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Web-based MINDfulness- and Skills-based distress reduction in cancer (MINDS): Study Protocol for a multicentre observational healthcare study.

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ABSTRACT

Introduction Although a high percentage of patients with cancer experience severe psychological distress, few of them receive psycho-oncological care, largely due to barriers on the side of patients and healthcare providers that pose great challenges to delivering such care. In response, low-threshold, self-guided eHealth interventions can enable patients with cancer to deal independently and effectively with disease-related challenges and distress. Mindfulness- and Skills-Based Distress Reduction in Oncology Training, nicknamed Make It Training, is one such innovative, self-guided eHealth intervention. In our study, we propose to assess different characteristics of such patients in order to define target populations for Make It Training, evaluate the intervention in terms of its usability, feasibility and sustainability and gather longitudinal data concerning the intervention's efficacy.

Methods and analysis Self-guided and web-based, Make It Training consists of eight 30-minute modules involving the use of techniques of mindfulness therapy, cognitive behavioural therapy and acceptance and commitment therapy to be completed in a 4-month period. In our observational study, adult patients with cancer who possess adequate German-language skills and provide their informed consent will be recruited at Essen, Erlangen and Tübingen University Hospitals, at outpatient oncological institutions and via online channels. Patients will undergo a baseline online assessment (T0), an assessment directly after completing the intervention (T1) and assessments 3 and 6 months later (T2 and T3, respectively). With the results of those assessments, we will perform descriptive analyses of their socio-demographic and medical data, compare means and conduct regression analyses.

Ethics and dissemination The Ethics Committees of the University Hospitals Essen, Erlangen and Tübingen have approved the study (19-8643-BO, 27_19 B, 293/2018BO1). Results will be published in peer-reviewed journals and conference presentations.

Trial registration This study was registered at the German Clinical Trials Register (DRKS00017119) on August 29, 2019.

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Strengths and limitations of this study

- The web-based intervention was developed using evidence-, theory- and person-based approaches.
- The study will evaluate the intervention in terms of acceptance, usability, feasibility and sustainability and collect longitudinal data on the effectiveness of the web-based approach.
- Provision of the web-based training for a large number of cancer patients independent of the tumor entity.
- No randomised controlled study design.

INTRODUCTION

Despite considerable improvements in the treatment of different tumour entities, every second patient with cancer suffers from acute psychological distress.[1] In fact, a third of all patients with cancer involving major tumour entities will meet the criteria for at least one mental health disorder at four-week prevalence.[2] Over a lifetime, however, the prevalence of any mental disorder in patients with cancer rises to more than 56%.[3] Psychological distress in patients with cancer is often associated with changed roles in their professional and family lives, financial problems and reduced quality of life (QoL),[4–6] and high distress can even reduce compliance with treatment.[7, 8] As a partial antidote, psycho-oncological interventions can significantly reduce the psychological distress and improve the QoL of patients with cancer.[9, 10] Although many patients with cancer demonstrate a great need for adequate psycho-oncological care in order to overcome disease-related distress, depression and anxiety,[11, 12] few of them receive such care.[13] In response, it is crucial for health care institutions to offer patients with cancer usable, sustainable and accessible interventions, such as eHealth interventions involving psycho-oncological treatment approaches for routine clinical care.[14]

Cognitive behavioral therapy and mindfulness in psycho-oncological interventions

Various studies have revealed that cognitive behavioural therapy (CBT) and mindfulness-based stress reduction (MBSR) significantly reduce distress, depression and anxiety in patients with cancer.[9, 15, 16] Such approaches can also increase their QoL and reduce the treatment-related side effects that patients with cancer may experience.[7, 8, 17] To date, the effect sizes of psycho-oncological interventions based on CBT and MBSR have been small to medium in randomised controlled trials (RCT).[18]

Psycho-oncological eHealth intervention

Given the increasing influence of internet use in daily life, web-based psycho-oncological care has the potential to reach high volumes of patients and to overcome barriers to healthcare provision on the side of patients and providers (e.g. rural areas, stigma, privacy, high costs and long wait times).[19, 20] In particular, eHealth interventions can be efficient approaches to reaching younger patients who report more unmet needs, are less likely to access psycho-oncological help but are generally more open to modern and web-based approaches.[21] At the same time, easy integration of psycho-oncological care through eHealth approaches into patients' lives prevents an additional workload for this vulnerable group.[21] Compared to the effects of face-to-face CBT interventions in several mental and somatic disorders, online CBT interventions lead to comparable efficacy outcomes.[22, 23] Other promising results suggest that online psycho-oncological interventions can improve the psychosocial and physical symptoms of patients with cancer.[24–26] There are more approaches to address the different needs of cancer patients.[27, 28] Nevertheless, due to the mixed findings and small sample sizes of studies on such interventions to date, high-quality research with larger, more diverse samples remain necessary.[29, 30]

Objectives and research questions

To overcome the current gap in the provision of psycho-oncological care for patients with cancer, we have developed an innovative eHealth intervention named Make It Training.

Highly time- and cost-efficient, Make It Training provides a novel way to support patients with cancer regardless of their physical conditions or location by improving their social and professional functioning and engagement. The chief objective of our study is to evaluate the acceptability, usability, feasibility and sustainability of Make It Training. In particular, we seek to identify the primary characteristics of patients with cancer in order to determine target populations for the intervention, namely by evaluating:

1. Acceptance and adherence to Make It Training; and
2. Dropout in and the usability of Make It Training.

Our secondary objectives refer to initial indications of the efficacy of Make It Training in order to identify patient characteristics that might determine potential benefits for patients with cancer. To that end, we developed two research questions:

1. Does Make It Training lead to increased self-efficacy, QoL and mindfulness among patients with cancer?
2. Does Make It Training lead to reduced distress, depression and anxiety among patients with cancer?

Because developing modern, issue-based interventions is important to improve patients' acceptance of eHealth interventions,[22] the results of our study promise to afford broad knowledge applicable to identifying and addressing specific groups of patients with cancer who are open to and may benefit from eHealth interventions in psycho-oncological care.

METHODS AND ANALYSIS

Study design

Our multicentre observational healthcare study is designed to offer the web-based intervention of Make It Training to a large number of patients with cancer. The proposed procedure for the study appears in Figure 1. Once cancer diagnosis is determined from their medical records, participating patients will complete the online baseline assessment (T0) and receive their personal Make It Training usernames from the research team. Further

assessments will be made directly after the completion of the intervention (T1) and at both 3 and 6 months later (T2 and T3, respectively). In the case of discontinuation (i.e. no login for 6 weeks after the first uncompleted module), patients will be asked to complete a questionnaire addressing their reasons for not completing Make It Training. During the intervention, each patient will receive a notification every 2 weeks stating that a new module is accessible. To improve study adherence, patients who have been inactive for 4 weeks will receive an additional notification to motivate them to continue Make It Training. The intervention will be considered to be complete when at least five of eight modules have been conducted.

Please insert Figure 1 here

Figure 1 Overall study design

Participant eligibility and recruitment

Patients with cancer will be included regardless of their demographic or medical characteristics (e.g. age and tumour entity), provided that they have a good command of the German language, internet access and basic computer skills, are at least 18 years of age and have given their informed consent. Patients will be recruited at University Hospitals Essen, Erlangen and Tübingen, at outpatient cancer institutions (e.g. established physicians), with the distribution of flyers and from the publicly accessible website for Make It Training.[31] Patients will be recruited from self-help and other groups on social media. At all three university hospitals, we will contact all patients with cancer who have indicated interest in participating in studies for patients with cancer and send them informational material about our study via email. Their informed consent will be given with their online confirmation of the study conditions in advance of the first assessment.

eHealth Intervention-Make It Training

Make It Training is a self-guided, interactive and web-based intervention that patients can use on their own personal computers, smartphones or tablets. Make It Training is based on established, effective methods of cognitive behavioural therapy, mindfulness therapy and

acceptance and commitment therapy.[9, 15, 16, 32] By combining both skills training and practices of mindfulness, Make It Training can address the different needs of psychologically burdened patients with cancer.[33] A previous pilot study with $n = 35$ has demonstrated the good acceptance and contentment rates of an exemplary module of the Make It Training.[34] The eight modules of Make It Training contain different media -tutorial videos, audio, individual skills boxes and patient-centred, interactive exercises- to enhance the acquisition of knowledge about specific disease-related topics (e.g. emotion management, resources, stress management and self-compassion). All guided mindfulness exercises are available as audio files and can be downloaded onto the patients’ devices. Table 1 gives an overview of the contents of the individual modules of Make It Training translated into English.[34] Make It Training consists of eight 30-minute modules offered at the rate of one module every 2 weeks for 4 months. In addition to the eight modules, mindfulness exercises to be performed at home should be integrated into patients’ daily routines. The interval of 2 weeks per module was chosen to afford patients sufficient time to integrate mindfulness exercises into their daily lives, which should improve their likelihood of continuing the exercises once the intervention has ended.

Table 1 Overview of the topics, contents and exercises of Make It Training

	Topic	Psychoeducation	Skills	Mindfulness
1. Module Introduction	The idea of the skills and mindfulness training and skills	<i>*No psycho-education because of introduction*</i>	<i>*No skills training because of intense mindfulness exercise*</i>	Mindful drinking
2. Module Emotions	Accepting and dealing with emotions	The presence of cancer-related emotions such as anxiety, sadness and anger	<ul style="list-style-type: none">Exercise: Giving emotions spaceDistance strategiesAcceptance cards	Mindful breathing
3. Module Experiencing	Experiencing one’s environment without judging it	<i>*No psycho-education because of intense mindfulness exercise*</i>	<i>*No skills training because of intense mindfulness exercise*</i>	Mindful experiencing
4. Module Sources of strength	Discovering and consciously using personal sources of strength	The emergence of vicious mental cycles and the meaning of individual sources of strength	<ul style="list-style-type: none">Exercise: Exiting the vicious cycle by using personal sources of strengthAction cards	Mindful listening

5. Module Body awareness	Feeling one's body in new and different ways	<i>*No psycho-education because of intense mindfulness exercise*</i>	<i>*No skills training because of intense mindfulness exercise*</i>	Mindful body awareness
6. Module Stress management	Mastering stress-intensive situations based on personal thoughts	The meaning of thoughts for subjective experience and feelings of stress	<ul style="list-style-type: none"> Exercise: ABC model Motivational quotations Reward cards 	Mindful vision
7. Module Self-care	To meet myself lovingly and benevolently	Self-esteem and its importance in the context of cancer	<ul style="list-style-type: none"> Exercise: Strengthen my self-esteem house My self-care Kind companion 	Mindful compassion
8. Module Emergency kit and skills boxes	Reviewing Make It Training and helpful skills	Use of the emergency kit with individual helpful skills	<ul style="list-style-type: none"> My emergency kit Exercise: Skills for emotional emergencies 	Favourite mindfulness exercise

Primary outcome measures

The schedule of the different assessments, each lasting between 10 and 25 minutes, is summarised in Table 2. Demographic data (e.g. gender, age, children, family status and employment status) and medical data (e.g. tumour entity, treatment method, date of diagnosis and type of therapy) will be self-reported and collected via the online survey application *Unipark* before the patients start the intervention (T0).[35]

Table 2 Assessment schedule

Instruments	T0: Baseline	T1: Post intervention	T2 & T3: Follow-up at 3 and 6 months	Dropout survey
Socio-demographic and medical history survey	x			
Distress Thermometer (DT)	x	x	x	x
Patient Health Questionnaire Depression Scale (PHQ-8)	x	x	x	x
Generalized Anxiety Disorder Scale-7 (GAD-7)	x	x	x	x
General Self-Efficacy Scale (GSE)	x	x	x	x
Freiburg Mindfulness Inventory (FMI)	x	x	x	x
Perceived Stress Questionnaire (PSQ-20)	x	x	x	x
Functional Assessment of Cancer Therapy – General, Physical Well-Being sub-scale (FACT-G)	x	x	x	x
European Quality of Life 5 Dimensions 3 Level Version (EQ-5D-3L)	x	x	x	x
Attitudes Towards Psychological Online	x	x		x

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Interventions (APOI)		
Self-generated evaluation items	x	x
System Usability Scale (SUS)	x	x
Client Satisfaction Questionnaire adapted to Internet-based interventions (CSQ-I)	x	x

Secondary outcome measures

We will use the German version of the Distress Thermometer (DT) to assess patients’ distress experienced in the past week.[36] By contrast, depression and anxiety will be assessed with the German versions of the Patient Health Questionnaire Depression Scale (PHQ-8) and the Generalized Anxiety Disorder Scale-7 (GAD-7), respectively.[37, 38] To gauge self-efficacy, we plan to use the German version of the General Self-Efficacy Scale (GSE),[39] whereas to assess mindfulness, we propose to use the German version of the Freiburg Mindfulness Inventory (FMI).[40] The German version of the Perceived Stress Questionnaire (PSQ) without the Joy sub-scale will be used to investigate and determine subjective perception, evaluation and the further processing of stressors.[41] To gather relevant information about the current somatic state of patients, we will use the Physical Well-Being sub-scale of the German version of the Functional Assessment of Cancer Therapy - General (FACT-G).[42] Last, to assess patients’ quality of life, we plan to use the German version of the 5-item European Quality of Life 5 Dimensions 3 Level Version (EQ-5D-3L) questionnaire.[43]

Evaluation of Make It Training

To evaluate the usability of and patients’ satisfaction with Make It Training, we will use a modified German version of the 10-item System Usability Scale (SUS),[44] the German version of the Client Satisfaction Questionnaire adapted to Internet-based interventions (CSQ-I)[45] and self-generated items, all to gather detailed information about the strengths and weaknesses of Make It Training. For each item-based topic, patients will have the possibility to add their personal thoughts and ideas. The patients’ acceptance of online psychological interventions in general and their possible changes in attitude will be collected with the

Attitudes Towards Psychological Online Interventions (APOI) instrument.[46] Reasons for not completing Make It Training will also be obtained, whereas data concerning adherence to the training (e.g. last login and time needed for modules) will be collected via backend functions of the Make It system.

Sample size calculation and statistical analyses

The sample size estimation will be done based on the BREATH study,[26] in which an effect size of Cohen's $d = 0.28$ was observed for General Self-Efficacy Scale.[39] Based on that effect size, we have calculated the need for a sample size of 103 patients using two-sided t tests for dependent samples with type 1 error of 0.05 and a power of 80%. Although a dropout rate of up to 50% for online interventions has been shown,[47] we might expect an even higher rate of dropout given the physically vulnerable patient group that will form our sample and because the last measurement will occur 6 months after the intervention has ended. Assuming that some patients will not complete the first online assessment and thus not start Make It Training after recruitment,[48] we plan to recruit 500 patients at T0. We will perform standard techniques of data preparation with tests of normality and homogeneity as well as conduct different descriptive analyses of socio-demographic and medical data. The primary statistical analyses will be an analysis of variance with repeated measurements, t tests for dependent samples (i.e. with two-sided p values and 95% confidence intervals) and regression analyses to identify potential predictors of treatment outcomes.

Patient and public involvement

Neither patients nor public were involved in the development of this study design, but as previously mentioned, patients were involved in developing the intervention content.[33] Furthermore, we conducted a pilot study on the acceptance of an exemplary module of Make It Training.[34] During the proposed study, we will also collect data on how Make It Training can be improved to subsequently improve it.

Ethics and dissemination

The Ethics Committees of the University Hospitals Essen, Erlangen and Tübingen have approved the study (19-8643-BO, 27_19 B, 293/2018BO1). Results will be disseminated in peer-reviewed journals and conference presentations. Key findings will also be published on the Make It Training website.

Trial status

Trial start date: 22th October 2019; Currently recruiting ($N_{\text{current}} = 60$ as of December 16, 2019).

DISCUSSION

In our study, we propose to evaluate whether specific groups of patients who differ in terms of socio-demographic data (e.g. age, sex and family status) and medical data (e.g. medical condition, time since cancer diagnosis and tumour entity) are generally open to using an innovative psycho-oncological eHealth intervention. Our evaluation is important in order to adapt modern interventions to the specific requirements and desires of such groups and to efficiently offer a low-threshold eHealth intervention. Our preliminary findings from a longitudinal perspective will suggest whether the self-guided, web-based Make It Training intervention is an efficient tool to support patients with cancer. In addition, we expect to be able to identify specific reasons for patient dropout that can help us to improve Make It Training in particular and to develop patient centred eHealth interventions in general. A key topic of discussion for subsequent research will be whether a self-guided online intervention can be effectively used to support patients with cancer. Although various studies have highlighted the importance of therapeutic contact in online interventions,[49] implementing such interventions in everyday healthcare necessarily faces numerous obstacles (e.g. higher costs and mostly accessibility during research work only).[50] In addition, evidence suggests that the efficacy of treatment between guided and self-guided online interventions for depression does not significantly differ.[51] Make It Training attempts to overcome the mentioned barriers by offering a completely self-guided tool to support all patients with

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3 cancer anytime and anywhere. One expected limitation of the study is the non-existence of a
4 control group to obtain sufficient data regarding the effectiveness of Make It Training.
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6 However, among its anticipated strengths is that we will offer Make It Training to all patients
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8 with cancer and gain valid information about the usability, feasibility and sustainability of
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10 web-based, self-guided psycho-oncological interventions. In a future study, we also plan to
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12 conduct a multicentre RCT to obtain valid information on the efficacy of Make It Training.
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15 Although many patients with cancer suffer from acute psychological distress, psycho-
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17 oncological support is often absent, unavailable or non-existent. Make It Training is one
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19 eHealth approach to overcome barriers on both the patient and provider side to offer patients
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21 with cancer a self-guided psycho-oncological intervention at any time and any place. Such
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23 interventions are time- and cost-efficient and afford broad availability in clinical routines for
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25 all patients at any stage of the disease, whether they are in acute care or have survived cancer.
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27 Make It Training in particular and self-guided eHealth interventions in general could be
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29 integrated in current healthcare systems to offer substantial benefits for patients and
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31 providers.
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40 **Author contributions** AB contributed to designing the study, administering the trial and
41
42 preparing the manuscript. MT initiated the study and contributed to designing the study,
43
44 developing the intervention, procuring funding and preparing the manuscript. JR contributed
45
46 to designing the study, developing the intervention, administering the trial and preparing the
47
48 manuscript. MB and ES contributed to preparing the manuscript. NS and FL contributed to
49
50 developing the intervention and helping with the manuscript. CS contributed to administering
51
52 the trial and preparing the manuscript. SZ contributed to designing the study, developing the
53
54 intervention and procuring funding. YE contributed to designing the study, procuring funding
55
56 and preparing the manuscript. All authors have read and approved the final manuscript.
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REFERENCES

1 Mehnert A, Hartung TJ, Friedrich M, et al. One in two cancer patients is significantly distressed: Prevalence and indicators of distress. *Psychooncology* 2018;27:75-82.

2 Mehnert A, Brähler E, Faller H, et al. Four-Week Prevalence of Mental Disorders in Patients With Cancer Across Major Tumor Entities. *J Clin Oncol* 2014;1;32:3540-6.

3 Kuhnt S, Brähler E, Faller H, et al. Twelve-Month and Lifetime Prevalence of mental Disorders in Cancer patients. *Psychother Psychosom* 2016;85:289-96.

4 Singer S, Das-Munshi J, Brähler E. Prevalence of mental health conditions in cancer patients in acute care-a meta-analysis. *Ann Oncol* 2010;21:925–30.

5 Mitchell AJ, Chan M, Bhatti H, et al. Prevalence of depression, anxiety, and adjustment disorder in oncological, haematological, and palliative-care settings: a meta-analysis of 94 interview-based studies. *Lancet Oncol* 2011;12:160–74.

6 Büttner M, König H-H, Löbner M, et al. Out-of-pocket-payments and the financial burden of 502 cancer patients of working age in Germany: results from a longitudinal study. *Support Care Cancer* 2019;27:2221-8.

7 Chambers SK, Meng X, Youl P, et al. A five-year prospective study of quality of life after colorectal cancer. *Qual Life Res* 2012;21:1551-64

8 Park CL, Gaffey AE. Relationships between psychosocial factors and health behavior change in cancer survivors: an integrative review. *Ann Behav Med* 2007;34:115-34.

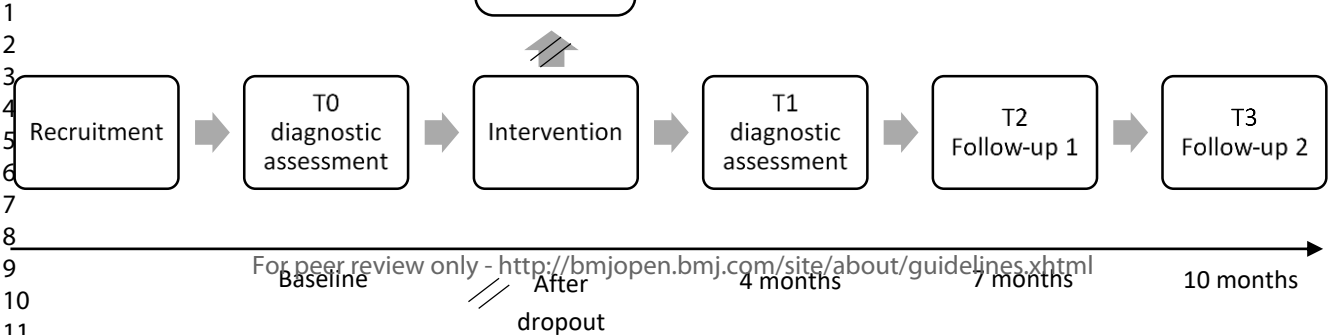
- 9 Faller H, Schuler M, Richard M, et al. Effects of psycho-oncologic interventions on
emotional distress and quality of life in adult patients with cancer: systematic review and
meta-analysis. *J Clin Oncol* 2013;20;31:786-93.
- 10 Cwikel JG, Behar LC. Social work with adult cancer patients: a vote-count review of
intervention research. *Soc Work Health Care* 1999;29:39-67.
- 11 Faller H, Weis J, Koch U, et al. Utilization of professional psychological care in a large
German sample of cancer patients. *Psychooncology* 2017;26:537-43.
- 12 Schaeffeler, N, Pfeiffer K, Ringwald J, et al. Assessing the need for psychooncological
support: screening instruments in combination with patients' subjective evaluation may
define psychooncological pathways. *Psychooncology* 2015;24:1784-1791.
- 13 Zeissig S.R, Singer S, Koch L, et al. Inanspruchnahme psychoonkologischer Versorgung
im Krankenhaus und in Krebsberatungsstellen durch Brust-, Darm- und
Prostatakrebsüberlebende. *Psychother Psych Med* 2015;65:177-82,
- 14 Aaronson NK, Mattioli V, Minton O, et al. Beyond treatment - Psychosocial and
behavioural issues in cancer survivorship research and practice. *EJC Suppl* 2014;12:54-
64.
- 15 Zainal NZ, Booth S, Huppert FA. The efficacy of mindfulness-based stress reduction on
mental health of breast cancer patients: A meta-analysis. *Psychooncology* 2013;22:1457-
65.
- 16 Rush SE, Sharman M. Mindfulness-based stress reduction as a stress management
intervention for cancer care: a systematic review. *J Evid Based Complementary Altern
Med* 2017;22:348-60.
- 17 Wells N, Hepworth JT, Murphy BA, et al. Improving cancer pain management through
patient and family education. *J Pain Symptom Manage* 2003;25:344-56.

- 18 Duijts SF, Faber MM, Oldenburg HS, et al. Effectiveness of behavioral techniques and physical exercise on psychosocial functioning and health-related quality of life in breast cancer patients and survivors—a meta-analysis. *Psychooncology* 2011;20:115-26.
- 19 Leykin Y, Thekdi SM, Shumay DM, et al. Internet interventions for improving psychological well-being in psycho-oncology: review and recommendations. *Psychooncology* 2012;21:1016-25.
- 20 Dilworth S, Higgins I, Parker V, et al. Patient and health professional's perceived barriers to the delivery of psychosocial care to adults with cancer: a systematic review. *Psychooncology* 2014;23:601-12.
- 21 Zebrack BJ, Block R, Hayes-Lattin B, et al. Psychosocial service use and unmet need among recently diagnosed adolescent and young adult cancer patients. *Cancer* 2013;119:201-14.
- 22 Andersson G. Internet-Delivered Psychological Treatments. *Annu Rev Clin Psychol* 2016;12:157-79.
- 23 Andersson G, Cuijpers P, Carlbringe P, et al. Guided Internet-based vs. face-to-face cognitive behavior therapy for psychiatric and somatic disorders: a systematic review and meta-analysis. *World Psychiatry* 2014;13:288-95.
- 24 Bouma G, Admiraal JM, de Vries EG, et al. Internet-based support programs to alleviate psychosocial and physical symptoms in cancer patients: A literature analysis. *Crit Rev Oncol Hematol* 2015;95:26–37.
- 25 Urech C, Grossert A, Alder J, et al. Web-Based Stress Management for Newly Diagnosed Patients With Cancer (STREAM): A Randomized, Wait-List Controlled Intervention Study. *J Clin Oncol* 2018;36:780-8.
- 26 Willems RA, Bolman CA, Mesters I, et al. Short-term effectiveness of a web-based tailored intervention for cancer survivors on quality of life, anxiety, depression, and fatigue: randomized controlled trial. *Psychooncology* 2016; 26:222-30.

- 27 Krusche A, Bradbury K, Corbett T, et al. Renewed: Protocol for a randomised controlled trial of a digital intervention to support quality of life in cancer survivors. *BMJ Open* 2019;9:e024862.
- 28 Akechi T, Yamaguchi T, Uchida M, et al. Smartphone problem-solving and behavioural activation therapy to reduce fear of recurrence among patients with breast cancer (SMartphone Intervention to LEssen fear of cancer recurrence: SMILE project): protocol for a randomised controlled trial. *BMJ Open* 2018;8: e024794.
- 29 Hong Y, Peña-Purcell NC, Ory MG. Outcomes of online support and resources for cancer survivors: A systematic literature review. *Patient Educ Couns* 2012;86:288-96.
- 30 Butow P, Smith A. Systematic reviews of pain and online interventions for cancer patients show evidence of mixed efficacy and highlight need for more rigorously designed research. *Patient Educ Couns* 2015;98:267-8.
- 31 Make It. <https://makeit-essen.medizin.uni-tuebingen.de>. Accessed 08 December 2019.
- 32 Casellas-Grau A, Font A, Vives J. Positive psychology interventions in breast cancer. A systematic review. *Psychooncology* 2014;23:9-19.
- 33 Ringwald J, Marwedel L, Junne F, et al. Demands and Need for Psycho-Oncological eHealth Interventions in Womend With Cancer: Cross-Sectional Study. *JMIR Cancer* 2017;24;3:e19.
- 34 Ringwald J, Gerstner L, Junne F, et al. Mindfulness and Skills Based Distress Reduction in Oncology: The Web-Based Psycho-Oncological Make It Training. *Psychother Psychosom Med Psychol* 2019; doi:10.1055/a-0835-6905
- 35 Questback GmbH. <https://www.unipark.com>. Accessed 08 December 2019.
- 36 Mehnert A, Müller D, Lehmann C, et al. Die deutsche Version des NCCN Distress-Thermometers Empirische Prüfung eines Screening Instruments zur Erfassung psychosozialer Belastung bei Krebspatienten. *Zeitschrift für Psychiatrie, Psychologie und Psychotherapie* 2006;54:213-23.

- 37 Kroenke K, Strine TW, Spitzer RL, et al. The PHQ-8 as a measure of current depression in the general population. *J Affect Disord* 2009;114:163–73.
- 38 Spitzer RL, Kroenke K, Williams JB, et al. A brief measure for assessing generalized anxiety disorder: The GAD-7. *Arch Intern Med* 2006;166:1092–7.
- 39 Schwarzer R, Jerusalem M. Skalen zur Erfassung von Lehrer- und Schülermerkmalen. Dokumentation der psychometrischen Verfahren im Rahmen der Wissenschaftlichen Begleitung des Modellversuchs Selbstwirksame Schulen. Berlin, Freie Universität Berlin 1999.
- 40 Walach H, Buchheld N, Buttenmüller V, et al. Measuring mindfulness - The Freiburg Mindfulness Inventory (FMI). *Pers Individ Dif* 2006;40:1543-55.
- 41 Fliege H, Rose M, Arck P, et al. Validierung des "Perceived Stress Questionnaire" (PSQ) an einer deutschen Stichprobe. *Diagnostica* 2001;47:142-152.
- 42 Cella D, Tulsky D, Gray G, et al. The Functional Assessment of Cancer Therapy Scale: Development and Validation of the General Measure. *J Clin Oncol* 1993;11:570-579.
- 43 The EuroQol Group. EuroQol-a new facility for the measurement of health-related quality of life. *Health Policy* 1990;16:199-208.
- 44 Brooke J. SUS: A 'quick and dirty' usability scale. In: Jordan PW, Thomas B, Weerdmeester BA, McClelland IL, eds. Usability Evaluation in Industry. London: Taylor & Francis 1996:189-94.
- 45 Boß L, Lehr D, Reis D, et al. Reliability and Validity of Assessing User Satisfaction With Web-Based Health Interventions. *J Med Internet Res* 2016;18: e234.
- 46 Schröder J, Sautier L, Kriston L, et al. Development of a questionnaire measuring Attitudes towards Psychological Online Interventions—the APOI. *J Affect Disord* 2015;187:136-41.
- 47 Christensen H, Griffiths KM, Farrer L. Adherence in internet interventions for anxiety and depression. *J Med Internet Res* 2009;11:e13.

- 1
2
3 48 Waller R, Gilbody S. Barriers to the uptake of computerized cognitive behavioural
4 therapy: a systematic review of the quantitative and qualitative evidence. *Psychol Med*
5 2009;39:705-712.
6
7
8
9
10 49 Palmqvist B, Carlbring P, Andersson G. Internet-delivered treatments with or without
11 therapist input: does the therapist factor have implications for efficacy and cost? *Expert*
12 *Rev Pharmacoecon Outcomes Res* 2007;7:291-7.
13
14
15
16
17 50 Andersson G, Titov N, Dear BF, et al. Internet-delivered psychological treatments: from
18 innovation to implementation. *World Psychiatry* 2019;18:20–28.
19
20
21 51 Berger T, Hämmerli K, Gubser N, et al. Internet-Based Treatment of Depression: A
22 Randomized Controlled Trial Comparing Guided with Unguided Self-Help. *Cogn Behav*
23 *Ther* 2011;40:251-266.
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Web-based MINDfulness- and Skills-based distress reduction in cancer (MINDS): Study Protocol for a multicentre observational healthcare study.

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ABSTRACT

Introduction Although a high percentage of patients with cancer experience severe psychological distress, few of them receive psycho-oncological care, largely due to barriers on the side of patients and healthcare providers that pose great challenges to delivering such care. In response, low-threshold, self-guided eHealth interventions can enable patients with cancer to deal independently and effectively with disease-related challenges and distress. Mindfulness- and Skills-Based Distress Reduction in Oncology Training, nicknamed Make It Training, is one such innovative, self-guided eHealth intervention. In our study, we propose to assess different characteristics of such patients in order to define target populations for Make It Training, evaluate the intervention in terms of its usability, feasibility and sustainability and gather longitudinal data concerning the intervention's efficacy.

Methods and analysis Self-guided and web-based, Make It Training consists of eight 30-minute modules involving the use of techniques of mindfulness therapy, cognitive behavioural therapy and acceptance and commitment therapy to be completed in a 4-month period. In our observational study, adult patients with cancer who possess adequate German-language skills and provide their informed consent will be recruited at Essen, Erlangen and Tübingen University Hospitals, at outpatient oncological institutions and via online channels. Patients will undergo a baseline online assessment (T0), an assessment directly after completing the intervention (T1) and assessments 3 and 6 months later (T2 and T3, respectively). With the results of those assessments, we will perform descriptive analyses of their socio-demographic and medical data, compare means and conduct regression analyses.

Ethics and dissemination The Ethics Committees of the University Hospitals Essen, Erlangen and Tübingen have approved the study (19-8643-BO, 27_19 B, 293/2018BO1). Results will be published in peer-reviewed journals and conference presentations.

Trial registration This study was registered at the German Clinical Trials Register (DRKS00017119) on August 29, 2019.

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Strengths and limitations of this study

- The web-based intervention was developed using evidence-, theory- and person-based approaches.
- The study will evaluate the intervention in terms of acceptance, usability, feasibility and sustainability and collect longitudinal data on the effectiveness of the web-based approach.
- Provision of the web-based training for a large number of cancer patients independent of the tumor entity.
- No randomised controlled study design.

INTRODUCTION

Despite considerable improvements in the treatment of different tumour entities, every second patient with cancer suffers from acute psychological distress.[1] In fact, a third of all patients with cancer involving major tumour entities will meet the criteria for at least one mental health disorder at four-week prevalence.[2] Over a lifetime, however, the prevalence of any mental disorder in patients with cancer rises to more than 56%.[3] Psychological distress in patients with cancer is often associated with changed roles in their professional and family lives, financial problems and reduced quality of life (QoL),[4–6] and high distress can even reduce compliance with treatment.[7, 8] As a partial antidote, psycho-oncological interventions can significantly reduce the psychological distress and improve the QoL of patients with cancer.[9, 10] Although many patients with cancer demonstrate a great need for adequate psycho-oncological care in order to overcome disease-related distress, depression and anxiety,[11, 12] few of them receive such care.[13] In response, it is crucial for health care institutions to offer patients with cancer usable, sustainable and accessible interventions, such as eHealth interventions involving psycho-oncological treatment approaches for routine clinical care.[14]

Cognitive behavioral therapy and mindfulness in psycho-oncological interventions

Various studies have revealed that cognitive behavioural therapy (CBT) and mindfulness-based stress reduction (MBSR) significantly reduce distress, depression and anxiety in patients with cancer.[9, 15, 16] Such approaches can also increase their QoL and reduce the treatment-related side effects that patients with cancer may experience.[7, 8, 17] To date, the effect sizes of psycho-oncological interventions based on CBT and MBSR have been small to medium in randomised controlled trials (RCT).[18]

Psycho-oncological eHealth intervention

Given the increasing influence of internet use in daily life, web-based psycho-oncological care has the potential to reach high volumes of patients and to overcome barriers to healthcare provision on the side of patients and providers (e.g. rural areas, stigma, privacy, high costs and long wait times).[19, 20] In particular, eHealth interventions can be efficient approaches to reaching younger patients who report more unmet needs, are less likely to access psycho-oncological help but are generally more open to modern and web-based approaches.[21] At the same time, easy integration of psycho-oncological care through eHealth approaches into patients' lives prevents an additional workload for this vulnerable group.[21] Compared to the effects of face-to-face CBT interventions in several mental and somatic disorders, online CBT interventions lead to comparable efficacy outcomes.[22, 23] Other promising results suggest that online psycho-oncological interventions can improve the psychosocial and physical symptoms of patients with cancer.[24–26] There are more approaches to address the different needs of cancer patients.[27, 28] Nevertheless, due to the mixed findings and small sample sizes of studies on such interventions to date, high-quality research with larger, more diverse samples remain necessary.[29, 30]

Objectives and research questions

To overcome the current gap in the provision of psycho-oncological care for patients with cancer, we have developed an innovative eHealth intervention named Make It Training.

Highly time- and cost-efficient, Make It Training provides a novel way to support patients with cancer regardless of their physical conditions or location by improving their social and professional functioning and engagement. The chief objective of our study is to evaluate the acceptability, usability, feasibility and sustainability of Make It Training. In particular, we seek to identify the primary characteristics of patients with cancer in order to determine target populations for the intervention, namely by evaluating:

1. Acceptance and adherence to Make It Training; and
2. Dropout in and the usability of Make It Training.

Our secondary objectives refer to initial indications of the efficacy of Make It Training in order to identify patient characteristics that might determine potential benefits for patients with cancer. To that end, we developed two research questions:

1. Does Make It Training lead to increased self-efficacy, QoL and mindfulness among patients with cancer?
2. Does Make It Training lead to reduced distress, depression and anxiety among patients with cancer?

Because developing modern, issue-based interventions is important to improve patients' acceptance of eHealth interventions,[22] the results of our study promise to afford broad knowledge applicable to identifying and addressing specific groups of patients with cancer who are open to and may benefit from eHealth interventions in psycho-oncological care.

METHODS AND ANALYSIS

Study design

Our multicentre observational healthcare study is designed to offer the web-based intervention of Make It Training to a large number of patients with cancer. The proposed procedure for the study appears in Figure 1. Once cancer diagnosis is determined from their medical records, participating patients will complete the online baseline assessment (T0) and receive their personal Make It Training usernames from the research team. Further

assessments will be made directly after the completion of the intervention (T1) and at both 3 and 6 months later (T2 and T3, respectively). In the case of discontinuation (i.e. no login for 6 weeks after the first uncompleted module), patients will be asked to complete a questionnaire addressing their reasons for not completing Make It Training. During the intervention, each patient will receive a notification every 2 weeks stating that a new module is accessible. To improve study adherence, patients who have been inactive for 4 weeks will receive an additional notification to motivate them to continue Make It Training. The intervention will be considered to be complete when at least five of eight modules have been conducted.

Please insert Figure 1 here

Figure 1 Overall study design

Participant eligibility and recruitment

Patients with cancer will be included regardless of their demographic or medical characteristics (e.g. age and tumour entity), provided that they have a good command of the German language, internet access and basic computer skills, are at least 18 years of age and have given their informed consent. Patients will be recruited at University Hospitals Essen, Erlangen and Tübingen, at outpatient cancer institutions (e.g. established physicians), with the distribution of flyers and from the publicly accessible website for Make It Training.[31] Patients will be recruited from self-help and other groups on social media. At all three university hospitals, we will contact all patients with cancer who have indicated interest in participating in studies for patients with cancer and send them informational material about our study via email. Their informed consent will be given with their online confirmation of the study conditions in advance of the first assessment.

eHealth Intervention-Make It Training

Make It Training is a self-guided, interactive and web-based intervention that patients can use on their own personal computers, smartphones or tablets. Make It Training is based on established, effective methods of cognitive behavioural therapy, mindfulness therapy and

acceptance and commitment therapy.[9, 15, 16, 32] By combining both skills training and practices of mindfulness, Make It Training can address the different needs of psychologically burdened patients with cancer.[33] A previous pilot study with $n = 35$ has demonstrated the good acceptance and contentment rates of an exemplary module of the Make It Training.[34] The eight modules of Make It Training contain different media -tutorial videos, audio, individual skills boxes and patient-centred, interactive exercises- to enhance the acquisition of knowledge about specific disease-related topics (e.g. emotion management, resources, stress management and self-compassion). All guided mindfulness exercises are available as audio files and can be downloaded onto the patients' devices. Table 1 gives an overview of the contents of the individual modules of Make It Training translated into English.[34] Make It Training consists of eight 30-minute modules offered at the rate of one module every 2 weeks for 4 months. In addition to the eight modules, mindfulness exercises to be performed at home should be integrated into patients' daily routines. The interval of 2 weeks per module was chosen to afford patients sufficient time to integrate mindfulness exercises into their daily lives, which should improve their likelihood of continuing the exercises once the intervention has ended.

Table 1 Overview of the topics, contents and exercises of Make It Training

	Topic	Psychoeducation	Skills	Mindfulness
1. Module Introduction	The idea of the skills and mindfulness training and skills	<i>*No psycho-education because of introduction*</i>	<i>*No skills training because of intense mindfulness exercise*</i>	Mindful drinking
2. Module Emotions	Accepting and dealing with emotions	The presence of cancer-related emotions such as anxiety, sadness and anger	<ul style="list-style-type: none">Exercise: Giving emotions spaceDistance strategiesAcceptance cards	Mindful breathing
3. Module Experiencing	Experiencing one's environment without judging it	<i>*No psycho-education because of intense mindfulness exercise*</i>	<i>*No skills training because of intense mindfulness exercise*</i>	Mindful experiencing
4. Module Sources of strength	Discovering and consciously using personal sources of strength	The emergence of vicious mental cycles and the meaning of individual sources of strength	<ul style="list-style-type: none">Exercise: Exiting the vicious cycle by using personal sources of strengthAction cards	Mindful listening

5. Module Body awareness	Feeling one's body in new and different ways	<i>*No psycho-education because of intense mindfulness exercise*</i>	<i>*No skills training because of intense mindfulness exercise*</i>	Mindful body awareness
6. Module Stress management	Mastering stress-intensive situations based on personal thoughts	The meaning of thoughts for subjective experience and feelings of stress	<ul style="list-style-type: none"> Exercise: ABC model Motivational quotations Reward cards 	Mindful vision
7. Module Self-care	To meet myself lovingly and benevolently	Self-esteem and its importance in the context of cancer	<ul style="list-style-type: none"> Exercise: Strengthen my self-esteem house My self-care Kind companion 	Mindful compassion
8. Module Emergency kit and skills boxes	Reviewing Make It Training and helpful skills	Use of the emergency kit with individual helpful skills	<ul style="list-style-type: none"> My emergency kit Exercise: Skills for emotional emergencies 	Favourite mindfulness exercise

Primary outcome measures

The schedule of the different assessments, each lasting between 10 and 25 minutes, is summarised in Table 2. Demographic data (e.g. gender, age, children, family status and employment status) and medical data (e.g. tumour entity, treatment method, date of diagnosis and type of therapy) will be self-reported and collected via the online survey application *Unipark* before the patients start the intervention (T0).[35]

Table 2 Assessment schedule

Measures	Assessment time points			
	T0: Baseline	T1: Post intervention	T2 & T3: Follow-up at 3 and 6 months	Dropout assessment
Primary outcome				
Demographic & medical characteristics	x			
Evaluation of Make It Training				
SUS		x		x
CSQ-I		x		x
APOI		x		x
Self-generated evaluation items		x		x
Secondary outcomes				
DT	x	x	x	x
PHQ-8	x	x	x	x
GAD-7	x	x	x	x
GSES	x	x	x	x
FMI	x	x	x	x
PSQ-20	x	x	x	x

EQ-5D-3L	EQ-5D-3L	X	X	X	X
FACT-G		X	X	X	X

Note: SUS = System Usability Scale; CSQ-I = Client Satisfaction Questionnaire adapted to Internet-based interventions; APOI = Attitudes Towards Psychological Online Interventions; DT = Distress Thermometer; PHQ-8 = Patient Health Questionnaire Depression Scale; GAD-7 = Generalized Anxiety Disorder Scale-7; GSES = General Self-Efficacy Scale; FMI = Freiburg Mindfulness Inventory; PSQ-20 = Perceived Stress Questionnaire; EQ-5D-3L = European Quality of Life 5 Dimensions 3 Level Version; FACT-G = Functional Assessment of Cancer Therapy – General.

Secondary outcome measures

We will use the German version of the Distress Thermometer (DT) to assess patients’ distress experienced in the past week.[36] By contrast, depression and anxiety will be assessed with the German versions of the Patient Health Questionnaire Depression Scale (PHQ-8) and the Generalized Anxiety Disorder Scale-7 (GAD-7), respectively.[37, 38] To gauge self-efficacy, we plan to use the German version of the General Self-Efficacy Scale (GSE),[39] whereas to assess mindfulness, we propose to use the German version of the Freiburg Mindfulness Inventory (FMI).[40] The German version of the Perceived Stress Questionnaire (PSQ) without the Joy sub-scale will be used to investigate and determine subjective perception, evaluation and the further processing of stressors.[41] To gather relevant information about the current somatic state of patients, we will use the Physical Well-Being sub-scale of the German version of the Functional Assessment of Cancer Therapy - General (FACT-G).[42] Last, to assess patients’ quality of life, we plan to use the German version of the 5-item European Quality of Life 5 Dimensions 3 Level Version (EQ-5D-3L) questionnaire.[43]

Evaluation of Make It Training

To evaluate the usability of and patients’ satisfaction with Make It Training, we will use a modified German version of the 10-item System Usability Scale (SUS),[44] the German version of the Client Satisfaction Questionnaire adapted to Internet-based interventions (CSQ-I)[45] and self-generated items, all to gather detailed information about the strengths and weaknesses of Make It Training. For each item-based topic, patients will have the possibility to add their personal thoughts and ideas. The patients’ acceptance of online psychological

interventions in general and their possible changes in attitude will be collected with the Attitudes Towards Psychological Online Interventions (APOI) instrument.[46] Reasons for not completing Make It Training will also be obtained, whereas data concerning adherence to the training (e.g. last login and time needed for modules) will be collected via backend functions of the Make It system.

Sample size calculation and statistical analyses

The sample size estimation will be done based on the BREATH study,[26] in which an effect size of Cohen's $d = 0.28$ was observed for General Self-Efficacy Scale.[39] Based on that effect size, we have calculated the need for a sample size of 103 patients using two-sided t tests for dependent samples with type 1 error of 0.05 and a power of 80%. Although a dropout rate of up to 50% for online interventions has been shown,[47] we might expect an even higher rate of dropout given the physically vulnerable patient group that will form our sample and because the last measurement will occur 6 months after the intervention has ended. Assuming that some patients will not complete the first online assessment and thus not start Make It Training after recruitment,[48] we plan to recruit 500 patients at T0. We will perform standard techniques of data preparation with tests of normality and homogeneity as well as conduct different descriptive analyses of socio-demographic and medical data. The primary statistical analyses will be an analysis of variance with repeated measurements, t tests for dependent samples (i.e. with two-sided p values and 95% confidence intervals) and regression analyses to identify potential predictors of treatment outcomes. We will consider above mentioned medical characteristics as potential covariates and include these in our primary analysis.

Patient and public involvement

Neither patients nor public were involved in the development of this study design, but as previously mentioned, patients were involved in developing the intervention content.[33] Furthermore, we conducted a pilot study on the acceptance of an exemplary module of Make

It Training.[34] During the proposed study, we will also collect data on how Make It Training can be improved to subsequently improve it.

Ethics and dissemination

The Ethics Committees of the University Hospitals Essen, Erlangen and Tübingen have approved the study (19-8643-BO, 27_19 B, 293/2018BO1). Results will be disseminated in peer-reviewed journals and conference presentations. Key findings will also be published on the Make It Training website.

Trial status

Trial start date: 22th October 2019; Currently recruiting ($N_{\text{current}} = 60$ as of December 16, 2019).

DISCUSSION

In our study, we propose to evaluate whether specific groups of patients who differ in terms of socio-demographic data (e.g. age, sex and family status) and medical data (e.g. medical condition, time since cancer diagnosis and tumour entity) are generally open to using an innovative psycho-oncological eHealth intervention. Our evaluation is important in order to adapt modern interventions to the specific requirements and desires of such groups and to efficiently offer a low-threshold eHealth intervention. Our preliminary findings from a longitudinal perspective will suggest whether the self-guided, web-based Make It Training intervention is an efficient tool to support patients with cancer. In addition, we expect to be able to identify specific reasons for patient dropout that can help us to improve Make It Training in particular and to develop patient centred eHealth interventions in general. A key topic of discussion for subsequent research will be whether a self-guided online intervention can be effectively used to support patients with cancer. Although various studies have highlighted the importance of therapeutic contact in online interventions,[49] implementing such interventions in everyday healthcare necessarily faces numerous obstacles (e.g. higher costs and mostly accessibility during research work only).[50] In addition, evidence suggests

that the efficacy of treatment between guided and self-guided online interventions for depression does not significantly differ.[51] Make It Training attempts to overcome the mentioned barriers by offering a completely self-guided tool to support all patients with cancer anytime and anywhere. One expected limitation of the study is the non-existence of a control group to obtain sufficient data regarding the effectiveness of Make It Training. However, among its anticipated strengths is that we will offer Make It Training to all patients with cancer and gain valid information about the usability, feasibility and sustainability of web-based, self-guided psycho-oncological interventions. In a future study, we also plan to conduct a multicentre RCT to obtain valid information on the efficacy of Make It Training. Although many patients with cancer suffer from acute psychological distress, psycho-oncological support is often absent, unavailable or non-existent. Make It Training is one eHealth approach to overcome barriers on both the patient and provider side to offer patients with cancer a self-guided psycho-oncological intervention at any time and any place. Such interventions are time- and cost-efficient and afford broad availability in clinical routines for all patients at any stage of the disease, whether they are in acute care or have survived cancer. Make It Training in particular and self-guided eHealth interventions in general could be integrated in current healthcare systems to offer substantial benefits for patients and providers.

Author contributions AB contributed to designing the study, administering the trial and preparing the manuscript. MT initiated the study and contributed to designing the study, developing the intervention, procuring funding and preparing the manuscript. JG contributed to designing the study, developing the intervention, administering the trial and preparing the manuscript. MB and ES contributed to preparing the manuscript. NS and FJ contributed to developing the intervention and helping with the manuscript. CS contributed to administering the trial and preparing the manuscript. SZ contributed to designing the study, developing the

intervention and procuring funding. YE contributed to designing the study, procuring funding and preparing the manuscript. All authors have read and approved the final manuscript.

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Ethics approval The Ethics Committees of the University Hospitals Essen (19-8643-BO), Erlangen (27_19 B) and Tübingen (293/2018BO1) have approved the study.

REFERENCES

- 1 Mehnert A, Hartung TJ, Friedrich M, et al. One in two cancer patients is significantly distressed: Prevalence and indicators of distress. *Psychooncology* 2018;27:75-82.
- 2 Mehnert A, Brähler E, Faller H, et al. Four-Week Prevalence of Mental Disorders in Patients With Cancer Across Major Tumor Entities. *J Clin Oncol* 2014;1;32:3540-6.
- 3 Kuhnt S, Brähler E, Faller H, et al. Twelve-Month and Lifetime Prevalence of mental Disorders in Cancer patients. *Psychother Psychosom* 2016;85:289-96.
- 4 Singer S, Das-Munshi J, Brähler E. Prevalence of mental health conditions in cancer patients in acute care-a meta-analysis. *Ann Oncol* 2010;21:925–30.
- 5 Mitchell AJ, Chan M, Bhatti H, et al. Prevalence of depression, anxiety, and adjustment disorder in oncological, haematological, and palliative-care settings: a meta-analysis of 94 interview-based studies. *Lancet Oncol* 2011;12:160–74.
- 6 Büttner M, König H-H, Löbner M, et al. Out-of-pocket-payments and the financial burden of 502 cancer patients of working age in Germany: results from a longitudinal study. *Support Care Cancer* 2019;27:2221-8.
- 7 Chambers SK, Meng X, Youl P, et al. A five-year prospective study of quality of life after colorectal cancer. *Qual Life Res* 2012;21:1551-64

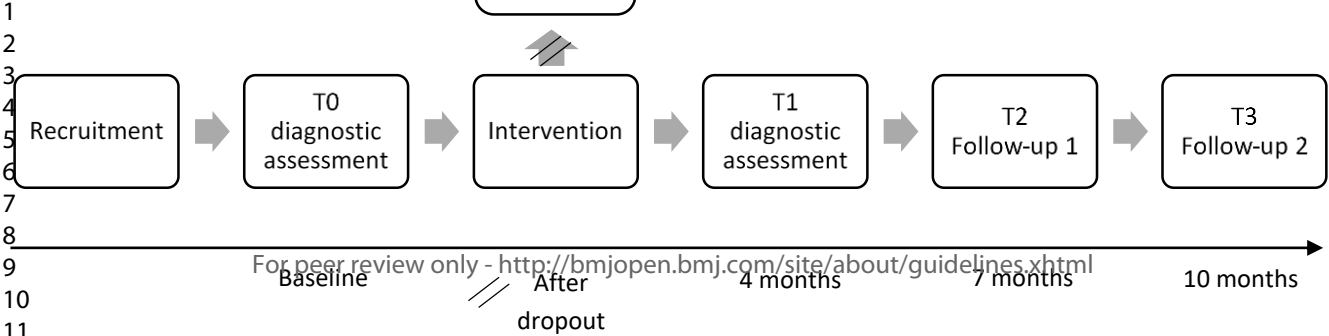
- 8 Park CL, Gaffey AE. Relationships between psychosocial factors and health behavior change in cancer survivors: an integrative review. *Ann Behav Med* 2007;34:115-34.
- 9 Faller H, Schuler M, Richard M, et al. Effects of psycho-oncologic interventions on emotional distress and quality of life in adult patients with cancer: systematic review and meta-analysis. *J Clin Oncol* 2013;20;31:786-93.
- 10 Cwikel JG, Behar LC. Social work with adult cancer patients: a vote-count review of intervention research. *Soc Work Health Care* 1999;29:39-67.
- 11 Faller H, Weis J, Koch U, et al. Utilization of professional psychological care in a large German sample of cancer patients. *Psychooncology* 2017;26:537-43.
- 12 Schaeffeler, N, Pfeiffer K, Ringwald J, et al. Assessing the need for psychooncological support: screening instruments in combination with patients' subjective evaluation may define psychooncological pathways. *Psychooncology* 2015;24:1784-1791.
- 13 Zeissig S.R, Singer S, Koch L, et al. Inanspruchnahme psychoonkologischer Versorgung im Krankenhaus und in Krebsberatungsstellen durch Brust-, Darm- und Prostatakrebsüberlebende. *Psychother Psych Med* 2015;65:177-82,
- 14 Aaronson NK, Mattioli V, Minton O, et al. Beyond treatment - Psychosocial and behavioural issues in cancer survivorship research and practice. *EJC Suppl* 2014;12:54-64.
- 15 Zainal NZ, Booth S, Huppert FA. The efficacy of mindfulness-based stress reduction on mental health of breast cancer patients: A meta-analysis. *Psychooncology* 2013;22:1457-65.
- 16 Rush SE, Sharman M. Mindfulness-based stress reduction as a stress management intervention for cancer care: a systematic review. *J Evid Based Complementary Altern Med* 2017;22:348-60.
- 17 Wells N, Hepworth JT, Murphy BA, et al. Improving cancer pain management through patient and family education. *J Pain Symptom Manage* 2003;25:344-56.

- 18 Duijts SF, Faber MM, Oldenburg HS, et al. Effectiveness of behavioral techniques and physical exercise on psychosocial functioning and health-related quality of life in breast cancer patients and survivors—a meta-analysis. *Psychooncology* 2011;20:115-26.
- 19 Leykin Y, Thekdi SM, Shumay DM, et al. Internet interventions for improving psychological well-being in psycho-oncology: review and recommendations. *Psychooncology* 2012;21:1016-25.
- 20 Dilworth S, Higgins I, Parker V, et al. Patient and health professional's perceived barriers to the delivery of psychosocial care to adults with cancer: a systematic review. *Psychooncology* 2014;23:601-12.
- 21 Zebrack BJ, Block R, Hayes-Lattin B, et al. Psychosocial service use and unmet need among recently diagnosed adolescent and young adult cancer patients. *Cancer* 2013;119:201-14.
- 22 Andersson G. Internet-Delivered Psychological Treatments. *Annu Rev Clin Psychol* 2016;12:157-79.
- 23 Andersson G, Cuijpers P, Carlbringe P, et al. Guided Internet-based vs. face-to-face cognitive behavior therapy for psychiatric and somatic disorders: a systematic review and meta-analysis. *World Psychiatry* 2014;13:288-95.
- 24 Bouma G, Admiraal JM, de Vries EG, et al. Internet-based support programs to alleviate psychosocial and physical symptoms in cancer patients: A literature analysis. *Crit Rev Oncol Hematol* 2015;95:26–37.
- 25 Urech C, Grossert A, Alder J, et al. Web-Based Stress Management for Newly Diagnosed Patients With Cancer (STREAM): A Randomized, Wait-List Controlled Intervention Study. *J Clin Oncol* 2018;36:780-8.
- 26 Willems RA, Bolman CA, Mesters I, et al. Short-term effectiveness of a web-based tailored intervention for cancer survivors on quality of life, anxiety, depression, and fatigue: randomized controlled trial. *Psychooncology* 2016; 26:222-30.

- 27 Krusche A, Bradbury K, Corbett T, et al. Renewed: Protocol for a randomised controlled trial of a digital intervention to support quality of life in cancer survivors. *BMJ Open* 2019;9:e024862.
- 28 Akechi T, Yamaguchi T, Uchida M, et al. Smartphone problem-solving and behavioural activation therapy to reduce fear of recurrence among patients with breast cancer (SMartphone Intervention to LEssen fear of cancer recurrence: SMILE project): protocol for a randomised controlled trial. *BMJ Open* 2018;8: e024794.
- 29 Hong Y, Peña-Purcell NC, Ory MG. Outcomes of online support and resources for cancer survivors: A systematic literature review. *Patient Educ Couns* 2012;86:288-96.
- 30 Butow P, Smith A. Systematic reviews of pain and online interventions for cancer patients show evidence of mixed efficacy and highlight need for more rigorously designed research. *Patient Educ Couns* 2015;98:267-8.
- 31 Make It. <https://makeit-essen.medizin.uni-tuebingen.de>. Accessed 08 December 2019.
- 32 Casellas-Grau A, Font A, Vives J. Positive psychology interventions in breast cancer. A systematic review. *Psychooncology* 2014;23:9-19.
- 33 Ringwald J, Marwedel L, Junne F, et al. Demands and Need for Psycho-Oncological eHealth Interventions in Women With Cancer: Cross-Sectional Study. *JMIR Cancer* 2017;24;3:e19.
- 34 Ringwald J, Gerstner L, Junne F, et al. Mindfulness and Skills Based Distress Reduction in Oncology: The Web-Based Psycho-Oncological Make It Training. *Psychother Psychosom Med Psychol* 2019; doi:10.1055/a-0835-6905
- 35 Questback GmbH. <https://www.unipark.com>. Accessed 08 December 2019.
- 36 Mehnert A, Müller D, Lehmann C, et al. Die deutsche Version des NCCN Distress-Thermometers Empirische Prüfung eines Screening Instruments zur Erfassung psychosozialer Belastung bei Krebspatienten. *Zeitschrift für Psychiatrie, Psychologie und Psychotherapie* 2006;54:213-23.

- 37 Kroenke K, Strine TW, Spitzer RL, et al. The PHQ-8 as a measure of current depression in the general population. *J Affect Disord* 2009;114:163–73.
- 38 Spitzer RL, Kroenke K, Williams JB, et al. A brief measure for assessing generalized anxiety disorder: The GAD-7. *Arch Intern Med* 2006;166:1092–7.
- 39 Schwarzer R, Jerusalem M. Skalen zur Erfassung von Lehrer- und Schülermerkmalen. Dokumentation der psychometrischen Verfahren im Rahmen der Wissenschaftlichen Begleitung des Modellversuchs Selbstwirksame Schulen. Berlin, Freie Universität Berlin 1999.
- 40 Walach H, Buchheld N, Buttenmüller V, et al. Measuring mindfulness - The Freiburg Mindfulness Inventory (FMI). *Pers Individ Dif* 2006;40:1543-55.
- 41 Fliege H, Rose M, Arck P, et al. Validierung des "Perceived Stress Questionnaire" (PSQ) an einer deutschen Stichprobe. *Diagnostica* 2001;47:142-152.
- 42 Cella D, Tulsky D, Gray G, et al. The Functional Assessment of Cancer Therapy Scale: Development and Validation of the General Measure. *J Clin Oncol* 1993;11:570-579.
- 43 The EuroQol Group. EuroQol-a new facility for the measurement of health-related quality of life. *Health Policy* 1990;16:199-208.
- 44 Brooke J. SUS: A 'quick and dirty' usability scale. In: Jordan PW, Thomas B, Weerdmeester BA, McClelland IL, eds. Usability Evaluation in Industry. London: Taylor & Francis 1996:189-94.
- 45 Boß L, Lehr D, Reis D, et al. Reliability and Validity of Assessing User Satisfaction With Web-Based Health Interventions. *J Med Internet Res* 2016;18: e234.
- 46 Schröder J, Sautier L, Kriston L, et al. Development of a questionnaire measuring Attitudes towards Psychological Online Interventions—the APOI. *J Affect Disord* 2015;187:136-41.
- 47 Christensen H, Griffiths KM, Farrer L. Adherence in internet interventions for anxiety and depression. *J Med Internet Res* 2009;11:e13.

- 1
2
3 48 Waller R, Gilbody S. Barriers to the uptake of computerized cognitive behavioural
4 therapy: a systematic review of the quantitative and qualitative evidence. *Psychol Med*
5 2009;39:705-712.
6
7
8
9
10 49 Palmqvist B, Carlbring P, Andersson G. Internet-delivered treatments with or without
11 therapist input: does the therapist factor have implications for efficacy and cost? *Expert*
12 *Rev Pharmacoecon Outcomes Res* 2007;7:291-7.
13
14
15
16
17 50 Andersson G, Titov N, Dear BF, et al. Internet-delivered psychological treatments: from
18 innovation to implementation. *World Psychiatry* 2019;18:20–28.
19
20
21 51 Berger T, Hämmerli K, Gubser N, et al. Internet-Based Treatment of Depression: A
22 Randomized Controlled Trial Comparing Guided with Unguided Self-Help. *Cogn Behav*
23 *Ther* 2011;40:251-266.
24
25
26
27
28
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Web-based MINDfulness- and Skills-based distress reduction in cancer (MINDS): Study Protocol for a multicentre observational healthcare study.

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Web-based MINDfulness- and Skills-based distress reduction in cancer (MINDS): Study Protocol for a multicentre observational healthcare study.

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ABSTRACT

Introduction Although a high percentage of patients with cancer experience severe psychological distress, few of them receive psycho-oncological care, largely due to barriers on the side of patients and healthcare providers that pose great challenges to delivering such care. In response, low-threshold, self-guided eHealth interventions can enable patients with cancer to deal independently and effectively with disease-related challenges and distress. Mindfulness- and Skills-Based Distress Reduction in Oncology Training, nicknamed Make It Training, is one such innovative, self-guided eHealth intervention. In our study, we propose to assess different characteristics of such patients in order to define target populations for Make It Training, evaluate the intervention in terms of its usability, feasibility and sustainability and gather longitudinal data concerning the intervention's efficacy.

Methods and analysis Self-guided and web-based, Make It Training consists of eight 30-minute modules involving the use of techniques of mindfulness therapy, cognitive behavioural therapy and acceptance and commitment therapy to be completed in a 4-month period. In our observational study, adult patients with cancer who possess adequate German-language skills and provide their informed consent will be recruited at Essen, Erlangen and Tübingen University Hospitals, at outpatient oncological institutions and via online channels. Patients will undergo a baseline online assessment (T0), an assessment directly after completing the intervention (T1) and assessments 3 and 6 months later (T2 and T3, respectively). With the results of those assessments, we will perform descriptive analyses of their socio-demographic and medical data, compare means and conduct regression analyses.

Ethics and dissemination The Ethics Committees of the University Hospitals Essen, Erlangen and Tübingen have approved the study (19-8643-BO, 27_19 B, 293/2018BO1). Results will be published in peer-reviewed journals and conference presentations.

Trial registration This study was registered at the German Clinical Trials Register (DRKS00017119) on August 29, 2019.

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Strengths and limitations of this study

- The web-based intervention was developed using evidence-, theory- and person-based approaches.
- The study will evaluate the intervention in terms of acceptance, usability, feasibility and sustainability and collect longitudinal data on the effectiveness of the web-based approach.
- Provision of the web-based training for a large number of cancer patients independent of the tumor entity.
- No randomised controlled study design.

INTRODUCTION

Despite considerable improvements in the treatment of different tumour entities, every second patient with cancer suffers from acute psychological distress.[1] In fact, a third of all patients with cancer involving major tumour entities will meet the criteria for at least one mental health disorder at four-week prevalence.[2] Over a lifetime, however, the prevalence of any mental disorder in patients with cancer rises to more than 56%.[3] Psychological distress in patients with cancer is often associated with changed roles in their professional and family lives, financial problems and reduced quality of life (QoL),[4–6] and high distress can even reduce compliance with treatment.[7, 8] As a partial antidote, psycho-oncological interventions can significantly reduce the psychological distress and improve the QoL of patients with cancer.[9, 10] Although many patients with cancer demonstrate a great need for adequate psycho-oncological care in order to overcome disease-related distress, depression and anxiety,[11, 12] few of them receive such care.[13] In response, it is crucial for health care institutions to offer patients with cancer usable, sustainable and accessible interventions, such as eHealth interventions involving psycho-oncological treatment approaches for routine clinical care.[14]

Cognitive behavioral therapy and mindfulness in psycho-oncological interventions

Various studies have revealed that cognitive behavioural therapy (CBT) and mindfulness-based stress reduction (MBSR) significantly reduce distress, depression and anxiety in patients with cancer.[9, 15, 16] Such approaches can also increase their QoL and reduce the treatment-related side effects that patients with cancer may experience.[7, 8, 17] To date, the effect sizes of psycho-oncological interventions based on CBT and MBSR have been small to medium in randomised controlled trials (RCT).[18]

Psycho-oncological eHealth intervention

Given the increasing influence of internet use in daily life, web-based psycho-oncological care has the potential to reach high volumes of patients and to overcome barriers to healthcare provision on the side of patients and providers (e.g. rural areas, stigma, privacy, high costs and long wait times).[19, 20] In particular, eHealth interventions can be efficient approaches to reaching younger patients who report more unmet needs, are less likely to access psycho-oncological help but are generally more open to modern and web-based approaches.[21] At the same time, easy integration of psycho-oncological care through eHealth approaches into patients' lives prevents an additional workload for this vulnerable group.[21] Compared to the effects of face-to-face CBT interventions in several mental and somatic disorders, online CBT interventions lead to comparable efficacy outcomes.[22, 23] Other promising results suggest that online psycho-oncological interventions can improve the psychosocial and physical symptoms of patients with cancer.[24–26] There are more approaches to address the different needs of cancer patients.[27, 28] Nevertheless, due to the mixed findings and small sample sizes of studies on such interventions to date, high-quality research with larger, more diverse samples remain necessary.[29, 30]

Objectives and research questions

To overcome the current gap in the provision of psycho-oncological care for patients with cancer, we have developed an innovative eHealth intervention named Make It Training.

Highly time- and cost-efficient, Make It Training provides a novel way to support patients with cancer regardless of their physical conditions or location by improving their social and professional functioning and engagement. The chief objective of our study is to evaluate the acceptability, usability, feasibility and sustainability of Make It Training. In particular, we seek to identify the primary characteristics of patients with cancer in order to determine target populations for the intervention, namely by evaluating:

1. Acceptance and adherence to Make It Training; and
2. Dropout in and the usability of Make It Training.

Our secondary objectives refer to initial indications of the efficacy of Make It Training in order to identify patient characteristics that might determine potential benefits for patients with cancer. To that end, we developed two research questions:

1. Does Make It Training lead to increased self-efficacy, QoL and mindfulness among patients with cancer?
2. Does Make It Training lead to reduced distress, depression and anxiety among patients with cancer?

Because developing modern, issue-based interventions is important to improve patients' acceptance of eHealth interventions,[22] the results of our study promise to afford broad knowledge applicable to identifying and addressing specific groups of patients with cancer who are open to and may benefit from eHealth interventions in psycho-oncological care.

METHODS AND ANALYSIS

Study design

Our multicentre observational healthcare study is designed to offer the web-based intervention of Make It Training to a large number of patients with cancer. The proposed procedure for the study appears in Figure 1. Once cancer diagnosis is determined from their medical records, participating patients will complete the online baseline assessment (T0) and receive their personal Make It Training usernames from the research team. Further

assessments will be made directly after the completion of the intervention (T1) and at both 3 and 6 months later (T2 and T3, respectively). In the case of discontinuation (i.e. no login for 6 weeks after the first uncompleted module), patients will be asked to complete a questionnaire addressing their reasons for not completing Make It Training. During the intervention, each patient will receive a notification every 2 weeks stating that a new module is accessible. To improve study adherence, patients who have been inactive for 4 weeks will receive an additional notification to motivate them to continue Make It Training. The intervention will be considered to be complete when at least five of eight modules have been conducted.

Please insert Figure 1 here

Figure 1 Overall study design

Participant eligibility and recruitment

Patients with cancer will be included regardless of their demographic or medical characteristics (e.g. age and tumour entity), provided that they have a good command of the German language, internet access and basic computer skills, are at least 18 years of age and have given their informed consent. Patients will be recruited at University Hospitals Essen, Erlangen and Tübingen, at outpatient cancer institutions (e.g. established physicians), with the distribution of flyers and from the publicly accessible website for Make It Training.[31] Patients will be recruited from self-help and other groups on social media. At all three university hospitals, we will contact all patients with cancer who have indicated interest in participating in studies for patients with cancer and send them informational material about our study via email. Their informed consent will be given with their online confirmation of the study conditions in advance of the first assessment.

eHealth Intervention-Make It Training

Make It Training is a self-guided, interactive and web-based intervention that patients can use on their own personal computers, smartphones or tablets. Make It Training is based on established, effective methods of cognitive behavioural therapy, mindfulness therapy and

acceptance and commitment therapy.[9, 15, 16, 32] By combining both skills training and practices of mindfulness, Make It Training can address the different needs of psychologically burdened patients with cancer.[33] A previous pilot study with $n = 35$ has demonstrated the good acceptance and contentment rates of an exemplary module of the Make It Training.[34] The eight modules of Make It Training contain different media -tutorial videos, audio, individual skills boxes and patient-centred, interactive exercises- to enhance the acquisition of knowledge about specific disease-related topics (e.g. emotion management, resources, stress management and self-compassion). All guided mindfulness exercises are available as audio files and can be downloaded onto the patients' devices. Table 1 gives an overview of the contents of the individual modules of Make It Training translated into English.[34] Make It Training consists of eight 30-minute modules offered at the rate of one module every 2 weeks for 4 months. In addition to the eight modules, mindfulness exercises to be performed at home should be integrated into patients' daily routines. The interval of 2 weeks per module was chosen to afford patients sufficient time to integrate mindfulness exercises into their daily lives, which should improve their likelihood of continuing the exercises once the intervention has ended.

Table 1 Overview of the topics, contents and exercises of Make It Training

	Topic	Psychoeducation	Skills	Mindfulness
1. Module Introduction	The idea of the skills and mindfulness training and skills	<i>*No psycho-education because of introduction*</i>	<i>*No skills training because of intense mindfulness exercise*</i>	Mindful drinking
2. Module Emotions	Accepting and dealing with emotions	The presence of cancer-related emotions such as anxiety, sadness and anger	<ul style="list-style-type: none">Exercise: Giving emotions spaceDistance strategiesAcceptance cards	Mindful breathing
3. Module Experiencing	Experiencing one's environment without judging it	<i>*No psycho-education because of intense mindfulness exercise*</i>	<i>*No skills training because of intense mindfulness exercise*</i>	Mindful experiencing
4. Module Sources of strength	Discovering and consciously using personal sources of strength	The emergence of vicious mental cycles and the meaning of individual sources of strength	<ul style="list-style-type: none">Exercise: Exiting the vicious cycle by using personal sources of strengthAction cards	Mindful listening

5. Module Body awareness	Feeling one's body in new and different ways	<i>*No psycho-education because of intense mindfulness exercise*</i>	<i>*No skills training because of intense mindfulness exercise*</i>	Mindful body awareness
6. Module Stress management	Mastering stress-intensive situations based on personal thoughts	The meaning of thoughts for subjective experience and feelings of stress	<ul style="list-style-type: none"> Exercise: ABC model Motivational quotations Reward cards 	Mindful vision
7. Module Self-care	To meet myself lovingly and benevolently	Self-esteem and its importance in the context of cancer	<ul style="list-style-type: none"> Exercise: Strengthen my self-esteem house My self-care Kind companion 	Mindful compassion
8. Module Emergency kit and skills boxes	Reviewing Make It Training and helpful skills	Use of the emergency kit with individual helpful skills	<ul style="list-style-type: none"> My emergency kit Exercise: Skills for emotional emergencies 	Favourite mindfulness exercise

Primary outcome measures

The schedule of the different assessments, each lasting between 10 and 25 minutes, is summarised in Table 2. Demographic data (e.g. gender, age, children, family status and employment status) and medical data (e.g. tumour entity, treatment method, date of diagnosis and type of therapy) will be self-reported and collected via the online survey application *Unipark* before the patients start the intervention (T0).[35]

Table 2 Assessment schedule

Measures	Assessment time points			
	T0: Baseline	T1: Post intervention	T2 & T3: Follow-up at 3 and 6 months	Dropout assessment
Primary outcome				
Demographic & medical characteristics	x			
Evaluation of Make It Training				
SUS		x		x
CSQ-I		x		x
APOI		x		x
Self-generated evaluation items		x		x
Secondary outcomes				
DT	x	x	x	x
PHQ-8	x	x	x	x
GAD-7	x	x	x	x
GSES	x	x	x	x
FMI	x	x	x	x
PSQ-20	x	x	x	x

EQ-5D-3L	EQ-5D-3L	X	X	X	X
FACT-G		X	X	X	X

Note: SUS = System Usability Scale; CSQ-I = Client Satisfaction Questionnaire adapted to Internet-based interventions; APOI = Attitudes Towards Psychological Online Interventions; DT = Distress Thermometer; PHQ-8 = Patient Health Questionnaire Depression Scale; GAD-7 = Generalized Anxiety Disorder Scale-7; GSES = General Self-Efficacy Scale; FMI = Freiburg Mindfulness Inventory; PSQ-20 = Perceived Stress Questionnaire; EQ-5D-3L = European Quality of Life 5 Dimensions 3 Level Version; FACT-G = Functional Assessment of Cancer Therapy – General; ; see Appendix 1 for detailed information on demographic & medical characteristics.

Secondary outcome measures

We will use the German version of the Distress Thermometer (DT) to assess patients’ distress experienced in the past week.[36] By contrast, depression and anxiety will be assessed with the German versions of the Patient Health Questionnaire Depression Scale (PHQ-8) and the Generalized Anxiety Disorder Scale-7 (GAD-7), respectively.[37, 38] To gauge self-efficacy, we plan to use the German version of the General Self-Efficacy Scale (GSE),[39] whereas to assess mindfulness, we propose to use the German version of the Freiburg Mindfulness Inventory (FMI).[40] The German version of the Perceived Stress Questionnaire (PSQ) without the Joy sub-scale will be used to investigate and determine subjective perception, evaluation and the further processing of stressors.[41] To gather relevant information about the current somatic state of patients, we will use the Physical Well-Being sub-scale of the German version of the Functional Assessment of Cancer Therapy - General (FACT-G).[42] Last, to assess patients’ quality of life, we plan to use the German version of the 5-item European Quality of Life 5 Dimensions 3 Level Version (EQ-5D-3L) questionnaire.[43]

Evaluation of Make It Training

To evaluate the usability of and patients’ satisfaction with Make It Training, we will use a modified German version of the 10-item System Usability Scale (SUS),[44] the German version of the Client Satisfaction Questionnaire adapted to Internet-based interventions (CSQ-I)[45] and self-generated items, all to gather detailed information about the strengths and weaknesses of Make It Training. For each item-based topic, patients will have the possibility to add their personal thoughts and ideas. The patients’ acceptance of online psychological

interventions in general and their possible changes in attitude will be collected with the Attitudes Towards Psychological Online Interventions (APOI) instrument.[46] Reasons for not completing Make It Training will also be obtained, whereas data concerning adherence to the training (e.g. last login and time needed for modules) will be collected via backend functions of the Make It system.

Sample size calculation and statistical analyses

The sample size estimation will be done based on the BREATH study,[26] in which an effect size of Cohen's $d = 0.28$ was observed for General Self-Efficacy Scale.[39] Based on that effect size, we have calculated the need for a sample size of 103 patients using two-sided t tests for dependent samples with type 1 error of 0.05 and a power of 80%. Although a dropout rate of up to 50% for online interventions has been shown,[47] we might expect an even higher rate of dropout given the physically vulnerable patient group that will form our sample and because the last measurement will occur 6 months after the intervention has ended. Assuming that some patients will not complete the first online assessment and thus not start Make It Training after recruitment,[48] we plan to recruit 500 patients at T0. We will perform standard techniques of data preparation with tests of normality and homogeneity as well as conduct different descriptive analyses of socio-demographic and medical data. The primary statistical analyses will be an analysis of variance with repeated measurements, t tests for dependent samples (i.e. with two-sided p values and 95% confidence intervals) and regression analyses to identify potential predictors of treatment outcomes. We will consider stage of disease, mindfulness experience and psychiatric co-morbidities as potential covariates, include these in an additional regression model, and perform moderator analyses considering these variables as moderator variables.

Patient and public involvement

Neither patients nor public were involved in the development of this study design, but as previously mentioned, patients were involved in developing the intervention content.[33]

Furthermore, we conducted a pilot study on the acceptance of an exemplary module of Make It Training.[34] During the proposed study, we will also collect data on how Make It Training can be improved to subsequently improve it.

Ethics and dissemination

The Ethics Committees of the University Hospitals Essen, Erlangen and Tübingen have approved the study (19-8643-BO, 27_19 B, 293/2018BO1). Results will be disseminated in peer-reviewed journals and conference presentations. Key findings will also be published on the Make It Training website.

Trial status

Trial start date: 22th October 2019; Currently recruiting ($N_{\text{current}} = 60$ as of December 16, 2019).

DISCUSSION

In our study, we propose to evaluate whether specific groups of patients who differ in terms of socio-demographic data (e.g. age, sex and family status) and medical data (e.g. medical condition, time since cancer diagnosis and tumour entity) are generally open to using an innovative psycho-oncological eHealth intervention. Our evaluation is important in order to adapt modern interventions to the specific requirements and desires of such groups and to efficiently offer a low-threshold eHealth intervention. Our preliminary findings from a longitudinal perspective will suggest whether the self-guided, web-based Make It Training intervention is an efficient tool to support patients with cancer. In addition, we expect to be able to identify specific reasons for patient dropout that can help us to improve Make It Training in particular and to develop patient centred eHealth interventions in general. A key topic of discussion for subsequent research will be whether a self-guided online intervention can be effectively used to support patients with cancer. Although various studies have highlighted the importance of therapeutic contact in online interventions,[49] implementing such interventions in everyday healthcare necessarily faces numerous obstacles (e.g. higher

costs and mostly accessibility during research work only).[50] In addition, evidence suggests that the efficacy of treatment between guided and self-guided online interventions for depression does not significantly differ.[51] Make It Training attempts to overcome the mentioned barriers by offering a completely self-guided tool to support all patients with cancer anytime and anywhere. One expected limitation of the study is the non-existence of a control group to obtain sufficient data regarding the effectiveness of Make It Training. However, among its anticipated strengths is that we will offer Make It Training to all patients with cancer and gain valid information about the usability, feasibility and sustainability of web-based, self-guided psycho-oncological interventions. In a future study, we also plan to conduct a multicentre RCT to obtain valid information on the efficacy of Make It Training. Although many patients with cancer suffer from acute psychological distress, psycho-oncological support is often absent, unavailable or non-existent. Make It Training is one eHealth approach to overcome barriers on both the patient and provider side to offer patients with cancer a self-guided psycho-oncological intervention at any time and any place. Such interventions are time- and cost-efficient and afford broad availability in clinical routines for all patients at any stage of the disease, whether they are in acute care or have survived cancer. Make It Training in particular and self-guided eHealth interventions in general could be integrated in current healthcare systems to offer substantial benefits for patients and providers.

Author contributions AB contributed to designing the study, administering the trial and preparing the manuscript. MT initiated the study and contributed to designing the study, developing the intervention, procuring funding and preparing the manuscript. JG contributed to designing the study, developing the intervention, administering the trial and preparing the manuscript. MB and ES contributed to preparing the manuscript. NS and FJ contributed to developing the intervention and helping with the manuscript. CS contributed to administering

the trial and preparing the manuscript. SZ contributed to designing the study, developing the intervention and procuring funding. YE contributed to designing the study, procuring funding and preparing the manuscript. All authors have read and approved the final manuscript.

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REFERENCES

- 1 Mehnert A, Hartung TJ, Friedrich M, et al. One in two cancer patients is significantly distressed: Prevalence and indicators of distress. *Psychooncology* 2018;27:75-82.
- 2 Mehnert A, Brähler E, Faller H, et al. Four-Week Prevalence of Mental Disorders in Patients With Cancer Across Major Tumor Entities. *J Clin Oncol* 2014;1;32:3540-6.
- 3 Kuhnt S, Brähler E, Faller H, et al. Twelve-Month and Lifetime Prevalence of mental Disorders in Cancer patients. *Psychother Psychosom* 2016;85:289-96.
- 4 Singer S, Das-Munshi J, Brähler E. Prevalence of mental health conditions in cancer patients in acute care-a meta-analysis. *Ann Oncol* 2010;21:925–30.
- 5 Mitchell AJ, Chan M, Bhatti H, et al. Prevalence of depression, anxiety, and adjustment disorder in oncological, haematological, and palliative-care settings: a meta-analysis of 94 interview-based studies. *Lancet Oncol* 2011;12:160–74.
- 6 Büttner M, König H-H, Löbner M, et al. Out-of-pocket-payments and the financial burden of 502 cancer patients of working age in Germany: results from a longitudinal study. *Support Care Cancer* 2019;27:2221-8.

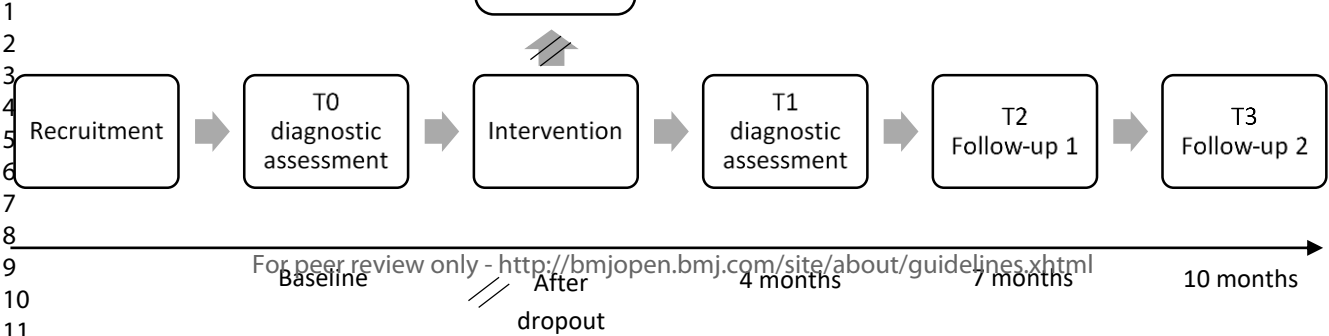
- 7 Chambers SK, Meng X, Youl P, et al. A five-year prospective study of quality of life after colorectal cancer. *Qual Life Res* 2012;21:1551-64
- 8 Park CL, Gaffey AE. Relationships between psychosocial factors and health behavior change in cancer survivors: an integrative review. *Ann Behav Med* 2007;34:115-34.
- 9 Faller H, Schuler M, Richard M, et al. Effects of psycho-oncologic interventions on emotional distress and quality of life in adult patients with cancer: systematic review and meta-analysis. *J Clin Oncol* 2013;20;31:786-93.
- 10 Cwikel JG, Behar LC. Social work with adult cancer patients: a vote-count review of intervention research. *Soc Work Health Care* 1999;29:39-67.
- 11 Faller H, Weis J, Koch U, et al. Utilization of professional psychological care in a large German sample of cancer patients. *Psychooncology* 2017;26:537-43.
- 12 Schaeffeler, N, Pfeiffer K, Ringwald J, et al. Assessing the need for psychooncological support: screening instruments in combination with patients' subjective evaluation may define psychooncological pathways. *Psychooncology* 2015;24:1784-1791.
- 13 Zeissig S.R, Singer S, Koch L, et al. Inanspruchnahme psychoonkologischer Versorgung im Krankenhaus und in Krebsberatungsstellen durch Brust-, Darm- und Prostatakrebsüberlebende. *Psychother Psych Med* 2015;65:177-82,
- 14 Aaronson NK, Mattioli V, Minton O, et al. Beyond treatment - Psychosocial and behavioural issues in cancer survivorship research and practice. *EJC Suppl* 2014;12:54-64.
- 15 Zainal NZ, Booth S, Huppert FA. The efficacy of mindfulness-based stress reduction on mental health of breast cancer patients: A meta-analysis. *Psychooncology* 2013;22:1457-65.
- 16 Rush SE, Sharman M. Mindfulness-based stress reduction as a stress management intervention for cancer care: a systematic review. *J Evid Based Complementary Altern Med* 2017;22:348-60.

- 17 Wells N, Hepworth JT, Murphy BA, et al. Improving cancer pain management through patient and family education. *J Pain Symptom Manage* 2003;25:344-56.
- 18 Duijts SF, Faber MM, Oldenburg HS, et al. Effectiveness of behavioral techniques and physical exercise on psychosocial functioning and health-related quality of life in breast cancer patients and survivors—a meta-analysis. *Psychooncology* 2011;20:115-26.
- 19 Leykin Y, Thekdi SM, Shumay DM, et al. Internet interventions for improving psychological well-being in psycho-oncology: review and recommendations. *Psychooncology* 2012;21:1016-25.
- 20 Dilworth S, Higgins I, Parker V, et al. Patient and health professional's perceived barriers to the delivery of psychosocial care to adults with cancer: a systematic review. *Psychooncology* 2014;23:601-12.
- 21 Zebrack BJ, Block R, Hayes-Lattin B, et al. Psychosocial service use and unmet need among recently diagnosed adolescent and young adult cancer patients. *Cancer* 2013;119:201-14.
- 22 Andersson G. Internet-Delivered Psychological Treatments. *Annu Rev Clin Psychol* 2016;12:157-79.
- 23 Andersson G, Cuijpers P, Carlbring P, et al. Guided Internet-based vs. face-to-face cognitive behavior therapy for psychiatric and somatic disorders: a systematic review and meta-analysis. *World Psychiatry* 2014;13:288-95.
- 24 Bouma G, Admiraal JM, de Vries EG, et al. Internet-based support programs to alleviate psychosocial and physical symptoms in cancer patients: A literature analysis. *Crit Rev Oncol Hematol* 2015;95:26–37.
- 25 Urech C, Grossert A, Alder J, et al. Web-Based Stress Management for Newly Diagnosed Patients With Cancer (STREAM): A Randomized, Wait-List Controlled Intervention Study. *J Clin Oncol* 2018;36:780-8.

- 26 Willems RA, Bolman CA, Mesters I, et al. Short-term effectiveness of a web-based tailored intervention for cancer survivors on quality of life, anxiety, depression, and fatigue: randomized controlled trial. *Psychooncology* 2016; 26:222-30.
- 27 Krusche A, Bradbury K, Corbett T, et al. Renewed: Protocol for a randomised controlled trial of a digital intervention to support quality of life in cancer survivors. *BMJ Open* 2019;9:e024862.
- 28 Akechi T, Yamaguchi T, Uchida M, et al. Smartphone problem-solving and behavioural activation therapy to reduce fear of recurrence among patients with breast cancer (SMartphone Intervention to LEssen fear of cancer recurrence: SMILE project): protocol for a randomised controlled trial. *BMJ Open* 2018;8: e024794.
- 29 Hong Y, Peña-Purcell NC, Ory MG. Outcomes of online support and resources for cancer survivors: A systematic literature review. *Patient Educ Couns* 2012;86:288-96.
- 30 Butow P, Smith A. Systematic reviews of pain and online interventions for cancer patients show evidence of mixed efficacy and highlight need for more rigorously designed research. *Patient Educ Couns* 2015;98:267-8.
- 31 Make It. <https://makeit-essen.medizin.uni-tuebingen.de>. Accessed 08 December 2019.
- 32 Casellas-Grau A, Font A, Vives J. Positive psychology interventions in breast cancer. A systematic review. *Psychooncology* 2014;23:9-19.
- 33 Ringwald J, Marwedel L, Junne F, et al. Demands and Need for Psycho-Oncological eHealth Interventions in Women With Cancer: Cross-Sectional Study. *JMIR Cancer* 2017;24;3:e19.
- 34 Ringwald J, Gerstner L, Junne F, et al. Mindfulness and Skills Based Distress Reduction in Oncology: The Web-Based Psycho-Oncological Make It Training. *Psychother Psychosom Med Psychol* 2019; doi:10.1055/a-0835-6905
- 35 Questback GmbH. <https://www.unipark.com>. Accessed 08 December 2019.

- 36 Mehnert A, Müller D, Lehmann C, et al. Die deutsche Version des NCCN Distress-Thermometers Empirische Prüfung eines Screening Instruments zur Erfassung psychosozialer Belastung bei Krebspatienten. *Zeitschrift für Psychiatrie, Psychologie und Psychotherapie* 2006;54:213-23.
- 37 Kroenke K, Strine TW, Spitzer RL, et al. The PHQ-8 as a measure of current depression in the general population. *J Affect Disord* 2009;114:163-73.
- 38 Spitzer RL, Kroenke K, Williams JB, et al. A brief measure for assessing generalized anxiety disorder: The GAD-7. *Arch Intern Med* 2006;166:1092-7.
- 39 Schwarzer R, Jerusalem M. Skalen zur Erfassung von Lehrer- und Schülermerkmalen. Dokumentation der psychometrischen Verfahren im Rahmen der Wissenschaftlichen Begleitung des Modellversuchs Selbstwirksame Schulen. Berlin, Freie Universität Berlin 1999.
- 40 Walach H, Buchheld N, Buttenmüller V, et al. Measuring mindfulness - The Freiburg Mindfulness Inventory (FMI). *Pers Individ Dif* 2006;40:1543-55.
- 41 Fliege H, Rose M, Arck P, et al. Validierung des "Perceived Stress Questionnaire" (PSQ) an einer deutschen Stichprobe. *Diagnostica* 2001;47:142-152.
- 42 Cella D, Tulsky D, Gray G, et al. The Functional Assessment of Cancer Therapy Scale: Development and Validation of the General Measure. *J Clin Oncol* 1993;11:570-579.
- 43 The EuroQol Group. EuroQol-a new facility for the measurement of health-related quality of life. *Health Policy* 1990;16:199-208.
- 44 Brooke J. SUS: A 'quick and dirty' usability scale. In: Jordan PW, Thomas B, Weerdmeester BA, McClelland IL, eds. Usability Evaluation in Industry. London: Taylor & Francis 1996:189-94.
- 45 Boß L, Lehr D, Reis D, et al. Reliability and Validity of Assessing User Satisfaction With Web-Based Health Interventions. *J Med Internet Res* 2016;18: e234.

- 46 Schröder J, Sautier L, Kriston L, et al. Development of a questionnaire measuring Attitudes towards Psychological Online Interventions—the APOI. *J Affect Disord* 2015;187:136-41.
- 47 Christensen H, Griffiths KM, Farrer L. Adherence in internet interventions for anxiety and depression. *J Med Internet Res* 2009;11:e13.
- 48 Waller R, Gilbody S. Barriers to the uptake of computerized cognitive behavioural therapy: a systematic review of the quantitative and qualitative evidence. *Psychol Med* 2009;39:705-712.
- 49 Palmqvist B, Carlbring P, Andersson G. Internet-delivered treatments with or without therapist input: does the therapist factor have implications for efficacy and cost? *Expert Rev Pharmacoecon Outcomes Res* 2007;7:291-7.
- 50 Andersson G, Titov N, Dear BF, et al. Internet-delivered psychological treatments: from innovation to implementation. *World Psychiatry* 2019;18:20–28.
- 51 Berger T, Hämmerli K, Gubser N, et al. Internet-Based Treatment of Depression: A Randomized Controlled Trial Comparing Guided with Unguided Self-Help. *Cogn Behav Ther* 2011;40:251-266.



Appendix 1

Sociodemographic Data

Gender

Age

Marital status

Native language

Children

Highest level of education

Employment status

Private usage of technology (*PC/Laptop, Tablet, Smartphone*)

Length of private internet usage per day

Aim of private internet usage

Financial burden

State of residence

Size of city

Mindfulness experience

How did you come across Make It Training?

Medical Data

Type of cancer

Stage of disease

Current aim of treatment (curative/ palliative/ not decided)

Type of cancer treatment

Other (non-oncological) physical diagnoses

Psychiatric co-morbidities

Current psychotropic drug/psychopharmacological usage

Experience with psychotherapy

Current utilization of psychotherapy