Behaviour Research and Therapy 150 (2022) 104028

Contents lists available at ScienceDirect

Behaviour Research and Therapy

journal homepage: www.elsevier.com/locate/brat

# Guided internet-based transdiagnostic individually tailored Cognitive Behavioral Therapy for symptoms of depression and/or anxiety in college students: A randomized controlled trial

Eirini Karyotaki [a,b,*], Anke M. Klein [c,f], Marketa Ciharova [a,b], Felix Bolinski [a,b,d], Lisa Krijnen [e], Lisa de Koning [f], Leonore de Wit [a,b], Claudia M. van der Heijde [j], David D. Ebert [g,h], Heleen Riper [a,b], Neeltje Batelaan [i], Peter Vonk [j], Randy P. Auerbach [k], Ronald C. Kessler [l], Ronny Bruffaerts [m], Sascha Struijs [a,b,n], Reinout W. Wiers [f,1], Pim Cuijpers [a,b,1]

[a] Department of Clinical, Neuro-, and Developmental Psychology, Vrije Universiteit Amsterdam, Van der Boechorststraat 7, BT 1081 Amsterdam, the Netherlands
[b] Amsterdam Public Health Research Institute, Faculty of Behavioural and Movement Sciences, Vrije Universiteit Amsterdam, the Netherlands
[c] Developmental and Educational Psychology of the Institute of Psychology, Leiden University, Leiden, the Netherlands
[d] Department of Public Mental Health and Prevention, Trimbos Institute (Netherlands Institute of Mental Health and Addiction), Utrecht, the Netherlands
[e] Department of Clinical Child and Family Studies, Utrecht University, Utrecht, the Netherlands
[f] Addiction, Development, And Psychopathology Lab, Department of Psychology, University of Amsterdam, Amsterdam, the Netherlands
[g] Psychology and Digital Mental Health Care, Technical University of Munich, Munich, Germany
[h] Clinical Psychology and Psychotherapy, Friedrich-Alexander-University Erlangen-Nuremberg, Erlangen, Germany
[i] Department of Psychiatry and Department of Epidemiology and Biostatistics, VU University Medical Centre Amsterdam, Amsterdam Public Health Research Institute, Amsterdam, the Netherlands
[j] Department of Research, Development and Prevention, Student Health Service University of Amsterdam, Amsterdam, the Netherlands
[k] Department of Psychiatry, Columbia University, New York, NY, USA
[l] Department of Health Care Policy, Harvard Medical School, Boston, MA, USA
[m] Universitair Psychiatrisch Centrum, Centre for Public Health Psychiatry, Katholieke Universiteit Leuven, Leuven, Belgium
[n] Institute of Psychology, Leiden University, Leiden, the Netherlands

ARTICLE INFO

*Keywords:*
Depression
Anxiety
College students
Transdiagnostic
Internet-based CBT
e-health

ABSTRACT

Common mental disorders, such as depression and anxiety, often emerge in college students during the transition into early adulthood. Mental health problems can seriously impact students' functioning, interpersonal relationships, and academic achievement. Actively reaching out to college students with mental health problems and offering them internet-based interventions may be a promising way of providing low-threshold access to evidence-based treatment in colleges. This randomized controlled trial aimed to assess the effectiveness of a guided web-based transdiagnostic individually tailored Cognitive Behavioral Therapy (iCBT) in treating college students with depression and/or anxiety symptoms. Through an online survey that screened college students' mental health, we recruited 100 college students aged ≥18 years who reported mild to moderate depression and/or anxiety symptoms and were attending colleges in the Netherlands. Participants were randomly allocated to guided iCBT (n = 48) or treatment as usual (TAU) control (n = 52). Primary outcomes were symptoms of depression and anxiety measured at post-treatment (7 weeks post-randomization). We also measured all outcomes at 6- and 12-months post-randomization. All analyses were based on the intention-to-treat principle and were repeated using the complete-case sample. We found no evidence of a difference between the effects of guided iCBT and TAU in any of the examined outcomes (i.e., symptoms of depression and anxiety, quality of life, educational achievement, and college dropout) across all time points ($p > .05$). There was no evidence that effects of iCBT were associated with treatment satisfaction and adherence. More research into transdiagnostic individually tailored iCBT is necessary. Further, future studies should recruit larger samples to investigate

* Corresponding author. Department of Clinical Psychology and Amsterdam Public Health Institute, VU Amsterdam, Van der Boechorststraat 7, 1081, BT Amsterdam, the Netherlands.
*E-mail address:* e.karyotaki@vu.nl (E. Karyotaki).
[1] Reinout W. Wiers and Pim Cuijpers share last authorship.

https://doi.org/10.1016/j.brat.2021.104028
Received 6 June 2021; Received in revised form 17 December 2021; Accepted 27 December 2021
Available online 4 January 2022

possible smaller but clinically relevant effects of internet-based interventions for college students with depression and/or anxiety.

## 1. Introduction

The mental health of college students is a growing concern worldwide. College years are particularly challenging due to the developmental transition from late adolescence to young adulthood (Arnett, 2000; Baghurst & Kelley, 2014). Students face various stressors such as independent living, adjustment to a new social environment, and academic pressure, making them particularly susceptible to experiencing mental health problems (Karyotaki et al., 2020; Pedrelli, Nyer, Yeung, Zulauf, & Wilens, 2015). Epidemiological studies have indicated that one in three college students has experienced at least one mental disorder over the past twelve months, with anxiety and depression being the most prevalent diagnoses (Auerbach et al., 2016). Symptoms of depression and anxiety impose a considerable burden on students and society due to their association with strained interpersonal relationships, poor functioning, and increased risk for premature mortality (Auerbach et al., 2018; Buchanan, 2012). Adding to the personal suffering of affected students, mental health problems jeopardize academic progress, thereby reducing the students' employment prospects (Wilks et al., 2020).

To effectively manage symptoms of depression and anxiety in college students, early interventions are warranted. Ample research suggests that psychological interventions are effective in addressing symptoms of depression and anxiety (Bandelow et al., 2015; Carl et al., 2020; Cuijpers et al., 2016; Cuijpers, Karyotaki, de Wit, & Ebert, 2020; Cuijpers, Noma, et al., 2020). Nevertheless, the majority of college students with mental health problems do not receive psychological care despite the available counseling services at many colleges (Auerbach et al., 2016; Blanco et al., 2008; Bruffaerts et al., 2019). We should note that such services, however, are often limited, focused on study-related issues (e.g., exam anxiety), and include long waiting lists (Bolinski et al., 2020; Cuijpers, Auerbach, et al., 2019). Next to the limited availability of counseling services, many students are reluctant to seek help from counsellors due to the stigma associated with depression and anxiety (Czyz, Horwitz, Eisenberg, Kramer, & King, 2013; Farrer, Christensen, Griffiths, & Mackinnon, 2011; Reichert, 2012). Other commonly reported barriers include the preference for self-management of psychological problems, lack of time, and the perception that treatment is unnecessary (Czyz et al., 2013; Ebert et al., 2019). To address some of the help-seeking barriers, exploring alternative modes of psychological interventions delivery is needed.

Actively reaching out to students and offering them an easily accessible psychological intervention via the internet may be a promising solution in expanding psychological services in colleges while overcoming many treatment barriers. The main advantage of actively reaching out to students (e.g., by offering all college students an online screening) is that common mental health problems can be recognized and treated at an earlier stage. Further, advantages of Internet-based interventions include patient empowerment, increased treatment accessibility, and low cost (Andersson & Titov, 2014; Samoocha, Bruinvels, Elbers, Anema, & van der Beek, 2010). Moreover, internet-based interventions can substantially reduce stigma fears and counsellors' time, allowing students to follow treatment at their own pace in any place and time (Titov, 2011). In this fast-growing field, Cognitive Behavioral Therapy (iCBT) is the most widely studied type of intervention (Cuijpers, Kleiboer, Karyotaki, & Riper, 2017). Previous research has shown that iCBT has moderate effects in reducing symptoms of adult depression and anxiety when delivered with some form of therapeutic support (Karyotaki et al., 2018; Karyotaki et al., 2021; Pauley, Cuijpers, Papola, Miguel, & Karyotaki, 2021). Nevertheless, recent meta-analytic evidence suggests that these effects are much smaller among college students, and thus, more clinical trials are needed to explore ways to increase treatment effectiveness (Bolinski et al., 2020; Harrer et al., 2019).

To optimize the effects of iCBT for depression and anxiety in college students, it is necessary to consider individual patient needs and potential comorbidities. In this context, internet-based transdiagnostic and individually tailored interventions have been rapidly emerging (Păsărelu, Andersson, Bergman Nordgren, & Dobrean, 2017). Such interventions simultaneously tackle core processes that contribute to the development and maintenance of multiple disorders (Craske, 2012). Given the high comorbidity between depression and anxiety (Auerbach et al., 2019), as well as common factors underlying both conditions (e.g. negative affect and information processing difficulties) (Garber & Weersing, 2010), a transdiagnostic approach is potentially more clinically relevant than disorder-specific approaches. Further, because "one-size doesn't fit all", it is important to address the specific needs of patients through individually tailored interventions. Research in this area has demonstrated that transdiagnostic and individually tailored interventions have moderate to large effects particularly in reducing adult depression (Păsărelu et al., 2017). Thus, such interventions may offer a viable way in exploiting the full potential of iCBT among college students.

Day, McGrath, and Wojtowicz (2013) conducted a randomized controlled trial to investigate the effects of an Internet-based guided transdiagnostic intervention compared to a waiting list in reducing symptoms of moderate depression, anxiety and/or stress among 66 college students (Day et al., 2013). The authors found moderate to large effects for anxiety and depression (Day et al., 2013). Similarly, Mullin et al. (2015) examined the effects of transdiagnostic iCBT against waiting list in a sample of 55 college students with depression and anxiety (Mullin et al., 2015). The intervention resulted in significantly lower symptoms of anxiety at post-treatment and 3 months follow-up. However, there were no significant differences between the intervention and the control group in reducing depressive symptoms (Mullin et al., 2015), which contradicts the respective findings of Day et al. (2013). Based on these conflicting findings, it remains unclear whether transdiagnostic internet-based interventions effectively reduce depressive symptoms. Moreover, both trials used a waiting list as a comparison condition, which may have artificially inflated the intervention's outcomes (Cunningham, Kypri, & McCambridge, 2013; Furukawa et al., 2014). Therefore, it is essential to examine further the effects of transdiagnostic and individually tailored approaches for college students with anxiety and depression against other control conditions that reflect the existing practices better.

Thus, in the present study, we aimed to evaluate the effects of a new guided Internet-based transdiagnostic individually tailored intervention called "ICare Prevent". This new program is based on established iCBT components (e.g., problem-solving, behavioral activation, and cognitive restructuring) that have been proven effective in previous RCTs in the general population (Furukawa et al., 2021). Several randomized trials are currently examining the effectiveness of the ICare Prevent, but all of them are still ongoing; thus, the effects of this program remain unclear. Nevertheless, ICare Prevent had promising outcomes in a recent pilot study examining its feasibility and acceptability in Indonesian college students with anxiety and/or depression (Rahmadiana et al., 2021). Moreover, similar promising findings were observed in a recent German mixed method study aimed at assessing the feasibility of the ICare Prevent intervention (Weisel et al., 2020). In a total sample of 49 adults with a diagnosis of anxiety disorders, the authors found that the intervention was feasible and potentially effective in reducing symptoms of anxiety and depression (Weisel et al., 2020). Finally, a smaller pilot by

Gericke, Ebert, Breet, Auerbach, and Bantjes (2021) found that this intervention facilitated self-disclosure, emotional expression, self-awareness, and skill acquisition in a sample of 22 South African first-year college students with depression (Gericke et al., 2021). Such preliminary evidence highlights the need to explore further this intervention's effectiveness in a randomized controlled trial.

This study aimed to investigate the effectiveness of ICare Prevent against treatment as usual in reducing mild to moderate depression and/or anxiety symptoms among college students. We hypothesized that iCBT would be more effective than treatment as usual (TAU).

## 2. Methods

### 2.1. Design

This study was embedded within the World Mental Health college surveys initiative (WHO WMH-ICS: http://www.hcp.med.harvard.edu/wmh/college_student_survey.php), which aims to assess the prevalence and correlates of mental health problems in college students around the world (Cuijpers, Auerbach, et al., 2019). The present study employed a two-arm randomized control superiority trial design to compare a guided transdiagnostic and individually tailored iCBT intervention to TAU in college students with mild to moderate symptoms of depression and/or anxiety. After eligibility screening, measures were administered at baseline, post-treatment, six months, and twelve months post-randomization. More details about study design and methods are provided in our study protocol (Karyotaki et al., 2019).

### 2.2. Study population

This study was carried out in two Dutch Universities, namely the Vrije Universiteit (VU) and Universiteit van Amsterdam (UvA). Participants were recruited from March 2018 through July 2019 and included in the RCT based on the following criteria: (a) 18 years of age or older, (b) enrolment as a bachelor's or master's student in a Dutch college, (c) fluency in Dutch or English, (d) mild to moderate symptoms of depression defined by scoring above the cut-off score of 4 on the Patient Health Questionnaire (PHQ-9) (Kroenke, Spitzer, & Williams, 2001) and/or anxiety symptoms as defining by scoring above the cut-off score of 4 on the Generalized Anxiety Disorder scale – 7 items (GAD – 7) (Spitzer, Kroenke, Williams, & Löwe, 2006), and (e) provision of a written informed consent before participation. We focused on mild to moderate depression after consultation with university stakeholders who advised encouraging students with more severe symptoms to seek high-intensity care since the present intervention was new and, thus, untested in the vulnerable group of students with more severe symptomatology.

Participants were excluded if they met any of the following criteria: (a) diagnosis of bipolar disorder according to the MINI International Neuropsychiatric Interview (MINI) (Sheehan et al., 1998), (b) moderately severe/severe depressive symptoms as defined by scoring above the cut-off score of 14 on the PHQ-9 and/or moderately severe/severe anxiety symptoms as defined by scoring above the cut-off score of 14 on the GAD-7 scale, (c) receiving psychological treatment for depression and/or anxiety in the past 12 months, and (e) or no Internet connection. The exclusion criterion (c) was chosen to eliminate possible confounding effects of face-to-face treatment.

### 2.3. Procedures

The study protocol was approved by the Medical Ethical Committee of the VU Medical Centre (VUMC; nr 2016-538) and it was prospectively registered at the Netherlands Trial Registry (NTR6797). The recruitment was conducted through the epidemiological e-survey of the WHO WMH-ICS (More information on the e-survey can be found in our study protocol, Karyotaki, et al., 2019). In this e-survey, we recruited participants through emails and advertisements (i.e., flyers, faculty newsletters, social media, study website, colleges websites, and a mental health awareness campaign). Moreover, study advisors, students' mentors and student ambassadors informed potential participants about the study and provided them with useful links in case they wished to participate in the e-survey. The participation was voluntary. After completing the e-survey, students who were eligible for the RCT, due to their mild to moderate symptoms on the GAD-7 and/or PHQ-9, received an information letter about the study and an informed consent form. Those who signed the latter were invited to a diagnostic interview by phone and further assessed against the study's eligibility criteria. Eligible participants were randomized to the trial's arms and completed the baseline questionnaires.

### 2.4. Randomization, treatment allocation, and blinding

The randomization was conducted by two independent researchers who were not involved in the study using a computer random sequence generator. Participants were randomized at an individual-level (1:1 ratio) and were stratified by recruitment location (VU and UvA). Block randomization was applied with randomly varied block sizes (6–12 allocations per block). Allocation was concealed from all researchers involved in this study. It was not possible to mask personnel and participants due to the nature of the intervention. However, the diagnostic interviews at 12 months were performed by interviewers who were blind to the allocation assignment.

### 2.5. Sample size calculation

The sample size calculation was based on depressive symptoms. We have decided to base our sample calculation on the effects of iCBT on depression because Internet-based interventions have overall higher effects on anxiety than depression (Andrews, Cuijpers, Craske, McEvoy, & Titov, 2010). We initially anticipated a moderate effect of Cohen's d = 0.70 based on the findings of previous meta-analyses on the effectiveness of psychological interventions in treating depressive symptoms among college students (Cuijpers et al., 2016; Davies, Morriss, & Glazebrook, 2014). Such a moderate effect was also in line with the results of the two former RCTs on transdiagnostic internet-based interventions for depression and/or anxiety among college students (Day et al., 2013; Mullin et al., 2015). Thus, based on the available evidence by the time we designed our study, the present RCT was powered to detect a conservative estimate of Cohen's d = 0.55. Approximately 100 participants were needed to achieve a d = 0.55 when adjusting for a dropout rate of ~25% (power 1- $\beta = 0.8$ and $\alpha = 0.05$).

### 2.6. Intervention & e-coaching

The guided iCBT used in this study is a transdiagnostic individually tailored intervention called 'ICare Prevent' (Weisel et al., 2019; Weisel et al., 2018). The content of this intervention was tailored to college student needs through focus group discussions (Bolinski et al., 2018). The ICare Prevent strategies were based mainly on CBT and were delivered in 7 weekly online sessions: (1) introduction, (2) identification of problems and behavioral activation, (3) psychoeducation, (4) cognitive restructuring, (5 & 6) problem solving or exposure in daily life, and (7) plan for the future. Four weeks after completion of the seventh session, participants were invited to a booster session, which aimed at reflecting on goal achievement and learned experiences. Further, in sessions 2 through 7, participants were free to choose elective modules based on their needs (i.e., worry and rumination, acceptance of unfulfilled needs, relaxation, alcohol consumption as emotion regulator, self-worth, perfectionism, appreciation and gratitude, and sleep hygiene). The intervention is defined as transdiagnostic because it tackles common underlying mechanisms of anxiety and depression in sessions 1–4, 7 and 8 next to the two individually tailored sessions (5th and 6th sessions). Also, all the optional modules tackle problems that are

common in both anxiety and depression. The "individually tailored" term was used because participants could focus either on depression or anxiety first based on their preferences and needs and received modules that were tailored to the primary condition (problem-solving vs. exposure). Further, in sessions 2 through 7, participants could choose between a range of optional modules based on their goals, needs, and preferences. Therefore, each participant could follow an individually tailored path throughout the intervention, meaning that participants did not follow the same sessions and in the exact same sequence from the beginning to the end. Such flexibility contradicts the standardized intervention approaches, and it is more well-suited to individually tailored approaches." The intervention included text, testimonials, (homework) exercises, audio–visual components, diaries, downloadable information sheets, a mood graph, and a messaging system that allowed participants to contact their online coach. The intervention was available in both Dutch and English.

Each session required between 45 and 60 min, which was self-paced. The sessions were delivered with manualized asynchronous support provided by trained psychology master's students (e-coaches) who were supervised by a senior PhD-level researcher (details about the e-coach training can be found in the protocol - (Karyotaki et al., 2019). More specifically, the e-coaches followed standard templates for providing feedback to participants, and they could tailor these templates to participants individual needs. At the beginning of the sessions, the e-coaches received feedback from a senior researcher who monitored the participants' progress. After the first sessions, the senior researcher randomly checked the e-coaches' responses to ensure fidelity to the feedback templates and provided additional feedback to the e-coaches whenever necessary. Finally, the e-coaches were advised to seek the support of the senior research staff at any time needed (e.g., presence of suicidal ideation during the trial). The e-coaches were advised to spend less than 30 min per feedback and reply within a maximum of two working days. The asynchronous support was given via the messaging function of the intervention platform. The reader is referred to our protocol for a more detailed description of our intervention (Karyotaki et al., 2019).

### 2.7. Treatment as usual (TAU)

Participants in the TAU group received detailed information about the available regular care services in the community (i.e., primary and secondary mental health services delivered by the student counseling services/general practitioners/psychologists/psychiatrists). This is in line with existing routine care practices in the Dutch universities, where students with mental health problems are advised to seek help through community services. In contrast, university counseling services are meant to manage study-related issues (e.g., exam anxiety). Thus, the present control reflected existing routine care practices in the universities where the study was conducted. It should be noted that info about the available services was also provided to participants in the intervention group. However, students in the TAU group were strongly advised to seek support, but they were free to decide whether they would follow this advice or not. We recorded the use of such services in both the intervention and control group throughout the trial assessments.

### 2.8. Measures

Depressive symptoms were assessed by the PHQ-9 (Kroenke et al., 2001). Item responses are on a 0–3 scale and total scores ranging from 0 to 27 with higher scores indicating more severe depression. The PHQ-9 has shown to have good psychometric properties (Wittkampf, Naeije, Schene, Huyser, & van Weert, 2007). Anxiety symptoms were measured by the GAD-7 (Spitzer et al., 2006). Items are each scored on a 0–3 scale and total score range is 0–21, with higher scores indicating more severe anxiety symptoms. The GAD-7 scale has shown to have good psychometrics properties (Dear et al., 2011). Diagnoses of mental health disorders were established based on the MINI (version 5.0) conducted via the telephone. The MINI is a brief structured diagnostic interview based on the Diagnostic and Statistical Manual of Mental disorders fourth edition (DSM-IV) and has good psychometric properties (Lecrubier et al., 1997).

Secondary outcome measures included EuroQol - 5 Dimensions (EQ-5D) (Group, 1990; König et al., 2010; van Agt, Essink-Bot, Krabbe, & Bonsel, 1994), Client satisfaction with treatment – 8 items (CSQ-8) (Attkisson & Greenfield, 1996, p. 120), university dropout, and educational achievement. The EQ-5D is a self-report questionnaire assessing quality of life, which consists of five dimensions (i.e., mobility, self-care, ordinary activities, discomfort, and mood state, related to anxiety or depression), and has shown to have adequate validity (Group, 1990; König et al., 2010; van Agt et al., 1994). The CSQ-8 is a self-report measure that consists of 8 items and assesses client satisfaction related to the treatment. Item responses are on a 1–4 scale and total scores range from 8 to 32, with higher scores of CSQ-8 indicating higher treatment satisfaction. The CSQ-8 has shown to have high internal consistency (Boβ et al., 2016). Educational achievement was measured using the Presenteeism Scale for Students (PSS), which measures academic impairment by addressing questions like "In the past 4 weeks, how often has your primary health condition affected your academic work?" The total score shows academic impairment due to presenteeism in percentages. PSS has shown to be a valid and reliable measure in college students (Matsushita et al., 2011). Students were also asked about the number of European Credit Transfer System (ECTs) achieved during a given study period, while university dropout was monitored through self-report questions.

Finally, treatment adherence was defined as the total number of online sessions completed divided by the total number of intervention sessions. Per protocol, adherence was also defined as completion of the 4th module in which the core component of iCBT (i.e., behavioral activation and cognitive restructuring) was delivered.

### 2.9. Analyses

All analyses were performed in STATA version 16.0. Baseline differences in demographic and clinical characteristics were examined with chi-square and t-tests. The results of the MINI interview were summarized by descriptive statistics. Primary analyses were based on the intention-to-treat (ITT) principle. Missing data were handled by multiple imputation. The effects of the iCBT intervention on depression and anxiety were analyzed using mixed effects linear regression with participants nested within the recruiting universities (VU and UvA). The post-treatment depression and anxiety scores were used as a dependent variable and trial arm condition as an independent variable while adjusting for baseline symptom severity ($OUT_{0ij}$) and major depression diagnosis ($MDD_{0ij}$). The main model used for the present analysis for continuous outcomes can be described as follows:

$$OUT_{ij} = \alpha_i + \beta_i OUT_{0ij} + \beta_i MDD_{0ij} + \theta_i x_{ij} + e_{ij}$$

$$\theta_i = \theta + u_i$$

$$u_i \sim N\ (0, \tau^2)$$

$$e_{ij} \sim N\ (0, \sigma^2_i)$$

In this expression, under the random effects model (random treatment effects), the *j*th participant provides their *OUT* (i.e., treatment outcome: depressive/anxiety symptoms) after treatment, $OUT_{ij}$, and their *OUT* at baseline $OUT_{0ij}$. The subscript, *i*, denotes that a separate parameter is estimated per each recruitment center. For instance, $\alpha i$ denotes that a separate intercept term is estimated per each recruitment center (clustering of participants within recruitment centers: VU and UvA). Similarly, $\beta_i$ and $\sigma^2_i$ denote a different adjustment term for

baseline values and a distinct residual variance per recruitment centers, respectively. Effect size Cohen's d was calculated by subtracting the average score on primary outcome measures (PHQ-9 and GAD-7 scales) of the iCBT group from the average scores of the TAU group at the post-treatment and dividing the results by the pooled SD. Accordingly, secondary outcomes were analyzed using mixed effects logistic or linear regression depending on whether the outcome was continuous or dichotomous. Finally, we performed sensitivity analysis with complete cases to test the robustness of our findings.

## 3. Results

### 3.1. Participant characteristics and flow

Fig. 1 shows the flow of participants throughout the study. Out of 3879 students who were assessed for eligibility, 3779 were excluded based on our eligibility criteria (n = 3758), because they declined to participate (n = 2) or for other reasons (n = 19). A total of 100 participants were randomized into the iCBT (n = 48) or the TAU (n = 52) groups. Study dropout was 24%, 26%, and 18% at post-test, 6- and 12-month follow-ups, respectively. Study dropout was well-balanced between the intervention and the control group (see Fig. 1). Participants who dropped out did not differ significantly from the participants who completed the assessment in most baseline characteristics apart from

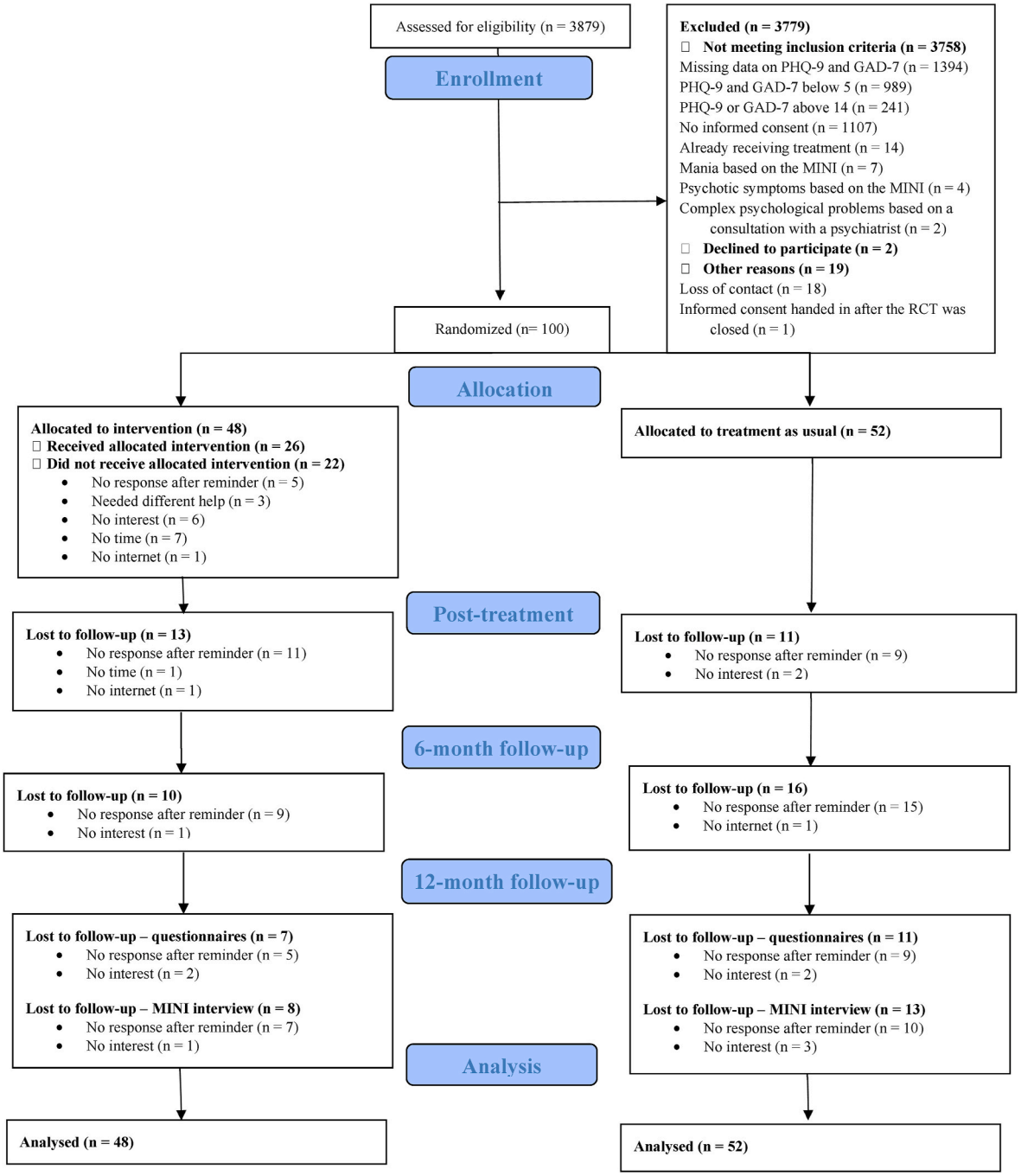


**Fig. 1.** Participant flow through study.

gender, with females being more likely to complete the post-treatment assessment than males (Cramer's V = .325, p = .003).

Table 1 shows the participant characteristics at baseline. The majority of participants were female (81%), full-time (99%), bachelor students (68%). The sample had a mean age of 21.91 (SD = 2.61). Most of the participants were Dutch (62%) while other prevalent nationalities were German (7%), Italian (5%) and Chinese (4%). According to the MINI diagnostic interview, 28% of participants had a major depressive episode in their lifetime, while 38% experienced a current major depression and 39% experience a current generalized anxiety disorder. Other diagnoses included: moderate suicidal risk (18%), current panic disorder (10%), lifetime panic disorder (21%), lifetime panic attacks (5%), current agoraphobia (20%), and current social phobia (22%). At 12-months, based on MINI, out of 79 respondents 12 had major depression (iCBT: 7/40; TAU: 5/39), 13 had generalized anxiety disorder (iCBT: 5/40; TAU 8/39), 3 had panic disorder (iCBT: 0/40; TAU: 3/39) and 9 had agoraphobia (iCBT: 4/40; TAU: 5/39).

Participants had a mean score of depression and anxiety of 8.23 (SD = 2.93) and 6.77 (SD = 2.82), respectively. Participants had a mean quality of life of 0.78 (SD = 0.13) at the baseline and reported having a GPA average of 6.2/10 (SD = 17.5, note: Dutch grades ranging from 1 to 10). Students had on average 49% impaired academic performance due to depression and/or anxiety symptoms, indicated by the results of PSS. We did not find any outliers in the sample after examining the normality of the variable distribution. As can be observed from the table, there were no significant differences between the conditions on any of the socio-demographic variables at baseline, with the exception of higher number of participants with current major depressive disorder in the intervention group (iCBT = 24/48 & TAU = 14/52; t = 5.6, p = .02; see Table 1). Thus, all subsequent analyses have been adjusted for this baseline imbalance.

### 3.2. Treatment adherence

Among the 48 participants allocated to the intervention, 26 (54.2%) completed the core modules of the intervention (all the sessions presenting the core techniques of cognitive restructuring and behavioral activation, i.e., at least 4 modules). Reasons stated for not completing the treatment included the following: 5 participants did not respond to repeated reminders. Three participants indicated in the post-assessment that they believed they needed different help, 6 indicated to have lost their interest, 7 did not to have time and 1 unexpectedly had no internet access during the intervention period. On average, the participants completed 4.50 (SD = 3.04) sessions, 19 participants (39.6%) completed all 7 sessions of the intervention, and 15 participants (31%) also completed the booster session. On average, participants completed 2.67 (SD = 2.14) optional modules and 36 participants (75%) completed at least 1 optional module.

As per our protocol, every e-coach spent approximately 2.48 (SD = 2.10) hour per participant. Finally, there were rare cases of direct correspondence between the e-coaches and participants. As per our protocol, feedback was mainly motivational, and e-coaches did not start a conversation with the participants. In some rare cases, participants responded to reminder emails stating their willingness to continue with the intervention. We should note that the e-coaches did not send feedback via a conversation function but through a feedback window at the end of each completed session. Therefore, the participants were not prompted to reply.

### 3.3. Use of mental health services

Table 2 presents the use of services in each of the two arms. During the 2 months before filling in the post-treatment questionnaire, the most common services used by the iCBT and the TAU group, respectively, were the service of a general practitioner (11 and 14 participants, respectively), study advisor (5 and 11 participants, respectively), and

**Table 1**
Socio-demographic characteristics and baseline scores.

| | Whole sample (*n* = 100) | iCBT (*n* = 48) | TAU (*n* = 52) | | | *p* |
|---|---|---|---|---|---|---|
| | *M (SD)* | *M (SD)* | *M (SD)* | *t* | *r* | |
| Age (years) | 21.91 (2.61) | 21.75 (2.70) | 22.06 (2.53) | 0.59 | .06 | .558 |
| | *N* | *n (%)* | *n (%)* | $\chi^2$ | *V* | |
| Gender | | | | 0.20 | 0.05 | .800 |
| Male | 19 | 10 (20.8) | 9 (17.3) | | | |
| Female | 81 | 38 (79.2) | 43 (82.7) | | | |
| Type of programme | | | | 0.93 | 0.10 | .999 |
| Full-time degree | 99 | 48 (100) | 51 (98.1) | | | |
| Part-time degree | 1 | 0 (0) | 1 (1.9) | | | |
| University | | | | 3.07 | .18 | .239 |
| VU | 70 | 35 (72.9) | 35 (67.3) | | | |
| UvA | 18 | 10 (20.8) | 8 (15.4) | | | |
| Windesheim | 12 | 3 (6.3) | 9 (17.3) | | | |
| Faculty | | | | | | |
| Behavioural, Social or Movement Sciences | 31 | 20 (41.7) | 11 (21.2) | 6.19 | .25 | .417 |
| Humanities | 9 | 3 (6.3) | 6 (11.5) | | | |
| Law | 9 | 4 (8.3) | 5 (9.6) | | | |
| Medicine | 5 | 3 (6.3) | 2 (3.8) | | | |
| Business or Economics | 7 | 3 (6.3) | 4 (7.7) | | | |
| Science | 19 | 8 (16.7) | 11 (21.2) | | | |
| No information | 20 | 7 (14.6) | 13 (25) | | | |
| Level of programme | | | | 0.50 | .07 | .525 |
| Bachelor | 68 | 31 (64.6) | 37 (71.2) | | | |
| Master | 32 | 17 (35.4) | 15 (28.8) | | | |
| Nationality | | | | 1.03 | .10 | .392 |
| Dutch | 68 | 35 (72.9) | 33 (63.5) | | | |
| International | 32 | 13 (27.1) | 19 (36.5) | | | |
| Ethnicity | | | | 0.01 | .01 | .999 |
| Dutch | 62 | 30 (62.5) | 32 (61.5) | | | |
| Other | 38 | 18 (37.5) | 20 (38.5) | | | |
| Diagnoses[a] | | | | | | |
| Current major depressive disorder | 38 | 24 (50) | 14 (26.9) | 5.64 | .24 | .023* |
| Dysthymia | 5 | 2 (4.2) | 3 (5.8) | 0.14 | .04 | .999 |
| Current panic disorder | 10 | 3 (6.3) | 7 (13.5) | 1.44 | .12 | .322 |
| Current generalized anxiety disorder | 39 | 20 (41.7) | 19 (36.5) | 0.28 | .05 | .683 |
| | *M (SD)* | *M (SD)* | *M (SD)* | *t* | *r* | |
| Scores on questionnaires[b] | | | | | | |
| Depressive symptoms | 8.23 (2.93) | 8.52 (2.87) | 7.96 (2.98) | −0.95 | .10 | .342 |
| Anxiety symptoms | 6.77 (2.82) | 6.81 (2.71) | 6.73 (2.95) | −0.14 | .01 | .886 |
| Quality of life | .78 (.13) | .77 (.12) | .79 (.15) | 0.59 | .06 | .557 |

*Note.* Abbreviations (alphabetical): $\chi^2$: Statistic of $\chi^2$-test; *M*: Mean; *n*: Number of participants; *p*: p-value; *r*: Pearson's r, *SD*: Standard deviation; *t*: Statistic of independent *t*-test; UvA: University of Amsterdam; *V*: Cramer's V; VU: Vrije

Universiteit Amsterdam.
*p < .05.
[a] based on the MINI-international neuropsychiatric interview.
[b] based on the Patient Health Questionnaire-9, Generalized Anxiety Disorder-7 and EuroQol – 5 dimensions (expressed in utility scores).

the services of a psychiatrist, psychologist, or psychotherapist (3 and 6 participants, respectively). These services remained the most used in both the intervention and the control condition during the 2 months before the 6-month follow-up period (general practitioner: 18 and 7 participants, respectively; study advisor: 9 and 7; psychiatrist/psychologist/psychotherapist: 10 and 6, respectively) as well as during the 2 months before the 12-month follow-up period (general practitioner: 12 and 13 participants, respectively; study advisor: 9 and 6; psychiatrist/psychologist/psychotherapist: 15 and 11, respectively).

In the TAU group, one participant reported the use of benzodiazepines, ADHD medication and cognitive enhancers at post-treatment, cognitive enhancers at 6-month follow-up and sleep medication or supplements at 12-month follow-up. In the iCBT group, one participant reported using cannabis oil at post-treatment and antidepressants and ADHD medication at 6-month follow-up. At the 12-month follow-up, 2 participants from the intervention group reported the use of antidepressants and ADHD medication, while one reported the use of benzodiazepines. In both groups and at all time-points, standard drugs were reported besides the medication described above, such as antihistamines, anti-asthmatics, antibiotics, pain killers, and contraceptives.

Overall, at post-test, the iCBT and TAU groups received similar services. Although a greater number of participants in the TAU than the iCBT group used these services, there was no significant difference in service use between the two groups at post-intervention. On the contrary, at 6-month post-randomization, participants of the intervention group were significantly accessing help from more health care providers on average (mean = 1.04, SD = 1.18; p = .033) compared to the control group. Reasons behind this significant difference remain largely unknown, but it could be attributed to possible increased awareness about the benefits of psychological help among the intervention participants or to the need for more substantial care after the end of the intervention. The use of services was more balanced between the iCBT and TAU groups at 12-months follow-up, with no significant differences between the groups in terms of service use.

### 3.4. Main outcomes

When including the full sample (intention-to-treat analysis), we found no significant differences between the intervention and the control in symptoms of depression and anxiety at post-test (depression: $\beta = -0.50$; anxiety: $\beta = -0.46$; $p > .05$). Similar outcomes were observed at 6- (depression: $\beta = 0.30$; anxiety: $\beta = 0.13$; $p > .05$) and 12-month follow-ups (depression: $\beta = -0.19$; anxiety: $\beta = -0.61$; $p > .05$), and in analyses including only the complete cases (see Table 3). In iCBT, within group effect sizes on depression ranged from small to moderate (d = .19 at post-test, d = 0.52 at 6-months, d = 39 at 12-months). Similar within group effects were observed for TAU, albeit slightly smaller in magnitude compared to within group effects of iCBT at post-test and 6 months (d = 0.06 at post-test, d = 0.47 at 6-months, d = 39 at 12-months). We observed much smaller in magnitude within group effects on anxiety in both iCBT (d = 0.18 at post-test, d = 0.22 at 6-months, d = 0.26 at 12-months) and TAU (d = 0.10 at post-test, d = 0.16 at 6-months, d = 0.25 at 12-months).

At 12 months, there was no significant difference in the rates of depression and anxiety current diagnoses based on MINI between the intervention and the control (MDD: $\beta = 0.12$, SE = 0.64; GAD: $\beta = -0.62$, SE = 1.0.; panic disorder: $\beta = -0.41$, SE = 1.5; Agoraphobia: $\beta = -0.22$, SE = 0.73; $p > .05$).

**Table 2**
Use of healthcare services during the follow-up period[a].

| | iCBT ($n$ = 48) | TAU ($n$ = 52) |
|---|---|---|
| **Post-treatment** | | |
| General practitioner | 11 (22.9%) | 14 (26.9%) |
| Study advisor | 5 (10.4%) | 11 (21.2%) |
| Student counsellor | 1 (2.1%) | 3 (5.8%) |
| Student psychologist | 2 (4.2%) | 3 (5.8%) |
| Psychiatrist/ psychologist/ psychotherapist | 3 (6.3%) | 6 (11.5%) |
| Medical specialist | 2 (4.2%) | 1 (1.9%) |
| Paramedical healthcare | 2 (4.2%) | 3 (5.8%) |
| Alternative medicine | 1 (2.1%) | 0 (0.0%) |
| Self-help groups | 0 (0.0%) | 2 (3.8%) |
| Other healthcare services[b] | 0 (0.0%) | Mindfulness practices (1; 1.9%)<br>Mental health care nurse (1; 1.9%) |
| Mental health medication[b] | Cannabis oil (1; 2.1%) | Benzodiazepines (1; 1.9%)<br>ADHD Medication (1; 1.9%)<br>Cognitive enhancers (1; 1.9%) |
| **6-month follow-up** | | |
| General practitioner | 18 (37.5%) | 7 (13.5%) |
| Study advisor | 9 (18.8%) | 7 (13.5%) |
| Student counsellor | 0 (0.0%) | 2 (3.8%) |
| Student psychologist | 2 (4.2%) | 3 (5.8%) |
| Psychiatrist/ psychologist/ psychotherapist | 10 (20.8%) | 6 (11.5%) |
| Medical specialist | 3 (6.3%) | 1 (1.9%) |
| Paramedical healthcare | 2 (4.2%) | 0 (0.0%) |
| Alternative medicine | 2 (4.2%) | 0 (0.0%) |
| Self-help groups | 1 (2.1%) | 3 (5.8%) |
| Other healthcare services[b] | Meditation group (1; 2.1%)<br>Social support (1; 2.1%) | Dietologist (1; 1.9%) |
| Medication[b] | Antidepressants (1; 2.1%)<br>ADHD medication (1; 2.1%) | Cognitive enhancers (1; 1.9%) |
| **12-month follow-up** | | |
| General practitioner | 12 (25%) | 13 (25%) |
| Study advisor | 9 (18.8%) | 6 (11.5%) |
| Student counsellor | 3 (6.3%) | 1 (1.9%) |
| Student psychologist | 1 (2.1%) | 3 (5.8%) |
| Psychiatrist/ psychologist/ psychotherapist | 15 (31.3%) | 11 (21.2%) |
| Medical specialist | 2 (4.2%) | 3 (5.8%) |
| Paramedical healthcare | 4 (8.3%) | 2 (3.8%) |
| Alternative medicine | 1 (2.1%) | 1 (1.9%) |
| Self-help groups | 1 (2.1%) | 1 (1.9%) |
| Other healthcare services[b] | Creative therapy (1; 2.1%)<br>Psycho-motor therapy (1; 2.1%)<br>Social support (3; 6.3%) | 0 (0.0%) |
| Medication[b] | Antidepressants (2; 4.2%)<br>ADHD medication (2; 4.2%)<br>Benzodiazepines (1; 2.1%) | Sleep medication (1; 1.9%)<br>Sleep supplement (1; 1.9%) |

*Note.* Medical specialist = e.g., cardiologist, rheumatologist, or neurologist. Paramedical healthcare provider = e.g., physiotherapist, speech therapist, occupational therapist. Alternative medicine practice = e.g., homeopath, acupuncturist, Reiki practitioner. Self-help group = e.g., Alcoholics Anonymous, patient association.
[a] Details are provided when some participants used the given service more than 3 times. If no details are provided, participants used the service 1–3 times only.
[b] The numbers in brackets relate to the number of participants who reported the use of the service or medication.

**Table 3**
Effects of iCBT compared to TAU for college students with depressive and/or anxiety symptoms at post-treatment, 6- and 1-month follow-up.

| | Post-treatment | | | | 6-month follow up | | | | 12-month follow-up | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | M (SE), n | d (95% CI) | β (95% CI) | p | M (SE), n | d (95% CI) | β (95%CI) | p | M (SE), n | d (95% CI) | β (95%CI) | p |
| **PHQ-9** | | | | | | | | | | | | |
| *ITT analysis* | | | | | | | | | | | | |
| iCBT | 7.66 (.83), 48 | .003 (−.38 to .39) | -.50 (−2.67 to 1.66) | .65 | 6.63 (.65), 48 | -.11 (−.50 to .29) | .30 (−1.46 to 2.06) | .74 | 6.73 (.85), 48 | -.06 (−.45 to .33) | -.19 (−2.46 to 2.08) | .87 |
| TAU | 7.68 (.75), 52 | | | | 6.17 (.59), 52 | | | | 6.39 (.68), 52 | | | |
| *Complete Cases* | | | | | | | | | | | | |
| iCBT | 7.37 (.78), 35 | .08 (−.36 to .54) | -.69 (−2.73 to 1.36) | .51 | 6.60 (.70), 38 | -.14 (−.59 to .32) | .29 (−1.50 to 2.08) | .75 | 6.83 (.84), 41 | -.06 (−.49 to .37) | -.12 (−2.12 to 1.87) | .90 |
| TAU | 7.78 (.75), 41 | | | | 6.08 (.54), 36 | | | | 6.54 (.64), 41 | | | |
| **GAD-7** | | | | | | | | | | | | |
| *ITT analysis* | | | | | | | | | | | | |
| iCBT | 6.15 (.64), 48 | .04 (−.35 to .43) | -.46 (−2.13 to 1.22) | .52 | 5.96 (.67), 48 | .008 (−.38 to .40) | .13 (−1.77 to 2.04) | .89 | 5.65 (.76), 48 | .04 (−.35 to .43) | -.61 (−2.81 to 1.58) | .58 |
| TAU | 6.33 (.64), 52 | | | | 6.00 (.76), 52 | | | | 5.84 (.57), 52 | | | |
| *Complete Cases* | | | | | | | | | | | | |
| iCBT | 6.00 (.63), 35 | .14 (−.32 to .59) | -.63 (−2.2 to .95) | .43 | 5.89 (.73), 38 | .08 (−.38 to .54) | -.02 (−1.93 to 1.88) | .98 | 5.63 (.76), 41 | .04 (−.39 to .47) | -.32 (−2.07 to 1.43) | .72 |
| TAU | 6.50 (.59), 40 | | | | 6.23 (.67), 35 | | | | 5.80 (.57), 41 | | | |
| **EQ-5D** | | | | | | | | | | | | |
| *ITT analysis* | | | | | | | | | | | | |
| iCBT | .75 (.03), 48 | .09 (−.30 to .49) | -.005 (−.11 to .10) | .92 | .78 (.02), 48 | .00 (−.04 to .39) | .01 (−.06 to .09) | .69 | .79 (.03), 48 | .05 (−.34 to .44) | .003 (−.08 to .09) | .93 |
| TAU | .77 (.03), 52 | | | | .78 (.03), 52 | | | | .80 (.03), 52 | | | |
| *Complete Cases* | | | | | | | | | | | | |
| iCBT | .77 (.02), 35 | .00 (−.45 to .45) | -.0004 (−.12 to .81) | .99 | .77 (.02), 33 | -.15 (−.67 to .36) | .03 (−.05 to .10) | .47 | .79 (.03), 41 | .06 (−.37 to .49) | -.002 (−.08 to .075) | .96 |
| TAU | .77 (.03), 40 | | | | .75 (.03), 26 | | | | .80 (.02), 41 | | | |
| **PSS** | | | | | | | | | | | | |
| *ITT analysis* | | | | | | | | | | | | |
| iCBT | 47 (2.56), 48 | .05 (−.34 to .44) | .08 (−7.50 to 7.66) | .98 | 40 (3.39), 48 | .19 (−.19 to .59) | −4.73 (−14.6 to 5.14) | .34 | 39 (3.10), 48 | .09 (−.31 to .48) | −2.80 (−12.9 to 7.34) | .59 |
| TAU | 48 (3.05), 52 | | | | 45 (3.85), 52 | | | | 41 (3.45), 52 | | | |
| *Complete Cases* | | | | | | | | | | | | |
| iCBT | 47 (2.54), 33 | -.06 (−.5 to .40) | -.36 (−8.05 to 7.32) | .92 | 40 (2.77), 34 | .33 (−.16 to .83) | −5.68 (−14.1 to 2.70) | .18 | 40 (3.17), 38 | .11 (−.35 to .56) | −2.61 (−11.0 to 5.81) | .54 |
| TAU | 46 (2.75), 38 | | | | 46 (3.81), 29 | | | | 42 (3.08), 36 | | | |
| **Average grade** | | | | | | | | | | | | |
| *ITT analysis* | | | | | | | | | | | | |
| iCBT | 7.0 (.12), 48 | .00 (−.39 to .39) | .081 (−.26 to .42) | .64 | 7.2 (.08), 48 | -.16 (−.55 to .24) | .13 (−.20 to .47) | .43 | 6.9 (.95), 48 | .22 (−.17 to .61) | −2.19 (−6.45 to 2.08) | .31 |
| TAU | 7.0 (.11), 52 | | | | 7.1 (.10), 52 | | | | 9.3 (1.9), 52 | | | |
| *Complete Cases* | | | | | | | | | | | | |
| iCBT | 7.1 (.13), 33 | -.15 (−.62 to .31) | .10 (−.20 to .41) | .50 | 7.2 (.07), 35 | -.45 (.95–.04) | .17 (−.07 to .42) | .17 | 7.0 (.10), 38 | .25 (−.21 to .70) | −1.86 (−6.09 to 2.37) | .39 |
| TAU | 7.0 (.09), 39 | | | | 7.0 (.09), 29 | | | | 9.2 (2.1), 37 | | | |

***Abbreviations***: *d = Cohen's d; EQ-5D = EuroQol - 5 Dimensions; GAD-7 = Generalized Anxiety Disorder 7-itmes; iCBT = Internet based Cognitive Behavioral Therapy; M = mean score; p = p-value; PHQ-9 = Patient Health Questionnaires 9-items; PSS = Presenteeism Scale for Students (PSS); SE = Standard error; TAU = Treatment as Usual; β = betta coefficient adjusted for diagnosis of Major Depression at baseline.*

### 3.5. Secondary outcomes

We found no evidence of a difference between iCBT and TAU in quality of life at post-treatment ($\beta = -0.005$; $p > .05$) and follow-up assessments (6 months: $\beta = 0.01$; 12 months: $\beta = 0.003$; $p > .05$). In addition, we found no differences in academic role impairment between the conditions at post-treatment ($\beta = 0.8$; $p > .05$) and follow-ups (6 months: $\beta = -4.73$; 12 months: $\beta = -2.80$; $p > .05$). Similarly, no significant differences were observed in the GPA at post-treatment ($\beta = 0.081$; $p > .05$) and follow-up assessments (6 months: $\beta = 0.13$; 12-months: $\beta = -2.19$; $p > .05$). All outcomes have been replicated in the complete case analyses and results are presented in Table 3. Regarding college dropout, in total 2 participants dropped out from the university at the post-treatment (iCBT = 1; TAU = 1), 6 at 6-month follow-up (iCBT = 2; TAU = 4) and 7 at 12 months follow up (iCBT = 3; TAU = 4). University dropout rates did not differ significantly between the conditions (post-treatment: $\beta = 0.17$, SE = 1.31; 6-months: $\beta = -0.72$, SE = 0.91; 12-months: $\beta = -0.47$, SE = 0.78; $p > .05$. Overall, participants reported a 72% (SD = 7.6%) rate of satisfaction with the intervention. On average, participants completed approximately half of the main 7 sessions of the iCBT intervention (55%). Treatment adherence and treatment (i.e., number of completed modules) satisfaction were not significantly associated with the effect size within the intervention group at post-treatment, 6- and 12-month follow-up. Nevertheless, the sample size of the iCBT group was small (n = 48 participants). So, we cannot rule out the possibility of an association between treatment adherence/satisfaction and effect sizes that we could not detect due to the limited statistical power.

## 4. Discussion

In this study, we examined the effects of a guided transdiagnostic individually tailored iCBT compared to TAU in reducing symptoms of depression and anxiety among college students. In contrast with our hypothesis, we found no evidence of a difference between the intervention and the control condition in any of the examined outcomes (i.e., depression, anxiety, quality of life, educational achievement, and college dropout) across the post-treatment and follow-up assessments. Overall, participants reported good satisfaction with the intervention, and more than half of the participants completed the core modules of the intervention, which is comparable to the findings of a previous meta-analysis on iCBT for depression in the general adult population (Van Ballegooijen et al., 2014). More specifically, van Ballegooijen and colleagues (2014) found that the percentage of completers of iCBT is on average 65.1%, which is somewhat higher than what we observed in the present trial. Nevertheless, we should bear in mind that the intervention type and target group differ between our study and van Ballegooijen and colleagues (2014) meta-analysis. Indicatively, a previous trial in the same field found a 43% intervention completion rate, which is in line with our findings (Mullin et al., 2015). We should note that the effects of the intervention were not significantly associated with treatment adherence and satisfaction.

The null findings found by the present study are in accordance with the results of previous literature on digital interventions for college students with depression. A recent meta-analysis by Harrer et al. (2019) showed a small but significant effect (g = 0.18) of internet-based interventions on depressive symptoms among college students (Harrer et al., 2019). Nevertheless, the authors reported that prediction intervals crossed zero (g = −0.26 to 0.62), indicating that results of future trials would probably range from negative to moderate (Harrer et al., 2019). A similar conclusion can be drawn using the personalized estimates of a recent individual patient data meta-analysis on iCBT for depression (Karyotaki et al., 2021). Setting the parameters to the mean age (22) and PHQ-9 score (8) of our target group (students) at the baseline (see https://bit.ly/3faSRdV), it can be seen that guided iCBT results in a small, but non-significant effect on depression compared to treatment as usual at post-treatment, 6- and 12-month follow-up assessments (Karyotaki et al., 2021).

However, the present findings on depression contrast with a previous trial on a transdiagnostic internet-based intervention for college students that found large effects on depression compared to a waiting list group (Day et al., 2013). Several reasons may explain these inconsistent findings. First, it is well known that waiting list controls may artificially inflate the outcomes (Cunningham et al., 2013; Furukawa et al., 2014). Based on previous literature findings, a waiting list control group may inflate the effects sizes of the intervention because participants are actively discouraged from seeking alternative help, which is reinforced by the expectation of receiving treatment in the future (Cuijpers, Karyotaki, Reijnders, & Ebert, 2019). It has also been suggested that a waiting list control may decrease the willingness to be engaged in positive activities, thereby acting as a nocebo (Furukawa et al., 2014). Therefore, the waiting list differs substantially from no treatment or TAU, where participants are actively encouraged to seek help. Thus, the discrepancy in our findings and the results of the trial by Day et al. (2013) may partly be explained by the different control conditions. Further, another plausible explanation may be the differences in baseline symptom severity. The trial of Day et al. (2013) had participants with moderate depression symptoms while in the present study, we included participants experiencing mild to moderate symptoms. Thus, the room for improvement was much smaller given the mild symptomatology of our sample. Finally, Day and colleagues administered a brief intervention (n = 5 core sessions) and weekly support via phone or email. Shorter programs and synchronous support may be more beneficial for college students than lengthier interventions with asynchronous support, but such a hypothesis should be examined by future studies. Our results, however, replicated the findings of Mullin and colleges (2015) who reported no significant effects for transdiagnostic iCBT on depressive symptoms (Mullin et al., 2015).

The present results on anxiety were in line with previous meta-analytic findings. Harrer and colleagues found no evidence of a difference in the effects of internet-based interventions compared to controls for college students with anxiety after adjusting for publication bias. Nevertheless, we did not replicate the conclusions of previous trials in this field that showed moderate to large effects in favor of transdiagnostic iCBT (Day et al., 2013; Mullin et al., 2015). Similarly to the above, possible explanations of this discrepancy include differences in the control condition, baseline symptom severity, intervention length and type of support. Finally, our secondary outcomes related to the quality of life, academic achievement, and college dropout are in accordance with previous literature findings. Recent meta-analyses have shown that internet-based interventions do not significantly improve quality of life and academic performance among college students with common mental disorders (Bolinski et al., 2020; Harrer et al., 2019).

The present results should be interpreted cautiously due to several limitations. First, although our sample was sufficiently powered to detect a moderate effect on symptoms of depression and anxiety, a bigger sample (>500 participants) would be required to detect a smaller but clinically relevant effect of d = 0.24 (Cuijpers, Turner, Koole, Van Dijke, & Smit, 2014). Thus, future studies should include a much bigger sample to investigate small effects of iCBT on mild-to-moderate anxiety and depression. To increase the sample size, future studies should consider lowering the recruitment threshold. For instance, the administration of MINI may have served as a barrier to participation for some students because they had no time to take such interview next to their busy schedules, or due to stigma around formal mental health diagnoses. Moreover, many potential participants were excluded because they did not sign the informed consent form. Plausible explanations for not completing the consent form include the lack of treatment motivation in general, and lack of interest in participating in iCBT or the clinical trial. Next, another probable reason is that the informed consent type was another barrier to participation. Based on the medical ethics committee regulations, participants had to print, sign, and mail through regular

post their informed consent form to participate in the trial. It is very well possible that a digital informed consent would have increased participation. Nevertheless, despite our systematic efforts, we either could not reach participants who did not complete the informed consent forms, or they did not provide us with specific explanations. Thus, the actual reasons behind not completing the forms remain unknown.

Second, we could not examine students' educational achievement in terms of the number of European Credit Transfer System (ECTs) achieved during a given study period. This resulted from differences in the number of ECTs/study periods among the participating universities and misinterpretations of the related questions (e.g., some students reported the ECTs achieved throughout the study years instead of a given period). Thus, we excluded these data from our analysis as unreliable. In addition, the most reliable way to measure education achievement would be through academic records. However, access to such records was not permitted due to ethical restrictions. Third, despite our continuous effort to approach participants who dropped out, we could not reach 23% of them. Thus, our overview of dropout reasons is limited. Finally, we used only the Client Satisfaction Questionnaire for measuring intervention satisfaction. Employing qualitative measures (e.g., in-depth interviews) may be more informative regarding participant satisfaction with the several aspects of the iCBT program ranging from coaching to the content and the interface.

Overall, it is unclear why we did not identify evidence of difference between the intervention and the control group. In the present study, we have included participants through systematic screening for mental health problems during the college years. Previous literature has suggested that psychological interventions do not result in significant improvements in depression if patients are recruited through systematic screening (Cuijpers, van Straten, van Schaik, & Andersson, 2009). Possibly, patients who are identified through systematic screening do not actively seek treatment. Thus, they are not enough motivated to be engaged in the therapeutic process (Cuijpers et al., 2009). Such lack of motivation is even more challenging in the case of self-help interventions that rely solely on the motivational readiness of the users to adapt the intervention strategies in their everyday lives.

Further, our sample was mildly impaired, suggesting that the overall room for improvement was much smaller than other treatment studies. The mild symptomatology of our sample is more comparable to what we see in indicative prevention studies that usually include much larger numbers of participants to detect small effects. However, we should note that our study was not indicative prevention (e.g., 38% of our sample met criteria for current major depressive disorder at baseline). Nevertheless, there is a possibility that focusing on participants with mild symptomatology makes the trial more susceptible to floor effects. Next, many individuals with mild concerns may remit spontaneously and thus, they may not necessarily need to follow an intervention. Future trials should consider including participants with more severe symptomatology as recent meta-analytic evidence suggests that guided interventions result in larger effects in moderately severe and severe depression in the general population (Karyotaki et al., 2021). Another point of interest is that we strongly advised the participants in the control group to seek help in the community. Thus, although we cannot be certain, it is possible that some participants followed this advice and sought help for their symptoms. Thus, in our study TAU is probably more than what students would typically do under different circumstances. This is also evident from the small-moderate within group effects on depression and anxiety that we observed in both iCBT and TAU conditions. Finally, since we used a new intervention program, some components or other aspects may have been suboptimal. We should note that the present intervention was adapted from its original version to meet college student needs. Thus, we cannot rule out the possibility that during this process important elements of the intervention were omitted. Nevertheless, such omissions are very improbable given that the adapted intervention content were reviewed by a licensed psychologist with ample experience in CBT. Further, although we performed a series of focus group discussions before the adaption of the original intervention to the student sample, these focus groups were generic (e.g., discussing possible topics that the intervention should cover). If we were to re-do these focus groups, it would seem essential to ask end-users to closely evaluate all intervention sessions and give concrete feedback on what to alter. Given that lack of time was reported as a reason for dropout, it would seem important to evaluate whether reducing the text and adding more audiovisual components would minimize the time needed to complete the intervention.

To conclude, based on the present findings, the transdiagnostic and individually tailored iCBT does not appear to lead to moderate effects in college students with mild to moderate depression and/or anxiety symptoms. Future trials in this field should include a larger sample to detect possible small effects of the iCBT in the given target group. Moreover, future research is needed to test whether the effects of the intervention would be improved if it is administered to students who actively seek help. Finally, given that actively reaching out to students offers key advantages (e.g., early detection and treatment), we need to explore ways to improve the effects of iCBT when it is delivered to students who are not actively seek help.

## CRediT authorship contribution statement

**Eirini Karyotaki:** Conceptualization, Methodology, Formal analysis, Supervision, Project administration, Writing – review & editing. **Anke M. Klein:** Conceptualization, Supervision, Project administration, Writing – review & editing. **Marketa Ciharova:** Formal analysis, Project administration, Writing – review & editing. **Felix Bolinski:** Conceptualization, Methodology, Project administration, Writing – review & editing. **Lisa Krijnen:** Project administration, Writing – review & editing. **Lisa de Koning:** Project administration, Writing – review & editing. **Leonore de Wit:** Conceptualization, Methodology, Supervision, Project administration, Writing – review & editing. **Claudia M. van der Heijde:** Project administration, Writing – review & editing. **David D. Ebert:** Conceptualization, Writing – review & editing. **Heleen Riper:** Conceptualization, Methodology, Supervision, Funding acquisition, Writing – review & editing. **Neeltje Batelaan:** Conceptualization, Methodology, Supervision, Writing – review & editing. **Peter Vonk:** Project administration, Writing – review & editing. **Randy P. Auerbach:** Conceptualization, Writing – review & editing. **Ronald C. Kessler:** Conceptualization, Writing – review & editing. **Ronny Bruffaerts:** Conceptualization, Writing – review & editing. **Sascha Struijs:** Project administration, Writing – review & editing. **Reinout W. Wiers:** Conceptualization, Methodology, Supervision, Funding acquisition, Writing – review & editing. **Pim Cuijpers:** Conceptualization, Methodology, Supervision, Funding acquisition, Writing – review & editing.

## Declaration of competing interest

In the past years, Dr. Kessler received support for his epidemiological studies from Sanofi Aventis; was a consultant for Johnson & Johnson Wellness and Prevention, Sage Pharmaceuticals, Shire, Takeda; and served on an advisory board for the Johnson & Johnson Services Inc. Lake Nona Life Project. Kessler is a co-owner of DataStat, Inc., a market research firm that carries out healthcare research.

## Acknowledgments

This trial was funded by ZonMw, Research Program GGz, grant number 636110005. We thank all student representatives as well as the university stakeholders of the Vrije Universiteit (VU) of Amsterdam and the Universiteit van Amsterdam (UvA) for their great help during the development of our study. Moreover, we thank the e-coaches and research assistants who worked hard throughout this trial.

## Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.brat.2021.104028.

## References


van Agt, H. M., Essink-Bot, M.-L., Krabbe, P. F., & Bonsel, G. J. (1994). Test-retest reliability of health state valuations collected with the EuroQol questionnaire. *Social Science & Medicine, 39*, 1537–1544.

Andersson, G., & Titov, N. (2014). Advantages and limitations of Internet-based interventions for common mental disorders. *World Psychiatry, 13*, 4–11.

Andrews, G., Cuijpers, P., Craske, M. G., McEvoy, P., & Titov, N. (2010). Computer therapy for the anxiety and depressive disorders is effective, acceptable and practical health care: A meta-analysis. *PLoS One, 5*, Article e13196.

Arnett, J. J. (2000). Emerging adulthood: A theory of development from the late teens through the twenties. *American Psychologist, 55*, 469.

Attkisson, C. C., & Greenfield, T. K. (1996). *The client satisfaction questionnaire (CSQ) scales and the service satisfaction scale-30 (SSS-30). Outcomes assessment in clinical practice*.

Auerbach, R. P., Alonso, J., Axinn, W. G., Cuijpers, P., Ebert, D. D., Green, J. G., et al. (2016). Mental disorders among college students in the World Health Organization world mental health surveys. *Psychological Medicine, 46*, 2955–2970.

Auerbach, R. P., Mortier, P., Bruffaerts, R., Alonso, J., Benjet, C., Cuijpers, P., et al. (2018). WHO world mental health surveys international college student Project: Prevalence and distribution of mental disorders. *Journal of Abnormal Psychology, 127*, 623.

Auerbach, R. P., Mortier, P., Bruffaerts, R., Alonso, J., Benjet, C., Cuijpers, P., et al. (2019). Mental disorder comorbidity and suicidal thoughts and behaviors in the world health organization world mental health surveys international college student initiative. *International Journal of Methods in Psychiatric Research, 28*, Article e1752.

Baghurst, T., & Kelley, B. C. (2014). An examination of stress in college students over the course of a semester. *Health Promotion Practice, 15*, 438–447.

Bandelow, B., Reitt, M., Röver, C., Michaelis, S., Görlich, Y., & Wedekind, D. (2015). Efficacy of treatments for anxiety disorders: A meta-analysis. *International Clinical Psychopharmacology, 30*, 183–192.

Blanco, C., Okuda, M., Wright, C., Hasin, D. S., Grant, B. F., Liu, S.-M., et al. (2008). Mental health of college students and their non–college-attending peers: Results from the national epidemiologic study on alcohol and related conditions. *Archives of General Psychiatry, 65*, 1429–1437.

Bolinski, F., Boumparis, N., Kleiboer, A., Cuijpers, P., Ebert, D. D., & Riper, H. (2020). *The effect of e-mental health interventions on academic performance in university and college students: A meta-analysis of randomized controlled trials*, 100321, Internet Interventions.

Bolinski, F., Kleiboer, A., Karyotaki, E., Bosmans, J. E., Zarski, A.-C., Weisel, K. K., et al. (2018). Effectiveness of a transdiagnostic individually tailored internet-based and mobile-supported intervention for the indicated prevention of depression and anxiety (ICare prevent) in Dutch college students: Study protocol for a randomised controlled trial. *Trials, 19*, 1–13.

Boß, L., Lehr, D., Reis, D., Vis, C., Riper, H., Berking, M., et al. (2016). Reliability and validity of assessing user satisfaction with web-based health interventions. *Journal of Medical Internet Research, 18*, e234.

Bruffaerts, R., Mortier, P., Auerbach, R. P., Alonso, J., Hermosillo De la Torre, A. E., Cuijpers, P., et al. (2019). Lifetime and 12-month treatment for mental disorders and suicidal thoughts and behaviors among first year college students. *International Journal of Methods in Psychiatric Research, 28*, Article e1764.

Buchanan, J. L. (2012). Prevention of depression in the college student population: A review of the literature. *Archives of Psychiatric Nursing, 26*, 21–42.

Carl, E., Witcraft, S. M., Kauffman, B. Y., Gillespie, E. M., Becker, E. S., Cuijpers, P., et al. (2020). Psychological and pharmacological treatments for generalized anxiety disorder (GAD): A meta-analysis of randomized controlled trials. *Cognitive Behaviour Therapy, 49*, 1–21.

Craske, M. G. (2012). *Transdiagnostic treatment for anxiety and depression*. Depression and anxiety.

Cuijpers, P., Auerbach, R. P., Benjet, C., Bruffaerts, R., Ebert, D., Karyotaki, E., et al. (2019). The world health organization world mental health international college student initiative: An overview. *International Journal of Methods in Psychiatric Research, 28*, Article e1761.

Cuijpers, P., Cristea, I. A., Ebert, D. D., Koot, H. M., Auerbach, R. P., Bruffaerts, R., et al. (2016). Psychological treatment of depression in college students: A metaanalysis. *Depression and Anxiety, 33*, 400–414.

Cuijpers, P., Karyotaki, E., de Wit, L., & Ebert, D. D. (2020). The effects of fifteen evidence-supported therapies for adult depression: A meta-analytic review. *Psychotherapy Research, 30*, 279–293.

Cuijpers, P., Karyotaki, E., Reijnders, M., & Ebert, D. D. (2019). Is psychotherapy effective? Pretending everything is fine will not help the field forward. *Epidemiology and Psychiatric Sciences, 28*, 356–357.

Cuijpers, P., Kleiboer, A., Karyotaki, E., & Riper, H. (2017). Internet and mobile interventions for depression: Opportunities and challenges. *Depression and Anxiety, 34*, 596–602.

Cuijpers, P., Noma, H., Karyotaki, E., Vinkers, C. H., Cipriani, A., & Furukawa, T. A. (2020). A network meta-analysis of the effects of psychotherapies, pharmacotherapies and their combination in the treatment of adult depression. *World Psychiatry, 19*, 92–107.

Cuijpers, P., Turner, E. H., Koole, S. L., Van Dijke, A., & Smit, F. (2014). What is the threshold for a clinically relevant effect? The case of major depressive disorders. *Depression and Anxiety, 31*, 374–378.

Cuijpers, P., van Straten, A., van Schaik, A., & Andersson, G. (2009). Psychological treatment of depression in primary care: A meta-analysis. *British Journal of General Practice, 59*, e51–e60.

Cunningham, J. A., Kypri, K., & McCambridge, J. (2013). Exploratory randomized controlled trial evaluating the impact of a waiting list control design. *BMC Medical Research Methodology, 13*, 1–7.

Czyz, E. K., Horwitz, A. G., Eisenberg, D., Kramer, A., & King, C. A. (2013). Self-reported barriers to professional help seeking among college students at elevated risk for suicide. *Journal of American College Health, 61*, 398–406.

Davies, E. B., Morriss, R., & Glazebrook, C. (2014). Computer-delivered and web-based interventions to improve depression, anxiety, and psychological well-being of university students: A systematic review and meta-analysis. *Journal of Medical Internet Research, 16*, Article e130.

Day, V., McGrath, P. J., & Wojtowicz, M. (2013). Internet-based guided self-help for university students with anxiety, depression and stress: A randomized controlled clinical trial. *Behaviour Research and Therapy, 51*, 344–351.

Dear, B. F., Titov, N., Sunderland, M., McMillan, D., Anderson, T., Lorian, C., et al. (2011). Psychometric comparison of the generalized anxiety disorder scale-7 and the Penn State Worry Questionnaire for measuring response during treatment of generalised anxiety disorder. *Cognitive Behaviour Therapy, 40*, 216–227.

Ebert, D. D., Mortier, P., Kaehlke, F., Bruffaerts, R., Baumeister, H., Auerbach, R. P., et al. (2019). Barriers of mental health treatment utilization among first-year college students: First cross-national results from the WHO World Mental Health International College Student Initiative. *International Journal of Methods in Psychiatric Research, 28*, Article e1782.

Farrer, L., Christensen, H., Griffiths, K. M., & Mackinnon, A. (2011). Internet-based CBT for depression with and without telephone tracking in a national helpline: Randomised controlled trial. *PLoS One, 6*.

Furukawa, T., Noma, H., Caldwell, D., Honyashiki, M., Shinohara, K., Imai, H., et al. (2014). Waiting list may be a nocebo condition in psychotherapy trials: A contribution from network meta-analysis. *Acta Psychiatrica Scandinavica, 130*, 181–192.

Furukawa, T., Suganuma, A., Ostinelli, E., Andersson, G., Beevers, C., Shumake, J., et al. (2021). Dismantling, optimising, and personalising internet cognitive behavioural therapy for depression: A systematic review and component network meta-analysis using individual participant data. *The Lancet Psychiatry, 8*, 500–511.

Garber, J., & Weersing, V. R. (2010). Comorbidity of anxiety and depression in youth: Implications for treatment and prevention. *Clinical Psychology: Science and Practice, 17*, 293–306.

Gericke, F., Ebert, D. D., Breet, E., Auerbach, R. P., & Bantjes, J. (2021). *A qualitative study of university students' experience of Internet-based CBT for depression*. Counselling and Psychotherapy Research.

Group, T. E. (1990). EuroQol-a new facility for the measurement of health-related quality of life. *Health Policy, 16*, 199–208.

Harrer, M., Adam, S. H., Baumeister, H., Cuijpers, P., Karyotaki, E., Auerbach, R. P., et al. (2019). Internet interventions for mental health in university students: A systematic review and meta-analysis. *International Journal of Methods in Psychiatric Research, 28*, e1759.

Karyotaki, E., Cuijpers, P., Albor, Y., Alonso, J., Auerbach, R. P., Bantjes, J., et al. (2020). Sources of stress and their associations with mental disorders among college students: Results of the world health organization world mental health surveys international college student initiative. *Frontiers in Psychology, 11*, 1759.

Karyotaki, E., Ebert, D. D., Donkin, L., Riper, H., Twisk, J., Burger, S., et al. (2018). Do guided internet-based interventions result in clinically relevant changes for patients with depression? An individual participant data meta-analysis. *Clinical Psychology Review, 63*, 80–92.

Karyotaki, E., Efthimiou, O., Miguel, C., Bermpohl, F. M. G., Furukawa, T. A., Cuijpers, P., et al. (2021). Internet-based cognitive behavioral therapy for depression: A systematic review and individual patient data network meta-analysis. *JAMA Psychiatry, 78*(4), 361–371.

Karyotaki, E., Klein, A. M., Riper, H., De Wit, L., Krijnen, L., Bol, E., et al. (2019). Examining the effectiveness of a web-based intervention for symptoms of depression and anxiety in college students: Study protocol of a randomised controlled trial. *BMJ Open, 9*, Article e028739.

König, H.-H., Heider, D., Lehnert, T., Riedel-Heller, S. G., Angermeyer, M. C., Matschinger, H., et al. (2010). Health status of the advanced elderly in six European countries: Results from a representative survey using EQ-5D and SF-12. *Health and Quality of Life Outcomes, 8*, 1–11.

Kroenke, K., Spitzer, R. L., & Williams, J. B. (2001). The PHQ-9: Validity of a brief depression severity measure. *Journal of General Internal Medicine, 16*, 606–613.

Lecrubier, Y., Sheehan, D. V., Weiller, E., Amorim, P., Bonora, I., Sheehan, K. H., et al. (1997). The mini international neuropsychiatric interview (MINI). A short diagnostic structured interview: Reliability and validity according to the CIDI. *European Psychiatry, 12*, 224–231.

Matsushita, M., Adachi, H., Arakida, M., Namura, I., Takahashi, Y., Miyata, M., et al. (2011). Presenteeism in college students: Reliability and validity of the presenteeism scale for students. *Quality of Life Research, 20*, 439–446.

Mullin, A., Dear, B. F., Karin, E., Wootton, B. M., Staples, L. G., Johnston, L., et al. (2015). The UniWellbeing course: A randomised controlled trial of a transdiagnostic internet-delivered cognitive behavioural therapy (CBT) programme for university students with symptoms of anxiety and depression. *Internet Interventions, 2*, 128–136.

Păsărelu, C. R., Andersson, G., Bergman Nordgren, L., & Dobrean, A. (2017). Internet-delivered transdiagnostic and tailored cognitive behavioral therapy for anxiety and

depression: A systematic review and meta-analysis of randomized controlled trials. *Cognitive Behaviour Therapy, 46*, 1–28.
Pauley, D., Cuijpers, P., Papola, D., Miguel, C., & Karyotaki, E. (2021). Two decades of digital interventions for anxiety disorders: A systematic review and meta-analysis of treatment effectiveness. *Psychological Medicine*, 1–13.
Pedrelli, P., Nyer, M., Yeung, A., Zulauf, C., & Wilens, T. (2015). College students: Mental health problems and treatment considerations. *Academic Psychiatry, 39*, 503–511.
Rahmadiana, M., Karyotaki, E., Schulte, M., Ebert, D. D., Passchier, J., Cuijpers, P., et al. (2021). Transdiagnostic internet intervention for Indonesian university students with depression and anxiety: Evaluation of feasibility and acceptability. *JMIR Ment Health, 8*, Article e20036.
Reichert, E. (2012). Reducing stigma barriers to help-seeking behaviors among college students. *Psychology, 3*, 892.
Samoocha, D., Bruinvels, D. J., Elbers, N. A., Anema, J. R., & van der Beek, A. J. (2010). Effectiveness of web-based interventions on patient empowerment: A systematic review and meta-analysis. *Journal of Medical Internet Research, 12*, e23.
Sheehan, D. V., Lecrubier, Y., Sheehan, K. H., Amorim, P., Janavs, J., Weiller, E., et al. (1998). The mini-international neuropsychiatric interview (MINI): The development and validation of a structured diagnostic psychiatric interview for DSM-IV and ICD-10. *Journal of Clinical Psychiatry, 59*, 22–33.
Spitzer, R. L., Kroenke, K., Williams, J. B., & Löwe, B. (2006). A brief measure for assessing generalized anxiety disorder: The GAD-7. *Archives of Internal Medicine, 166*, 1092–1097.
Titov, N. (2011). Internet-delivered psychotherapy for depression in adults. *Current Opinion in Psychiatry, 24*, 18–23.
Van Ballegooijen, W., Cuijpers, P., Van Straten, A., Karyotaki, E., Andersson, G., Smit, J. H., et al. (2014). Adherence to internet-based and face-to-face cognitive behavioural therapy for depression: A meta-analysis. *PLoS One, 9*, Article e100674.
Weisel, K. K., Zarski, A.-C., Berger, T., Krieger, T., Moser, C. T., Schaub, M. P., et al. (2020). User experience and effects of an individually tailored transdiagnostic internet-based and mobile-supported intervention for anxiety disorders: Mixed-methods study. *Journal of Medical Internet Research, 22*, Article e16450.
Weisel, K. K., Zarski, A.-C., Berger, T., Krieger, T., Schaub, M. P., Moser, C. T., et al. (2019). Efficacy and cost-effectiveness of guided and unguided internet-and mobile-based indicated transdiagnostic prevention of depression and anxiety (ICare prevent): A three-armed randomized controlled trial in four European countries. *Internet Interventions, 16*, 52–64.
Weisel, K. K., Zarski, A.-C., Berger, T., Schaub, M. P., Krieger, T., Moser, C. T., et al. (2018). Transdiagnostic tailored internet-and mobile-based guided treatment for major depressive disorder and comorbid anxiety: Study protocol of a randomized controlled trial. *Frontiers in Psychiatry, 9*, 274.
Wilks, C. R., Auerbach, R. P., Alonso, J., Benjet, C., Bruffaerts, R., Cuijpers, P., et al. (2020). The importance of physical and mental health in explaining health-related academic role impairment among college students. *Journal of Psychiatric Research, 123*, 54–61.
Wittkampf, K. A., Naeije, L., Schene, A. H., Huyser, J., & van Weert, H. C. (2007). Diagnostic accuracy of the mood module of the patient health questionnaire: A systematic review. *General Hospital Psychiatry, 29*, 388–395.