Predictors of Dropout in a Digital Intervention for the Prevention and Treatment of Depression in Patients With Chronic Back Pain: Secondary Analysis of Two Randomized Controlled Trials

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Abstract

Background: Depression is a common comorbid condition in individuals with chronic back pain (CBP), leading to poorer treatment outcomes and increased medical complications. Digital interventions have demonstrated efficacy in the prevention and treatment of depression; however, high dropout rates are a major challenge, particularly in clinical settings.

Objective: This study aims to identify the predictors of dropout in a digital intervention for the treatment and prevention of depression in patients with comorbid CBP. We assessed which participant characteristics may be associated with dropout and whether intervention usage data could help improve the identification of individuals at risk of dropout early on in treatment.

Methods: Data were collected from 2 large-scale randomized controlled trials in which 253 patients with a diagnosis of CBP and major depressive disorder or subclinical depressive symptoms received a digital intervention for depression. In the first analysis, participants' baseline characteristics were examined as potential predictors of dropout. In the second analysis, we assessed the extent to which dropout could be predicted from a combination of participants' baseline characteristics and intervention usage variables following the completion of the first module. Dropout was defined as completing <6 modules. Analyses were conducted using logistic regression.

Results: From participants' baseline characteristics, lower level of education (odds ratio [OR] 3.33, 95% CI 1.51-7.32) and both lower and higher age (a quadratic effect; age: OR 0.62, 95% CI 0.47-0.82, and age^2: OR 1.55, 95% CI 1.18-2.04) were significantly associated with a higher risk of dropout. In the analysis that aimed to predict dropout following completion of the first module, lower and higher age (age: OR 0.60, 95% CI 0.42-0.85; age^2: OR 1.59, 95% CI 1.13-2.23), medium versus high social support (OR 3.03, 95% CI 1.25-7.33), and a higher number of days to module completion (OR 1.05, 95% CI 1.02-1.08) predicted a higher risk of dropout, whereas a self-reported negative event in the previous week was associated with a lower risk of dropout (OR 0.24, 95% CI 0.08-0.69). A model that combined baseline characteristics and intervention usage data generated the most accurate predictions (area under the receiver operating curve [AUC]=0.72) and was significantly more accurate than models based on baseline characteristics only (AUC=0.70) or intervention usage data only (AUC=0.61). We found no significant influence of pain, disability, or depression severity on dropout.

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Conclusions: Dropout can be predicted by participant baseline variables, and the inclusion of intervention usage variables may improve the prediction of dropout early on in treatment. Being able to identify individuals at high risk of dropout from digital health interventions could provide intervention developers and supporting clinicians with the ability to intervene early and prevent dropout from occurring.

Introduction

Background

Chronic back pain (CBP) is a major global health concern with lifetime prevalence rates of 60%-70% [1]. CBP is the leading cause of activity limitation and work absenteeism and accounts for the highest number of disability-adjusted life years worldwide [2]. Approximately 1 in 5 adults with CBP are diagnosed with major depression and many more experience subclinical symptoms [3]. In patients with CBP, comorbid depression is often associated with lower treatment adherence, poorer treatment outcomes, increased medical complications, and higher health care use [4-6].

Psychological interventions have been demonstrated to be effective in the treatment of depression for individuals with CBP [7]. Accordingly, cognitive behavioral therapy is now recommended as the first-line treatment in most international guidelines, for example, the National Institute for Health and Care Excellence [8]. However, the ability to access psychotherapy is a significant barrier to treatment. On average, less than 1 in 5 people in high-income countries and less than 1 in 27 people in low- and middle-income countries receive appropriate treatment [9], giving rise to a *treatment gap* in mental health care [10].

Digital interventions, which deliver psychotherapeutic components via a web browser or smartphone app, have been proposed as a scalable, cost-effective way to meet the growing demand for psychological treatment and address many of the challenges associated with accessing traditional face-to-face therapy [11-15]. There is now a large body of evidence supporting the efficacy of digital interventions for the prevention and treatment of depression [16-20], with recent studies providing promising evidence for the treatment of depression in patients with comorbid physical conditions [21-25].

Despite the demonstrated efficacy, adherence to digital interventions remains a major challenge. A recent meta-analysis on digital interventions for depression identified that, on average, little more than half of the participants completed the full intervention and only 25% of the participants completed the full intervention when the intervention was delivered within routine health care settings [16]. The same meta-analysis also identified that completing the full intervention was the strongest predictor of outcomes, underscoring the importance of treatment adherence [26]. Similar rates of intervention dropout have been reported in other studies on digital health interventions [27-30], giving rise to what Eysenbach [31] has referred to as the "law

of attrition," the observation that a substantial proportion of users in eHealth apps will stop using the intervention before completing the full treatment protocol.

Several studies have assessed predictors of dropout in digital mental health interventions [27,32-34]. In a systematic review of internet-based interventions for anxiety and depression, Christensen et al [34] found that higher baseline depression severity and older age were associated with higher rates of intervention dropout. In a meta-analysis of individual patient data, Karyotaki et al [33] found that being male, having a lower education level, younger age, and comorbid anxiety symptoms significantly increased the risk of dropout from self-guided digital interventions for depression.

However, to the best of our knowledge, no research has been published to date that assesses which factors may predict dropout in a digital intervention for depression in patients with comorbid somatic illness. This question may be particularly pertinent for these individuals as chronic pain and depression are often associated with reduced motivation to initiate or complete goal-directed tasks [35,36]. As the treatment schedules of patients with multimorbidities can already be quite demanding [37,38], higher levels of pain disability—or lower confidence in performing activities while in pain (pain self-efficacy)—may therefore influence an individual's ability to adhere to a digital intervention and thus experience the benefits [39].

Knowing which patient characteristics predict a higher likelihood of dropout may be valuable for identifying individuals in advance of treatment that might benefit from alternative care pathways [33,40]. However, it is unclear how useful the baseline predictors may be once a patient has already started treatment. In most digital health interventions, there is a steady attrition over time, with most users dropping out after completing the first 1 or 2 modules—the "attrition-phase" [31,41,42]. The ability to identify which individuals are at high risk of dropout early on in treatment could be valuable for supporting clinicians, especially within stepped-care models where rapid identification of nonresponders and the speed of providing alternative treatment can have a significant influence on outcomes [43,44].

Although the field is still nascent, there is a wealth of data generated from digital interventions that may aid the prediction of dropout once a patient has started treatment. In the same way that many digital apps outside of health care use *churn-prediction models* to identify if a user is likely to churn (ie, stop using the app as intended), similar models and principles of human-computer interaction may be valuable to predict dropout and maximize adherence within the field of

digital health. For example, in a digital intervention for a chronic lifestyle disease, Pedersen et al [45] were able to predict dropout with 89% precision using a model that included the number of messages received from the health coach, 2 weeks of inactivity, and the provider of the intervention as the most significant predictors. In a study of a self-help digital intervention for the treatment of insomnia, Bremer et al [46] identified individuals at risk of dropout with an area under the receiver operating curve (AUC) of 0.719 using a combination of baseline characteristics (eg, self-reported stress levels) and intervention usage data (eg, number of days to complete each module). One of the most significant findings of the study was that the prediction of user dropout was possible early on in the intervention (after completion of the introductory module).

Objectives

As digital mental health interventions are being increasingly adopted by health care systems worldwide [13,47], the ability to identify patients at risk of dropout may provide valuable information to improve the adherence, and thus effectiveness, of digital interventions. This study aimed to identify the factors that may predict dropout in a digital intervention for depression in individuals with CBP. In particular, we sought to assess which participant characteristics may be associated with a higher risk of dropout and whether intervention usage data could help improve the identification of individuals at risk of dropout early on in treatment.

Drawing from 2 recent studies on a guided digital intervention for the treatment and prevention of depression in individuals with comorbid CBP, we asked the following research questions:

1. Can we predict intervention dropout from participant baseline characteristics? If so, which participant characteristics predict a higher likelihood of dropout?
2. Can we develop an "early warning system" that identifies participants at risk of dropout early on in the intervention? Specifically, how accurately can we predict which participants will drop out after completion of the first module and what is the most accurate model for classifying at-risk individuals?
3. Do predictors of dropout differ between patients clinically diagnosed with major depressive disorder (where the intervention is targeting treatment) and patients with subclinical depressive symptoms (where the intervention is targeting prevention)?

Methods

Study Design

This study was a secondary analysis of data from 2 trials that assessed the efficacy of a therapist-guided internet-based intervention for the treatment [48] and prevention [21] of depressive symptoms in patients with comorbid CBP. Both trials were observer-masked, multicenter, pragmatic, and randomized controlled trials with a parallel design. The trials were conducted simultaneously using the same intervention, procedures, and research setting but targeted individuals with different levels of depressive symptomatology (diagnosed depressive disorder of mild to moderate severity in the study

by Baumeister et al [48] and subclinical but at least mild levels of depressive symptoms in the study by Sander et al [21]). For the purpose of this study, the trial data were combined. All the participants provided written informed consent.

Participants

All participants (N=253) assigned to the intervention arms of the primary studies were included in this analysis. The inclusion criteria of the primary studies were as follows: (1) age ≥18 years; (2) presence of depressive symptoms, either reported persistent subthreshold depressive symptoms in the past 3 months or meeting the Diagnostic and Statistical Manual of Mental Disorders, 4th Edition, criteria for a mild to moderate depressive episode or persistent depressive disorder; (3) diagnosed back pain chronicity of at least 6 months; (4) have German language skills; and (5) access to internet and PC. The exclusion criteria were as follows: (1) having ongoing or planned psychotherapy within the forthcoming 3 months, (2) being currently suicidal or having had suicidal attempts within the past 5 years, or (3) having had a severe depressive episode within the past 6 months. In the primary studies, participants were recruited during or following discharge from 1 of the 82 orthopedic clinics across Germany. They were recruited personally by a clinician or on the web using a flyer and information letters distributed by the clinic.

Intervention

The intervention is a guided internet- and mobile-based intervention for the treatment (eSano BackCare-D [49]) or prevention (eSano BackCare-DP [50]) of depression in patients with comorbid CBP. The content of the intervention is based on cognitive behavioral therapy for depression and includes elements of psychoeducation, social skills, problem-solving, behavioral activation, relaxation, motivation for physical exercises, and psychological pain intervention elements. Modules consist of information provided by text, video, audio, and interactive exercises and include a homework assignment. At the start of each module, participants reported their perceived stress level at the time and whether they had experienced any negative events in the previous 7 days. There are 6 regular modules and 3 optional modules focusing on sleep, partnership and sexuality, and work. Participants were advised to complete 1 session per week. During the intervention, participants were guided by trained and supervised psychologists (e-coaches) who provided written feedback within 48 hours of each completed module and by answering any queries.

Measures

Baseline Measures

In this study, 8 baseline characteristic variables were assessed as potential predictors of dropout. Variables were chosen on the basis of previous research pointing to demonstrated or hypothetical relationships between the predictor variables and intervention adherence or dropout [32-34,45,46,51]. Demographic characteristics included age, sex (male or female), education level (based on the International Standard Classification of Education by UNESCO [52], low: level 1-2, medium: level 3-4, and high: level 5+), marital status (single, in a relationship, or divorced or widowed), and social support

(low, medium, or high). Clinical characteristics included depression, as measured by the Hamilton Depression Rating Scale (HAM-D; [53]); pain disability, as measured by the Oswestry Disability Index (ODI; [54]); and pain self-efficacy, as measured by the Pain Self-Efficacy Questionnaire (PSEQ). The process variables included internet affinity, as measured by the Internet Affinity Scale. Further details on all measurements are provided in the original study protocols [49,50].

Intervention Usage Measures

Intervention usage measures included both active and passive measures. The active measures were the stress level reported by the participant at the start of each module ("Burden") and the occurrence of any negative events experienced in the past 7 days, self-reported by the participant at the start of each module ("Negative Events"). Burden was assessed using a Likert scale from 0 to 10, where 0="not burdened at all" and 10="extremely burdened." Negative events were dummy coded as 0="no negative event in the past week" and 1="at least one negative event in the past week." For passive measures, we included the number of days taken to complete each module ("N Days to complete module") and the number of minutes spent on the web completing each module ("Time spent online completing module").

Dropout

Dropout was defined as completing <6 intervention modules, in accordance with the intervention developers [49,50]. It was operationalized as a binary outcome (dropped out or did not drop out).

Analytic Strategy

Predicting Dropout From Participant Baseline Characteristics

To assess whether participants' baseline characteristics could predict dropout, analyses were conducted using logistic regression in 3 steps. First, we conducted a series of bivariate analyses to assess the odds ratios (ORs) of each baseline variable (bivariate "bivariate model"). Second, we repeated the analyses with all baseline variables simultaneously entered into the binomial model (the "complete model"). Finally, we built a "parsimonious model" in which we excluded nonsignificant predictors with no incremental predictive power from the complete model in a stepwise procedure.

Akaike information criterion (AIC) and Bayesian information criterion (BIC) were used as measures of model fit and for model comparison. For nested models, likelihood ratio tests were used to directly compare whether 2 models were significantly different from one another [55]. Collinearity was assessed using variance inflation factors and tolerance (1/variance inflation factors). The assumption of linearity of the logit (a linear relationship between the predictors and dropout) was assessed for all continuous predictor variables, and any variables found violating the assumption were transformed based on a visual inspection of the plot.

As this was an exploratory study, we did not adjust for multiple testing. The study was not powered for confirmatory analysis

of the predictors, and alpha adjustment may have increased the likelihood of type II errors.

Predicting Dropout Early on in the Intervention

To assess whether we could identify people at risk of dropout early on in the intervention, we first created a subset of the data available up until the point of module 1 completion (ie, baseline assessment data and intervention data captured until participants had completed the first module). We then compared the performance of three separate logistic regression models using the constrained data set: (1) a model based on participant baseline characteristics only—the "baseline characteristics model," (2) a model based on intervention usage variables only—the "intervention usage model," and (3) a model combining all baseline characteristics and intervention usage variables—the "combined model." The quality of the models was assessed using the area under the receiver operating characteristic curve (AUROC) and related measures of sensitivity and specificity [55]. The optimal threshold for AUROC was determined using Youden J statistic [56].

Sensitivity analyses were conducted to assess whether predictors differed in the prevention and treatment studies. Here, study was included as a dummy-coded variable (0=PROD-BP for the prevention study and 1=WARD-BP for the treatment study) in all parsimonious models, first as an additional predictor to assess for a main effect of study type on dropout and then as an interaction term with other predictors in the model to assess whether the effect of a predictor differed across studies.

To assess whether the number of modules completed influenced the relative risk of dropout, we conducted sensitivity analyses using Cox proportional hazards regression [57]. In this study, we assessed whether significant predictors of dropout differed between the 2 methods. Analyses were conducted according to the procedures outlined by Eysenbach [31]. The number of completed modules was used as a proxy for time. Models were built using the same 3-step procedure outlined above for logistic regression.

Missingness occurred in 111 out of 3084 (3.6%) data points and was assumed to be missing at random, indicating that missingness depended on observed data [58]. To avoid bias introduced by missingness, missing data were imputed using multiple imputation by chained equations [59,60]. Predictors for missing values were selected based on (1) model-induced predictors, (2) predictors based on bivariate correlation, and (3) bivariate correlation with missingness according to the procedures outlined by van Buuren and Groothuis-Oudshoorn [60]. Predictive mean matching was used as the imputation method. The number of imputed data sets was set to 20, and the number of iterations was set to 10. Convergence was visually assessed and confirmed. Regression analysis was performed on each imputed data set, and the results were pooled according to the rules by Rubin [61]. Sensitivity analyses were conducted using observed (nonimputed) data to compare with the results of the complete models using imputed data.

All analyses were conducted in R using R Studio (RStudio, PBC; [62]). The pROC package was used to calculate the AUROC [63]. The Caret package (R Foundation for Statistical

Computing) was used to calculate the sensitivity and specificity [64]. The multiple imputation by chained equations (MICE) package was used for multiple imputation and likelihood ratio tests [60].

Ethics Approval

This study was a secondary of analysis of data from two RCTs—Sander et al [21] and Baumeister et al [48]. In the original studies, all the participants provided written informed consent. The trial in Sander et al [21] was registered at German Clinical Trials Register (DRKS00007960). The trial in Baumeister et al [48] was registered at the World Health Organization International Clinical Trials Registry (DRKS00009272). All procedures were approved by the ethics committee of the Albert Ludwigs University of Freiburg, Germany (REC No. 8022-6-BW-H-2015; No. 297/14_150513 for the WARD-BP trial, EK-297/14_150513 for the PROD-BP study).

Results

Descriptive Statistics

Among the 253 participants, 149 (58.9%) were female and 104 (41.1%) were male. The age of participants ranged from 24 to 78 years, with a mean age of 51.1 (SD 8.88) years. Of the 253 participants, 171 (67.6%) reported having a low level of education. Of the 253 participants, 34 (13.4%) were single, 180 (71.1%) were in a relationship or married, and 39 (15.4%) were divorced or separated. The mean depression severity at baseline was 10.3 (SD 5.93), as measured by the HAM-D, and 9.94 (SD 4.41), as measured by the Patient Health Questionnaire-9. The mean level of pain disability was 31.3 (SD 14.7), as measured by the ODI, and the mean level of pain self-efficacy was 34.9 (SD 13.0), as measured by the PSEQ. Table 1 provides a detailed summary of the demographic and clinical characteristics of the participants.

On average, the participants completed 4.65 out of the 6 regular and 3 optional modules (SD 3.48). The participants took an average of 17.64 (SD 19.55) days to complete each module, and the mean time on the web taken to complete a module was 80.26 (SD 136.96) minutes. The mean self-reported burden was 4.55 (SD 1.97), and the mean number of self-reported negative events across the intervention was 0.80 (SD 1.33). Table 2 shows that 45.1% (114/253) of the participants dropped out of the intervention before completing at least six modules. The table also shows that the number of participants completing the modules decreased steadily as the intervention progressed.

Table 1. Demographic and clinical characteristics of the participants (N=253).

Variable	Value[a]
Age (years)	
Mean (SD)	51.1 (8.88)
Median (range)	52 (24-78)
Sex, n (%)	
Male	104 (41.1)
Female	149 (58.9)
Education level, n (%)	
Low	171 (67.6)
Medium	45 (17.8)
High	37 (14.6)
Marital status, n (%)	
Single	34 (13.4)
In a relationship (including married)	180 (71.1)
Divorced or separated	39 (15.4)
Children, n (%)	
Yes	200 (79.1)
No	53 (20.9)
Social support, n (%)	
None	9 (3.6)
Low	67 (26.5)
Sufficient	81 (32)
High	73 (28.9)
Very high	23 (9.1)
Internet affinity (IAS[b])	
Mean (SD)	9.33 (4)
Median (range)	8.5 (5-25)
Missing, n (%)	1 (0.4)
HAM-D[c]	
Mean (SD)	10.3 (5.93)
Median (range)	9 (0-30)
Missing, n (%)	1 (0.4)
PHQ-9[d]	
Mean (SD)	9.94 (4.41)
Median (range)	10.0 (1-24)
Missing, n (%)	3 (1.2)
Pain disability (ODI[e])	
Mean (SD)	31.3 (14.7)
Median (range)	30.0 (0-72)
Missing, n (%)	1 (0.4)
Pain self-efficacy (PSEQ[f])	
Mean (SD)	34.9 (13)

Variable	Value[a]
Median (range)	36 (0-59)
Missing, n (%)	1 (0.4)
Dropout, n (%)	
No	139 (54.9)
Yes	114 (45.1)

[a]Values are based on observed data.

[b]IAS: Internet Affinity Scale.

[c]HAM-D: Hamilton Depression Rating Scale.

[d]PHQ-9: Patient Health Questionnaire-9.

[e]ODI: Oswestry Disability Index.

[f]PSEQ: Pain Self-Efficacy Questionnaire.

Table 2. Intervention usage data.

Variable	Value
Modules completed, mean (SD)	4.65 (3.48)
Participants completing modules, n (%)	
Module 1	188 (74.31)
Module 2	174 (68.77)
Module 3	159 (62.85)
Module 4	148 (58.5)
Module 5	136 (53.75)
Module 6	128 (50.59)
Module 7	109 (43.08)
Module 8	71 (28.06)
Module 9	61 (24.11)
Days to module completion, mean (SD)	17.64 (19.55)
Time spent on the web completing module (minutes), mean (SD)	80.26 (136.96)
Burden, mean (SD)	4.55 (1.97)
Negative events, mean (SD)	0.81 (1.33)
Dropout, n (%)	114 (45.1)

Predicting Dropout Using Participant Baseline Characteristics

Table 3 displays the performance of the models used to predict dropout based on the participant baseline characteristics. As the Patient Health Questionnaire-9 and PSEQ scores were highly correlated with HAM-D and ODI ($r=0.63$ and $r=-0.73$, respectively) and were not significant in the bivariate analyses, they were not included in the multivariate predictor models to prevent collinearity. The results of the bivariate analysis indicated that a lower level of education was significantly associated with a higher risk of dropout (OR 2.43, 95% CI 1.19-4.97; $P=.01$, whereas higher age predicted a lower risk of dropout (OR 0.97, 95% CI 0.94-0.99; $P=.02$). None of the other potential predictors (sex, social support, internet affinity, baseline depression severity, and baseline pain intensity) were statistically significant at the level of $P<.05$ in the bivariate analysis.

In the complete model, being single was found to be an additional significant predictor of dropout (OR 2.54, 95% CI 1.09-5.90; $P=.03$). When age was added as a quadratic term (age^2) to the model to account for the nonlinear relationship between age and dropout, we found that both age (OR 0.63, 95% CI 0.47-0.84; $P<.001$) and age^2 (OR 1.55, 95% CI 1.17 to –2.05; $P<.001$) were significant predictors, such that both lower and higher age were associated with increased risk of dropout.

In the parsimonious model, where predictors were reduced stepwise to relevant predictors only, low education (OR 3.33, 95% CI 1.51-7.32; $P<.001$) and age (OR 0.62, 95% CI 0.47-0.82; $P<.001$ and age^2: OR 1.55, 95% CI 1.18-2.04; $P<.001$) remained significant predictors of dropout. Marital status, internet affinity, baseline depression severity, and baseline pain intensity were found to be nonsignificant after controlling for the other predictors.

Table 3. Predictors of dropout from participant baseline characteristics.

Predictors	Bivariate model[a]		Complete model[a]		Parsimonious model[a]	
	OR[b] (95% CI)	P value	OR (95% CI)	P value	OR (95% CI)	P value
Age	0.97 (0.94-0.99)	.02	0.63 (0.47-0.84)	<.001	0.62 (0.47-0.82)	<.001
Age^2	N/A[c]	N/A	1.55 (1.17-2.05)	<.001	1.55 (1.18-2.04)	<.001
Sex (male)	1.60 (0.96-2.66)	.07	1.68 (0.96-2.94)	.07	N/A	N/A
Marital status						
Single vs in a relationship	1.97 (0.93-4.20)	.08	2.54 (1.09-5.90)	.03	N/A	N/A
Divorced or widowed vs in a relationship	0.54 (0.26-1.14)	.11	0.62 (0.27-1.42)	.25	N/A	N/A
Education						
Low vs medium	2.43 (1.19-4.97)	.01	3.77 (1.68-8.49)	<.001	3.33 (1.51-7.32)	<.001
High vs medium	1.88 (0.75-4.71)	.18	2.08 (0.74-5.83)	.16	2.08 (0.78-5.57)	.15
Social support						
Low vs high	0.83 (0.45-1.53)	.55	0.83 (0.41-1.69)	.60	N/A	N/A
Medium vs high	1.60 (0.88-2.90)	.13	1.64 (0.86-3.14)	.13	N/A	N/A
IAS[d]	1.02 (0.96-1.09)	.53	1.02 (0.95-1.10)	.58	N/A	N/A
HAM-D[e]	0.99 (0.95-1.03)	.67	0.98 (0.93-1.03)	.36	N/A	N/A
Pain disability	1.00 (0.98-1.02)	.85	1.00 (0.97-1.02)	.69	N/A	N/A
Pain self-efficacy (PSEQ[f])	1.00 (0.98-1.02)	.92	N/A	N/A	N/A	N/A
PHQ-9[g]	0.97 (0.91-1.02)	.24	N/A	N/A	N/A	N/A

[a]Models based on imputed data.

[b]OR: odds ratio.

[c]N/A: Not applicable.

[d]IAS: Internet Affinity Scale.

[e]HAM-D: Hamilton Depression Rating Scale.

[f]PSEQ: Pain Self-Efficacy Questionnaire.

[g]PHQ-9: Patient Health Questionnaire-9.

Predicting Dropout Early on in the Intervention

Tables 4-6 provide a comparison of the models used to predict dropout following the completion of the first module. In the parsimonious model using only participant baseline characteristics, higher and lower age (OR 0.57, 95% CI 0.41-0.79; P=.001 and age^2: OR 1.68, 95% CI 1.22-2.31; P=.001) and low education (OR 2.98, 95% CI 1.04-8.56; P=.04) were significant predictors of dropout. The AUROC for the model was 0.70, the sensitivity was 68%, and the specificity was 62%.

In the parsimonious model using only intervention usage data, a higher number of days to module completion predicted a higher risk of dropout (OR 1.04, 95% CI 1.01-1.07; P=.005), whereas a self-reported negative event in the previous week was associated with a lower risk of dropout (OR 0.30, 95% CI 0.11-0.81; P=.02). The AUROC for the model was 0.61, the sensitivity was 56%, and the specificity was 54%.

In the parsimonious model that combined participant baseline characteristics and intervention usage variables as predictors, higher and lower age (OR 0.60, 95% CI 0.42-0.85; P=.004 and age^2: OR 1.59, 95% CI 1.13-2.23; P=.008), medium versus high social support (OR 3.03, 95% CI 1.25-7.33; P=.02), and a higher number of days to module completion (OR 1.05, 95% CI 1.02-1.08; P=.002) all predicted a higher risk of dropout, whereas a self-reported negative event in the previous week was associated with a lower risk of dropout (OR 0.24, 95% CI 0.08-0.69; P=.008). The AUROC for the model was 0.72, the sensitivity was 76%, and the specificity was 59%.

As shown in Table 7, a comparison of the parsimonious models based on participant baseline characteristics and intervention usage variables revealed that the model that combined baseline and intervention usage variables was the most accurate in predicting dropout (AIC=198.9; BIC=253.9) and significantly more accurate than the model using participant baseline characteristics only (AIC=212.6; BIC=254.7; χ^2_{181}=5.3; P=.006).

Table 4. Predictors of dropout following module 1 completion—participant baseline characteristics.

Predictors	Bivariate model[a]		Complete model[a]		Parsimonious model[a]	
	OR[b] (95% CI)	P value	OR (95% CI)	P value	OR (95% CI)	P value
Age	0.96 (0.92-1.00)	.048	0.61 (0.43-0.87)	.006	0.57 (0.41-0.79)	.001
Age^2	0.97 (0.93-1.01)	.12	1.58 (1.12-2.24)	.01	1.68 (1.22-2.31)	.001
Sex (male)	1.45 (0.75-2.82)	.27	1.37 (0.65-2.92)	.41	N/A[c]	N/A
Marital status						
Single vs in a relationship	1.79 (0.68-4.72)	.24	2.06 (0.67-6.27)	.20	N/A	N/A
Divorced or widowed vs in a relationship	0.75 (0.30-1.90)	.55	1.01 (0.35-2.93)	.99	N/A	N/A
Education						
Low vs medium	2.17 (0.83-5.68)	.11	3.60 (1.19-10.88)	.02	2.98 (1.04-8.56)	.04
High vs medium	2.03 (0.61-6.75)	.25	1.77 (0.46-6.80)	.40	2.18 (0.60-7.85)	.23
Social support						
Low vs high	0.84 (0.34-2.07)	.69	0.80 (0.29-2.22)	.66	N/A	N/A
Medium vs high	2.65 (1.22-5.80)	.01	2.32 (1.00-5.38)	.05	N/A	N/A
IAS[d]	1.02 (0.94-1.11)	.59	1.02 (0.92-1.13)	.72	N/A	N/A
HAM-D[e]	0.99 (0.94-1.05)	.79	1.00 (0.94-1.07)	.98	N/A	N/A
Pain disability	0.99 (0.97-1.01)	.38	0.98 (0.95-1.01)	.28	N/A	N/A
Pain self-efficacy (PSEQ[f])	1.00 (0.97-1.02)	.97	N/A	N/A	N/A	N/A
PHQ-9[g]	0.97 (0.90-1.04)	.41	N/A	N/A	N/A	N/A

[a]Models based on imputed data.

[b]OR: odds ratio.

[c]N/A: not applicable.

[d]IAS: Internet Affinity Scale.

[e]HAM-D: Hamilton Depression Rating Scale.

[f]PSEQ: Pain Self-Efficacy Questionnaire.

[g]PHQ-9: Patient Health Questionnaire-9.

Table 5. Predictors of dropout following module 1 completion—intervention usage variables.

Predictors	Bivariate model[a]		Complete model[a]		Parsimonious model[a]	
	OR[b] (95% CI)	P value	OR (95% CI)	P value	OR (95% CI)	P value
Number of days to module 1 completion	1.04 (1.01-1.06)	.007	1.04 (1.01-1.07)	.005	1.04 (1.01-1.07)	.005
Negative events	0.34 (0.13-0.87)	.03	0.30 (0.11-0.81)	.02	0.30 (0.11-0.81)	.02
Burden	0.98 (0.84-1.15)	.83	1.01 (0.85-1.19)	.91	N/A[c]	N/A
Time spent on the web completing module 1	1.00 (0.99-1.01)	.81	1.00 (0.99-1.01)	.94	N/A	N/A

[a]Models based on imputed data.

[b]OR: odds ratio.

[c]N/A: not applicable.

Table 6. Predictors of dropout following module 1 completion—baseline and intervention usage variables.

Predictors	Complete model[a]		Parsimonious model[a]	
	OR[b] (95% CI)	*P* value	OR (95% CI)	*P* value
Age	0.54 (0.36-0.80)	.003	0.60 (0.42-0.85)	.004
Age^2	1.76 (1.19-2.61)	.005	1.59 (1.13-2.23)	.008
Sex (male)	1.53 (0.65-3.59)	.33	N/A[c]	N/A
Marital status				
Single vs in a relationship	1.88 (0.56-6.34)	.31	N/A	N/A
Divorced or widowed vs in a relationship	1.21 (0.38-3.78)	.75	N/A	N/A
Education				
Low vs medium	3.21 (0.91-11.33)	.07	N/A	N/A
High vs medium	1.17 (0.26-5.23)	.84	N/A	N/A
Social support				
Low vs high	0.83 (0.27-2.56)	.75	0.92 (0.34-2.51)	.88
Medium vs high	3.40 (1.33-8.64)	.01	3.03 (1.25-7.33)	.02
IAS[d]	0.99 (0.88-1.11)	.84	N/A	N/A
HAM-D[e]	0.99 (0.92-1.06)	.78	N/A	N/A
Pain disability	0.97 (0.94-1.00)	.08	N/A	N/A
Number of days to module 1 completion	1.05 (1.02-1.08)	.004	1.05 (1.02-1.08)	.002
Negative events	0.22 (0.07-0.68)	.009	0.24 (0.08-0.69)	.008
Burden	0.96 (0.80-1.17)	.71	N/A	N/A
Time spent on the web completing module 1	1.01 (0.99-1.02)	.28	N/A	N/A

[a]Models based on imputed data.

[b]OR: odds ratio.

[c]N/A: not applicable.

[d]IAS: Internet Affinity Scale.

[e]HAM-D: Hamilton Depression Rating Scale.

Table 7. Predictors of dropout following completion of module 1: model comparison (models based on imputed data).

Model	AIC[a]	BIC[b]	AUROC[c]	Sensitivity (%)	Specificity (%)
Model 1: baseline variables	212.6	254.7	0.70	68	62
Model 2: intervention variables	207.5	223.7	0.61	56	54
Model 3: baseline+intervention variables	198.9	253.9	0.72	76	59

[a]AIC: Akaike information criterion.

[b]BIC: Bayesian information criterion.

[c]AUROC: area under the receiver operating characteristic curve.

Sensitivity Analyses

Sensitivity analyses assessing whether findings differed between the treatment (WARD-BP) and prevention (PROD-BP) studies found no significant difference between the two, either in terms of main effect or interaction effects with other predictors. Sensitivity analyses assessing whether findings differed when using Cox proportional hazards regression versus logistic regression found no difference in the significant predictors. Multimedia Appendix 1 presents the results from the Cox regression analyses. Sensitivity analyses assessing whether the results differed between the models using observed data and those using imputed data revealed no difference in the predictors found to be significant. Results from the models using observed data are presented in Multimedia Appendix 2.

Discussion

Principal Findings

This study aimed to identify the predictors of treatment dropout in a digital intervention for the treatment and prevention of depression in patients with comorbid CBP. From the participants' baseline characteristics, we found that a lower education level and lower and higher age (a quadratic effect) predicted a higher risk of dropout. From the intervention usage variables, we found that a higher number of days to module completion predicted a higher risk of dropout, whereas the occurrence of a negative event in the previous week predicted a lower risk of dropout.

Participants with lower education levels were more likely to drop out of treatment, which is consistent with a large body of research on adherence to both digital interventions and face-to-face psychotherapy [33,51,65-67]. This may reflect the fact that these individuals find it harder to comprehend the intervention material or the digital format, and thus, they lose the motivation to continue [30,51]. It is worth noting that 67.5% (171/253) of the participants in this study were classified as having low levels of education. Lower levels of education have also been associated with longer duration or higher occurrence of back pain [68], underscoring the need for additional research on digital interventions for this particular patient group. The finding that both younger and older age predicted higher risk of dropout suggests that the relationship between age and dropout may be more complex than has been previously identified, either owing to the nonlinear relationship between the two or a possible interaction between age and other factors such as computer literacy [33,69]. More pertinently, it points to the challenges of predicting which individuals are likely to drop out of a digital intervention based on baseline characteristics alone [70]. Finally, the finding that neither pain disability nor depression severity levels were associated with an increased risk of dropout is important as it suggests that digital interventions targeting comorbid depression are acceptable for patients with varying levels of pain intensity and depression symptom severity. This is further supported by the fact that we found no significant difference in predictors when the intervention was aimed at prevention and when it was aimed at treatment. Taken together, these findings provide promising evidence that digital interventions may provide a scalable approach for integrating psychological treatment within pain management routines in health care settings.

This study also demonstrated the feasibility of predicting dropout early on in the intervention based on data restricted to the first module and participant baseline characteristics. Our finding that the number of days taken to complete the first module significantly predicted dropout is consistent with the study by Bremer et al [46] that identified the average number of days taken to complete each module as one of the strongest predictors of dropout in a digital intervention for insomnia. This may reflect a number of underlying causes, including challenges interacting with the intervention, low motivation, lack of time, or low perceived value [40]. The finding that a self-reported negative event in the previous week predicted a lower risk of

dropout may be because of the fact that experiencing a negative event (or being asked to report on one) provided greater intrinsic motivation to complete the module and is consistent with research demonstrating that some people drop out from an intervention because they no longer feel they need it [30,31,40]. However, it is worth highlighting that the CIs for the predictor were wide, so the results should be interpreted with caution and examined in future studies using larger sample sizes to determine whether the findings replicate. Notwithstanding, this is the first study to identify that a simple 1-item self-report questionnaire may be used to aid the prediction of dropout during a digital intervention, thus highlighting the potential of incorporating such assessments within digital interventions in the future. Interestingly, the relationship between participant education level and dropout was no longer significant in the models that combined baseline characteristics and intervention usage variables (Table 6). This suggests that a patient's education level may be less important at predicting dropout when including variables that reflect how the patient interacts with the intervention, such as how long it takes them to complete a specific module.

Indeed, a comparison of models using baseline characteristics and intervention usage variables revealed that a model that combined baseline characteristics and intervention usage data generated the most accurate predictions and was significantly more accurate than models based on baseline characteristics only or intervention usage data only. Moreover, in terms of clinical utility, the AUROC of 0.72 and sensitivity of 76% exceeded the accuracy threshold of 65%-70%, at which clinicians reportedly become willing to act on predictions [71]. Implemented within an intervention, dropout risk models such as this could be used to alert supporting clinicians and health care workers when an individual is at high risk of dropout, so that they are able to intervene early and ideally prevent it.

Notwithstanding the above, there is still significant room for improving model performance. In particular, the development of models that are able to predict dropout *before* completion of the first module would be especially valuable as a significant proportion of individuals drop out before then [65,69]. Developing more accurate models will require intervention developers to capture more granular data related to engagement with the intervention, for example, the number and timing of log-ins, interaction with specific components of the modules (eg, homework; [72]), data specifically related to the intervention target (eg, sleep data for an insomnia intervention; [46]), and additional self-report data such as early measures of therapeutic alliance with the coach [40,73]. Armed with comprehensive intervention usage data such as this, researchers will be better positioned to engineer both handcrafted (theory-driven) and automated features and assess their impact on predictive accuracy. Exploring the role of nonlinear machine learning models in improving model performance is also an area that holds potential, as has been demonstrated in several studies comparing the classification performance of machine learning algorithms with logistic regression in the prediction of dropout [45,46].

Finally, as the findings of this study were specific to one intervention, future research would also benefit from assessing

whether the predictors found herein are valuable for predicting dropout in other digital interventions, alternative disorders, and different populations. If it is consistently found that there are a set of variables such as "number of days to module completion" that are associated with higher risk of dropout, these predictors may then be used to inform the basis of models for other interventions in the future. In the same way that outcome feedback technology that identifies individuals at risk of deterioration during treatment has been shown to improve eventual treatment outcomes [43,44], dropout warning systems could be used to alert the supporting clinician, guide care pathways (eg, in stepped-care models), or personalize the intervention itself in the case of self-help interventions. Given the high dropout rates found in real-world settings [16], this will become increasingly important as interventions are implemented within public and private health care systems to meet the growing demand for psychotherapy [47].

Strengths and Limitations

To the best of our knowledge, this is the first study to examine the predictors of dropout in a digital intervention for depression in individuals with a comorbid somatic illness. This is also the first study to compare whether predictors of dropout differ when the intervention is aimed at prevention (in a subclinical population) versus treatment (in a clinically diagnosed population) and using study samples with clinically verified diagnoses at baseline. Finally, in contrast to most studies conducted to date, which have been based on efficacy trials with small sample sizes and convenient samples [33], this analysis was based on data from 2 large-scale effectiveness trials. These trials were conducted within routine health care settings, where dropout rates are typically significantly higher [16], thereby providing high ecological validity.

Despite these strengths, we acknowledge several limitations of this study. First, the analyses were based on data specific to a prevention and treatment version of one intervention and one population, namely, individuals with depressive symptoms and CBP. As such, the predictors we found to be significant and the subsequent accuracy of the classification models may not generalize to other interventions or other populations. For example, dropout has been found to be significantly greater in unguided interventions than in guided interventions, and the

mechanisms underlying dropout may differ between the two [33,51]. Future research would, therefore, benefit from assessing whether the predictors found to be significant in this study generalize to other interventions, populations, and settings. Second, as this was an exploratory study, we did not just adjust for multiple testing as alpha adjustment may have increased the likelihood of type II errors. Future research aimed at replicating the current findings in studies that are sufficiently powered for a confirmatory analysis would be valuable. Third, we had only a limited set of data from the intervention available for analysis. Several studies have demonstrated that a number of other variables derived from intervention usage are valuable in the prediction of both adherence and outcomes, including in-depth measures of engagement such as the frequency of log-ins [45] and interactions with specific content formats [72]. Accordingly, there may be other variables with further explanatory power that were not included in our models. The same applies to baseline characteristics, where studies have shown that data obtained from electronic medical records may be used to identify those at risk of dropout during face-to-face therapy [74,75]. Finally, although dropout in this study was operationalized according to the usage intended by the clinicians who developed the intervention [76], it is important to highlight that it is not always necessary for patients to complete the full per-protocol treatment to benefit clinically [30]. In other words, dropout is not always representative of a negative experience [31,40].

Conclusions

The high dropout rates associated with digital health interventions remain one of the biggest challenges to their successful implementation in real-world health care settings. Being able to identify individuals at high risk of dropout early on in treatment may provide clinicians and intervention developers with a valuable opportunity to intervene early and prevent dropout from occurring. Using a combined set of predictors from patient baseline characteristics and intervention usage data, we were able to identify individuals at risk of dropout early on in a digital intervention for depression in patients with comorbid CBP. Future research should explore ways of improving model accuracy and investigate the feasibility and efficacy of using these models directly within the interventions themselves to improve adherence.

Data Availability

The data that support the findings of this study are available on reasonable request from HB (harald.baumeister@uni-ulm.de). Data requesters will need to sign a data access agreement. Provision of data is subject to data security regulations. Investigator support depends on the available resources. The statistical code may be made available to an investigator upon reasonable request to the corresponding author.

Authors' Contributions

IM, YT, HB, LBS, and DDE contributed to the study conception and design. IM, YT, HB, and DDE contributed to the methods and analysis. IM prepared the original draft. YT, SP, SS, LPR, HB, LBS, and DDE critically reviewed and edited the manuscript. All authors read and approved the final manuscript and account for all aspects of this work.

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Conflicts of Interest

SS has received fees for lectures or workshops from training institutes for psychotherapists in the context of digital health research. HB has received consultancy fees, fees for lectures or workshops from chambers of psychotherapists and training institutes for psychotherapists in the context of digital health research and license fees for an Internet-intervention. LBS has received consultancy fees, fees for lectures and workshops from chambers of psychotherapists and training institutes for psychotherapists in the context of digital health research. DDE has received consultancy fees/served in the scientific advisory board from several companies such as Minddistrict, Lantern, Novartis, Sanofi, Schoen Kliniken, Ideamed, German health insurance companies (BARMER, Techniker Krankenkasse) and a number of federal chambers for psychotherapy. He is a stakeholder of the Institute for health training online (GET.ON), which aims to implement scientific findings related to digital health interventions into routine care. The authors have no further conflicts to declare.

Multimedia Appendix 1

Survival analyses assessing risk of dropout using Cox proportional hazards regression.
[DOCX File , 40 KB-Multimedia Appendix 1]

Multimedia Appendix 2

Results of the models using observed (nonimputed) data.
[DOCX File , 34 KB-Multimedia Appendix 2]

References

1. Wu A, March L, Zheng X, Huang J, Wang X, Zhao J, et al. Global low back pain prevalence and years lived with disability from 1990 to 2017: estimates from the Global Burden of Disease Study 2017. Ann Transl Med 2020 Mar;8(6):299 [FREE Full text] [doi: 10.21037/atm.2020.02.175] [Medline: 32355743]
2. GBD 2015 Disease and Injury Incidence and Prevalence Collaborators. Global, regional, and national incidence, prevalence, and years lived with disability for 310 diseases and injuries, 1990-2015: a systematic analysis for the Global Burden of Disease Study 2015. Lancet 2016 Oct 08;388(10053):1545-1602 [FREE Full text] [doi: 10.1016/S0140-6736(16)31678-6] [Medline: 27733282]
3. Bair MJ, Robinson RL, Katon W, Kroenke K. Depression and pain comorbidity: a literature review. Arch Intern Med 2003 Nov 10;163(20):2433-2445. [doi: 10.1001/archinte.163.20.2433] [Medline: 14609780]
4. Nicholas MK, Coulston CM, Asghari A, Malhi GS. Depressive symptoms in patients with chronic pain. Med J Aust 2009 Apr 06;190(S7):S66-S70. [doi: 10.5694/j.1326-5377.2009.tb02473.x] [Medline: 19351296]
5. Miles CL, Pincus T, Carnes D, Homer KE, Taylor SJ, Bremner SA, et al. Can we identify how programmes aimed at promoting self-management in musculoskeletal pain work and who benefits? A systematic review of sub-group analysis within RCTs. Eur J Pain 2011 Sep;15(8):775.e1-775.11. [doi: 10.1016/j.ejpain.2011.01.016] [Medline: 21354838]
6. Costa LC, Maher CG, McAuley JH, Hancock MJ, Herbert RD, Refshauge KM, et al. Prognosis for patients with chronic low back pain: inception cohort study. BMJ 2009 Oct 06;339:b3829 [FREE Full text] [doi: 10.1136/bmj.b3829] [Medline: 19808766]
7. Williams AC, Eccleston C, Morley S. Psychological therapies for the management of chronic pain (excluding headache) in adults. Cochrane Database Syst Rev 2012 Nov 14;11(11):CD007407 [FREE Full text] [doi: 10.1002/14651858.CD007407.pub3] [Medline: 23152245]
8. Depression in adults with a chronic physical health problem: recognition and management. National Institute for Health and Care Excellence. 2009 Oct 28. URL: https://www.nice.org.uk/guidance/cg91 [accessed 2020-10-27]
9. Thornicroft G, Chatterji S, Evans-Lacko S, Gruber M, Sampson N, Aguilar-Gaxiola S, et al. Undertreatment of people with major depressive disorder in 21 countries. Br J Psychiatry 2017 Feb;210(2):119-124 [FREE Full text] [doi: 10.1192/bjp.bp.116.188078] [Medline: 27908899]
10. Kohn R, Saxena S, Levav I, Saraceno B. The treatment gap in mental health care. Bull World Health Organ 2004 Nov;82(11):858-866 [FREE Full text] [Medline: 15640922]
11. Campion J, Javed A, Sartorius N, Marmot M. Addressing the public mental health challenge of COVID-19. Lancet Psychiatry 2020 Aug;7(8):657-659 [FREE Full text] [doi: 10.1016/S2215-0366(20)30240-6] [Medline: 32531299]
12. Paganini S, Teigelkötter W, Buntrock C, Baumeister H. Economic evaluations of Internet- and mobile-based interventions for the treatment and prevention of depression: a systematic review. J Affect Disord 2018 Jan 01;225:733-755. [doi: 10.1016/j.jad.2017.07.018] [Medline: 28922737]
13. Richards D, Enrique A, Eilert N, Franklin M, Palacios J, Duffy D, et al. A pragmatic randomized waitlist-controlled effectiveness and cost-effectiveness trial of digital interventions for depression and anxiety. NPJ Digit Med 2020 Jun 15;3:85 [FREE Full text] [doi: 10.1038/s41746-020-0293-8] [Medline: 32566763]
14. Singla DR, Raviola G, Patel V. Scaling up psychological treatments for common mental disorders: a call to action. World Psychiatry 2018 Jun;17(2):226-227 [FREE Full text] [doi: 10.1002/wps.20532] [Medline: 29856556]

15. Torous J, Bucci S, Bell IH, Kessing LV, Faurholt-Jepsen M, Whelan P, et al. The growing field of digital psychiatry: current evidence and the future of apps, social media, chatbots, and virtual reality. World Psychiatry 2021 Oct;20(3):318-335 [FREE Full text] [doi: 10.1002/wps.20883] [Medline: 34505369]

16. Moshe I, Terhorst Y, Philippi P, Domhardt M, Cuijpers P, Cristea I, et al. Digital interventions for the treatment of depression: a meta-analytic review. Psychol Bull 2021 Aug;147(8):749-786. [doi: 10.1037/bul0000334] [Medline: 34898233]

17. Karyotaki E, Efthimiou O, Miguel C, Bermpohl FM, Furukawa TA, Cuijpers P, Individual Patient Data Meta-Analyses for Depression (IPDMA-DE) Collaboration, et al. Internet-based cognitive behavioral therapy for depression: a systematic review and individual patient data network meta-analysis. JAMA Psychiatry 2021 Apr 01;78(4):361-371 [FREE Full text] [doi: 10.1001/jamapsychiatry.2020.4364] [Medline: 33471111]

18. Wright JH, Owen JJ, Richards D, Eells TD, Richardson T, Brown GK, et al. Computer-assisted cognitive-behavior therapy for depression: a systematic review and meta-analysis. J Clin Psychiatry 2019 Mar 19;80(2):18r12188 [FREE Full text] [doi: 10.4088/JCP.18r12188] [Medline: 30900849]

19. Sander L, Rausch L, Baumeister H. Effectiveness of Internet- and mobile-based psychological interventions for the prevention of mental disorders: a systematic review and meta-analysis protocol. Syst Rev 2016 Feb 16;5:30 [FREE Full text] [doi: 10.1186/s13643-016-0209-5] [Medline: 26880167]

20. Ebert DD, Van Daele T, Nordgreen T, Karekla M, Compare A, Zarbo C, et al. Internet- and mobile-based psychological interventions: applications, efficacy, and potential for improving mental health: a report of the EFPA E-Health Taskforce. Eur Psychol 2018 May;23(2):167-187. [doi: 10.1027/1016-9040/a000318]

21. Sander LB, Paganini S, Terhorst Y, Schlicker S, Lin J, Spanhel K, et al. Effectiveness of a guided Web-based self-help intervention to prevent depression in patients with persistent back pain: the PROD-BP randomized clinical trial. JAMA Psychiatry 2020 Oct 01;77(10):1001-1011 [FREE Full text] [doi: 10.1001/jamapsychiatry.2020.1021] [Medline: 32459348]

22. O'moore KA, Newby JM, Andrews G, Hunter DJ, Bennell K, Smith J, et al. Internet cognitive-behavioral therapy for depression in older adults with knee osteoarthritis: a randomized controlled trial. Arthritis Care Res (Hoboken) 2018 Jan;70(1):61-70. [doi: 10.1002/acr.23257] [Medline: 28426917]

23. Meyer B, Weiss M, Holtkamp M, Arnold S, Brückner K, Schröder J, et al. Effects of an epilepsy-specific Internet intervention (Emyna) on depression: results of the ENCODE randomized controlled trial. Epilepsia 2019 Apr;60(4):656-668. [doi: 10.1111/epi.14673] [Medline: 30802941]

24. Ebert DD, Nobis S, Lehr D, Baumeister H, Riper H, Auerbach RP, et al. The 6-month effectiveness of Internet-based guided self-help for depression in adults with type 1 and 2 diabetes mellitus. Diabet Med 2017 Jan;34(1):99-107. [doi: 10.1111/dme.13173] [Medline: 27334444]

25. Schlicker S, Baumeister H, Buntrock C, Sander L, Paganini S, Lin J, et al. A Web- and mobile-based intervention for comorbid, recurrent depression in patients with chronic back pain on sick leave (Get.Back): pilot randomized controlled trial on feasibility, user satisfaction, and effectiveness. JMIR Ment Health 2020 Apr 15;7(4):e16398 [FREE Full text] [doi: 10.2196/16398] [Medline: 32293577]

26. Musiat P, Johnson C, Atkinson M, Wilksch S, Wade T. Impact of guidance on intervention adherence in computerised interventions for mental health problems: a meta-analysis. Psychol Med 2022 Jan;52(2):229-240. [doi: 10.1017/S0033291721004621] [Medline: 34802474]

27. Donkin L, Christensen H, Naismith SL, Neal B, Hickie IB, Glozier N. A systematic review of the impact of adherence on the effectiveness of e-therapies. J Med Internet Res 2011 Aug 05;13(3):e52 [FREE Full text] [doi: 10.2196/jmir.1772] [Medline: 21821503]

28. Richards D, Richardson T. Computer-based psychological treatments for depression: a systematic review and meta-analysis. Clin Psychol Rev 2012 Jun;32(4):329-342. [doi: 10.1016/j.cpr.2012.02.004] [Medline: 22466510]

29. Wells MJ, Owen JJ, McCray LW, Bishop LB, Eells TD, Brown GK, et al. Computer-assisted cognitive-behavior therapy for depression in primary care: systematic review and meta-analysis. Prim Care Companion CNS Disord 2018 Mar 01;20(2):17r02196 [FREE Full text] [doi: 10.4088/PCC.17r02196] [Medline: 29570963]

30. 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 May;39(5):705-712. [doi: 10.1017/S0033291708004224] [Medline: 18812006]

31. Eysenbach G. The law of attrition. J Med Internet Res 2005 Mar 31;7(1):e11 [FREE Full text] [doi: 10.2196/jmir.7.1.e11] [Medline: 15829473]

32. Kok RN, Beekman AT, Cuijpers P, van Straten A. Adherence to a Web-based pre-treatment for phobias in outpatient clinics. Internet Interv 2017 Sep;9:38-45 [FREE Full text] [doi: 10.1016/j.invent.2017.05.004] [Medline: 30135835]

33. Karyotaki E, Kleiboer A, Smit F, Turner DT, Pastor AM, Andersson G, et al. Predictors of treatment dropout in self-guided Web-based interventions for depression: an 'individual patient data' meta-analysis. Psychol Med 2015 Oct;45(13):2717-2726. [doi: 10.1017/S0033291715000665] [Medline: 25881626]

34. Christensen H, Griffiths KM, Farrer L. Adherence in Internet interventions for anxiety and depression. J Med Internet Res 2009 Apr 24;11(2):e13 [FREE Full text] [doi: 10.2196/jmir.1194] [Medline: 19403466]

35.   Jonsson T, Christrup LL, Højsted J, Villesen HH, Albjerg TH, Ravn-Nielsen LV, et al. Symptoms and side effects in chronic non-cancer pain: patient report vs. systematic assessment. Acta Anaesthesiol Scand 2011 Jan;55(1):69-74. [doi: 10.1111/j.1399-6576.2010.02329.x] [Medline: 21039361]

36.   Felger JC, Treadway MT. Inflammation effects on motivation and motor activity: role of dopamine. Neuropsychopharmacology 2017 Jan;42(1):216-241 [FREE Full text] [doi: 10.1038/npp.2016.143] [Medline: 27480574]

37.   Knowles S, Hays R, Senra H, Bower P, Locock L, Protheroe J, et al. Empowering people to help speak up about safety in primary care: using codesign to involve patients and professionals in developing new interventions for patients with multimorbidity. Health Expect 2018 Apr;21(2):539-548 [FREE Full text] [doi: 10.1111/hex.12648] [Medline: 29266797]

38.   Wallace E, Salisbury C, Guthrie B, Lewis C, Fahey T, Smith SM. Managing patients with multimorbidity in primary care. BMJ 2015 Jan 20;350:h176. [doi: 10.1136/bmj.h176] [Medline: 25646760]

39.   Thompson EL, Broadbent J, Bertino MD, Staiger PK. Do pain-related beliefs influence adherence to multidisciplinary rehabilitation?: a systematic review. Clin J Pain 2016 Feb;32(2):164-178. [doi: 10.1097/AJP.0000000000000235] [Medline: 26735864]

40.   Knowles SE, Lovell K, Bower P, Gilbody S, Littlewood E, Lester H. Patient experience of computerised therapy for depression in primary care. BMJ Open 2015 Nov 30;5(11):e008581 [FREE Full text] [doi: 10.1136/bmjopen-2015-008581] [Medline: 26621513]

41.   Norlund F, Wallin E, Olsson EM, Wallert J, Burell G, von Essen L, et al. Internet-based cognitive behavioral therapy for symptoms of depression and anxiety among patients with a recent myocardial infarction: the U-CARE heart randomized Controlled trial. J Med Internet Res 2018 Mar 08;20(3):e88 [FREE Full text] [doi: 10.2196/jmir.9710] [Medline: 29519777]

42.   Farvolden P, Denisoff E, Selby P, Bagby RM, Rudy L. Usage and longitudinal effectiveness of a Web-based self-help cognitive behavioral therapy program for panic disorder. J Med Internet Res 2005 Mar 26;7(1):e7 [FREE Full text] [doi: 10.2196/jmir.7.1.e7] [Medline: 15829479]

43.   Delgadillo J, de Jong K, Lucock M, Lutz W, Rubel J, Gilbody S, et al. Feedback-informed treatment versus usual psychological treatment for depression and anxiety: a multisite, open-label, cluster randomised controlled trial. Lancet Psychiatry 2018 Jul;5(7):564-572. [doi: 10.1016/S2215-0366(18)30162-7] [Medline: 29937396]

44.   Shimokawa K, Lambert MJ, Smart DW. Enhancing treatment outcome of patients at risk of treatment failure: meta-analytic and mega-analytic review of a psychotherapy quality assurance system. J Consult Clin Psychol 2010 Jun;78(3):298-311. [doi: 10.1037/a0019247] [Medline: 20515206]

45.   Pedersen DH, Mansourvar M, Sortsø C, Schmidt T. Predicting dropouts from an electronic health platform for lifestyle interventions: analysis of methods and predictors. J Med Internet Res 2019 Sep 04;21(9):e13617 [FREE Full text] [doi: 10.2196/13617] [Medline: 31486409]

46.   Bremer V, Chow PI, Funk B, Thorndike FP, Ritterband LM. Developing a process for the analysis of user journeys and the prediction of dropout in digital health interventions: machine learning approach. J Med Internet Res 2020 Oct 28;22(10):e17738 [FREE Full text] [doi: 10.2196/17738] [Medline: 33112241]

47.   Titov N, Dear B, Nielssen O, Staples L, Hadjistavropoulos H, Nugent M, et al. ICBT in routine care: a descriptive analysis of successful clinics in five countries. Internet Interv 2018 Sep;13:108-115 [FREE Full text] [doi: 10.1016/j.invent.2018.07.006] [Medline: 30206525]

48.   Baumeister H, Paganini S, Sander LB, Lin J, Schlicker S, Terhorst Y, et al. Effectiveness of a guided Internet- and mobile-based intervention for patients with chronic back pain and depression (WARD-BP): a multicenter, pragmatic randomized controlled trial. Psychother Psychosom 2021;90(4):255-268. [doi: 10.1159/000511881] [Medline: 33321501]

49.   Lin J, Sander L, Paganini S, Schlicker S, Ebert D, Berking M, et al. Effectiveness and cost-effectiveness of a guided Internet-and mobile-based depression intervention for individuals with chronic back pain: protocol of a multi-centre randomised controlled trial. BMJ Open 2017 Dec 28;7(12):e015226 [FREE Full text] [doi: 10.1136/bmjopen-2016-015226] [Medline: 29288172]

50.   Sander L, Paganini S, Lin J, Schlicker S, Ebert DD, Buntrock C, et al. Effectiveness and cost-effectiveness of a guided Internet- and mobile-based intervention for the indicated prevention of major depression in patients with chronic back pain-study protocol of the PROD-BP multicenter pragmatic RCT. BMC Psychiatry 2017 Jan 21;17(1):36 [FREE Full text] [doi: 10.1186/s12888-017-1193-6] [Medline: 28109247]

51.   Schmidt ID, Forand NR, Strunk DR. Predictors of dropout in Internet-based cognitive behavioral therapy for depression. Cognit Ther Res 2019 Jun;43(3):620-630 [FREE Full text] [doi: 10.1007/s10608-018-9979-5] [Medline: 32879540]

52.   International Standard Classification of Education (ISCED). Institute for Statistics, The United Nations Educational, Scientific and Cultural Organization. 2017. URL: http://uis.unesco.org/sites/default/files/documents/international-standard-classification-of-education-isced-2011-en.pdf [accessed 2021-12-20]

53.   Hamilton M. A rating scale for depression. J Neurol Neurosurg Psychiatry 1960 Feb;23(1):56-62 [FREE Full text] [doi: 10.1136/jnnp.23.1.56] [Medline: 14399272]

54.   Mannion AF, Junge A, Grob D, Dvorak J, Fairbank JC. Development of a German version of the Oswestry disability index. part 2: sensitivity to change after spinal surgery. Eur Spine J 2006 Jan;15(1):66-73 [FREE Full text] [doi: 10.1007/s00586-004-0816-z] [Medline: 15856340]

55.   Hosmer DW, Lemeshow S. Applied Logistic Regression. 2nd edition. Hoboken, NJ, USA: Wiley Online Library; 2000.

56.   Youden WJ. Index for rating diagnostic tests. Cancer 1950 Jan;3(1):32-35. [doi: 10.1002/1097-0142(1950)3:1<32::aid-cncr2820030106>3.0.co;2-3] [Medline: 15405679]

57.   Cox DR. Regression models and life-tables. J R Stat Soc Series B Stat Methodol 1972 Jan;34(2):187-202. [doi: 10.1111/j.2517-6161.1972.tb00899.x]

58.   Enders CK. Applied Missing Data Analysis. New York, NY, USA: The Guilford Press; 2010.

59.   van Buuren S. Flexible Imputation of Missing Data. 2nd edition. Boca Raton, FL, USA: CRC Press; 2018.

60.   van Buuren S, Groothuis-Oudshoorn K. mice: multivariate imputation by chained equations in R. J Stat Soft 2011 Dec 12;45(3):1-67. [doi: 10.18637/jss.v045.i03]

61.   Rubin DB. Multiple imputation after 18+ years. J Am Stat Assoc 1996 Jun;91(434):473-489. [doi: 10.1080/01621459.1996.10476908]

62.   R Core Team. R: a language and environment for statistical computing. R Foundation for Statistical Computing. Vienna, Austria: R Foundation for Statistical Computing; 2016. URL: https://www.r-project.org/about.html [accessed 2022-08-17]

63.   Robin X, Turck N, Hainard A, Tiberti N, Lisacek F, Sanchez J, et al. pROC: an open-source package for R and S+ to analyze and compare ROC curves. BMC Bioinformatics 2011 Mar 17;12:77 [FREE Full text] [doi: 10.1186/1471-2105-12-77] [Medline: 21414208]

64.   Kuhn M. Building predictive models in R using the caret package. J Stat Soft 2008 Nov 10;28(5):1-26. [doi: 10.18637/jss.v028.i05]

65.   Batterham PJ, Neil AL, Bennett K, Griffiths KM, Christensen H. Predictors of adherence among community users of a cognitive behavior therapy website. Patient Prefer Adherence 2008 Feb 02;2:97-105 [FREE Full text] [Medline: 19920949]

66.   Al-Asadi AM, Klein B, Meyer D. Pretreatment attrition and formal withdrawal during treatment and their predictors: an exploratory study of the anxiety online data. J Med Internet Res 2014 Jun 17;16(6):e152 [FREE Full text] [doi: 10.2196/jmir.2989] [Medline: 24938311]

67.   Jarrett RB, Minhajuddin A, Kangas JL, Friedman ES, Callan JA, Thase ME. Acute phase cognitive therapy for recurrent major depressive disorder: who drops out and how much do patient skills influence response? Behav Res Ther 2013 May;51(4-5):221-230 [FREE Full text] [doi: 10.1016/j.brat.2013.01.006] [Medline: 23485420]

68.   Dionne CE, Von Korff M, Koepsell TD, Deyo RA, Barlow WE, Checkoway H. Formal education and back pain: a review. J Epidemiol Community Health 2001 Jul;55(7):455-468 [FREE Full text] [doi: 10.1136/jech.55.7.455] [Medline: 11413174]

69.   Enrique A, Palacios JE, Ryan H, Richards D. Exploring the relationship between usage and outcomes of an Internet-based intervention for individuals with depressive symptoms: secondary analysis of data from a randomized controlled trial. J Med Internet Res 2019 Aug 01;21(8):e12775 [FREE Full text] [doi: 10.2196/12775] [Medline: 31373272]

70.   Beatty L, Binnion C. A systematic review of predictors of, and reasons for, adherence to online psychological interventions. Int J Behav Med 2016 Dec;23(6):776-794. [doi: 10.1007/s12529-016-9556-9] [Medline: 26957109]

71.   Eisenberg JM, Hershey JC. Derived thresholds. Determining the diagnostic probabilities at which clinicians initiate testing and treatment. Med Decis Making 1983;3(2):155-168. [doi: 10.1177/0272989X8300300203] [Medline: 6415358]

72.   Chien I, Enrique A, Palacios J, Regan T, Keegan D, Carter D, et al. A machine learning approach to understanding patterns of engagement with Internet-delivered mental health interventions. JAMA Netw Open 2020 Jul 01;3(7):e2010791 [FREE Full text] [doi: 10.1001/jamanetworkopen.2020.10791] [Medline: 32678450]

73.   Lawler K, Earley C, Timulak L, Enrique A, Richards D. Dropout from an Internet-delivered cognitive behavioral therapy intervention for adults with depression and anxiety: qualitative study. JMIR Form Res 2021 Nov 12;5(11):e26221 [FREE Full text] [doi: 10.2196/26221] [Medline: 34766909]

74.   Davis A, Smith T, Talbot J, Eldridge C, Betts D. Predicting patient engagement in IAPT services: a statistical analysis of electronic health records. Evid Based Ment Health 2020 Feb;23(1):8-14 [FREE Full text] [doi: 10.1136/ebmental-2019-300133] [Medline: 32046987]

75.   Chekroud AM, Foster D, Zheutlin AB, Gerhard DM, Roy B, Koutsouleris N, et al. Predicting barriers to treatment for depression in a U.S. national sample: a cross-sectional, proof-of-concept study. Psychiatr Serv 2018 Aug 01;69(8):927-934 [FREE Full text] [doi: 10.1176/appi.ps.201800094] [Medline: 29962307]

76.   Sieverink F, Kelders SM, van Gemert-Pijnen JE. Clarifying the concept of adherence to eHealth technology: systematic review on when usage becomes adherence. J Med Internet Res 2017 Dec 06;19(12):e402 [FREE Full text] [doi: 10.2196/jmir.8578] [Medline: 29212630]

Abbreviations

AIC: Akaike information criterion
AUC: area under the receiver operating curve
AUROC: area under the receiver operating characteristic curve
BIC: Bayesian information criterion
CBP: chronic back pain
HAM-D: Hamilton Depression Rating Scale
MICE: multiple imputation by chained equations

ODI: Oswestry Disability Index
OR: odds ratio
PSEQ: Pain Self-Efficacy Questionnaire

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