Internetbasierte Interventionen

zur Reduktion von riskantem Alkoholkonsum und zur Bewältigung

von Depressionen

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Danksagung

Inhalt

Zusammenfassung

Gesundheitlich riskanter Alkoholkonsum und Depressionen führen in Deutschland und weltweit zu großen Lebenseinschränkungen und hohen ökonomischen Kosten. Obwohl es bewährte Präventionsmaßnahmen für alkoholbezogene Erkrankungen und evidenzgesicherte Behandlungsverfahren zur Bewältigung von Depressionen gibt, nimmt nur ein Bruchteil der Betroffenen Hilfe in Anspruch. Mit internetbasierten Gesundheitsinterventionen wird ein in Deutschland neuer Ansatz zur Prävention alkoholbezogener Erkrankungen vorgestellt und in einer drei-armigen randomisiert-kontrollierten Studie mit 428 Erwachsenen mit riskantem Alkoholkonsum erprobt (Studie I). Auf Grundlage der vorhandenen Evidenz für die Wirksamkeit internetbasierter Interventionen gegen depressive Beschwerden wird zudem ein Online-Training zur Bewältigung von Depressionen entwickelt und anhand von 131 Personen evaluiert (Studie II). Aufgrund des relativ neuen Interventionsansatzes beschränkten sich bisherige Evaluationsstudien weitgehend auf die klinische Wirksamkeit als Ergebnismaß. Mit zunehmender Evidenz spielen weitere Evaluationskriterien, wie die Nutzerzufriedenheit, eine wichtige Rolle für die Etablierung dieses Ansatzes. In der Vergangenheit mangelte es jedoch an validierten Messinstrumenten. Zu diesem Zweck wurde in einer dritten Studie (Studie III) die psychometrische Qualität eines Fragebogens zur Messung der Zufriedenheit mit internetbasierten Gesundheitstrainings anhand von zwei unabhängigen Stichproben im Umfang von 174 (Stichprobe 1) und 111 Personen (Stichprobe 2) untersucht.

In Studie I konnte gezeigt werden, dass das entwickelte Online-Training Clever weniger trinken nach sechs Wochen zu einem Rückgang des wöchentlichen Alkoholkonsums um durchschnittlich acht Standardgläser à 12 Gramm Reinalkohol und damit zu einer signifikant stärkeren Reduktion führte ($p < 0,001$) als die Wartebedingung, durch die lediglich eine Reduktion von durchschnittlich 3 Standardgläsern erreicht wurde. Selbst nach sechs Monaten konnte noch ein signifikanter Trainingseffekt nachgewiesen werden. Dabei zeigten sich keine Unterschiede zwischen Personen, die an einer Selbsthilfevariante des Trainings teilgenommen haben und denen, die zusätzlich von einem Online-Coach begleitet wurden. Darüber hinaus führte das Training zu Verbesserungen des allgemeinen und des arbeitsbezogenen Wohlbefindens.

In Studie II konnte gezeigt werden, dass sowohl das entwickelte Online-Training GET.ON Mood Enhancer als auch eine kurze Online-Psychoedukation zur Reduktion depressiver Beschwerden bei Personen mit Depression führte. Das Online-Training zeigte sich mit einem Effekt nach Cohen's d in Höhe von 0,36 ($p = 0,028$) der Psychoedukation zumindest kurzfristig signifikant überlegen. Die Ergebnisse weisen darauf hin, dass Personen ohne Psychotherapieerfahrung vom Online-Training, nicht aber von reiner Psychoedukation profitieren. Das Online-Training erwies sich zudem im Vergleich zur Psychoedukation als nebenwirkungsarm.

Die psychometrische Analyse des Fragebogens zur Zufriedenheit mit internetbasierten Gesundheitstrainings in Studie III bestätigte die Einfachstruktur des Fragebogens, die sich über zwei unabhängige Stichproben hinweg als messinvariant erwies. Die hohe Reliabilität des Fragebogens zeigte sich in McDonald's Omegas von 0,95 in Stichprobe 1 und 0,93 in Stichprobe 2. Die erwarteten mittleren Korrelationen zwischen der Zufriedenheit mit dem Training und den primären Zielkriterien der jeweiligen Trainings (die Reduktion der Depressivität in Stichprobe 1 und die Stressreduktion in Stichprobe 2) weisen auf die gute Validität des Fragebogens hin.

Mit dieser Arbeit konnte erstmals gezeigt werden, dass eine internetbasierte Intervention zur Reduktion des Alkoholkonsums, sowohl als Selbsthilfevariante als auch mit Begleitung durch einen Online-Coach, wirksam ist. Weiter belegt die Arbeit die kurzfristige Überlegenheit einer internetbasierten Intervention zur Bewältigung von Depressionen gegenüber Psychoedukation, die zudem nebenwirkungsarm ist. Mit dem Fragebogen zur Zufriedenheit mit internetbasierten Gesundheitstrainings liegt nun ein validiertes, ökonomisches Instrument zur Ergänzung klinischer Evaluationskriterien um die Nutzerperspektive vor.

Abstract

Risky alcohol consumption and depression lead to major life restrictions and high economic costs in Germany and worldwide. Although there are proven prevention measures for alcohol-related diseases and evidence-based treatments for coping with depression, only a fraction of those affected receive help. Internet-based health interventions are introduced as a new approach for the prevention of alcohol-related diseases in Germany and tested in a three-arm randomized-controlled trial with 428 adults who show risky alcohol consumption (study I). Based on existing evidence for the efficacy of Internet-based interventions against depressive disorders, an Internet-based intervention for coping with depression will also be developed and evaluated in a sample of 131 people (study II). Due to the relatively new intervention approach, previous evaluation studies were largely limited to clinical efficacy as a measure of results. With increasing evidence, further evaluation criteria, such as user satisfaction, become more important in establishing this approach. In the past, however, there has been a lack of validated measuring instruments. To this end, a third study (study III) examines the psychometric quality of a questionnaire to measure satisfaction with Internet-based health interventions using two independent samples of 174 (sample 1) and 111 persons (sample 2).

In Study I, it was shown that the Internet-based training "GET.ON Clever weniger trinken" (be smart – drink less) led to a reduction in weekly alcohol consumption of an average of eight standard glasses of 12 grams of pure alcohol each after six weeks. The training was superior to a waiting control ($P < 0.001$), which only led to a reduction of an average of three standard glasses. Even after six months, a significant training effect could still be proven. There were no differences between people who participated in a self-help version of the training and those who were additionally accompanied by an e-coach. In addition, the training led to significant improvements in general and work-related well-being.

Study II showed that both the Internet-based training "GET.ON Mood Enhancer" and a short online psychoeducation can reduce depressive symptoms in people with depression. With an effect of 0.36 according to Cohen's d, the online training was significantly superior to psychoeducation at least in the short term ($p = 0.028$). The results indicated that people without psychotherapy experience benefit from the Internet-based training but not from pure psychoeducation. In comparison to psychoeducation, the Internet-based training has also proven to have few side effects.

The psychometric analysis of the questionnaire on satisfaction with Internet-based health interventions in study III confirmed the simple structure of the questionnaire, which showed measurement invariance across two independent samples. The high reliability of the questionnaire was demonstrated in McDonald's Omegas of 0.95 in sample 1 and 0.93 in sample 2. The expected mean correlations between satisfaction with the training and the primary outcome of the respective training

(the reduction of depression in sample 1 and the stress reduction in sample 2) indicated the good validity of the questionnaire.

With this work it has been shown for the first time that an Internet-based intervention to reduce alcohol consumption, both as self-help and accompanied by an online coach, is effective. Furthermore, this work demonstrates the short-term superiority of an Internet-based intervention for coping with depression over psychoeducation, which is also low in side effects. With the questionnaire on satisfaction with Internet-based health trainings, a validated, economic instrument to supplement clinical evaluation criteria with the user perspective is now available.

Kapitel 1 – Allgemeiner Hintergrund

Epidemiologie alkoholbezogener und depressiver Störungen

Psychische und subtanzbezogene Störungen werden für 7,4 % aller weltweiten Gesundheitsbeeinträchtigungen in Form von disability adjusted life years (DALYs) verantwortlich gemacht [1]. Unter den Störungen gilt die Alkoholabhängigkeit als die Erkrankung, die mit ca. 44 % für den größten Anteil vorzeitiger Mortalität verantwortlich ist. In Deutschland liegt die 12-Monatsprävalenz für die Alkoholabhängigkeit und den -missbrauch bei ca. 6,5 % [2]. Diese Prävalenzrate spiegelt jedoch nur einen Teil des Problems wider, da auch ein Alkoholkonsum unterhalb der diagnostischen Abhängigkeits- oder Missbrauchsschwelle mit erheblichen gesundheitlichen Risiken und gesundheitsökonomischen Folgen verbunden ist. Als riskanter Alkoholkonsum gilt die Menge konsumierten Alkohols, mit der das Risiko für alkoholbedingte Folgeschäden als sehr wahrscheinlich angenommen wird [3]. Laut der aktuellen S3-Leitlinie zu alkoholbezogenen Störungen [4] gilt als riskanter Alkoholkonsum bei Erwachsenen ohne körperliche Erkrankungen in Deutschland der tägliche Konsum von mehr als 24 g Reinalkohol für Männer und von mehr als 12 g für Frauen. Bevölkerungsrepräsentativen Studien zufolge weisen zwischen 14,2 % [2] und 21,4 % [5] aller Erwachsenen in Deutschland ein riskantes Konsummuster auf. Selbst geringer bis moderater Alkoholkonsum (bis zu zwei alkoholische Getränke pro Tag) geht mit einer erhöhten Wahrscheinlichkeit für verschiedene Krebserkrankungen einher [6]. Der globale Alkoholkonsum zählt zu einem der größten vermeidbaren Gesundheitsrisiken, der zudem mit erheblichen Gesundheitskosten verbunden ist [7]. Gesundheitskosten entstehen dabei nicht primär durch direkte Versorgungsangebote (z. B. durch Behandlungskosten für den Alkoholentzug und die Entwöhnungstherapie), sondern vor allem indirekt (z. B. aufgrund von Produktivitätsverlusten durch Arbeitsausfälle, Arbeitsunfälle oder eingeschränkte Leistungsfähigkeit) [1].

In der Allgemeinbevölkerung treten zudem häufig Wechselwirkungen zwischen alkoholbezogenen Störungen und psychischen Erkrankungen, vor allem Depressionen, auf [8–10]. So können sich in der Folge einer Abhängigkeitserkrankung depressive Symptome entwickeln oder sich im Zuge einer Depression alkoholbezogene Probleme manifestieren oder es entstehen Symptome beider Störungsbereiche nebeneinander [11]. Statistisch gesehen erfüllen in Deutschland 6 % der Erwachsenen die diagnostischen Kriterien einer akuten depressiven Episode (12-Monatsprävalenz). Schätzungsweise 12% der Erwachsenen in Deutschland durchleben wenigstens einmal in ihrem Leben eine depressive Episode [12]. Depressionen stellen damit ein erhebliches Krankheitsleiden da, das auch die physische Gesundheit beeinträchtigt sowie soziale und ökonomische Folgen nach sich zieht [13].

Prognosen zufolge werden im Jahr 2030 Depressionen und Alkoholabhängigkeiten neben Herzinfarkten und Alzheimer in hochindustriellen Ländern zu den vier Erkrankungen mit der höchsten Lebenseinschränkung zählen [14].

Aufbau der Dissertation

Die vorliegende Dissertation widmet sich den Fragen, ob und wie der Einsatz von E-Mental-Health-Interventionen zur Lösung der eingangs skizzierten Problembereichen, riskanter Alkoholkonsum und Depressionen, beitragen kann.

In Kapitel 2 wird die aktuelle Problemlage bei der Prävention und Versorgung von Menschen mit riskantem Alkoholkonsum dargelegt. Es folgt die Einführung von internetbasierten Gesundheitsinterventionen als innovativer Ansatz zur Ergänzung der bestehenden Interventionsangebote in diesem Bereich. Als konkreter Lösungsansatz wird die Entwicklung und Evaluation eines internetbasierten Trainings zur Alkoholkonsumreduktion bei Erwachsenen anhand von zwei Manuskripten (Studienprotokoll sowie Wirksamkeitsstudie) vorgestellt, die im Rahmen dieser Arbeit veröffentlicht wurden.

In Kapitel 3 wird mit der aktuellen Versorgungslage für Menschen mit Depression ein weiterer Gesundheitsbereich beschrieben, in dem das große Potenzial von E-Mental-Health-Interventionen bereits nachgewiesen werden konnte. Der aktuelle Forschungsbedarf in diesem Forschungsfeld wird aus vorhandenen Erkenntnissen zur Wirksamkeit internetbasierter Interventionen zur Reduktion depressiver Beschwerden abgeleitet. Schließlich wird die Entwicklung eines internetbasierten Trainings zur Bewältigung von Depressionen und dessen Evaluation in Bezug auf die inkrementelle Wirksamkeit gegenüber anderen Interventionsvarianten und in Bezug auf mögliche Nebenwirkungen beschrieben. Auch hierfür wurden zwei Manuskripte, ein Studienprotokoll sowie eine Wirksamkeitsstudie veröffentlicht.

In Kapitel 4 wird erläutert, warum die bisherige Fokussierung auf klinische Wirksamkeitsindikatoren bei der Evaluation von internetbasierten Gesundheitsinterventionen zunehmend um andere Evaluationskriterien wie die Nutzerzufriedenheit erweitert werden sollte. Da es bislang an Messinstrumenten für solche nicht-klinischen Indikatoren fehlt, wird in dem Kapitel die Adaptation und Evaluation eines Online-Fragebogens zur Messung der Zufriedenheit mit internetbasierten Gesundheitstrainings beschrieben. Auch hierzu wurde ein Manuskript veröffentlicht.

In den Kapiteln 5 und 6 werden die Erkenntnisse aus den vorherigen Kapiteln zusammengefasst und vor dem Hintergrund des aktuellen Forschungsstandes reflektiert. Das Kapitel wird mit einem Ausblick auf zukünftige Fragestellungen, die sich aus dieser Arbeit ergeben, abgeschlossen.

Kapitel 2 – E-Mental-Health zur Alkoholreduktion

Versorgungssituation für Menschen mit riskantem Alkoholkonsum

Für Personen mit einer Alkoholabhängigkeitserkrankung existiert in Deutschland eine Vielzahl unterschiedlicher Hilfsangebote. Dazu zählen etwa die hausärztliche Behandlung, die ambulante Suchtberatung, die stationäre Entgiftung und Entwöhnungsbehandlung, ambulante Psychotherapie sowie Selbsthilfegruppen [15]. Jedoch wird mit diesen Maßnahmen nur ein Bruchteil der Betroffenen erreicht [16]. Gerade für Konsumenten unterhalb der diagnostischen Schwelle fehlen leicht zugängliche Angebote zur frühzeitigen Prävention alkoholbezogener Störungen. Laut aktueller S3-Leitlinie zur Behandlung alkoholbezogener Probleme sind bei riskantem Konsummuster insbesondere „Kurzinterventionen ein Weg, Menschen mit problematischem Alkoholkonsum in nicht-spezialisierten Settings zu einer Trinkmengenreduktion oder ggf. zur Abstinenz zu motivieren." [4]. Kurzinterventionen werden dabei als Interventionen verstanden, die (ohne Festlegung einer Untergrenze) eine Dauer von 60 Minuten und maximal fünf Sitzungen nicht überschreiten. Sie zielen auf eine Verringerung des Alkoholkonsums und alkoholassoziierter Probleme ab und integrieren verschiedene Behandlungsbausteine. Zu den wichtigsten Bausteinen zählt das personalisierte normative Feedback (PNF) zum eigenen Alkoholkonsum, in dem der individuelle Alkoholkonsum mit den gesundheitlichen Normen oder dem Konsum der jeweiligen Peer-Group in Beziehung gesetzt wird. Weitere Bausteine sind die Förderung der Änderungsbereitschaft, die individuelle Zielfindung sowie konkrete Ratschläge zur Zielerreichung. Laut Leitlinie können solche Kurzinterventionen durch schriftliches Informationsmaterial ergänzt oder auch computergestützt dargeboten werden.

Konkrete Angebote solcher Kurzinterventionen sind jedoch rar. Unter Nutzung von Kurzscreenings wie dem CAGE-Fragebogen oder dem AUDIT-C [17,18], verschiedenen Beratungsleitfäden oder der Empfehlung zum Führen eines Trinktagebuchs können beispielsweise im Rahmen der hausärztlichen Versorgung erste Formen von Kurzinterventionen eingeleitet werden [19,20]. Die oft unzureichende Qualifikation der Hausärzte oder schlicht das fehlende Wissen um solche Interventionen schränken die Versorgung in diesem Bereich ein [21]. Ein alternatives Angebot besteht in der Integration von alkoholbezogenen Kurzinterventionen in die Therapie von anderen primären Beschwerden, z. B. im Rahmen einer Depressionsbehandlung [3]. In so einem Setting beschränkt sich die Alkoholintervention i. d. R. auf grundlegende Informationen und Empfehlungen zu Trinkmengen und zur Abstinenz für Hochrisikogruppen (z. B. bei Vorliegen organischer Erkrankungen oder während der Schwangerschaft).

Neben der geschilderten Versorgungslücke bei riskantem Alkoholkonsum ist ein weiteres Problem in der mangelnden Inanspruchnahme verfügbarer Hilfsangebote zu sehen [15,22,23]. Studienergebnisse deuten auf verschiedene Gründe für die geringe Rate der Inanspruchnahme hin: So scheint vielen Betroffenen schlicht das Wissen um die Gefahren ihres gesundheitsgefährdenden Verhaltens zu fehlen

[15]. Andere Untersuchungen weisen darauf hin, dass viele Betroffene über eine stark ausgeprägte Selbsthilfetendenz verfügen, die sie womöglich von der Suche nach externer Unterstützung abhält [24]. Untersuchungen im betrieblichen Kontext weisen zudem auf die verbreitete Angst vor Stigmatisierung hin, die Personen ebenfalls an der Suche nach Unterstützung hindert [25,26]. Schließlich stellt das mangelnde Wissen um verfügbare Unterstützungsangebote eine Barriere zu ihrer Inanspruchnahme dar [24].

Ergänzung des Präventions- und Versorgungsangebots durch E-Mental-Health

Angesichts der geschilderten Situation stellen internetbasierte Gesundheitsinterventionen eine vielversprechende Ergänzung von bestehenden Angeboten zur Prävention von alkoholbezogenen Störungen dar, da sie orts- und zeitunabhängig nutzbar sind und sich mit wenig Aufwand auf die individuellen Erfordernisse Einzelner zuschneiden lassen. Internetbasierte Interventionen basieren in der Regel auf etablierten evidenzgesicherten Konzepten der kognitiven Verhaltenstherapie. Die Interventionen gliedern sich typischerweise in mehrere, meistens 5 bis 10, Trainingseinheiten, die in einem wöchentlichen Rhythmus absolviert werden. Sie können entweder als reine Selbsthilfeinterventionen (im Englischen: unguided interventions) oder zusätzlich mit persönlicher Unterstützung durch einen Online-Coach (guided interventions), meistens PsychologInnen oder PsychotherapeutInnen, durchgeführt werden. Das allgemeine Ziel der persönlichen Unterstützung besteht im Allgemeinen darin, die an der Intervention teilnehmende Person dabei zu unterstützen, das beabsichtigte Interventionsergebnis zu erreichen [27]. Die persönliche Unterstützung kann je nach Intervention in der Intensität, in der Dauer und dem inhaltlichen Fokus variieren. Inzwischen liegt eine Reihe metaanalytischer Ergebnisse vor, die die Wirksamkeit internetbasierter Interventionen im Vergleich zu Wartekontrollgruppen bei Depressionen [28], Angststörungen [29], Stress [30], und Schlafproblemen [31] belegen. Wenngleich auch Wirksamkeitshinweise zur Reduktion des Alkoholkonsums vorliegen [32,33], wurden in Deutschland bislang kaum internetbasierte Ansätze zur Konsumreduktion untersucht.

Entwicklung und Evaluation von Clever weniger trinken

Wie im ersten Abschnitt beschrieben fehlen in Deutschland vor allem niedrigschwellige Angebote zur frühzeitigen Intervention bei riskantem Alkoholkonsum. Internetbasierte Alkoholinterventionen könnten eine wertvolle Ergänzung des Präventionsangebots darstellen, um die Lücke zwischen primärpräventiven Aufklärungskampagnen (z. B. kenn-dein-limit.de) und der Versorgung alkoholbezogener Erkrankungen (z. B. Suchtberatung, stationärer Entzug und Entwöhnung) zu schließen. Aus den Erkenntnissen zur Inanspruchnahme ambulanter und stationärer Angebote des Suchthilfesystems zeigte sich in der Vergangenheit, dass Frauen hier unterrepräsentiert sind [16]. Das gilt auch dann, wenn die unterschiedlich hohen Prävalenzraten alkoholbezogener Störungen bei Männern (ca. 4,8 % für Alkoholabhängigkeit) und Frauen (ca. 2,0 % für Alkoholabhängigkeit) berücksichtigt werden [2]. Demgegenüber zeigen Erkenntnisse aus der E-Mental-Health-Forschung, dass sich hauptsächlich Frauen von diesen relativ neuen Ansätzen angesprochen fühlen. Insofern könnten internetbasierte Alkoholinterventionen ein geeignetes Mittel sein, um auch vermehrt Frauen anzusprechen.

Zur Wirksamkeit deutschsprachiger Alkoholinterventionen liegen bislang kaum Wirksamkeitsnachweise vor (Beispiel: „Alkohol - Alles im grünen Bereich?!" [34]). Ungeklärt ist zudem, welchen Nutzen die persönliche Unterstützung in Form eines begleitenden Online-Coaching für die Wirksamkeit von Alkoholinterventionen bietet [35]. Hierzu liegen bislang auch international kaum Erkenntnisse vor, da die meisten Alkoholinterventionen in der Vergangenheit als Selbsthilfeinterventionen konzipiert und untersucht worden sind [33,36]. Eine bessere Evidenz in diesem Bereich ist nicht zuletzt aus kostenökonomischer Perspektive von Bedeutung, da die Implementierung begleiteter Interventionen höhere Kosten erwarten lässt als die von reinen Selbsthilfeinterventionen. Ausgehend von dem zuvor geschilderten Forschungsstand werden in der vorliegenden Arbeit die nachfolgenden Fragestellungen bearbeitet:

Fragestellung 1: Wie lässt sich ein niedrigschwelliges Online-Training zur Reduktion des Alkoholkonsums unter Nutzung zeitgemäßer IT-Technologie entwickeln und in einer randomisiert-kontrollierten Studie evaluieren?

Das Ziel war die Entwicklung eines internetbasierten Trainingskonzepts für Erwachsene mit einem riskanten Alkoholkonsum. Das entwickelte Training Clever weniger trinken (CWT) wurde so konzipiert, dass es sowohl in Begleitung durch einen persönlichen Online-Coach als auch in Form reiner Selbsthilfe dargeboten werden kann. Des Weiteren wurde ein Studiendesign entwickelt, um die Wirksamkeit beider Darbietungsformen des Trainings im Vergleich zu einer Warte-Kontroll-Bedingung zu untersuchen und in Form eines Studienprotokolls veröffentlicht.

Fragestellung 2: Kann ein Online-Alkoholreduktionstraining den wöchentlichen Alkoholkonsum bei Erwachsenen im Vergleich mit der Routineversorgung signifikant stärker reduzieren?

Auf Basis des Studienprotokolls wurde eine dreiarmige randomisiert-kontrollierte Studie (Studie I) durchgeführt, um die Wirksamkeit von Clever weniger trinken bei Erwerbstätigen zu untersuchen, die ein riskantes Konsummuster (wöchentlicher Konsum von mehr als 21 Standardgläsern bei Männern bzw. mehr als 14 bei Frauen sowie ein AUDIT-Wert von über 8 bzw. über 6) aufwiesen. Gruppe 1 erhielt Zugang zum Training mit begleitetem Online-Coaching, Gruppe 2 erhielt Zugang zum Training ohne zusätzliches Online-Coaching und Gruppe 3 fungierte als Warte-Kontrollgruppe, die erst zu einem späteren Zeitpunkt Zugang zum Training erhielt. Primäres Zielkriterium der Wirksamkeitsanalyse war die Reduktion des wöchentlichen Alkoholkonsums sechs Wochen nach Trainingsbeginn im Vergleich zur Kontrollgruppe. Sekundäre Zielkriterien waren die Reduktion des Alkoholkonsums nach einem halben Jahr sowie weitere alkoholkonsumbezogene Parameter und die Reduktion psychosomatischer Beschwerden wie Depressivität und Stress. Es wurde angenommen, dass das Training sowohl mit als auch ohne ein zusätzliches Online-Coaching zu einer signifikant stärkeren Reduktion des wöchentlichen Alkoholkonsums führt als die Kontrollbedingung.

Die Bearbeitung der zuvor genannten Fragestellungen wurde in zwei wissenschaftlichen Manuskripten veröffentlicht, die im nächsten Kapitel einsehbar sind. Das Studienprotokoll mit dem Titel „Evaluating the (cost-)effectiveness of guided and unguided Internet-based self-help for problematic alcohol use in employees - a three arm randomized controlled trial" beschreibt die Entwicklung der Intervention Clever weniger trinken und das Untersuchungsdesign, mit dem die Wirksamkeit der Intervention untersucht werden sollte. Im Manuskript mit dem Titel „Efficacy of a web-based intervention with and without guidance for employees with risky drinking: results of a three-arm randomized controlled trial" werden die Evaluationsergebnisse der Intervention ausführlich beschrieben.

Manuskript 1 – Studienprotokoll Clever weniger trinken

Boß L, Lehr, D, Berking M, Riper H, Schaub M, Ebert DD. Evaluating the (cost-)effectiveness of guided and unguided Internet-based self-help for problematic alcohol use in employees - a three arm randomized controlled trial. *BMC Public Health. 2015*;15(1):1043. DOI:10.1186/s12889-015-2375-0.

Abstract

Background: Problematic alcohol consumption is associated with a high disease burden for affected individuals and has a detrimental impact on companies and society due to direct and indirect health costs. This protocol describes a study design to evaluate the (cost)-effectiveness of a guided and unguided Internet-based self-help intervention for employees called "GET.ON Clever weniger trinken" (be smart – drink less) compared to a waiting list control group.

Methods: In a three-arm randomized controlled trial, 528 German adults who are currently members of the workforce will be recruited by occupational health departments of major health insurance companies. Employees aged 18 and older displaying problematic drinking patterns (> 21/14 drinks per week and an AUDIT score > 8/6 for men/women) will be randomly assigned to one of three following study conditions: 1. unguided web-based self-help for problematic drinking, 2. adherence-focused guided self-help, and 3. waiting list control. Self-report data will be collected at baseline (T1), 6 weeks (T2), and 6 months (T3) after randomization. The primary outcome will be the reduction of alcohol standard units during the 7 days prior to T2, using the Timeline Followback method. Cost-effectiveness analyses to determine direct and indirect costs will be conducted from the perspectives of employers and the society. Data will be analyzed on an intention-to-treat basis and per protocol.

Discussion: There is a need to identify effective low-threshold solutions to improve ill-health and reduce the negative economic consequences due to problematic alcohol drinking in workforces. If the proposed web-based intervention proves both to be efficacious and cost-effective, it may be a useful tool to increase utilization rates of interventions for problematic drinking in occupational settings.

Trial Registration: German Register of Clinical Studies (DRKS): DRKS00006105, date of registration: 2014-07-07.

Keywords: Internet intervention, alcohol, work-related stress, occupational health, cost-effectiveness, self-help, problematic alcohol use, alcohol use disorders, randomized controlled trial

Theoretical Background

Problematic alcohol use - a global health problem

Problematic alcohol consumption is associated with a high burden of disease [1, 2]. Alcohol use disorders (AUDs) are projected to become the fourth leading cause of disability in high-income countries by 2030 [3]. The 12-month prevalence for alcohol dependence in the U.S. population is estimated to be 7% [4] and in the German population 3.4% [5]. AUDs are also linked to mental health problem domains, such as mood and anxiety disorders [6], work stress [7] and are associated with an increased risk for premature mortality [8].

However, the proportion of people with problematic drinking patterns that exceed the low-risk threshold but do not result in an AUD is even higher and might be more suitable to illustrate the actual dimension of the health problem [9]. Prevalence rates of such patterns vary considerably because there is no consensus when problematic drinking begins [10, 11]. For example, in 2013, 24.6% of the U.S. population reported binge drinking, i.e., having five or more drinks in one occasion within the last month [4]. In the German population, 14.2% of men and women drink more than 24 and 12 grams of alcohol per day, respectively [5], and 33.6% engage in hazardous drinking as defined by the short form Alcohol Use Disorders Identification Test [12].

In the present study, problematic drinking is alcohol consumption that is likely to lead to physical or psychosocial harm and will be defined based on the recommendations of the World Health Organization [13]. According to this, people engaging in problematic drinking consume more than 14 (women) or 21 (men) standard units of alcohol per week. Problematic alcohol consumption is associated with considerable costs due to impaired productivity and absence from work [14, 15]. Total alcohol-attributable costs per person range between $358 and $837 in high-income countries [2]. Indirect costs such as those due to productivity losses have shown to be the predominant cost-category with an average 72.1% of all alcohol-attributable costs in high-income countries [2].

There are good reasons for offering services that help to reduce alcohol consumption in occupational settings. Workplaces offer a high potential for delivering alcohol prevention by reaching a high proportion of the target group [16, 17]. As there are correlations between alcohol drinking, absence from work, and related costs [18], occupational prevention programs may help to reduce impaired productivity due to, for example, alcohol-related absenteeism and presenteeism [19]. Moreover, Siegrist and Roedel [20] found evidence from prospective studies that work-related stress is a risk factor for problematic alcohol consumption. Based on a social learning paradigm, people may use alcohol as an alternative mechanism to cope with stressful situations (e.g. work stress) [21]. Such situations may include difficulties to relax from work or to cope with negative emotions. According to social environment models, peer pressure and the omnipresent availability of alcohol may add to the risk of increase drinking in those situations. Reducing these risk factors by providing exercises of emotional coping as a major part of the intervention might be beneficial.

Existing treatments at the workplace

Different approaches have been tested in occupational settings, for example, education programs, personal counseling, individual feedback, brief mail-out interventions, and management training [22]. However, effects of these interventions are mixed, and many studies lack sufficient methodological quality [22, 23]. Traditional occupational interventions are typically offered in large businesses that have an employee assistance program or other health-promoting plans. Thus, especially people in smaller businesses are less likely to have access to these kinds of prevention programs [16]. Another barrier for implementing health interventions at the workplace may be low participation rates [23]. Reasons for these low rates include a preference for self-helping attempts [24] and a fear of stigmatization [25, 26].

Potential of web-based interventions

Using the Internet to provide brief self-help interventions may help to overcome some of the barriers for implementing traditional occupational health programs. People can access the intervention at any time and at any place without disclosing their identity [16]. Other advantages include the fact that participants can work at their own pace and review materials as often as they want. In addition, such interventions possibly reach affected people earlier than traditional health services, thereby preventing the onset of more severe health problems [27].

Efficacy of web-based interventions for problematic alcohol use

In recent years, studies on web-based interventions for alcohol reduction have been on the rise [28, 29]. Meta-analyses have revealed effect sizes of these kinds of interventions for reducing weekly alcohol units ranging from $g = 0.2$ [28] to $d = 0.4$ [29].

Web-based occupational health interventions for problematic alcohol use

There have only been a few studies on web-based alcohol interventions in occupational settings. For example, employees from an U.S. technology company participated in a web-based health promotion program designed for universal prevention of depression, anxiety, and problematic substance use [30]. This study showed that employees participating in this program were slightly more willing to change their drinking behavior compared to those in the control group. However, data of the total amount of drinking was not reported. Doumas and Hannah [31] tested a brief website that provides personalized normative feedback (PNF) on drinking to young employees in the 18-24-year age group. The study group found small effects on reductions of weekend drinking ($d = 0.3$), peak consumption ($d = 0.3$), and intoxication ($d = 0.2$) compared to a control group. Pemberton and his co-authors [32] tested a brief web-based intervention for high-risk drinkers and a web-based universal prevention program including PNF, motivational interviewing elements, and skills for behavioral change in military personnel. They found small effects for the intervention for high-risk drinkers on average drinks per

drinking occasion, frequent heavy episodic drinking status, and estimated peak blood alcohol concentration (all about d = 0.1 compared to a control group). In contrast, the effects of the prevention program were not significant. In a more recent study, Khadjesari and colleagues [33] analyzed the effects of an online screening and PNF in a workforce in the UK, but did not find improvements with regard to drinking behavior. In the long term, after 6 months, none of these interventions showed significant effects.

However, all described interventions were tested in very specific populations, for example, military personnel [32], adolescents [31], individual companies [33], thus, it is questionable, if findings can be generalized to other workforce populations. Moreover, to the best of our knowledge, none of these studies included an economic evaluation. All of the interventions mentioned above are based on a self-help paradigm. However, unguided web-based interventions, that means those without any human support (i.e., pure self-help), have been found to be less effective than guided interventions for depression and social phobia [34]. With regard to interventions for problematic alcohol consumption, the picture is less clear. In a recent meta-analysis, Riper and her co-authors [28] did not find differences in terms of efficacy between guided and unguided interventions across different studies, but the number of trials with guidance was very small (n=5). Thus, there is a need to explore the (cost-)effectiveness of web-based interventions for reducing problematic alcohol consumption with and without guidance in the same study.

Aims of the study

The scope of this study is to evaluate the (cost-)effectiveness of a newly developed web-based cognitive-behavioral self-help intervention called GET.ON Clever weniger trinken (CWT) for employees with problematic alcohol consumption. The study has the following aims: 1) to assess the effectiveness of self-help CWT for reducing alcohol consumption compared to a control group, 2) to assess the effectiveness of CWT with adherence-focused guidance compared to a control group, 3) to assess the incremental cost-effectiveness ratio (ICER), that is the ratio between costs and clinical outcome, of guided and unguided CWT compared to a control group. We expect both intervention groups to be superior compared to the control group in terms of alcohol consumption reduction from baseline to the post-assessment. We hypothesize guided and unguided self-help CWT both to be more cost-effective compared to the control group at the 6-month follow-up assessment. As a secondary aim we explore the differences of additional professional support, i.e., adherence-focused guidance [35].

Methods

Study Design

A three-arm randomized controlled trial (RCT) will be conducted to evaluate the web-based intervention CWT with and without guidance compared to a waiting list control group (WLC). Assessments will take place before the allocation to the study conditions (T1), 6 weeks (T2), and 6 months (T3) after the allocation (Figure 1). All procedures involved in the study will be consistent with the generally accepted standards of ethical practice approved by the University of Lueneburg (Germany) ethics committee (No. Boss201404_OT). The trial is registered in the German clinical trials register DRKS00006105.

Participants & Procedure

Inclusion and exclusion criteria

We include (a) working people, (b) who are above the age of 18, (c) who report drinking of at least 14/21 (women/men) standard units per week, (d) who have a score of at least 6/8 for women/men on the Alcohol Use Disorders Identification Test (AUDIT) [36], (e) who have Internet access, (f) who have sufficient German language reading and writing skills (self-reported), and (g) who are willing to give informed consent. We exclude subjects (a) who indicate that they have been diagnosed with psychosis or a drug dependency in the past, (b) who show a notable suicidal risk as indicated by a score greater than 1 on BDI [37] Item 9 ("I feel I would be better off dead"), (c) who have received medication or have begun psychotherapy to treat their problematic alcohol consumption, and (d) who are participating in another study on online-health training of our study group at the same time.

Recruitment

Participants will be recruited nationwide from the German-speaking population. The recruitment process is scheduled from autumn 2014 to autumn 2015 and will be conducted by several health insurance companies (BARMER GEK, KKH, BKK). The insurance companies advertise the study in their member-journals that will be sent to all of their insurants and they promote the study participation on their websites. Nevertheless, participation is not limited to the insurants of these companies and is not restricted to specific industrial sectors or occupational groups. An open access website (http://www.geton-training.de/alkohol) provides information on the intervention and study conditions. Potential participants sign up by providing an email address and name or pseudonym on the website.

Assessment of eligibility and randomization

The trial will be open to all people who meet criteria listed above. After registering, applicants receive an email with detailed information about the study procedures. Then, they will be informed that they can withdraw from the intervention and/or study at any time without any negative consequences. Applicants who continue to participate in the study will be asked to complete an online screening questionnaire. They must fulfill all criteria of inclusion and none of the exclusion criteria, have to complete the baseline assessment (T1), and return the informed consent form to participate in the study.

Eligible applicants will be randomly allocated in a 1/1/1 ratio to one of the three trial arms: adherence-focused guided CWT, unguided CWT, or WLC. Randomization will take place at an individual level. The allocation will be performed by an independent researcher not otherwise involved in the study, using an automated computer-based random integer generator (randomisation.eu). During the randomization process, allocation will be concealed from participants, researchers involved in recruitment, and eCoaches. After being informed about the outcome of the randomization, participants in the two intervention groups will receive immediate access to the training. All data is collected using a secure web-based assessment system (AES, 256-bit encrypted).

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┌─────────────────────────┐
│       Enrollment        │
└─────────────────────────┘

┌─────────────────────────┐
│ Assessment for eligibility │
└─────────────────────────┘
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Inclusion:
- Currently employed
- Age >18
- Past week drinking of at least 14/21 standard units for w/m
- AUDIT-score of at least 6/8 for w/m
- Internet access
- Sufficient German language skills in reading and writing
- Given informed consent

Exclusion:
- Diagnosed with drug dependency or psychosis
- BDI-II suicide item > 1
- Currently in psychotherapy due to alcohol consumption
- Currently receiving medication to inhibit alcohol consumption
- Participating in another web-based health intervention of the study group

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┌─────────────────────────┐
│     Assessment T1       │
└─────────────────────────┘

┌─────────────────────────┐
│     Randomization       │
└─────────────────────────┘

┌─────────────────────────┐
│       Allocation        │
└─────────────────────────┘
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| Unguided intervention group (n=176) | Adherence-focused guided group (n=176) | Waiting list control group (n=176) |

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┌─────────────────────────┐
│        Follow-Up        │
└─────────────────────────┘
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| Assessment T2 6 weeks after randomization | Assessment T2 6 weeks after randomization | Assessment T2 6 weeks after randomization |

| Assessment T3 6 months after randomization | Assessment T3 6 months after randomization | Assessment T3 6 months after randomization |

Fig. 1. Study Flow

Intervention

The web-based intervention CWT comprises five modules (Table 1). Each includes general information, illustrative examples, interactive exercises, quizzes, audio and video files, and downloadable work sheets (Figures 2-4). The intervention combines different examples of good clinical practice in alcohol treatment [38], tools to control drinking behavior [39], and an emotion regulation training [40]. The combination of these elements is meant to initiate and promote the

processes of change that allow participants to move from one stage of behavioral change to another, as defined by the Transtheoretical Model of Health Behavior Change [41].

Table 1 Content of the web-based training GET.ON CWT

Module	Intervention content
1	Psychoeducation Personalized normative feedback Motivational interviewing
2	Planning of behavioral change
3	Maintenance of behavioral change Emotion regulation Behavioral activation
4	Maintenance of behavioral change Emotion regulation
5	Planning for the future

Participants are advised to complete each module within one week. The Module 1 includes three major sections: section a) provides an overview of the training content, an explanatory model of conditions that may lead to increased consumption of alcohol (e.g. the wish to relax after work or some kind of peer pressure), and an explanation of alcohol standard units and why this measure is useful to monitor alcohol consumption. Section b) consists of personalized normative feedback. By completing a short self-assessment, participants identify their own drinking patterns in comparison to normative drinking guidelines. Participants who show a drinking pattern of high risk for alcohol dependency receive information about health services they should use in addition to the online intervention. Participants belonging to a high-risk group (e.g. pregnant participants) are advised to abstain from alcohol. This kind of a normative feedback element as stand-alone-intervention has been shown to effectively reduce drinking [42]. It aims to enable participants to reconsider their drinking habits by comparing their own alcohol consumption to that of peers and health norms [43]. In section c) different exercises are presented in a non-directive style based on motivational interviewing principles [44] that are meant to elicit behavioral change. The participants reflect on advantages and disadvantages of their drinking, think of reasons for change, and determine a personal goal (e.g. to reduce alcohol consumption in specific situations, to become abstinent, or to just monitor drinking habits).

An additional tool of the training program is an online-diary, which participants can use to record how much they drank on the previous day and to set a personal limit for the next day. At the beginning of each subsequent module, participants reflect on their drinking on the previous days. The diary is accessible via Internet or smartphone.

The core element in Module 2 is a four-step plan to control alcohol consumption in specific situations. It is theoretically based on the Health Action Process Approach (HAPA) [45] and elements

of the Problem Solving Therapy (PST) [46]. The plan consists of the following steps: 1) Participants choose a typical situation in which it is hard for you to abstain from alcohol, 2) determine a drinking limit for this situation, 3) explore possible solutions for behavioral change in this kind of situation, and 4) describe in detail how to put their solution into practice. At the end of Modules 2 to 5, participants receive additional information and techniques they can use to achieve their goals. This optional toolbox contains information on the following topics: how to refuse alcohol in social contexts, how to control situations in which alcohol is easily available (stimulus control), how to change drinking habits, and how to relax after work without drinking (relaxation techniques).

In Module 3, participants reflect on their first efforts of controlling alcohol, adopt or adapt a plan for behavioral change, or develop a new plan in response to another problematic drinking situation. Participants are then introduced to the nature of different emotions and how these are linked to alcohol consumption. There is evidence for the detrimental impact of negative emotional states on maladaptive drinking [47, 48]. Furthermore, participants start to learn evoking positive emotions without using alcohol, for example, by planning enjoyable activities. This planning process can be continued throughout the other modules.

Module 4 comprises techniques of emotional regulation to cope with negative affective situations. The core exercise is to accept and tolerate negative emotional states based on the Affect Regulation Training (ART) [40, 49]. Acquiring these competencies may help individuals to improve their drinking habits [50]. Participants begin this exercise by recognizing a situation in the past when they had to struggle with their emotions. Then, they reflect on the usefulness and positive aspects of the unwanted (negative) emotions and develop strategies for coping with them in this kind of situation (i.e., by accepting the current emotional state). At the end of the exercise, they are reminded that they are able to bear the acute emotion and that this state will pass.

Finally, in Module 5, participants think of their progress and describe how they can continue to improve. They define an alcohol limit for the future and choose techniques that appeared to be useful to stay within the limit that they have set for themselves.
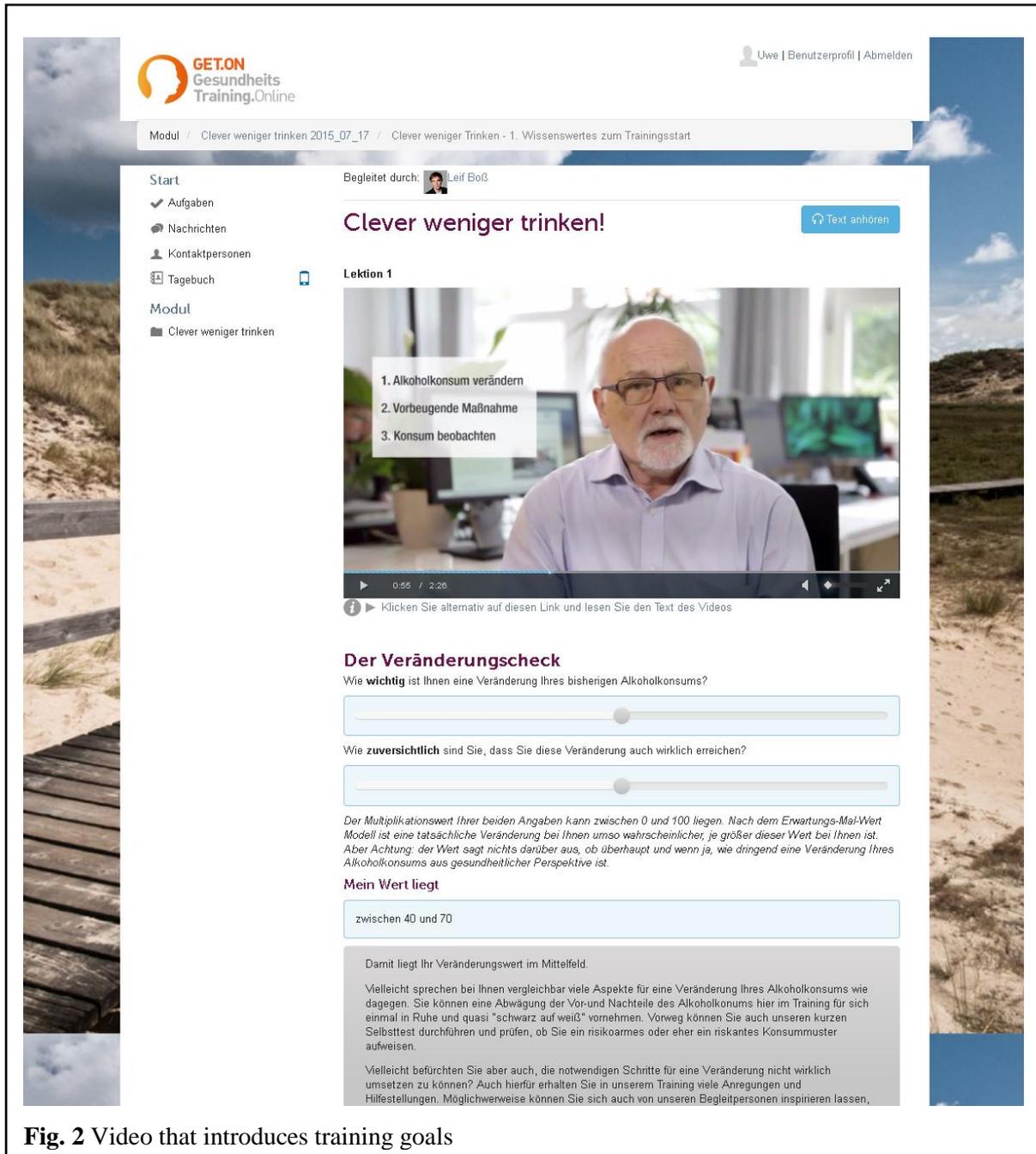
Fig. 2 Video that introduces training goals

Study conditions

Unguided CWT

Participants of the unguided intervention group will communicate with the team organizing the study during the study period but will not be supported by an eCoach. In the case of any technical problems, they can contact support via email.

Fig. 3 Example of adaptive content

Adherence-focused guided CWT

Participants of the guided intervention group will be supported by an eCoach. Guidance is mainly based on the supportive-accountability model of guidance in Internet interventions [51]. In this study, the primary aim of guidance will be to support participants to adhere to the training schedule. Every participant in this study group will be assigned to an eCoach during the training. The eCoaches are trained psychologists and will follow guidelines for the feedback process that are defined according to the content and structure of the intervention. At the beginning of the training, eCoachs send a message to the participants clarifying their supportive role in the program.

Fig. 4 Example of a writing exercise for behavioral change planning

Coaching guidance consists of two elements: a) adherence monitoring and b) feedback on demand. These principles of guidance have already been described elsewhere [35].

Adherence monitoring includes regularly checking whether participants have completed the intervention modules on time and sending reminders if they did not complete at least one module within 7 days. The reminders are formulated in an encouraging and motivational style to avoid reactance. In addition, all participants receive a standardized message after having completed the first module to make sure that they stick to the program.

Feedback on demand includes offering participants the opportunity to contact their eCoach via the internal messaging system of the training platform and to receive individual feedback whenever such a need may arise. Within 48 hours, the participants will receive personalized written feedback. The time required for coaching including all reminders and feedback is estimated to be up to 1 hour per participant.

Waiting list control (WLC)

Participants of the WLC will not get any kind of active training intervention. But they are informed that monitoring and reflecting on their drinking behavior by completing online-assessments can be a first step toward healthier drinking habits. In addition, participants will get access to the training after the 6-month follow-up assessment.

Measures

Primary Outcome

Primary outcome will be the self-reported alcohol consumption (standard units) during the 7 days prior to T2, using the Timeline Followback (TLFB) method [52]. The TLFB has been shown to be a valid and reliable procedure to document recent drinking histories [53]. The procedure has been proven to capture drinking levels very well compared to a daily diary [54]. It has been also validated as a web-based version [55]. Respondents retrospectively record their daily drinking by choosing the amount and kind of drinks they had out of a set of typical alcoholic drinks (e.g. a 330ml bottle of beer or a 100ml glass of wine). These quantities will be automatically converted to alcohol standard units and added to calculate the total sum score of units for the last 7 days.

As a secondary drinking measure, participants will be coded as responders if their drinking remains within the margin of low-risk, i.e., drinking not more than 14 (women) or 21 (men) standard units per week. Besides the drinking level, several other variables will be assessed as secondary outcomes (Table 2).

Secondary Outcome Measures

Alcohol-related problems The Alcohol Problems Questionnaire (APQ) [56] will be used to measure common (23 items, e.g. "Have your friends criticized you for drinking too much?") and occupational (8 items, e.g. „Have you been unable to arrive on time for work due to your drinking?") alcohol-related problems. All items apply to a 6-month period prior to the assessment and can be answered by 1 = "Yes" or 0 = "No.". Item scores can be added to calculate a common problems subdomain score (APQC) ranging from 0 to 23 and a work problems subdomain score (WORK), ranging from 0 to 8. The subdomains show internal consistencies of $\alpha = .92$ for the APQC and $\alpha = .82$ for WORK [57].

Table 2 Secondary outcome measures and assessment points

Outcome measures	T1	T2	T3
Alcoholic Drinks (Timeline Followback method)	✓	✓	✓
Alcohol Problems Questionnaire (APQ)	✓		✓
Readiness to Change Questionnaire (RTCQ)	✓	✓	✓
Depression Anxiety Stress Scale (DASS-21)	✓	✓	✓
Irritation Scale (IS)	✓	✓	✓
Effort Reward Imbalance Questionnaire (ERI-SF)	✓		✓
Work Limitations Questionnaire (WLQ)	✓	✓	✓
Single-Item Presenteeism Question	✓	✓	✓
Single item question on work ability	✓	✓	✓
General Self-Efficacy Scale (GSE)	✓	✓	✓
Assessment of Quality of Life (AQoL-8D)	✓	✓	✓
Trimbos and institute of Medical Technology Assessment Cost Questionnaire for Psychiatry (TiC–P-G)	✓		✓
Attitudes toward seeking psychological help (ATSPPH-SF)	✓	✓	✓
Use of other health services		✓	✓
Negative-Effects of Psychotherapy Inventory (INEP)			✓
Client Satisfaction Questionnaire (CSQ-8)		✓	

Note: T1 = baseline assessment before randomization, T2 = post assessment after 6 weeks, T3 = follow-up assessment after 6 months.

Readiness to change The Readiness to Change Questionnaire (RTCQ) [58, 59] is based on the stage of change model of Prochaska and DiClemente. It consists of three subdomains with four items each, corresponding to the stages through which a person moves in an attempt to resolve a drinking problem: precontemplation (e.g. "I don't think I drink too much"), contemplation (e.g. "I enjoy my drinking, but sometimes I drink too much"), and action (e.g. "I am trying to drink less than I used to"). Respondents rate all items on a five-point Likert-type scale, ranging from 1 = "strongly disagree" to 5 = "strongly agree". The subdomains show internal consistencies of $\alpha = .82$ for precontemplation, $\alpha = .86$ for contemplation, and $\alpha = .78$ for action.

Depression, anxiety, and stress The Depression Anxiety Stress Scale (DASS-21) [60] will be used to assess symptoms of depression, anxiety, and stress with seven items each. Respondents rate each item (e.g. "I found it hard to wind down") on a four-point Likert-type scale, ranging from 0 = "Did not apply to me at all" to 3 = "Applied to me very much, or most of the time". Total scores of the three subdomains range from 0 to 21. The DASS-21 show internal consistencies of $\alpha = .88$ for depression, $\alpha = .82$ for anxiety, and $\alpha = .90$ for stress [61].

Work-related stress We will use two different measures to assess work-related stress. The Irritation Scale (IS) [62] operationalizes work-related stress in terms of cognitive (CI) and emotional irritation (EI), as reactions on uncertainty in the working environment. The CI subdomain consists of three items (e.g. "Even at home I often think of my problems at work."). The EI subdomain consists of five items (e.g. "I get grumpy when others approach me."). Respondents rate all items on a seven-point Likert-type scale (1 = "strongly disagree", 2 = "largely disagree", 3 = "rather disagree", 4 = "moderately agree", 5 = "partly agree", 6 = "largely agree", 7 = "strongly agree"). The items are added to a total irritation scale. Both subdomains show good internal consistencies, ranging from $\alpha = .85$ to .97 [62].

The Effort Reward Imbalance Questionnaire – Short Form (ERI-SF) [63] assesses stress based on the model of effort-reward imbalance. The subdomain "effort" consists of three items (e.g. "I have constant time pressure due to a heavy work load"). The subdomain "reward" consists of seven items (e.g. "My job promotion prospects are poor"). Respondents rate all items on a four-point Likert-type scale (1 = "strongly agree", 2 = "agree", 3 = "disagree", 4 = "strongly disagree"). The subdomains show moderate to good consistencies, $\alpha = .77$ for effort and $\alpha = .82$ for reward [64].

Presenteeism We will use the short form of the Work Limitations Questionnaire (WLQ-8) [65, 66]. It consists of eight items, measuring the degree to which health problems interfere with the ability to perform in the job. All items are to be rated on a five-point Likert-type scale, ranging from 1 = "the whole time" to 5 = "none of the time" (e.g. "In the past 2 weeks, how much of the time did your physical health or emotional problems make it difficult for you to concentrate on your work?"). In addition, we will use an adapted version of the Single-Item Presenteeism Question ("To what extent has your physical or mental health problems affected your performance at work over the past 30 days?") [67], ranging from 0 = "not at all" to 10 "extremely", and a single item question on work ability ("Current work ability compared with the lifetime best") [68], ranging from 0 = "completely unable to work" to 10 "work ability at its best".

Self-efficacy The 10-item General Self-Efficacy Scale (GSE) [69] assesses a general sense of perceived self-efficacy, with the goal of predicting the ability to cope with daily problems and adapt after experiencing stressful life events. The respondents evaluate statements on a four-point Likert-

type scale, ranging from 1 = „not at all true" to 4 = "completely true" (e.g. "I can typically handle whatever comes my way"). A higher score indicates higher self-efficacy. The item values can be added to a total score, ranging from 10 to 40. The internal consistency of the GSE is varying from α = .76 to .90 in different samples [69].

Attitudes toward seeking professional psychological help The Attitudes Toward Seeking Professional Psychological Help Scale – Short Version (ATSPPHS-SF) [70] assesses attitudes toward seeking professional help for psychological problems. Respondents rate all of the ten items of this scale on a four-point Likert-type scale, ranging from 0 = "disagree" to 3 = "agree" (e.g. "If I believed I was having a mental breakdown, my first inclination would be to get professional attention."). The items can be added to a total score, ranging from 0 to 30. The scale shows an internal consistency of α = .84.

Negative side-effects Adverse effects will be measured with an adapted version of the Negative-Effects of Psychotherapy Inventory (INEP) [71]. The version used in this study consists of 15 items, assessing negative effects participants experienced within or after the completion of the web-based training. The INEP covers the following domains: negative intrapersonal changes, negative effects in an intimate relationship, family/friends, perceived dependence on the eCoach/intervention, and stigmatization (e.g. "I am anxious that my colleagues or friends could find out about my training participation"). Respondents rate all items on a four-point Likert scale, ranging from 0 = "no agreement at all" to 3 = "total agreement". For each item, participants also state whether they attribute the adverse effects on the training participation or on other factors. Only item scores of those negative effects that were attributed on participating in the training are added to the total score. Higher total scores indicate more negative effects. The INEP show an internal consistency of α = 0.85.

Course evaluation To evaluate the course satisfaction we used the Client Satisfaction Questionnaire (CSQ-8) [72, 73] and adapted it to the context of web-based trainings. The CSQ consists of eight items, measuring the global client's satisfaction with the training. Respondents rate all items (e.g. "How would you rate the quality of service you received?") on a four-point Likert-type scale, with different responses (e.g. 1 = "Poor" to 4 = "Excellent"). Previous research indicated a high internal consistency of α = .92 for the general version [74] and α = .92 for the adapted version [75, 76].

Quality of life The Assessment of Quality of Life (AQoL-8D) [77] will be used as multi-attribute utility instrument. This measure consists of 35 items, covering eight subdomains of health-related quality of life which can be combined to a physical super dimension (independent living, pain, senses) and a mental super dimension (mental health, happiness, coping, relationships, self-worth). The respondents rate all items on a four-, five-, or six-point Likert-type scale, ranging from 1 = "very

rarely" to 4 = "most of the time" (e.g. "Thinking about how often you experience serious pain: I experience it…"), from 1 = "never" to 5 = "always" (e.g. "How often do you feel socially excluded or left out?"), or from 1 = "very satisfying" to 6 = "very unpleasant" (e.g. "Your close relationships (family and friends) are:"). The scale show internal consistencies of $\alpha = .88$ for the physical health dimension and $\alpha = .96$ for the mental health dimension [77].

Cost measure A German version of the Trimbos and Institute of Medical Technology Assessment Cost Questionnaire for Psychiatry (TiC–P-G) [78] will be used to record direct and indirect medical costs over the previous three months. Direct costs can be derived from information on the participants' use of health services (e.g. general practice visits, sessions with psychiatrists, hospital days). To assess indirect costs participants register the number of "work loss" days (absenteeism from work) and the number of "work cut-back" days, i.e., days on that they were showing up for work despite of feeling ill (presenteeism). The questionnaire shows a good retest-reliability and achieves comparable results between patient-reported data and data derived from medical registrations [78].

Sample size calculation

We expect that both intervention groups will be, compared to the control group, superior in terms of the primary outcome from T1 to T2. The latest meta-analysis on mainly unguided web-based interventions for reducing alcohol consumption [28] yielded an overall effect size of $d = 0.20$. Subgroup analyses revealed no significant differences in effect size regarding the type of intervention (personalized normative feedback vs. more extended interventions) or the number of sessions. However, in an earlier meta-analysis, the same research group found indications for extended interventions to be more effective than personalized normative feedback with an average effect size of $g = 0.61$ for extended and $g = 0.27$ for PNF [79]. Because GET.ON CWT contains evidence-based cognitive-behavioral components over and above PNF and motivational interviewing, we expect a slightly greater effect than the one that was found in the meta-analysis [28]. We aim to include 528 participants. This sample size will allow us to detect an effect size of $d = 0.30$ based on a power (1-ß) of 80% and an alpha error of .05 in a two-sided test, calculated using G*Power software [80].

Statistical analyses

The trial will be conducted in compliance with the study protocol and the Declaration of Helsinki. Aiming at an intention-to-treat design, we will include all participants who will have been randomly assigned to the conditions. Missing data will be handled using multiple imputations. In addition, per protocol analyses (PPA) will be performed, including only participants followed the intervention outlined in the study protocol. The evaluation will be conducted in accordance with the consolidated standards of reporting trials (CONSORT) [81].

Clinical evaluation

Analyses of covariance with baseline scores as covariate will be conducted to explore the effects of the interventions compared to the control group on all primary and secondary outcomes. A-priori contrasts will be defined to test the separate effects of the guided and unguided interventions compared to the control condition. For all analyses, Cohen's d will be calculated by subtracting the average change scores from baseline to post-assessment (T1-T2) of one study group from the other one and then dividing it by the pooled standard deviations of the change scores. We will also calculate the number needed to treat (NNT) with adherence-focused guided and unguided CWT to achieve one response, i.e., complying with the low-risk guideline, compared to the control group. For all statistical analyses, significance level will be set at $p<.05$ for two-sided tests.

Economic evaluation

To compare relative costs and outcomes of the study conditions, we will conduct cost-effectiveness and cost-utility analyses from the perspectives of employers and the society. In both analyses, the incremental cost-effectiveness ratio (ICER) will be calculated for a 6-months period using the following formula: ICER=(Cost intervention group-Cost control group)/(Effect intervention group-effect control group) [82]. Treatment response will be the outcome to estimate the cost-effectiveness of the intervention whereas quality-adjusted life years (QALYs) will be the outcome to estimate cost-utility. The incremental cumulative costs will be calculated as the differences in the costs between the intervention groups and the control group. Costs to be estimated consist of direct costs for developing and maintaining the intervention, costs for staffing (i.e., for providing feedback and technical support), and opportunity costs caused by time spending on the intervention. The non-parametric bootstrap method will be used to handle uncertainty in the ICER. In addition, results will be shown in a cost-effectiveness acceptability curve [82].

Ethical considerations

This study has been approved by the ethics committee of the Leuphana University of Lueneburg, Germany (No. Boss201404_OT).

Discussion

Problematic alcohol consumption among the workforce is a high-risk factor for individuals in terms of disease burden, and it can lead to high costs for employers and society [1, 2, 8]. As a low-threshold health program, web-based interventions can help people displaying problematic drinking behavior [29]. However, the effects of interventions for reducing alcohol consumption are, on average, small [28, 29, 79]. While there have been a few studies on the efficacy of these kinds of interventions in the workforce [30–32], to the best of our knowledge, no research has been done on cost-effectiveness.

Based on a sample of employees from different sectors, this study provides further evidence for the (cost-)effectiveness of web-based interventions for reducing problematic alcohol consumption in the workforce. The CWT intervention draws on components of traditional methods to treat alcoholism, such as self-monitoring and reflecting on drinking behavior. In addition, techniques commonly used in cognitive-behavioral therapy and emotion regulation trainings are integral elements of the training. To the best of our knowledge, there has been no web-based intervention for reducing problematic alcohol consumption that has integrated emotional psychoeducation and emotion regulation techniques. Given that recent research provide evidence for the relevance of emotion regulation skills for abstinence from alcohol [50], integrating these techniques in interventions for problematic alcohol use may be a promising strategy to further increase the effectiveness of such interventions.

Although there are hints that guided interventions are superior compared to unguided interventions in different health problem domains [34, 84, 85], it is unclear whether this holds for interventions for reducing problematic alcohol consumption. There may be only one study directly comparing different types of guidance in a web-based intervention within the same trial [86], but there is no study on the workforce. Research on the cost-effectiveness of these interventions is also scarce. Because the operational costs of these interventions may particularly be related to the level of guidance, it is of major interest to both employers and health care providers which type of intervention is more cost-effective. The more people use an unguided intervention, the lower the costs [87]. In contrast, the costs for personnel in guided interventions are fixed and will not decrease when the number of users rises. In this three-armed trial, it will be possible to explore both the clinical effectiveness and cost-effectiveness of guided and unguided interventions.

This study has the following limitations: First, we chose a recruiting strategy that is based on the occupational health programs of several health insurance companies and did not focus on specific industrial sectors (e.g. finance, social services, health care, manufacturing, retail, or government) or specific occupational groups (e.g. managers or blue-collar workers). On the one hand, this allows us to estimate the mean (cost-)effectiveness of the intervention for the workforce. On the other hand, this certainly reduces the internal validity of the study because we cannot determine the (cost-)effectiveness for specific industrial sectors or occupational groups. Moreover, employees need to apply actively for study participation. Hence, the results may not generalize to non-help seeking populations. Second, the economic evaluation to be conducted in this study will be based on actual intervention costs (direct intervention costs + opportunity costs for the participants). Costs associated with the implementation of the intervention (e.g. marketing) will not be considered. Third, attrition is often a problem in web-based interventions [88, 89]. Although we developed the intervention in a way that we hope keeps participants on track (e.g. they engage with integrated multimedia tools, keep an online-diary, and learn about individuals who successfully navigated exemplary situations), we expect several participants to stop using the intervention. We also expect participants to drop out of the study, i.e., to fail to take part in the follow-up assessments. Fourth, the primary aim of guidance in this study

is to support participants to adhere to the intervention schedule. However, it may be the case that the level of support may be too low to have a meaningful incremental impact on the guided intervention in terms of psychopathological outcomes and cost-effectiveness compared to the unguided intervention. Fifth, due to limitations with regard to feasibility, only self-reported measurements will be used. Sixth, even though most of the self-rated measures show good psychometric properties, only a few have been validated in the context of online-assessments, for example the TLFB [55]. Seventh, in this trial, we will use a waiting list control group. This may increase the risk of overestimating intervention effects compared to an assessment-only control group [28]. However, due to practical and ethical reasons, we decided to give all control participants access to the unguided intervention after they will have finished the follow-up assessment.

Conclusions

This study allows us to assess the (cost-)effectiveness of a web-based intervention for reducing alcohol consumption in a heterogeneous workforce. If shown effective, the CWT intervention would be a flexible solution for employees who do not use traditional services for alcohol treatment and for companies and society to overcome the high risk of ill-health and productivity losses due to alcohol-related problems. If the intervention works as intended, the next step would be to investigate which guidance format is the most feasible for dissemination to a broad community.

Abbreviations

AUD: Alcohol use disorder; PNF: Personalized normative feedback; CWT: Clever weniger trinken (name of the intervention); RCT: Randomized controlled trial; WLC: Waiting list control group; AUDIT: Alcohol Use Disorders Identification Test; BDI: Beck Depression Inventory; HAPA: Health Action Process Approach; PST: Problem Solving Therapy; ART: Affect Regulation Training; TLFB: Timeline follow back; APQ: Alcohol Problems Questionnaire; RTCQ: Readiness to Change Questionnaire; DASS-21: Depression Anxiety Stress Scale (short form); IS: Irritation Scale; ERI-SF: Effort Reward Imbalance Questionnaire (short form); WLQ-8: Work Limitations Questionnaire; GSE: General Self-Efficacy Scale; ATSPPHS-SF: Attitudes Toward Seeking Professional Psychological Help Scale (short form); INEP: Negative-Effects of Psychotherapy Inventory; CSQ-8: Client Satisfaction Questionnaire; AQoL-8D: Assessment of Quality of Life; TiC–P-G: Trimbos and Institute of Medical Technology Assessment Cost Questionnaire for Psychiatry; PPA: Per protocol analyses; CONSORT: Consolidated standards of reporting trials; NNT: Number needed to treat; ICER: Incremental cost-effectiveness ratio; QALYs: Quality-adjusted life years

Competing interests

The authors declare that they have no competing interest.

Authors' contribution

DE, DL, and MB obtained funding for this study. LB, DL, DE, and HR contributed to the development of the GET.ON CWT training. DE was responsible for the initial study design draft, DL, HR and LB contributed to the final study design. LB drafted the manuscript. DE and DL supervised the writing process. All authors contributed to the further writing of the manuscript, all authors read and approved the final manuscript.

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Manuskript 2 – Wirksamkeitsstudie Clever weniger trinken

ABSTRACT

Aims To test the efficacy of a web-based alcohol intervention with and without guidance. **Design** Three parallel groups with primary endpoint after 6 weeks. **Setting** Open recruitment in the German working population. **Participants** Adults (178 males/ 256 females, mean age of 47) consuming at least 21/14 weekly standard units of alcohol (SUA) and scoring ≥8/6 on the Alcohol Use Disorders Identification Test. **Intervention** Five web-based modules including personalized normative feedback, motivational interviewing, goal setting, problem solving, and emotion regulation over 5 weeks. One intervention group received an unguided self-help version (n=146), the second received additional adherence-focused guidance by eCoaches (n=144). Controls were on a waiting list with full access to usual care (n=144). **Measurements** Primary outcome was weekly consumed SUA after 6 weeks. SUA after 6 months was examined as secondary outcome, next to numbers of participants drinking within the low-risk range, and general and work-specific mental health measures. **Findings** All groups showed reductions of mean weekly SUA after six weeks (unguided: -8.0; guided: -8.5; control: -3.2). There was no significant difference between the unguided and guided intervention (P=0.37). Participants in the combined intervention group reported significantly fewer SUA than controls (B=-4.85, 95%-CI=-7.02 to -2.68, P<0.001). The intervention groups also showed significant reductions in SUA consumption after six months (B=-5.72, 95%-CI=-7.71 to -3.73, P<0.001) and improvements regarding general and work-related mental health outcomes after six weeks and 6 months. **Conclusions** This web-based alcohol intervention, whether administered with or without personal guidance, yielded significant reductions in mean weekly alcohol consumption, and improvements in mental health and work-related outcomes in employees.

Keywords Internet, occupational health, mental health, drinking, alcohol, treatment, training, employee

INTRODUCTION

Alcohol consumption is an important risk factor for conditions like cancer, cardiovascular disease, and mental and behavioral disorders [1-3]. It is also associated with considerable economic costs, which include sick leave and impaired productivity at work [4].

Among a multitude of risk factors, several studies have highlighted associations between specific work-related factors — like job strain [5], long work hours [6], and effort-reward imbalance [7,8] — and alcohol consumption. Concurrently, workplaces provide opportunities to deliver alcohol-related interventions (e.g., via health promotion programs, alcohol policies, or screening and brief interventions) [9]. While some studies have revealed small effects on alcohol consumption [10-12], others failed to demonstrate any beneficial effects among subjects offered such interventions relative to controls [13]. In Germany, health insurance companies have been legally obligated to offer and reimburse for preventative measures to reduce alcohol consumption since the late eighties. As a result, a variety of public and occupational services have been established during the past decades. Still, a general problem with such services are low utilization rates [14-16]. This is a common issue for both public [17] and occupational [18] alcohol-related health services. Reasons for this include preferences for self-help attempts [17] and fears of stigmatization [18,19]. It therefore would be of great value to investigate the use of lower-threshold and less-stigmatizing approaches. Web-based interventions are a potentially promising solution, by which evidence-based measures designed to prevent alcohol-related problems in employees can be delivered less intrusively and conspicuously [9,20].

Several web-based alcohol interventions have been evaluated in the general population, producing small effects in terms of alcohol reduction, relative to controls [21-23]. However, research on interventions targeting working populations is scarce and largely restricted to very specific sub-populations. For example, in young employees, Doumas and Hannah tested a website that provided personalized normative feedback (PNF) [24]. In turn, other studies focusing either on screening [25] or very brief interventions [26] have shown such measures not to be effective. All interventions have focused upon a single problem area (i.e., alcohol consumption). However, alcohol-related problems are associated with other mental health problem domains, like depression and anxiety [27]. It therefore seems worthwhile to explore whether or not web-based alcohol interventions can exert any positive effect on co-occurring mental problems [28]. In particular, recent findings indicate an impact of work-related rumination on alcohol use after work [29]. People may use alcohol as a coping strategy to reduce work-related rumination on the one hand, while on the other hand there also is evidence that workers facing high-level work stress, in terms of effort-reward imbalance, consume more alcohol than those with low-work stress [7,8,30,31]. However, to our knowledge, there have been neither studies investigating the effects of web-based alcohol interventions on work-related outcomes, nor studies that have considered work-stress as a factor that predicts drinking.

There also is a lack of evidence regarding the optimal form of personal support in web-based alcohol interventions. Findings on meta-analysis suggest that, on average, guided interventions may be better than pure self-help interventions [21]. To the best of our knowledge, however, only one study explored a web-based alcohol intervention with different guidance formats [32], demonstrating greater effects for the intervention plus intensive accompanying chat therapy (d=0.59) than for the self-help intervention (d=0.35), when compared against controls. Nonetheless, there was no significant difference in efficacy between both interventions.

The purpose of the present study was to test the efficacy of a web-based alcohol intervention named "GET.ON Clever weniger trinken" (CWT; be smart – drink less) in employees with a problematic drinking pattern [33]. We tested two versions of the intervention: unguided/purely self-help and guided, including additional support from eCoaches.

METHODS

Study design

This study was conducted in compliance with the study protocol [33] and the Declaration of Helsinki. Within the context of a three-arm randomized controlled trial (RCT), 434 participants were randomly assigned (at a ratio of 1:1:1 and block size of three) to either (1) the unguided web-based self-help intervention (unguided CWT, n=146); (2) to CWT with additional adherence-focused guidance (guided CWT, n=144); or to a waiting list control group (WLC, n=144) that was offered delayed access to unguided CWT. All groups otherwise had full access to usual care. Online outcome assessments took place before subjects were allocated to a study group (T1), six weeks later (T2), and at six months of follow-up (T3).

Procedures

Individuals 18 years old or older were included if they were currently employed or self-employed, if they reported drinking at least 14/21 (women/men) SUA per week, and if they had a score of at least 6/8 for women/men on the Alcohol Use Disorders Identification Test (AUDIT) [34]. They were excluded if they had been diagnosed with any past psychosis or drug dependence (self-disclosed); exhibited a notable suicidal risk, as indicated by a score greater than 1 on item 9 ("I feel I would be better off dead") of the Beck Depression Inventory [35]; or if they had received any other kind of treatment for alcohol-related problems or work-related stress prior to the baseline assessment.

Subjects were recruited nationwide from the German-speaking working population between October 2014 and February 2016. The recruitment process was supported by several health insurance companies (BARMER, KKH) and by the German company health insurance fund (BKK) via announcements in print membership magazines and on their websites. Participation was not limited to

the insurants of these companies. Additionally, the intervention was announced in print newspaper articles. Potential participants signed up by providing an email address and name or pseudonym on an open-access website (www.geton-training.de). After registration, applicants received an email with detailed information about the study procedures and were asked to complete an online screening questionnaire to assess their eligibility. Applicants who fulfilled all inclusion but no exclusion criteria, provided informed consent, and completed the baseline assessment (T1) were assigned to one of the three study groups. Randomization took place at an individual level and was performed by an independent researcher not otherwise involved in the study, using an automated, computer-based, random integer generator (randomisation.eu). Prior to any subject recruitment, all procedures involved in the study had been approved by the University of Lueneburg (Germany) ethics committee (No. Boss201404_OT) and registered in the German clinical trials register (No. DRKS00006105).

Interventions

The web-based intervention (CWT) consisted of five modules and participants were advised to complete one module per week. Each module contained general information, illustrative examples, interactive exercises, quizzes, audio and video files, and downloadable work sheets. Exercises in the intervention were adapted from evidence-based treatment elements for alcohol use disorders [36,37], such as motivational interviewing and tools to control drinking behaviors. The exercises included personalized normative feedback, pros and cons of drinking, goal setting, monitoring of drinking by an online-diary, action and coping planning to control drinking behavior, and relapse prevention. In addition, we integrated emotional regulation techniques [38], that have not been tested in web-based alcohol interventions so far. The study protocol contains a detailed description of the intervention's content and theoretical background [33].

All participants in either one of the two active intervention groups received the same web-based CWT. The unguided intervention group could contact the study team via email only if technical problems arose. In the guided intervention group, each participant was assigned an eCoach, a trained psychologist who gave feedback following a semi-structured manual. In this study, guidance primarily aimed at encouraging participants to adhere to their training schedule (i.e., adherence-focused guidance) [39,40]. At the beginning of training, the eCoaches sent a message to each participant clarifying their supportive role in the program. Coaching guidance had two elements: a) adherence monitoring and b) feedback on demand. Adherence monitoring included regular monitoring of whether participants had completed the intervention modules on time. If subjects did not complete a module within seven days, the eCoaches sent reminders written in an encouraging and motivational style. Feedback on demand referred to the opportunity to contact the eCoaches for any question via the internal messaging system provided in the training platform. Individual feedback was provided within 48 hours. Participants in the waiting list group were informed that monitoring and reflecting on their

drinking behaviors, by completing the online-assessments, could be their first step towards developing healthier drinking habits. Furthermore, they were informed that they would ultimately receive access to the unguided training program after their six-month follow-up assessment.

Primary outcome

The primary outcome was the average self-reported quantity of alcohol consumption in standard units of alcohol (SUA) over seven days prior to T2, using the Timeline Followback (TLFB) method [41]. One SUA contains 10-12 grams of pure alcohol. The TLFB has been shown to be a valid and reliable procedure to document recent drinking histories, with average retest-reliability of .90 [42,43].

Secondary outcomes and predictors

Secondary drinking outcomes included alcohol consumption in terms of SUA weekly prior to T3 and the number of responders who complied with the low-risk guideline for problematic drinking at T2 and T3. Responders were defined as having consumed no more than 14 (for women) or 21 (for men) SUA weekly. The Depression Anxiety Stress Scale (DASS-21) [44] was used to assess symptoms of depression, anxiety, and stress at T2 and T3, via seven items and subscores that ranged from 0 to 21 each. We used the Irritation Scale (IS) [45] with its subdomains cognitive irritation (3 items; range 3-21) and emotional irritation (5 items; range 5-35) to assess rumination in the context of the working environment at T2 and T3. The Effort Reward Imbalance Questionnaire – Short Form (ERI-SF) [46] was also used, with the subdomains effort (3 items; range 3-12) and reward (7 items; range 7-28) that covers aspects of the working context as possible baseline predictors of the intervention effects. Further measures used in this trial [33] will be considered in subsequent publications.

Statistical Analyses

All analyses are reported in accordance with the Consolidated Standards of Reporting Trials (CONSORT) [47] following intention-to-treat (ITT) procedures. For the main analyses, we used multiple imputations (MI) to deal with missing data. MI techniques are recommended as they provide the best estimate for missing data [48]. We employed a Markov Chain Monte Carlo multivariate imputation algorithm, using the missing data module in SPSS v. 23, with 100 estimations per missing value. These estimations were aggregated to a single value that was included for all further analyses. In addition, we conducted sensitivity analyses with replacing missing values by the baseline score, assuming that study dropouts did not change their drinking behavior. All statistics were conducted using IBM SPSS (SPSS Inc, Chicago, IL, USA). For all statistical analyses, the significance level was set at $P<0.05$ for two-sided tests. Based on a power of 80%, we aimed to recruit 528 participants to detect an intervention effect of d=0.30 relative to the control condition at T2 [33]. Eventually,

recruitment was slower than anticipated, so we closed the trial with 434 participants. Considering this sample size, the trial had 80% power to detect an intervention effect of d=0.33.

To test the effects of the intervention, we conducted hierarchical multiple regression analyses. We included the study condition and the baseline score of the relevant outcome in the regression model, as well as the following baseline predictors: gender, age, education (high vs. low and mid-level), depression, irritation and effort and reward at work. The analysis plan followed a two-stage procedure. First, we compared unguided CWT with guided CWT. Second, if these groups did not significantly differ, both groups were combined into a single intervention group that was compared with the control group then. For all continuous analyses, Cohen's d [49] was calculated based on imputed data by subtracting the average post-assessment score of one study group from the other and then dividing this value by the pooled standard deviations of the post scores. To analyze interventional effects at an individual level, we tested for group differences in the number of responders using Pearson chi-square analysis and calculated the odds ratio (OR) with 95% confidence intervals (CI).

RESULTS

Participants

A total of 434 participants were randomly allocated to the three study arms (Figure 1). This was lower than the initially intended sample size [33]. Recruitment in this trial was difficult compared to earlier studies on web-based health interventions conducted by our research group, since this phase took substantially longer than expected. Due to a limited funding period, we had to stop recruitment after 17 months. In the guided intervention group, two participants withdrew from study participation and called for deletion of their datasets, which was a necessary option requested from the ethics committee. Thus, the final study sample consisted of 432 participants with an average age of 47, among whom more than a half were female (Table 1). The majority of participants were employed full time, with an average working experience of 23 years.

Missing Data

Data on sociodemographic and outcome variables were available for the entire sample at T1. In total, 339 participants (78.4%) attended the post-assessment (T2), while 270 (62.5%) came to the six-month follow-up (T3) (Figure 1). The three groups differed with regard to missing data on primary and secondary outcomes at T2 ($P=0.032$), but not at T3 ($P=0.092$). Missing of outcome data appeared only in terms of wave non-response and Little's overall test of randomness indicated that missing occurred completely at random ($P=0.817$); as such, multiple imputations of the missing data could be conducted [48].
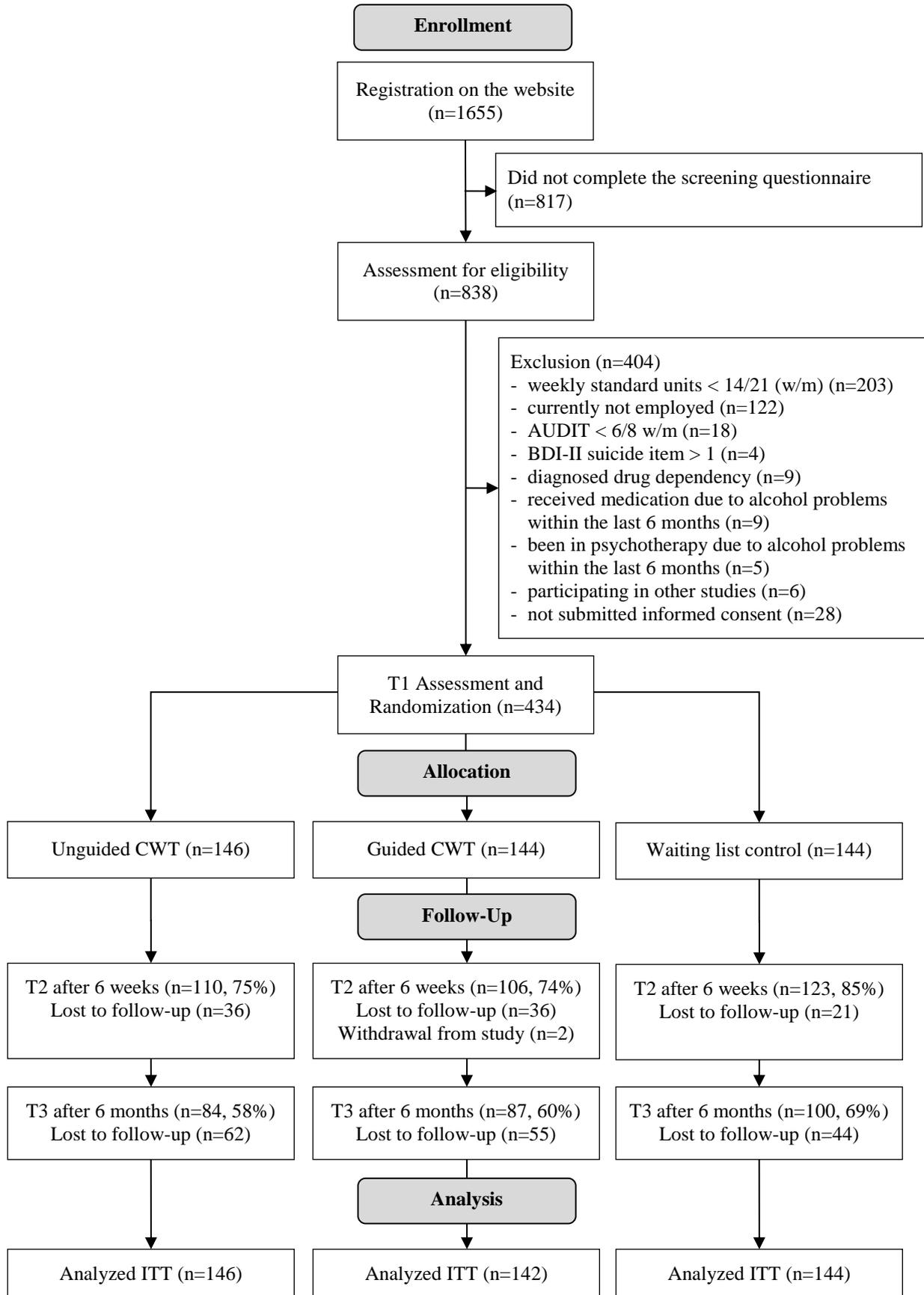
Figure 1 Study flow

Table 1 Baseline characteristics

Characteristics	Control (n=144)	Unguided CWT (n=146)	Guided CWT (n=142)
Sociodemographic			
Age, mean (SD)	47.3 (10.3)	47.6 (9.3)	47.5 (9.8)
Women, n (%)	89 (61.8)	84 (57.5)	83 (58.5)
Married or in a partnership, n (%)	85 (59.0)	100 (68.5)	81 (57.1)
Educational level			
Low, n (%)	5 (3.5)	11 (7.5)	7 (4.9)
Middle, n (%)	41 (28.5)	47 (32.2)	38 (26.8)
High, n (%)	98 (68.1)	88 (66.3)	97 (68.3)
Work characteristics			
Full-time employed, n (%)	102 (70.8)	97 (66.4)	102 (71.8)
Part-time employed, n (%)	34 (23.6)	38 (26.0)	33 (23.2)
On sick leave, n (%)	3 (2.1)	-	-
Seeking work, n (%)	4 (2.8)	10 (6.8)	5 (3.5)
Not gainfully employed, n (%)	1 (0.7)	1 (0.7)	2 (1.4)
Work experience in years, mean (SD)	23.5 (11.1)	23.0 (11.1)	23.2 (11.6)
Efforts spent at work[a], mean (SD)	8.30 (2.2)	8.7 (2.3)	8.5 (2.4)
Rewards received from work[a], mean (SD)	18.9 (4.0)	18.0 (3.8)	18.0 (4.0)
Effort-Reward Imbalance[b], mean (%)	76 (52.8)	92 (63.0)	87 (60.4)
Work sectors			
Service, n (%)	33 (22.9)	34 (23.3)	36 (25.4)
Economy, n (%)	25 (17.4)	21 (14.4)	16 (11.3)
Health, n (%)	16 (11.1)	20 (13.7)	23 (16.2)
Social, n (%)	13 (9.0)	26 (17.8)	17 (12.0)
Information Technologies, n (%)	9 (6.3)	7 (4.8)	9 (6.3)
Others, n (%)	48 (33.3)	38 (26.0)	41 (28.9)
Income in Euro, per month			
< 1.000, n (%)	13 (9.1)	10 (6.8)	4 (2.8)
1.000-2.000, n (%)	29 (20.3)	29 (19.9)	31 (21.8)
2.000-3.000, n (%)	25 (17.5)	26 (17.8)	30 (21.1)
3.000-4.000, n (%)	19 (13.3)	29 (19.9)	22 (15.5)
4.000-5.000, n (%)	16 (11.2)	14 (9.6)	14 (9.9)
> 5.000, n (%)	23 (16.1)	20 (13.7)	22 (15.5)
Prefer not to say, n (%)	6 (4.2)	3 (2.1)	7 (4.9)
No paid employment, n (%)	13 (9.1)	15 (10.3)	12 (8.5)
Previous use of health services			
Previous health training, n (%)	12 (8.3)	17 (11.6)	22 (15.5)
Previous psychotherapy, n (%)	64 (44.4)	55 (37.7)	60 (42.3)
Current psychotherapy, n (%)	1 (0.7)	3 (2.1)	2 (1.4)

Note: SD=standard deviation; [a]=subdomains of the Effort-Reward Imbalance (ERI) questionnaire; [b]=according to Siegrist et al. (2004) ERI ratio values > 1 indicate high work stress.

Intervention Usage

On average, participants in the unguided CWT group completed 2.5 training modules, while participants in the guided CWT group completed 3.0 training modules (Figure 2). Adherence — defined as completing a minimum of the first three intervention modules — was significantly greater in the guided CWT group (t_{277}=2.86, P=0.005). There were two major forms of interaction between participants and eCoaches in the guided CWT group (n=142). First, 47 participants (33.1%) engaged in conversation with an eCoach as a response to reminder messages that were sent by eCoaches when participants had not completed a training module in time. Typically, participants used these conversations to state when they were going to finish the outstanding training session. Second, some requested feedback on specific topics or exercises of the intervention; however this only amounted to 15 participants (10.6%). In the waiting list control group, eight participants (5.6%) indicated that they had received other help within the study period (e.g., visits to their general practitioner, psychotherapy, addiction services, online-forums, health training other than the CWT), versus seven participants (4.8%, P=0.927) in the unguided CWT group and six (4.2%, P=0.770) in the guided CWT group.
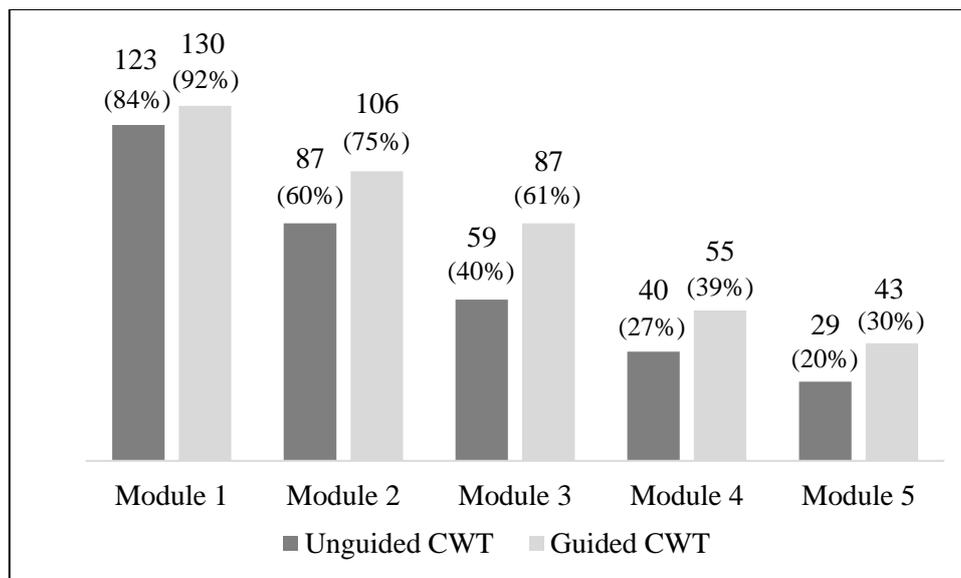
Figure 2 Participants who completed the intervention modules (based on log-data). CWT = 'clever weniger trinken' (be smart - drink less)

Primary Outcome Analysis

All study groups showed a reduction of mean weekly SUA from T1 to T2 (control: -3.2; unguided CWT: -8.0; guided: -8.5; Table 2). There was no significant difference between unguided and guided CWT in the unadjusted model or in any other model including possible baseline confounders (Table 3). Accordingly, we combined both active intervention groups and compared it with the control group. The fully adjusted regression model revealed a significant group effect (B=-4.85, 95% CI: -7.02 to -2.68, $P<0.001$; Table 3). Participants who received any type of CWT reduced their weekly drinking by 4.9 SUA on average, relative to controls.

Table 2 Means, standard deviations, and effect sizes on weekly standard units alcohol

	Baseline		Six weeks after baseline[a]					Six months after baseline[a]				
	M	SD	M	SD	d[b]	95% CI		M	SD	d[b]	95% CI	
Control (n=144)	28.99	13.38	25.79	12.33				24.04	13.18			
Unguided CWT (n=146)	30.26	16.11	22.31	14.66	0.25	0.02	0.48	17.89	12.16	0.45	0.22	0.68
Guided CWT (n=142)	29.44	17.68	20.96	14.39	0.38	0.14	0.61	19.63	11.70	0.38	0.14	0.61
Combined CWT (n=288)	29.87	16.89	21.59	14.47	0.30	0.10	0.51	18.79	12.12	0.42	0.22	0.62

Note: [a]=Missing data handled by multiple imputation; [b]=effect size Cohen's d based on differences between the intervention and the control group.

Table 3 Results of the primary outcome regression analyses

	Guided vs. Unguided CWT after 6 weeks			Combined CWT vs. Control after 6 weeks		
	B	95% CI	*P*	B	95% CI	*P*
Model 1 (R²=0.020)[a]						
Condition	-1.70	-5.08 1.68	0.324	-4.19	-6.97 -1.41	0.003
Model 2 (ΔR²=0.386, *P*<0.001)[a]						
Condition	-1.23	-3.90 1.45	0.367	-4.66	-6.82 -2.49	<0.001
SUA	0.53	0.45 0.60	<0.001	0.55	0.48 0.61	<0.001
Model 3 (ΔR²=0.016, *P*=0.010)[a]						
Condition	-1.29	-3.92 1.35	0.338	-4.71	-6.85 -2.56	<0.001
SUA	0.48	0.39 0.56	<0.001	0.51	0.44 0.58	<0.001
Gender	-4.99	-7.86 -2.11	0.001	-3.53	-5.76 -1.31	0.002
Age	-0.08	-0.22 0.06	0.238	-0.03	-0.14 0.07	0.519
Education	1.03	-1.74 3.80	0.463	1.09	-1.08 3.25	0.324
Model 4 (ΔR²=0.000, *P*=0.762)[a]						
Condition	-1.29	-3.93 1.35	0.336	-4.72	-6.87 -2.57	<0.001
SUA	0.48	0.39 0.56	<0.001	0.51	0.44 0.58	<0.001
Gender	-4.97	-7.86 -2.09	0.001	-3.56	-5.79 -1.33	0.002
Age	-0.08	-0.22 0.06	0.239	-0.03	-0.14 0.07	0.529
Education	1.04	-1.74 3.81	0.462	1.08	-1.09 3.25	0.329
Depression	-0.03	-0.32 0.25	0.816	0.03	-0.19 0.26	0.762
Model 5 (ΔR²=0.006, *P*=0.376)[a]						
Condition	-1.32	-3.97 1.33	0.326	-4.85	-7.02 -2.68	<0.001
SUA	0.48	0.39 0.56	<0.001	0.51	0.44 0.58	<0.001
Gender	-5.26	-8.18 -2.35	<0.001	-3.69	-5.93 -1.44	0.001
Age	-0.08	-0.23 0.06	0.241	-0.03	-0.13 0.08	0.639
Education	0.77	-2.06 3.59	0.594	0.98	-1.23 3.19	0.384
Depression	-0.11	-0.43 0.22	0.519	-0.03	-0.28 0.23	0.834
Emotional irritation	-0.04	-0.29 0.21	0.770	0.01	-0.18 0.20	0.919
Efforts	0.20	-0.43 0.83	0.537	0.30	-0.20 0.79	0.240
Rewards	-0.03	-0.40 0.33	0.856	0.00	-0.28 0.28	0.992

Note: SUA=standard units alcohol at baseline; CI=confidence interval; [a]=R², ΔR², and *P* values refer to the comparison of combined CWT vs. control; A negative score on the beta weight for condition indicates a lower consumption level in the guided and the combined intervention group compared to the control group. A negative score on the beta weight for gender indicates that females drink less than males. A positive score on the beta weight for education indicates that higher educated participants drink more than lower educated participants.

Secondary Outcome Analyses

The regression analysis showed that the combined intervention group was also significantly effective after 6 months, indicated by an adjusted lower mean SUA score of 5.7, compared to controls (95%-CI=-7.71 to -3.73, $P<0.001$). Analyzing the intervention effects at an individual level, we found that in the unguided and guided CWT group, n=52 (36%) and n=62 (43%) of the participants fell below the low-risk threshold at T2, respectively. The difference between both intervention groups was not significant ($\chi^2=1.948$, $P=0.185$). The combined intervention group yielded higher rates of response to the low-risk threshold at T2 ($\chi^2=14.00$, $P<0.001$; OR=2.39, 95%-CI: 1.51-3.77) and at T3 ($\chi^2=21.63$, $P<0.001$; OR=2.83, 1.82-4.38) than the control group (Figure 3).

The comparison of combined CWT with the controls revealed significant group effects on depression, stress, and anxiety (Table 5), with small effect sizes in terms of Cohen's d (Table 4). Significant effects were also found on emotional and cognitive irritation.
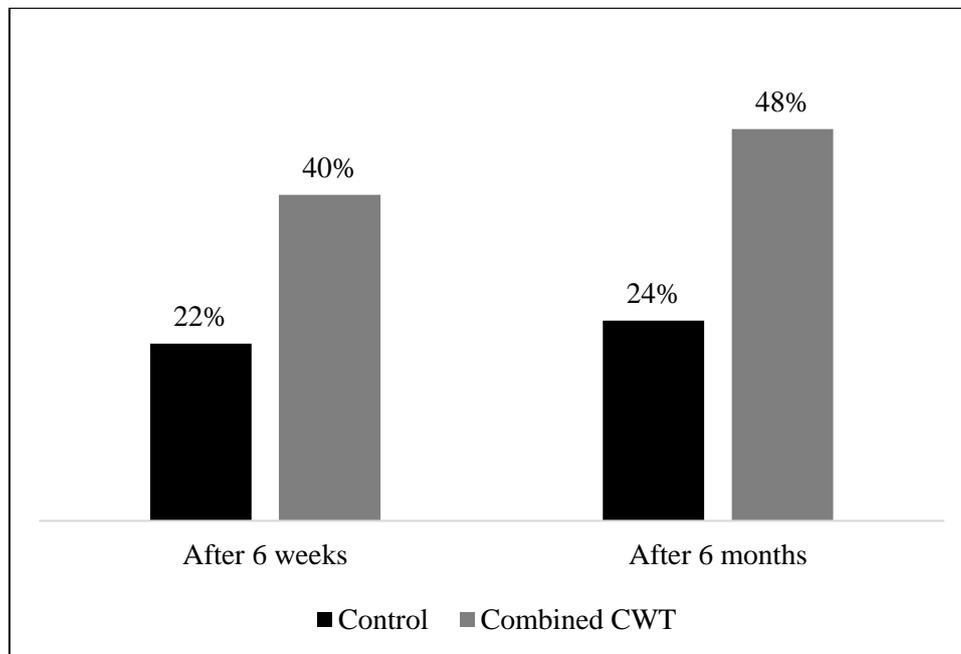
Figure 3 Participants complying with the low-risk guideline (< 21/14 standard units/week for men/women) after 6 weeks and 6 months. CWT = 'clever weniger trinken' (be smart - drink less)

Sensitivity Analyses

An analysis using baseline observation carried forward for missing data showed similar results like the main-analyses of the multiple imputed dataset. This was indicated by a significant small effect of combined CWT on the primary outcome (B=-3.99, 95% CI: -6.31 to -1.68, $P=0.001$, d=0.20), compared to controls. Detailed results of the sensitivity analyses for all continuous outcomes can be downloaded as supplemental file.

Table 4 Means, SDs and effect sizes on secondary outcomes.

Outcome	Baseline		6 weeks after baseline[a]					6 months after baseline[a]				
	M	SD	M	SD	d[b]	95% CI		M	SD	d[b]	95% CI	
Control (n=144)												
DASS-S	6.72	4.81	6.46	4.50				6.10	4.43			
DASS-D	4.60	4.50	4.69	4.43				4.60	4.27			
DASS-A	2.31	2.71	2.22	2.64				2.51	2.87			
IS-E	14.24	7.22	13.47	6.57				13.35	6.74			
IS-C	11.64	5.38	10.72	4.91				10.52	4.61			
Unguided CWT (n=146)												
DASS-S	7.33	4.67	5.10	3.73	0.33	0.10	0.56	5.00	4.00	0.26	0.03	0.49
DASS-D	5.17	4.71	3.77	4.12	0.22	-0.02	0.45	4.04	3.76	0.14	-0.09	0.37
DASS-A	2.42	2.97	1.63	2.28	0.24	0.01	0.47	2.04	2.53	0.18	-0.05	0.41
IS-E	15.66	6.89	12.26	5.67	0.20	-0.03	0.43	12.03	5.95	0.21	-0.02	0.44
IS-C	11.93	5.50	10.22	4.65	0.11	-0.12	0.34	9.53	4.64	0.21	-0.02	0.45
Guided CWT (n=142)												
DASS-S	6.64	4.80	5.13	3.40	0.33	0.10	0.57	4.39	2.92	0.46	0.22	0.69
DASS-D	4.96	4.73	3.30	3.10	0.36	0.13	0.60	3.43	3.30	0.31	0.08	0.54
DASS-A	1.90	2.42	1.20	1.73	0.46	0.22	0.69	1.51	1.60	0.43	0.20	0.67
IS-E	14.66	7.03	12.61	5.73	0.14	-0.09	0.37	11.58	5.39	0.29	0.06	0.52
IS-C	12.01	5.05	10.36	4.91	0.07	-0.16	0.30	9.00	4.17	0.35	0.11	0.58
Combined CWT (n=288)												
DASS-S	6.98	4.74	5.11	3.56	0.34	0.14	0.55	4.69	3.51	0.37	0.16	0.57
DASS-D	5.07	4.71	3.54	3.65	0.29	0.09	0.49	3.74	3.53	0.23	0.03	0.43
DASS-A	2.16	2.72	1.41	2.03	0.36	0.16	0.56	1.77	2.13	0.31	0.11	0.51
IS-E	15.16	6.96	12.43	5.69	0.17	-0.03	0.37	11.81	5.67	0.26	0.05	0.46
IS-C	12.00	5.28	10.29	4.77	0.09	-0.11	0.29	9.27	4.41	0.28	0.08	0.48

Note: DASS-S=Stress; DASS-D=Depression; DASS-A=Anxiety; IS-E=Emotional Irritation; IS-C=Cognitive Irritation; CI=confidence interval; [a]=Missing data handled by multiple imputation; [b]=effect size Cohen's d based on differences between the intervention and the control group.

**Table 5** Summarized results of secondary outcomes regression analyses for the combined intervention groups compared to the control group.

	Combined CWT vs. Control after 6 weeks				Combined CWT vs. Control after 6 months			
	B[a]	95% CI		P	B	95% CI		P
DASS-S	-1.48	-2.07	-0.90	<0.001	-1.54	-2.12	-0.97	<0.001
DASS-D	-1.40	-2.01	-0.78	<0.001	-1.11	-1.68	-0.54	<0.001
DASS-A	-0.74	-1.11	-0.36	<0.001	-0.65	-0.99	-0.31	<0.001
IS-E	-1.57	-2.45	-0.70	<0.001	-2.15	-2.93	-1.37	<0.001
IS-C	-0.67	-1.33	-0.02	0.045	-1.48	-2.07	-0.89	<0.001

Note: DASS-S=Stress; DASS-D=Depression; DASS-A=Anxiety; IS-E=Emotional Irritation; IS-C=Cognitive Irritation; [a]=group effect based on multiple regression model including condition and baseline score of the outcome as predictors; CI=confidence interval.

Discussion

In this study, we tested whether the web-based intervention "GET.ON Clever weniger trinken" is effective at reducing weekly standard units of alcohol in employees with problematic drinking. The study was designed around the concept that tailoring interventions to the needs of certain target groups — like employees — could enhance both their beneficial effects and reach. The intervention was effective, whether offered with or without guidance, at reducing weekly alcohol consumption. We detected a small effect of the intervention in terms of an average reduction of 4.9 SUA per week (d=0.30), relative to usual care, after six weeks. This effect was slightly higher than the average effect found in the latest published meta-analysis (g=0.20) [21]. Contrary to the results of recent meta-analyses, which failed to uncover any significant effects in the long-term [21] or at the most minimal significant effects (about 1 SUA/week) [23,50], our findings showed that the effects were sustained over time, indicated by a mean difference of 5.7 SUA/week, relative to care as usual at six months.

The direct comparison of the guided and unguided groups failed to reveal any significant differences in the quantity of self-reported SUA. This result corresponds to Blankers et al. [32], who detected similar advantages over standard care with an unguided intervention and the intervention plus chat therapy in a general population sample, without significant differences in effects between both interventions. Despite this, several points must be considered when interpreting our results. First, the intensity of guidance offered in this trial was relatively low [40], as it focused mainly on adherence promotion using standardized messages and only optional support in terms of feedback from eCoaches. Second, although the guided intervention group showed better adherence than the unguided group, which is consistent with previous reports [51], very few participants actually made use of this option and asked for feedback from their eCoaches. Concerns regarding fears of stigmatization and of giving up self-disclosure when asking for help might have caused this result, especially as these concerns may be significant barriers against the use of alcohol interventions [17,52]. An alternative explanation might be that the addition of guidance to a web-based alcohol intervention exerts no beneficial effect on drinking. Such an assumption is supported by recent meta-analytic findings that found web-based interventions with guidance not to be superior than unguided interventions for depression [53] and for anxiety disorders [54].

As alcohol-related problems are often closely associated with stress and depressive symptoms, the intervention included therapeutic techniques like problem solving and emotion regulation. These techniques are commonly employed in stress management or depression interventions. We identified small-size effects for the intervention, relative to usual care, on depression, stress, and anxiety at both follow-up appointments. Accordingly, it seems worthwhile to conduct further studies testing the incremental effect of transdiagnostic interventions compared to pure alcohol interventions [28].

The workplace is considered a good setting in which to deliver alcohol-related interventions [9], and work-related stress is associated with drinking behaviors [5,7,8,29]. Therefore, it was assumed

that a tailored, low-threshold intervention might be an attractive approach to supplement established health care services and increase the overall reach of alcohol-related interventions. That assumption was supported by the observation that the vast majority of employees in this study had never partaken in any occupational health services for alcohol-related problems before. However, it also must be noted that more than half of our subjects had received psychotherapy for some psychological disorder in the past. This rate is much higher than the public health service utilization rates usually found among people with alcohol-related problems [15,16].

However, effects on work-related outcomes were mixed. The intervention might help employees to find ways other than drinking to detach mentally from work-related problems, indicated by small effects on emotional irritation at both follow-ups. Hierarchical regression models analyzed in this study did not indicate that work-related mental health variables in terms of irritation or effort and rewards had meaningful predictive effects on weekly alcohol consumption. Thus, longitudinal studies are needed to have a closer look at moderators of alcohol intervention success in the working context.

Limitations

This study had several limitations. First, the actual sample size was smaller than the intended sample size. For pragmatic reasons, we recruited via announcements in print membership magazines of health insurance companies and on their websites. As a result of being one of the first web-based alcohol interventions in Germany, perhaps many lacked sufficient knowledge about the nature of such interventions. Low participation rates have been reported for other alcohol reduction approaches in various contexts [14], indicating that recruiting subjects can be challenging. However, it would have been beneficial to extend our impersonal recruiting strategy involving newspapers and the Internet, by collaborating closer with occupational health practitioners and other existing services. Health practitioners might be perceived as particularly trustworthy and, as such, their recommendations regarding study participation could have had a significantly positive effect on subject numbers. Second, the study was not intended nor powered to directly compare the effects between the guided and unguided groups. Therefore, any conclusions drawn about the two approaches' comparative efficacy should be made cautiously. Nonetheless, as this was one of the first studies to compare different intervention formats directly, our results should provide future investigators with invaluable information for power calculations and the design of appropriate studies like non-inferiority trials [55]. Third, because so few people actually made use of the guidance offered in this study, the generalizability of our findings regarding guidance is limited. One explanation for the low rate of guidance utilization could be the guidance format that we selected for this study, which was of very low intensity. Another explanation relates to fears regarding stigmatization [19] that might surface when participants think about interacting with eCoaches. One potential solution could be a more intensive, content-focused guidance format [40] combined with introduction videos about guidance

and the role of eCoaches in the intervention to increase acceptance [56]. Anyhow, the results of the intervention should only be generalized to situations where comparable recruiting strategies were employed and participants actively searched for help by their own. Lastly, due to feasibility and ethical reasons, participants in the control group were offered access to the intervention after a waiting time of six months. Such waiting conditions have been discussed as being potentially associated with a nocebo effect. Participants might be discouraged to initiate behavioral changes or seek otherwise help because they expect to get help after the waiting time. Hence, delayed treatment access control conditions might overestimate intervention effects [57].

CONCLUSIONS

In this study, we found the intervention "GET.ON Clever weniger trinken" to be effective at reducing weekly alcohol consumption, whether offered with or without additional guidance and support from eCoaches. Furthermore, the intervention led to significant reductions in subjects' depression, anxiety, general stress, and work-related irritation. The present sample seemed to be more willing to accept psychological help and to make use of the web-based intervention than traditional alcohol-related health services. These findings indicate that the intervention could be a promising approach to enhance established services for alcohol-related problems among employees. However, recruitment difficulties and the low use of guidance in this study highlight the need for innovative and effective strategies to increase the rate of intervention usage.

Randomized trial registration

This trial was registered at the German Register of Clinical Studies (DRKS): DRKS00006105, date of registration: 2014-07-07. All procedures involved in the study were consistent with the generally-accepted standards of ethical practice approved by the University of Lueneburg (Germany) ethics committee (No. Boss201404_OT).

Declaration of interests

Leuphana University, Lueneburg, has full exploitation rights for the University Lueneburg. However, DE, DL, and MB report holding shares of the Institute for Online Health Training, which aims to transfer scientific knowledge related to the present research into routine mental health care in Germany. This institute licenses the intervention under study at Leuphana University, Lueneburg, to provide the intervention within routine preventative services of health insurance companies in Germany. Having the foundation of such an institute to disseminate the findings and products from the research project was the primary aim of the European Union for funding the presented research. MB reports receiving research grants from the German Ministry of Research and the German Research Association and receiving personal fees from various institutions providing ongoing training for

psychotherapists. DE reports receiving funds from the European Union, German Ministry of Education and Research, as well as fees as scientific advisor from several companies such as Minddistrict Holding, Lantern Inc., BARMER, Techniker Krankenkasse.

Acknowledgements

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Supporting Information

Additional Supporting Information may be found online in the supporting information tab for this article.

Table S1 Means, standard deviations and effect sizes of all study groups on weekly standard units alcohol [imputation by baseline observation carried forward (BOCF)].

Table S2 Means, standard deviations and effect sizes of all study groups on secondary outcomes [imputation by baseline observation carried forward (BOCF)].

Table S3 Results of the primary outcome regression analyses [imputation by baseline observation carried forward (BOCF)].

Table S4 Summarized results of secondary outcomes regression analyses for the combined intervention groups compared to the ntrol group [imputation by baseline observation carried forward (BOCF)]

Table S1 Means, standard deviations and effect sizes of all study groups on weekly standard units alcohol [imputation by baseline observation carried forward (BOCF)]

	Baseline		Six weeks after baseline[a]					Six months after baseline[a]				
	M	SD	M	SD	d[b]	95% CI		M	SD	d[b]	95% CI	
Control (n=144)	28.99	13.38	26.59	13.72				25.85	15.38			
Unguided CWT (n=146)	30.26	16.11	24.05	16.56	0.17	-0.06	0.40	23.32	17.05	0.16	-0.07	0.39
Guided CWT (n=142)	29.44	17.68	22.72	16.58	0.25	0.02	0.49	22.85	15.67	0.19	-0.04	0.43
Combined CWT (n=288)	29.87	16.89	23.39	16.55	0.20	0.00	0.40	23.09	16.36	0.17	-0.03	0.37

Note: [a]=Missing data handled by baseline observation carried forward (BOCF); [b]=effect size Cohen's d based on differences between the intervention and the control group; CI=confidence interval.

Table S2 Means, standard deviations and effect sizes of all study groups on secondary outcomes [imputation by baseline observation carried forward (BOCF)].

	Baseline		Six weeks after baseline[a]					Six months after baseline[a]				
	M	SD	M	SD	d[b]	95% CI		M	SD	d[b]	95% CI	
Control (n=144)												
DASS-S	6.72	4.81	6.67	4.85				6.39	4.94			
DASS-D	4.60	4.50	4.85	4.64				4.69	4.58			
DASS-A	2.31	2.71	2.37	2.99				2.56	3.15			
IS-E	14.24	7.22	13.76	7.15				13.65	7.49			
IS-C	11.64	5.38	10.86	5.33				10.99	5.39			
Unguided CWT (n=146)												
DASS-S	7.33	4.67	5.72	4.37	0.21	-0.02	0.44	6.08	4.75	0.06	-0.17	0.29
DASS-D	5.17	4.71	4.31	4.71	0.12	-0.11	0.35	4.56	4.61	0.03	-0.20	0.26
DASS-A	2.42	2.97	1.86	2.75	0.18	-0.05	0.41	2.32	3.30	0.07	-0.16	0.30
IS-E	15.66	6.89	13.01	6.60	0.11	-0.12	0.34	13.63	7.44	0.00	-0.23	0.23
IS-C	11.93	5.50	10.65	5.28	0.04	-0.19	0.27	10.64	5.68	0.06	-0.17	0.29
Guided CWT (n=142)												
DASS-S	6.64	4.80	5.64	4.23	0.23	0.00	0.46	5.27	4.25	0.24	0.01	0.47
DASS-D	4.96	4.73	3.87	4.10	0.22	-0.01	0.46	3.90	4.42	0.17	-0.06	0.41
DASS-A	1.90	2.42	1.45	2.19	0.35	0.12	0.58	1.67	2.26	0.32	0.09	0.55
IS-E	14.66	7.03	13.19	6.75	0.08	-0.15	0.31	13.21	7.04	0.06	-0.17	0.29
IS-C	12.01	5.05	10.86	5.51	0.00	-0.23	0.23	10.46	5.38	0.10	-0.13	0.33
Combined CWT (n=288)												
DASS-S	6.98	4.74	5.68	4.29	0.22	0.02	0.42	5.68	4.52	0.15	-0.05	0.35
DASS-D	5.07	4.71	4.09	4.42	0.17	-0.03	0.37	4.23	4.52	0.10	-0.10	0.30
DASS-A	2.16	2.72	1.66	2.49	0.27	0.07	0.47	2.00	2.85	0.19	-0.01	0.39
IS-E	15.16	6.96	13.10	6.66	0.10	-0.10	0.30	13.42	7.23	0.03	-0.17	0.23
IS-C	12.00	5.28	10.76	5.39	0.02	-0.18	0.22	10.55	5.52	0.08	-0.12	0.28

Note: DASS-S=Stress; DASS-D=Depression; DASS-A=Anxiety; IS-E=Emotional Irritation; IS-C=Cognitive Irritation; [a]=Missing data handled by baseline observation carried forward (BOCF); [b]=effect size Cohen's d based on differences between the intervention and the control group; CI=confidence interval.

Table S3 Results of the primary outcome regression analyses [imputation by baseline observation carried forward (BOCF)].

	Guided vs. Unguided CWT after 6 weeks			Combined CWT vs. Control after 6 weeks		
	B	95% CI	P	B	95% CI	P
Model 1 ($\Delta R^2=0.009$)[a]						
Condition	-1.43	-5.29 2.42	0.465	-3.24	-6.39 -0.09	0.044
Model 2 ($\Delta R^2=0.456$, $P<0.001$)[a]						
Condition	-0.91	-3.81 1.99	0.537	-3.78	-6.10 -1.47	0.001
SUA	0.64	0.56 0.73	<0.001	0.67	0.60 0.74	<0.001
Model 3 ($\Delta R^2=0.014$, $P=0.011$)[a]						
Condition	-0.87	-3.73 1.98	0.547	-3.85	-6.15 -1.56	0.001
SUA	0.59	0.50 0.69	<0.001	0.63	0.56 0.71	<0.001
Gender	-5.31	-8.42 -2.19	0.001	-3.49	-5.87 -1.12	0.004
Age	-0.14	-0.30 0.01	0.063	-0.09	-0.20 0.02	0.110
Education	0.07	-2.93 3.07	0.965	-0.08	-2.40 2.23	0.945
Model 4 ($\Delta R^2=0.001$, $P=0.508$)[a]						
Condition	-0.87	-3.73 1.99	0.550	-3.89	-6.19 -1.59	0.001
SUA	0.59	0.50 0.69	<0.001	0.63	0.55 0.70	<0.001
Gender	-5.31	-8.44 -2.19	0.001	-3.55	-5.93 -1.17	0.004
Age	-0.14	-0.30 0.01	0.063	-0.09	-0.20 0.02	0.118
Education	0.07	-2.94 3.07	0.966	-0.11	-2.42 2.21	0.929
Depression	0.02	-0.29 0.32	0.923	0.08	-0.16 0.32	0.508
Model 5 ($\Delta R^2=0.004$, $P=0.465$)[a]						
Condition	-0.96	-3.84 1.91	0.511	-3.99	-6.31 -1.68	0.001
SUA	0.59	0.50 0.68	<0.001	0.63	0.56 0.71	<0.001
Gender	-5.56	-8.72 -2.40	0.001	-3.66	-6.06 -1.25	0.003
Age	-0.15	-0.31 0.00	0.053	-0.08	-0.20 0.03	0.151
Education	-0.33	-3.40 2.73	0.831	-0.26	-2.62 2.10	0.829
Depression	-0.01	-0.36 0.34	0.970	0.03	-0.24 0.30	0.822
Emotional irritation	-0.11	-0.39 0.16	0.412	-0.01	-0.21 0.19	0.903
Cognitive irritation	0.28	-0.06 0.62	0.106	0.13	-0.12 0.39	0.297
Efforts	0.18	-0.50 0.87	0.602	0.27	-0.26 0.80	0.317
Rewards	-0.02	-0.41 0.38	0.931	0.01	-0.29 0.31	0.947

Note: SUA=standard units alcohol at baseline; CI=confidence interval; [a]=R^2, ΔR^2, and P values refer to the comparison of combined CWT vs. control; A negative score on the beta weight for condition indicates a lower consumption level in the guided and the combined intervention group compared to the control group. A negative score on the beta weight for gender indicates that females drink less than males. A positive score on the beta weight for education indicates that higher educated participants drink more than lower educated participants.

Table S4 Summarized results of secondary outcomes regression analyses for the combined intervention groups compared to the control group [imputation by baseline observation carried forward (BOCF)]

	Combined CWT vs. Control after 6 weeks				Combined CWT vs. Control after 6 months			
	B$_a$	95% CI		P	B	95% CI		P
DASS-S	-1.18	-1.79	-0.56	<0.001	-0.91	-1.52	-0.31	0.003
DASS-D	-1.08	-1.72	-0.45	0.001	-0.82	-1.40	-0.23	0.006
DASS-A	-0.62	-1.01	-0.22	0.002	-0.43	-0.76	-0.10	0.010
IS-E	-1.29	-2.21	-0.36	0.006	-1.11	-1.93	-0.30	0.007
IS-C	-0.36	-1.05	-0.33	0.302	-0.70	-1.34	-0.06	0.031

Note: DASS-S=Stress; DASS-D=Depression; DASS-A=Anxiety; IS-E=Emotional Irritation; IS-C=Cognitive Irritation; [a]=group effect based on multiple regression model including condition and baseline score of the outcome as predictors; CI=confidence interval.

Kapitel 3 – E-Mental-Health zur Bewältigung von Depressionen

Versorgungssituation für Menschen mit Depression

Es existieren hoch wirksame psychotherapeutische [38–40] und pharmakologische [40,41] Maßnahmen zur Behandlung von Depressionen. Dementsprechend wird in der aktuellen S3-Leitlinie Unipolare Depression bei länger anhaltender leichter oder mittelgradiger depressiver Episode die Psychotherapie oder Psychopharmakotherapie als Behandlungsmethode empfohlen [42]. Die höchste Evidenz zur Wirksamkeit psychotherapeutischer Verfahren besteht für die kognitive Verhaltenstherapie (KVT) [38]. Zu den Behandlungszielen der KVT bei Depressionen gehören die Psychoedukation, die Schaffung einer Balance von angenehmen, verstärkenden Aktivitäten und aversiven Aktivitäten, die Steigerung positiv erlebter Erfahrungen, die Überwindung sozialer Defizite durch Verbesserung der interaktionellen Kompetenz, die Korrektur überzogener Ansprüche sowie der Aufbau differenzierenden Denkens [43]. Nichtsdestotrotz besteht eine große Versorgungslücke für Betroffene [22,44,45]. Ein Grund ist in der eingeschränkten Verfügbarkeit qualifizierter Therapeuten zu sehen [46]. Diejenigen, die aktiv nach Hilfe suchen, haben bis zum Behandlungsbeginn oft lange Wartezeiten zu überbrücken [44,47]. Aber selbst, wenn Therapieangebote vorhanden sind, werden diese nicht immer in Anspruch genommen. Eine Hürde scheint auch darin zu bestehen, die Zeit für eine entsprechende Therapieteilnahme unter Alltagsbedingungen aufzubringen [46]. Dies trifft vor allem auf Betroffene zu, die trotz Einschränkungen ihrer Leistungsfähigkeit noch voll berufstätig sind. Weitere Barrieren der Inanspruchnahme vorhandener Hilfsangebote sind erwartete negative (soziale) Konsequenzen bei Inanspruchnahme entsprechender Angebote (u. a. Stigmatisierungsangst), ein als gering eingeschätzter Behandlungsbedarf vieler Betroffener sowie eine erhöhte Neigung zu Selbsthilfeverhalten [48]. Ein weiteres Problem besteht in den hohen Abbruchraten von Therapieangeboten, die sich sowohl im Forschungskontext [49,50] als auch in der klinischen Praxis [51] zeigen.

Entwicklung und Evaluation von GET.ON Mood Enhancer

Für keinen anderen Bereich psychischer Erkrankungen liegen so viele Wirksamkeitsnachweise zu internetbasierten Interventionen vor wie für depressive Beschwerden. Internetbasierte Interventionen zeigen sich, zumindest im Forschungskontext, in der Reduktion depressiver Beschwerden ähnlich effektiv wie die Psychotherapie [52]. In der Vergangenheit erwiesen sich solche Interventionen, die durch ein persönliches Online-Coaching ergänzt wurden (guided interventions), tendenziell wirksamer als reine Selbsthilfe-Interventionen (unguided interventions) [28,53,54]. Allerdings wurden bislang selten beide Interventionsformate direkt miteinander verglichen [35]. Subgruppenanalysen legen vielmehr nahe, dass sich gefundene Wirksamkeitsunterschiede wenigstens zum Teil durch die jeweils gewählte Kontrollbedingung erklären lassen [28]. Vor allem bei Verwendung von Wartekontrollgruppen könnten Interventionseffekte überschätzt werden [55]. Während in der

Vergangenheit die meisten Interventionen mit Wartegruppen verglichen wurden, existieren nur wenige Studien mit aktiven Kontrollgruppen (z. B. Psychoedukation) [56]. Zurückliegende Studien wiesen darauf hin, dass schon die bloße Psychoedukation helfen kann, depressive Beschwerden zu lindern [56].

In jedem Fall besteht ein dringender Forschungsbedarf hinsichtlich der vergleichenden Wirksamkeit internetbasierter Depressionsinterventionen und internetbasierter Psychoedukation. Daneben findet ein weiterer Aspekt in der Wirksamkeitsuntersuchung internetbasierter Interventionen zu wenig Berücksichtigung. Während es bei neuen medikamentösen Behandlungen selbstverständlich ist, mögliche Nebenwirkungen zu untersuchen, fehlen entsprechende Untersuchungen bei internetbasierten Interventionen weitgehend. Dementsprechend wurden im Rahmen der Dissertation auch negative Effekte internetbasierter Interventionen bei Depression analysiert.

Aufgrund des in Deutschland relativ neuen Interventionsansatzes wurde zu Beginn eines von der EU geförderten Forschungsprojekts (GesundheitsTrainings.Online des Innovations-Inkubators Lüneburg; EFRE: CCI2007DE161PR001), aus dem die vorliegende Arbeit entstand, eine Pilotstudie durchgeführt [57]. Die Pilotstudie diente dem Zweck, die in Kooperation mit dem Projektpartner Minddistrict GmbH entwickelte Trainingsplattform zu erproben und erste Wirksamkeitshinweise in Deutschland zu untersuchen. In der Studie wurde die Wirksamkeit eines internetbasierten Problemlösetrainings zur Reduktion depressiver Beschwerden unter LehrerInnen untersucht. Dabei zeigte sich in der Trainingsgruppe eine signifikante Reduktion der Beschwerden im Vergleich zu LehrerInnen in einer Wartekontrollgruppe. Um dem zuvor skizzierten Forschungsbedarf zum Einsatz internetbasierter Interventionen zur Bewältigung von Depressionen zu begegnen, werden in dieser Arbeit die nachfolgenden weiteren Fragestellungen bearbeitet:

Fragestellung 3: Wie lässt sich ein kurzes Online-Training zur Bewältigung von Depressionen entwickeln und dessen Wirksamkeit evaluieren?

Ziel war es, ein kurzes internetbasiertes Training namens GET.ON Mood Enhancer zu entwickeln, um Erwachsene mit akuter depressiver Episode (Major Depressive Disorder, MDD) bei der Bewältigung der Depression zu unterstützen. Um die Wirksamkeit des Trainings adäquat untersuchen zu können, wurde ein Studiendesign entwickelt, mit dem sowohl positive als auch potenziell negative Wirkungen des Trainings beurteilt werden können.

Fragestellung 4: Führt ein Online-Depressionsbewältigungstraining zu einer signifikant stärkeren Reduktion depressiver Beschwerden als reine Psychoedukation?

Im Rahmen einer zweiarmigen randomisiert-kontrollierten Studie (Studie II) wurde das Training GET.ON Mood Enhancer bei erwachsenen Personen mit depressiver Episode evaluiert. Die Studienteilnehmenden in Gruppe 1 erhielten Zugang zum Online-Training und ein wöchentliches

Feedback durch einen Online-Coach. Die Studienteilnehmenden in Gruppe 2 erhielten Zugang zu einem kurzen psychoedukativen Online-Modul auf Basis der aktuellen S3-Behandlungsleitlinie für unipolare Depressionen. Primäres Zielkriterium der Evaluation war die Reduktion der depressiven Symptomatik sechs Wochen nach Trainingsbeginn im Vergleich zu reiner Psychoedukation. Es wurde angenommen, dass das Online-Training zu einer signifikant stärkeren Reduktion der depressiven Beschwerden führt als die Online-Psychoedukation. Sekundäre Zielkriterien umfassten weitere depressionsspezifische Parameter sowie potenzielle negative Nebenwirkungen durch das Training. Es wurde angenommen, dass das Online-Training im Vergleich zu reiner Online-Psychoedukation zu keinen unerwünschten Nebenwirkungen führt.

Das Manuskript, „GET.ON Mood Enhancer: efficacy of Internet-based guided self-help compared to psychoeducation for depression: an investigator-blinded randomised controlled trial", ist das Studienprotokoll, das die Entwicklung der Intervention GET.ON Mood Enhancer sowie das geplante Design beschreibt, mit dem die Wirksamkeit der Intervention bei Erwachsenen mit Depression untersucht werden sollte. Im Manuskript, „The more I got, the less I need? Efficacy of Internet-based guided self-help compared to online psychoeducation for Major Depressive Disorder", werden die Ergebnisse der Wirksamkeitsuntersuchung dargestellt.

Manuskript 3 – Studienprotokoll GET.ON Mood Enhancer

Abstract

Background: Major depressive disorder (MDD) imposes a considerable disease burden on individuals and societies. A large number of randomised controlled trials (RCTs) have shown the efficacy of Internet-based guided self-help interventions in reducing symptoms of depression. However, study quality varies considerably. The aim of this study is to evaluate the efficacy of a new Internet-based guided self-help intervention (GET.ON Mood Enhancer) compared to online-based psychoeducation in an investigator-blinded RCT.

Methods/design: A RCT will be conducted to compare the efficacy of GET.ON Mood Enhancer with an active control condition receiving online psychoeducation on depression (OPD). Both treatment groups will have full access to treatment as usual. Adults with MDD (n = 128) will be recruited and randomised to one of the two conditions. Primary outcome will be observer-rated depressive symptoms (HRSD-24) by independent assessors blind to treatment conditions. Secondary outcomes include changes in self-reported depressive symptom severity, anxiety and quality of life. Additionally, potential negative effects of the treatments will systematically be evaluated on several dimensions (for example, symptom deteriorations, attitudes toward seeking psychological help, relationships and stigmatisation). Assessments will take place at baseline, 6 and 12 weeks after randomisation.

Discussion: This study evaluates a new Internet-based guided self-help intervention for depression using an active control condition (psychoeducation-control) and an independent, blinded outcome evaluation. This study will further enhance the evidence for Internet-based guided self-help interventions for MDD. Trial registration: German Clinical Trial Registration (DRKS): DRKS00005025

Keywords: Guided self-help, Internet-based, Major depressive disorder, Randomised controlled trial, Negative effects of psychotherapy, Active control

Background

Major depressive disorder (MDD) is one of the most prevalent psychiatric disorders with a lifetime prevalence of more than 16% [1-3]. Moreover, MDD is related to a considerable quality of life decrement [4,5], increased mortality rates [6], and substantial economic costs [7-9]. Currently, MDD ranks as the fourth disorder with the highest disease burden and is projected to be the leading cause of disability in high-income countries by 2030 [10].

Although there is ample evidence for the effectiveness of psychotherapy in the treatment of depression [11,12], many individuals remain untreated [13]. People who could particularly benefit from treatment disregard treatment for several reasons including a lack of knowledge of what to do, prohibitive costs, anticipated negative (social) consequences or preference for self-help [14]. Moreover, those seeking help hardly receive immediate access to evidence-based treatment because of long waiting lists for psychotherapeutic treatment [14,15]. Limited availability of clinicians, geographical inaccessibility and difficulties to 'attend therapy during usual business hours' are further barriers.

Using the Internet to provide guided self-help interventions may help to overcome some of the limitations of traditional treatment services. Internet-based guided selfhelp strategies have several advantages over face-to-face approaches. These include: (1) interventions are more easily accessible at any time and place; (2) anonymity is assured when patients want to avoid stigmatisation; (3) a greater potential for the integration of acquired skills in daily life exists because of an emphasis on the participants' active role in (guided) self-help interventions [16]; (4) participants can work at their own pace and go through materials as often as they want; (5) travel time and costs for both participants and clinicians are eliminated; (6) Internet-based interventions may attract people who do not (want to) make use of traditional mental health services [17]; and (7), Internet-based interventions are easily scalable, implying that only a small increase of therapeutic resources is required for reaching a greater proportion of the eligible population using these interventions.

Accumulating empirical evidence suggests that Internet-based interventions are well-accepted by participants [18] and effective in the treatment of MDD [19], subthreshold depression [20] and as maintenance treatment [21]. A systematic review of 19 randomised controlled trials (RCTs) evaluating Internet-based interventions for symptoms of depression in 2,996 individuals [19] found a mean effect size of d = 0.56. Interventions including at least some guidance by a clinician were more effective (d = 0.78) than interventions without guidance (d = 0.36). Cuijpers (2010) showed that guided self-help interventions for depression (and anxiety disorders) could have comparable effects to traditional face-to-face therapy even when they are directly compared to each other [22].

However, a recent methodological analysis of 75 RCTs of computer- and Internet-based interventions for psychiatric disorders [23] criticised the mean methodological quality of published trials in the field as rather low. They criticised, for example, that many studies used weak control

conditions (that is, wait-list control), that most studies relied solely on participants' self-report, and that they failed to include an independent assessment such as blind ratings or biological indicators. Moreover, they found that low overall methodological quality scores were associated with higher reported effect sizes. In fact, the latest systematic review in the field on Internet-based treatments for depression [19] did not include any study that used an independent outcome assessment by assessors blind to the treatment condition. Moreover, half of the included studies used a wait-list control-only comparison. To the best of our knowledge no study on Internet-based treatment for major depression published so far, has applied an independent, blinded outcome evaluation.

Another important issue not adequately addressed to date is the potential negative effects of Internet-based treatments for depression. One particularly unfavourable outcome of psychotherapy is deterioration of symptoms during treatment. However, RCTs evaluating psychological treatments seldom report the number of patients who had deteriorated while being treated [24]. Critics of Internet-based treatments have often emphasised that treatment might be provided that is less intensive than required to treat severely affected or symptomatic individuals [23]. This inadequate treatment allocation may result in less treatment expectations for psychotherapy in general and discourage individuals from seeking more intensive treatment. Hence, not only is there a pressing need for research on potential adverse events of psychotherapy in general [24] but also specifically for Internet-based treatments.

Objective and research questions

The aim of this study is to evaluate the efficacy of a newly developed guided self-help Internet-based intervention (GET.ON Mood Enhancer) compared to an online psychoeducation on depression (OPD).

We expect that observer-rated depressive symptomatology assessed by raters blind to treatment conditions will be reduced to a greater extent in the intervention group than in the control condition. Moreover, we hypothesise that GET.ON Mood Enhancer is superior in terms of self-reported depressive symptoms, wellbeing, quality of life, symptoms of anxiety and problem-solving skills compared to the OPD-control condition. Potential negative effects with regard to (1) numbers of patients with symptom deteriorations, (2) attitudes towards seeking psychological help, and (3) other adverse events will be systematically evaluated. We hypothesise that both treatment conditions will not have a negative effect on attitudes towards seeking psychological help.

Methods/design

Design

A two-arm RCT will be conducted to compare GET.ON Mood Enhancer with an online psychoeducation on depression (OPD) condition. Both treatment arms will have full access to treatment as usual. Assessments will take place at baseline (T1), post-treatment (6 weeks, T2) and 12-week follow-up (T3; see Figure 1 for a detailed overview of assessments). All procedures involved in the study will be consistent with the generally accepted standards of ethical practice approved by the University of Marburg ethics committee (No. 2013–08 K). The trial is registered in the German clinical trials register under DRKS00005025.
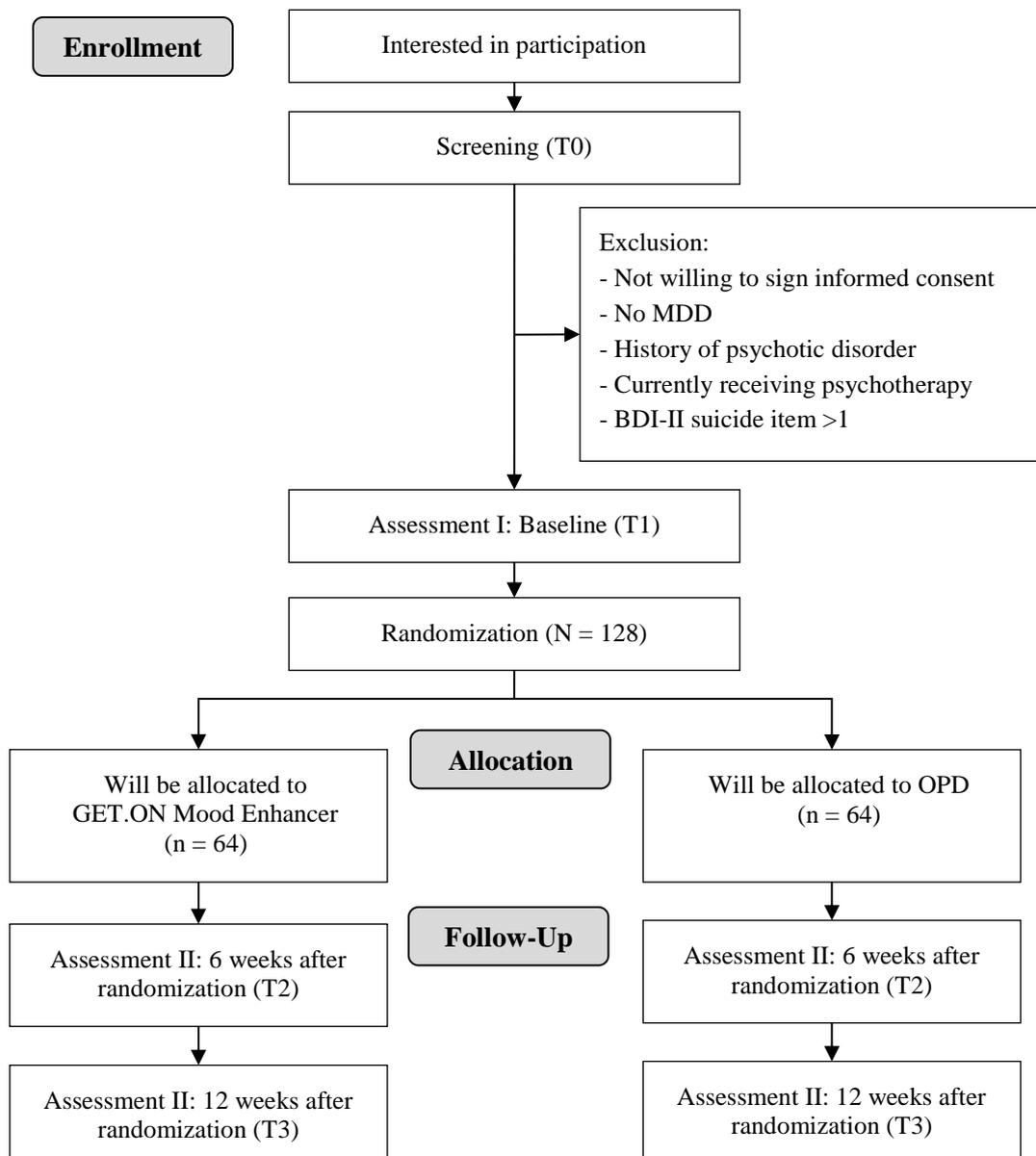
Figure 1 Study flow.

Trial status

By the time of submission, recruitment for the trial was still ongoing. Recruitment started in June 2013 and will approximately last until February 2014.

Participants and procedure

Inclusion and exclusion criteria

We will include adults (1) above the age of 18 years (2) with MDD according to DSM-5 criteria (3) who have Internet access, (4) have sufficient German skills in reading and writing (self-report), and (5) are willing to give informed consent. We will exclude subjects (1) with a history of manic/ hypomanic episodes, (2) with a history of psychotic disorders, (3) currently receiving psychotherapy for any kind of mental health problems, (4) showing a notable suicidal risk as indicated by a score greater than 1 on BDI Item 9 ('I feel I would be better off dead'), or (5) a change in antidepressive medication dosage/drug within 4 weeks before baseline.

Recruitment

Participants will be recruited via the GET.ON research website [25] that is announced in newspapers, on-air media and related websites. The research website provides information about the GET.ON Mood Enhancer training and details about another study evaluating GET.ON Mood Enhancer in a sample with subthreshold depression (Trial registration: DRKS00004709, [26]). Those participants who do fulfil criteria for a MDD are excluded from that study, and instead offered to participate in this trial.

Assessment of eligibility and randomisation

People who apply for study participation will receive an information letter with detailed information about the study procedures. Full written informed consent will be obtained from all participants. They will be informed that they can withdraw from the intervention and/or study at any time without any negative consequences. Nevertheless, we will ask those who withdraw from the trial treatment to attend all the remaining research appointments or at least provide minimal data (primary outcome measure). Applicants who continue to participate in the study will be asked to complete online screening questionnaires to assess the severity of their depressive symptoms (CES-D >16), whether they are currently receiving any kind of treatment for any mental health disease and whether they have a high suicidal risk (BDI Item 9 > 1). Subjects screened positive and are willing to give informed consent will be scheduled for a structured clinical interview (SCID) conducted via the telephone [27]. SCIDs will be conducted by trained clinicians. Participants meeting all of the inclusion and none of the exclusion criteria, who have completed the baseline assessment, and returned the informed consent form will enter the study and will be randomly allocated to study conditions. Randomisation will take

place at an individual level. The allocation will be performed by an independent researcher not otherwise involved in the study using an automated computer-based random integer generator (randlist). The allocation will be concealed in advance from participants, researchers involved in recruitment, and therapists.

Assessments

Self-report and observer-rated assessments will take place at baseline, post-intervention and 12-week follow-up. See Figure 1 for a detailed overview. Self-report data will be collected using a secured online-based assessment system (AES, 256-bit encrypted), and observer-based assessments will be conducted via the telephone by trained interviewers. Observer-rated assessments will be recorded to examine inter-rater reliability. In case of disagreement, the two raters will discuss until a consensus is formed, and the agreed rating will be used for analysis. If no agreement is reached after discussion, the assessment will be rated by an experienced diagnostic-rater (gold standard), and this rating will be used for analysis.

Blinding

The research staff conducting the observer-based rating of depressive symptoms will be blinded to the condition the participants are assigned to. Considerable effort is undertaken to ensure blindness, including (1) an explanation to the participants why it is important not to inform the interviewer about the condition they were assigned to, (2) a written reminder in the interview manual for the interviewer to ask the participant not to mention anything about their randomisation status, (3) verbal reminders to the patient before the interview, and (4) a documentation after the assessment of whether or not the interviewer is still blind to the treatment condition. In the event of a blind violation, the interviewer will be changed to the following assessment. Participants know about the content of both conditions, but are blinded with regard to which intervention is the experimental and which the control condition.

Intervention

GET.ON Mood Enhancer

GET.ON Mood Enhancer is a brief intervention consisting of six lessons with modules concerning psychoeducation, behavioral activation (BA), problem solving (PS) and relapse prevention. Additionally, participants are offered four modules that can be chosen based on individual need and/ or preference. Additional modules are directed at sleep problems, relaxation techniques and dealing with worrying thoughts (see Table 1 for a session overview). Lessons consist of text, exercises and testimonials and also include interactive elements such as audio and video clips. A strong focus of the intervention lies on transfer tasks (homework assignments) to integrate newly acquired strategies and techniques into daily life. In the beginning of each subsequent lesson, participants are invited to reflect

on their experiences with the newly acquired skills. The training is adaptive as the content is tailored to the specific needs of the individual participant by continuously asking participants to respond by choosing among various response options. Subsequent content is then tailored to the participant's response. Using responsive web design, participants can follow the program on the Internet, a tablet or mobile phone. An integrated read-aloud function allows participants to follow narrated lessons. Participants are advised to complete at least one but preferably two lessons per week, because a previous meta-regression analysis about the role of treatment intensity for treatment outcome in the treatment of depression indicated that more frequent therapy sessions might be associated with a better outcome compared to a lower frequency of sessions [28]. Consequently, the training lasts about 3 to 6 weeks. We decided that we will not include more modules, because (1) a recent meta-analysis [19] found that web-based interventions for depression including more than seven modules were less effective (d = 0.36) than interventions with seven or less modules (d = 0 .75), and (2) we want to lower the threshold for individuals as much as possible. In terms of a stepped-care model participants will be encouraged to seek more intensive help in routine mental health services, if their progress is not sufficient at the end of the intervention. During the last treatment session, they will be provided with information about evidence-based treatments in routine mental healthcare and how to obtain access to it.

The main modules used in GET.ON Mood Enhancer are based on evidence-based face-to-face manuals that have been found to be effective in the treatment of depression, such as behaviour therapy (BT) [29] and problem-solving therapy (PST) [30]. In BT, a strong focus rests on daily pleasurable activity scheduling that is integrated in each lesson. The PST elements implemented in GET.ON Mood Enhancer have been used in various web-based interventions, such as the Dutch web-based 'Alles onder Controle' course, which has been shown to be effective in reducing depressive symptomatology across several RCTs [31,32].

During the training, participants will be supported by an online therapist. Every participant will be assigned to one therapist for the duration of the study. The total time a therapist spends on a participant will be approximately 2 to 3 hours. Guidance is provided by psychotherapists in training supervised by an experienced clinician. Participants will communicate with their therapist through the internal messaging function of the system on which GET. ON Mood Enhancer is implemented. The guidance is mainly based on the supportive-accountability model of providing guidance in Internet-based interventions [33]. In the current study, the purpose of the guidance will be to support participants to adhere to the treatment modules, and therapists will not teach therapeutic techniques beyond techniques used in the treatment modules. All feedback from therapists is stored for supervision and adherence checks.

Table 1 Overview of GET.ON Mood Enhancer lessons

Session	Topic	Content
1	Psychoeducation	•Information about symptoms, causes and types of depression •Role of motivation •Introduction of the mood and activity diary
2	Behavioural activation (BA) I	•Relationship between activities and depression •Introduction of daily activity scheduling
3	Behavioural activation (BA) II	•Reflection on experiences with newly acquired skills and on activities/behaviour that might have influenced the mood (from now on in every session at the beginning) •Coping with difficulties with regard to daily activity scheduling •Goal setting for the upcoming days •Additional: sleeping problems
4	Problem-solving techniques (PST) I	•BA: reflection of goal attainment and goal setting for the upcoming days •PST: distinction between solvable and unsolvable problems •PST: introduction of 6-step PST procedure: (1) defining the problem, (2) defining the goal, (3) brainstorming about possible solutions and choosing the best one, (4) making a plan how to implement this solution, (5) putting the solution into practice, and (6) evaluating the outcome. •PST: choosing one personal problem, filling out steps 1 to 4, step 5 as homework
5	Problem-solving techniques (PST) II	•BA: reflection of goal attainment and goal setting for the upcoming days •PST: deepening the 6-step procedure: step 6 of the 6-step procedure: evaluating outcome; depending on the evaluation: coping with difficulties, revising steps 1 to 4 or choosing another problem •Additional: stop-worrying techniques
6	Relapse prevention	•BA: reflection goal attainment and goal setting for the future •PST: step 6 of the 6-step procedure: evaluating outcome •Evaluation: summarising gains and learned strategies •Developing an individual relapse prevention plan •Information about further healthcare services

Psychoeducation on depression condition (OPD)

The OPD intervention is also Internet-based and is implemented on the same platform as GET.ON Mood Enhancer. In the current study, the psychoeducational intervention is based on the patient version of the German S3-Guideline/ National Disease Management Guideline Unipolar Depression [34]. It informs participants about the nature and evidence-based treatments of depression including information about symptoms, strategies to overcome depression and sources of help. In this study, the psychoeducational intervention requires no explicit homework assignments from the participants and provides no therapist support. Passive psychoeducational interventions have been shown to be effective in reducing depressive symptoms with a pooled standardised effect size of d = 0.26 [35].

Treatment as usual

There will be no restriction on the use of treatment as usual in routine mental health services during the study period, such as psychotherapeutic and psychiatric treatment or antidepressant medication. However, to control for potential confounding effects, treatment utilisation and changes in the dosage of antidepressant medication intake will be monitored during the study period.

Primary and secondary outcomes

The primary outcome will be observer-rated depression severity. In the secondary analyses, we will explore the effects of the treatments on self-reported depression severity, wellbeing, anxiety symptoms, quality of life and the number of patients who (1) responded and (2) are in remission. Moreover, we will also systematically evaluate potential negative treatment effects (that is, symptom deteriorations, negative effects on attitudes towards seeking psychological help; other adverse events).

Measures

Primary outcome

The primary outcome will be observer-based rating of depressive symptom severity measured by the Hamilton Rating Scale for Depression HRSD-24 [36-38]. The HRSD is likely to be the most widely used clinician-rated scale for measuring depression in research. The self-report measure assesses depressed mood, vegetative and cognitive symptoms of depression, and anxiety symptoms. Items are rated on either a 5-point or a 3-point scale, and the total score is derived by summing the individual item scores. Higher scores indicate greater symptom severity. The HRSD is sensitive to change, inter-rater reliability is 0.90 [36], and the scale corresponds well with overall clinical ratings of severity [39,40]. The cutoff points of 10, 19, 27 and 35 represent the threshold for mild, moderate, severe and very severe depression, respectively.

Secondary outcomes

Depressive symptoms As the secondary outcome, observer-based rating of depression will also be measured using the Quick Inventory of Depressive Symptomatology - Clinician-Rating QIDS-CR16 [41,42]. The 16-item QIDS-CR16 is a brief clinician-report rating scale developed from the 30-item Inventory of Depressive Symptomatology [41-43]. In contrast to the HRSD, it evaluates only the nine depression criterion symptom domains (that is, sad mood, concentration, self-criticism, suicidal ideation, interest/involvement, energy/fatigability, sleep disturbance, appetite/weight change and psychomotor agitation/retardation) from the Diagnostic and Statistical Manual of Mental Disorders [44] during the prior 7 days. Each item is scored on a scale from 0 to 3 points, with higher scores indicating higher symptom severity. This measure has shown good psychometric properties, such as strong internal consistency ($\alpha = 0.85$), concurrent validity and sensitivity to symptom change in

patients with MDD [42]. The cutoff points of 6, 11, 16 and 21 represent the threshold for mild, moderate, severe and very severe depression, respectively. Self-reported depressive symptoms will be assessed with the Patient Health Questionnaire (PHQ-9). This measure has comparable sensitivity and specificity to many other depression measures, although it is only half the length. Its internal reliability reaches values between $\alpha = 0.86$ and 0.89 [45,46]. Each item assesses the frequency of a symptom in the last 2 weeks on a scale ranging from 0 ('not at all') to 3 ('nearly every day'). In contrast to the primary outcome measure HRSD-24, the PHQ-9 only assesses frequency of symptoms, not their intensity. The total score ranges from 0 to 27, with a higher score indicating more frequent symptoms. The cutoff points of 5, 10, 15 and 20 represent the threshold for mild, moderate, moderately severe and severe depression, respectively [45,46].

Quality of life Health-related quality of life will be assessed with the SF-12v1 Health Survey [47]. The SF12v1 has 12 items covering eight health domains (physical functioning, physical and emotional role functioning, body pain, general health, vitality, social functioning and mental health). The SF-12 generates a physical and a mental health summary score.

Anxiety Anxiety will be measured with the anxiety subscale of the Hospital Anxiety and Depression Scale HADS-A [48]. The anxiety subscale consists of seven questions and each is scored from 0 to 3 with total scores ranging from 0 to 21. A score between 0 and 7 indicates no anxiety, between 8 and 10 possible anxiety, and above 11 or 12 a clinical anxiety disorder. Psychometric properties are well established [49].

Problem-solving skills Problem-solving ability (that is, generalised appraisal, beliefs, expectancies and emotional responses) will be measured with two subscales of the Social Problem-Solving Inventory-Revised (SPSI-R). The positive problem orientation (PPO) subscale represents a constructive dimension, and the negative problem orientation (NPO) subscale is viewed as a dysfunctional dimension. Cronbach's alphas are $\alpha = 0.76$ for the PPO dimension and 0.83 for the NPO dimension [50].

Behavioural activation Participants' activation towards goals or values and pleasant activities and avoidance behaviours will be measured with the BADS-Short Form BADS-SF [51]. The BADS-SF entails nine items comprising two subscales (activation and avoidance). The items are rated on a 7-point Likert-type scale. Higher scores indicate that the participant scores high on the area of interest. The internal consistency is $\alpha = 0.82$ [51].

Wellbeing Psychological wellbeing will be measured by the World Health Organization's (WHO) 5 Wellbeing Index [52]. Participants indicate for each of the five statements, which one is closest to how they have been feeling over the prior 2 weeks. Each question is scored from 0 to 5 with the total score ranging from 0 to 25. Higher scores indicate better wellbeing.

Problematic alcohol use The Alcohol Use Disorders Identification Test (AUDIT) is a 10-item questionnaire designed by the WHO to screen for hazardous alcohol intake. It assess three conceptual domains: alcohol intake (items 1 to 3), dependence (items 4 to 6) and adverse consequences (items 7 to 10). Sum-scores can range from 0 to 40, and the generally accepted cutoff point for identifying a potential alcohol problem is 8 [53].

Treatment credibility/patient expectancy Training credibility and participants' expectancy for improvement will be measured with the credibility and expectation questionnaire (CEQ). The CEQ consists of six items which are rated on a 9- or sometimes 10-point Likert scale. The psychometric properties of the instrument are well established [54].

Course evaluation In absence of a standardised measure for evaluating course satisfaction in Internet-based treatments, user satisfaction will be measured with a selfdesigned questionnaire based on the Client Satisfaction Questionnaire CSQ-8, German Version [55,56]. This selfreport measure consists of eight items measuring the global client satisfaction with the Internet-based training. Previous research indicated a high internal consistency [57].

Response and remission Participants will be coded as responders when they demonstrate a reliable change according to the widely used reliable change index (RCI) [58]. Participants with an RCI of 1.96 or above on the primary outcome measure HRSD-24 will be considered responders. Remission is defined a priori as a nonpathological score of ≤10 on the HRSD-24.

Negative effects Negative effects will be measured on (1) symptom deterioration during treatment (2), attitudes towards seeking psychological help, and (3) other adverse events.

(1) Symptom deteriorations

Patients will be classified as deteriorated when they display a reliable negative change (−1.96) in the primary outcome measure HRSD-24 according to the reliable change index, proposed by Jacobsen & Truax (1991) [58].

(2) Negative effects on attitudes towards seeking professional psychological help

A potential negative influence on attitudes towards seeking mental healthcare service utilisation will be measured with the Attitudes Toward Seeking Professional Psychological Help Scale-SF ATSPPH-SF [59]. The ATSPPH-SF consists of 10 items that are rated on a 4-point Likert scale from 0 to 3, yielding a total score ranging from 0 to 30. High scores indicate more positive treatment attitudes. The instrument showed good psychometric properties [60].

Other adverse events Other adverse events will be measured with the negative effects of psychotherapy inventory (INEP). The INEP is a relatively new measure and was developed for assessing systematic and potentially negative effects of psychotherapeutic interventions in different

domains. The version used in this study consists of 15 items assessing any negative effects participants experienced within or after the completion of the Internet-based training on (1) negative intrapersonal changes (for example, 'During treatment or since the end of my therapy, I suffered from suicidal thoughts or intentions for the first time ever'), (2) negative effects in an intimate relationship (for example, 'My partner is or has been jealous of my therapist'), (3) family/friends (for example, 'The relationships with my friends has worsened'), (4) perceived dependence on the psychotherapist/psychotherapeutic intervention (for example, 'I feel dependent on my therapist'), and (5) stigmatisation (for example, 'I am anxious that my colleagues or friends could find out about my psychotherapy'). The items are rated on a 4-point Likert scale (0 = no agreement at all; 3 = total agreement). Chronbach's alpha is $\alpha = 0.85$ (Table 2).

Table 2 Overview of measurements

| Instrument | Aim | Time of measurement | | |
		T1 (Baseline)	T2 (6 weeks)	T3 (12 weeks)
SCID	Diagnostic interview	x		
HRSD$_{24}$	Hamilton Rating Scale for Depression	x	x	x
QIDS-C$_{16}$	Quick Inventory for Depressive Symptomatology	x	x	x
PHQ-9	Depressive symptomatology	x	x	x
WHO-5	Wellbeing	x	x	x
SF-12	Quality of life	x	x	x
HADS-A	Anxiety symptoms	x	x	x
SPSI-R	Problem-solving skills	x	x	x
BADS-SF	Behavioural activation	x	x	x
CEQ	Patient expectancy/treatment credibility	x		
ATSPPH-SF	Attitudes toward seeking psychological help	x	x	
BFI	Big Five Inventory	x		
INEP	Inventory of negative effects in psychotherapy		x	x
CSQ-8	Clients' satisfaction with the online training		x	
AUDIT	Alcohol use disorder identification test	x		
Other questions	Socio-demographics	x		

Sample size calculation

We aim to include 128 participants. This sample will allow us to detect a between-group effect size (ES) of d = 0.50 with a power (1-ß) of 80% and an alpha of 0.05 (calculated using PASS 12). The most recent meta-analytic review found a mean ES of d = 0.78 for therapist-supported web-based interventions for depression [19]. However, most of the included studies used a waiting-list control comparison only, and these studies showed a considerably larger ES than those studies including a treatment-as-usual condition. Our comparison condition will include psychoeducation and full access to treatment as usual and participants are encouraged to seek further help. Thus, we expect a somewhat smaller ES of d = 0.50 at post-treatment.

Statistical analyses

The clinical trial will be conducted in compliance with the Declaration of Helsinki, the CONSORT guidelines, GCP and the protocol. Aiming at an intention-to-treat design [61] we will include all participants who will be randomly assigned to one of the two conditions. Additional per protocol analyses (PPA) will be conducted, including only participants' satisfying protocol treatment (completed at least 4 of 6 modules). Mixed-model analyses of variance will be conducted to explore the effects of the treatments on all continuous outcomes. Missing data will be handled using multiple imputations (MI). MI is especially robust with respect to missing data [62]. Nevertheless, to assess systematic effects of non-ignorable missing data, pattern mixture analyses for multi-level longitudinal approaches [63] will be conducted. To determine if the treatment effect is dependent on missing data, the missing-data pattern of each participant will be first coded and then included in a three-way interaction (missing pattern × condition × change in depression severity) in the main outcome analyses. If no significant interactions between missing-data pattern and treatment outcome are found, we will conclude that no missing data bias occurred in the results. For all mixed-model analyses, Cohen's d [64] will be calculated by standardising the differences between baseline and follow-up scores by the pooled standard deviation of the baseline scores. Response and remission rates will be compared across groups with the help of contingency tables and χ2 tests. We will also calculate the number needed-to-be-treated (NNT) with GET. ON Mood Enhancer to achieve one response and remission, respectively, compared to the control group. We will also calculate the number needed-to-harm, which indicates the number of participants treated in the experimental condition for one extra person to have a symptom deterioration. Because the differential risk of the intervention ideally needs to be set into relation with its benefits we will also calculate a benefit-risk ratio [65]. Benefit-risk ratio will be calculated by dividing the NNH to achieve one symptom deterioration through the NNT to achieve one response. If this benefit-risk ratio is greater than 1, the benefits outweigh the risks; if it is 1, the balance between benefit and risks are equal across the groups; if it is less than 1, the risks

outweigh the benefits (LIT). Benefit-risk ratios will only be calculated when differences in risk for symptom deteriorations are statistically significant.

For other negative effects, we will use independent t-tests for continuous, $\chi2$ for categorical, and logistic regression for binary outcomes. In a pre-planned subgroup analysis, we will explore negative effects of GET.ON Mood Enhancer on attitudes towards seeking psychological help in patients who do not reach the response criteria up to post-assessment (6 weeks). For all statistical analyses, significance level will be set at $P < 0.05$. All analyses will be conducted using SPSS 20.

Discussion

MDD is a highly prevalent disorder associated with a considerable loss in quality of life, increased mortality rates and substantial economic costs. Several reasons lead to the fact that patients remain untreated although they are in need of help. Internet-based guided self-help approaches could be an attractive, efficient and cost-effective approach to offer an evidence-based treatment alternative. Numerous studies have shown the acceptance and efficacy of guided self-help interventions in the treatment of depression. However, recent reviews have criticised that the methodological quality of studies are low and more high quality studies are needed, before such Internet-based therapies are widely disseminated. Moreover, as is also the case for face-to-face psychotherapy, hardly anything is empirically known about the potential negative effects of Internet-based guided self-help approaches. This study will evaluate a new Internet-based intervention for depression (GET.ON Mood Enhancer) compared to an online psychoeducation control in an investigator-blinded RCT. Special emphasis will be given to systematically evaluate potential negative effects, such as symptom deterioration, effects on attitudes towards seeking psychological help and other adverse events (that is, perceived intrapersonal negative change, relationships, friendships, family, therapeutic malpractice and stigmatisation).

This study will also have some limitations. First, as in most longitudinal studies we will need to deal with the problem of missing values. Although the planned adjustment for missing data (Multiple Imputation) is a highly recommended method to handle missing data [62], we will nevertheless additionally conduct pattern-mixture analyses [63] to minimise a possible risk for bias. Second, ideally the risk for negative effects when providing an Internet-based guided self-help intervention to patients with MDD needs to be compared with the risk for negative effects in face-to-face psychotherapy. However, a systematic evaluation of potentially negative effects of treatment has seldom been conducted for face-to-face psychotherapeutic interventions for Major Depression. Therefore, drawing conclusions on the differential risk of this guided self-help treatment compared to traditional psychotherapeutic treatment will not be possible. Third, the comparison condition does not control for unspecific effects through human support. Finally, the study sample will be too small to test for potential moderating effects. Thus, which patients are likely to profit from this type of treatment

delivery or which patients are especially likely to experience negative effects will remain unclear.

There will also be several strengths of this study, including the strong methodology of a randomised controlled design with an active control condition, outcome assessment with validated assessments by independent raters blind to treatment condition, a sample defined by a standard diagnostic measure, an appropriate statistical analyses plan and handling of missing data with state of the art methods. Given these strengths, the results of the study should further enhance the evidence-base for Internet-based guided self-help interventions for Major Depression. Moreover, a systematic evaluation of potentially negative effects of an Internet-based treatment as it is conducted in the present study has to the best of our knowledge not been conducted before. This study will therefore provide valuable information to the field as the basis for a wide dissemination of such concepts.

Overall, to overcome the gap between the need for treatment and evidence-based treatment availability and treatment utilisation, (cost-) effective low-threshold interventions are needed that are accessible for as many people as possible. Internet-based guided self-help interventions might be a promising strategy not only as a first step in a stepped-care approach but by providing treatments that are more intensive when patients fail to respond. If at some point this strategy becomes classified as evidence-based treatment, such approaches could provide evidence-based services to patients in areas or countries where psychotherapeutic treatment is not readily available [66]. If the proposed trial shows that the investigated intervention is not only effective in reducing depressive symptoms but also shows an acceptable riskbenefit balance, it would further strengthen the arguments for a wide dissemination of Internet-based guided selfhelp approaches for Major Depression.

Competing interests

MB is a minority shareholder of Minddistrict GmbH, which will provide the technical platform for the web-based interventions.

Authors' contribution

MB obtained funding for this study. DE, CB, JR, LB and DL contributed to the development of the GET.ON Mood Enhancer training. DE was responsible for the initial draft of design of the study, LB, PC, HR, HB, MB and DL further contributed to the study design. DE drafted the manuscript. LB, JR and CB are responsible for trial management and carrying out the diagnostic assessments. All authors contributed to the further writing of the manuscript. All authors read and approved the final manuscript.

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Manuskript 4 – Wirksamkeitsstudie GET.ON Mood Enhancer

Abstract

Background: This study's aims were to compare the efficacy and negative effects of guided Internet-based cognitive behavior therapy (iCBT) and online psychoeducation (OPE) in people with major depression.

Methods: A total of 131 individuals were randomized. Assessments took place at baseline (T1), six weeks (T2), and three months (T3). The primary endpoint was change in observer-based depression severity from T1 to T2. Potential negative effects were analyzed in terms of suicidal ideations, symptom deterioration, attitudes toward seeking further help, and other adverse events.

Results: iCBT (n=65) and OPE (n=66) both reduced depressive symptoms from T1 to T2, with large changes observed for iCBT and medium for OPD (iCBT: Cohen's d=1.09; OPE: d=0.60). Differences between groups were significant at the primary endpoint (d=0.36, p=0.028). OPD continued to have a positive effect from post-treatment to follow-up, while the effect of iCBT remained stable, with differences between groups not being significant anymore at follow-up. Participants who had undergone prior psychotherapy benefited from both treatments; but for those without prior psychotherapy, iCBT was superior also at follow-up. In the iCBT group 26.2% of the participants reported at least one side-effect.

Limitations: The history of psychotherapy was imbalanced between the groups. Some negative effects were assessed in the iCBT group only.

Conclusions: Both iCBT and OPE were effective in reducing depressive symptoms, but with iCBT having a more rapid effect. iCBT was specifically superior in those with no prior history of psychotherapy. Negative effects occurred frequently and should be considered when implementing iCBT.

Trial registration: German clinical trials register: DRKS00005025

Background

Although numerous studies provide evidence supporting the efficacy of available psychological and pharmacological treatments for major depressive disorder (MDD) (Cuijpers et al., 2014a, 2008), most affected individuals remain untreated (Bebbington et al., 2003; Kessler et al., 2001; Mack et al., 2014). Reasons for these seemingly-low treatment rates do not appear to solely relate to supply shortfalls — like prolonged waiting times, or long distances to therapy in rural areas. Anticipating negative (social) consequences, a low perceived need for treatment, and a preference for self-help are major barriers against seeking help (Andrade et al., 2014).

Internet-based self-help interventions could aid in solving some of these difficulties. Meta-analysis evidence indicates the efficacy of guided Internet-based interventions for major depressive disorder, in terms of large pre-to-post reductions in depressive symptoms, ranging from Hedges' $g=0.64$ to $g=2.24$, and beneficial effects when compared to controls ($g=0.90$) (Königbauer et al., 2017). However, one criticism is that many comparisons in this field rely on control conditions, like a waiting list with no active intervention component. These comparisons convey only little regarding the efficacy of this strategy of treatment delivery at the current level of research (Kiluk et al., 2011).

Nowadays, it is increasingly common to use brief unguided self-help interventions, like psychoeducation, as an active control condition for testing the effectiveness of Internet-based guided self-help interventions (Karyotaki et al., 2018). Furthermore, online psychoeducational information represents a realistic condition of care as usual in health information seeking behavior as the Internet may be the first source for most people who search for health information (Jacobs et al., 2017). There is evidence that psychoeducation can also be effective at reducing depressive symptoms, in terms of within-group effects, with effect sizes ranging from Cohen's $d=0.29$ to $d=0.65$ (Beiwinkel et al., 2017; Buntrock et al., 2015; Christensen et al., 2004; Imamura et al., 2016; Nobis et al., 2015). However, little is known about the comparative efficacy of online psychoeducation versus guided Internet-based self-help interventions for adult depression. Any such comparisons are scarce and reveal mixed results, with some studies yielding medium to large between-group differences, favoring iCBT over OPE ($d=0.41$ to $d=0.89$) (Beiwinkel et al., 2017; Buntrock et al., 2015; Nobis et al., 2015), while other studies have generated non-significant differences (Christensen et al., 2004).

Given the high prevalence (Kessler, 2005; Wittchen et al., 2011) and the chronic nature of depressive illness (Eaton et al., 2008), MDD is responsible for high medical service use (Greenberg and Birnbaum, 2005). In the literature, there are indications that people with depression repeatedly seek psychological treatment (Bender et al., 2001; Comninos and Grenyer, 2007). Research on the impact of past psychotherapy on psychological intervention success is scarce and mixed in its findings. One study showed a higher likelihood for significant change in depressive symptoms if people had no previous history of mental health service utilization (Boswell et al., 2012), while other studies found no significant correlations between previous psychotherapy and treatment efficacy

(Button et al., 2012; Grenyer et al., 2008; Junge et al., 2015). Thus, it also seems worthwhile to acquire further insights into how previous psychotherapy experiences influence Internet-based intervention success.

However, while Internet-based, guided self-help interventions are assumed to have great potential for decreasing depressive symptoms, there also might be negative effects associated with participating in online psychological treatments; for example, symptom deterioration, negative intrapersonal changes, suicidal ideations, and adverse effects on intimate relationships (Rozental et al., 2014). A recent meta-analysis on Internet-based guided self-help treatments identified a significantly-lower risk of 'reliable deterioration' amongst those in the intervention group than in waiting list controls (Ebert et al., 2016a). However, there are unfortunately only very few investigators reporting non-responder rates, or the frequency of symptom deterioration, negative effects on help-seeking attitudes, and other adverse events (Boettcher et al., 2014; Ebert et al., 2018). Further analysis of the different domains of negative effects seems mandatory, given the increasing use of internet-based interventions (Boettcher et al., 2014; Emmelkamp et al., 2014; Rozental et al., 2014).

Objectives

The primary aim of this study was to compare the efficacy of a guided self-help iCBT (a shortened version of GET.ON Mood Enhancer) against an online psychoeducational module on depression. We further aimed to compare a range of secondary outcome variables (i.e. mental and physical health, clinical response, and reliable change and remission rates), as well as potential negative effects of treatment.

Methods

Study design and sample size

A guided self-help iCBT group was compared to an online psychoeducation group, with full access to usual treatment for both treatment arms. Assessments took place at baseline (T1), as well as six weeks (T2) and 12 weeks (T3) after randomization. Recruitment started in May 2013 and ended in March 2014. Power analysis (calculated using PASS 12) indicated that 128 subjects were required to detect a between-group effect size of d=0.50 (power=80%; α=.05). Further details on study design have been published elsewhere (Ebert et al., 2014a).

Participants and Procedures

Recruitment

A major scope of our research group was to develop interventions for various levels of depressive symptoms. Consequently, we evaluated two versions of an Internet-based program, called GET.ON

Mood Enhancer, in two independent randomized controlled trials at the same time. For the first of these trials, the sample population had subthreshold depression (trial registration: DRKS00004709) (Buntrock et al., 2014). The currently-presented trial used a shortened version of the intervention to be evaluated in a sample with MDD. Participants were primarily recruited from the general population via a large German health insurance company, as well as through on-air media, newspaper articles, and related websites (GesundheitsTraining.online, 2014). Those interested in participating were invited to send an e-mail to the research team or apply online on the research website, where they were asked to provide their e-mail address.

Inclusion and exclusion criteria

All subjects had to a) be ≥ 18 years of age; b) be diagnosed with MDD, according to DSM-IV-criteria assessed via SCID (First et al., 2002); c) have Internet access; d) possess sufficient German skills both for reading and writing; and e) agree to the terms of the trial by providing informed written consent. Individuals were excluded if they a) had a history of manic/hypomanic episodes; b) had a history of psychotic disorders; c) were currently receiving psychotherapy for any kind of mental health problem; d) exhibited a notable suicidal risk, as indicated by a score greater than 1 on item 9 of the Beck Depression Inventory (BDI (Beck et al., 1996); 'I feel I would be better off dead'); or e) had changed either their antidepressant medication or its dose over the four weeks prior to the baseline assessment.

Assessment of eligibility and randomization

Applicants who met all inclusion and none of the exclusion criteria were permitted to enter the study, at which time they were randomly allocated — using an automated computer-based random integer generator (randlist) — to either of the two study conditions by an independent researcher who was not otherwise involved in the study.

Intervention Conditions

Guided Internet-based cognitive behavioural therapy

The guided self-help iCBT intervention — GET.ON Mood Enhancer — consists of six interactive sessions. Each session lasts about 30 minutes, though the duration might vary between users. Since a previous meta-regression analysis indicated that more frequent therapy sessions may be associated with better outcomes than less frequent sessions (Cuijpers et al., 2013), participants were advised to finish at least one, but preferably two modules per week. The program was also available beyond the post assessment at 6 weeks.

The modules rely on evidence-based face-to-face manuals that have been shown to be effective at reducing depressive symptomatology, including psychoeducation, and exercises for behavioral activation, problem solving, and relapse prevention; with three additional modules (sleep

problems, relaxation techniques, worrying) that can be chosen, depending on individual users' needs or preferences. A strong emphasis was placed on homework assignments designed to integrate acquired coping skills into daily life. Relative to the standard version of the intervention, which was originally developed to target subclinical depressive symptoms, and proven to be both effective (Buntrock et al., 2016a; David Daniel Ebert et al., 2018; Ebert et al., 2016b; Nobis et al., 2015) and cost-effective (Buntrock et al., 2017) across a range of target conditions, the current version was shortened and simplified to account for potentially-reduced ability to concentrate among individuals with severe depression. Changes to the standard version included reducing the lengths of explanatory text, as well as reducing the choice options for participants (e.g., elective modules like increasing social support, progressive muscle relaxation). Participants were supported by eCoaches (psychotherapists-in-training supervised by an experienced clinician). Guidance took place in the form of individualized written feedback after each module. The total time an eCoach spent per user averaged two hours. All feedback was stored for supervision and adherence checks.

Online Psychoeducation on Depression

The online psychoeducation intervention used the same platform as GET.ON Mood Enhancer. It was based on the patient version of the National Disease Management Guideline Unipolar Depression (VersorgungsLeitlinien.de, 2009). Participants were informed about the nature of depression, its symptoms, and strategies to overcome depressive episodes, including existing evidence-based treatments and sources of help. Neither specific homework assignments nor any eCoach support was provided. This online psychoeducation module has been shown to reduce the severity of depressive symptoms in patients with concomitant depression and diabetes (Nobis et al., 2015), and in a sample with subthreshold depressive symptoms (Buntrock et al., 2015).

Treatment as usual

At the end of both treatments participants received information of how to access further help and were encouraged to use routine mental health services, like psychotherapy or antidepressant medication, throughout the study period. However, we monitored treatment utilization and changes in antidepressant medication doses over the trial period to control for potential confounding.

Primary and secondary outcomes

'Change in observer-based depression severity from baseline to posttreatment' was considered the primary outcome. Secondary outcome measures were used to explore treatment effects on self-reported depressive symptomatology, anxiety symptoms, overall well-being, and general physical and mental health, as well as the rates of response, remission, and reliable improvement in the two study groups. We also evaluated for potential negative effects, including reliable symptom deterioration,

effects on attitudes toward seeking psychological help, and other adverse events deemed attributable to the GET.ON Mood Enhancer program.

Measures

Primary outcome measure

Observer-based depression severity was measured using the widely used Hamilton Rating Scale for Depression, HRSD-24 (Hamilton, 1960; Miller et al., 1984). The HRSD contains depressed mood, vegetative and cognitive symptoms of depression, and anxiety symptoms. In this study, the HRSD-24 exhibited very good inter-rater reliability, with an intraclass correlation coefficient (ICC) of .97 (95%-CI: .91-.99) at T2, based on recorded audio data from randomly-selected participants (10% of cases). In two subjects, assessor blinding to treatment condition was violated. In these cases the interviewer was changed for the following assessment.

Secondary outcome measures

Mental and physical health

We also used a second observer-based rating of depression: the Quick Inventory of Depressive Symptomatology - Clinician-Rating QIDS-CR16 (Rush et al., 2003; Trivedi et al., 2004). Contrary to the HRSD, it only addresses the nine depression criteria from the Diagnostic and Statistical Manual of Mental Disorders (American Psychiatric Association, 2000) over the preceding seven days. The Patient Health Questionnaire, PHQ-9 (Kroenke and Spitzer, 2002, 2001), was used to assess depressive symptomatology by self-report. Contrary to the primary outcome measure, HRSD-24, the PHQ-9 does not assess the intensity, but rather the frequency of symptoms, in nine items. Anxiety was measured with the anxiety subscale of the Hospital Anxiety and Depression Scale HADS-A (Zigmond and Snaith, 1983). The SF-12v1 Health Survey (Gandek et al., 1998) was used to assess health-related quality of life. We used two subscales of the Social Problem-Solving Inventory-Revised, SPSI-R (D'Zurilla TJ and Nezu AM, 2002), to measure problem-solving ability: the positive problem orientation (PPO) subscale measures a constructive dimension; while the negative problem orientation (NPO) subscale can be seen as a dimension of dysfunction. The Behavioral Activation for Depression Scale-Short Form, BADS-SF (Fuhr et al., 2016), was used to measure participants' active motivation for goals or values, as well as pleasant activities and avoidance behaviors. Psychological well-being was measured using the World Health Organization's (WHO) 5 Wellbeing Index (Primack, 2003).

Clinical significance

To assess improvements in the primary outcome at an individual level, for both study groups we examined according to the study protocol a) the number of participants with a clinical response, defined as 50% reduction from baseline symptom severity (Rush et al., 2006); and b) the number of participants exhibiting 'reliable improvement', employing the widely-used reliable change index

(RCI) proposed by Jacobson and Truax, 1991. Participants were defined as reliably improved if their HRSD-24-score declined, from baseline to post-assessment, with a reliable change index greater than 1.96 (one standard deviation, which equaled 4.42 points on the HRSD-24, based on SDpost = 9.2 and ICCpost = .97). In addition, we examined c) the number of participants who exhibited complete remission of their depression, defined a-priori as a post-assessment HRSD-24 score ≤ 10 (Kyle et al., 2016).

Adverse effects from the Internet-based intervention

According to Rozental et al., 2014, adverse effects should be analyzed in multitude domains. Increased suicidal risk of subjects in either group over the study course is one potential negative effect. A clinically-significant increase in the suicidal ideation item score on the HRSD-24 from baseline to post-treatment or follow-up was considered any increase ≥ 2 (0="Absent", 1="Feels life is not worth living", 2="Wishes he were dead or any thoughts of possible death to self", 3="Suicidal ideas, gestures, or plans", 4="Attempted suicide"). A score of 3 or 4 was considered a severe risk.

We also measured depressive symptom deterioration over the course of treatment. Participants were coded as having 'deteriorated' if they experienced a reliable negative change (−1.96) in the HRSD-24, as per RCI.

The Inventory of Negative Effects in Psychotherapy, INEP (Ladwig et al., 2014), was used to measure other adverse events. The version used in this study consists of 15 items that inquired about any negative effects that individuals experienced during or after completion of the Internet-based training program that were attributed to the program itself, including a) negative intrapersonal changes; b) negative changes in an intimate relationship; c) adverse effects on family/friends; d) perceived dependence on the psychotherapist/psychotherapeutic intervention; and e) stigmatization. The items are rated on a 7-point Likert scale that ranges from -3 (very negative experience) to +3 (very positive experience) or on a 4-point Likert scale that ranges from -3 (total agreement) to 0 (no agreement at all). Adverse events were counted by any negative response on one of the items.

To evaluate whether bad experiences with Internet-based interventions could have a negative effect on future utilization rates of other help, we used the Attitudes Toward Seeking Professional Psychological Help Scale-SF, ATSPPH-SF (Fischer and Farina, 1995), to measure potential negative influences on attitudes toward seeking mental healthcare service utilization in participants who did not respond to their allocated intervention (Ebert et al., 2018).

Course evaluation

User satisfaction was measured with the CSQ-I (Boss et al., 2016). This questionnaire consists of eight items measuring global client satisfaction.

Data Analysis

All analyses followed an intention-to-treat (ITT) protocol, including all participants who were randomly assigned to either of the two study groups, regardless of nonadherence to the intervention or non-attendance at follow-up assessments. For all ITT analyses, missing data were handled via multiple imputations (Schafer and Graham, 2002). Hundred single imputations of the missing values were calculated based on the valid data for all outcome measures at all assessment points (T1, T2, and T3) as well as age and gender and were aggregated into a single overall estimate of each outcome variable.

As a first step of our primary analysis, we examined for group differences in the primary outcome variable over time by employing mixed effects models, with fixed effects for *symptomatology*, *group*, and *assessment point*, and a random intercept to account for clustering within each participant. The model also included a twofold interaction term — *group x assessment point* — allowing us to analyze for differences in the intervention effect between baseline (T1) and the two follow-up assessments (T2 and T3). Although the study was initially not powered to identify moderators, we conducted a second analysis step because of baseline imbalances in the number of participants with a history of psychotherapy between the study groups. This incorporated a fixed effect for *history of psychotherapy* (yes/no), a twofold interaction term — *assessment point x history of psychotherapy* — and a three-factor interaction term — *assessment point x group x history of psychotherapy*. For this, we deviated from the initial study protocol to adjust for covariate imbalances at baseline, as recommended by Pocock et al., 2002. The fixed effect of most interest was the *assessment point × group* interaction, which indicated that the difference between the intervention and control groups was a change in psychopathological symptoms over time. We calculated Cohen's d with 95% confidence intervals (Cohen, 1988) for pre-to-post differences on the primary outcome for each study group. Additionally, we calculated Cohen's d for all inter-group differences by subtracting the difference between baseline and follow-up in the online psychoeducation group from the difference between baseline and follow-up in the iCBT group, and dividing this by the pooled standard deviation of the change scores.

Clinical response, reliable improvement, remission, increased suicidal risk and deterioration rates were analyzed using contingency tables and Pearson χ2 analysis. For significant findings, we also calculated the number needed-to-treat (NNT, with 95% confidence intervals) with GET.ON Mood Enhancer to achieve one additional response, one reliable change, and one remission, relative to online psychoeducation.

In a pre-planned subgroup analysis, we explored negative effects of the GET.ON Mood Enhancer program on attitudes toward seeking psychological help in participants who did not reach the response criteria by T2. To investigate the hypothesis that GET.ON Mood Enhancer does not lead to more negative attitudes toward psychological interventions among those who failed to experience a clinical response, relative to online psychoeducation, a confidence interval approach was used for the effect size of the difference between the two treatment groups. The equivalence margin that corresponds to the smallest value that would represent a relevant negative effect was set, a priori, at d=-0.20, which has been set 20% lower compared to what has been defined as a minimal important

difference in the treatment of depression (Cuijpers et al., 2014b). The lower bound of the 95% CI for the effect size was compared with the predefined equivalence margin of d=-0.20, and had to be above the margin to exhibit equivalence. One-sided hypotheses were tested using one-sided tests; while two-sided hypotheses (e.g., tests on negative effects) were conducted using two-sided test. The a priori criterion for statistical significance was set at $p < 0.05$.

Results

Participant flow

In total, 131 individuals gave their informed consent and were randomized into the two study groups (Figure 1). Participants were predominantly female (n=99; 75.6%), with an average age of 41.6 years (SD=10.8; Table 1). Nearly half of the participants (n=60; 45.8%) suffered from a chronic course of depression. There were no meaningful differences in baseline characteristics between the groups, except for the number of participants with a history of psychotherapy, who were overrepresented in the Internet-based self-help cognitive behavioral therapy (iCBT, n=45; 69.2%) group relative to the online psychoeducation (OPE, n=32; 48.5%) group. Therefore, we included 'history of psychotherapy' as a baseline predictor in a separate mixed-effects model, to analyze its impact on the primary outcome.

Table 1. Demographic characteristics: means/counts and standard deviations/percentages.

	All				iCBT				OPE			
	N	%	M	SD	N	%	M	SD	N	%	M	SD
Age			41.6	10.8			40.6	10.7			42.7	10.8
Females	99	75.6			45	69.2			54	81.8		
Married/partnership	61	46.6			27	41.5			34	51.5		
Higher education	94	71.8			44	67.7			50	75.8		
Currently employed	94	71.8			42	64.6			52	78.8		
Chronicity of MDD[a]	60	45.8			33	50.8			27	40.9		
Suicidal ideation at baseline[b]	8	6.1			4	6.2			4	6.1		
History of psychotherapy at baseline	77	58.8			45	69.2			32	48.5		
Baseline medication	26	19.8			14	21.5			12	18.2		
Started psychotherapy during treatment	16	12.2			9	13.8			7	10.6		
Changed medication during treatment	32	24.4			16	24.6			16	24.6		

Abbreviations: iCBT= Internet-based cognitive behavior therapy; OPE=online psychoeducation on depression; [a]=referring to DSM-V criteria for chronic major depressive disorder; [b]=as defined by a score of 2 on the Hamilton Rating Scale for Depression suicidal ideation item ("thoughts about being dead or of possible death to self").
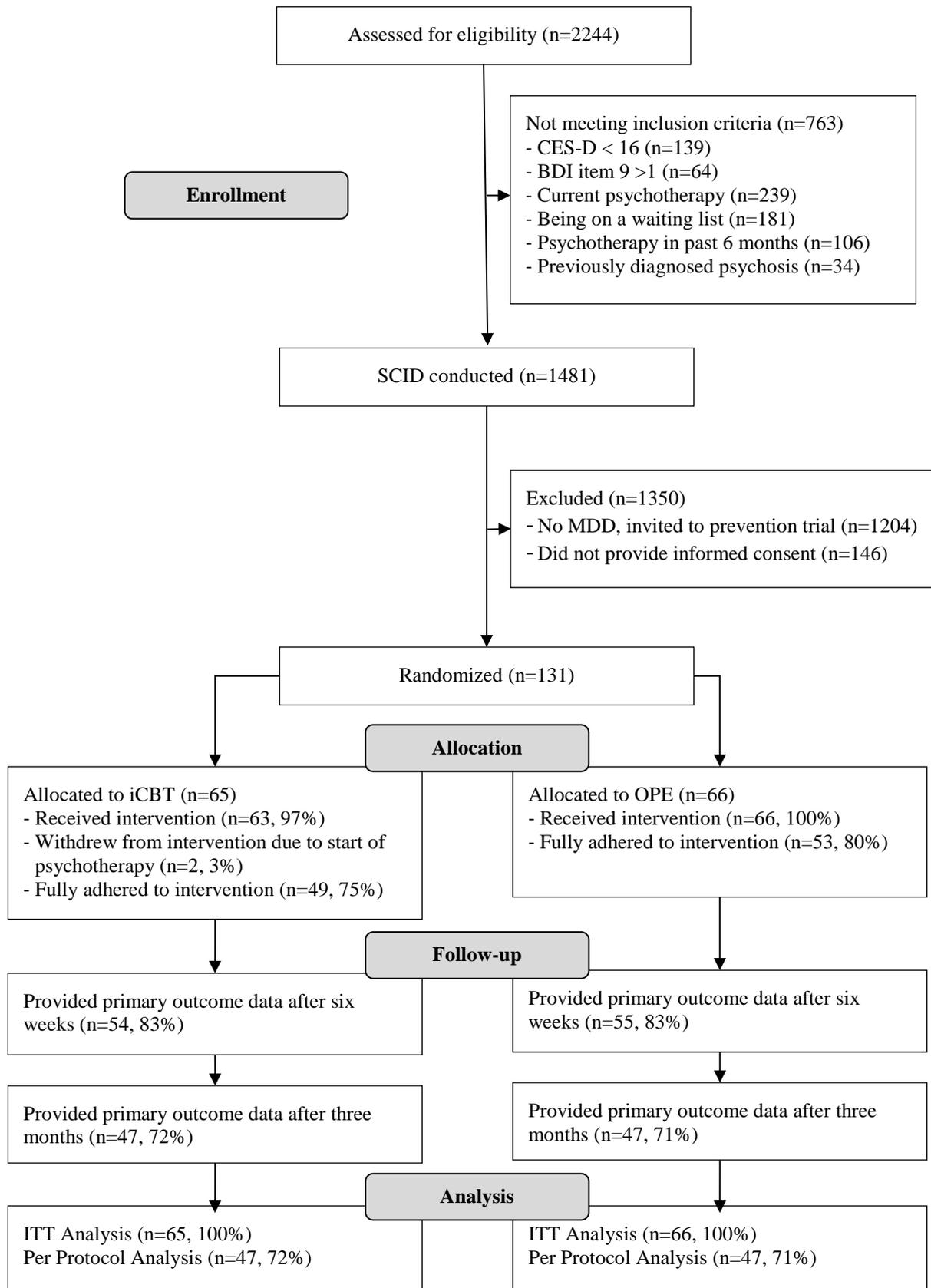
Figure 1. Study Flow

Intervention usage and service utilization

Of the 65 participants in the iCBT group, 63 (96.9%) completed at least one training module, 61 (93.8%) completed two modules, 60 (92.3%) completed three, 54 (83.1%) completed four, 52 (80%) completed five, and 49 (75.4%) completed all six modules of the intervention. In the iCBT group 37 participants (56.9%) finished the training prior to the post-assessment and 24 (36.9%) continued with the training afterwards. Participants needed an average of 39 days to complete the program (SD=20.8; range 3 – 87 days). Of the 66 participants in the OPE group, 53 (80.3%) read the psychoeducation material, as determined by their log-in history.

In the iCBT group, eight (12.3%) experienced some change (drug or dose) in their anti-depressant medication, while nine (13.8%) began psychotherapy over the course of the study, with two withdrawing from the study for the latter reason. Baseline data from these two participants was included in the analyses. Missing values at the post- and follow-up-assessment were handled like other missing data by multiple imputations in accordance to the intention to treat principle. Among those participants receiving psychoeducation, six (9.1%) experienced some change in their medication, while seven (10.6%) began psychotherapy.

Primary outcome analysis

Both study groups exhibited statistically-significant reductions in observer-based depression severity from baseline (T1) to post-treatment scores (T2) on the HRSD (Table 2). Mixed-effects model (MEM) analysis of the base model, unadjusted for any baseline imbalances, showed that in those who received iCBT, there was a mean reduction of 8.31 points on the HRSD (p<0.001; d=1.09, 95% CI 0.72-1.46). In the OPE group, the mean reduction on the HRSD was 5.42 points (p<0.001; d=0.59, 0.24-0.94). Both groups also exhibited significant decreases from T1 to 3-month follow-up (T3), of 8.62 points in the iCBT group (p<0.001; d=1.02, 0.65-1.38) and 7.70 points in their OPE counterparts (p<0.001; d=0.87, 0.51-1.23). The analysis of group differences revealed a significantly-greater reduction in depression severity from T1 to T2 with iCBT than with OPE (T1-T2 x group: p=0.028; d=0.36, 0.01–0.70). However, there was no difference in change from T1 to T3 between the groups (T1-T3 x group: p=0.197).

Table 2. Means and standard deviations of outcome variables at baseline, post-treatment, and at three-month follow-up based on multiple imputations (intention-to-treat sample)

| | T1 | | | | T2 | | | | T3 | | | |
| | iCBT | | OPE | | iCBT | | OPE | | iCBT | | OPE | |
Outcome	M	SD	M	SD	M	SD	M	SD	M	SD	M	SD
HRSD	22.06	7.71	21.83	8.62	13.75	7.52	16.47	9.45	13.44	9.19	14.39	8.49
QIDS	12.02	4.49	11.82	4.43	7.99	4.53	9.46	5.14	7.74	4.84	7.98	4.49
PHQ-D	15.72	4.41	16.06	4.31	10.62	4.99	12.11	5.44	10.35	5.15	11.09	5.42
BADS	19.35	6.58	22.00	6.60	28.86	8.97	23.96	8.35	27.46	9.03	25.75	8.60
HADS-A	11.82	3.91	11.72	3.20	8.90	4.26	10.08	4.39	8.99	4.00	9.51	3.55
WHO5	4.49	2.87	4.35	2.75	7.82	4.63	6.47	4.52	8.67	5.08	7.59	4.95
SPSI-PPO	7.54	3.81	7.75	4.57	9.87	3.44	8.76	4.19	9.67	3.88	8.70	4.09
SPSI-NPO	8.39	4.77	8.13	5.08	6.98	4.27	8.21	4.98	6.90	4.35	7.73	4.50
SF12-PH	44.59	11.10	46.16	8.68	43.12	10.92	45.81	9.68	44.20	10.34	46.43	10.02
SF12-MH	26.84	7.10	26.52	6.85	34.93	10.10	31.74	10.13	36.67	10.62	35.04	9.53
ATSPPH	21.72	4.32	21.24	4.41	22.00	3.91	21.57	4.34	/	/	/	/

Abbreviations: T1=baseline; T2=post-treatment after six weeks; T3=follow-up after three months; iCBT=Internet-based cognitive behavior therapy; OPE=online psychoeducation on depression; /= No assessment; HRSD=Hamilton Rating Scale for Depression; QIDS=Quick Inventory of Depressive Symptomatology - Clinician-Rating; PHQ=Patient Health Questionnaire-Depression; BADS=Behavioral Activation Depression Scale; HADS-A=Hospital Anxiety and Depression Scale – Anxiety Subscale; WHO5= World Health Organization's 5 Wellbeing Index; SPSI-PPO=Social Problem-Solving Inventory – Positive Problem Orientation; SPSI-NPO=Social Problem-Solving Inventory – Negative Problem Orientation; SF12-PH=SF-12 Health Survey – Physical Health Subdomain; SF12-MH=SF-12 Health Survey – Mental Health Subdomain; ATSPH=Attitudes Toward Seeking Professional Psychological Help.

Following our analysis plan, we conducted further MEM analyses including *baseline psychotherapy history (yes/no)* as a predictor and potential moderator of change in observer-based depression severity over time (Tables 3, 4). The adjusted MEM revealed a) a significant decrease in depression severity from baseline to post-treatment (*T1-T2*, Table 3) and from baseline to final follow-up (*T1-T3*) with both iCBT and OPE; and b) a significantly-greater reduction in depression severity only among participants in the OPE who had undergone psychotherapy prior to their entry into the current study (*T1-T2 x psychotherapy history*/ *T1-T3 x psychotherapy history*) versus those with no psychotherapy history. The twofold interaction (*T1-T2 x group*, Table 4) indicated c) a significantly-greater decrease

(-7.1 HRSD points) in depression severity from baseline to T2 in the iCBT than OPE group, among participants with no psychotherapy history. Finally, d) a significantly-positive threefold interaction coefficient (*T1-T2 x psychotherapy history x group*) indicated that, comparing the reduction in depression severity from T1 to T2 between participants with versus without a psychotherapy history, the mean T1-T2 difference was smaller in those receiving iCBT than those receiving OPE. The contrary impact of this interaction on the change in depression severity over time in participants with compared to those without a psychotherapy history is depicted in Figure 2. In summary, on MEM analysis adjusted for psychotherapy history, no difference was detected between the two treatment arms, in terms of T1-to-T2 depression severity among participants with a psychotherapy history (d=0.09, 95% CI -0.37-0.54), but a significant difference in the two treatments was observed in those with no prior psychotherapy; and this effect was large (d=0.82, 95% CI 0.25-1.40).
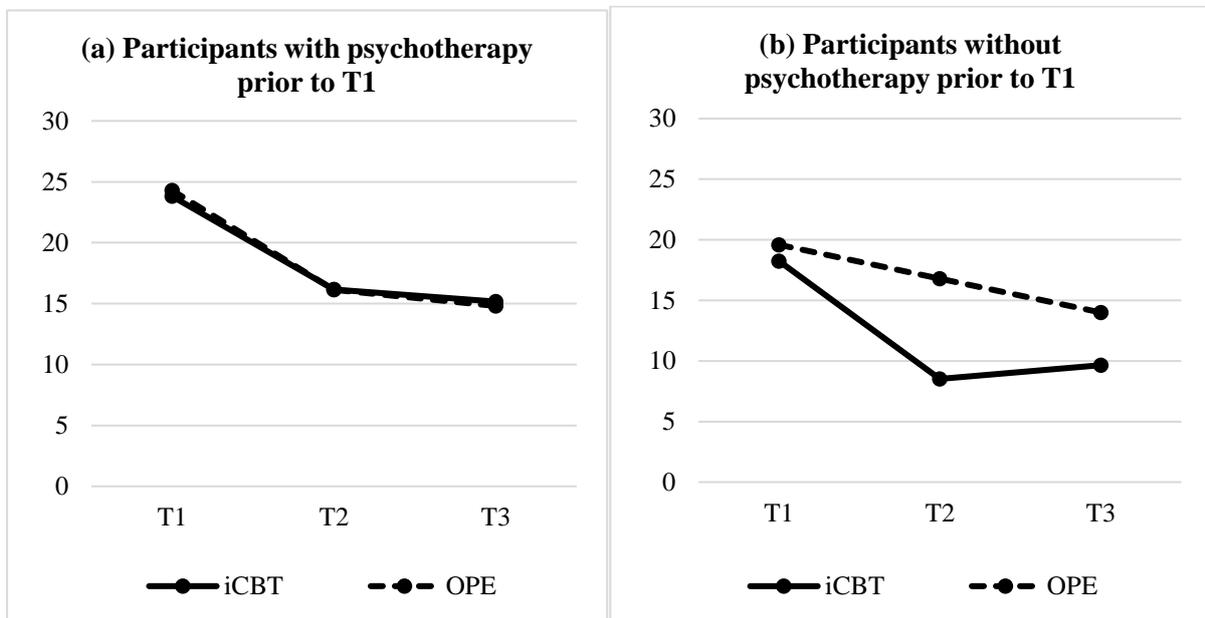
Figure 2. Course of depressive symptomatology on the HRSD in the subgroups of participants (a) with and (b) without psychotherapy experiences prior to the baseline assessment. T1=baseline; T2=post-treatment after six weeks; T3=follow-up after three months; iCBT=Internet-based cognitive behavior therapy; OPE=online psychoeducation on depression.

Table 3. Estimated differences in change from baseline to six weeks and three month follow-up of the primary outcome in each group based on mixed-effect-model including psychotherapy history, time, and its interaction as predictors.

	Intercept Baseline		Psychotherapy history		T1-T2		T1-T2 x Psychotherapy history		T1-T3		T1-T3 x Psychotherapy history	
	B	SE	B	SE	B	SE	B	SE	B	SE	B	SE
iCBT	18.47	1.47	5.19[a]	1.51	-9.85[a]	1.78	2.21	2.09	-8.73[a]	1.78	-0.13	2.09
OPE	19.46	1.26	5.19[a]	1.51	-2.73[c]	1.40	-5.72[b]	1.95	-5.52[a]	1.40	-4.25[c]	1.95

Abbreviations: [a]=$p<0.001$; [b]=$p<0.01$; [c]=$p<0.05$; [d]=$p<0.10$; T1=baseline; T3=follow-up after three months; iCBT=Internet-based cognitive behavior therapy; OPE=online psychoeducation on depression.

Table 4. Estimated group differences of the primary outcome based on mixed-effect-model including two- and threefold interaction terms with group, time, and history of psychotherapy as predictors.

Group Baseline		T1-T2 x Group				T1-T2 x Psychotherapy history x Group				T1-T3 x Group				T1-T3 x Psychotherapy history x Group			
B	SE	B	SE	CI$_{low}$	CI$_{upp}$	B	SE	CI$_{low}$	CI$_{upp}$	B	SE	CI$_{low}$	CI$_{upp}$	B	SE	CI$_{low}$	CI$_{upp}$
-0.99	1.49	-7.12[b]	2.18	2.84	11.40	7.94[b]	2.64	2.75	13.12	-3.20[d]	2.18	-7.48	1.08	4.12[d]	2.64	-1.07	9.31

Abbreviations: [a]=$p<0.001$; [b]=$p<0.01$; [c]=$p<0.05$; [d]=$p<0.10$; T1=baseline; T3=follow-up after three months; negative coefficients indicate a decreased depression severity for Internet-based cognitive behavior therapy compared to online psychoeducation on depression.

Secondary outcome analysis

Clinical significance

There were no significant differences between the two treatment groups in terms of the percentage of subjects experiencing a clinical response from T1 to T2 (χ^2=0.420, p=0.279) or from T1 to T3 (χ^2=0.062, p=0.402). There also were no significant inter-treatment differences in remission rates at either T2 (χ^2=0.654, p=0.210) or T3 (χ^2=0.374, p=0.271) (Figure 3). In the iCBT versus OPE group, significantly more participants exhibited a reliable improvement in depression severity from T1 to T2 (χ^2=5.152, p=0.012), indicated by a number needed to treat to achieve one reliable improvement from T1 to T2 of 5.12 (95% CI 2.77-33.11). There was no significant inter-treatment difference from T1 to T3 (χ^2=0.719, p=0.198).
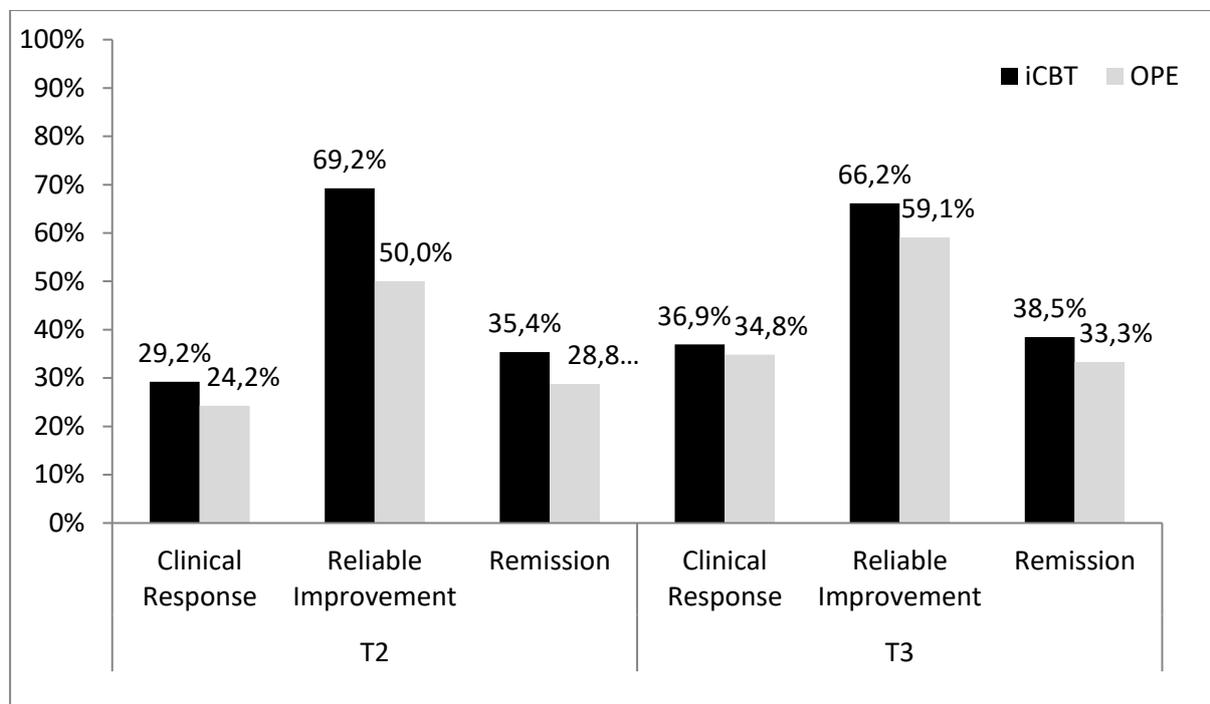
Figure 3. Rates of clinical response, reliable improvement, and remission. T1=baseline; T2=post-treatment after six weeks; T3=follow-up after three months; iCBT=Internet-based cognitive behavior therapy; OPE=online psychoeducation on depression.

Mental and physical health

To analyze intervention effects on continuous secondary outcomes, we used MEM adjusted for psychotherapy history, analogous to the primary outcome analysis model. Significant cross-level interaction effects indicated between-group differences in change from baseline to posttreatment (*T1-T2 × group*) that favored iCBT, with respect to improved severity of depression criteria symptoms (d=0.36), self-rated depression (d=0.25), behavioral activation (d=1.16), and anxiety (d=0.40; Table S1). No inter-group differences were identified for changes in overall well-being, problem-solving

skills, or general physical health (Table S3). The cross-level interaction effect *T1–T3 × group* was significant only for behavioral activation (d=0.70) and overall well-being (d=0.44), indicating larger improvements in the iCBT than OPE group at T3 (Table S3). The threefold interaction effect *T1-T2 x psychotherapy history x group* only was significant for self-rated depression and anxiety, indicating a smaller difference between those with versus without prior psychotherapy in symptom reduction from baseline to post-treatment in participants in the iCBT than OPE group. Effect sizes and MEM coefficients for all secondary outcome variables are available for viewing in downloadable supplemental tables.

Adverse effects from the Internet-based intervention

Suicidal ideations

In the iCBT and OPE groups, four (7.4%) and one subject (1.9%), respectively, reported "thoughts about being dead or of possible death to self" (score = 2 on the HRSD-24 suicide item) at any time over the week prior to the T2 interview. At T3, corresponding numbers were four (7.7%) and four (8.3%). Comparing to the baseline (Table 1), the prevalence of suicidal ideation remained stable in both groups. All suicidal ideations were documented by the interviewer and corresponding subjects supervised by an experienced clinician. No participant in either treatment arm reported suicidal ideas, gestures, plans, or attempts (HRSD-24 suicide item score = 3 or 4).

Reliable deterioration in depressive symptoms

Assessing the number of participants with increased baseline symptomatology ($\geq$ 4.42 points on the HRSD-24), six (9.2%) and five (7.6%) of the subjects in the iCBT and OPE groups experienced a reliable deterioration from T1 to T2, respectively; these rates were not statistically different (χ^2=0.117, p=0.732). From T1 to T3, corresponding numbers with reliable symptom deterioration were three (4.6%) and six (9.1%), a difference that, again, was not statistically significant (χ^2=0.311, p=0.492). There was no association between the deterioration rates and adherence to the intervention from T1 to T2 (χ^2=1.520, p=0.252) or from T1 to T3 (χ^2=2.135, p=0.222). There was also no association between deterioration and study attrition from T1 to T2 (χ^2=0.011, p=1.000) or from T1 to T3 (χ^2=0.024, p=1.000).

Attitudes toward seeking help

Potential negative effects on help-seeking attitudes (ATSPPH) were examined in participants who did not reach our a priori criterion for a clinical response (iCBT: n=46, 70.8%; OPE: n=50, 75.8%). Attitudes toward seeking psychological help increased in both study groups (iCBT: 0.28 points; OPE: 0.33 points), with no significant difference between the two treatments (T1-T2 x group, p=0.321; d=0.04; 95%-CI -0.37 to 0.46). As the effect sizes were positive and did not cross the lower bound of

the confidence interval for the predefined equivalence margin of d=-0.20, it can be concluded that there were no negative effects on attitudes toward seeking psychological help in those who failed to respond to the intervention.

Other negative side-effects

At T2, 17 of the 65 subjects (26.2%) in the iCBT group reported negative side-effects that they attributed to participating in the intervention. Most frequently, they reported effects in the area of negative intrapersonal changes, with most ratings on the item "During the training or since completing the training there were phases I was feeling mentally unwell." (n=6, 9.2%). Some reported perceived stigmatization, partnership problems, problems with family or friends, or perceived dependence on the eCoach (Table S4).

Program evaluation

Among those in the iCBT group, 45 of the 54 who answered questions on their satisfaction with the program (83.4%) said that they were satisfied, overall, with the intervention. The majority perceived the training as being of high quality (n=50, 92.6%), and said they: received the kind of training they had wanted to receive (n=43, 79.6%); perceived that their needs had been met (n=41, 75.9%); were satisfied with the amount of assistance they received (n=39, 72.2%); would use the program again, should the need arise (n=48, 88.9%); found that the training helped them to deal effectively with their problems (n =41, 79.9%). Forty-seven of the 54 (87.0%) said they would recommend the intervention to a friend.

Discussion

Primary outcome

In the current randomized controlled trial, a shortened version of original GET.ON Mood Enhancer program was associated with significant improvements in depressive symptoms in a sample of moderate to severely depressed individuals with Major Depressive Disorder and a high chronicity of depressive symptoms. Large effects were found in changes of observer-based depression severity from baseline to immediately post-treatment (d=1.10) and three-month follow-up (d=1.01). These findings are consistent with those of a recent meta-analysis on internet- and mobile-based depression interventions for those with diagnosed depression (Königbauer et al., 2017). Results are also in line with the findings from earlier studies that our group has conducted using other (non-shortened) versions of GET.ON Mood Enhancer, which yielded within-group-effects of d=1.06 in those with subthreshold depressive symptoms (Buntrock et al., 2015). However, changes were somewhat smaller

compared to findings in a group of patients with diabetes mellitus and co-morbid depression with effects of d=1.40 (Nobis et al., 2015).

Surprisingly, participants in our trial who received online psychoeducation also experienced substantial reductions in observer-based depression severity from baseline to immediate post-treatment, with a medium within-group effect of d=0.60 and a large effect for changes from baseline to follow-up (d=0.87). This result is somewhat higher than findings from earlier studies on guided iCBT interventions, in which only small within-group effects were observed for online psychoeducation (Beiwinkel et al., 2017), even in studies of our own group that used exactly the same online psychoeducation intervention (Buntrock et al., 2015; Ebert et al., 2017; Nobis et al., 2015).

In the first step of mixed-effect-model (MEM) analysis, unadjusted for any baseline imbalances, we found a significant superiority of GET.ON Mood Enhancer over OPE at the primary endpoint post-treatment, with a small to medium between-group effect of d=0.36, but no differences for change from baseline to follow-up. Results from previous comparable studies are inconsistent, however, some identifying no between-group effects at all (Christensen et al., 2004), while others using the original non-shortened version of GET.ON Mood Enhancer, found medium (Buntrock et al., 2015) or large between-group effects in favor of iCBT both in short-term (Nobis et al., 2015) and in long-term (Buntrock et al., 2016b; Ebert et al., 2017). Interestingly, the mean values indicated a stable effect for iCBT between T2 and T3, while psychoeducation initially showed a lower improvement, but continued to have a positive impact on depression severity from post-treatment to follow-up. These results indicate that both kinds of interventions can reduce depression severity, but iCBT might work more rapidly than psychoeducation. An explanation for the non-superiority of iCBT vs. psychoeducation at follow-up might lie in the fact that we tested a shortened version of the GET.ON Mood Enhancer intervention, because we wanted to account for potential concentration difficulties in subjects with severe depression. However, this might have led to a lower perceived credibility or inadequate intervention intensity for some participants and not enough additional value of guided self-help vs. psychoeducation. Such an assumption is supported by the fact that satisfaction ratings in the present trial were much lower than in various previous studies that utilized the original, longer version of GET.ON Mood Enhancer (Buntrock et al., 2015; David Daniel Ebert et al., 2018; Nobis et al., 2015). An alternative explanation for the lower satisfaction rates and non-superiority of guided-self-help vs. psychoeducation compared to prior evaluations might be associated with differences in the various samples' baseline characteristics, such as the large proportion (51%) of individuals that reported chronicity of their depressive symptoms at baseline.

When we included baseline psychotherapy history as a potential predictor and moderator of change in an adjusted MEM, we only found the iCBT program to be superior to OPE, in terms of reducing observer-based depression severity from T1 to T2, in people with no prior psychotherapy experience (between-group effect d=0.87). No such significant effect was identified for those with a psychotherapy history (between-group effect d=0.08). This is in line with Boswell et al., 2012, who

found students to be more likely to experience a clinically-significant change in depressive symptoms if they had no history of psychotherapy. However, it is contrary to the results of Button et al., 2012 and Junge et al., 2015, who did not find previous psychotherapy to significantly predict or moderate iCBT efficacy.

Internet–based guided self-help might be especially beneficial compared to simple psychoeducation when the intervention is the first service that people with MDD use, because it contains specific therapeutic strategies that may provide a novel way for them to cope with their problems ("novelty hypothesis"). This possible explanation links to the phase model of psychotherapy outcomes (Howard et al., 1993), a model that describes different treatment phases to go along with different experiences that individuals have with regard to changes in symptoms and well-being. On the other hand, for recurrent help seekers who have already accumulated knowledge from previous treatments, online psychoeducation might be a kind of refresher course, unearthing previously-learned knowledge and coping behaviors to address their depressive episode ("refreshing hypothesis"). For these people, guided self-help might provide no meaningful incremental benefit over and above a psychoeducational refresher course, which might be sufficient for at least some patients. Such an assumption is supported by our finding that average pre-post changes of participants in the psychoeducation group with no previous experience in psychotherapy were significantly larger (d=1.18) than in those with prior psychotherapy (d=0.31). Future studies are needed to test this assumption.

Secondary outcomes

We analyzed intervention effects on several secondary outcomes. While significantly more participants in the iCBT versus OPE group experienced a reliable improvement in their depression scores immediately post-treatment, no between-treatment differences were found in either the rate of clinical response or the rate of remission, either immediately post intervention or at 3-month follow-up. However, guided self-help iCBT was superior to online psychoeducation, with medium-to-large effects on behavioral activation, and small-to-medium effects on problem-solving skills and anxiety. These findings were expected, because the intervention emphasizes behavioral activation and problem solving, both of which have already been proven to be effective as stand-alone interventions (Ebert et al., 2014b; Ekers et al., 2014; Hoek et al., 2012).

Negative intervention effects

In this study, we systematically analyzed potential negative effects and were unable to detect any instances of severe suicidal ideations. In both groups, a very small percentage (under 10%) of subjects experienced a statistically-reliable increase in the severity of their depression. There was no difference between iCBT and OPE in this percentage, as opposed to prior studies comparing Internet-based

interventions and a non-treatment (e.g., waiting list) control group, in which deterioration in depressive symptoms was more common in controls (Ebert et al., 2016a). Clearly, this discrepancy between our and prior results might be explained by our comparison of two active treatments, instead of comparing an intervention versus no intervention. Nonetheless, our findings still highlight the need for a closer look at those who use either of these two approaches — an Internet program like GET.ON Mood Enhancer or online psychoeducation — perhaps monitoring the severity of depression more frequently and offering additional support (e. g., medication and/or psychotherapy) to those who start to feel worse over the course of the intervention.

Seventeen subjects (26%) in the iCBT group attributed at least minor expressions of negative side-effects, besides worsened depression, to the intervention. Very few data have been published on potential negative effects from either Internet-based interventions or psychotherapy. However, the rate of negative side-effects reported in the present trial is much lower than that found in a recent study of traditional face-to-face psychotherapy in both inpatients and outpatients with major depression and co-morbid disorders, with about 70% of subjects reporting at least one negative side-effect (Abeling et al., 2017). The side-effect most frequently reported in the present trial was decreased mood during the intervention phase (Table S4). One explanation might be that CBT-based exposure exercises can evoke uncomfortable thoughts and emotions, which could adversely impact a person's mood. A negative side-effect like diminished mood could be considered a normal phenomenon during the course of any psychological intervention (Foulkes, 2010). Others indicated a fear of negative consequences when other people or institutions found out that they had participated in a depression study intervention. Additional information about Internet-based interventions and e-coaching prior to study entry might have been beneficial to enhance potential participants' beliefs in the intervention's credibility. For example, introduction videos have been shown to increase users' acceptance of Internet-based interventions and reduce barriers like the fear of stigmatization in previous studies (Ebert et al., 2015), and might be a way to reduce negative effects associated with negative expectations about the intervention.

One further potential adverse effect of Internet-based interventions might be that they are less intensive than required to treat severely-affected individuals (Kiluk et al., 2011), and that this might discourage non-responders from seeking more intensive treatments. Our subgroup analysis of participants who did not reach the criterion for a clinical response, revealed no difference in attitudes or changes in attitude toward seeking professional psychological help between those in the GET.ON Mood Enhancer and psychoeducation group. This corresponds to other research that has evaluated the impact of iCBT on help-seeking attitudes, suggesting that, even if someone fails to respond to iCBT, this does not appear to adversely impact their decision to seek other sources of help in the future (Moritz et al., 2013).

Limitations

Our study had several limitations. First, the results of our analysis indicate that past psychotherapy prior to study entry exerted a meaningful impact on the interventions' overall success. Although the statistical methods we used in analysis are presumed to be robust, with respect to baseline imbalances, our findings still must be interpreted with caution. Nonetheless, as ours is one of the first studies to include psychotherapy experiences as a potential confounder of treatment effects, our results should provide future investigators with valuable information for power calculations and analysis planning. Secondly, some participants in our iCBT group experienced a number of negative side-effects after starting the intervention. It is important to bear in mind that any negative response on one of the 15 INEP statements was counted as adverse event, independent of the intensity of the item response. Therefore, the negative side-effects derived from this measure may be overestimated. Unfortunately, at the time the study was conducted, there existed, to our knowledge, no better accurate instrument for measuring negative effects in psychotherapy. Moreover, we did not assess these negative side-effects in the online psychoeducation group. However, the findings about negative effects of the guided self-help iCBT can only be interpreted in relation to the psychoeducational control in this trial. An additional passive control condition would have been helpful to derive conclusions about the general efficacy and negative effects of both guided self-help iCBT and online psychoeducation on depression.

Conclusions

Both guided self-help Internet-based CBT and online psychoeducation appear to substantially reduce the severity of depression in patients with a Major Depressive Disorder, with the former significantly superior only immediately post treatment, but not at the follow-up. Given that satisfaction ratings were much lower for the shortened version of GET.ON Mood Enhancer in the present study compared to prior evaluations of the program, future studies should explore the comparable credibility and perceived effectiveness of the two versions. Moreover, the superiority of iCBT over online psychoeducation seems specific for those who have not had prior psychotherapy. Although we can conjecture that, perhaps, those who have had prior psychotherapy already have at least some of the knowledge and tools our iCBT program provided, further research to clarify this issue is warranted. Finally, no subject in either group reported serious suicidal ideations, and no real difference was detected between the two studied treatments with respect to other adverse effects and outcomes. Nonetheless, since a small percentage in both treatment groups did experience considerable worsening of their depression, it behooves clinicians and investigators alike to monitor individuals using these interventions closely, so such worsening can be detected and appropriately countered.

Authors' contribution

DE, DL, and MB obtained funding for this study. JR, LB, DL, and DE contributed to the development of the GET.ON Mood Enhancer program. DE was responsible for the initial study design draft, while JR and LB contributed to the final study design. LB conducted the main data analyses. JR drafted the manuscript. DE supervised the writing process. All authors contributed to further writing of the manuscript, and all authors read and approved the final manuscript.

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All procedures involved in the study were consistent with the generally-accepted standards of ethical practice approved by the University of Marburg ethics committee (No. 2013–08 K). The trial is registered in the German clinical trials register under DRKS00005025.

Declaration of competing interests

Mr. Ebert, Mr. Lehr, and Mr. Berking hold shares of the GET.ON Institute for Online Health Training, which aims to transfer scientific knowledge related to the present research into routine mental health care in Germany. The foundation of such an institute to disseminate findings and products from the research project was the primary aim of the European Union for funding the currently-presented research. Mr. Berking has received research grants from the German Ministry of Research and the German Research Association and personal fees from various institutions providing ongoing training for psychotherapists. Mr. Ebert has received funds from the German Ministry of Research and the German Research Association, the European Union, the BARMER, the SVLFG and consultancy fees from Schoen Kliniken, Agaplesion Kliniken, Sanofi, Novartis, BARMER, Techniker Krankenkasse. No other disclosures are reported.

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Supplement

Table S1. Effect sizes of changes from baseline to the follow-ups between the groups on the continuous secondary outcomes based on descriptive data with multiple imputations (intention-to-treat sample).

Outcome	Baseline to 6 weeks			Baseline to 3 months		
	d^a	CI_{low}^b	CI_{upp}	d	CI_{low}	CI_{upp}
QIDS	0.36	0.01	0.70	0.15	-0.19	0.49
PHQ-D	0.25	-0.09	0.59	0.12	-0.22	0.46
BADS	1.16	0.79	1.53	0.70	0.35	1.05
HADS-A	0.40	0.05	0.74	0.23	-0.12	0.57
WHO5	0.47	0.12	0.81	0.44	0.10	0.79
SPSI-PPO	0.33	-0.02	0.67	0.29	-0.06	0.63
SPSI-NPO	0.30	-0.04	0.65	0.24	-0.11	0.58
SF12-PH	-0.15	-0.49	0.19	-0.07	-0.42	0.27
SF12-MH	0.39	0.05	0.74	0.24	-0.10	0.59

Abbreviations: [a]Cohen's d was calculated by standardizing differences from baseline to follow-up scores by the pooled standard deviation of the baseline scores; positive d indicates a superiority of GET.ON Mood Enhancer compared to online psychoeducation; [b]CI: 95% confidence intervals for Cohen's d; /=No assessment; HRSD=Hamilton Rating Scale for Depression; QIDS=Quick Inventory of Depressive Symptomatology - Clinician-Rating; PHQ=Patient Health Questionnaire-Depression; BADS=Behavioral Activation Depression Scale; HADS-A=Hospital Anxiety and Depression Scale – Anxiety Subscale; WHO5= World Health Organization's 5 Wellbeing Index; SPSI-PPO=Social Problem-Solving Inventory – Positive Problem Orientation; SPSI-NPO=Social Problem-Solving Inventory – Negative Problem Orientation; SF12-PH=SF-12 Health Survey – Physical Health Subdomain; SF12-MH=SF-12 Health Survey – Mental Health Subdomain.

Table S2 a. Estimated differences in change from baseline to six weeks and three month follow-up of secondary outcomes in each group based on mixed-effect-model including psychotherapy history, time, and its interaction as predictors.

Outcome	Condition	Intercept Baseline		Psychotherapy history		T1-T2		T1-T2 x Psychotherapy history		T1-T3		T1-T3 x Psychotherapy history	
		B	SE	B	SE	B	SE	B	SE	B	SE	B	SE
QIDS	iCBT	10.41	0.82	2.31[b]	0.84	-3.89[a]	1.03	-0.19	1.20	-3.96[a]	1.03	-0.63	1.20
	OPE	10.76	0.70	2.32[b]	0.84	-1.39[c]	0.81	-2.11[c]	1.12	-3.16[a]	0.81	0.90[d]	1.51
PHQ-D	iCBT	15.39	0.88	0.48	0.90	-7.06[a]	1.01	2.72[b]	1.19	-6.86[a]	1.01	1.93[d]	1.19
	OPE	15.88	0.74	0.48	0.90	-3.40[a]	0.80	1.14	1.10	-4.79[a]	0-79	-0.37	1.10
BADS	iCBT	20.50	1.43	-1.65	1.47	11.10[a]	1.80	-2.19	2.10	8.94[a]	1.80	-0.77	2.10
	OPE	22.74	1.24	-1.65	1.47	2.18[d]	1.42	-0.34	1.96	3.99[b]	1.42	-0.37	1.96
HADS-A	iCBT	11.69	0.68	0.19	0.70	-4.89[a]	0.73	2.83[b]	0.87	-4.17[a]	0.73	1.83	0.87
	OPE	11.65	0.59	0.19	0.70	-1.61[b]	0.58	-0.10	0.81	-2.49[a]	0.58	0.54	0.81
WHO5	iCBT	4.95	0.76	-0.67	0.79	3.89[a]	0.92	-0.81	1.08	5.33[a]	0.92	-1.40[d]	1.08
	OPE	4.77	0.66	-0.67	0.79	2.07[d]	1.12	0.41	1.01	2.95[a]	0.73	0.40	1.01

Abbreviations: HRSD=Hamilton Rating Scale for Depression; QIDS=Quick Inventory of Depressive Symptomatology - Clinician-Rating; PHQ=Patient Health Questionnaire-Depression; BADS=Behavioral Activation Depression Scale; HADS-A=Hospital Anxiety and Depression Scale – Anxiety Subscale; WHO5= World Health Organization's 5 Wellbeing Index; SPSI-PPO=Social Problem-Solving Inventory – Positive Problem Orientation; SPSI-NPO=Social Problem-Solving Inventory – Negative Problem Orientation; SF12-PH=SF-12 Health Survey – Physical Health Subdomain; SF12-MH=SF-12 Health Survey – Mental Health Subdomain; iCBT=Internet-based cognitive behavior therapy; OPE=online psychoeducation on depression; [a]=$p<0.001$; [b]=$p<0.01$; [c]=$p<0.05$; [d]=$p<0.10$.

Table S2 b. Estimated differences in change from baseline to six weeks and three month follow-up of secondary outcomes in each group based on mixed-effect-model including psychotherapy history, time, and its interaction as predictors.

Outcome	Condition	Intercept Baseline		Psychotherapy history		T1-T2		T1-T2 x Psychotherapy history		T1-T3		T1-T3 x Psychotherapy history	
		B	SE	B	SE	B	SE	B	SE	B	SE	B	SE
SPSI-PPO	iCBT	7.60	0.71	-0.09	0.73	2.37[b]	0.72	-0.10	0.83	2.34[b]	0.73	-0.31	0.83
	OPE	7.74	0.61	-0.09	0.73	1.06[c]	0.55	0.01	0.77	0.93[d]	0.55	0.15	0.77
SPSI-NPO	iCBT	8.02	0.83	0.68	0.85	-1.88[c]	0.89	0.60	1.06	-1.75[c]	0.89	0.18	1.36
	OPE	7.91	0.71	-0.21	0.98	0.07	0.70	0.80	1.36	0.02	0.70	-1.08	0.98
SF12-PH	iCBT	44.81	1.80	-0.29	1.85	0.27	1.84	-2.53	2.19	0.94	1.84	-1.74	2.18
	OPE	46.40	1.55	-0.29	1.85	0.19	1.46	-1.36	2.04	-0.71	1.46	1.82	2.04
SF12-MH	iCBT	26.90	1.65	-0.39	1.70	9.84[a]	2.13	-2.25	2.49	11.79[a]	2.13	-2.10	2.49
	OPE	26.85	1.43	-0.39	1.70	6.03[a]	1.70	-1.95	2.33	8.41[a]	1.70	-0.06	2.33

Abbreviations: HRSD=Hamilton Rating Scale for Depression; QIDS=Quick Inventory of Depressive Symptomatology - Clinician-Rating; PHQ=Patient Health Questionnaire-Depression; BADS=Behavioral Activation Depression Scale; HADS-A=Hospital Anxiety and Depression Scale – Anxiety Subscale; WHO5= World Health Organization's 5 Wellbeing Index; SPSI-PPO=Social Problem-Solving Inventory – Positive Problem Orientation; SPSI-NPO=Social Problem-Solving Inventory – Negative Problem Orientation; SF12-PH=SF-12 Health Survey – Physical Health Subdomain; SF12-MH=SF-12 Health Survey – Mental Health Subdomain; iCBT=Internet-based cognitive behavior therapy; OPE=online psychoeducation on depression; [a]=$p<0.001$; [b]=$p<0.01$; [c]=$p<0.05$; [d]=$p<0.10$.

Table S3. Estimated group differences of secondary outcomes based on mixed-effect-model including two- and threefold interaction terms with group, time, and history of psychotherapy as predictors.

Outcome	Group Baseline		T1-T2 x Group				T1-T2 x Psychotherapy history x Group				T1-T3 x Group				T1-T3 x Psychotherapy history x Group			
	B	SE	B	SE	CI_{low}	CI_{upp}	B	SE	CI_{low}	CI_{upp}	B	SE	CI_{low}	CI_{upp}	B	SE	CI_{low}	CI_{upp}
QIDS	-0.35	0.83	-2.50[b]	1.25	-4.96	0.04	1.92	1.51	-1.04	4.88	-0.80	1.25	-3.26	1.66	0.90	1.51	-2.06	3.87
PHQ-D	-0.44	0.89	-3.66[b]	1.24	-6.10	-1.22	3.86[b]	1.52	0.87	6.84	-2.08[c]	1.24	-4.52	0.36	2.30[d]	1.52	-0.68	5.29
BADS	-2.25[d]	1.45	8.92[a]	2.19	4.61	13.23	-1.85	2.64	-7.04	3.33	4.95[c]	2.19	0.64	9.26	-0.40	2.64	-5.59	4.78
HADS-A	0.04	0.69	-3.27[a]	0.91	-5.06	-1.49	2.93[b]	1.12	0.73	0.51	-1.68[c]	0.91	-3.46	0.10	1.30	1.12	-0.90	3.49
WHO5	0.18	0.77	2.07[c]	1.13	-0.15	4.29	-1.22	1.36	-3.91	1.46	2.38[c]	1.13	0.16	4.60	-1.80[d]	1.36	-4.49	0.88
SPSI-PPO	-0.14	0.72	1.31[d]	0.87	-0.40	3.02	-0.11	1.08	-2.24	2.02	1.40[d]	0.87	-0.31	3.11	-0.46	1.08	-2.60	1.67
SPSI-NPO	0.11	0.84	-1.95[c]	1.10	-4.12	0.22	0.80	1.36	-1.87	3.48	-1.77[d]	1.10	-3.94	0.40	1.27	1.36	-1.41	3.94
SF12-PH	-1.59	1.82	0.07	2.28	-4.42	4.57	-1.17	2.83	-6.74	4.39	1.66	2.28	-2.84	6.15	-3.56	2.83	-9.13	2.00
SF12-MH	0.05	1.67	3.81[d]	2.59	-1.29	8.97	-0.30	3.09	-6.38	5.79	3.37[d]	2.59	-1.73	8.48	-2.03	3.09	-8.11	4.05

Abbreviations: HRSD=Hamilton Rating Scale for Depression; QIDS=Quick Inventory of Depressive Symptomatology - Clinician-Rating; PHQ=Patient Health Questionnaire-Depression; BADS=Behavioral Activation Depression Scale; HADS-A=Hospital Anxiety and Depression Scale – Anxiety Subscale; WHO5= World Health Organization's 5 Wellbeing Index; SPSI-PPO=Social Problem-Solving Inventory – Positive Problem Orientation; SPSI-NPO=Social Problem-Solving Inventory – Negative Problem Orientation; SF12-PH=SF-12 Health Survey – Physical Health Subdomain; SF12-MH=SF-12 Health Survey – Mental Health Subdomain; iCBT=Internet-based cognitive behavior therapy; OPE=online psychoeducation on depression; [a]=p<0.001; [b]=p<0.01; [c]=p<0.05; [d]=p<0.10.

Table S4. Negative Side-Effects from the intervention.

No.	Statement of the INEP[a]	n[b]	%
1	Since completing the training I feel worse.	1	1.5
2	Since the end of the training it is hard for me to trust others than it was before.	0	0
3	Since completing the training I have suffered more from past events than I did before.	5	7.7
4	Since completing the training I experience more conflicts with my partner than before.	4	6.2
5	Since completing the training my relationship with my family is worse than before.	1	1.5
6	Since completing the training my relationships with my friends is worse than before.	1	1.5
7	Since the beginning or after completing this training, I worry that my classmates/colleagues/fellow students may find out that I participated in this study	3	4.6
8	During the training or since completing the training I got in trouble regarding my insurances or I fear that problems may appear in the future.	4	6.2
9	During the training or since completing the training I worry more about financial problems than before.	0	0
10	During the training or since completing the training I felt dependent on my e-Coach.	3	4.6
11	During the training or since completing the training I struggle more with making my own decisions	2	3.1
12	My partner was jealous of my relationship with my e-Coach.	0	0
13	During the training or since completing the training there were phases I was feeling mentally unwell.	6	9.2
14	During the training or since completing the training I have changed for the worse.	2	3.7
15	During the training or since completing the training I have had, for the first time, suicidal thoughts	0	0

Abbreviations: [a]INEP= Inventory for the Assessment of Negative Effects of Psychotherapy; [b]Multiple choices made by 17 out of 65 participants in the intervention group.

Kapitel 4 – Messung der Zufriedenheit mit internetbasierten Gesundheitstrainings

Erweiterung der Evaluationskriterien von E-Mental-Health um die Nutzerperspektive

Um die Versorgungslücke bei Maßnahmen zur Bewältigung psychischer und substanzbezogener Probleme, u. a. bei riskantem Alkoholkonsum und bei Depressionen, durch neue Interventionsansätze schließen zu können, bedarf es in erster Linie evidenzgesicherter Wirksamkeitsnachweise. Der Evaluationsfokus bei internetbasierten Interventionen liegt dementsprechend auf klinischen Wirksamkeitsindikatoren. Der klinische Wirksamkeitsnachweis einer Intervention kann zwar als notwendige aber nicht als hinreichende Bedingung dafür gelten, dass eine Intervention Einzug in die Praxis erhält [58,59]. Bislang scheitern viele innovative Ansätze bei der Implementierung in die Routineversorgung [60]. Aufschluss über das Implementierungspotenzial neuer Gesundheitsinterventionen können „patientenorientierte" Outcomes liefern. Ein wichtiger Indikator zur Beurteilung des Implementierungspotentials neuer Interventionen ist die Zufriedenheit der Interventionsteilnehmenden [61]. Das Potenzial von wirksamen Maßnahmen bei der Prävention und Versorgung von Personen bleibt beschränkt, wenn sie aufgrund unerfüllter Erwartungen, eines unästhetischen Designs oder gar unerwünschter Nebenwirkungen nicht genutzt werden. Aus der Konsumentenforschung entlehnt beschreibt die Zufriedenheit das Verhältnis zwischen den Erwartungen an ein Produkt oder eine Dienstleistung und der wahrgenommenen Leistung [62]. Auf internetbasierte Gesundheitsinterventionen übertragen ist anzunehmen, dass eine Intervention mit höherer Wahrscheinlichkeit Einzug in die Versorgung erhält, wenn sie zu den gewünschten Effekten führt und darüber hinaus den Erwartungen der Teilnehmenden entspricht. Erst durch die Beurteilung von Interventionen unter Zuhilfenahme von Indikatoren wie der Nutzerzufriedenheit können die Chancen und mögliche Barrieren für eine Implementierung wirksamer Interventionen beurteilt und Maßnahmen zum Abbau entsprechender Hürden abgeleitet werden.

Evaluation des Fragebogens zur Zufriedenheit mit internetbasierten Gesundheitstrainings

Um die Nutzerzufriedenheit mit internetbasierten Gesundheitstrainings messen zu können, bedarf es valider Indikatoren [61,63]. Bislang fehlen jedoch validierte Instrumente zur Erfassung der Zufriedenheit. Mit dem Fragebogen zur Patientenzufriedenheit (im Original: Client Satisfaction Questionnaire, CSQ) existiert bereits ein ökonomisches Instrument für die Evaluation stationärer Versorgungseinrichtungen [64], von dem auch eine deutsche Übersetzung vorliegt [65]. Im Rahmen dieser Arbeit wurde deshalb die folgende Fragestellung bearbeitet:

Fragestellung 5: Ist ein Online-Fragebogen zur Erfassung der Trainingszufriedenheit ein geeignetes Instrument, um die Nutzerzufriedenheit mit Online-Gesundheitstrainings zu erfassen?

In einer weiteren Studie (Studie III) wurde der Online-Fragebogen zur Messung der Zufriedenheit mit internetbasierten Gesundheitstrainings (Client Satisfaction Questionnaire adapted to Internet-based interventions, CSQ-I) evaluiert. Anhand von zwei unabhängigen Stichproben wurde die innere Konsistenz, die faktorielle Struktur sowie die Messinvarianz über mehrere Gruppen hinweg untersucht. Anschließend wurde beurteilt, ob der Fragebogen ein geeignetes Instrument ist, die Teilnehmerzufriedenheit mit Online-Trainings zu erfassen und als zusätzliches Erfolgskriterium bei der Evaluation internetbasierter Trainings dienen kann. Das folgende Manuskript mit dem Titel „Reliability and Validity of Assessing User Satisfaction With Web-Based Health Interventions" beschreibt die Adaptation und Evaluation des Fragebogens.

Manuskript 5 – Fragebogenevaluation

Abstract

Background: The perspective of users should be taken into account in the evaluation of web-based health interventions. Assessing the user's satisfaction with the intervention they receive could enhance the evidence for the intervention effects. Thus, there is a need for valid and reliable measures on online-assessed satisfaction with web-based health interventions.

Objective: The objective of this study was to analyze the reliability, factorial structure, and construct validity of the Client Satisfaction Questionnaire adapted to Internet -based interventions (CSQ-I).

Methods: The psychometric quality of the CSQ-I was analyzed in user samples from two separate web-based randomized controlled trials, one from a depression prevention intervention (Sample 1, N=174) and the other from a stress management intervention (Sample 2, N=111). At first, the underlying measurement model of the CSQ-I was analyzed in order to determine the internal consistency. The factorial structure of the scale and the measurement invariance across groups were tested by multigroup confirmatory factor analyses. Additionally, the construct validity of the scale was examined by comparing satisfaction scores with the primary clinical outcome.

Results: Multigroup confirmatory analyses on the scale yielded a one-factorial structure with a good fit (RMSEA=0.09, CFI=0.96, SRMR=0.05) that showed partial strong invariance across the two samples. The scale showed very good reliability, indicated by McDonald's omegas of 0.95 in Sample 1 and 0.93 in Sample 2. Significant correlations with change in depressive symptoms (r=-0.35, P<.001) and perceived stress (r=-0.48, P<.001) demonstrated the construct validity of the scale.

Conclusion: The proven internal consistency, factorial structure, and construct validity of the CSQ-I indicate a good overall psychometric quality of the online measure to assess the user's general satisfaction with web-based interventions for depression and stress management. Multigroup analyses indicate its robustness across different samples. Thus, the CSQ-I seems to be a suitable measure to consider the user's perspective in the overall evaluation of web-based health interventions.

Keywords: Internet, online training, mental health, evaluation, clinical effectiveness, personal satisfaction

Introduction

State of Research on Web-Based Health Interventions

In recent years, development and usage of web-based health interventions have been on the rise, and these interventions show potential in expanding upon established services for preventing and treating impaired health [1]. Many studies so far have shown that web-based interventions are effective for various conditions, including depression [2,3], anxiety [4,5], sleep disorders [6], alcohol consumption [7], and stress [8–11]. However, there is a lack of published knowledge regarding aspects of effectiveness that are related to external validity, such as the applicability of proven interventions in routine care practice [12]. There are different reasons why evaluators should also examine how affected users directly evaluate the intervention. First, adding to the discussion on the importance of external validity [12,13], the evaluation should go beyond clinical effects that are directly assessed by healthcare professionals using observer- or self-rated health measures (eg, assessing depressive symptoms) [14]. The user's satisfaction with their intervention can be an important source for this metric. Adapting the definition from Ware and colleagues [15] for this study, satisfaction is a user's evaluation of the received web-based intervention. Thus, it provides information beyond what is assessed by healthcare professionals. Second, it also provides information beyond the design qualities of a web-based intervention that can be assessed by usability experts [16]. Thus, it delivers important information to service providers so that they can improve their interventions. Third, studying satisfaction can help to successfully implement and disseminate clinically effective web-based interventions as a part of routine healthcare [17,18]. Fourth, there are ongoing debates on the relationship between user satisfaction and clinical intervention outcomes [14]. Previous studies found significant correlations between satisfaction with face-to-face interventions and psychological health [19–22] insofar as people with better health were more satisfied. One problem in web-based interventions is the rate of users who do not fully adhere to the intervention protocol [23]. Satisfaction with the delivered intervention may play an important role for understanding adherence to web-based interventions and vice versa. Some studies, most of which focused on in-patient settings, found that adherent patients are more satisfied than patients who stop participating in the intervention [24]. Investigating the user satisfaction in web-based health interventions could therefore add to the understanding of such relations. However, there is a strong need for thoroughly studied online measures [25]. To the best of our knowledge, there is yet no validated measure for the assessment of user satisfaction with web-based interventions.

Review of established satisfaction measures

Various satisfaction measures have already been developed, such as the Patient Satisfaction Questionnaire PSQ-18 [26], the Service Satisfaction Scale SSS-30 [27], the Satisfaction with Stroke Care Questionnaire SASC [28], and the Client Satisfaction Questionnaire CSQ-8 [29]. Most of these

instruments were designed to evaluate healthcare in hospitals or the GP's office. In these settings, satisfaction ratings evaluate some dimensions that are not or less relevant to web-based interventions, including satisfaction with the clinical staff (eg, "I have been treated with kindness and respect by the staff at the hospital", SASC), the waiting time (eg, "waiting time between asking to be seen and the appointment (date and time) given", SSS-18), the time spent with a doctor (eg, "Doctors usually spend plenty of time with me", PSQ-18), or the technical quality (eg, "I think my doctor's office has everything needed to provide complete care", PSQ-18). Therefore, satisfaction measures for web-based interventions must be modified to address their unique characteristics that are not represented in traditional health services. For example, web-based interventions can be delivered with or without direct contact to healthcare professionals or can be accessed immediately after registration without any waiting time. In order to address all of these variations, any developed generic measure should be applicable to a wide range of web-based interventions. Moreover, especially for ease of usage in routine care settings, it is important to have an economically efficient instrument that requires little time to administer by staff and to complete by users. The Client Satisfaction Questionnaire (CSQ) seems to be a feasible candidate for adaptation and application to web-based interventions. The original CSQ has shown good psychometric properties in a study (N=45) to investigate the effects of pre-therapy orientation on psychotherapy outcome [30]. The German adaptation has been validated in a sample (N=300) of inpatient treatment within a psychosomatic clinic [31] and has already been integrated as a measure of routine monitoring in inpatient rehabilitation (N=53177) [32].

The CSQ has also become a widely used instrument for assessing user satisfaction with web-based health interventions [33-36]. It has been used as secondary outcome in a study comparing Internet-based Interpersonal Psychotherapy and Internet-based Cognitive Behavioral Therapy for adults with depressive symptoms, indicating that participants of the first intervention group were more satisfied than the second group [33]. In another study, the CSQ was used as a secondary outcome to compare an Internet-based intervention for depression with and without weekly therapist support, indicating that participants of the supported intervention were more satisfied than participants without support [34]. A modified version of the scale was also used in a pilot study of an Internet-based screening and brief intervention for student marijuana use, yielded 95 out of 123 participants (75%) being at least moderately satisfied with the intervention [35]. In a previous study of our research group, the CSQ was used as secondary outcome of an Internet-based recovery training for employees and yielded that 44 out of 49 participants (90%) would recommend the training to a friend in need (item 4 of the CSQ) [36]. However, to our knowledge, there is yet to be a study evaluating the psychometric quality of online assessed user satisfaction that tests its factorial structure and its association with indicators of effectiveness such as training adherence and health outcomes in web-based interventions.

Aim of the Study

This study aims to validate an adapted version of the German Client Satisfaction Questionnaire to assess the user satisfaction with Internet and mobile-based interventions (CSQ-I). First, we will examine the internal consistency of the scale, particularly, whether the measurement model underlying its eight items is at least essentially tau equivalent [37], which means that each item measures the same latent variable but with possibly different degrees of precision. Second, considering previous findings [29,31], we expect a single-factorial structure of user satisfaction that should be invariant across both samples in this study. The measurement model and the factorial structure of the scale will be cross-validated in two independent samples to increase the generalizability of the findings. We will further evaluate the validity of the scale by analyzing its correlation with other indicators of effectiveness. The overall evaluation of the psychometric quality of the scale will be conducted according to recommendations derived from the COSMIN checklist (Consensus-based Standards for the Selection of Health Status Measurement Instruments) [38,39].

Methods

Study Design

The CSQ-I was evaluated across two randomized controlled trials (RCT). The first trial was conducted to evaluate the efficacy of a web-based intervention in preventing the onset of major depression disorder [40,41]. Participants were recruited from 2013 to 2014 from the general population via newspaper articles, on-air media and through a campaign of a large insurance company. After completing an online screening questionnaire and telephone interview, individuals of at least 18 years of age with elevated depressive symptoms (Center for Epidemiological Studies Depression Scale, CES-D $\geq$ 16), not having a major depressive episode were randomly assigned to either the intervention or to a control group. The full inclusion and exclusion criteria are described in the efficacy paper of this trial [41]. The intervention consisted of six modules that were based on cognitive behavioral therapy. The participants were intended to complete each module within one week. All study outcomes were assessed using self-report measures at baseline (T1) and in post-intervention assessment after seven weeks (T2). Study outcomes relevant for the CSQ validation were the reduction of depressive symptoms between T1 and T2, adherence to the intervention, negative side-effects, and user satisfaction at T2. The second trial was conducted to evaluate a web-based stress management intervention in employees [42,43]. Participants of this trial were recruited in 2013 from the general population via newspaper articles, on-air media and through a campaign of a large insurance company. After completing an online screening questionnaire, individuals of at least 18 years of age with elevated symptoms of stress (Perceived Stress Scale, PSS $\geq$ 22) were randomly assigned to either the web-based intervention or to a control group. The full inclusion and exclusion criteria are described in the efficacy paper of this trial [43]. The stress management intervention

consisted of seven modules, each to be completed within one week. Outcome assessments took place at baseline (T1) and after seven weeks (T2). The primary outcome was symptom reduction of perceived stress between T1 and T2. Secondary outcomes included adherence to the intervention, negative side-effects, and user satisfaction at T2.

Measures

Client Satisfaction Questionnaire adapted for Internet Interventions (CSQ-I)

The CSQ-I consists of eight items measuring global satisfaction with the web-based intervention (Table 1). On the original German scale [31], respondents rate each of the items on a four-point Likert-type scale, but wording of response categories differed between the items. For example, the responses for item 1, "How would you rate the quality of service you received?" are rated between 4="Excellent" and 1="Poor", and the responses for item 2, "Did you get the kind of service you wanted?" are rated between 1="No, definitely not" to 4="Yes, definitely". Furthermore, four items are scored in inverse to minimize stereotypic response sets. However, after pilot testing (N=15) of the scale, discussion of the results in a focus group consisting of members of our research group, and inquiring for advice from experts in the field of Internet research, we decided to adapt the questionnaire in the following way. First, all questions were rephrased as statements to have constant response scales across the items, ranging from 1= "Does not apply to me" to 4="Does totally apply to me". In addition, we replaced the word "service" with "training" in all items because we expected that this wording would be more precise and common for users of web-based interventions. As in the original version, the scores from all eight items can be summed to a total score that ranges from 8 to 32. On five items (items 1, 2, 3, 5, and 7) participants rate the degree to which the intervention fulfilled their general satisfaction with the quality, kind of training, and amount of help they received. On item 6, respondents rate the degree to which the intervention helped them to deal with their problems. Item 4 assesses the degree to which respondents would recommend the intervention to others. Finally, on item 8, respondents rate their likelihood of using the intervention for themselves again.

Clinical Outcome

Depressive symptoms were assessed using the German version of the Center for Epidemiological Studies Depression Scale (CES-D) [44]. The CES-D is a self-report scale and consists of 20 items (eg, "During the past week I felt sad"), each scored from 0 to 3. The total score ranges from 0 to 60, with a higher score indicating more severe depressive symptoms. A cutoff of 16 is usually regarded as indicating clinically relevant depressive symptom severity.

Symptoms of stress were assessed using the German version of the ten-item Perceived Stress Scale (PSS-10) [45,46]. The PSS assesses the degree to which people perceive their lives as stressful.

Participants are asked to answer questions regarding the previous week (eg, "In the past week, how often have you felt that you were unable to control the important things in your life?") on a five-point Likert-type scale, with responses ranging from 0 to 4. The total score ranges from 0 to 40, with a higher score indicating higher perceived stress.

Adherence

The number of training modules that participants completed was used as the definition of adherence to the intervention in both trials. Full adherence was achieved when participants completed all six modules in the depression prevention intervention or all seven modules in the stress management intervention.

Side Effects

Side effects of participating in the trainings were measured with the side effects of psychotherapy inventory (INEP) [47] that was adapted to training settings. The adapted version consists of 15 items assessing negative changes participants experienced after completing the web-based training in their social and/or work environments that they directly attribute to their participation in the training (eg, "During or after finishing the training, I got worse in making important decisions by myself" or "Compared to the time before the training, my relationship to my family is worse"). For the analysis, the negative side effects will be counted and summed to a total amount of negative effects. The total score ranges from 0 to 15, with a higher score indicating more negative side effects.

Table 1. Item labels and descriptive analysis of the Client Satisfaction Questionnaire adapted to Internet-based interventions.

Item[a]	Sample 1				Sample 2			
	Mean (SD)	n_low[b] (%)	n_high[c] (%)	L[d]	Mean (SD)	n_low (%)	n_high (%)	L
1. The training I attended was of high quality or Das Training, an dem ich teilgenommen habe, hatte eine hohe Qualität.	3.48 (0.66)	3 (1.7)	94 (54.0)	0.73	3.45 (0.57)	0	54 (48.6)	0.67
2. I received the kind of training I wanted or Ich habe die Art von Training erhalten, die ich wollte.	3.11 (0.72)	5 (2.9)	54 (31.0)	0.83	3.09 (0.72)	3 (2.7)	31 (27.9)	0.82
3. The training has met my needs or Das Training hat meinen Bedürfnissen entsprochen.	3.13 (0.73)	5 (2.9)	58 (33.3)	0.83	3.05 (0.72)	3 (2.7)	3 (26.1)	0.80
4. I would recommend this training to a friend, if he/she were in need of similar help or Ich würde einem Freund/einer Freundin dieses Training empfehlen, wenn er/sie eine ähnliche Hilfe benötigen würde.	3.36 (0.73)	6 (3.4)	87 (50.0)	0.77	3.50 (0.67)	2 (1.8)	65 (58.6)	0.80
5. I am satisfied with the amount of help I received through the training or Ich bin zufrieden mit dem Ausmaß der Hilfe, die ich durch das Training erhalten habe.	3.18 (0.81)	9 (5.2)	71 (40.8)	0.82	3.12 (0.88)	6 (5.4)	44 (39.6)	0.78
6. The training helped me deal with my problems more effectively or Das Training hat mir dabei geholfen, angemessener mit meinen Problemen umzugehen.	3.25 (0.78)	9 (5.2)	76 (43.7)	0.82	3.09 (0.84)	7 (6.3)	37 (33.3)	0.82
7. In an overall, general sense, I am satisfied with the training or Im Großen und Ganzen bin ich mit dem Training zufrieden.	3.43 (0.80)	8 (4.6)	99 (56.9)	0.90	3.40 (0.70)	1 (0.9)	57 (51.4)	0.89
8. I would come back to such a training if I were to seek help again or Ich würde ein solches Training wieder nutzen, wenn ich Hilfe bräuchte.	3.36 (0.84)	8 (4.6)	101 (58.0)	0.89	3.35 (0.88)	6 (5.4)	63 (56.8)	0.81

[a] Item scoring: 1=does not apply to me or trifft nicht zu; 2=does rather not apply to me or trifft eher nicht zu; 3=does partly apply to me or trifft teilweise zu; 4=does totally apply to me or trifft voll und ganz zu.
[b] n_low=number of participants achieving the lowest possible score.
[c] n_high=number of participants achieving the highest possible score.
[d] L=standardized factor loadings.

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Data analyses

The analyses were conducted through structural equation modeling using the R package *lavaan* [48]. The covariance matrix was analyzed using the maximum likelihood method with robust (Huber-White) standard errors (MLR), which is asymptotically equivalent to the Yuan-Bentler T2* test statistic [49] recommended for non-normally distributed data. In the first step, to estimate the internal consistency of the scale, we examined the underlying measurement model of the scale. Essential tau equivalency [37] of the scale indicates that all items can be assumed to assess the same latent variable with the same units of measurement (ie, equal factor loadings). Essential tau equivalency is a necessary assumption for the use of the Cronbach alpha index; if the underlying model violates this assumption, Cronbach alpha will underestimate the reliability of the scale, and McDonald's omega should be used instead as a more precise estimate [50]. In the second step, we evaluated whether the one-factor structure proposed by the authors of the original CSQ [30,31] holds across our two training samples by conducting multigroup CFAs. The idea underlying the estimation of multigroup CFAs is that mean scores of different samples can only be compared in a meaningful way when the requirements of measurement invariance across groups are satisfied. Additionally, multigroup CFAs allow to test if participants in different training groups interpret and respond to the items in the same way. The procedure to establish measurement invariance (MI) involves several steps [51,52] which can be described as follows: Configural invariance means that the same common factor structure is shared across groups. Weak invariance indicates that all participants, regardless of their group membership (ie, the received training) respond to the scale items in the same way. Thus, to achieve weak invariance in addition to configural invariance, equivalent factor loadings across the groups are required. Next, we tested for strong measurement invariance by imposing additional constraints on the intercepts of the items (ie, the intercepts of the items were set to be equal across the groups). Strong invariance implies that individuals who have the same score on the latent variable (true score) will obtain the same score on the observed variable regardless of their training group membership.

To assess the fit of the models to the data, we used the following measures: the chi-square statistic, the relative chi-square (χ^2/df), the comparative fit index (CFI), the root mean square error of approximation (RMSEA), and the standardized root mean square residual (SRMR). In general, a χ^2/df value ≤3.00, CFI and TLI values ≥0.95, and RMSEA and SRMR values ≤0.08 indicate an acceptable fit to the data. Because the chi-square difference test commonly used to compare nested models is sensitive to sample size, we used additional criteria for model comparisons. For the Akaike's Information Criterion (AIC), models with lower AIC fit the data better than those with higher AIC values. In addition, we used ΔCFI, ΔRMSEA, and ΔSRMR to evaluate test invariance. Considering the number of items and the size of our samples, the following criteria proposed by Chen [53] were applied: ΔCFI<-0.005, ΔRMSEA<0.010, and ΔSRMR<0.005 for testing strong measurement invariance.

To test the convergent validity of the scale, we correlated the CSQ-I scores with the primary clinical outcomes in terms of symptom status at T2 and change of symptoms between T1 and T2. In addition, we compared participants with and without reliable symptom reductions. To assess symptom reductions on an individual level, we examined the number of participants who were classified as having reliably changed according to the reliable change index described by Jacobsen and Truax [54]. Participants were defined as having reliably changed if their symptoms declined from T1 to T2 with a reliable change index greater than 1.96 (8.65 points on the CES-D and 5.16 points on the PSS, respectively). Furthermore, we conducted explorative subgroup analyses on sex, adherence, and negative side effects from the intervention.

Discriminant validity was evaluated by means of the Average Variance Extracted (AVE). Fornell and Larcker introduced the AVE as an extension of chi-square based statistics for measuring the goodness of fit between theoretical models with unobservable variables and the empirical data [55]. The index also provides a procedure for establishing discriminant validity. The use of the AVE for this purpose has shown to be robust in various studies, primarily in the field of marketing research. For example, McKinney and colleagues used the AVE as an additional measure of the reliability for the evaluation of a web-customer satisfaction questionnaire and compared the AVE values to other established measures, such as Cronbach's alpha and the Composite Factor Reliability [56]. Liao and colleagues used the AVE as an additional measure to estimate the validity of a planned behavior model, including consumer satisfaction, to predict the customer's intention towards continued use of online services [57]. In this study, we compared the AVE values for the CSQ-I with the squared correlation estimate between satisfaction and clinical outcome at T2. The AVE was calculated as the total of all squared standardized factor loadings divided by the number of items [58]. Assuming discriminant validity, the AVE should be greater than the squared correlation estimate. This would indicate that user satisfaction is a separate construct, distinguishable from clinical symptoms.

All correlations and subgroup analyses were conducted using IBM SPSS version 22. All analyses were done only on complete data samples. Cases with missing values in the outcome variables were excluded from the analyses.

Results

Samples Characteristics

The depression intervention sample consisted of 201 adults from the German population with clinically relevant levels of depression (CES-D≥16). Complete data on the study outcome variables were available for 174 participants (86.6%). The participants were on average 45 years of age (SD=11.84), and 130 were female (74.7%) (Table 2).

Satisfaction with the web-based intervention to prevent major depression ranged from M=3.11 (SD=0.72) on item 2 to M=3.48 (SD=0.66) on item 1 (Table 1). Each of the items showed a ceiling effect, as at least 54 participants (31.0%) achieved the highest possible score (4="does totally apply to me") on the items (eg. "I got the kind of training I wanted"). In terms of quality criteria for measurement properties [38], ceiling effects are considered to be present if more than 15% of respondents achieved the highest possible score. The average total CSQ-I score was M=26.26 (SD=5.34), with 23 participants (13.2%) achieving the highest possible total score and only one participant achieving the lowest possible total score. The sample showed a negatively skewed distribution of satisfaction scores (skewness=-1.294, SE=0.184).

The stress management intervention sample consisted of 132 employees from the German population with elevated symptoms of stress (PSS≥22). Complete data of primary and secondary outcome variables were available for 111 participants (84.0%). The participants were on average 42 years of age (SD=9.79). The majority (n=94, 84.7%) was female (Table 2).

The satisfaction ranged from M=3.05 (SD=0.72) on item 3 to M=3.50 (SD=0.67) on item 4. At least 29 participants (26.1%) achieved the highest possible score on the items (Table 1). The total CSQ-I score was M=26.05 (SD=4.96) with 14 participants (12.6%) achieving the highest possible total score, whereas none of the participants achieved the lowest possible score. The sample showed a distribution skewed to the left (skewness=-0.909, SE=0.211).

Table 2. Samples' description

Characteristics	Sample 1 (N=174), n (%)	Sample 2 (N=111), n (%)
Gender		
Female	130 (74.7)	94 (84.7)
Male	44 (25.3)	16 (14.4)
Other[a]	-	1 (0.9)
Marital status		
Single	55 (31.6)	33 (29.7)
Married/partnership	87 (50.0)	52 (46.8)
Divorced/separated	32 (18.4)	10 (14.4)
Education		
High school	77 (42.0)	48 (43.3)
College/University	91 (54.6)	59 (53.1)
PhD	6 (3.4)	4 (3.6)
Occupation		
Employed full-time	92 (52.9)	85 (76.6)
Employed part-time	55 (31.6)	25 (22.5)
Not employed	21 (12.1)	-
Unemployed	3 (1.7)	-
Unable to work due to illness	3 (1.7)	1 (0.9)
History of psychotherapy		
Have not been in psychotherapy	101 (58.0)	72 (64.9)
Have been in psychotherapy	73 (42.0)	39 (35.1)

[a]Participants who wanted to specify their gender as neither female nor male.

Test of the CSQ-I Measurement Model

The tau congeneric model indicated that the one-factor model proposed for the original instrument [30,31] was supported in our adapted version. We found that in both samples, the one-factor model showed an acceptable fit to the data with a CFI=0.96 and SRMR=0.029 in Sample 1 and CFI=0.95 and SRMR=0.035 in Sample 2, but the RMSEA values were questionable: In Sample 1, RMSEA was 0.10 (*P*=.002), and in Sample 2, RMSEA was 0.10 (*P*=.02), indicating that the tested model did not perfectly fit to the data in Sample 2. In the next step, our results revealed that the essentially tau equivalent model was rejected by the data in both samples. In Sample 1, ΔCFI was -0.032, ΔRMSEA=0.021, and ΔSRMR=0.105. In Sample 2, ΔCFI was -0.052, ΔRMSEA=0.031, and ΔSRMR=0.140. Also, in both samples, the AICs were lower for the tau congeneric model. Hence, the assumptions for the computation of Cronbach alpha indices were not met [50], and the more precise McDonald's omegas were computed instead. Using this metric, the CSQ-I showed very good

reliability in both samples, where Sample 1 had ω=0.95 (bias corrected and accelerated [BCa] confidence interval [CI], 0.93-0.96), and Sample 2 had ω=0.93 (BCa CI, 0.91-0.95).

CSQ-I Structure Across the 2 Study Sample*s*

In the next step, we examined whether the test scores of the CSQ-I are comparable across the two study samples. To do so, we performed multigroup CFAs to test for configural, weak, and strong measurement invariance. The unconstrained model (M1) we used to test for configural invariance fit the data well across Sample 1 and Sample 2 (Table 3). Furthermore, the model that was used to test for weak invariance (M2) also fit the data well, and the differences in the relevant indices (ΔCFI, ΔRMSEA, ΔSRMR) showed that the additional constraints imposed on the data (ie, equal factor loadings) did not significantly alter the fit of the model. Subsequently, we tested for strong measurement invariance by imposing equality on the intercepts (M3). Our results indicated that our data did not support strong measurement invariance, although the corresponding cut-offs were only slightly missed (ΔCFI=-0.006, ΔRMSEA=0.001, ΔSRMR=0.005) and the AIC was almost the same: AIC=3581.5 for the model with weak invariance vs. AIC=3583.1 for the model with strong invariance. Given that full strong invariance was not supported, we tested for partial strong measurement invariance. The inspection of the means residual matrix revealed a substantial standardized residuum for item 4 ("I would recommend that training to a friend, if he/she were in need of similar help.") with a value of 4.84. This indicated a lack of invariance for this item across the two training samples. When the intercept of item 4 was freely estimated, partial strong invariance was supported (M4).

Table 3. Tests of invariance for the proposed one-factor structure of the CSQ-I between sample 1 (N = 174) and sample 2 (N = 111): results of multigroup confirmatory factor analyses with MLR estimator.

Model	χ^2	df^a	χ^2 / df	CFI[b]	RMSEA[c]	SRMR[d]
M1. configural invariance	99.20	40	2.48	0.964	0.102	0.031
M2. weak invariance	104.52	47	2.22	0.965	0.093	0.043
M3. strong invariance	120.23	54	2.23	0.959	0.093	0.048
M4. partial strong invariance	111.33	53	2.10	0.964	0.088	0.045

[a]*df*=degrees of freedom.
[b]CFI=comparative fit index.
[c]RMSEA=root mean square error of approximation.
[d]SRMR=standardized root mean square residual.

Convergent Validity

In Sample 1, the CSQ-I score was significantly correlated with depressive symptoms at T2 (r=-0.35, *P*<.001) (Table 4), indicating that higher satisfaction corresponded to a lower score of depressive symptoms after the intervention. The CSQ-I score was also significantly correlated with a change of depressive symptoms between T1 and T2 (r=0.27, *P*<.001), meaning that on average, participants with larger reductions in depressive symptoms appeared to be more satisfied with the intervention compared to those with smaller symptom reductions. The group of participants who met the criteria for reliable reduction of depressive symptoms (n=102, 58.6%) showed significantly greater satisfaction (M=27.45, SD=4.45) than the group without reliable symptom reduction (M=24.58, SD=6.03; t$_{(172)}$=3.609, *P*< .001; Cohen's d=0.52).

Most of the participants (n=134, 77.0%) fully adhered to the training protocol by completing all six training modules. The fully adherent participants (n=134, M=26.48, SD=5.38) did not appear to be more or less satisfied with the training than participants who did not fully adhere (n=40, M=25.55, SD= 5.21; t$_{(172)}$=0.964, *P*=.34). There was no meaningful difference in satisfaction between women (M=26.17, SD=5.51) and men (M=26.30, SD=4.87; t$_{(172)}$=0.086, *P*=.93). In this sample, 36 out of 174 participants (21%) reported negative side effect due to the training. In terms of satisfaction scores, participants who reported side effects (M=26.64, SD=6.26) did not significantly differ from participants without such negative effects (M=26.17, SD=5.09; t$_{(172)}$=0.472, *P*=.64).

Table 4. Means, standard deviations, and intercorrelations of relevant outcomes in sample 1.

Outcome	Mean (SD)	Intercorrelations (*P*)			
		1	2	3	4
1. Satisfaction at T2	26.26 (5.34)	-			
2. Depressive symptoms at T1	26.29 (7.66)	-0.04 (.59)	-		
3. Depressive symptoms at T2	17.10 (8.89)	-0.35 (<.001)	0.35 (<.001)	-	
4. Depressive symptoms T1-T2	-9.19 (9.50)	0.27 (<.001)	0.49 (<.001)	-0.58 (<.001)	-

In Sample 2, the CSQ-I score significantly correlated with perceived stress at T2 (r=-0.48, *P*<.001) (Table 5), indicating that higher satisfaction corresponded to a lower score of stress symptoms after the intervention. The CSQ-I score was also significantly correlated with change in perceived stress between T1 and T2 (r=0.52, *P*<.001), meaning that on average, participants with larger reductions of perceived stress appeared to be more satisfied with the intervention compared to those with smaller symptom reductions. The group of participants who met the criteria for reliable reduction in perceived stress (n=60, 54.1%) showed significantly greater satisfaction (M=28.12, SD=3.8) than the group without reliable symptom reduction (M=23.63, SD=5.10; t$_{(109)}$=5.302, *P*<.001; d=1.01). Most of the participants (n=90, 81%) fully adhered to the training protocol by completing all seven training

modules. The fully adherent participants (n=90, M=26.81, SD=4.55) were more satisfied with the training compared to the participants who did not fully adhere (n=21, M=22.81, SD=5.44; $t_{(109)}$=3.492, P<.001; d=0.85). There was no meaningful difference in satisfaction between women (M=26.37, SD=4.76) and men (M=24.13, SD=5.95; $t_{(109)}$=1.681, P=.10). In this study, 12 out of 111 participants (11%) reported they experienced at least one negative side effect due to the training. In terms of satisfaction scores, participants who reported side effects (M=27.75, SD=3.25) did not significantly differ from participants without such negative effects (M=25.85, SD=5.11; $t_{(109)}$=1.257, P=.21).

Table 5. Means, standard deviations, and intercorrelations of relevant outcomes in sample 2.

Outcome	Mean (SD)	Intercorrelations (P)			
		1	2	3	4
1. Satisfaction at T2	26.05 (4.96)	-			
2. Stress at T1	25.28 (4.60)	0.08 (.42)	-		
3. Stress at T2	18.68 (6.27)	-0.48 (<.001)	0.22 (.02)	-	
4. Stress T1-T2	-6.60 (7.00)	0.52 (<.001)	0.45 (<.001)	-0.74 (<.001)	-

Discriminant Validity

In sample 1, the AVE values for both measures (CSQ-I AVE=0.681, CES-D AVE=0.446) were greater than the squared correlation between these outcomes (R^2=0.123), indicating that the CSQ-I construct explained more of the variance in its items than it shared with the CES-D. In Sample 2, the Average Variance Extracted values for both measures (CSQ-I AVE=0.512, PSS-10 AVE=0.411) were also greater than the squared correlation between the CSQ-I and the PSS (R^2=0.230), indicating that the adapted CSQ-I explained more of the variance in its items than it shared with the PSS-10.

Discussion

Principal Findings

In the evaluation of Web-based health interventions, the user's perspective should be taken into account [15,24]. For this purpose, online measures with proven psychometric quality are needed [25]. In this study, we investigated the factorial structure, the measurement model, and construct validity of an adapted version of the Client Satisfaction Questionnaire in two samples of adults who had participated in web-based health interventions for either preventing major depression or improving stress management.

Multigroup factor analyses on the CSQ-I confirmed the proposed one-factorial structure [29,31] of the original scale across two independent samples. Our results showed that, although the assumptions needed for Cronbach alpha were not met, the scale demonstrated excellent reliability

through McDonald's ω [50] with ω=.95 in Sample 1 and ω=.93 in Sample 2. These findings correspond to previous studies that showed a very good reliability of the original scale, indicated by Cronbach's alphas of α=.93 [30], α=.87 [31], and α=.90 [32], respectively. The results on measurement invariance across the groups imply that the factor structure was replicated between the two samples; however this should be interpreted with caution since the differences found in the latent means were due to partial rather than full strong measurement invariance. While some researchers argue that in order to test for latent means between two samples at least two items must have invariant loadings and intercepts [59], Thompson and Green [60] reason that "in models with equivalent factor loadings but differing intercepts, differences in the means on that measure are a function of both the latent factors and the varying intercepts which can be interpreted in terms of a biased measure" (p. 149). However, we stress that the differences in the indices comparing weak and strong invariance were very small, indicating that the lack of invariance was marginal.

In line with previous findings [30,31,32,61], the satisfaction scores were on average very high, indicating that the participants tended to be very satisfied with the delivered intervention. This result may be restricted due to a ceiling effect [38], because many participants achieved the highest possible satisfaction score in both samples. However, the results showed that participants with reliable symptom reductions due to the received intervention were more satisfied than those without reliable reductions. Thus, these findings indicate the ability of the scale to discriminate between more and less satisfied intervention users, despite potential ceiling effects. Nevertheless, some studies suggest that modifying the response choice pattern from a 4-point format to a 5-point format with three positive choices and two negative choices can increase the variability of satisfaction scores [62-64]. Thus, testing a further adaptation of the CSQ-I response format may be useful in the future. The content validity of the scale was primarily investigated in relation to clinical outcomes in terms of psychopathological symptoms after the intervention and change of symptoms between baseline and post-assessment. The correlations between satisfaction and symptoms at the post-intervention assessment were r=-.35 in Sample 1 and r=-.48 in Sample 2. These results are in line with findings from the original CSQ version with correlation coefficients of r=-.34 for satisfaction x psychosomatic symptoms at post-assessment [30], r=.40 for satisfaction x health condition at discharge [31], and r=.40 for satisfaction x health condition at discharge [32]. The correlation between satisfaction and change of symptom severity from baseline to post-assessment were r=.27 in Sample 1 and r=.52 in Sample 2 in our study. These results also correspond to findings from the original CSQ regarding correlations between satisfaction and psychosomatic symptom reduction of r=-.40 [30], health condition improvement of r=.52 [31], and r=.60 [32], respectively. In summary, the results of the content validity analysis can lead to the assumption that participants might have rated their satisfaction to be high merely because they felt improved after the training. In this case, the satisfaction score would display a proxy measure for the clinical outcome. However, the discriminant validity analyzed in terms of the Average Variance Extracted values of the CSQ-I indicates that the satisfaction measure

and the clinical outcome measure assessed different constructs. The relation between satisfaction and adherence remains unclear. In the second sample only, we found a marginal but statistically significant difference between the satisfaction scores of participants who did and did not fully adhere to the intervention. In general, low satisfaction with the intervention is assumed to be associated with low adherence [25]; notwithstanding that individuals experiencing a high burden (eg, due to depressive symptoms) may be under considerable pressure to find relief. Those individuals may also adhere to an existing intervention, although they do not evaluate all aspects of the intervention as favorable. This might rather apply to the participants in the depressive intervention sample than to those in the stress intervention sample.

Nevertheless, some limitations of this study should be taken into account. First, the study drop-out rates were very low in both samples (13.4% in Sample 1, 16% in Sample 2), corresponding to drop-out rates in other validation studies [31,61,65]. However, it is possible that participants who did not complete post-treatment assessments may have rated their satisfaction lower than participants who attended the post-assessment [65]. Second, we were not able to control for the interference between satisfaction and post-intervention health state in terms of psychopathological symptoms, because both variables were assessed at the same time point. Thus, we could not exclude that the participants' health state, after participating in the trainings, biased their satisfaction rating. Further experimental studies are needed to investigate the clinical effects of web-based interventions on satisfaction using different time points for the assessment of user satisfaction and health outcomes, and also consider follow-up assessments. Third, because we used the same clinical outcome measure for state and for change of psychological health, it was not possible to estimate the predictive impact of both health outcomes on satisfaction independently. Thus, it may be beneficial to use different measures for a) health condition at the post-intervention assessment and b) change of health over time. Fourth, it was not possible to analyze the impact of adherence on satisfaction. Adherence was operationalized by the number of completed training modules. In both samples most of the participants completed all modules (77% in Sample 1 and 81% in Sample 2), so that it would not have been of value to determine the correlation between adherence and satisfaction. Future research should use additional measures of adherence (eg, login counts or time spent on the training website) to investigate the construct validity of the scale. Unfortunately, such data was not available for our study. Fifth, the subgroup-analyses of gender and negative side effects from the intervention were underpowered. Hence, future studies are needed to explore potential relevant subgroup effects such as gender and negative intervention effects that may influence satisfaction ratings. Finally, one theoretical limitation must be taken into account when using the CSQ-I for the evaluation of web-based health interventions. There have been previous discussions regarding the usefulness of user satisfaction in assessing quality of healthcare interventions, mainly because of its construct validity and unclear evidence for its association to other health outcomes [14]. It is important to note that the CSQ-I covers the user's satisfaction with web-based health interventions in a broader sense rather than focusing on specific intervention aspects. Thus, it is not

clear on which aspects of the intervention the participants actually based their satisfaction rating. Most of the CSQ-I items cover the fulfilled expectancy in terms of the general quality of the intervention, their intention to use it again, or their likeliness of recommending it to other affected people. The items do not cover specific aspects and surrounding conditions of the intervention (eg, usability of the online program, registration and login procedures, psychological and technical guidance) that may also be relevant for clinical success [1] and adherence [16] in web-based health interventions. Thus, it may be valuable to evaluate additional, more specific quality dimensions of web-based interventions (eg, technical support, usability, simplicity of the intervention content).

Conclusions

In this study the CSQ-I has shown to be a robust measure with a clear factorial structure across different samples. Thus, the CSQ-I seems to be a suitable measure to consider the user's satisfaction in the overall evaluation of web-based health interventions. It can provide an important source of information for service providers who wish to improve or implement their interventions into routine healthcare. Furthermore, satisfaction scores derived from the CSQ-I may serve as a useful reference for other people who are seeking help via the Internet.

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Authors' Contributions

DE, DL, and MB obtained funding for this study. LB and DE drafted the study design and the adaptation of the questionnaire. DL contributed to the final study design. LB drafted the manuscript. DL and DE supervised the writing process. LB and DR conducted the analyses. All authors read and approved the final manuscript.

Conflicts of Interest

None declared.

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Abbreviations

AIC: Akaike information criterion

AVE: average variance extracted

BCa: bias-corrected and accelerated

CES-D: Center for Epidemiologic Studies Depression Scale

CFA: confirmatory factor analysis

CFI: comparative fit index

CSQ: Client Satisfaction Questionnaire

CSQ-I: Client Satisfaction Questionnaire adapted to Internet-based interventions

PSQ-18: Patient Satisfaction Questionnaire Short Form

PSS-10: Perceived Stress Scale, 10-item version

RMSEA: root-mean-square error of approximation

SASC: Satisfaction with Stroke Care Questionnaire

SRMR: standardized root-mean-square residual

SSS-30: Service Satisfaction Scale-30

Kapitel 5 – Zusammenfassung der Ergebnisse

In diesem Kapitel werden die Ergebnisse der im Rahmen dieser Arbeit durchgeführten Studien zusammengefasst und vor dem Hintergrund anderer Studienergebnisse kritisch reflektiert. Den Abschluss dieser Arbeit bilden die Einordnung der durch diese Arbeit gewonnenen Erkenntnisse in den bisherigen Forschungsstand sowie ein Ausblick auf zukünftige Forschungsvorhaben, die sich aus der vorliegenden Arbeit ergeben.

Alkoholbezogene Störungen und ein riskanter Alkoholkonsum sowie Depressionen stellen bedeutsame Probleme für die Betroffenen und für das Gesundheitssystem dar. Obwohl es wirksame Verfahren zur Linderung dieser Probleme gibt, bleibt eine Vielzahl der Betroffenen unbehandelt. Die Gründe hierfür liegen zum einen in der mangelnden Verfügbarkeit entsprechender Gesundheitsangebote und zum anderen in einer geringen Bereitschaft, die vorhandenen Angebote in Anspruch zu nehmen.

Internetbasierte Interventionen wurden als Ansatz mit großem Potenzial beschrieben, um das aktuelle Präventions- und Versorgungsangebot zu ergänzen. Im Bereich alkoholbezogener Störungen beschränken sich die Versorgungsangebote in Deutschland weitgehend auf Personen, die bereits an einer diagnostizierbaren Erkrankung leiden. Für Personen unterhalb des Diagnosespektrums existieren praktisch keine individuellen Unterstützungsangebote, abgesehen von punktuellen Settingprogrammen, wie sie zum Beispiel im Rahmen der betrieblichen Suchtprävention erfolgen. Das Potenzial internetbasierter Interventionen zur Reduktion von riskanten Alkoholkonsummustern ist in Deutschland kaum erforscht. Vergleichende Wirksamkeitsuntersuchungen unterschiedlicher Interventionsformate (mit oder ohne Coaching) fehlen bislang auch international.

Mit der Versorgung von Menschen mit Depression wurde ein zweiter Problembereich skizziert. Trotz vorliegender Evidenz zur Wirksamkeit von internetbasierten Intervention bei Depressionen im Vergleich zu Wartekontrollgruppen war bislang unklar, ob solche Interventionen auch einem Vergleich mit anderen aktiven Interventionsformen, wie Gesundheitsinformationen zum Erkrankungsbild (Psychoedukation), überlegen sind. Des Weiteren fehlte es bislang an Untersuchungen potenzieller Nebenwirkungen von internetbasierten Interventionen bei Depressionen.

Ein weiteres Manko bisheriger Evaluationen internetbasierter Interventionen wurde in Bezug auf die starke Fokussierung auf klinische Ergebnismaße identifiziert. Mit der wachsenden Evidenz zur Wirksamkeit der Interventionen bedarf es einer Erweiterung des Evaluationsfokus um die Perspektive der NutzerInnen von internetbasierten Interventionen. Geeignete und vor allem nach psychometrischen Gütekriterien validierte Messinstrumente fehlten in diesem Bereich bislang.

Mit der vorliegenden Arbeit wurden deshalb die folgenden Fragen beantwortet:

1. Wie lässt sich ein niedrigschwelliges Online-Training zur Reduktion des Alkoholkonsums unter Nutzung zeitgemäßer IT-Technologie entwickeln und in einer randomisiert-kontrollierten Studie evaluieren? 2. Kann ein Online-Alkoholreduktionstraining den wöchentlichen Alkoholkonsum bei

Erwachsenen im Vergleich mit der Routineversorgung signifikant stärker reduzieren (Studie I)? 3. Wie lässt sich ein kurzes Online-Training zur Bewältigung von Depressionen entwickeln und dessen Wirksamkeit evaluieren? 4. Führt ein Online-Depressionsbewältigungstraining zu einer signifikant stärkeren Reduktion depressiver Beschwerden als reine Psychoedukation (Studie II)? 5. Ist ein Online-Fragebogen zur Erfassung der Trainingszufriedenheit ein geeignetes Instrument, um die Nutzerzufriedenheit mit Online-Gesundheitstrainings zu erfassen (Studie III)?

Es wurde angenommen, 1. dass die internetbasierte Intervention Clever weniger trinken sowohl mit als auch ohne Coaching-Unterstützung, verglichen mit der Wartekontrollgruppe, zu einer signifikant stärkeren Reduktion des wöchentlichen Alkoholkonsums führt, 2. dass die internetbasierte Intervention GET.ON Mood Enhancer mit Coaching-Unterstützung zu einer signifikant stärkeren Reduktion der Depressivität führt als reine Psychoedukation, 3. dass die Intervention gegenüber reiner Psychoedukation keine bedeutsamen unerwünschten Nebenwirkungen nach sich zieht, und schließlich 4. dass mit dem adaptierten Fragebogen zur Erfassung der Zufriedenheit mit internetbasierten Interventionen ein Online-Fragebogen vorliegt, mit dem sich die Trainingszufriedenheit psychometrisch adäquat erfassen lässt. Zur Überprüfung der oben genannten Annahmen wurden zwei randomisiert-kontrollierte Studien mit insgesamt 559 teilnehmenden Personen sowie eine Sekundäranalyse mit Daten von weiteren 285 Personen durchgeführt. Insgesamt wurden damit Effekte von internetbasierten Gesundheitsinterventionen anhand von 844 Personen untersucht.

Ergebnisse aus Studie I:

Mit Clever weniger trinken wurde in Kooperation mit internationalen Experten auf dem Gebiet internetbasierter Alkoholinterventionen ein Online-Training entwickelt, das auf bewährten Elementen der motivierenden Gesprächsführung und der kognitiv-behavioralen Verhaltenstherapie zur Alkoholkonsumreduktion beruht. Der theoretische Hintergrund und das Evaluationskonzept des Trainings wurden im Rahmen eines Studienprotokolls publiziert. Damit wurde die Fragestellung 1 beantwortet. Um die Wirksamkeit des Trainings mit und ohne zusätzlicher Coaching-Begleitung im Vergleich zu einer Wartekontrollgruppe (KG) zu untersuchen, wurden insgesamt 428 Personen mit riskantem Alkoholkonsum [> 14 Standardgläser (SG) pro Woche bei Frauen und > 21 bei Männern] in Studie I aufgenommen. Das Durchschnittsalter der Studienteilnehmenden betrug 47 Jahre (SD = 9,8), mehr als die Hälfte waren Frauen (n = 256, 59 %). Fast die Hälfte der Teilnehmenden (n = 185, 42,8 %) hat zuvor schon einmal psychotherapeutische Hilfe in Anspruch genommen. Teilnehmende des Selbsthilfetrainings absolvierten durchschnittlich 2,5 der insgesamt 5 Trainingseinheiten, von ihnen durchliefen 29 Personen (20 %) das komplette Training. Teilnehmende des begleiteten Trainings absolvierten durchschnittlich 3 von 5 Trainingseinheiten, 43 von ihnen (30 %) durchliefen das komplette Training. Von den Teilnehmenden des Selbsthilfetrainings zeigten sich 88 (85,4 %) und von denen des begleiteten Trainings 89 Personen (87,3 %) insgesamt zufrieden oder sehr zufrieden mit dem Training.

In allen drei Studiengruppen zeigte sich eine Reduktion des durchschnittlichen wöchentlichen Alkoholkonsums sechs Wochen nach der Randomisierung (KG: -3,2 SG; Selbsthilfe: -8,0 SG; mit Begleitung: -8,5 SG). Somit wurde auch die Fragestellung 2 in dem Sinne positiv beantwortet, dass die Annahme einer Überlegenheit des Online-Trainings gegenüber der Wartekontrollgruppe bestätigt werden konnte. Dabei zeigte sich kein signifikanter Unterschied zwischen der Selbsthilfeversion und dem begleiteten Training. Personen in den Trainingsgruppen konnten ihren wöchentlichen Alkoholkonsum jedoch um durchschnittlich 5 SG stärker reduzieren als Personen in der Kontrollgruppe. Dieser Unterschied war statistisch signifikant [B = -4,85; 95 %-Konfidenzintervall (KI): -7,02 bis -2,68; $p < 0,001$] und erwies sich auch sechs Monate nach der Randomisierung noch als stabil. Daneben zeigte die Analyse nach sechs Monaten, dass es in den Trainingsgruppen prozentual signifikant mehr Personen geschafft haben, ihren Alkoholkonsum auf ein risikoarmes Niveau zu reduzieren (n = 138, 48 %) als in der Kontrollgruppe [n = 35, 24 %; $\chi2 = 21,63$; $p < 0,001$; Odds ratio = 2,83; 95 % KI: 1,82 bis 4,38)]. Darüber hinaus wiesen Personen in den Trainingsgruppen im Vergleich zu denen der Kontrollgruppe eine signifikante Reduktion depressiver Symptomatik (d = 0,29; 0,09 bis 0,49), Angst (d = 0,36; 0,16 bis 0,56) und Stress (d = 0,34; 0,14 bis 0,55) auf.

Ergebnisse aus Studie II

Zur Beantwortung der Fragestellung 3 wurde das internetbasierte Training GET.ON Mood Enhancer auf Basis der kognitiv-behavioralen Psychotherapie bei Depressionen entwickelt. Die Kernübung des Trainings besteht in dem Aufbau positiver Aktivitäten sowie deren Integration in den Alltag der Teilnehmenden. Der Hintergrund des Trainings sowie dessen Evaluationsdesign wurden ebenfalls in einem Studienprotokoll veröffentlicht. Um die Wirksamkeit des Trainings zu untersuchen, wurden 131 Personen mit vorliegender Depression (Major Depressive Disorder nach DSM-IV) in die Studie II aufgenommen. Das Durchschnittsalter der Studienteilnehmenden betrug 42 Jahre (SD = 10,8), die meisten von ihnen waren Frauen (n = 99, 75,6 %). Etwas mehr als die Hälfte der Teilnehmenden (n = 77, 60,2 %) hatte bereits vor Beginn der Studienteilnahme wenigstens einmal psychotherapeutische Hilfe in Anspruch genommen. Der Anteil an Teilnehmenden mit Psychotherapieerfahrung war in der Trainingsgruppe (iCBT; internet-based Cognitive-Behavioral Therapy) (n = 45, 69,2 %) deutlich höher als in der psychoedukativen Kontrollgruppe (OPE; Online-Psychoeducation) (n = 32, 69,2 %). Von den insgesamt 65 Personen, die in die iCBT randomisiert wurden, absolvierten 49 (75,4 %) alle sechs Trainingseinheiten und benötigten dazu durchschnittlich 39 Tage. Von den insgesamt 66 Personen der OPE haben 53 (80,3 %) die psychoedukative Einheit absolviert. Die Trainingsteilnehmenden zeigten sich zum überwiegenden Teil zufrieden oder sehr zufrieden mit dem Training (n = 45, 83,4 %).

Sechs Wochen nach der Randomisierung wiesen sowohl die Teilnehmenden der iCBT als auch die der OPE eine signifikante Reduktion der depressiven Symptomatik auf. In der iCBT zeigte sich eine mittlere Reduktion von 8,47 Punkten auf der Hamilton-Skala, was mit d = 1,1 [95 %

Konfidenzintervall (KI): 0,72 bis 1,46] nach der Konvention von Cohen [66] einem großen Effekt entspricht. In der OPE zeigte sich eine mittlere Reduktion von 5,7 Punkten, was einem mittleren Effekt entspricht (d = 0,6; 95% KI: 0,25 bis 0,95). Die Analyse der Intergruppeneffekte zeigte eine stärkere Reduktion der Depressivität durch iCBT im Vergleich zu OPE mit einem kleinen Effekt in Höhe von d = 0,36 (0,02 bis 0,71). Somit wurde die Fragestellung 4 eindeutig beantwortet, indem die Annahme einer Überlegenheit von iCBT gegenüber OPE bestätigt werden konnte. Jedoch beschränkt sich die Überlegenheit auf den kurzfristigen Vergleich nach Abschluss der Intervention. Eine mittelfristige Überlegenheit nach drei Monaten konnte nicht belegt werden. Subanalysen zeigten zudem, dass die iCBT der OPE nur bei Personen überlegen war, die zuvor noch keine psychotherapeutische Hilfe in Anspruch genommen hatten (d = 0,87; 95% KI: 0,29 bis 1,45). Bei Personen mit vorhandener Psychotherapieerfahrung zeigte sich kein signifikanter Unterschied in der Reduktion der Depressivität (d = 0,08; 95 % KI: -0,37 bis 0,54). Die Analyse potenzieller Nebenwirkungen ergab, dass einige der Studienteilnehmenden im Verlauf ihrer Studienteilnahme negative Nebeneffekte erlebt haben. Suizidale Gedanken berichteten eine Person in der iCBT (1,9 %) und 4 Personen in der OPE (7,4 %); eine Symptomverschlechterung wiesen sechs Personen in der iCBT (9,2 %) und fünf in der OPE auf (7,6 %). Daneben zeigten sich selbst bei Personen, die keine Verbesserungen hinsichtlich der Depressivität zeigten, leicht erhöhte Werte in Bezug auf ihre Einstellung gegenüber der Inanspruchnahme weiterer psychologischer Hilfe (iCBT: Anstieg um 0,28 Punkte; OPE: 0,33 Punkte). In keiner dieser potenziell negativen Nebenwirkungen zeigten sich signifikante Unterschiede zwischen den Gruppen. Daneben gaben jedoch 17 Teilnehmende der iCBT (26,2 %) an, im Verlauf des Trainings oder danach andere negative Erfahrungen gemacht zu haben.

Ergebnisse aus Studie III

In der dritten Studie wurde eine Sekundäranalyse zweier unabhängiger Stichproben vorgenommen, um die psychometrische Qualität des adaptierten Fragebogens zur Erfassung der Trainingszufriedenheit mit internetbasierten Trainings zu untersuchen. Die erste Stichprobe (S 1) bestand aus 174 Teilnehmenden an einem Online-Training zur Prävention von Depressionen, die im Durchschnitt 45 Jahre alt und zu 74,7 % weiblich waren. Die zweite Stichprobe (S 2) umfasste 111 Teilnehmende eines Online-Stressmanagement-Trainings, die durchschnittlich 42 Jahre alt und zu 84,7 % Frauen waren. Eine Faktorenanalyse über beide Teilnehmendengruppen bestätigte die einfaktorielle Struktur des Konstrukts. Die Modell-Anpassungs-Indizes [Root Mean Square Error of Approximation (RMSEA) = 0,09; Comparative Fit Index (CFI) = 0,96; Standardized Root-Mean-Square Residual (SRM-R) = 0,05] wiesen auf eine hohe Modellgüte sowie die Messinvarianz über beide Stichproben hinweg hin. Eine akzeptable Passung des Modells zu den Daten ist durch CFI-Werte ≥ 0,95; RMSEA- und SRMR- Werte ≤ 0,08 gekennzeichnet. Die Skala zeigte sich zudem als sehr reliabel (McDonald's omega in S 1 = 0,95; omega in S 2 = 0,93). Signifikant negative Korrelationen zwischen der Trainingszufriedenheit

und psychischen Beschwerden nach dem Training (S 1: r = -0,35; p < 0,001; S 2: r = -0,48; p < 0,001) sowie signifikant positive Korrelationen zwischen der Zufriedenheit und der Reduktion der Beschwerden (S 1: r = 0,27; p < 0,001; S 2: r = 0,52; p < 0,001) kennzeichneten die Konstruktvalidität des Fragebogens. Durch die umfangreiche psychometrische Analyse des Fragebogens konnte die Fragestellung 5 eindeutig beantwortet werden.

Kapitel 6 – Allgemeine Diskussion der Ergebnisse

Wer nahm an den Interventionen teil?

Im Rahmen der vorliegenden Dissertation wurden die Effekte internetbasierter Interventionen bei verschiedenen Stichproben erwachsener Personen aus der Allgemeinbevölkerung untersucht. Das Durchschnittsalter über alle Stichproben hinweg lag bei 44 Jahren [Standardabweichung (SD) = 10,5]. Das Alter war in allen Stichproben ähnlich verteilt, sodass das jüngste Viertel aller Teilnehmenden jünger als 37 Jahre und das älteste Viertel älter als 53 Jahre war (Abbildung 1). Daran lässt sich erkennen, dass internetbasierte Gesundheitsinterventionen weitgehend unabhängig vom Alter in Anspruch genommen werden.
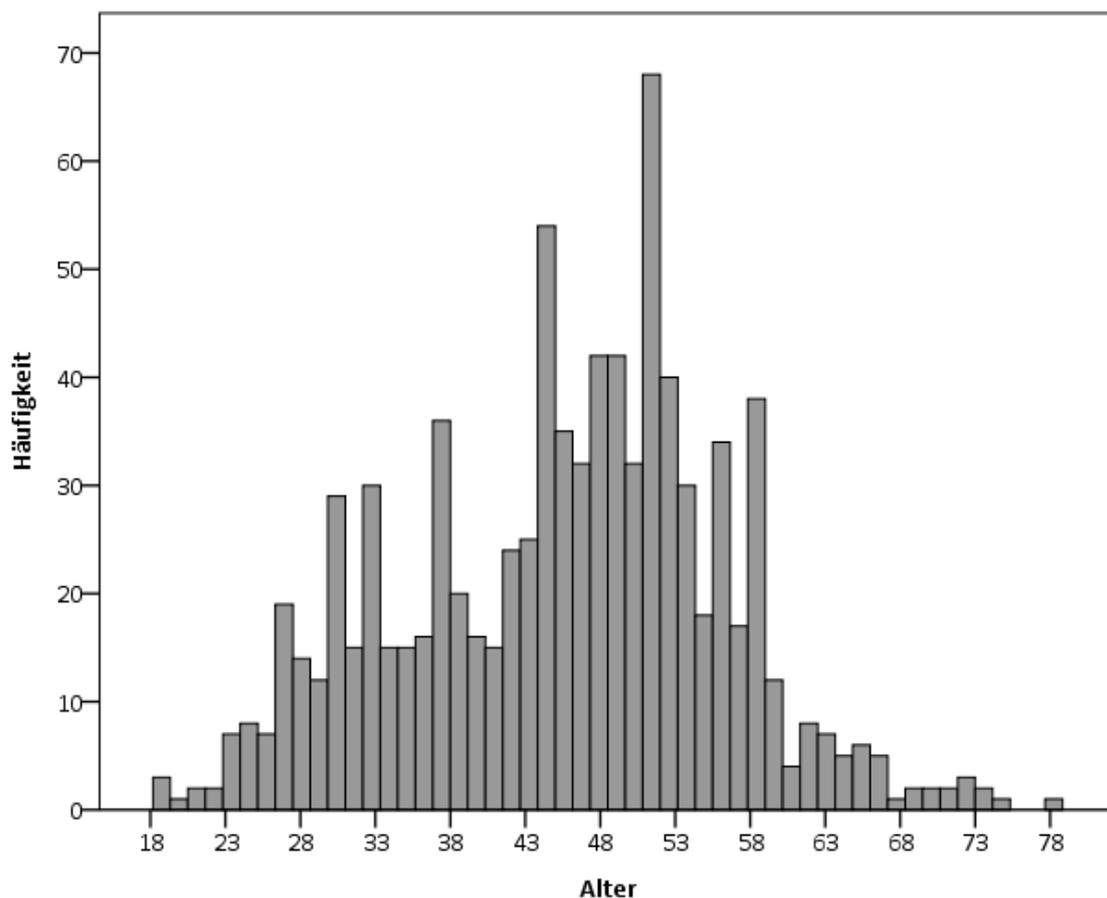
Abbildung 1. Altersverteilung über alle Stichproben der Studien I, II und III (N = 844)

Die Mehrheit der Personen war weiblich (69 %), wobei der Anteil der Frauen von 60 % in der Stichprobe mit riskantem Alkoholkonsum (Studie I) über 75 % in den beiden Stichproben mit depressiven Beschwerden (Studien II und III) bis zu 85 % in der Stichprobe mit erhöhtem Stress (Studie III) variierte. Der durchweg hohe Anteil an Frauen reiht sich in Erfahrungen mit traditionellen Gesundheitsangeboten ein, die zeigen, dass sowohl präventive Maßnahmen zu Themen wie Ernährung, Bewegung und Entspannung [67] sowie Stressbewältigung [68] als auch Behandlungsangebote wie Psychotherapie [69] mehrheitlich von Frauen in Anspruch genommen werden. Auch wenn der Männeranteil bei präventiven Setting-Angeboten (z. B. im Rahmen der betrieblichen Suchthilfe) im Vergleich zu anderen Gesundheitsthemen höher ausfällt, nehmen Männer hierzulande kaum individuelle Kursangebote wahr [68]. Hervorzuheben ist vor diesem Hintergrund der Anteil männlicher Teilnehmer am Training Clever weniger trinken in Höhe von immerhin 40 %.

In den durchgeführten Studien nahmen mit insgesamt 63 % mehrheitlich Personen mit Abitur oder höherem Bildungsabschluss teil. Damit bestätigt sich auch hier das Bild zu Inanspruchnahmeraten traditioneller Präventionsangebote, die in einem positiven Zusammenhang mit dem Bildungsgrad stehen [67]. Insofern können die Ergebnisse dieser Arbeit nicht auf Personen mit niedrigem Bildungsgrad übertragen werden.

Insgesamt hatten 44 % der Probanden vor Studienbeginn schon einmal eine psychotherapeutische Behandlung begonnen, mit einem vergleichswese geringeren Anteil in den Stichproben mit erhöhtem Stress (35 %), unterschwelliger Depressivität (42 %), riskantem Alkoholkonsum (43 %) und einem vergleichsweise hohen Anteil in der Stichprobe mit ausgeprägter Depression (59 %), was aufgrund des gewählten Einschlusskriteriums (diagnostizierbare depressive Episode) nicht überrascht. Einerseits zeigen diese Befunde, dass sich durch den Einsatz internetbasierter Interventionen Personen erreichen lassen, die traditionelle Hilfsangebote nicht in Anspruch nehmen [60]. Andererseits zeigen die Daten, dass auch ein erheblicher Anteil der Teilnehmenden, insbesondere Betroffene mit depressiven Beschwerden, verschiedenen Formaten von Hilfsangeboten gegenüber aufgeschlossen zu sein scheint. Sekundäre Analysen der vorliegenden Datensätze wiesen zudem darauf hin, dass die Einstellung der Studienteilnehmenden gegenüber der Inanspruchnahme traditioneller Hilfsangebote (i.e. Psychotherapie) im Studienzeitraum unverändert blieb. Insofern deuten die Ergebnisse nicht darauf hin, dass sich internetbasierte Interventionen negativ auf die Inanspruchnahme bewährter psychotherapeutischer Angebote auswirken.

Wie ist das Nutzungspotential der Interventionen zu beurteilen?

Um das Potenzial neuer Interventionen in der Praxis beurteilen zu können, spielt neben ihrer Wirksamkeit die Adhärenz eine wichtige Rolle [70,71]. Die Adhärenz beschreibt, inwiefern Personen an einer Gesundheitsintervention tatsächlich teilnehmen, sodass sich die beabsichtigte Wirkung einstellen kann [72]. In den durchgeführten Interventionsstudien wurde die Adhärenz durch die Anzahl durchgeführter Trainingseinheiten operationalisiert.

In Studie I wurde die Trainingsadhärenz wie folgt definiert: Da alle Trainingsteilnehmenden in der dritten Trainingseinheit festlegen konnten, mit welchem persönlichen Ziel sie das Training fortführen wollen (z. B. Beobachtung des eigenen Alkoholkonsums, Reduktion des wöchentlichen Konsums oder Erreichen der Abstinenz), wurde adhärentes Verhalten durch das Absolvieren der ersten drei Trainingseinheiten definiert. In der Trainingsvariante mit Coaching-Unterstützung zeigten sich mit 61 % signifikant mehr Teilnehmende adhärent als in der Selbsthilfevariante mit 40 % der Teilnehmenden (p = 0,005). Insgesamt fügen sich die Ergebnisse in andere Befunde zur Adhärenz alkoholbezogener Interventionen ein, die sowohl bei internetbasierten [33,73] als auch in Face-to-face-Angeboten oft weniger als 70 % beträgt [74,75].

In Studie II absolvierten 75 % der Teilnehmenden alle sechs Einheiten des Trainings GET.ON Mood Enhancer. Damit lag die Trainingsadhärenz leicht über der mittleren Adhärenz anderer internetbasierter Interventionen zur Reduktion depressiver Beschwerden (63%) [28]. Die Adhärenz ist vergleichbar mit der von psychotherapeutischen Behandlungen [38,52,76].

Wie ist die Wirksamkeit der Interventionen zu beurteilen?

In Studie I konnte gezeigt werden, dass das Online-Training Clever weniger trinken den wöchentlichen Alkoholkonsum in beiden getesteten Varianten, mit und ohne zusätzliche Coaching-Unterstützung, effektiv reduzieren kann. Die Stärke des statistischen Trainingseffekts (d = 0,30) fügt sich in die bisherige Befundlage ein, obwohl der erzielte Effekt leicht über dem durchschnittlichen Effekt vergleichbarer Interventionen liegt (d = 0,24) [33]. Darüber hinaus zeigte sich kein statistisch signifikanter Unterschied in der Wirksamkeit zwischen dem Training mit und dem ohne zusätzliche Coaching-Unterstützung. Auch dieser Befund passt zur bisherigen Evidenzlage [32], wenngleich es bislang nur wenige Studien gab, die überhaupt ein unterstützendes Online-Coaching untersucht haben. Zudem müssen die Ergebnisse zur Wirksamkeit des Trainings mit Coaching-Unterstützung vor dem Hintergrund interpretiert werden, dass nur ein geringer Anteil der Trainingsteilnehmenden vom Coaching-Angebot Gebrauch gemacht hat. Im Rahmen der Wirksamkeitsuntersuchung wurde auch der Einfluss verschiedener sozioökonomischer Faktoren und von arbeitsbezogenem Stress auf die Alkoholkonsumreduktion durch das Training analysiert, da in der Vergangenheit sowohl Querschnittstudien [77,78] als auch prospektive Studien [77,79,80] auf einen Zusammenhang zwischen solchen Faktoren und dem Alkoholkonsum hingewiesen haben. In der durchgeführten Studie

erwies sich lediglich das Geschlecht als signifikanter Prädiktor für den Alkoholkonsum nach dem Training. Ein bedeutsamer Einfluss arbeitsbezogener Stressfaktoren konnte nicht identifiziert werden.

In Studie II wurde die Wirksamkeit der internetbasierten Intervention GET.ON Mood Enhancer mit zusätzlicher Coaching-Begleitung im Vergleich zu internetbasierter Psychoedukation untersucht. Beide Interventionen wurden nach evidenzbasierten Verfahren und Empfehlungen konzipiert [81]. Dabei konnte die Annahme bestätigt werden, dass das Training mit Coaching-Unterstützung kurzfristig zu einer stärkeren Reduktion der Depressivität bei Personen mit depressiver Episode führt als reine Psychoedukation. Zur Nacherhebung drei Monate später fand sich keine Überlegenheit einer der beiden Interventionen. Damit unterscheidet sich das Ergebnis von denen früherer Studien unserer Forschungsgruppe, in denen verschiedene Versionen von GET.ON Mood Enhancer gegenüber Psychoedukation untersucht wurden. So zeigte sich eine Version der Intervention bei Personen mit unterschwelliger Depression (diagnostische Kriterien für eine depressive Episode waren nicht erfüllt) deutlich effektiver als reine Psychoedukation [82]. Eine weitere Version, die sich an Personen mit unterschwelliger Depression und komorbidem Diabetes mellitus richtete, erwies sich ebenfalls als deutlich effektiver gegenüber reiner Psychoedukation [83]. Anders als in den erwähnten Studien, in denen lediglich kleine Prä-/Post-Effekte für Psychoedukation gefunden wurden ($d = 0,29$ bzw. $d = 0,32$), führte in der vorliegenden Studie sowohl GET.ON Mood Enhancer ($d = 1,1$) als auch internetbasierte Psychoedukation ($d = 0,6$) zu einer deutlichen Reduktion der Depressivität. Dieses Ergebnis fügt sich in den bisherigen Kenntnisstand zu psychoedukativen Interventionen ein, die sich in der Vergangenheit ebenfalls als wirksam erwiesen haben [56,84]. Möglicherweise benötigen Personen mit voll ausgeprägter Depression, die an der vorliegenden Studie teilgenommen haben, eine intensivere Unterstützung, um einen deutlichen Nutzenzuwachs gegenüber einer Psychoedukation zu erfahren. Der geringe Interventionseffekt lässt sich möglicherweise auch durch den Umstand erklären, dass sich in der Interventionsgruppe mehrheitlich Personen mit Psychotherapieerfahrung befanden. Die Ergebnisse zeigten, dass bei dieser Personengruppe bereits die reine Psychoedukation zu einer bedeutsamen Reduktion der depressiven Symptomatik führt, während die Subgruppe der Personen, die zuvor noch keinerlei Hilfe in Anspruch genommen hatte, nur von GET.ON Mood Enhancer profitierten, nicht aber von der Online-Psychoedukation. Demnach deuten die Ergebnisse darauf hin, dass die Behandlungshistorie von Personen mit Depression eine Rolle für die Wirksamkeit internetbasierter Interventionen spielt. Dieser Befund widerspricht den Ergebnissen der einzigen beiden Studien, die in der Vergangenheit den Einfluss der Psychotherapiehistorie auf die Wirksamkeit internetbasierter Interventionen untersucht, aber keinen signifikanten Zusammenhang gefunden haben [85,86]. Um die Bedeutung der Therapieerfahrung für den inkrementellen Nutzen internetbasierter Trainings gegenüber psychoedukativen Interventionen besser beurteilen zu können, sollten die Ergebnisse dieser Arbeit als Basis für weitere a priori geplante experimentelle Untersuchungen mit Stichproben mit und ohne Therapieerfahrung genutzt werden.

Welche nicht-klinischen Erfolgskriterien sind von Bedeutung?

In Studie III wurde der Fragebogen zur Messung der Patientenzufriedenheit [64,65] für internetbasierte Gesundheitsinterventionen adaptiert und evaluiert [87]. Dabei zeigte er sich über zwei unabhängige Stichprobe hinweg als reliables und valides Instrument. Im Zuge der Evaluation konnte ein erwartungskonformer moderater Zusammenhang zwischen der Zufriedenheit mit dem Training und der Wirksamkeit der Interventionen festgestellt werden. Der Zusammenhang zwischen der Zufriedenheit und der Trainingsadhärenz bleibt jedoch unklar, da hier nur in einer der beiden untersuchten Stichproben ein positiver Zusammenhang erkennbar war. Das Ergebnis fügt sich damit in die bestehende Befundlage ein [88]. Zusammenfassend steht nun ein ökonomisches Instrument zur Verfügung, mit dessen Hilfe sich internetbasierte Interventionen auch direkt aus der Perspektive ihrer NutzerInnen beurteilen lassen. Da jedoch unklar ist, welche Interventionsmerkmale (z. B. Verständlichkeit der Übungen oder Attraktivität des Designs) für das Zufriedenheitsurteil ausschlaggebend sind, ist das Instrument nur eingeschränkt von Nutzen, wenn das Ziel der Evaluation darin besteht, daraus detaillierte technische Optimierungen der Intervention abzuleiten. Die Integration des Fragebogens als Indikator für die generelle externe Validität einer Intervention erlaubt jedoch in Zukunft eine ganzheitlichere Beurteilung entsprechender Maßnahmen. Dementsprechend wurde der Fragebogen in den Studien I und II eingesetzt, um die Perspektive der Teilnehmenden in die Beurteilung der Online-Trainings einfließen zu lassen.

In Studie I wurde die Zufriedenheit der Teilnehmenden mit dem Training Clever weniger trinken erhoben. Die Ergebnisse konnten im Rahmen der Veröffentlichung des Manuskripts 4 jedoch nicht berücksichtigt werden. Sowohl in der Trainingsversion mit als auch in der ohne Coaching-Unterstützung zeigten sich 85 % der Teilnehmenden insgesamt zufrieden oder sehr zufrieden mit dem Training. Ein Vergleich zu anderen Studien ist nicht möglich, da die Zufriedenheit in anderen Studien nicht untersucht oder berichtet wurde.

Im Vergleich mit vorherigen Versionen des Trainings GET.ON Mood Enhancer [82,83], in denen 98 % bzw. 88 % der Teilnehmenden berichtet haben, mit dem erhaltenen Training zufrieden oder sehr zufrieden zu sein, zeigten sich in der in Studie II untersuchten Version weniger Teilnehmende zufrieden (83 %). Insgesamt ergab die Untersuchung jedoch, dass weder das Online-Training noch die reine Psychoedukation zu schwerwiegenden Nebeneffekten führt und dass das Online-Training nicht mehr ungewollte Nebenwirkungen hervorruft als reine Psychoedukation. Insgesamt zeigten sich aber in beiden Untersuchungsgruppen in Studie I mehr Personen mit Symptomverschlechterungen als in anderen Studien [89]. Daraus ergibt sich die Notwendigkeit, auch die Konzeption des Online-Trainings an sich kritisch zu reflektieren [81]. Möglicherweise reichte die Intensität oder der Umfang der gebotenen Unterstützung nicht aus, um allen Teilnehmenden die Unterstützung zu bieten, die sie benötigten, um ihr Befinden zu verbessern oder wenigstens eine Verschlechterung zu verhindern.

Welche Limitationen gilt es zu berücksichtigen?

Die vorliegende Arbeit und die dadurch gewonnenen Erkenntnisse unterliegen einigen Limitationen. Die in den Studien erhobenen Daten stammen von Personen, die selbstselektiv an den Untersuchungen teilgenommen haben und nicht per Zufall aus der Gesamtbevölkerung ausgewählt wurden. Somit ist einerseits davon auszugehen, dass die Studienteilnehmenden überdurchschnittlich motiviert waren, etwas zur Verbesserung ihres Befindens zu unternehmen. So wiesen die untersuchten Probanden bei der Eingangsbefragung im Vergleich zur Gesamtbevölkerung überdurchschnittlich starke gesundheitliche Beschwerden oder gesundheitsgefährdende Verhaltensweisen auf, die auf ein überdurchschnittlich starkes Gesundheitsrisiko hindeuteten. Andererseits spiegelt diese Tatsache höchstwahrscheinlich ein realistisches Abbild der Personengruppe wider, die auch unter Routinebedingungen von solchen Interventionen Gebrauch machen würde, da es sich bei den hier untersuchten Interventionen um Maßnahmen der indizierten Prävention (Reduktion riskanten Alkoholkonsums) und der akuten Behandlung (Bewältigung von bereits vorhandener Depression) handelt. Eine weitere Spezifität der Stichproben besteht in Bezug auf das Bildungsniveau. Über alle Studien hinweg verfügten zwei Drittel der Teilnehmenden über einen Fach-/Hochschulabschluss und damit überproportional mehr als in der deutschen Allgemeinbevölkerung mit ca. einem Drittel [90]. Dieser Befund reiht sich in die bisherigen Untersuchungen internetbasierter Gesundheitsinterventionen ein, unabhängig vom untersuchten Gesundheitsproblem. Damit ist die Generalisierbarkeit der Ergebnisse auf die Allgemeinbevölkerung eingeschränkt. Darüber hinaus unterliegen die Ergebnisse der einzelnen Studien weiteren Limitationen:

So zeigte sich in Studie I, dass ein internetbasiertes Training geeignet ist, den Alkoholkonsum bei Erwachsenen mit Risikokonsum zu reduzieren. Die Rekrutierung der Studienprobanden erwies sich jedoch als besonders schwierig. Daher ist fraglich, ob eine, wenngleich wirksame, internetbasierte Intervention tatsächlich ein niedrigschwelliges Angebot für alkoholbezogene Probleme darstellt, das auch von einer nennenswerten Anzahl an Personen genutzt werden würde, wenn es einer größeren Personengruppe zur Verfügung gestellt wird.

In Studie II konnte eine kurzfristige Überlegenheit des internetbasierten Trainings zur Bewältigung von Depressionen gegenüber internetbasierter Psychoedukation gezeigt werden, die geringer ausfiel als in vergleichbaren Untersuchungen. Dieses Resultat muss unter Berücksichtigung zweier Randergebnisse interpretiert werden. So zeigte sich zum einen ein moderierender Einfluss der Psychotherapievorerfahrung auf den Zusammenhang zwischen Trainingsteilnahme und Symptomreduktion derart, dass diejenigen Personen ohne Vorerfahrung stärker vom Training als von der reinen Psychoedukation profitierten. Zum anderen fanden sich in der Trainingsgruppe deutlich weniger Personen ohne Psychotherapievorerfahrung als in der Psychoedukationsgruppe. Damit ist die Interpretation des Gesamtergebnisses durch die unterschiedliche Verteilung der Therapieerfahrung zwischen den Studiengruppen eingeschränkt.

In Studie III wurde mit dem Fragebogen zur Messung der Trainingszufriedenheit ein geeignetes Instrument vorgestellt, um die Zufriedenheit der NutzerInnen von internetbasierten Gesundheitsinterventionen zu erfassen. Dabei wurde ein generelles Problem bei der Erfassung des Zufriedenheitskonstrukts sichtbar, nämlich die mangelnde Streuung in den Item-Antworten. Aufgrund der durchschnittlich relativ hohen Antwortausprägungen konnte die Gefahr eines Deckeneffektes nicht ausgeschlossen werden. Insofern vermag der Fragebogen gerade im oberen Antwortsegment nicht ausreichend zwischen zufriedenen und sehr zufriedenen Personen zu unterscheiden. Dies ist jedoch ein generelles Problem des Zufriedenheitskonstrukts. Eine weitere Einschränkung ergibt sich aus der inhaltlichen Bandbreite der Skala. Mit lediglich acht Items liegt ein sehr ökonomisches Messinstrument vor. Gleichzeitig ermöglicht eine solch kurze Skala nur eine allgemeine Einschätzung der Zufriedenheit und keine detailliertere Identifikation der interventionsspezifischen Merkmale, die dem Gesamtzufriedenheitsurteil zugrunde liegen.

Welche Schlussfolgerungen ergeben sich für den Einsatz der Interventionen und die weitere Forschung?

Vor dem Hintergrund der geringen Inanspruchnahme traditioneller Präventionsangebote zum Alkoholkonsum stellt Clever weniger trinken ein innovatives Ergänzungsangebot dar. Selbst die Darbietung der Intervention ohne jegliche Coaching-Unterstützung kann zu substanziellen Konsumreduktionen führen. Daneben stellen die hohen Abbruchraten in Bezug auf die Adhärenz des Trainings ein unbefriedigendes Ergebnis dar, obwohl sie weitgehend den Abbrüchen von klassischen Hilfsangeboten bei problematischem Substanzkonsum entsprechen. Nichtsdestotrotz unterstreichen diese Erkenntnisse sowie die Erfahrungen bei der Probandenrekrutierung die Herausforderung, innovative Interventionsangebote zur Reduktion riskanten Alkoholkonsums zukünftig so zu platzieren, dass mehr Personen erreicht werden, um das Potential dieser Angebote ausschöpfen zu können. Eine vielversprechende Möglichkeit dazu könnte die Verknüpfung internetbasierter Alkoholinterventionen mit bestehenden Setting-Ansätzen sein. Diese Ansätze zielen darauf ab, potentielle NutzerInnen „in ihrem unmittelbaren Lebensumfeld anzusprechen und zu erreichen" [91]. Ein solcher Setting-Ansatz hat sich bereits in der Vergangenheit gerade für den Bereich des Substanzkonsums als vielversprechend erwiesen, um auch Männer mit gesundheitsfördernden Maßnahmen zu erreichen [68].

Die Evaluation des Trainings GET.ON Mood Enhancer zeigte, dass Personen, die unter Depressionen leiden, von einer Online-Intervention substanziell profitieren können. Die Ergebnisse deuten ferner darauf hin, dass je nach Behandlungshistorie eine unterschiedliche Intensität der Interventionen notwendig ist, um substanzielle Verbesserungen depressiver Beschwerden zu erzielen. Zudem wurden erstmalig auf verschiedenen Ebenen potentielle Nebenwirkungen einer KVT-basierten Online-Intervention analysiert. In den entsprechenden Analysen fanden sich keine Hinweise darauf, dass GET.ON Mood Enhancer systematisch negative Nebenwirkungen nach sich zieht. Dennoch ergibt sich

aus einzelnen berichteten negativen Erfahrungen in Zusammenhang mit ihrer Trainingsteilnahme die Notwendigkeit, entsprechende Interventionen so zu implementieren, dass sie an den individuellen Bedarf der Betroffenen angepasst werden können. Das gilt sowohl für die Individualisierung der Intervention vor dem Beginn als auch für die Zeit während der Interventionsteilnahme. So könnte ein vorgeschaltetes Feinscreening dazu genutzt werden, für jedes Individuum bereits vor Beginn eines Trainings Empfehlungen für bestimmte Übungen zu erteilen. Mithilfe eines kontinuierlichen Kurz-Monitorings während der Trainingsteilnahme könnte die Online-Coaching-Unterstützung noch mehr an den individuellen Unterstützungsbedarf angepasst werden, indem z. B. die Unterstützungsintensität erhöht wird, wenn Teilnehmende eine Verschlechterung der depressiven Symptomatik aufweisen. Auf diese Weise ließen sich internetbasierte Interventionen, sowohl solche zur Reduktion depressiver Beschwerden als auch zur Reduktion alkoholbezogener Probleme individualisieren [92–94].

Vor dem Hintergrund der vorgestellten Ergebnisse stellen sich folgende weitergehende Fragen, die sowohl für internetbasierte Alkoholinterventionen als auch für Depressionsinterventionen gelten: Welchen Nutzergruppen genügt eine fundierte Psychoedukation, um ihr Befinden zu verbessern, welche profitieren von Selbsthilfevarianten der Online-Trainings und welche benötigen eine engmaschigere, persönliche Unterstützung? Welches Ausmaß an persönlicher Unterstützung ist unter Berücksichtigung klinischer Notwendigkeit und kostenökonomischen Gesichtspunkten am effizientesten? Mit der vorliegenden Arbeit konnten bereits Anhaltspunkte zur Beantwortung einiger dieser Fragen identifiziert werden. Auf Basis der vorliegenden Ergebnisse können diese Fragen weiterbearbeitet werden. Zu diesem Zweck könnte es sinnvoll sein, das Untersuchungsparadigma randomisiert-kontrollierter Wirksamkeitsstudien insofern zu erweitern, dass verschiedene potenzielle Moderatoren (z. B. Psychotherapieerfahrung vs. keine Vorerfahrung) und Unterstützungsvarianten (z. B. Intensives Coaching vs. minimales Coaching vs. Selbsthilfe) mit realisierbarem Aufwand hinsichtlich der Anzahl zu rekrutierender Probanden untersucht werden können [95]. Ein effizienter methodologischer Ansatz zur Untersuchung dieser Komponenten könnten faktorielle Designs bieten [95,96]. Dies setzt voraus, dass die Modalitäten der verschiedenen Interventionsvarianten und – komponenten im Vorfeld klar definiert werden. Für die Konzeption unterschiedlicher Coaching-Varianten kann das Efficiency Model of Human Support eine gute Hilfestellung bieten [27]. Des Weiteren deuten die Wirksamkeitsergebnisse der vorliegenden Arbeit auch auf das Potenzial transdiagnostischer Interventionen hin, insbesondere für die Themen Depression, Alkohol und Stress [97,98]. Mit dem Fragebogen zur Zufriedenheit mit internetbasierten Trainings liegt nun ein erwiesenermaßen valides und reliables Instrument vor, mit dessen Hilfe sich auch das Implementierungspotenzial internetbasierter Interventionen besser beurteilen lässt.

Letztendlich gilt es, in Zukunft konkrete Disseminations- und Implementierungsstrategien zu erproben, um die wirksamen Interventionen möglichst vielen Betroffenen zur Verfügung zu stellen, damit sie ihre Wirkung entfalten können. Eine Möglichkeit dazu besteht in der Integration entsprechender Interventionen in bestehende oder auch zu schaffende Angebote betrieblicher

Gesundheitsförderung, um potentielle NutzerInnen „in ihrem unmittelbaren Lebensumfeld anzusprechen und zu erreichen" [91]. Ein solcher Setting-Ansatz hat sich bereits in der Vergangenheit gerade für den Bereich des Substanzkonsums als vielversprechend erwiesen, um auch Männer für die Teilnahme für Programme der Gesundheitsförderung zu gewinnen [68]. Im Rahmen eines im Jahr 2016 begonnenen Förderprojekts (www.digi-exist.de) des Bundesministeriums für Bildung und Forschung (BMBF) wurden die Trainings GET.ON Mood Enhancer und Clever weniger trinken für die Zielgruppe junger Unternehmen adaptiert [99]. Seit dem Frühjahr 2018 werden sie als Bestandteile eines digitalen Gesundheitsmanagementprogramms erstmalig in einem Pilotunternehmen erprobt.

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