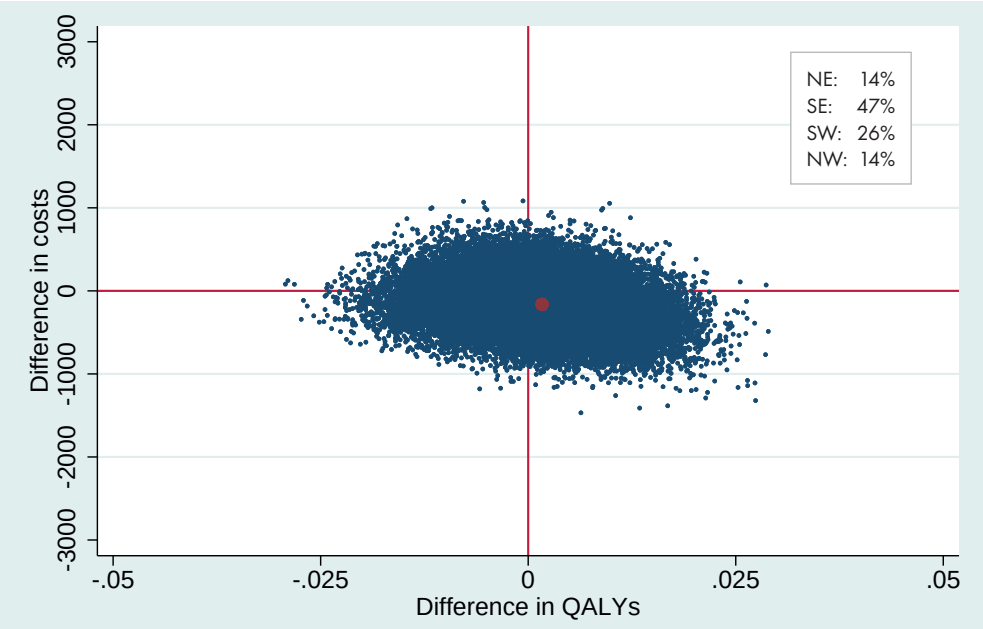


Figure 2 – Cost-utility plane of the base case analysis

QALYs, quality-adjusted life years; NE, north-east; SE, south-east; SW, south-west; NW, north-west quadrant. The percentages indicate the percentage of bootstrap replications in a certain quadrant

QLQ-C30). However, that study also showed that the effects of Oncokompas were also found on tumour-specific symptoms (measured with EORTC tumour-specific modules). In the present study, QALYs are based on the generic EQ-5D, which does not take cancer-generic and tumour-specific symptoms into account. Also, ceiling effects were found in the EQ-5D utility scores, as many participants had a high or the maximum EQ-5D score at baseline, and the group performed relatively well at baseline on other outcome measures. In future research, the EORTC QLU-C10D can be used for measuring utilities, of which data can be derived from the QLQ-C30.[26]

The previous study also showed that for some tumour-specific symptoms, beneficial effects of Oncokompas occurred at 3- or even 6-month follow-up, and not directly post-intervention.[14] It may be that survivors need time to follow-up on the provided advice and use the preferred interventions or supportive care options, before seeing improvements in HRQOL. The possible subsequent cost-saving effect as a result of the improvements is expected to take even longer to become visible. Since the follow-up period of the study was only 6 months, it is possible that this long-term cost-saving effect was not captured within the follow-up period in this study. More research is therefore needed on

Table 2 – Results of the cost-utility analyses; base case and sensitivity analyses

Analysis		**QALYs**		**Costs (€)**		**Incremental effects**		**Incremental costs**	
Group	n	Mean	SEM	Mean	SEM	QALY	95% CI	€	95% CI
Base case						0.0017	−0.0121 to 0.0155	−163	−665 to 326
Intervention	320	0.4452	0.0052	1,935	224				
Control	305	0.4435	0.0045	2,098	191				
Sensitivity analyses [1]									
Base case with correction for baseline						−0.0057	−0.0161 to 0.0048	2	−441 to 443
Intervention	320	NA	NA	NA	NA				
Control	305	NA	NA	NA	NA				
Intervention costs									
€ 15						−0.0057	−0.0161 to 0.0048	−8	−451 to 433
Intervention	320	NA	NA	NA	NA				
Control	305	NA	NA	NA	NA				
€ 100						−0.0057	−0.0161 to 0.0048	77	−366 to 518
Intervention	320	NA	NA	NA	NA				
Control	305	NA	NA	NA	NA				
Complete cases						−0.0023	−0.0112 to 0.0054	68	−452 to 602
Intervention	205	NA	NA	NA	NA				
Control	240	NA	NA	NA	NA				
Healthcare perspective (direct medical costs)						−0.0043	−0.0148 to 0.0061	−40	−344 to 241
Intervention	320	NA	NA	NA	NA				
Control	305	NA	NA	NA	NA				

[1] *All sensitivity analyses were corrected for baseline costs and EQ-5D utility score*

long-term effects of BITs such as Oncokompas, for instance by performing a budget impact analysis on real-world data, when Oncokompas has been implemented and scaled up in clinical practice. Together with the results on the efficacy of Oncokompas[14] and the fact that Internet skills of cancer survivors are expected to improve over time and eHealth will be more commonly used, it is expected that long-term cost-utility of BITs such as Oncokompas will be even more positive. It is expected that the effects related to the use of the proposed healthcare options in Oncokompas will positively influence utilities (i.e. better quality of life and higher QALYs), as well as reduce costs (as a result of (earlier) use of healthcare options or applying self-help advice, more expensive treatment and productivity losses can be prevented or reduced). Performing these analyses on real-world data, it is possible to measure over a longer period and include all survivors, which improves the generalizability of the results. Furthermore, implementation and upscaling will lead to more users, which leads to less intervention costs per user, which improves the cost-utility in favour of Oncokompas.

With an increasing number of cancer survivors, the costs of cancer survivorship healthcare are growing, together with an increasing healthcare workforce shortage.[1,27] The present study showed that from a healthcare perspective (taking only direct medical costs into account), costs were not significantly lower (−€40) in the intervention group. It is promising that the tailored approach in Oncokompas does not seem to lead to increased medical costs: users are encouraged to apply personalized tips and information provided within Oncokompas and use self-help interventions first, before turning to professional care. This may prevent worsening of symptoms and may be cost-saving in the long-term.

Economic evaluations of eHealth interventions among patients with chronic diseases are scarce and mostly performed among patients with diabetes and cardiovascular disease.[28,29] To the best of our knowledge, this study was the first economic evaluation of an eHealth intervention among cancer survivors. A strength of this study is that we performed the cost-utility analysis from a societal as well as a healthcare perspective.

Potential limitations of this study were that several assumptions were made regarding missing data on healthcare resource use. Missing data was replaced based on assumptions or imputed using multiple imputation techniques. This might not reflect reality, but since we made similar assumptions and imputations in both groups, it is not expected that this has influenced our findings. Also, since the cost prizes of unit resource and productivity costs in this study are based on the Dutch tariff, the results

might not be generalizable to other countries. The Dutch healthcare system and reimbursement of care, and thereby the low barrier to seek care, might also not be representative of other countries. Furthermore, the attrition rate was higher in the intervention group than in the control group, and there were also more complete cases in the control group than in the intervention group. This might be explained by the fact that participants in the wait-list control group obtain access to Oncokompas after the last follow-up measurement, which might have been an extra motivation to complete the follow-up assessments. We cannot be sure whether this has under- or overestimated the results, but since the results from the sensitivity analysis with only taken into account the complete cases did not differ much from the sensitivity analysis with all participants, it is expected that this influence is limited. Finally, the participation rate of the randomised controlled trial was 21%, and participants were mostly long-term survivors and had relatively good baseline scores, which might limit the generalizability of the results. Further research is needed to see whether these results can be confirmed among representative samples of cancer survivors, also diagnosed with other tumour types.

In conclusion, results indicate that a fully automated BIT such as Oncokompas is at least as effective as usual cancer survivorship care, and not more expensive. Implementation and upscaling of Oncokompas may help to improve cancer survivorship care in a (cost-)effective manner.

REFERENCES

1. Mayer DK, Alfano CM. Personalized Risk-Stratified Cancer Follow-Up Care: Its Potential for Healthier Survivors, Happier Clinicians, and Lower Costs. J. Natl. Cancer Inst. 2019; 111: 442–8.

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. 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.

7. 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.

8. Kim SH, Kim K, Mayer DK. Self-management intervention for adult cancer survivors after treatment: A systematic review and meta-Analysis. Oncol. Nurs. Forum. 2017; 44: 719–28.

9. 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.

10. 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.

11. Duman-Lubberding S, van Uden-Kraan CF, Jansen F, et al. Durable usage of patient-reported outcome measures in clinical practice to monitor health-related quality of life in head and neck cancer patients. Support Care Cancer 2017; 25: 3775–83.

12. Duman-Lubberding S, Van Uden-Kraan CF, Peek N, Cuijpers P, Leemans CR, Verdonck-DeLeeuw IM. An eHealth application in head and neck cancer survivorship care: Health care professionals' perspectives. J Med Internet Res 2015; 17: e235.

13. 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 (Madr) 2018; 57: 924–34.

14. van der Hout A, van Uden-Kraan CF, Holtmaat K, et al. Role of eHealth application Oncokompas in supporting self-management of symptoms and health-related quality of life in cancer survivors: a randomised, controlled trial. Lancet Oncol 2020; 21: 80–94.

15. de Wit LM, 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.

16. 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.

17. van De Poll-Franse L V., 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.

18. Bouwmans C, Hakkaart-van Roijen L, Koopmanschap M, Krol M, Severens H, Brouwer W. Handleiding iMTA Medical Cost Questionnaire (iMCQ). 2013.

19. Kanters TA, Bouwmans CAM, Van Der Linden N, Tan SS, Hakkaart-van Roijen L. Update of the Dutch manual for costing studies in health care. PLoS One 2017; 12: e0187477.

20. Hakkaart-van Roijen L, van der Linden N, Bouwmans C, Kanters T, Tan S. Costing manual: Methodology of costing research and reference prices for economic evaluations in healthcare [in Dutch: Kostenhandleiding: Methodologie van kostenonderzoek en referentieprijzen voor economische evaluaties in de gezondheidszorg]. 2015.

21. Bouwmans C, Krol M, Severens H, Koopmanschap M, Brouwer W, Roijen LH Van. The iMTA Productivity Cost Questionnaire: A Standardized Instrument for Measuring and Valuing Health-Related Productivity Losses. Value Heal 2015; 18: 753–8.

22. Lamers LM, Stalmeier PFM, McDonnell J, Krabbe PFM, Busschbach JJ Van. Measuring the quality of life in economic evaluations: the Dutch EQ-5D tariff. Ned Tijdschr Geneeskd 2005; 149: 5.

23. Integraal Kankercentrum Nederland (IKNL). Cijfers over kanker. https://www.cijfersoverkanker.nl (accessed May 22, 2020).

24. 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.

25. Watson M, Homewood J. Mental Adjustment to Cancer Scale©: Psychometric properties in a large cancer cohort. Psychooncology 2008; 17: 1146–51.

26. King MT, Costa DSJ, Aaronson NK, et al. QLU-C10D: a health state classification system for a multi-attribute utility measure based on the EORTC QLQ-C30. Qual Life Res 2016; 25: 625–36.

27. Mariotto AB, Robin Yabroff K, Shao Y, Feuer EJ, Brown ML. Projections of the cost of cancer care in the United States: 2010-2020. J Natl Cancer Inst 2011; 103: 117–28.

28. Sanyal C, Stolee P, Juzwishin D, Husereau D. Economic evaluations of eHealth technologies: A systematic review. PLoS One. 2018; 13: e0198112.

29. Michaud TL, Zhou J, McCarthy MA, Siahpush M, Su D. Costs of home-based telemedicine programs: a systematic review. Int J Technol Assess Health Care 2018; 34: 400–9.

SUPPLEMENTARY MATERIAL

Socio-demographic and clinical characteristics

Socio-demographic and clinical characteristics were measured with a study-specific questionnaire (marital status, employment status, comorbidities), or extracted from the Netherlands Cancer Registry (NCR) (age, tumour stage, time since cancer diagnosis).

Health-related quality of life

The summary score (SumSC) of the EORTC QLQ-C30 is based on the five functional scales (physical, cognitive, emotional, social, and role functioning), three symptom scales (fatigue and nausea/vomiting, and pain), and five single items (dyspnoea, insomnia, appetite loss, constipation, diarrhoea) of the QLQC30. The SumSC ranges from 0 to 100. A higher SumSC score represents better HRQOL.[24]

Mental adjustment to cancer

The Mental Adjustment to Cancer (MAC) scale comprises two summary subscales: summary positive adjustment (SPA) and summary negative adjustment (SNA). Scores range from 17 to 68 on SPA, with a higher score indicating more positive adjustment, and 16 to 64 on SNA, a higher score indicating more negative adjustment.[25]

Supplementary Table 1 – Frequencies, mean costs (sd) (€) per time point for complete cases

		Baseline (T0)						3-months follow-up (T2)						6-months follow-up (T3)					
		Intervention (n = 205)			Control (n = 240)			Intervention (n = 205)			Control (n = 240)			Intervention (n = 205)			Control (n = 240)		
	Price*	%	Mean	SD	%	Mean	SD	%	Mean	SD	%	Mean	SD	%	Mean	SD	%	Mean	SD
Direct medical costs			*639*	*1,215*		*816*	*1,54*		*510*	*803*		*625*	*1,135*		*600*	*1,407*		*625*	*1,688*
General practitioner																			
Phone	17	39%	11	17	32%	9	17	34%	9	26	34%	10	18	26%	7	14	38%	10	17
Home visit	51	2%	2	18	4%	4	26	1%	0	4	3%	2	19	1%	0	5	3%	2	14
Consultation	34	53%	31	43	49%	31	44	46%	27	37	49%	33	69	40%	27	47	43%	30	49
Nurse consultation	17	2%	0	5	0%	0	4	2%	1	6	1%	0	4	0%	-	-	1%	0	3
Company doctor	70	7%	5	21	6%	6	27	4%	3	16	6%	6	25	4%	3	18	5%	5	24
Social worker	67	3%	4	26	3%	3	15	2%	4	36	3%	4	28	3%	5	27	3%	4	28
Physiotherapist	34	24%	74	187	36%	134	268	27%	81	182	34%	127	255	27%	70	170	30%	95	206
Ergotherapist	34	3%	3	25	2%	2	17	1%	0	3	0%	-	-	1%	0	2	0%	0	2
Dietitian	30	6%	3	14	9%	4	16	5%	2	11	7%	6	31	6%	2	11	6%	4	15
Speech therapist	31	2%	2	26	2%	2	17	2%	3	30	3%	3	37	1%	3	43	2%	2	14
Oral hygienist	26	25%	7	14	24%	7	15	23%	6	12	23%	7	15	22%	6	12	27%	8	18
Psychologist/ psychiatrist [a]	96-126	4%	17	115	6%	17	84	3%	19	135	4%	13	91	6%	15	71	5%	21	144
Medical specialist																			
General hospital	82	55%	99	181	60%	95	123	43%	69	101	46%	80	185	46%	71	113	46%	77	157
Academic hospital	167	36%	99	217	30%	93	264	31%	72	138	23%	63	161	25%	70	149	23%	50	108

Supplementary Table 1 – continued

		Baseline (T0)						3-months follow-up (T2)						6-months follow-up (T3)					
		Intervention (n = 205)			Control (n = 240)			Intervention (n = 205)			Control (n = 240)			Intervention (n = 205)			Control (n = 240)		
	Price*	%	Mean	SD	%	Mean	SD	%	Mean	SD	%	Mean	SD	%	Mean	SD	%	Mean	SD
Spiritual counsellor	132	2%	5	41	1%	4	37	1%	1	9	2%	5	46	2%	2	16	3%	6	40
Alternative treatment	62	4%	11	69	5%	10	50	8%	9	38	7%	22	140	6%	10	58	4%	9	47
Emergency care visit	265	4%	16	77	7%	23	89	3%	8	45	4%	11	53	3%	12	66	4%	10	50
Ambulance to hospital	527	2%	10	73	3%	13	82	1%	3	37	1%	4	48	2%	8	63	1%	4	48
Day treatment																			
Hospital	310	7%	77	489	6%	81	579	7%	65	288	4%	22	123	9%	82	561	5%	56	433
Care center [b]	69-313	1%	3	44	0%	29	444	1%	3	48	0%	-	-	0%	-	-	0%	-	-
Admission																			
Hospital	487	4%	105	635	7%	162	765	5%	86	547	5%	112	734	7%	121	649	4%	73	661
Care center [b]	172-471	0%	-	-	0%	-	-	0%	-	-	0%	13	199	1%	39	559	0%	75	1,157
Personal care	51	1%	0	7	0%	3	43	0%	-	-	1%	5	58	0%	-	-	1%	11	138
Nursing care	75	1%	3	38	2%	17	194	0%	-	-	1%	13	189	0%	-	-	1%	13	189
Medication	0-38	66%	51	163	70%	65	206	66%	39	66	69%	63	188	65%	46	162	73%	58	183
Direct non-medical costs			*204*	*782*		*235*	*597*		*139*	*490*		*252*	*857*		*146*	*434*		*227*	*609*
Transport [c]	0-9	-	18	26	-	19	27	-	14	18	-	16	23	-	14	19	-	15	26
Home care	20	2%	5	44	3%	16	123	2%	8	68	2%	5	48	2%	10	73	2%	9	91
Informal care	15	10%	117	714	12%	80	338	11%	71	376	14%	118	747	13%	79	373	12%	75	374
Supportive care [d]	15-65	8%	64	276	13%	120	427	7%	46	242	10%	113	426	6%	43	208	12%	128	468

Supplementary Table 1 – continued

			Baseline (T0)					3-months follow-up (T2)					6-months follow-up (T3)				
			Intervention (n = 205)			Control (n = 240)			Intervention (n = 205)			Control (n = 240)			Intervention (n = 205)			Control (n = 240)	
	Price*	%	Mean	SD	%	Mean	SD	%	Mean	SD	%	Mean	SD	%	Mean	SD	%	Mean	SD
Indirect non-medical costs			*124*	*708*		*160*	*837*		*193*	*1,397*		*251*	*1,385*		*240*	*1,526*		*95*	*518*
Absenteeism	36/hour	*7%*	114	*705*	11%	147	814	*5%*	187	1,378	9%	241	1,369	*5%*	235	1,523	*7%*	88	*507*
Presenteeism	36/hour	10%	9	46	11%	14	92	6%	6	37	10%	10	43	8%	4	21	10%	*7*	36
Total costs			***967***	***1,778***		***1,211***	***2,021***		***842***	***1,711***		***1,128***	***2,058***		***986***	***2,221***		***947***	***2,002***

** Reference price per unit (€) %: Percentage of participants that used the care at least once.*

[a] Psychologic or psychiatric help = psychological help at a private practice (€96), mental health service (out-patient) (€100), addiction clinic (€126), and/or psychologic help in hospital (€126) [b] Care center = residential center (treatment: €69, admission: €172), rehabilitation center (treatment: €313, admission: €471) and/or psychiatric institution (treatment: €173, admission: €309); [c] Transport = transportation and parking costs: €0.21/km + €3.07 parking costs per visit; [d] Self-management interventions = help with coping (€65), support groups (€65), sport rehabilitation programs (€65), body image care (€15) and/or online self-help programs (€15)

Reasons for not reaching or using web-based self-management applications, and the use and evaluation of Oncokompas among cancer survivors

A. (Anja) van der Hout, C.F. (Nelly) van Uden-Kraan, K. (Karen) Holtmaat, F. (Femke) Jansen, B.I. (Birgit) Lissenberg-Witte, G.A.P. (Grard) Nieuwenhuijzen, J.A. (José) Hardillo, R.J. (Robert) Baatenburg de Jong, N.L. (Nicolette) Tiren-Verbeet, D.W. (Dirkje) Sommeijer, K. (Koen) de Heer, C.G. (Cees) Schaar, R.J.E. (Robert-Jan) Sedee, K. (Koop) Bosscha, M.W.M. (Michiel) van den Brekel, J.F. (Marije) Petersen, M. (Matthijs) Westerman, J. (Jimmie) Honings, R.P. (Robert) Takes, I. (Ilse) Houtenbos, W.T. (Wim) van den Broek, R. (Remco) de Bree, P. (Patricia) Jansen, S.E.J. (Simone) Eerenstein, C.R. (René) Leemans, J.M. (Josée) Zijlstra, P. (Pim) Cuijpers, L.V. (Lonneke) van de Poll-Franse, I.M. (Irma) Verdonck-de Leeuw

Submitted

ABSTRACT

Introduction: The web-based self-management application Oncokompas was developed to support cancer survivors to monitor health-related quality of life and symptoms (Measure) and to provide tailored information (Learn) and supportive care options (Act). Reach was seen as the eligibility for Oncokompas (access to internet and e-mail), and participation in the randomised clinical trial (RCT). In a previously reported RCT, 68% of 655 recruited survivors were eligible, and of those 45% participated in the RCT. Among participants, 52% used Oncokompas as intended. The aim of this study was to explore reasons for not participating in the RCT, and reasons for not using Oncokompas.

Methods: Reasons were assessed with a study-specific questionnaire. Usage was investigated via system data, and evaluation of Oncokompas was explored with a study-specific questionnaire 1 week after usage.

Results: Main reasons for not participating were not interested in participation in scientific research (68%) and not interested in Oncokompas (46%). Main reasons for not being interested in Oncokompas were wanting to leave the period of being ill behind (29%), no symptom burden (23%), or lacking internet skills (18%). Main reasons for not using Oncokompas were no symptom burden (32%) or lack of time (26%). Satisfaction and user-friendliness were rated with a 7 (scale 0–10). Within 3 (IQR 1–4) sessions, users selected 32 (IQR 6–37) topics. After each component, users stepped out: 19% after account activation, 17% after Measure, and 43% after Learn. Main reasons for not using healthcare options in Act were that the information in Learn was already sufficient (44%) or no supportive care needs (32%).

Discussion: Main reasons for not reaching or using Oncokompas were no internet access or lacking skills, no symptom burden, no supportive care needs, or lack of time. Users selected many cancer-generic and tumour-specific topics to address.

INTRODUCTION

Cancer survivors are nowadays expected to manage effects of cancer treatment, adopt a healthy lifestyle in order to reduce or prevent late effects, and cope with psychological consequences.[1–3] Self-management of these effects and navigating through available care options is not just for highly motivated cancer survivors, but is becoming necessary for all cancer survivors.[3] Web-based self-management interventions can have positive effects on health-related quality of life (HRQOL) and symptom burden in cancer patients,[4–8] and have the advantage that content can be tailored to the individual user, and are available at relatively low costs.[9,10] However, knowledge is scarce on who is reached by such interventions, (i.e. who is eligible for such interventions, and who participates in such interventions), and who uses those interventions as intended.

The web-based self-management application Oncokompas was developed to support cancer survivors in self-management, and contains three components: 1) Measure: monitoring health-related quality of life and cancer-generic and tumour-specific symptoms by means of patient reported outcome measures (PROMs), 2) Learn: providing tailored information based on PROM scores, and 3) Act: providing a personalised overview with recommended supportive care options.[11] A randomised controlled trial (RCT) showed that Oncokompas is effective to reduce symptoms and improve HRQOL in cancer survivors,[12] and is not more expensive than usual cancer survivorship.[13] These are important conditions in order to implement Oncokompas in routine cancer survivorship care. However, to tailor implementation strategies it is also important to know which cancer survivors are reached and reasons why people are not reached, and to evaluate the actual usage of Oncokompas and reasons why cancer survivors are not using Oncokompas.

In our previous report, we investigated the reach by assessing the eligibility rate and participation rate, in the context of an RCT on the efficacy and cost-utility of Oncokompas.[11–13] We found that 68% of the respondents were eligible to use Oncokompas (they had access to the internet and an e-mail address), of whom 45% agreed to participate in the RCT on Oncokompas. Factors associated with eligibility were male sex, younger age, higher health literacy, higher positive adjustment to cancer, no unmet needs regarding health system information and supportive care, and tumour type. Factors associated with participation were a medium and higher education level, unmet supportive care needs for sexual problems, and a higher belief of control of health by powerful others.[12] However, specific reasons why eligible people decided not to participate in the RCT are not known. It is

known that eHealth applications are not always used as intended.[14,15] Initial results on the usage of Oncokompas showed that 52% of the users, used Oncokompas as intended.[12] Usage as intended was defined as the minimal use that was expected to improve outcomes, and was defined as completing at least the components Measure and Learn for at least one topic. Factors associated with usage as intended were a higher education level, having a partner, and not being employed.[12] Reasons for not using Oncokompas among those who did not use Oncokompas, as well as the evaluation of Oncokompas among users may provide more insight into how to improve usage.

The aim of this study was to investigate the reach and usage of Oncokompas, by investigating reasons for not participating in the RCT studying Oncokompas, and reasons for not using Oncokompas, and to investigate system data and evaluate Oncokompas among users. The results are important in the continuous cycle of improvement and updating the content and design of web-based self-management interventions.[16,17]

METHODS

Study design

The study was conducted in the context of an RCT on efficacy and cost-utility of Oncokompas. Details of the study procedures are described elsewhere.[11,12] To investigate the reach, a two-step inclusion method was used: a survey on supportive cancer care (part 1), and the actual RCT (part 2) (**Figure 1**). Respondents of the survey were invited to participate in the RCT if they were eligible to use Oncokompas. They were eligible when they had internet access and an e-mail address. Via this two-step inclusion method associations of eligibility and participation could be investigated, because information on non-eligible survivors and non-participants was available from the survey. The study protocol was approved by the Medical Ethics Committee of the VU University Medical Center (2015.523), published previously,[11] and registered in the Netherlands Trial Register (NTR5774). All participants provided (online) written informed consent.

Cancer survivors were invited from October 2016 until July 2017 by a letter from their (former) treating physician. Of the 1491 cancer survivors who were invited to participate in the survey (part 1), 655 (44%) completed the survey, and 201 (13%) consented to participate in the RCT. Later, cancer survivors were invited for participation in the RCT directly. From July 2017 to May 2018, 1462 cancer

survivors were invited to participate directly. Of these, 424 (29%) consented to participate. In total, 625 survivors participated in the RCT, of whom 320 were randomised into the intervention group, and had access to Oncokompas (**Figure 1**).

To investigate the usage of Oncokompas, system data was extracted from RCT participants randomised into the intervention group, who had access to Oncokompas. To evaluate the usage of Oncokompas, data from the first follow-up assessment in the RCT was used. The link to the follow-up assessment was sent by mail, 1 week after Oncokompas was used as intended. If Oncokompas was not used, the link was sent 2 weeks after randomisation.

In- and exclusion criteria

The inclusion criteria for the survey (part 1) were: being diagnosed with breast cancer, colorectal cancer, head and neck cancer or lymphoma; being ≥18 years, and having completed treatment with curative intent 3 months to 5 years ago (all treatment modalities). Cancer survivors who had not yet completed endocrine therapy or immunotherapy were included 3 months to 5 years after their previous treatment, and patients diagnosed with lymphoma who had a wait-and-see regimen, were included 3 months to 5 years after the date of diagnosis. The exclusion criteria for part 1 were: male cancer survivors diagnosed with breast cancer, severe cognitive impairment, insufficient mastery of the Dutch language, or physical inability to complete a questionnaire (e.g. blind, or paralyzed). Additional eligibility criteria for the RCT (part 2) were: having access to the internet and having an e-mail address.

Intervention

A detailed description of Oncokompas has been published previously.[11,12] In short, Oncokompas is an eHealth self-management application that supports cancer survivors to monitor their HRQOL and cancer-generic and tumour-specific symptoms. Oncokompas includes 32 topics in 5 cancer-generic domains: physical, psychological, and social functioning, lifestyle, and existential issues. In addition, tumour-specific modules are available targeting head and neck cancer (6 topics), colorectal cancer (8 topics), breast cancer (9 topics) and (non-)Hodgkin lymphoma survivors (7 topics). Oncokompas consists of three components: 'Measure', 'Learn', and 'Act'. In the 'Measure' component, cancer survivors complete PROMs on the topic(s) of choice. Data from the 'Measure' component are processed in real-time and linked to feedback in the 'Learn' component. In the 'Learn'

component feedback is provided by means of a 3-colour system: green (no elevated well-being risks), orange (elevated well-being risks), and red (seriously elevated well-being risks). Cancer survivors receive personalized information on the outcomes (Learn, information), and comprehensive self-care advice (Learn, advice). In the 'Act' component, cancer survivors obtain a personalised overview with supportive care options. If a user has elevated well-being risks (orange score), the feedback includes suggestions for self-help interventions, and if a user has seriously elevated well-being risks, the feedback includes suggestions for medical specialists or their general practitioner.[11,12]

Outcome measures

Reach

Reach was investigated by eligibility and participation rate in the RCT, among those who were invited with the two-step inclusion method (**Figure 1**, two-step inclusion), and reported previously.[12] The eligibility rate was calculated as the number of respondents of the survey that were eligible for participation in eHealth interventions, divided by the number of survey respondents. The participation rate was calculated as the number of survivors who consented to participate in the RCT, divided by the number of eligible survivors.

Among survivors who were not willing to participate in the RCT, reasons for not participating were assessed in an online form with response options: 'not interested in Oncokompas', 'not interested in scientific research', 'not interested in Oncokompas and scientific research', and 'other reasons'. Reasons for not being interested in Oncokompas were further explored with pre-set response options, and multiple reasons were allowed. In case the online form was not completed, but the reason for not participating was indicated by phone or e-mail, the reasons were categorized into one of the categories manually.

Usage

Usage was evaluated among those who were randomised into the intervention group in the RCT (**Figure 1**, usage), and reported previously.[12] Usage was investigated via system data from Oncokompas and data from an evaluation questionnaire. System data was extracted separately for each component of Oncokompas (Measure, Learn and Act). For the component Measure: number of completed topics per user, and number of completions per topic; for the component Learn: number of green (no elevated well-being risk), orange (elevated well-being risk) and red scores (seriously

elevated well-being risk) per user, and the number of green, orange, and red scores per topic, and for the component Act: number of clicks to supportive care options.

Usage as intended was defined as the completion of the components Measure and Learn for at least one topic, at least once during the 6-month follow-up period. It was expected that the use of at least these components are needed to improve outcomes. The usage rate was calculated as the number of users who used Oncokompas as intended, divided by the total number of users.

In the first follow-up assessment in the RCT (1 week after usage of Oncokompas, with a maximum of 2 weeks after randomisation), participants were invited to complete the study-specific evaluation questionnaire. Satisfaction and user-friendliness were evaluated via items on an 11-point rating scale (0 – 10). User experiences and satisfaction on several aspects of the components Measure, Learn and Act were evaluated via multiple-choice questions. Among survivors who were randomised into the intervention group but who did not use Oncokompas, reasons for not using Oncokompas were explored with pre-set response options.

Statistical analyses

Descriptive statistics were generated to characterize the study sample (by means of frequency and percentage for categorical data and median and interquartile range (IQR) for continuous data), calculate the eligibility, participation and usage rates and describe the reasons for not participating and not using Oncokompas, and system data. Statistical analyses were performed using IBM SPSS Statistics version 26 (IBM Corp., Armonk, NY, USA).

RESULTS

The flow chart of the study is shown in **Figure 1**. Characteristics of the study population are shown in **Table 1**.

Reach

Among those who were invited with the two-step inclusion method, the reach was determined (**Figure 1**, two-step inclusion). Of the 655 respondents of the survey (part 1), 444 were eligible for participation in Oncokompas (eligibility rate: 68%), and 211 (32%) were not eligible (no access to the internet or e-mail address, or did not want to provide their e-mail address) (**Figure 1**, eligibility).[12]

The eligibility rate was 60% among head and neck cancer, 68% among breast cancer, 69% among colorectal cancer (69%) and 79% among (non-)Hodgkin lymphoma survivors. Of the 444 eligible cancer survivors invited to participate in the RCT on Oncokompas (part 2), 201 agreed to participate (participation rate: 45%) (**Figure 1**, participation). The participation rate was 39% among (non-) Hodgkin lymphoma, 43% among head and neck cancer survivors, 46% among colorectal cancer, and 48% among breast cancer survivors (48%).

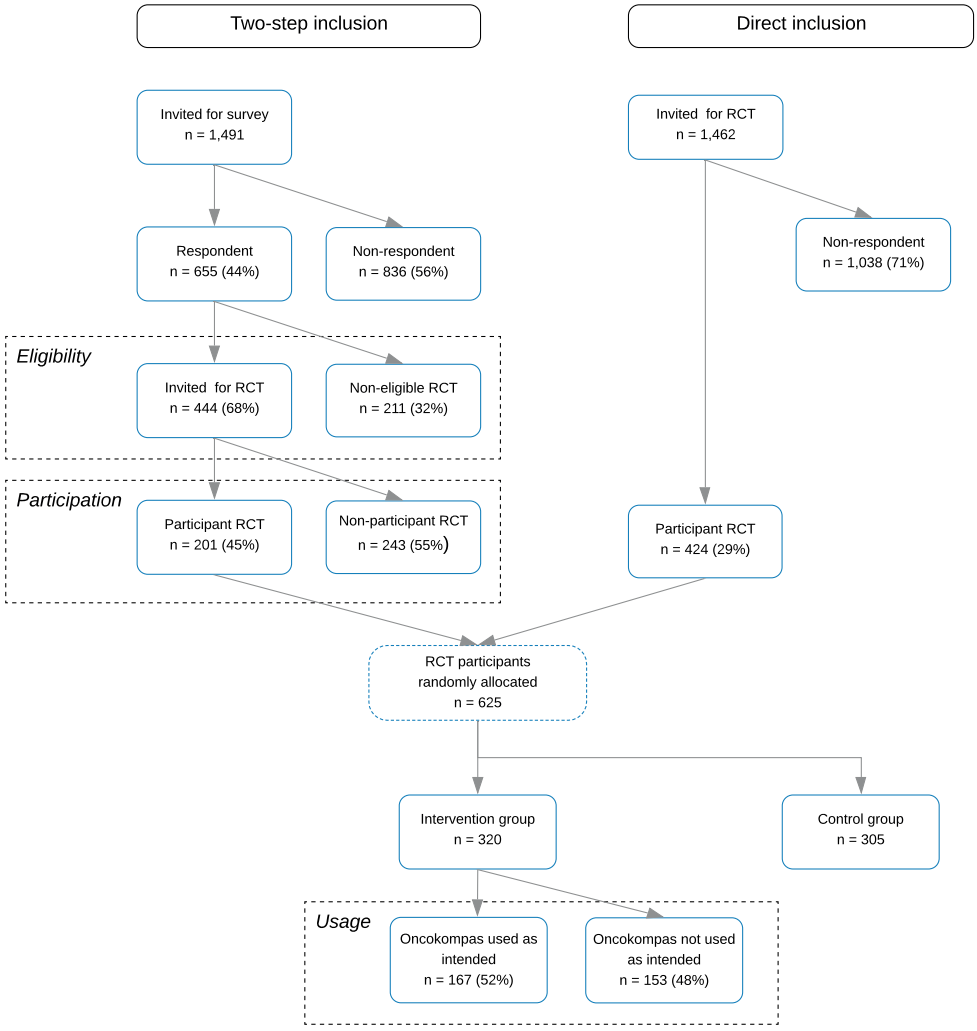


Figure 1 – Flow chart of the study

Of the 243 eligible survivors who did not participate, 152 (63%) responded and actively declined, and 91 (37%) did not respond. Among those who responded, most often indicated reason for not participating was that survivors did not want to participate in scientific research (67%), followed by not being interested in Oncokompas (46%). Most often reasons for not being interested in Oncokompas (n = 70) was that someone wanted to leave the period of being ill behind (29%), did not experience any symptom burden (23%), thought they would lack sufficient internet skills (18%) or had no need for supportive care (14%). Reasons are shown in **Table 2**.

Table 1 – Baseline characteristics of cancer survivors analysed for the reach and usage

	Reach		Usage	
Characteristics *	Eligible cancer survivors (n = 444)	Participants of RCT (n = 201)	Intervention group of RCT (n = 320)	Users as intended (n = 167)
Age (years)	64 (56 – 70)	64 (56 – 70)	65 (56 – 71)	65 (57 – 70)
Sex (female)	268 (60%)	120 (60%)	158 (49%)	85 (51%)
Marital status (partner)	367 (83%)	174 (87%)	265 (83%)	144 (86%)
Education level				
Low	177 (40%)	67 (33%)	111 (35%)	52 (31%)
Medium	135 (30%)	71 (35%)	105 (33%)	51 (31%)
High	131 (30%)	63 (31%)	103 (32%)	63 (38%)
Employment status (employed)	144 (32%)	69 (34%)	122 (38%)	56 (34%)
Tumour type				
Breast cancer	170 (38%)	82 (41%)	66 (21%)	31 (19%)
Colorectal cancer	134 (30%)	61 (30%)	80 (25%)	39 (23%)
Head and neck cancer	79 (18%)	34 (17%)	99 (31%)	59 (35%)
Lymphoma	61 (14%)	24 (12%)	75 (23%)	38 (23%)
Tumour stage				
Stage I	150 (34%)	77 (38%)	106 (35%)	54 (32%)
Stage II	108 (24%)	44 (22%)	73 (24%)	42 (25%)
Stage III	93 (21%)	40 (20%)	61 (20%)	33 (20%)
Stage IV	54 (12%)	26 (13%)	64 (21%)	32 (20%)
Unknown	39 (9%)	14 (7%)	16 (5%)	6 (4%)
Time since diagnosis				
3-<12 months	51 (12%)	22 (11%)	39 (12%)	16 (10%)
12-<24 months	156 (35%)	66 (33%)	104 (33%)	54 (32%)
24-60 months	237 (53%)	113 (56%)	177 (55%)	97 (58%)
Treatment type (multimodal)	294 (66%)	140 (70%)	183 (57%)	93 (56%)
Comorbidities (multiple)	103 (23%)	48 (24%)	71 (22%)	34 (20%)

** Median (IQR), or n (%)*

Table 2 – Reasons for not participating in the RCT on the efficacy of Oncokompas and reasons for not being interested in Oncokompas

	Total	Head and neck cancer	Colorectal cancer	Breast cancer	(non-) Hodgkin lymphoma
Reasons for not participating in the RCT *	(n = 152) **	(n = 25)	(n = 53)	(n = 58)	(n = 16)
Not interested in participation in scientific research	103 (67%)	20 (80%)	39 (74%)	34 (59%)	10 (63%)
Not interested in Oncokompas	70 (46%)	13 (52%)	28 (53%)	26 (45%)	3 (19%)
Personal reasons	13 (9%)	2 (8%)	3 (6%)	6 (10%)	2 (13%)
Did not want to provide reasons	8 (5%)	0 (0%)	3 (6%)	3 (5%)	2 (13%)
Reasons for not being interested in Oncokompas *	(n = 70)	(n = 13)	(n = 28)	(n = 26)	(n = 3)
Want to leave the period of being ill behind	20 (29%)	6 (46%)	4 (14%)	10 (38%)	0 (0%)
No symptom burden	18 (23%)	2 (15%)	7 (25%)	7 (27%)	2 (67%)
Lacking sufficient internet skills	14 (18%)	4 (31%)	8 (29%)	2 (8%)	0 (0%)
No need for supportive care	11 (14%)	2 (15%)	3 (11%)	6 (23%)	0 (0%)
Not fitting to personal situation	10 (13%)	1 (8%)	3 (11%)	6 (23%)	0 (0%)
No time/motivation	8 (11%)	0 (0%)	5 (18%)	3 (12%)	0 (0%)
Too confronting	8 (11%)	3 (23%)	4 (14%)	0 (0%)	1 (33%)
No need for information and advice	7 (9%)	1 (8%)	0 (0%)	5 (19%)	1 (33%)
The aim of Oncokompas was unclear	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)

*n (%). * Multiple reasons could be given, so percentage adds up to more than 100%. ** Among 152 non-participants who actively declined*

Usage

Among all RCT participants who were randomised into the intervention group (n = 320), the usage was evaluated (**Figure 1**, usage). Of them, 248 (78%) activated their account, and 167 used Oncokompas as intended (usage rate: 52%).[12] The flow chart of the usage, with the completion per subsequent component is shown in **Figure 2**. The usage rate was 47% among breast cancer, 49% among colorectal cancer, 51% among (non-)Hodgkin lymphoma, and 60% among head and neck cancer survivors.

Among the 72 cancer survivors who did not activate their account, 31 (43%) completed the first assessment of the RCT, two weeks after being provided access to Oncokompas. Among them, reasons for not using Oncokompas are shown in **Table 3**. The most often mentioned reasons for not

using Oncokompas was that no symptom burden was experienced (32%) or that they lacked time to use Oncokompas (26%) within the two-week time frame.

System data and evaluation

During the 6-months follow-up period of the RCT, the median number of logins in Oncokompas was 3 (IQR 1 – 4) among the 248 who activated their account, and 3 (IQR 2 – 5) among the 167 who used Oncokompas as intended.

Among the 248 participants who activated their Oncokompas account, 217 (88%) completed the first follow-up assessment (one week after using Oncokompas for the first time). The median score on satisfaction was 7 (IQR 6 – 8), and on user-friendliness 7 (IQR 5 – 8). The median score on the

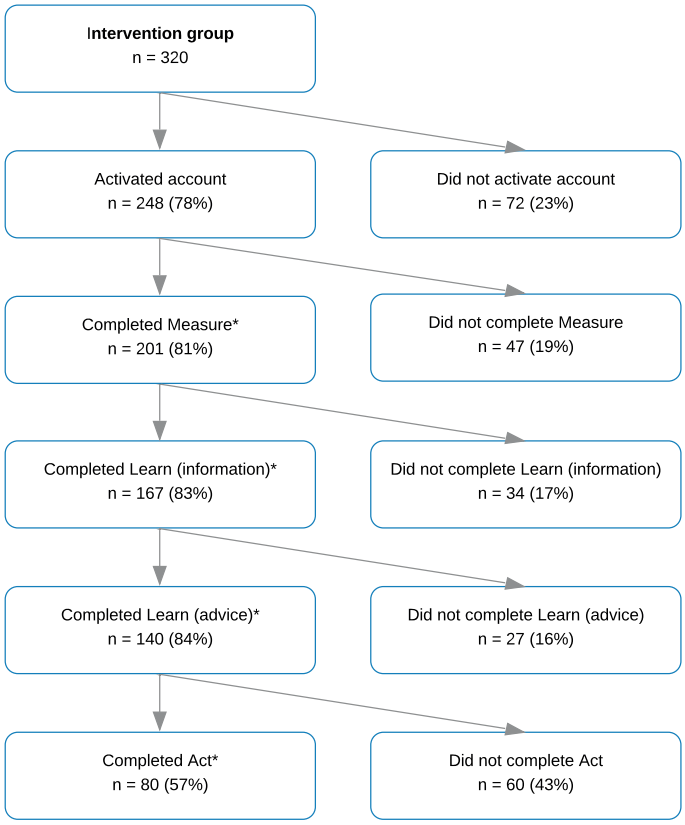


Figure 2 – Flow chart of usage of Oncokompas.

** for at least 1 topic*

Table 3 – Reasons for not using Oncokompas among those in the intervention group of the RCT

	Total	Head and neck cancer	Colorectal cancer	Breast cancer	(non-) Hodgkin lymphoma
*Reasons for not using Oncokompas**	(n = 31)	(n = 10)	(n = 9)	(n = 6)	(n = 6)
No symptom burden	10 (32%)	4 (40%)	3 (33%)	2 (33%)	1 (17%)
Lack of time	8 (26%)	1 (10%)	1 (11%)	4 (67%)	2 (33%)
Not interested	3 (10%)	0 (0%)	2 (22%)	0 (0%)	1 (17%)
Not fitting to personal problems	3 (10%)	0 (0%)	2 (22%)	1 (17%)	0 (0%)
Personal reasons	3 (10%)	1 (10%)	1 (11%)	1 (17%)	0 (0%)
Login details lost or not received	3 (10%)	2 (20%)	1 (11%)	0 (0%)	0 (0%)
Forgotten to activate Oncokompas account	2 (6%)	0 (0%)	0 (0%)	1 (17%)	1 (17%)
Aim of Oncokompas was not clear	2 (6%)	2 (20%)	0 (0%)	0 (0%)	0 (0%)
Too difficult	1 (3%)	1 (10%)	0 (0%)	0 (0%)	0 (0%)
Too comprehensive	1 (3%)	0 (0%)	0 (0%)	0 (0%)	1 (17%)
Technical problems	1 (3%)	1 (10%)	0 (0%)	0 (0%)	0 (0%)
Too confronting	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)

*n (%). * Multiple reasons could be given, so percentage adds up to more than 100%.*

question 'How likely is it that you will recommend Oncokompas to other cancer survivors' was 6 (IQR 5 – 7). Self-reported time spent in Oncokompas was less than 30 minutes as reported by 28%, between 30 and 60 minutes by 48%, and more than 60 minutes by 23% of the users. The time it took to complete Oncokompas was evaluated as 'way too long' by 6%, 'too long' by 25%, 'exactly right' by 66%, and 'too short' by 3% of the users. A minority (15%) indicated that they had help of others (e.g. partner) using Oncokompas, and none of the participants reported that they e-mailed or called the helpdesk of Oncokompas. Most users (75%) intended to login to Oncokompas again and read the information and advice, and supportive care options once again. Most users (71%) indicated that they wanted to use Oncokompas again.

Measure

In total, 201 participants (81% of those who activated their account) completed the component Measure for at least 1 topic (**Figure 2**), during the 6-months follow-up period. The median number of topics completed per person was 32 (IQR: 6 – 37). The cancer-generic topics that were chosen most often were: fatigue, sleep, and daily functioning, all from the physical quality of life domain (**Figure 3**). The number of questions in the Measure component was rated as 'not feasible' by 6%, 'a

little feasible' by 41%, 'feasible' by 41%, and 'very feasible' by 9%. The overlap between questions in Measure was rated as 'not' by 16%, 'a little' by 57%, 'much' by 24%, and 'very much' by 3%.

Learn

In total, 167 users (83% of those who completed the Measure component) read the page with information for at least 1 topic. Of them, 140 users (84% of those who read the information page) also read the page with advice and self-help tips for at least 1 topic. In total, 4497 topics were completed, on which 73% of the users had a green score, 18% had an orange score, and 9% had a red score. Per user, the median number of green scores was 21 (IQR 2 – 28), the median number of orange scores was 4 (IQR: 2 – 8), and the median number of red topics was 2 (IQR: 0 – 4). The scores on cancer-generic topics are shown in **Figure 3** and the scores on tumour-specific topics are shown in **Figure 4**.

The question 'Did the score correspond with your personal experience?' was answered as 'not corresponding' by 7%, 'little corresponding' by 43%, 'much corresponding' by 45%, and 'very much corresponding' by 5% of the users. Most users (74%) rated the scores as clear and understandable. The information accompanying the scores was rated by most users as clear (72%), complete (63%), and useful (53%). Of the users, 61% indicated that the provided information and advice in the Learn component did not fit their personal situation, 57% that it not fit their health status, and 35% indicated that the information had added value for them. Slightly more than half (52%) of the users indicated that they received sufficient information to cope with their problem.

Act

In total, 80 users (57% of those who completed the Learn component) completed the Act component for at least 1 topic (**Figure 2**). The number of proposed supportive care options was rated as 'too little' by 13%, 'exactly right' by 66%, and 'too much' by 21% of the users.

Nineteen percent of the users indicated that they had already used supportive care options suggested by Oncokompas after 1-week follow-up, and 41% of the users indicated that they wanted to use the proposed supportive care options in the near future. Reasons for not wanting to use the proposed supportive care options are shown in **Table 4.** The most indicated reasons for not wanting to use the proposed healthcare options was that the information and advice given in the Learn component was already sufficient (44%) or that they did not want supportive care (32%).

Table 4 – Reasons for not using the proposed supportive care options in the Act component

	Total	Head and neck cancer	Colorectal cancer	Breast cancer	(non-) Hodgkin lymphoma
Reasons for not using the proposed supportive care options *	*(n = 72)*	*(n = 29)*	*(n = 10)*	*(n = 17)*	*(n = 16)*
The information and advice provided in Oncokompas was already sufficient	32 (44%)	13 (45%)	6 (60%)	8 (47%)	5 (31%)
Not interested or no need for the supportive care option	23 (32%)	10 (35%)	4 (40%)	2 (12%)	7 (44%)
Already using the supportive care option	10 (14%)	4 (14%)	1 (10%)	4 (24%)	1 (6%)
Used the supportive care option before	9 (13%)	4 (14%)	0 (0%)	4 (24%)	1 (6%)
Limited in functioning, therefore using supportive care options was not possible	6 (8%)	3 (10%)	0 (0%)	0 (0%)	3 (19%)
Lack of time	5 (7%)	1 (3%)	0 (0%)	2 (12%)	2 (13%)
Too little information on the supportive care option	3 (4%)	0 (0%)	0 (0%)	0 (0%)	3 (19%)
Supportive care option was not available or had a wait-list	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Supportive care option was too far away	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Supportive care option was too expensive and/or was not reimbursed	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)

*n (%). * Multiple reasons could be given, so percentage adds up to more than 100%.*

DISCUSSION

In this study, we investigated reasons for not reaching or not using the web-based self-management application Oncokompas among cancer survivors. One third of the cancer survivors was not reached by web-based self-management interventions, because they did not have access to internet or e-mail. Half of the eligible cancer survivors did not want to participate in the RCT investigating Oncokompas. The most often indicated reason for not participating in the RCT was that cancer survivors did not want to participate in scientific research (68%), followed by not being interested in Oncokompas (46%). Main reasons for not being interested in Oncokompas were that cancer survivors wanted to leave the period of being ill behind, did not experience symptom burden, thought they would lack sufficient internet skills, or they did not have a need for supportive care. The main reason for not using Oncokompas among RCT participants was that no symptom burden was experienced.

Among breast cancer survivors, the RCT participation rate was highest, but actual Oncokompas usage rate was lowest compared to the other tumour types. It might be that breast cancer survivors are

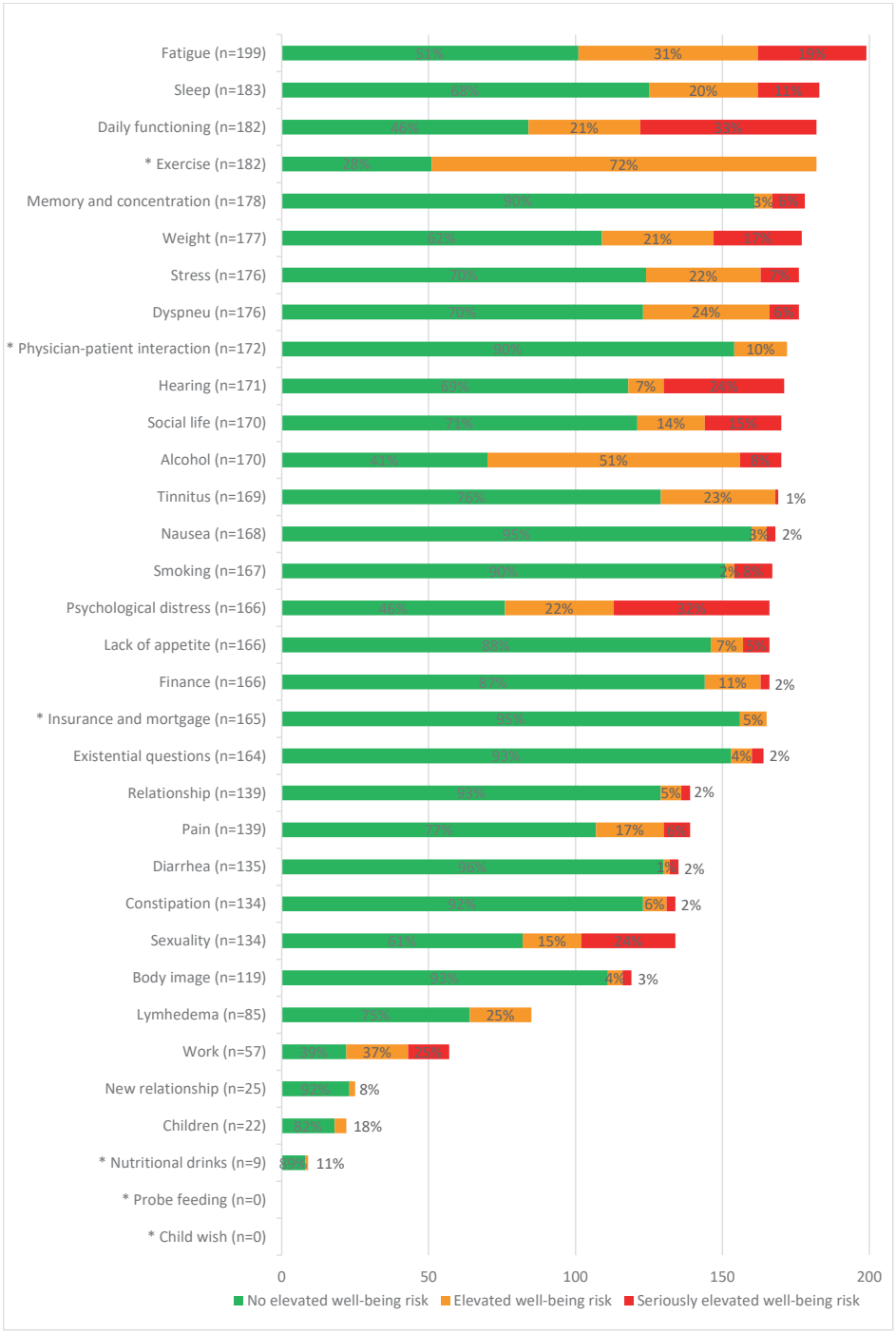


Figure 3 – Number of completions per cancer-generic topic within Oncokompas, and corresponding scores, based on system data. ** on these topics users can only score green or orange*

Figure 4 – Number of completions per tumour-specific topic within Oncokompas, and corresponding scores, based on system data. ** on these topics users can only score green or orange*

willing to participate in scientific research, but that they are performing relatively well, and therefore did not use Oncokompas as often. In contrast, head and neck cancer survivors were participating less frequently in the RCT, but if they did, they used Oncokompas more often, possibly because they were suffering from symptoms more often. This corresponds with the percentage of seriously elevated well-being risks on tumour-specific symptoms, which was lowest among breast cancer survivors (5% of completed tumour-specific topics), and highest among head and neck cancer survivors (18% of completed tumour-specific topics).

While reasons such as no symptom burden or no supportive care needs are legitimate reasons for not participating or using Oncokompas, other reasons mentioned might be useful to improve (access to) web-based interventions. These include no time, not fitting to personal situation and that people think they lack skills to use such an intervention. These reasons emphasize the need for easy to use applications, with simple login procedures, which do not take much time to use. Tailoring evidence-based information to the individual cancer survivor is seen as an advantage of Oncokompas, as this makes the information applicable to the users' situation and needs, and can be directly applied.[9] However, further tailoring might improve Oncokompas, as more than half of the users indicated that the information did not match with their personal situation and health status, and one third of the users indicated that it took too much time to complete Oncokompas.

The number of topics that users chose to address during 6-months follow-up was high (median of 32 topics, during a median of 3 sessions). This may explain why one third of the users rated the time it took to complete Oncokompas as too long. Encouraging users to address one or two topics at a time, that are the most important for them, and stimulate repeated use to cover multiple topics is recommended to improve usage as intended. Multimedia tools such as podcasts, videos, infographics and gamifications elements may also increase usage and stimulate repeated use.[14,18–22] Moreover, instructions for healthcare professionals on how to recommend Oncokompas to cancer survivors might increase the reach.

Users had no elevated well-being risks on 73% of the topics they completed and had (seriously) elevated well-being risks on 27% of the topics. The cancer-generic topics that were most often selected were fatigue, sleep, and daily functioning, all from the physical quality of life domain. Topics with the highest percentage of seriously elevated well-being risk (red score) were daily functioning, psychological problems, work, and sexuality, which are symptoms often observed among cancer

survivors.[23–27] Whereas some other web-based self-management interventions target a single topic, or a limited amount of topics,[28–30] we think that the variety of topics that are incorporated in Oncokompas is valuable in self-management of HRQOL and symptoms, because of the wide range of symptoms that cancer survivors can experience.[23,25,31,32] This is supported by the fact that the 20 most selected topics in did not differ much in absolute numbers.

It was found that after each step of Oncokompas (Measure, Learn, Act), some users were not going to the next step. After activation of the account 19% did not go to the Measure component, 17% of them did not go to the Learn component with information, 16% of them did not go the Learn component with advice, and 43% of them did not go to the Act component. About half of the users indicated that the information and advice provided in the component Learn was already sufficient to cope with their problem, and therefore, the component Act might not be necessary for all users. Oncokompas is a complex intervention, with multiple components, domains and topics, and every cancer survivor has other preferences and needs. Therefore, it is difficult to measure the dose-response relation of usage, and determine the accurate cut-off point when it is used as intended.[9,33] In this study, we used the definition of used as intended when the components Measure and Learn were completed for at least one topic. Only 52% of the participants met the defined criteria, which is similar to other studies, showing that about 50% of the participants fully adhere to web-based interventions.[15] Among users, Oncokompas was evaluated positively and most users indicated that they wanted to use Oncokompas again. In contrast, only 35% of the cancer survivors reported that the information had added value for them, and the question whether they would recommend Oncokompas to other cancer survivors was rated with a median of 6. This seems contradictory to the 71% of users that indicated that they want to use Oncokompas again. This might suggest that knowing that support is available when needed, or when symptoms are present is already sufficient. Further research into usage patterns is needed to gain insight into which specific components and topics contribute to the intervention effect of Oncokompas, and to be able to predict which user needs which components.[34] Usage patterns would be helpful to gain insight into ways to improve usage.[35]

A limitation of this study is that we used 'willing to participate in an RCT on Oncokompas' as a proxy for 'being interested in Oncokompas', while these measures might not correspond in practice. Another limitation is that the findings reported per tumour type are based on relatively small study samples. Further research on real-world data is necessary to extend our knowledge on the reach

and usage of web-based self-management applications as Oncokompas. The scientific context in which Oncokompas was offered to cancer survivors, might have led to selection bias, and the results might have been different when offered in routine care. We found that the scientific context plays a role in the decision not to participate in web-based self-management interventions, as this was the main reason for not participating. When Oncokompas was offered directly to cancer survivors, the response rate was lower than the response rate of the survey of supportive care (step 1) (29% vs. 44%). Furthermore, respondents of the survey were older and had a shorter time since diagnosis than non-respondents of the survey.[12] There were no differences regarding sex, tumour type, or tumour stage.[12] However, due to ethical and practical reasons, we think this was the best method to investigate the reach of Oncokompas.

In conclusion, main reasons for not reaching or using Oncokompas were no internet access or lack of internet skills, no symptom burden, no need for supportive care, or lack of time. The variety of topics within Oncokompas seems valuable, as users selected a large number of generic cancer as well as tumour-specific topics to address.

REFERENCES

1. Jansen F, van Uden-Kraan CF, van Zwieten V, Witte BI, Verdonck-de Leeuw IM. Cancer survivors' perceived need for supportive care and their attitude towards self-management and eHealth. Support Care Cancer 2015; 23: 1679–88.

2. Greene J, Hibbard JH, Sacks R, Overton V, Parrotta CD. When patient activation levels change, health outcomes and costs change, too. Health Aff 2015; 34: 431–7.

3. Howell D, Mayer DK, Fielding R, et al. Management of cancer and health after the clinic visit: A call to action for self-management in cancer care. JNCI J Natl Cancer Inst 2020; : djaa083.

4. 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.

5. 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.

6. 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.

7. 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.

8. 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.

9. Murray E. Web-based interventions for behavior change and self-management: Potential, pitfalls, and progress. J Med Internet Res 2012; 14: 1(2):e3.

10. Bashshur RL, Shannon G, Krupinski EA, Grigsby J. Sustaining and Realizing the Promise of Telemedicine. Telemed e-Health 2013; 19: 339–45.

11. 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.

12. van der Hout A, van Uden-Kraan CF, Holtmaat K, et al. Role of eHealth application Oncokompas in supporting self-management of symptoms and health-related quality of life in cancer survivors: a randomised, controlled trial. Lancet Oncol 2020; 21: 80–94.

13. van der Hout A, Jansen F, van Uden-Kraan CF, et al. Cost-utility of an eHealth application 'Oncokompas' that supports cancer survivors in self-management: results of a randomised controlled trial. J Cancer Surviv 2020.

14. Sieverink F, Kelders SM, Gemert-Pijnen V. Clarifying the concept of adherence to ehealth technology: Systematic review on when usage becomes adherence. J Med Internet Res 2017; 19: e402.

15. Kelders SM, Kok RN, Ossebaard HC, Van Gemert-Pijnen JEWC. Persuasive system design does matter: A systematic review of adherence to web-based interventions. J Med Internet Res 2012; 14: e152.

16. Catwell L, Sheikh A. Evaluating eHealth interventions: The need for continuous systemic evaluation. PLoS Med 2009; 6: e1000126.

17. Granja C, Janssen W, Johansen MA. Factors determining the success and failure of ehealth interventions: Systematic review of the literature. J Med Internet Res 2018; 20: e10235.

18. Sardi L, Idri A, Fernández-Alemán JL. A systematic review of gamification in e-Health. J Biomed Inform 2017; 71: 31–48.

19. Perski O, Blandford A, West R, Michie S. Conceptualising engagement with digital behaviour change interventions: a systematic review using principles from critical interpretive synthesis. Transl Behav Med

2017; 7: 254–67.

20. Araújo-Soares V, Hankonen N, Presseau J, Rodrigues A, Sniehotta FF. Developing Behavior Change Interventions for Self-Management in Chronic Illness: An Integrative Overview. Eur. Psychol. 2019; 24: 7–25.

21. Kelders SM, T. Bohlmeijer E, Van Gemert-Pijnen JEWC. Participants, usage, and use patterns of a web-based intervention for the prevention of depression within a randomized controlled trial. J Med Internet Res 2013; 15: e172.

22. Moore GF, Evans RE, Hawkins J, et al. From complex social interventions to interventions in complex social systems: Future directions and unresolved questions for intervention development and evaluation. Evaluation 2019; 25: 23–45.

23. Aaronson NK, Mattioli V, Minton O, et al. Beyond treatment - Psychosocial and behavioural issues in cancer survivorship research and practice. Eur J Cancer Suppl 2014; 12: 54–64.

24. Harden SM, Gaglio B, Shoup JA, et al. Fidelity to and comparative results across behavioral interventions evaluated through the RE-AIM framework: A systematic review. Syst Rev 2015; 4: 155.

25. Stein KD, Syrjala KL, Andrykowski MA. Physical and psychological long-term and late effects of cancer. Cancer 2008; 112: 2577–92.

26. Eeltink CM, Rood JAJ, Nauta IH, et al. Reply to: "Discussing sexuality in cancer care: towards personalized information for cancer patients and survivors". Support Care Cancer 2020; : 1–3.

27. Foster C, Wright D, Hill H, Hopkinson J, Roffe L. Psychosocial implications of living 5 years or more following a cancer diagnosis: A systematic review of the research evidence. Eur J Cancer Care (Engl) 2009; 18: 223–47.

28. Willems RA, Bolman CAWA, Mesters I, Kanera IM, Beaulen AAAJM, Lechner L. The Kanker Nazorg Wijzer (Cancer Aftercare Guide) protocol: the systematic development of a web-based computer tailored intervention providing psychosocial and lifestyle support for cancer survivors. BMC Cancer 2015; 15: 580.

29. Foster C, Grimmett C, May CM, et al. A web-based intervention (RESTORE) to support self-management of cancer-related fatigue following primary cancer treatment: a multi-centre proof of concept randomised controlled trial. Support Care Cancer 2016; 24: 2445–53.

30. Kim AR, Park H. Web-based Self-management Support Interventions for Cancer Survivors: A Systematic Review and Meta-analyses. Stud Health Technol Inform 2015; 216: 142–7.

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

32. Given CW, Given BA. Symptom management and psychosocial outcomes following cancer. Semin Oncol 2013; 40: 774–83.

33. Sieverink F, Kelders S, Poel M, van Gemert-Pijnen L. Opening the Black Box of Electronic Health: Collecting, Analyzing, and Interpreting Log Data. JMIR Res Protoc 2017; 6: e156.

34. Jonkman NH, Schuurmans MJ, Groenwold RHH, Hoes AW, Trappenburg JCA. Identifying components of self-management interventions that improve health-related quality of life in chronically ill patients: Systematic review and meta-regression analysis. Patient Educ Couns 2016; 99: 1087–98.

35. Kelders SM, Van Gemert-Pijnen JEWC. Using log-data as a starting point to make eHealth more persuasive. In: International conference on persuasive technology. Springer, Berlin, Heidelberg, 2013: 99–109.

7

General Discussion

The web-based self-management application Oncokompas was developed to support cancer survivors in self-management by monitoring health-related quality of life (HRQOL), and cancer-generic and tumour-specific symptoms, and by providing tailored information and advice, and a personalized overview of supportive care options. The aim of this thesis was to investigate the efficacy, cost-utility and reach of Oncokompas, in order to evaluate whether web-based self-management is a sustainable option in cancer survivorship care.

Main findings

The first research question 'Is Oncokompas effective compared to usual cancer survivorship care?' comprised 3 sub-questions: a) What is the effect on cancer survivors' knowledge, skills and confidence for self-management?; b) What is the effect on HRQOL and symptoms, self-efficacy, personal control, supportive care needs, mental adjustment to cancer and perceived efficacy in patient-physician interaction?; and c) What are moderating factors of the observed effects of Oncokompas? It was shown that Oncokompas did not improve knowledge, skills and confidence for self-management (patient activation) in the total group (**Chapter 3**), nor in subgroups (**Chapter 4**). There was also no significant effect on secondary outcomes such as self-efficacy, needs for supportive care and mental adjustment to cancer in the total group. However, there was a beneficial effect of Oncokompas on the course of health-related quality of life (HRQOL) and several tumour-specific symptoms (**Chapter 3**). Moderation analyses showed that Oncokompas was more effective in improving HRQOL in cancer survivors with low to moderate self-efficacy, in cancer survivors with higher personal control, and in cancer survivors with higher health literacy. Also, cancer survivors with some degree of symptom burden at baseline benefit from Oncokompas, and the intervention effect became larger when symptom burden was higher (**Chapter 4**).

The finding that Oncokompas had no effect on patient activation may be explained by the study population, which comprised cancer survivors who had access to the internet, who were doing relatively well, and were mostly long-term survivors (>2 years after diagnosis). These cancer survivors might already have found the information and support they needed to build their skills and confidence to manage cancer-related concerns (**Chapter 3**). Another explanation may be the validity and/or reliability of the patient reported outcome measure (PROM) with which patient activation was measured, the Patient Activation Measure (PAM). Although measurement properties of the PAM

among a Dutch population of chronically ill patients were generally good,[1,2] it could be questioned what the influence of measurement error is on the results, because no score could be calculated when multiple questions (3 out of 13 items) are answered with the option 'not applicable'.[3] Patient activation was improved in a pilot study on Oncokompas,[4] but other interventions had inconsistent effects on patient activation among populations with chronic diseases.[5,6]

Most effects on symptom burden were found in survivors of head and neck cancer, several in survivors of colorectal cancer and non-Hodgkin lymphoma, but no effects were found in breast cancer survivors (**Chapter 3**). This might be explained by the differences in the effect of the type of cancer itself and its treatment, but also the availability of (online) information and supportive care between various tumour types, and the supportive care needs.[7–9] Oncokompas was found to be more effective among those with higher symptom burden at baseline (**Chapter 4**). The intervention effect of Oncokompas on HRQOL was largest among cancer survivors with low to moderate self-efficacy, and among those with high personal control and high health literacy. Examining the study population, persons with lower self-efficacy were not the same persons as those with higher personal control and higher health literacy. It could be that cancer survivors with lower self-efficacy need a push to act, and with Oncokompas, they have the tools to do that and improve HRQOL. The effect among cancer survivors with higher personal control might be because they feel in control with Oncokompas, which leads to an earlier improvement in HRQOL (**Chapter 4**).

The second research question 'Is Oncokompas cost-effective compared to usual cancer survivorship care?' was addressed in **Chapter 5**. The economic evaluation of Oncokompas showed that survivors in the intervention group had slightly (but not significantly) lower societal costs than the survivors in the care as usual group. The base case cost-utility analysis indicated that the probability that Oncokompas was both more effective and less costly compared to usual cancer survivorship care was 47%, seen from a societal perspective. When seen from a healthcare perspective and adjusted for baseline costs and quality adjusted life years (QALYs), the probability that QALYs were higher was 20%, with the effect in favour of usual cancer survivorship care. It should be noted that the incremental effect was −0.0043, which reflects a difference of 1.6 days living in perfect health. The probability that the total healthcare costs were lower was 57%, with incremental costs in favour of Oncokompas (−€40), but this difference was not statistically significant. Therefore, we concluded that Oncokompas is equally effective in terms of QALYs, and not more expensive as seen

from a societal and healthcare perspective. Economic evaluations of web-based self-management interventions among patients with chronic diseases are scarce, and mostly performed among patients with diabetes and cardiovascular disease.[10,11] The majority of interventions costs of web-based interventions are made during development, and the additional costs per extra user are relatively low.[12,13] Therefore, the cost-benefit relies on reaching and achieving large numbers of users.

The third research question 'Who is reached by web-based self-management interventions', was addressed in **Chapter 3** and **Chapter 6**. To gain insight into factors associated with eligibility for and participation in Oncokompas, a two-step inclusion method was used to recruit participants in the randomised controlled trial (RCT). Among the respondents of the survey on supportive care (step 1), 68% was eligible for using web-based self-management interventions, i.e. they had access to the internet and had an email address. This percentage seems low, when compared to the percentage of Dutch households with access to the internet access rate, which is estimated on >95% in 2019.[14] Some of the survey respondents indicated that they had access to the internet, but did not have a laptop or personal computer to use the internet. Others indicated that they did not have a personal e-mail address, which made them not eligible to participate in the study. Although an upward trend in internet access and use is seen in the last years,[15,16] it is also expected that there will remain a group of cancer survivors who will not be reached because of other reasons. In the second step, eligible survivors were invited to participate in the RCT on Oncokompas. In total, 45% agreed to participate in Oncokompas as part of the RCT. This indicates that 31% (45% of 68%) could potentially be reached by web-based self-management interventions in clinical practice, which is similar to other interventions among cancer survivors.[17–20] While factors such as age and health literacy were associated with eligibility (**Chapter 3**), and factors such as educational level and a higher belief in control of their health by powerful others were associated with participation, many other investigated factors such as HRQOL, time since diagnosis and other clinical factors were not associated. This suggests that it is not needed to screen for sociodemographic and clinical factors when offering Oncokompas in clinical practice. However, Oncokompas could especially be recommended to cancer survivors who benefit most from it, which are cancer survivors who are suffering from one or more symptoms. This was also emphasized by the reasons for not reaching and not using Oncokompas that were mentioned often; cancer survivors wanted to leave the period of being ill behind, did not experience symptom burden, or did not have supportive care needs (**Chapter 6**). These types of reasons are frequently seen in trials among cancer survivors.[17,18] Other reasons for not reaching cancer survivors included no time,

not fitting to personal situation and lacking skills to use such an intervention. Besides, reasons for not using Oncokompas were also that participants had no time, or that technical difficulties were present (e.g. problems with login procedure). This emphasizes the need for user-friendly applications, with simple login procedures, which do not take much time to use.

Strengths and limitations

A strength of this thesis is that a large RCT was conducted (n = 625) to evaluate the web-based self-management application Oncokompas. The study population of the RCT consisted of a broad population of cancer survivors with prevalent (breast cancer, colorectal cancer) and less prevalent (head and neck cancer and lymphoma) tumour types, men and women, solid and non-solid tumours, and short and long term cancer survivors (3 months to 5 years after treatment). The RCT performed in this thesis was judged as possibly the largest RCT of web-based self-management interventions reported, and therefore contributes to the literature on web-based self-management.[21] To the best of our knowledge, we are among the first who investigated the reach of a web-based self-management application among cancer survivors, and performed an economic evaluation. The strength of the cost-utility analyses is that we took both a societal and healthcare perspective into account, which provides a broad overview of costs that may be influenced by Oncokompas, and is interesting for healthcare policy makers and healthcare insurance companies. However, there are some limitations that should be borne in mind when interpreting the results of this thesis.

The participants of the RCT were performing relatively well at baseline, with most of the baseline scores in the upper 10-30% of the scale.[22] Within this well-performing group of cancer survivors, still an improvement in HRQOL and symptom burden was found in the intervention group, compared to the control group, although some of the differences are possibly not clinically relevant. Clinically relevant differences reflect whether the difference in PROM scores, really makes a meaningful difference for participants.[23,24] Effects on self-management interventions are often measured with PROMs, which are so-called 'soft' outcome measures, as self-management interventions do not have 'hard' clinical outcomes such as overall survival with medical interventions.[25] On HRQOL, the effect size was small (Cohen's d was 0.18 at 6 months follow-up), and on symptoms effect sizes ranged from small to large (Cohen's d ranged from 0.17 to 0.80 at 6 months follow-up), which is mainly explained by the high baseline scores, which does not leave much room for improvement. Although,

in studies on efficacy of web-based interventions or self-management interventions, large effect sizes are rarely found.[12,26–28] A common problem with web-based interventions is the low usage and adherence, limiting the efficacy.[29]

The power calculation performed before the study started was done to determine the required sample size in order to detect clinically relevant differences on the primary outcome (patient activation) between Oncokompas and usual survivorship care. The found effect on the outcome HRQOL should therefore be interpreted with caution, as this was a secondary outcome measure. Furthermore, many secondary outcomes were tested, and also secondary moderation analyses were performed. As these analyses were exploratory, no corrections were applied to the secondary analyses. Besides, this study is likely to be underpowered to detect differences in the cost-utility analyses. Therefore, the cost-utility analyses were performed with a probabilistic approach.[30]

A potential limitation regarding the reach is that we used 'willing to participate in a RCT on Oncokompas' as a proxy for 'being interested in the use of Oncokompas', while these measures might not correspond completely in daily clinical routine and practice. For instance, breast cancer survivors were more willing to participate in the RCT than other tumour types, but the actual usage rate of Oncokompas was the lowest compared to the other tumour types. In contrast, among head and neck cancer survivors, usage rate was the highest, but eligibility and participation rates were the lowest compared to the other tumour types. The study context in which Oncokompas was offered to cancer survivors, might have introduced selection bias, and the results might have been slightly different when offered in clinical practice. As mentioned before, the participants in the RCT were performing relatively well at baseline, with most of the baseline scores in the upper 10-30% of the scale (**Chapter 3**). Also, no symptom burden was among the most often mentioned reasons for not participating or not using Oncokompas (**Chapter 6**). Research on implementation and upscaling of Oncokompas is therefore recommended to see whether the effects remain when Oncokompas is part of routine care.

Drop-out is often an issue in studies on (web-based) interventions. Participants may drop-out because symptom burden is reduced or persist despite using the intervention, they do not like the intervention, or for other unknown reasons.[31] The drop-out rate in the RCT differed between the intervention and control condition, with 19% and 12% respectively at 6 months follow-up. Participants in the control

group might have been extra motivated to complete the follow-up assessments, because it was a wait-list control group, and they were told to get access to Oncokompas after completing the 6-months follow-up assessment. Participants in the intervention group might have experienced Oncokompas as too time consuming in addition to the time it took to complete the follow-up assessments, or Oncokompas did not meet expectations. Unfortunately, reasons for drop-out were not listed in this study.

Implications for clinical practice

With increasing numbers of cancer survivors, the need for sustainable, affordable cancer survivorship care is growing. It is important that cancer survivors have access to optimal supportive care, which is tailored to the individual. However, cancer survivors are often unaware of available supportive care options, and healthcare professionals have limited time and knowledge to refer to optimal supportive care. Web-based self-management interventions can be tailored to the individual user, when algorithms are used to link PROM scores to tailored content.[12] Fully automated interventions do not need health professionals to guide users through the intervention or to discuss the results, which might help to organize healthcare more efficiently. Access to evidence-based information is seen as an important part of supportive care.[32] Tailoring this evidence-based information to the individual cancer survivor is seen as an advantage for cancer survivors, as this makes the information directly applicable to their situation and needs.

The impact of web-based self-management interventions in clinical practice can be illustrated through the RE-AIM framework, with the factors Reach, Efficacy, Adoption, Implementation, Maintenance. This framework is developed to translate research results into clinical practice.[33] Within the RE-AIM framework reach and efficacy are both measured at an individual level. These two factors combined indicate the public health impact of a new intervention.[33,34] When an intervention has a high efficacy, but low reach, or a low efficacy but a high reach, the impact might be limited. From a public health perspective, however, even a small difference can have an impact across a large population.[12,35] Oncokompas does not reach all cancer survivors, and is mainly used by those who are relatively performing well, but Oncokompas can relieve the pressure on the healthcare. When Oncokompas is used by those who have the skills, or are relatively performing well but have some symptoms, it ensures that this group is not going to the healthcare professional or uses medical care when it is not

necessary. This leaves more time and attention for cancer survivors who are not reached by web-based self-management, or who need more complex care. Since the absolute number of cancer survivors are high,[12,36] and Oncokompas does not lead to increased cost from a societal as well as healthcare perspective, Oncokompas can therefore be a sustainable addition to usual cancer survivorship care.

Ideally, an intervention reaches the subgroup which also benefits most from the intervention, to maximize the impact. Besides offering Oncokompas to cancer survivors with high symptom burden, it may also be worthwhile to pay attention to health literacy. Health literacy is known to be an important factor in the optimal use of eHealth interventions,[37] and found to be associated with internet use.[38,39] In our research, health literacy was found to be associated with eligibility for web-based self-management interventions; cancer survivors with lower health literacy were less likely to be eligible. Health literacy was also found to be moderating the effect of Oncokompas on HRQOL; cancer survivors with high health literacy were found to benefit from Oncokompas in terms of HRQOL, while the intervention effect was limited among cancer survivors with lower health literacy. (**Chapter 3** and **Chapter 4**). When developing web-based interventions it is good to keep in mind that the subgroup of low-literate cancer survivors is less likely to be reached by and benefit from such interventions. This subgroup might benefit more from other types of interventions, e.g. face-to-face or group interventions. The content of Oncokompas, including the cut-off scores on PROMs for elevated and seriously elevated well-being risks, the information and advice, and the overview of healthcare options per topic can also be valuable for healthcare professionals in their clinical practice, as it can be used as guidance to support their patients during consultations, short and long after cancer treatment.

Within the RE-AIM framework, adoption and implementation are measured at setting level, in this case hospital level.[33] In a pilot study in the Netherlands, it was shown that 20 out of the 65 invited hospitals adopted Oncokompas (adoption rate 31%), i.e. they agreed to offer Oncokompas to cancer patients, before, during or after treatment. Of the 20 hospitals that adopted Oncokompas, 44 out of the 61 healthcare professionals who completed a questionnaire on implementation, indicated that Oncokompas was offered to their patients (implementation rate 72%).[40] Maintenance of the effect of Oncokompas in terms of efficacy, adoption and implementation in the longer term can be measured at an individual level and setting level,[33] and is topic of ongoing research.

Systematic reviews on the effect of web-based self-management interventions often have inconclusive results, as studies are heterogeneous because of the different types of interventions, and different outcome measures.[41–43] Different target populations, content, and delivery modes make that some interventions are more effective than others, but it is hard to untangle which part contributes specifically to the beneficial effect.[12] While other interventions are often developed targeting one specific tumour type (often high prevalent tumour types, such as breast cancer[44] or prostate cancer[45]), are developed focusing on one specific symptom, for instance fatigue,[46] or distress,[47,48] or are targeting lifestyle improvements, such as physical activity,[49] Oncokompas targets all tumour types with the cancer-generic domains, and contains a variety of topics within multiple quality of life domains. Of the 32 available cancer-generic topics in Oncokompas, the 20 most selected topics among users of Oncokompas did not differ much in absolute numbers. Therefore it can be assumed that the various number of topics is valuable in self-management of HRQOL and symptoms, also because of the wide range of symptoms that cancer survivors can experience.[50–53]

Oncokompas distinguishes from other web-based interventions that can be used for monitoring HRQOL, or interventions that provide information. In interventions that can be used to monitor HRQOL with PROMs, sometimes tailored feedback on PROM scores is provided, but often they do not refer to supportive care. These types of interventions are used as part of value-based healthcare and in routine care, for instance OncoQuest,[54] and CHESS.[55] While there is growing evidence that implementing PROMs in routine care improves communication between patients and healthcare providers and patient satisfaction,[56] the addition of tailored information and a personalised overview of suitable supportive care options in Oncokompas seems valuable for the individual cancer survivor. Effects of information-based interventions are variable,[57] and the information provided in these interventions is often generic. The added value of Oncokompas compared to these types of interventions might be that it provides tailored information on the symptoms or well-being risks the user is suffering from. In the Learn component, it outlines information on the specific (seriously) elevated well-being risks, by providing background information, indicating how many other cancer survivors suffer from the same problems or symptoms, but it also provides self-care advice and tips. The well-being overview in the Learn component gives insight in their own scores, and it might confirm their feelings, and with the information and self-help advice, users can make a start with reducing the symptom burden, or improve quality of life themselves. When necessary, the personalised overview of supportive care options in Act give insight into what interventions or healthcare options can be

used to (further) reduce symptom burden. While a considerably percentage (43%) of users did not use of the Act component, 44% of those who did not use the supportive care options in Act said that they did not use it, because the information in Learn was already sufficient. This suggest that not everyone needs the Act component. The tailored approach in Oncokompas seems therefore beneficial, compared to interventions that only provide generic information.

Oncokompas does not have an active therapy component, but instead refers to (web-based) interventions with an active therapy component, such as BREATH for breast cancer survivors,[58,59] LIVE for lymphoma patients,[19,60] and the Kanker Nazorg Wijzer (Cancer Aftercare Guide).[20,61] These types of interventions comprise active therapy components such as psychotherapy or (internet-based) cognitive behavioural therapy.[42,43,62,63] In Oncokompas users are supported in their self-management by providing a personalised overview of supportive care options which are tailored to the users' well-being risk (elevated or seriously elevated) and preferences (for instance online, individual or group interventions) in the Act component. The actual referral and use of the supportive care options need to be arranged by the cancer survivor itself, as it is a self-management intervention. As mentioned before, not everyone used the Act component, because they indicated that the information was already sufficient. This might suggest that those who used the Act component, are the ones with higher symptom burden. This is supported by the finding that head and neck cancer survivors had the most seriously elevated well-being scores and also the highest usage rates, while for instance breast cancer survivors had less seriously elevated well-being scores and also lower usage rates. This also may explain the limited effect of other interventions with an active therapy component, when offered in a general population that performs relatively well and does not have high levels of distress at baseline. Therefore, the various number of topics in Oncokompas seem valuable, because users can select the most relevant topic, and improve on that specific symptom.

eHealth interventions are often developed in a scientific context, but even when proven effective, they are often not easily accessible in clinical practice.[12,34,64] Oncokompas could be a good solution to provide access to these eHealth interventions. Supportive care options in the Act component in Oncokompas are tailored to the needs and preferences of users, and therefore can be used to match users with evidence-based interventions and improve their usage.

Recommendations

The studies presented in this thesis provide valuable knowledge on web-based self-management among cancer survivors, but also provide directions for further research. The efficacy, cost-utility and reach of Oncokompas has been comprehensively investigated. These results can be used for improving those factors, and thereby improve the impact of Oncokompas on cancer survivorship care. These results can also be used in the development of new web-based self-management interventions. Based on the findings in this thesis, the following recommendations can be made.

First, looking into how the effect of web-based self-management applications as Oncokompas can be improved is recommended. Self-management support can lead to increased engagement and thereby increase the effect of interventions.[65,66] More actively supporting cancer survivors might also improve their self-management skills.[67,68] Further research is needed on what type of support is best for cancer survivors, and whether online support or support in the form of a healthcare professional is most effective.

It is recommended to further investigate moderating factors on the effect of Oncokompas on HRQOL and symptoms. Adapting the intervention to those groups who benefit less from Oncokompas in its current format, might lead to an overall better intervention effect. Since positive effects were found on tumour-specific symptoms, developing more tumour-specific modules could be explored, especially for tumours with high symptom burden.

For efficacy as well as cost-utility it is recommended to see whether the effect is maintained or even better on the long-term, since this study has only evaluated the impact of the intervention until 6 months follow-up. It might be that the cost-saving potential of Oncokompas was not yet visible in the 6-months follow-up period that we used in this study, and also the effects on HRQOL and symptom burden might be different in the longer term. A budget impact analysis can be performed to provide insight in the financial impact of healthcare budgets, when it is implemented in clinical practice.[69] Cost-utility analyses can also be conducted with the cancer-specific EORTC QLU-C10D, instead of the generic EQ-5D; this might lead to a better insight into the QALYs gained by cancer survivors, which is more sensitive to cancer-specific symptoms.[70]

Usage of web-based self-management interventions need to be further investigated, and engagement needs to be improved. Web-based self-management applications are often complex interventions, due to the complexity of interacting components, involved behaviours, individual levels of the outcome at baseline, and tailoring.[71–73] Usage of those interventions is therefore difficult to measure, since it is complex to measure the dose-response using the intervention. Analysing system data, with a good framework is recommended to investigate usage patterns of complex web-based interventions.[74–76] Usage of Oncokompas might be improved by further tailoring information to the user, and adding persuasive elements, e.g. by encouraging a user to address only one or two topics at a time, and help them select the most important topics at that time.[12,29,77] Usage might also be improved by gamification, in which gaming elements are applied to a non-gaming context.[78] Gaming elements can motivate users to change their health behaviours and stay engaged with the interventions,[78] and it can be used to make complex health information interactive and attracting,[72,78–80] leading to better usage rates and improved efficacy.[81,82] Furthermore, in Oncokompas, automated reminders are sent every two months to encourage repeated use. More frequent or personal reminders might help increase adherence and treatment response of interventions.[29]

Web-based self-management interventions such as Oncokompas might also be valuable for other populations than cancer survivors. Patients with incurable cancer might benefit from web-based self-management, as this might support them in finding and obtaining optimal palliative care. RCTs on the efficacy and cost-utility of a version of Oncokompas among patients with incurable cancer, and a version for their partners are currently ongoing.[83,84]

Besides efficacy, cost-utility and reach, also other aspects of evaluation play a role in the translation of research into practice. Evaluation of web-based self-management interventions needs to be conducted continuously, by evaluating, adapting and updating content and features, and implementing and disseminating new versions.[85]

CONCLUSION

This thesis provides evidence on the efficacy, cost-utility and reach of web-based self-management among cancer survivors. It is estimated that one third of cancer survivors is not eligible for the use of web-based self-management, due to not having internet access or email. It is estimated that half of the eligible survivors is willing to participate in (research on) web-based self-management interventions. Among those who participated, Oncokompas had a small effect on HRQOL, and small to large effects on several tumour-specific symptoms, but it did not improve cancer survivors' knowledge, skills and confidence for self-management, or other secondary outcomes such as self-efficacy and unmet supportive care needs. Oncokompas was most effective in reducing symptom burden in those with higher symptom burden, and in improving HRQOL in those with low to moderate self-efficacy, and in those with high personal control, and high health literacy. From a societal and healthcare perspective, Oncokompas was found to be equally effective in terms of QALYs, and not more expensive than usual cancer survivorship care. Therefore, it is recommended to implement Oncokompas, as it is likely to be a sustainable and affordable addition to high quality cancer survivorship care.

REFERENCES

1. Rademakers J, Nijman J, Van Der Hoek L, Heijmans M, Rijken M. Measuring patient activation in the Netherlands: Translation and validation of the American short form Patient Activation Measure (PAM13). BMC Public Health 2012; 12: 577.

2. Rademakers J, Maindal HT, Steinsbekk A, Gensichen J, Brenk-Franz K, Hendriks M. Patient activation in Europe: an international comparison of psychometric properties and patients' scores on the short form Patient Activation Measure (PAM-13). BMC Health Serv Res 2016; 16: 1–7.

3. Linden A. Estimating Measurement Error of the Patient Activation Measure for Respondents with Partially Missing Data. Biomed Res Int 2015; 2015: 1–7.

4. 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 (Madr) 2018; 57: 924–34.

5. Struwe LA, Schmaderer MS, Zimmerman L. Changes in Patient Activation in a Self-Management Intervention. West J Nurs Res 2020; 42: 194–200.

6. Roberts NJ, Kidd L, Dougall N, Patel IS, McNarry S, Nixon C. Measuring patient activation: The utility of the Patient Activation Measure within a UK context—Results from four exemplar studies and potential future applications. Patient Educ Couns 2016; 99: 1739–46.

7. Fiszer C, Dolbeault S, Sultan S, Brédart A. Prevalence, intensity, and predictors of the supportive care needs of women diagnosed with breast cancer: A systematic review. Psychooncology. 2014; 23: 361–74.

8. Boyes AW, Girgis A, D'Este C, Zucca AC. Prevalence and correlates of cancer survivors' supportive care needs 6 months after diagnosis: a population-based cross-sectional study. BMC Cancer 2012; 12: 150.

9. Armes J, Crowe M, Colbourne L, et al. Patients' supportive care needs beyond the end of cancer treatment: A prospective, longitudinal survey. J Clin Oncol 2009; 27: 6172–9.

10. Sanyal C, Stolee P, Juzwishin D, Husereau D. Economic evaluations of eHealth technologies: A systematic review. PLoS One. 2018; 13: e0198112.

11. Michaud TL, Zhou J, McCarthy MA, Siahpush M, Su D. Costs of home-based telemedicine programs: a systematic review. Int J Technol Assess Health Care 2018; 34: 400–9.

12. Murray E. Web-based interventions for behavior change and self-management: Potential, pitfalls, and progress. J Med Internet Res 2012; 14: 1(2):e3.

13. Tate DF, Finkelstein EA, Khavjou O, Gustafson A. Cost effectiveness of internet interventions: Review and recommendations. Ann. Behav. Med. 2009; 38: 40–5.

14. Centraal Bureau voor de Statistiek. Households–connection to the internet. https://opendata.cbs.nl/statline/#/CBS/nl/dataset/83291NED/table?ts=1560934345782 (accessed Aug 8, 2020).

15. Jiang S, Hong YA, Liu PL. Trends of online patient-provider communication among cancer survivors from 2008 to 2017: a digital divide perspective. J Cancer Surviv 2019; 13: 197–204.

16. van Eenbergen MCHJ, Vromans RD, Boll D, et al. Changes in internet use and wishes of cancer survivors: A comparison between 2005 and 2017. Cancer 2019; 126: 408–15.

17. Kampshoff CS, Mechelen W, Schep G, et al. Participation in and adherence to physical exercise after completion of primary cancer treatment. Int J Behav Nutr Phys Act 2016; 13: 100.

18. van Waart H, van Harten WH, Buffart LM, Sonke GS, Stuiver MM, Aaronson NK. Why do patients choose (not) to participate in an exercise trial during adjuvant chemotherapy for breast cancer? Psychooncology 2016; 25: 964–70.

19. Arts LPJ, Oerlemans S, Posthuma EFM, et al. Web-Based Self-Management for Patients With Lymphoma: Assessment of the Reach of Intervention of a Randomized Controlled Trial. J Med Internet Res 2020; 22:

e17018.

20. Willems RA, Bolman CAW, Mesters I, Kanera IM, Beaulen AAJM, Lechner L. Short-term effectiveness of a web-based tailored intervention for cancer survivors on quality of life, anxiety, depression, and fatigue: randomized controlled trial. Psychooncology 2017; 26: 222–30.

21. Girgis A. The role of self-management in cancer survivorship care. Lancet Oncol 2020; 21: 8–9.

22. van der Hout A, van Uden-Kraan CF, Holtmaat K, et al. Role of eHealth application Oncokompas in supporting self-management of symptoms and health-related quality of life in cancer survivors: a randomised, controlled trial. Lancet Oncol 2020; 21: 80–94.

23. Wyrwich KW, Nienaber NA, Tierney WM, Wolinsky FD. Linking Clinical Relevance and Statistical Significance in Evaluating Intra-Individual Changes in Health-Related Quality of Life. Med Care 1999; 37: 469–78.

24. Norman GR, Sloan JA, Wyrwich KW. Interpretation of changes in health-related quality of life the remarkable universality of half a standard deviation. Med Care 2003; 41: 582–92.

25. Baker TB, Gustafson DH, Shaw B, et al. Relevance of CONSORT reporting criteria for research on eHealth interventions. Patient Educ Couns 2010; 81: S77–86.

26. Cuthbert CA, Farragher JF, Hemmelgarn BR, Ding Q, McKinnon GP, Cheung WY. Self-management interventions for cancer survivors: A systematic review and evaluation of intervention content and theories. Psychooncology 2019; 28: 2119–40.

27. Webb TL, Joseph J, Yardley L, Michie S. Using the Internet to promote health behavior change: A systematic review and meta-analysis of the impact of theoretical basis, use of behavior change techniques, and mode of delivery on efficacy. J Med Internet Res 2010; 12: e4.

28. Sieverink F, Kelders SM, Gemert-Pijnen V. Clarifying the concept of adherence to ehealth technology: Systematic review on when usage becomes adherence. J Med Internet Res 2017; 19: e402.

29. Kelders SM, Kok RN, Ossebaard HC, Van Gemert-Pijnen JEWC. Persuasive system design does matter: A systematic review of adherence to web-based interventions. J Med Internet Res 2012; 14: e152.

30. Drummond M, Sculpher M, Torrance G, O'Brien B SG. Methods for the Economic Evaluation of Health Care Programmes, 3rd edn. Oxford: Oxford Univ Press, 2005.

31. Crutzen R, Viechtbauer W, Spigt M, Kotz D. Differential attrition in health behaviour change trials: A systematic review and meta-analysis. Psychol Health 2015; 30: 122–34.

32. Harrison JD, Young JM, Price MA, Butow PN, Solomon MJ. What are the unmet supportive care needs of people with cancer? A systematic review. Support Care Cancer 2009; 17: 1117–28.

33. Glasgow RE, Vogt TM, Boles SM. Evaluating the public health impact of health promotion interventions: The RE-AIM framework. Am J Public Health 1999; 89: 1322–7.

34. Glasgow RE. eHealth evaluation and dissemination research. Am J Prev Med 2007; 32: S119-26.

35. Rose G. The Determinants of Individual Cases Sick individuals and sick populations. Int J Epidemiol 2001; 30: 427–32.

36. Integraal Kankercentrum Nederland (IKNL). Cijfers over kanker. https://www.cijfersoverkanker.nl (accessed May 22, 2020).

37. Kim H, Xie B. Health literacy in the eHealth era: A systematic review of the literature. Patient Educ. Couns. 2017; 100: 1073–82.

38. Estacio EV, Whittle R, Protheroe J. The digital divide: Examining socio-demographic factors associated with health literacy, access and use of internet to seek health information. J Health Psychol 2019; 24: 1668–75.

39. Aydın GÖ, Kaya N, Turan N. The Role of Health Literacy in Access to Online Health Information. Procedia - Soc Behav Sci 2015; 195: 1683–7.

40. de Wit LM, 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.

41. 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.

42. Kim SH, Kim K, Mayer DK. Self-management intervention for adult cancer survivors after treatment: A systematic review and meta-Analysis. Oncol. Nurs. Forum. 2017; 44: 719–28.

43. 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.

44. Triberti S, Savioni L, Sebri V, Pravettoni G. eHealth for improving quality of life in breast cancer patients: A systematic review. Cancer Treat. Rev. 2019; 74: 1–14.

45. 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.

46. Foster C, Grimmett C, May CM, et al. A web-based intervention (RESTORE) to support self-management of cancer-related fatigue following primary cancer treatment: a multi-centre proof of concept randomised controlled trial. Support Care Cancer 2016; 24: 2445–53.

47. Krebber AMH, Jansen F, Witte BI, et al. Stepped care targeting psychological distress in head and neck cancer and lung cancer patients: A randomized, controlled trial. Ann Oncol 2016; 27: 1754–60.

48. Braamse AMJ, van Meijel B, Visser OJ, et al. A randomized clinical trial on the effectiveness of an intervention to treat psychological distress and improve quality of life after autologous stem cell transplantation. Ann Hematol 2016; 95: 105–14.

49. Kampshoff CS, Chinapaw MJM, Brug J, et al. Randomized controlled trial of the effects of high intensity and low-to-moderate intensity exercise on physical fitness and fatigue in cancer survivors: Results of the Resistance and Endurance exercise After ChemoTherapy (REACT) study. BMC Med 2015; 13: 275.

50. Aaronson NK, Mattioli V, Minton O, et al. Beyond treatment - Psychosocial and behavioural issues in cancer survivorship research and practice. Eur J Cancer Suppl 2014; 12: 54–64.

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

52. Given CW, Given BA. Symptom management and psychosocial outcomes following cancer. Semin Oncol 2013; 40: 774–83.

53. Stein KD, Syrjala KL, Andrykowski MA. Physical and psychological long-term and late effects of cancer. Cancer 2008; 112: 2577–92.

54. Duman-Lubberding S, van Uden-Kraan CF, Jansen F, et al. Durable usage of patient-reported outcome measures in clinical practice to monitor health-related quality of life in head and neck cancer patients. Support Care Cancer 2017; 25: 3775–83.

55. McTavish FM, Gustafson DH, Owens BH, et al. CHESS: An interactive computer system for women with breast cancer piloted with an underserved population. J Ambul Care Manage 1995; 18: 35–41.

56. Chen J, Ou L, Hollis SJ. A systematic review of the impact of routine collection of patient reported outcome measures on patients, providers and health organisations in an oncologic setting. BMC Health Serv Res 2013; 13: 211.

57. White V, Farrelly A, Pitcher M, Hill D. Does access to an information-based, breast cancer specific website help to reduce distress in young women with breast cancer? Results from a randomised trial. Eur J Cancer Care (Engl) 2018; 27: e12897.

58. van Den Berg SW, Gielissen MFM, Custers JAE, Van Der Graaf WTA, Ottevanger PB, Prins JB. BREATH: Web-based self-management for psychological adjustment after primary breast cancer-results of a

multicenter randomized controlled trial. J Clin Oncol 2015; 33: 2763–71.

59. 59 Van Den Berg SW, Peters EJ, Kraaijeveld JF, Gielissen MFM, 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: e170.

60. Arts LPJ, van de Poll-Franse L V., van den Berg SW, et al. 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. Trials 2017; 18: 199.

61. Willems RA, Bolman CAWA, Mesters I, Kanera IM, Beaulen AAAJM, Lechner L. The Kanker Nazorg Wijzer (Cancer Aftercare Guide) protocol: the systematic development of a web-based computer tailored intervention providing psychosocial and lifestyle support for cancer survivors. BMC Cancer 2015; 15: 580.

62. Atema V, Van Leeuwen M, Kieffer JM, et al. Efficacy of internet-based cognitive behavioral therapy for treatment-induced menopausal symptoms in breast cancer survivors: Results of a randomized controlled trial. J Clin Oncol 2019; 37: 809–22.

63. van Der Spek N, Vos J, Van Uden-Kraan CF, et al. Efficacy of meaning-centered group psychotherapy for cancer survivors: A randomized controlled trial. Psychol Med 2017; 47: 1990–2001.

64. Harvey J, Dopson S, McManus RJ, Powell J. Factors influencing the adoption of self-management solutions: An interpretive synthesis of the literature on stakeholder experiences. Implement. Sci. 2015; 10: 159.

65. Jordan JE, Briggs AM, Brand CA, Osborne RH. Enhancing patient engagement in chronic disease self-management support initiatives in Australia: the need for an integrated approach. Med J Aust 2008; 189: S9–13.

66. Sabharwal A, Fields S, Hilliard ME, DeSalvo DJ. Digital technologies to support behavior change: challenges and opportunities. In: Klonoff, DC, Kerr D, Mulvaney SA, eds. Diabetes Digital Health. Elsevier, 2020: 37–50.

67. Alvarez C, Greene J, Hibbard J, Overton V. The role of primary care providers in patient activation and engagement in self-management: A cross-sectional analysis. BMC Health Serv Res 2016; 16: 85.

68. McCusker J, Lambert SD, Haggerty J, Yaffe MJ, Belzile E, Ciampi A. Self-management support in primary care is associated with improvement in patient activation. Patient Educ Couns 2019; 102: 571–7.

69. Castañeda-Orjuela C, García-Molina M, De la Hoz-Restrepo F. Is There Something Else Beyond Cost-Effectiveness Analysis for Public Health Decision Making? Value Heal Reg Issues 2020; 23: 1–5.

70. King MT, Costa DSJ, Aaronson NK, et al. QLU-C10D: a health state classification system for a multi-attribute utility measure based on the EORTC QLQ-C30. Qual Life Res 2016; 25: 625–36.

71. Craig P, Dieppe P, Macintyre S, Mitchie S, Nazareth I, Petticrew M. Developing and evaluating complex interventions: The new Medical Research Council guidance. BMJ. 2008; 337: 979–83.

72. Araújo-Soares V, Hankonen N, Presseau J, Rodrigues A, Sniehotta FF. Developing Behavior Change Interventions for Self-Management in Chronic Illness: An Integrative Overview. Eur. Psychol. 2019; 24: 7–25.

73. Moore GF, Evans RE, Hawkins J, et al. From complex social interventions to interventions in complex social systems: Future directions and unresolved questions for intervention development and evaluation. Evaluation 2019; 25: 23–45.

74. Sieverink F, Kelders S, Poel M, van Gemert-Pijnen L. Opening the Black Box of Electronic Health: Collecting, Analyzing, and Interpreting Log Data. JMIR Res Protoc 2017; 6: e156.

75. Miller S, Ainsworth B, Yardley L, et al. A framework for analyzing and measuring usage and engagement data (AMUSED) in digital interventions: Viewpoint. J Med Internet Res 2019; 21: e10966.

76. Short CE, DeSmet A, Woods C, et al. Measuring engagement in eHealth and mHealth behavior change interventions: Viewpoint of methodologies. J. Med. Internet Res. 2018; 20: e292.

77. Bernat JK, Wittman DA, Hawley ST, et al. Symptom burden and information needs in prostate cancer survivors: a case for tailored long-term survivorship care. BJU Int 2016; 118: 372–8.

78. Sardi L, Idri A, Fernández-Alemán JL. A systematic review of gamification in e-Health. J Biomed Inform 2017; 71: 31–48.

79. Perski O, Blandford A, West R, Michie S. Conceptualising engagement with digital behaviour change interventions: a systematic review using principles from critical interpretive synthesis. Transl Behav Med 2017; 7: 254–67.

80. Kelders SM, T. Bohlmeijer E, Van Gemert-Pijnen JEWC. Participants, usage, and use patterns of a web-based intervention for the prevention of depression within a randomized controlled trial. J Med Internet Res 2013; 15: e172.

81. Donkin L, Christensen H, Naismith SL, Neal B, Hickie IB, Glozier N. A systematic review of the impact of adherence on the effectiveness of e-therapies. J Med Internet Res 2011; 13: e52.

82. Ludden GDS, Van Rompay TJL, Kelders SM, Van Gemert-Pijnen JEWC. How to increase reach and adherence of web-based interventions: A design research viewpoint. J Med Internet Res 2015; 17: e172.

83. Schuit AS, Holtmaat K, Hooghiemstra N, et al. Efficacy and cost-utility of the eHealth application 'Oncokompas', supporting patients with incurable cancer in finding optimal palliative care, tailored to their quality of life and personal preferences: A study protocol of a randomized controlled trial. BMC Palliat Care 2019; 18: 85.

84. Schuit AS, Holtmaat K, Hooghiemstra N, et al. Efficacy and cost-utility of the eHealth self-management application 'Oncokompas', helping partners of patients with incurable cancer to identify their unmet supportive care needs and to take actions to meet their needs: A study protocol of a randomized controlled trial. Trials 2020; 21: 124.

85. Catwell L, Sheikh A. Evaluating eHealth interventions: The need for continuous systemic evaluation. PLoS Med 2009; 6: e1000126.

SUMMARY

Chapter 1 presents the general introduction of this thesis. First, common problems among cancer survivors during cancer survivorship are described, as well as how data from patient reported outcome measures (PROMs) can be used to improve cancer survivorship care. Second, the importance of supportive care is emphasized, and how it seen as an integral part of quality cancer treatment. In addition, it is described how self-management interventions empower cancer survivors to achieve optimal health and well-being. Special attention is paid to web-based self-management interventions, which can be used to tailor content to the individual user. Furthermore, the background and development process of the web-based self-management application Oncokompas is described in this chapter. Oncokompas was developed with the aim to support cancer survivors in self-management by monitoring health-related quality of life (HRQOL) and cancer-generic and tumour-specific symptoms, providing feedback and information on their personal scores, as well as a personalized overview of supportive care options. The aim of this thesis was to investigate the web-based self-management application Oncokompas among cancer survivors, in terms of efficacy, cost-utility, and reach.

The **Intermezzo** presents a visual overview of Oncokompas, with screenshots of the application. Oncokompas consists of three components: Measure, Learn, and Act. In the component Measure, users complete PROMs on the topics they selected. In the component Learn feedback on their PROM scores is given by means of a 3-colour system: green (no elevated well-being risks), orange (elevated well-being risks), and red (seriously elevated well-being risks). Users also receive tailored information and comprehensive self-care advice. In the component Act, a personalised overview of supportive care options is provided, based on users' PROM scores and expressed preferences.

Chapter 2 presents the study protocol of the randomised controlled trial (RCT). The aim of the proposed study was to investigate the efficacy, cost-utility and reach of Oncokompas. Survivors diagnosed with head and neck cancer, colorectal cancer, or breast cancer, or (non-)Hodgkin lymphoma, who were treated with curative intent 3 months to 5 years ago were included via their (former) treating physician. Participants were randomised to either the intervention group, in which they had direct access to Oncokompas, or the wait-list control group, with usual supportive care during the study, and access to Oncokompas after 6 months. The assessments were at baseline,

1-week post-intervention, and at 3- and 6-months follow-up. The primary outcome was patient activation, i.e. knowledge, skills and confidence for self-management, and was measured with the Patient Activation Measure (PAM). Secondary outcomes included HRQOL and symptoms, self-efficacy, personal control, mental adjustment to cancer, supportive care needs, and perceived patient-physician interaction. Cost outcomes included quality-adjusted life years (QALYs), and costs.

Chapter 3 describes the results of the RCT on the efficacy of Oncokompas. In total, 625 cancer survivors were randomised to the intervention group (n = 320) or control group (n = 305). Linear mixed model analyses (intention-to-treat) showed that the primary outcome patient activation was not statistically significant different between the intervention and control group over time. Oncokompas did improve the course of secondary outcomes HRQOL, and tumour-specific symptoms in head and neck cancer, and colorectal cancer and non-Hodgkin lymphoma survivors over time. No effects were found on the other secondary outcomes self-efficacy, personal control, mental adjustment to cancer and perceived efficacy in patient-physician interaction. This chapter concluded that Oncokompas may be effective amongst cancer survivors to improve HRQOL and reduce the burden of several tumour-specific symptoms.

Chapter 4 further explored these results by investigating for which subgroups of cancer survivors Oncokompas is especially effective in terms of HRQOL, and whether there are subgroups for which Oncokompas improves patient activation. These secondary analyses suggested that Oncokompas seems to be more effective in cancer survivors with low to moderate self-efficacy, higher personal control, and higher health literacy in terms of HRQOL. Also, cancer survivors with some degree of symptom burden at baseline seems to benefit from Oncokompas, and the intervention effect on head and neck cancer-specific symptoms pain in the mouth, social eating, swallowing, coughing, and trismus, and the colorectal cancer-specific symptom weight, became larger when the symptom burden was higher. No specific subgroups were identified that benefit from Oncokompas in terms of patient activation.

Chapter 5 presents the cost-utility analyses of Oncokompas compared to usual cancer survivorship care. Cost-utility analyses were performed from a societal perspective, including direct medical costs (costs of healthcare resource use and medication), direct non-medical costs (traveling to and parking at healthcare services, costs of informal care, and support groups), indirect non-medical costs (costs

due to absence from paid work, and productivity loss), and intervention costs. Mean cumulative costs and QALYs were compared for the intervention and control group. The incremental costs were –€163 (95% CI: –665 to 326), and incremental QALYs were 0.0017 (95% CI, –0.0121 to 0.0155) in the intervention group compared to the control group. The probability that, compared to usual cancer survivorship care, Oncokompas is more effective was 60%, less costly 73%, and both more effective and less costly 47%. Sensitivity analyses showed that incremental costs vary between –€40 and €69, and incremental QALYs vary between –0.0023 and –0.0057. This chapter concluded that Oncokompas is likely to be equally effective on utilities, and not more expensive than usual cancer survivorship care.

Chapter 6 describes the reach and usage of Oncokompas in more detail and elaborates on the results of the reach and usage described in **Chapter 3**. Of the first 655 respondents of the RCT, 68% was eligible to use Oncokompas (they had access to the internet and an e-mail address). Of the 444 eligible cancer survivors, 201 (45%) agreed to participate in the RCT on Oncokompas. Factors associated with eligibility were male sex, younger age, higher health literacy, higher positive adjustment to cancer, no unmet needs regarding health system information and supportive care, and tumour type. Factors associated with participation were a medium education level, unmet supportive care needs for sexual problems, and a higher belief in control of health by powerful others. The main reasons that cancer survivors were not reached by Oncokompas were no internet access, wanting to leave the period of being ill behind, no symptom burden, or lack of internet skills. The main reasons for not using Oncokompas were that no symptom burden was experienced, or lack of time. Users selected many cancer-generic and tumour-specific topics to address in Oncokompas. Oncokompas was generally positively evaluated among users, and most users indicated that they want to use Oncokompas again.

Chapter 7 provides the general discussion of this thesis, in which the results of all chapters were combined and discussed. It also includes the strengths and limitations, implications for clinical practice, recommendations for further research and improvements, and the conclusion. The findings of this thesis are that Oncokompas has positive effects on HRQOL and symptom burden, but it did not improve cancer survivors' knowledge, skills and confidence for self-management. In addition, it was shown that Oncokompas is not more expensive than usual cancer survivorship care. The main study limitations are that the RCT participants were performing relatively well at baseline, and that many

analyses were performed for which statistical power was lacking. The efficacy, cost-utility and reach of Oncokompas has been comprehensively investigated in this thesis, and based on these findings, it is recommended to implement Oncokompas as it is likely to be a sustainable and affordable addition to high quality cancer survivorship care.

SAMENVATTING

Hoofdstuk 1 betreft de algemene inleiding van dit proefschrift. Allereerst worden veelvoorkomende problemen bij overlevers van kanker in de periode na de behandeling beschreven, evenals hoe scores op patiënt gerapporteerde uitkomstmaten (PROMs) kunnen worden gebruikt om de nazorg na kanker te ondersteunen. Ten tweede wordt het belang van deze ondersteunende zorg benadrukt als een integraal onderdeel van een kwalitatief goede nazorg bij kanker. Daarnaast wordt beschreven hoe zelfmanagementinterventies overlevers van kanker in staat stellen om optimale gezondheid en welzijn te bereiken. Er wordt specifieke aandacht besteed aan online zelfmanagement interventies, die kunnen worden gebruikt om inhoud op maat aan te bieden, afgestemd op de individuele gebruiker. Verder wordt in dit hoofdstuk de achtergrond en ontwikkeling beschreven van de online zelfmanagement applicatie Oncokompas. Oncokompas is ontwikkeld met als doel om overlevers van kanker te ondersteunen bij het zelfstandig omgaan met klachten die een negatief effect kunnen hebben op hun kwaliteit van leven. Oncokompas ondersteunt hen bij het monitoren van gezondheids-gerelateerde kwaliteit van leven en kanker generieke en tumor specifieke symptomen, geeft feedback en informatie op hun persoonlijke scores evenals een gepersonaliseerd overzicht van opties voor ondersteunende zorg. Het doel van dit proefschrift was om de online zelfmanagement applicatie Oncokompas te onderzoeken bij overlevers van kanker, voor wat betreft de effectiviteit, kosteneffectiviteit en het bereik.

Het **Intermezzo** geeft een visueel overzicht van Oncokompas met screenshots van de applicatie. Oncokompas bevat 3 componenten: Meten, Weten en Doen. In de eerste component Meten vullen gebruikers PROMs in op onderwerpen die ze hebben gekozen. In de tweede component Leren wordt er feedback gegeven op hun PROM-scores door middel van een 3 kleurensysteem: groen (geen verhoogd gezondheidsrisico), oranje (verhoogd gezondheidsrisico) en rood (zeer verhoogd gezondheidsrisico). Gebruikers ontvangen tevens informatie op maat en uitgebreide zelfhulp adviezen. In de derde component Doen krijgen gebruikers een gepersonaliseerd overzicht van opties voor ondersteunende zorg dat is gebaseerd op hun PROM-scores en aangegeven voorkeuren.

Hoofdstuk 2 beschrijft het studieprotocol van een gerandomiseerde, gecontroleerde studie (RCT). Het doel van deze studie was om de effectiviteit, kosteneffectiviteit en het bereik van Oncokompas

te onderzoeken. Overlevers van kanker konden deelnemen aan de RCT als ze gediagnosticeerd waren met hoofd-hals kanker, colorectaal kanker, borstkanker of (non-)Hodgkin lymfoom en 3 maanden tot 5 jaar geleden waren behandeld met een curatieve opzet. Deelnemers werden gerandomiseerd in de interventiegroep, waar men direct toegang tot Oncokompas kreeg, of de wachtlijst controlegroep, waarin men gebruikelijke ondersteunende zorg kreeg tijdens de studie en toegang tot Oncokompas na 6 maanden. De metingen vonden plaats op baseline (bij de start van de studie) en na 1 week en 3 en 6 maanden follow up. De primaire uitkomstmaat was patiëntactivatie (kennis, vaardigheden en vertrouwen in zelfmanagement) en werd gemeten met de Patient Activation Measure (PAM). Secundaire uitkomstmaten waren kwaliteit van leven en symptomen, zelfeffectiviteit, ervaren regie, mentale aanpassing aan kanker, behoefte aan ondersteunende zorg en de ervaren interactie tussen patiënt en arts. Uitkomsten op het gebied van kosten waren kwaliteit-gecorrigeerde levensjaren (QALY's) en kosten.

Hoofdstuk 3 beschrijft de resultaten van de RCT voor wat betreft de effectiviteit van Oncokompas. In totaal werden 625 overlevers van kanker gerandomiseerd in de interventiegroep (n = 320) of de controlegroep (n = 305). Linear mixed model analyses (intention-to-treat) lieten zien dat het beloop van de scores op de PAM over tijd niet statistisch significant verschillend waren tussen de interventie- en controlegroep. Wel was het beloop van de secundaire uitkomstmaten kwaliteit van leven en een aantal tumor specifieke symptomen bij overlevers van hoofd-halskanker, colorectaal kanker en non-Hodgkin lymfoom beter in de interventiegroep, vergeleken met de controlegroep. Er werd geen effect gevonden op de andere secundaire uitkomstmaten zelfeffectiviteit, ervaren regie, mentale aanpassing aan kanker, behoefte aan ondersteunende zorg en ervaren interactie tussen patiënt en arts. De conclusie in dit hoofdstuk was dat Oncokompas effectief is bij overlevers van kanker om hun kwaliteit van leven te verbeteren en om verschillende tumor specifieke symptomen te verminderen.

Hoofdstuk 4 gaat verder in op deze resultaten door te onderzoeken voor welke subgroepen van overlevers van kanker Oncokompas vooral effectief was voor wat betreft kwaliteit van leven en symptomen en of er subgroepen zijn die wel baat hebben bij Oncokompas voor wat betreft patiëntactivatie. Wat betreft kwaliteit van leven lijkt Oncokompas effectiever te zijn voor mensen met een lagere zelfeffectiviteit, voor mensen met meer ervaren regie en voor mensen met betere gezondheidsvaardigheden. Ook lijken mensen die meer last hadden van symptomen voorafgaand aan het gebruik van Oncokompas meer te profiteren van Oncokompas. Dit gold voor de symptomen

pijn in de mond, eten in gezelschap, slikken, hoesten en beperkte mondopening (hoofd-halskanker) en gewicht (colorectaal kanker). Er werden geen subgroepen geïdentificeerd die baat hadden bij Oncokompas voor wat betreft patiëntactivatie.

Hoofdstuk 5 presenteert het onderzoek naar de kosteneffectiviteit van Oncokompas vergeleken met standaard nazorg. Kostenutiliteit analyses werden uitgevoerd vanuit een maatschappelijk perspectief, met daarin meegenomen directe medische kosten (kosten van het gebruik van zorg en medicatie), directe niet-medische kosten (kosten van het reizen naar en parkeren bij zorginstellingen, informele zorg, steungroepen), indirecte niet-medische zorg (kosten door ziekteverzuim of verminderde productiviteit bij betaald werk) en interventiekosten. De gemiddelde cumulatieve kosten en QALY's werden vergeleken voor de interventie- en controlegroep. De incrementele kosten waren −€163 (95% BI: −665 tot 326) en incrementele QALY's waren 0.0017 (95% BI, −0.0121 tot 0.0155). De waarschijnlijkheid dat Oncokompas effectiever is dan standaard nazorg was 60%, dat het minder kost was 73% en dat het zowel effectiever is en minder kost was 47%. Sensitiviteitsanalyses lieten zien dat de incrementele kosten varieerden tussen −€40 en €69 en dat de incrementele QALY's varieerden tussen −0.0023 en −0.0057. De conclusie in dit hoofdstuk was dat Oncokompas waarschijnlijk even effectief is in termen van utiliteiten en niet duurder is dan standaard nazorg.

Hoofdstuk 6 beschrijft het bereik en gebruik van Oncokompas in meer detail en gaat verder in op de resultaten van bereik en gebruik, beschreven in **Hoofdstuk 3**. Van de eerste 655 respondenten hadden 444 (68%) toegang tot internet en een e-mailadres, waarvan er 201 (45%) wilden deelnemen aan de RCT. Factoren die geassocieerd waren met het hebben van internet en e-mailadres waren het mannelijke geslacht, jongere leeftijd, betere gezondheidsvaardigheden, betere positieve aanpassing aan kanker, geen onvervulde behoeften met betrekking tot informatie over het gezondheidssysteem en ondersteunende zorg en het type kanker. Factoren die geassocieerd waren met deelname aan de RCT waren een middelbaar opleidingsniveau, onvervulde behoefte met betrekking tot seksuele problemen en een hoger vertrouwen in de controle van hun gezondheid door invloedrijke anderen. De belangrijkste redenen dat mensen niet bereikt werden door Oncokompas waren geen internet toegang, de behoefte om de periode van ziek zijn achter zich te laten, geen last van symptomen of onvoldoende internetvaardigheden. De belangrijkste redenen dat mensen Oncokompas niet gebruikten waren dat mensen geen last hadden van symptomen of een gebrek aan tijd. Het onderzoek naar het gebruik van Oncokompas liet zien dat mensen een groot aantal onderwerpen

kozen. Dit betroffen zowel kanker generieke als tumor specifieke onderwerpen. Oncokompas werd over het algemeen goed beoordeeld en de meeste gebruikers gaven aan dat ze Oncokompas nogmaals wilden gebruiken.

Hoofdstuk 7 betreft de algemene discussie van dit proefschrift en beschrijft de belangrijkste bevindingen, beperkingen, implicaties en conclusie van dit proefschrift. De uitkomsten van dit proefschrift zijn dat Oncokompas positieve effecten heeft op kwaliteit van leven en symptomen, maar het niet de kennis, vaardigheden en zelfvertrouwen in zelfmanagement verbeterde. Daarnaast liet de economische evaluatie zien dat Oncokompas niet duurder is dan de standaard nazorg na kanker. De belangrijkste beperkingen van dit proefschrift waren dat de deelnemers aan de RCT relatief goed presteerden bij aanvang van de studie en dat er veel analyses zijn uitgevoerd waarvoor statistische power ontbrak. De effectiviteit, kosteneffectiviteit en het bereik van Oncokompas is uitgebreid onderzocht in dit proefschrift. Op basis van de bevindingen wordt er aanbevolen om Oncokompas te implementeren, omdat het waarschijnlijk een duurzame en betaalbare aanvulling zal zijn op kwalitatief goede nazorg na kanker.

DANKWOORD

"Who we travel with is as important as where we are headed" - Tim Garrety (Ventura)

De afgelopen jaren hebben veel mensen een bijdrage geleverd aan dit proefschrift. Ik wil graag **iedereen** daarvoor bedanken en in het bijzonder de volgende personen.

Als eerste wil ik de **deelnemers aan het Oncokompas onderzoek** bedanken. Zonder jullie inzet, tijd en bereidheid om de vragenlijsten in te vullen was dit proefschrift er niet geweest. De persoonlijke verhalen die jullie soms met mij deelden als ik belde hebben mij doen beseffen hoe belangrijk het is om dit soort onderzoek te doen. Zoals een van jullie het een keer heel mooi verwoorde: "Het gaat niet alleen om het onderzoek naar een toekomstig nieuw medicijn wat ooit, in de verre toekomst, iedereen gaat genezen van kanker". Op dit moment leven er heel veel mensen die kanker hebben gehad en daar nog altijd directe of indirecte effecten van ondervinden. Daarom wil ik ook graag het **Alpe d'HuZes fonds** en **KWF Kankerbestrijding** bedanken voor het financieel mogelijk maken van dit onderzoek.

Heel veel dank aan mijn promotieteam. **Prof. dr. I.M. Verdonck-de Leeuw**, beste Irma, hartelijk dank dat jij mij in de afgelopen jaren de kans hebt gegeven om dit mooie onderzoek te doen en om daarnaast ook de master Epidemiologie te volgen. Jij hebt me laten zien dat alles mogelijk is als je er in gelooft. Bedankt voor je brede blik en je snelle feedback. **Prof. dr. L.V. van de Poll-Franse**, beste Lonneke, bedankt voor je betrokkenheid bij mijn promotieonderzoek. Ik vond het altijd fijn om tijdens onze, vaak telefonische, overleggen de mening te horen van iemand die niet direct betrokken was bij Oncokompas, maar er iets verder vanaf stond. Bedankt voor jouw verfrissende input op dit proefschrift. **Dr. C.F. van Uden-Kraan**, beste Nelly, wat was het fijn om met jou samen te werken. Jij hebt in het begin van het onderzoek en later wat meer op de achtergrond een hele belangrijke bijdrage geleverd aan dit proefschrift. Jij hebt me wegwijs gemaakt in de wetenschappelijke wereld en in de wondere wereld van Oncokompas. Bedankt voor het vertrouwen dat je mij op de juiste momenten gaf en dat ik altijd met alle vragen bij jou terecht kon.

Leden van de leescommissie en promotiecommissie, **prof. dr. Heleen Riper**, **prof. dr. Sabine Siesling**, **prof. dr. Niels Chavannes**, **prof. dr. Hanneke van Laarhoven**, **prof. dr. Judith Bosmans**, **dr. Maarten Lahr** en **dr. Jiska Aardoom**, hartelijk dank voor de bereidheid om zitting te nemen in de lees- en/of promotiecommissie en voor het beoordelen van mijn proefschrift.

Graag wil ik ook alle **co-auteurs** bedanken. Het was lang niet altijd makkelijk om bijna 30 co-auteurs te hebben, maar jullie kritische en klinische blik heeft er wel voor gezorgd dat de artikelen goed aansloten bij het publiek dat we voor ogen hadden. In het bijzonder wil ik graag **dr. Birgit Lissenberg-Witte** bedanken voor de hulp bij de statistische analyses en **dr. Femke Jansen** voor de hulp bij de kostenanalyses.

Nicole Horevoorts, **Britt Tuerlings** en **Erna de Winter** van IKNL, heel veel dank voor jullie hulp en ondersteuning met PROFIEL. Het duurde even voordat het allemaal liep zoals we wilden, maar uiteindelijk is alles goed gekomen!

Dan wil ik ook heel graag **Michelle Fris** bedanken. Michelle, jij was in de uitvoerende fase van het onderzoek echt onmisbaar als onderzoeksassistent. Wat heb jij veel werk verzet met alle telefoontjes die je hebt gedaan, brieven en mailtjes die je hebt verstuurd en al het werk dat je me uit handen hebt genomen. Je enthousiasme was aanstekelijk en gelukkig was jij net zo precies als ik. Dankjewel!

Iedereen van de onderzoeksgroep Samen Leven Met Kanker (SLMK) en het Oncokompas team, in het bijzonder **Angelina**, **Anouk**, **Femke, Florie**, **Heleen**, **Inge**, **Margot**, **Matthijs**, **Michelle**, **Nienke**, **Karen**, **Koen**, **Sandra** en **Vina**, bedankt dat ik zo veel van jullie heb mogen leren en voor de gezelligheid!

Fijne collega's van de afdeling Klinische Psychologie, in het bijzonder **Tanja**, **Lisette**, **Felix** en **Simon**, bedankt voor jullie gezelligheid en het lotgenotencontact. Ook veel dank aan het **secretariaat**! En natuurlijk mijn kamergenootjes door de jaren heen: **Inge**, **Karen**, **Matthijs**, **Anouk**, **Michelle**, **Nienke**, **Angelina** en **Florie**. Wat hebben we lekkere taartjes gebakken met z'n allen, natuurlijk met de lekkere koffie van Matthijs' koffiemachine erbij. Zonder jullie was het niet zo leuk om naar de VU te komen!

Verder wil ik **dr. Leti van Bodegom-Vos** bedanken. Jij hebt mijn interesse in de wetenschap aangewakkerd. Helaas ben ik niet bij jou mijn promotie onderzoek gaan doen, maar ik heb als onderzoekassistent bij het LUMC wel heel veel van je geleerd.

Hanna, we zijn al lang geen collega's meer, maar spreken elkaar nog regelmatig. Bedankt voor de gezellige koffiemomentjes op de VU, waarin we konden bijpraten, stoom afblazen en brainstormen over onze artikelen en proefschriften. Ik weet zeker dat die van jou ook heel mooi wordt!

Afleiding was vaak zeer welkom en die vond ik dan ook vaak op de fiets en op het ijs. Daarom wil ik ook mijn fiets- en/of schaatsmaatjes **Paul**, **Willemijn**, **Lennart** en **Koen** bedanken. Paul, hopelijk is het veel mooi weer, anders ben ik bang dat ik niet meer met je wil fietsen op mijn nieuwe fiets! Willemijn en Lennart, jullie wonen nu wat verder weg, maar gelukkig wel in een hele mooie fietsomgeving! Afleiding vond ik ook op reis: **Anouk Elzerman**, wat hebben we een mooie reizen gemaakt in Jordanië en India. Hopelijk kunnen we snel bij jullie op bezoek komen in Goa! **Anouk Schuit**, wat was het gaaf in Amerika! Ik heb genoten van onze prachtige hikes in Yosemite en het suppen op Lake Tahoe.

Vina, bedankt voor je goede voorbeeld met jouw promotie en dat je altijd bereid bent om te helpen en mee te denken. Ik vind het heel leuk dat wij elkaar nog regelmatig zien en spreken.

Lieve vriendinnen **Ankie** en **Adinda**, ik vind het zo leuk dat ik jullie heb leren kennen bij de opleiding Epidemiologie. Ankie, ik ben zo trots op je! Hoewel je nu ver weg woont, ben ik blij dat we elkaar nog veel spreken. Ik hoop dat ik je snel kan komen opzoeken. Adinda, ik heb jou eigenlijk niet eens tijdens de opleiding leren kennen, maar op de fiets. Ik hoop dat we nog vele fiets en schaatsritjes gaan maken samen! Beiden heel veel dank voor alle afleiding en gezelligheid.

Nienke en **Heleen**, dankjulliewel dat jullie mijn paranimf willen zijn! Nienke, jij maakte het zoveel leuker om naar de VU te komen in het laatste jaar van mijn contract, door samen koffietjes te drinken, te tafeltennissen en af en toe samen te reizen van en naar de VU. Dat hebben we nu ingeruild voor biertjes drinken en wandelen in het Haagse bos, alleen maar beter! Heleen, wat was het fijn om samen op te trekken met ons proefschrift, zeker in de laatste fase. Onze schrijfdagen met timers en lekkere lunches en koffietjes hebben ervoor gezorgd dat mijn proefschrift heel wat sneller af was. Ik vind het een eer om ook jouw paranimf te mogen zijn!

Dan mijn lieve familie en schoonfamilie. **Jan** & **Tjitske** en **Lieke** & **Glenn**, wat fijn dat jullie mij zo goed hebben opgenomen in de familie van der Meulen en dat jullie zo geïnteresseerd waren in mijn onderzoek. Ik voel mij heel erg thuis bij jullie.

Linda, dankjewel voor je goede zorgen op de momenten dat ik het druk had. Dankjewel dat je zulke lieve kaartjes schreef, voor me kookte en dat we samen leuke dingen gingen doen. Ik kan me geen betere zus wensen dan jij! **Nico**, hoe bijzonder was het dat wij allebei op dezelfde dag in

Limburg hoorden dat ons artikel geaccepteerd was in een goed tijdschrift! Ik ben stiekem wel blij dat je me niet hebt ingehaald met jouw proefschrift.

Cees & **Nelline**, lieve pap en mam, jullie denken misschien dat je niet veel hebt bijgedragen aan dit proefschrift. Maar ik weet zeker dat ik wat van jullie doorzettingsvermogen heb meegekregen en ik ben jullie zo ontzettend dankbaar voor al die jaren dat jullie mij om 5.00 uur 's ochtends naar de zwemtraining en in het weekend naar wedstrijden door het hele land brachten. Deze discipline en sportiviteit hebben zeker weten een bijdrage geleverd aan mijn carrière zoals die nu is. Bedankt voor jullie steun en liefde!

En dan tot slot, lieve **Mark**, jij hebt de laatste fase van mijn proefschrift zoveel leuker gemaakt. Ik ben zo blij dat ik jou ben tegengekomen. Bedankt voor je vertrouwen, je optimisme en dat je me hebt geleerd dat af beter is dan perfect. Bedankt voor alles. Op naar de toekomst!

ABOUT THE AUTOR

Anja van der Hout was born on June 18th, 1990 in Naaldwijk, the Netherlands. After graduating from secondary education at the Interconfessionele Scholengemeenschap Westland (ISW) in 2008, she started her study Biomedical Sciences at the Vrije Universiteit Amsterdam. After obtaining her bachelor's degree in 2011, she continued with the master Health Sciences, with the specialization Nutrition and Health. She graduated in 2012 as a health scientist and started working as a research assistant on the department of Medical Decision-making at Leiden University Medical Center (LUMC) in 2013. In 2015, she started as a PhD student at the department Clinical Psychology, at the Vrije Universiteit Amsterdam. Her research focussed on the web-based self-management application Oncokompas for cancer survivors. During this time, she did the post-initial master Epidemiology at EpidM (Epidemiology & Biostatistics, Amsterdam UMC, location VUmc), of which she was a student member of the curriculum committee. She graduated in 2019 as an epidemiologist. She was also actively involved in the Dutch Association of Psychosocial Oncology (Nederlandse Vereniging Psychosociale Oncologie, NVPO). Anja is currently working at the Knowledge Institute of the Dutch Association of Medical Specialists (Kennisinstituut van de Federatie Medisch Specialisten) and contributes to the development of evidence-based medical guidelines.

LIST OF PUBLICATIONS

Publications included in this thesis

van der Hout A, van Uden-Kraan CF, Witte BI, Coupé VMH, Jansen F, Leemans CR, Cuijpers P, van de Poll-Franse LV, Verdonck-de Leeuw IM (2017). 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,* 18(1), 228.

van der Hout A, van Uden-Kraan CF, Holtmaat K, Jansen F, Lissenberg-Witte BI, Nieuwenhuijzen GAP, Hardillo JA, Baatenburg de Jong RJ, Tiren-Verbeet NL, Sommeijer DW, de Heer K, Schaar CG, Sedee RE, Bosscha K, van den Brekel MWM, Petersen JF, Westerman M, Honings J, Takes RP, Houtenbos I, van den Broek WT, de Bree R, Jansen P, Eerenstein SEJ, Leemans CR, Zijlstra JM, Cuijpers P, van de Poll-Franse LV, Verdonck-de Leeuw IM (2020). Role of eHealth application Oncokompas in supporting self-management of symptoms and health-related quality of life in cancer survivors: a randomised, controlled trial. *The Lancet Oncology,* 21(1), 80-94.

van der Hout A, Holtmaat K, Jansen F, Lissenberg-Witte BI, van Uden-Kraan CF, Nieuwenhuijzen GAP, Hardillo JA, Baatenburg de Jong RJ, Tiren-Verbeet NL, Sommeijer DW, de Heer K, Schaar CG, Sedee RE, Bosscha K, van den Brekel MWM, Petersen JF, Westerman M, Honings J, Takes RP, Houtenbos I, van den Broek WT, de Bree R, Jansen P, Eerenstein SEJ, Leemans CR, Zijlstra JM, Cuijpers P, van de Poll-Franse LV, Verdonck-de Leeuw IM (2020). The eHealth self-management application 'Oncokompas' that supports cancer survivors to improve health-related quality of life and reduce symptoms: which groups benefit most?. *In press*

van der Hout A, Jansen F, van Uden-Kraan CF, Coupé VM, Holtmaat K, Nieuwenhuijzen GAP, Hardillo JA, Baatenburg de Jong RJ, Tiren-Verbeet NL, Sommeijer DW, de Heer K, Schaar CG, Sedee RE, Bosscha K, van den Brekel MWM, Petersen JF, Westerman M, Honings J, Takes RP, Houtenbos I, van den Broek WT, de Bree R, Jansen P, Eerenstein SEJ, Leemans CR, Zijlstra JM, Cuijpers P, van de Poll-Franse LV, Verdonck-de Leeuw IM (2020). Cost-utility of an eHealth application 'Oncokompas' that supports cancer survivors in self-management: results of a randomised controlled trial. *Journal of Cancer Survivorship,* 1-10.

van der Hout A, van Uden-Kraan CF, Holtmaat K, Jansen F, Lissenberg-Witte BI, Nieuwenhuijzen GAP, Hardillo JA, Baatenburg de Jong RJ, Tiren-Verbeet NL, Sommeijer DW, de Heer K, Schaar CG, Sedee RE, Bosscha K, van den Brekel MWM, Petersen JF, Westerman M, Honings J, Takes RP, Houtenbos I, van den Broek WT, de Bree R, Jansen P, Eerenstein SEJ, Leemans CR, Zijlstra JM, Cuijpers P, van de Poll-Franse LV, Verdonck-de Leeuw IM. Reasons for not reaching or using web-based self-management applications, and the use and evaluation of Oncokompas among cancer survivorsbased self-management application Oncokompas among cancer survivors. *Submitted*

Publications not included in this thesis

Neijenhuijs KI, **van der Hout A**, Veldhuijzen E, Scholten-Peeters GGM, van Uden-Kraan CF, Cuijpers P, Verdonck-de Leeuw IM (2019). Translation of the eHealth Impact Questionnaire for a population of Dutch electronic health users: validation study. *Journal of Medical Internet Research*, 21(8), e13408.

van der Hout A, Neijenhuijs KI, Jansen F, van Uden-Kraan CF, Aaronson NK, Groenvold M, Holzner B, Terwee CB, van de Poll-Franse LV, Cuijpers P, Verdonck-de Leeuw IM (2019). Measuring health-related quality of life in colorectal cancer patients: systematic review of measurement properties of the EORTC QLQ-CR29. *Supportive Care in Cancer*, 1-18.

Voorn VMA, Marang-van de Mheen PJ, **van der Hout A**, So-Osman C, van den Akker-van Marle ME, Koopman-van Gemert AWMM, Dahan A, Vliet Vlieland TPM, Nelissen RGHH, van Bodegom-Vos L (2017). Hospital variation in allogeneic transfusion and extended length of stay in primary elective hip and knee arthroplasty: a cross-sectional study. *BMJ Open*, *7*(7), e014143.

Voorn VMA, Marang-van de Mheen PJ, **van der Hout A**, Hofstede SN, So-Osman C, van den Akker-van Marle ME, Kaptein AA, Stijnen T, Koopman-van Gemert AWMM, Dahan A, Vliet Vlieland TPMM, Nelissen RGHH, van Bodegom-Vos L (2017). The effectiveness of a de-implementation strategy to reduce low-value blood management techniques in primary hip and knee arthroplasty: a pragmatic cluster-randomized controlled trial. *Implementation Science*, 12(1), 72.

Engelhardt EG, Pieterse AH, **van der Hout A**, de Haes HJ, Kroep JR, Quarles van Ufford-Mannesse P, Portielje JE, Smets EM, Stiggelbout AM (2016). Use of implicit persuasion in decision making about adjuvant cancer treatment: a potential barrier to shared decision making. *European Journal of Cancer*, 66, 55-66.

Voorn VM, Marang-van de Mheen PJ, So-Osman C, Kaptein AA, **van der Hout A**, van den Akker-van Marle ME, Koopman-van Gemert AW, Dahan A, Nelissen RG, Vliet Vlieland TP, van Bodegom-Vos L (2014). De-implementation of expensive blood saving measures in hip and knee arthroplasties: study protocol for the LISBOA-II cluster randomized trial. *Implementation Science*, 9(1), 48.

Leistra E, van Bokhorst-de van der Schueren MA, Visser M, **van der Hout A**, Langius JA, Kruizenga HM (2014). Systematic screening for undernutrition in hospitals: predictive factors for success. *Clinical Nutrition*, 33(3), 495-501.