Statistical Analysis Plan (SAP)

for

Final Analysis

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Authors:	Lukas Lange-Drenth Anja Holz (Review) Anne Daubmann (Review) Holger Schulz (Review)
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Responsible Bio statistician:
Anne Daubmann
University Medical Center Hamburg-Eppendorf, Department of Medical Biometry and Epidemiology

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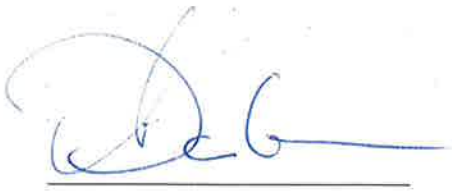
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Principal Investigator / Representative and Sponsor / Representative:
Prof. Holger Schulz, University Medical Center Hamburg-Eppendorf, Department of Psychosomatic Medicine and Psychotherapy

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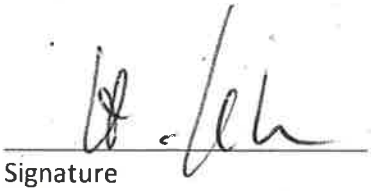
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Document History:

Version No.	Date	Chapter / Attachment	Reason for Review / Modification
00-1	24.06.2025	All chapters	Comments from statisticians
00-2	19.08.2025	All chapters	Comments from principal investigator
01-0	28.08.2025		Final version after implementation of review comments

Abbreviations

Abbreviation	Definition
SAP	Statistical Analysis Plan
DHLI	Digital health literacy Instrument
RIMMS	Reduced Instructional Materials Motivation
AIM	Acceptability of Intervention Measure
IAM	Intervention Appropriateness Measure
FIM	Feasibility of Intervention Measure
FAS	Full analysis set

Content

1 Introduction

This Statistical Analysis Plan (SAP) is based on the study protocol version (Lange-Drenth et al., 2025) and follows the guideline for statistical analysis plans (Gamble et al., 2017).
Some aspects of the statistical methods and the study design are already described in the study protocol (Lange-Drenth et al., 2025). This SAP aims to further specify the procedures and statistical methods applied during the analysis of the study data.

1.1 Background and Rationale

The Internet allows cancer patients to access information about their disease at any time. However, the quality of online information varies widely. Information is often inaccurate or does not provide all the details patients need to make informed decisions. Patients' often inadequate ability to find and critically evaluate cancer-related online information can lead to misinformation. Therefore, an interactive e-learning environment to promote digital health literacy will be developed and evaluated for its effectiveness.
Overall, five different groups (IG1.1-1.3, IG2, control group) will be included in the eHK-Strong study. There are three different versions of the e-learning environment (IG1.1-1.3), tailored to examine different instructional features. Participants in the IG1.1 will receive the e-learning environment with all primary task support elements described. Participants in IG1.2 will receive the same content but will not be guided through the content step by step in a predetermined sequence (tunneling), but can determine the order of the content themselves. Participants in IG1.3 will also receive the same content, but all rehearsal elements such as quizzes, tests or the summary of key points at the end of each chapter will be removed from the e-learning environment. Participants in IG2 will receive the same content as participants in the IG1.1-IG1.3, but not within the interactive e-learning environment, but in a non-interactive PDF format. Participants in the control group will not receive any intervention and will only be referred to the German Cancer Information Service (CIS) brochure “Your journey through cancer”. The brochure, while emphasizing informed decision-making and offering practical advice on medical, psychological, and social aspects of cancer care, does not include guidance on how to search for cancer-related information online.

1.2 Study Objective

The primary objective of the eHK-Strong study is to determine the effectiveness of an interactive e-learning environment (IG1.1–IG1.3) compared to a non-interactive PDF version (IG2) and compared to a control group in improving digital health literacy measured with the German version of the Digital Health Literacy Instrument (DHLI) in cancer patients from baseline (T0) to eight weeks after baseline (T2).
Secondary objectives are to examine: (2) whether cancer patients who use the full e-learning environment (IG1.1) show greater improvements in digital health literacy from baseline (T0) to follow-up (T2) compared to those using the e-learning environment without tunneling elements (IG1.2) or without rehearsal elements (IG1.3);(3) whether the interactive e-learning environments (IG1.1–IG1.3) are more effective in improving digital health literacy from baseline (T0) to eight weeks (T2) in cancer patients compared to the non-interactive PDF version (IG2); (4) whether the effectiveness can also be observed from baseline to two weeks after baseline (T1); (5) whether the effectiveness of the intervention can be demonstrated using the total score of the performance-based items of the DHLI as the outcome;

1.2.1 Other objectives

In addition the following other endpoints are assessed: (6) whether participants’ self-reported motivation mediates the relationship between group assignment and changes in digital health literacy

from T0 to T2; and (7) whether the interactive e-learning environment is perceived by cancer patients as more user-friendly, appropriate, and feasible than the non-interactive PDF format.

1.3 Study Endpoint(s)

1.3.1 Primary endpoint

The primary endpoint of the study is the change (T2 mean score- T0 mean score) in mean self-reported digital health literacy score from baseline to T2 (eight weeks after baseline), as measured by the DHLI (van der Vaart & Drossaert, 2017). A higher mean score indicates higher digital health literacy. A higher change score (T2 mean score-T0 mean score) indicates a greater change in digital health literacy.

1.3.2 Secondary endpoints

- DHLI mean score change from baseline to two weeks after randomization. A higher change score (T1 mean score-T0 mean score) indicates a greater improvement in digital health literacy.
- The change in the performance-based assessment of digital health literacy total score from baseline to eight weeks after baseline, measured with the six performance-based items of the DHLI (van der Vaart & Drossaert, 2017). A higher change score (T2-T0) indicates a greater improvement in digital health literacy.

1.3.3 Other endpoints

- The mean score of self-reported motivation to use the e-learning environment measured with the Reduced Instructional Materials Motivation (RIMMS) (Loorbach, Peters, Karreman, & Steehouder, 2014) two weeks after baseline. A higher mean score indicates greater motivation.
- The mean score of the self-reported acceptability of the e-learning environment as measured by the Acceptability of Intervention Measure (AIM) questionnaire (Weiner et al., 2017) two weeks after baseline. A higher mean score indicates greater acceptance.
- The mean score of the self-reported appropriateness of the e-learning environment as measured by the Intervention Appropriateness Measure (IAM) questionnaire two weeks after baseline. A higher mean score indicates greater appropriateness.
- The mean score of the self-reported feasibility of the e-learning environment as measured by the Feasibility of Intervention Measure (FIM) questionnaire (Weiner et al., 2017) two weeks after baseline. A higher mean score indicates greater feasibility.
- The number of discontinuations of the e-learning environment or deviations from the treatment protocol to determine the acceptability of the e-learning environment will be measured at T1. Participants in the intervention groups will be asked which (1) chapters of the e-learning environment they completed, (2) if they did not complete all chapters, and (3) the reasons why they stopped the e-learning environment early (open-ended question).
- E-learning usage data, such as (1) time spent in the e-learning environment in minutes and (2) which learning blocks were clicked on, is collected anonymously to measure the engagement with the e-learning environment. “These data will be collected for each participant during the active intervention period, defined as first log-in until submission of the last study questionnaire.

1.3.4 Safety endpoints

No safety endpoints are defined in this study, as no medical intervention or risk to participants is involved.

1.3.5 Participants' sociodemographic, recruitment and medical characteristics and Internet use:

Participants characteristics recorded at baseline (T0) include:
- Sociodemographic data (Age, sex, marital status and educational level)
- Recruitment route (recruitment route associated with CIS vs. recruitment route not associated with the CIS)
- Medical data (cancer type, self-reported health status, time since cancer diagnosis)
- Frequency of Internet use, preferred digital device used to access the Internet, preferred mobile operating system (IOS vs. Android vs. other operating system), preferred computer or laptop operating system (Window, macOS or other operating system), frequency of accessing web pages on the subject of health, frequency of using social media (including online forums) for health-related purposes, frequency of using health apps on a mobile phone, frequency of digital interaction with healthcare providers (e.g., video consultations, online appointment scheduling)

2 Study Methods

2.1 Trial Design

This eHK-Strong trial is a stratified randomized controlled superiority trial with five parallel groups (IG1.1-1.3, IG2, and control group) with a 1:1:1:1:1 allocation. To enhance the objectivity of the outcomes and minimize expectation-related bias, single blinding will be applied: participants will be blinded to their group assignment, while the study team is aware of group allocations. Double blinding was not possible due to practical constraints during study planning and implementation.
Participants in the control group will not receive any intervention and will instead be referred to the CIS brochure “Your Journey Through Cancer”, which does not provide any guidance on how to search for cancer-related information online.

The five study arms are:
- IG1.1: Participants receiving an interactive e-learning environment with all primary task supports.
- IG1.2: Participants receiving the same content as IG1.1 without tunnelling, i.e. they will not be guided through the content step by step.
- IG1.3: Participants receiving the same content as IG1.1, but all rehearsal elements such as quizzes will be removed from the e-learning environment.
- IG2: Participants receiving the same content as participants in the IG1.1, but not within the interactive learning environment, but in a non-interactive PDF format.
- Control group: Participants in the control group will not receive any intervention and will only be referred to the CIS brochure "Your journey through cancer”.

2.2 Randomization

Participants will be randomized to the five treatment groups, based on a stratified randomization sequence with variable block length in an allocation ratio of 1:1:1:1:1.
Stratification will be based on two factors: (1) Recruitment route (CIS-associated vs. non-CIS-associated), and (2) Cancer type (breast cancer vs. other cancers). These strata were chosen to reflect relevant population characteristics.

2.3 Sample Size

The sample size calculation for the primary hypothesis was calculated using PASS 2008 for a one-way ANOVA. We set the two-sided significance level at 5% and the power at 80%. For the sample size

calculation, we expected that at T2 there will be a greater improvement in digital health literacy in the e-learning groups (IG1.1 to IG1.3) and IG2 (non-interactive PDF group) compared to the control group. The study by Mitsuhashi (32) found an effect size of Cohen's d=0.25 at 2 weeks. We assume that we will achieve a slightly higher effect size: First, because we involve patients in the design process of the digital learning offerings, and second, because the content of our e-learning environment is presented in a more interactive and engaging manner. In the case number design, we assume an effect size between the e-learning environment (IG1.1, IG1.2 and IG1.3) and the control group and between IG2 and the control group of Cohen's d=0.35. These assumptions correspond to an effect size of f=0.165. The sample size calculation results in 297 participants for the three e-learning environment groups (IG1.1, IG1.2, and IG1.3) and 99 each for IG2 and the control group, for a total of 495 participants (Figure 4).
In the above-mentioned study by Mitsuhashi (2018), 6% of participants dropped out in the two weeks between baseline and follow-up. In other RCTs involving the promotion of digital health literacy in older adults, dropout rates ranged from 13% to 26% in the period between 2 weeks and 9 months (Chu, Huber, Mastel-Smith, & Cesario, 2009; Nahm et al., 2019; Woodward et al., 2010; B. Xie, 2011). With a period of 8 weeks between T0 and T2, we assume a dropout rate of 25%. To compensate for this dropout rate, a total of 660 subjects must be enrolled. 396 people will be equally assigned to the groups IG1.1, IG1.2 and IG1.3 and 132 each for IG2 and the control group.

2.4 Framework

The eHK-Strong study is a superiority trial designed to determine the effectiveness of a digital e-learning environment compared to a non-interactive PDF version and compared to a control group in cancer patients.
Secondary endpoints are analyzed descriptively.

2.5 Statistical Interim Analyses and Stopping Guidance

No interim analysis is conducted.

2.6 Timing of Outcome Assessments

Table 1. Measures and assessment time points for endpoints

Measures	T0	T1	T2
Primary outcome			
digital health literacy, DHLI	X	X	x
Secondary outcomes / other outcomes			
Digital health literacy, performance-based items of the DHLI	X	X	X
Motivation to use e-learning environment, RIMMS		[a]X	
Acceptance of e-learning environment, AIM		[a]X	
Appropriateness of the e-learning environment, IAM		[a]X	
Feasibility of the e-learning environment, IAM		[a]X	
Acceptance of the e-learning environment, completion of chapters and reasons for stopping e-learning early		[a]X	
Safety endpoints			
Protocol deviations in the intervention group		[a]X	
Protocol deviations in the control group		X	
Adverse events			
Characteristics			
Participants' sociodemographic characteristics	X		

Medical data	X
Internet use	X

Note. T0 = baseline survey right before randomization; T1 = 2 weeks after randomization; T2 = 8 weeks follow-up; DHLI = Digital health literacy Instrument; RIMMS = Reduced Instructional Materials Motivation Survey; AIM = Acceptability of Intervention Measure; IAM = Intervention Appropriateness Measure; FIM = Feasibility of Intervention Measure.

[a] Instruments will only be administrated to the intervention group

2.7 Timing of Final Analysis

The final analysis of the EHK-Strong trial will take place once we have collected data for baseline and two follow-up visits for 495 participants, divided among the three e-learning environment groups (IG1.1, IG1.2, IG1.3), IG2, and the control group. According to our current planning, no new participants will be enrolled after August 8, 2025. The final data transfer will take place in October 2025, followed by the final analysis. If we are unable to recruit the planned number of participants, the final analysis will still commence based on the available data.

3 Statistical Principles

3.1 Confidence Intervals and *P* Values

All statistical tests are two-sided and conducted at a 5% significance level. Confidence intervals are 95% and two-sided. Analyses of secondary, other outcomes are performed exploratory without adjustment for multiple testing.

3.2 Adherence and Protocol Deviations

3.2.1 Intervention Adherence

Adherence will be defined as completion of at least 50% of the chapters in the e-learning environment, as assessed by 'the number of chapters completed' item at T1.
The absolute and relative frequencies of adherent participants will be reported in tabular form, both for the overall sample as well as separately for each intervention/control group.
To rule out protocol deviations:

- Participants in the intervention groups (IG1.1-IG1.3 und IG2) will be asked at T1 whether the content of the intervention was completed by themselves or by someone close to them (e.g., spouse or child).
- Participants in the control group will be asked at T2 whether they had access to the content of the intervention groups (e.g. through friends/acquaintances in a patient support group).

3.2.2 Protocol deviations

Major protocol deviations are predefined as follows:

- Participants of the IG1.1-IG1.3 group who did not complete at least 50% of the chapters in the e-learning environment.
- Participants who report having participated in the study before
- Participants who indicate that the intervention content was completed by someone else (e.g., a family member or close acquaintance).
- Participants who report not having a cancer diagnosis.
- Participants who did not complete the T1 follow-up questionnaire
- Participants in the control group who reported having accessed the content of the intervention group (e.g. through friends/acquaintances in a patient support group)

- Participants of the IG1.1-IG1.3 group who reported not having access to the e-learning environment

3.3 Analysis Populations

3.3.1 Full Analysis Set

The evaluation of the primary and secondary hypotheses is based on the full analysis set (FAS). It is as complete as possible and as similar as possible to the intention-to-treat population. The intention-to-treat population includes all randomized patients belonging to the group to which they were originally randomized, regardless of whether protocol violations are known. For the FAS at least a valid baseline and one valid post-baseline value of the primary outcome needs to be available.

3.3.2 Per Protocol Population

The Per Protocol (PP) population is a subset of the FAS and includes only patients without major protocol violations (see chapter 3.2.2).

4 Trial Population

4.1 Screening Data

Our study does only have one screening item (patient-based screening): participants are asked at the very beginning of the baseline REDCap questionnaire whether they have ever received a cancer diagnosis during their life time. If participants indicate that they have not had cancer, they are not able to proceed with the questionnaire.
Additionally, we will report the number of participants who started at T0 and the number of participants who did not respond to any of the follow-up questionnaires. We will also report socio-demographic and medical characteristics as well as the mean digital health literacy score of these drop-outs. We will also conduct a drop-out analysis using logistic regression to examine whether socio-demographic factors and baseline digital health literacy (DHLI) scores are associated with study attrition.

4.2 Eligibility

The following eligibility criteria according to the study protocol are assessed within a self-report online survey at T0 immediately prior to randomization. Potential participants can read the eligibility criteria on the contact website (www.uke.de/orientiertinformiert) and again in the informed consent:

Patients are eligible for the trial if they are:
- 18 years of age or older
- self-report a diagnosis of cancer of any type
- have sufficient knowledge of the German language, as all study materials and questionnaires are available in German only
- are able to use a digital device (e.g., smartphone, tablet, PC, laptop) with an Internet connection, as all study content and questionnaires are accessible online only
- have their own email address, as all reminders for follow-up questionnaires will be sent via email

Patients are excluded, if they are:

- severely cognitively impaired due to their cancer or other illnesses

- unable to operate a digital device

4.3 Recruitment / Withdrawal / Follow-up

A CONSORT flow diagram is used to summarize the number of participants who:

- Started to complete the questionnaire at T0
- Completed the questionnaire T0
- became ineligible after completing the questionnaire (i.e., reported not having cancer or email address is not logically correct) *.
- eligible and randomized
- lost to follow-up at T1*
- lost to follow-up at T2*
- randomized and included in the primary analysis
- randomized and excluded from the primary analysis*

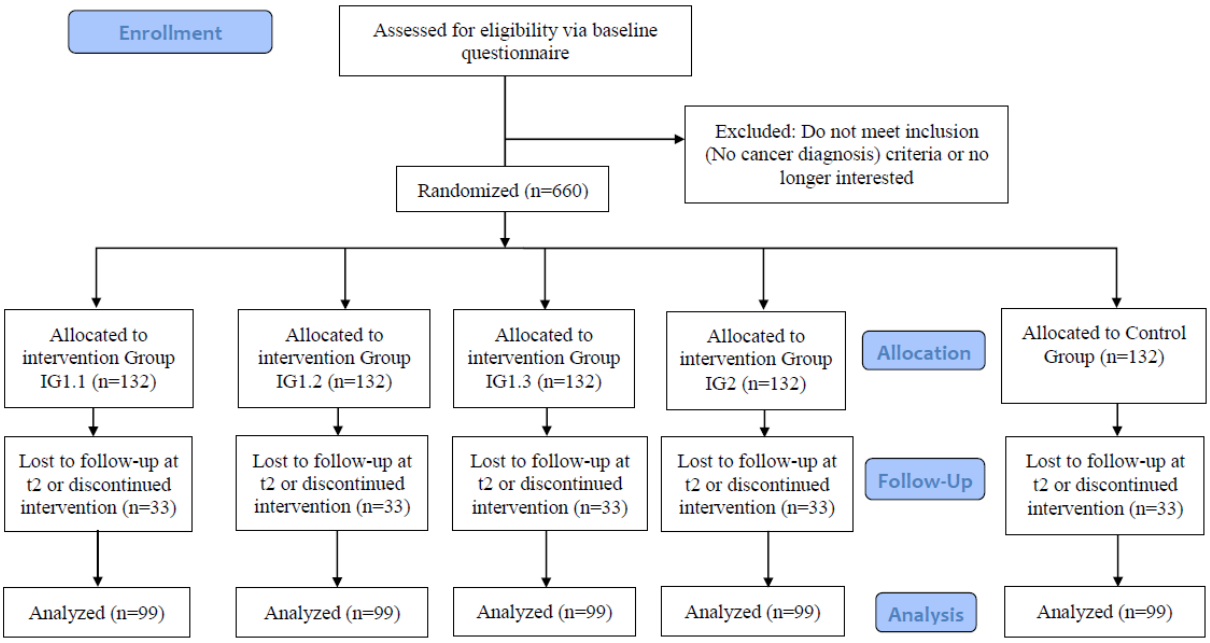

Figure 1. Expected flow chart for participation in the study.

4.4 Baseline Participant Characteristics

Summary statistics are reported for baseline participant characteristics (see Chapter 1.3.5).
Categorical data are summarized as absolute and relative frequencies. Continuous data are summarized by mean, standard deviation or median, interquartile range, minimum and maximum. These measures are presented for the total population that completed the T0 questionnaire and separated by treatment group.

5 Analysis

5.1 Outcome Definitions

Primary Outcome

- Change in mean DHLI score (21 items) (T2 (8 weeks after randomization) - T0 (baseline)).

Secondary Outcome

- Change in total score of the performance-based DHLI (6 items) (T2 (8 weeks after randomization) – T0 (baseline)
- Change in mean DHLI score (21 items) (T1 (2 weeks after randomization) - T0 (baseline))

Other Outcomes

- Mean score of the RIMMS at t1
- Mean score of the AIM at t1
- Mean score of the IAM at t1
- Mean score of the FIM at t1
- Mean number of chapter completed at t1

The following other endpoints are binary or categorical outcomes.

- Completing the e-learning (yes/no)
- Completed the e-learning by themselves
- Had access to the content of the intervention groups (only for participants of the control group).

5.2 Missing Data

In the full analysis set, we will not impute missing data. However, as a further sensitivity analysis, the primary analysis will be performed with a multiply imputed dataset. For the imputation, we will use the "mice" package (version 1.8.1 in R (Buuren & Groothuis-Oudshoorn, 2011)), which allows us to generate 100 imputations of missing values using a bootstrapping-based algorithm. For the imputation of missing DHLI values at T2 (ordinal Likert-type items), we will use proportional odds logistic regression (polr method in mice). As a robustness check, we may also explore predictive mean matching (pmm) if model convergence issues arise. We will pool the results of the linear mixed model for the 100 imputed datasets based on Rubin's rules (Rubin, 1987).
Furthermore, it is expected that respondents who do not use social media or do not post on forums cannot answer the items belonging to the two subscales adding self-generated content and protecting privacy. This may legitimately lead to up to 6 missing items. To ensure comparability across participants, mean scores (range 1–4) will be computed if at least 15 of the 21 items (71%) are available. In line with this study, one study (L. Xie & Mo, 2023) reported high proportions of missing responses on the protecting privacy subscale and excluded it from analysis; the second (Kim, Yang, Ryu, Kim, Jang, & Chang, 2021) treated those items as optional. A previous validation study also applied the rule of requiring at least 15 of 21 items to calculate mean scores (Zeeb, Pohlabeln, Preising, Schulz, Naczinsky, & Kolpatzik, 2022).

5.3 Efficacy Evaluation

Primary and secondary endpoints will be analysed in the FAS.

5.3.1 Analysis of Primary Endpoint(s)

The primary, global hypothesis is: There is a difference between at least two out of three groups (IG1.1-IG1.3 pooled, IG2, control group).
The following pairwise hypotheses are:

- Cancer patients who use a digital interactive e-learning environment (IG1.1-IG1.3) or the content of the e-learning environment as a non-interactive PDF file (IG2) will show a greater improvement in their digital health literacy from T0 to T2 as compared to cancer patients who receive no intervention.
- Cancer patients who use the full e-learning environment (IG1.1) will show a greater improvement in their digital health literacy from T0 to T2 compared to cancer patients

who use the e-learning environment without tunnelling elements (IG1.2) or the e-learning environment without rehearsal elements (IG1.3).
- Cancer patients who use a digital interactive e-learning environment (IG1.1-IG1.3) will show a greater improvement in their digital health literacy from T0 to T2 as compared to cancer patients who receive the non-interactive PDF version (IG2).

The evaluation of the primary hypothesis is based on the closed testing principle (Ruth, Peritz, & Gabriel, 1976) with the randomization groups being analysed as a combined digital e-learning intervention group (IG1.1–IG1.3 pooled), a non-interactive PDF group, and a control group: In the first step, a global test is carried out to determine whether the change in the digital health literacy value from T0 to T2 differs significantly between at least two of the three randomization groups (digital e-learning (IG1.1–IG1.3), non-interactive PDF group and control group). The two-sided significance level is set to 5%. A linear mixed model is calculated to analyse this primary hypothesis. The R package "lme4" will be used for this purpose (Bates, Mächler, Bolker, & Walker, 2015). The randomization group, the follow-up time points T1 and T2, the recruitment route (CIS vs. non-CIS), the cancer type (breast cancer vs. other cancer types) and the interaction between the follow-up time points and the randomization group will be included as fixed factors. To control for differences in baseline DHLI scores, regression to the mean, and to reduce the error variance in the dependent variable (Glymour, Weuve, Berkman, Kawachi, & Robins, 2005; Schad, Vasishth, Hohenstein, & Kliegl, 2020), the baseline DHLI value will be included as a covariate. In addition, a random intercept will be estimated for the patients. The global hypothesis shows a significant result if the p-value of the global comparison between the three randomization groups at time T2 is smaller than the two-sided significance level of 5%. Only if the result is significant, the pairwise comparisons between the three randomization groups at time T2 will be calculated in the second step using the R package "emmeans" (Lenth R, 2024). A pairwise comparison is significant, if the associated p-value is smaller than the two-sided significance level of 5%. In this way, we keep the overall two-sided type I error at a maximum of 5%.
Along the model estimates corresponding 95% CI will be presented.

5.3.2 Analysis of Secondary Endpoint(s)

To evaluate the fourth research objective — whether the primary hypothesis also applies to the change from baseline to two weeks after baseline (T1) — we will use the same linear mixed model as specified for the primary analysis. The model includes the randomization group, follow-up time points (T1 and T2), recruitment route, cancer type, the interaction between the follow-up time points and the randomization group, and the baseline DHLI score as fixed factors, with a random intercept for patients. The same closed testing principle will be applied: a global test will first determine whether the change in DHLI from T0 to T1 differs significantly between the three randomization groups. If the global test yields a significant result, pairwise comparisons will be performed with the emmeans package. We will estimate the following contrasts: (1) IG1 (IG1.1–IG1.3 pooled) vs control group; (2) IG2 vs control group. Secondary: (3) IG1.1 vs IG1.2; (4) IG1.1 vs IG1.3; (5) IG1 (IG1.1–IG1.3 pooled) vs IG2.

To address the fifth research objective, we will analyze whether the randomization groups differ in total score on the performance-based items of the DHLI. This analysis will also be performed using linear mixed models analogous to the primary hypothesis. The model specification, including fixed factors and covariates, will follow the same structure as described for the primary endpoint.

5.3.3 Sensitivity Analyses

In the full analysis set, we will not impute missing data. However, as a further sensitivity analysis, the primary analysis will be performed with a multiply imputed dataset, as described in section 5.2 "Missing Data".
As a second sensitivity analyses, the primary evaluation is repeated in the per-protocol (PP) population.

5.3 Safety Evaluation

Not applicable.

5.4 Additional Analyses

5.4.1 Check of Assumptions

Normality of residuals and linearity
The assumptions regarding normality of residuals, and linearity between the independent variables and the dependent variable in case of linear mixed models and the log odds of the dependent variable in case of mixed logistic regressions, respectively, are examined graphically. Partial residual plots are used to examine linearity. Residual plots and quantile-quantile plots are used to evaluate normality of residuals. In case of unmet assumptions, the Box-Cox transformation is applied in order to find out which power transformation is reasonable in terms of not violating the assumption.

5.4.2 Evaluation of Perceived User-Friendliness, Appropriateness and Feasibility

To evaluate whether the e-learning environment is perceived as more user-friendly, appropriate and feasible that the non-interactive PDF file (research question 7), we will use Analysis of Variance (ANOVA) tests.

5.4.3 Drop Out Analysis

If applicable, we will perform a dropout analysis to investigate potential systematic differences between participants who complete all three measurement time points (baseline, T1 at two weeks, and T2 at eight weeks) and those who complete only the baseline questionnaire. For this purpose, we will use a binary dependent variable (dropout: yes vs. no) in a logistic regression model. As covariates, we will include the fixed factors specified in the linear mixed model as well as the baseline value of the primary outcome measure.

5.4.4 Mediation Analysis

A mediation model is used to analyse whether motivation mediates the association between randomization groups and the change in digital health literacy from T0 to T2 (research question 6). The mediation model is calculated with patient motivation (mean RIMMS score) as the mediator; the intervention group as the independent variable. The dependent variable is the difference in digital health literacy from T0 to T2. The mediation analysis is performed based on the model of Hayes (Hayes, 2013).

5.6 Data Challenges

Not applicable.

5.7 Differences to Trial Protocol

One deviation from the original trial protocol concerns the method used for imputing missing data. Initially, we planned to use the Amelia II package for multiple imputation. However, during the course of the project, we changed to the mice package (Buuren & Groothuis-Oudshoorn, 2011). This decision was made for several reasons. First, mice provides greater flexibility in specifying imputation models tailored to the type of missing data (e.g., proportional odds logistic regression for ordinal variables). Second, mice is widely used and well-supported in the scientific community, which facilitates transparency and reproducibility. Third, practical experience indicated that mice offered greater stability and ease of use in the context of our dataset, while Amelia II resulted in convergence issues and imputed values that were not well suited for our ordinal outcome measures.

In addition, we will conduct a drop-out analysis using logistic regression to examine whether socio-demographic characteristics and baseline digital health literacy (DHLI) scores are associated with study attrition.
One deviation from the original trial protocol concerns blinding. The protocol broadly stated that double blinding (participants and data analysts) would be maintained throughout. In the SAP, we specify a single-blind in which participants are blinded to group assignment. Data analysts are blinded to group assignment via masked group codes (A–E). However, data analysts were not blinded to group allocation due to practical considerations during study planning and conduct.
In the SAP, we added a third hypothesis comparing the interactive e-learning environments (IG1.1–IG1.3) with the non-interactive PDF version (IG2). This addition was made to explicitly test the added value of interactivity, which had not been separately specified in the original protocol.

5.8 Statistical Software

- R 3.4.1 or newer

6 References

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