Monitoring and improving mental health with internet- and mobile-based approaches

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CONTENT

Abstract

Internet- and mobile technologies are increasingly used to deliver mental health care. E-Mental Health is promising for the prevention and treatment of mental disorders, in particular due to its wide population access, a low threshold, the active role of the client, lower costs compared to traditional care, and the possibility to integrate interventions in real-world settings. However, while E-Mental Health was shown to be an effective treatment tool, fewer studies investigated the prevention of mental health problems with E-Mental Health approaches. In a series of three studies, this dissertation examines internet- and mobile-based approaches for the early monitoring and supporting of mental health. First, a pilot study investigates the use of smartphone data as collected by daily self-reports and sensor information for the self-monitoring of bipolar disorder symptoms. It was found that some, but not all smartphone measurements predicted clinical symptoms of mania and depression, indicating that smartphones could be used as an early-warning system for patients with bipolar disorder. Second, a randomized controlled trial evaluates the effectiveness of an internet-based intervention among persons with depression and sickness absence. The intervention was found to be effective in reducing depressive symptoms compared to a control group, suggesting that the internet can provide effective support for people with sickness absence due to depression. Third, a study protocol proposes to combine self-monitoring with a mobile intervention to support mental health in daily life. Supportive self-monitoring will be evaluated in a fully mobile randomized controlled trial among a sample of smartphone users with psychological distress. If supportive self-monitoring on the basis of a smartphone application is effective, it could be widely distributed to monitor and support mental health on a population level. Finally, the contribution of the presented studies to current research topics in E-Mental Health is discussed.

Zusammenfassung

Internet- und mobil-basierte Technologien werden in zunehmenden Maße zur Gesundheitsversorgung psychisch erkrankter Menschen eingesetzt. E-Mental Health ist ein vielversprechender Ansatz zur Prävention und Behandlung psychischer Störungen, insbesondere aufgrund des breiten Zugangs in der Bevölkerung, der Bereitstellung niedrigschwelliger Angebote, der aktiven Rolle des Klienten, geringeren Kosten im Vergleich zu traditioneller Versorgung, sowie der Möglichkeit, die psychische Gesundheit im Kontext des alltäglichen Leben zu untersuchen. Während die Effektivität von E-Mental Health zur Behandlung psychischer Störungen bereits gut nachgewiesen ist, liegen weniger Studien zur Prävention psychischer Störungen mit E-Mental Health vor. In einer Reihe von drei Studien untersucht die vorliegende Dissertation internet- und mobilbasierte Ansätze zum Früh-Monitoring und zur Unterstützung der psychischen Gesundheit. Erstens untersucht eine Pilotstudie, ob per Smartphone erhobene tägliche Selbstberichte und Sensorik-Messungen für das Monitoring von Symptomen bipolarer Störungen eingesetzt werden können. Die Ergebnisse zeigen, dass einige, aber nicht alle per Smartphone erhobenen Daten klinische Symptome von Manie und Depression vorhersagen, was auf den möglichen Einsatz von Smartphones als „Frühwarnsystem“ für Patienten mit bipolarer Störung hinweist. Zweitens wird in einer randomisiert-kontrollierten Studie die Effektivität einer internetbasierten Intervention für Personen mit Depression und Arbeitsunfähigkeit untersucht. Die Ergebnisse belegen die Effektivität der internetbasierten Intervention hinsichtlich einer Reduzierung depressiver Symptome im Vergleich zur Kontrollgruppe. Dieses Ergebnis zeigt, dass das Internet von Arbeitsunfähigkeit aufgrund Depression betroffener Menschen effektiv unterstützen kann. Drittens wird basierend auf den vorherigen Befunden ein Studiendesign entwickelt. Es wird vorgeschlagen, Monitoring mit einer mobilen Intervention zur Unterstützung der psychischen Gesundheit im alltäglichen Leben von Personen mit psychischer Belastung zu kombinieren. Unterstützendes Monitoring soll in einer mobilen randomisiert-kontrollierten Studie an einer Stichprobe von psychisch belasteten Benutzern eines Smartphones untersucht werden. Sofern der Ansatz des unterstützenden Monitorings auf Basis einer Smartphone Applikation effektiv ist, könnte er großflächig eingesetzt werden, um die psychische Gesundheit der Bevölkerung zu unterstützen. Abschließend wird der Beitrag der vorgestellten Studien zu aktuellen Forschungsfragen im Bereich E-Mental Health zusammenfassend diskutiert.

Chapter 1: General Introduction

General Introduction

Mental health is a global challenge of the 21st century. Up to 27% of the adult population is affected by at least one mental disorder each year [1], and by the age of 50, three-quarters of the population have experienced some kind of mental disorder in their lifetime [2]. Among the most common mental disorders are mood disorders, anxiety disorders, insomnia, somatoform disorders, and substance abuse disorders [3]. Mental ill-health is responsible for substantial disability, accounting for 28.5% of global years lived with disability (YLD) [4]. By 2030, mental health problems are expected to be the leading contributor to overall disease burden in high-income countries [5].

For the individual, maintaining good mental health is fundamental not only for well-being and quality of life, but also for positive functioning and social connectedness. Poor mental health can be both a determinant and a consequence of poverty, and people with mental health problems face an elevated risk of unemployment [6]. There are strong links between mental health and work productivity, social inclusion, quality of relationships, and life opportunities in general [7, 8]. People with mental illnesses are subject to stereotypes, prejudice, and discrimination due to the stigma associated with mental illness [9]. Mental illness also has a high co-morbidity with other health conditions, and poor mental health acts as a risk factor for poor physical health [10]. Over an individual's lifespan, mental health problems often occur episodically, where relatively symptom-free periods alternate with more severe episodes of illness [6]. Mental ill-health frequently develops in young adults and tends to become chronic in older age if not adequately treated and managed [7].

From a societal perspective, mental health has a substantial impact on the economy. It is estimated that the total cost of all mental disorders taken together amounts to €240 billion each year in Europe [11]. The majority of costs are not a result of direct expenditures, e.g., for mental health services and treatment, but are rather results of indirect costs from work absenteeism and decreased productivity while at work (presenteeism). These productivity losses are paid by employers and the social security system. In Germany, the contribution of mental health problems to total sickness absence among employees is growing. Between 2005 and 2015, the share of mental health problems from overall sickness absences more than doubled, reaching 15.1% [12], and making mental health problems the third largest contributor to sickness absences. Actions to target the increase in absenteeism and inability to work due to mental health problems has been demanded.

The existing health care system offers effective treatment options to those affected by mental health problems. For example, the recommended treatment for depression includes a combination of psychotherapy and medication and is provided in an inpatient or outpatient setting based on severity [13]. But even in Germany, where there are comprehensive health care systems with free

access to mental health care, only up to one-quarter of all individuals with mental disorders receive adequate professional help [14]. This means that 75% of people with mental health problems remain untreated. Manifold barriers to help-seeking exist [15], and these include geographical restrictions of services, fear of stigmatization, a preference for self-care, and negative attitudes towards mental health care [16, 17]. Another reason for the under-treatment of mental ill-health is the low detection rate of people with mental health problems. In primary care, only about 55% of patients are correctly diagnosed by general practitioners as having a clinically significant depressive disorder [18]. It can be inferred that there is a significant amount of unmet treatment need in the population due to the high number of individuals who are unaware of their mental health issues and consequently do not seek treatment.

To address the treatment gap in mental health care, the global expert commission, the National Institute of Mental Health (NIMH), has identified several "Grand Challenges" that contribute to the global state of mental ill-health [19]. These include identifying its root causes and risk and protective factors, advancing prevention and implementation of early interventions, improving treatments and expanding access to care, and raising awareness on the global burden of mental ill-health. On the policy level, several countries have made effective, accessible, and high-quality mental health care a priority and have called for increasing action to promote mental health in the population [19, 20]. Within this framework, it is the role of clinical psychology and psychiatry to develop broadly accessible and evidence-based interventions for mental health.

Recently, the use of the Internet and mobile technology in mental health care has emerged as a promising opportunity to increase access to mental health care [21]. In the past years, an increasing number of internet- and mobile-based approaches have been developed to complement existing traditional treatment options. This is generally referred to as E-Mental Health. E-Mental Health has several delivery options, including via websites, email, or smartphones, and can be offered as a standalone treatment or as a component of traditional care, as in stepped care approaches. E-Mental Health has several advantages. Due to its relative anonymity, E-Mental Health has a low threshold and is easily accessible. Since it is accessible at any time or place, geographical barriers to care can be circumvented and patients can progress through the content at their own pace. A major advantage compared to traditional care is that E-Mental Health is easily scalable, and once a tool has been developed, can be delivered on a large scale with low additional costs. The use of mobile technology even allows for real-time, real-world intervention. It is assumed that E-Mental Health encourages the client to take an active role, empowering them to manage their own health. Due to this, E-Mental Health is likely to reach affected individuals earlier than traditional care, thus preventing the onset of more severe mental health problems and providing support at the most critical moments.

While E-Mental Health has been found to be generally effective for a broad variety of mental health problems, there are several gaps in this emerging field of research. Internet-based programs can be comparably effective as face-to-face care for depression, anxiety, and other mental health conditions [22, 23]. However, few studies have examined the role of E-Mental Health in the prevention of mental ill-health. Furthermore, meta-analyses indicate broad heterogeneity in the effectiveness of E-Mental Health programs [24, 25]. Internet-based programs differ considerably in their effect sizes, making it necessary to evaluate each program separately. For example, the amount of additional human therapeutic support moderates the degree to which patients benefit from participating in E-Mental Health and how they engage and adhere to the content [26]. In mobile self-monitoring, the clinical usefulness of passively collected sensor-based information has not yet been shown. Regarding the safety of E-Mental Health, concerns have been raised over possible detrimental effects and acute crisis intervention in unsupervised settings [27]. Another concern is that high self-management skills are required for E-Mental Health, and there is a low threshold for drop-out, making it more likely for some individuals to discontinue participation before any sustainable effects occur. Thus, it is necessary to identify the subgroups for which E-Mental Health interventions are most efficient, and to target those subgroups specifically before E-Mental Health can be integrated into the healthcare system.

Two major research areas, prevention and therapy of mental ill-health, are highly relevant for E-Mental Health given the impact of mental illness. Prevention refers to actions taken in order to prevent illness from starting or becoming more serious by minimizing risk factors and promoting healthy behavior. Due to the increasing integration of mobile technology into everyday life, mobile-based approaches are considered to be especially suitable for the prevention of mental illness in its early stages. With mobile-based approaches, it is possible to monitor symptoms of mental illness and health-related behavior over time, assisting patients and providers in the identification of early-warning signs and the self-management of mental health. Mobile technology is also capable of collecting ecologically valid data from daily life, which can contribute to knowledge on the phenomenology and epidemiology of mental disorders. However, the potential of E-Mental Health for the early prevention of mental disorders has not yet been explored. Currently, in terms of therapy, the most common modes of delivery are Internet-based programs (non-mobile), since they are capable of presenting therapeutic content over websites that can display text, graphics, audio, video, and interactive exercises within the format of structured sessions. Among the available therapeutic approaches, cognitive-behavioral therapy (CBT) is most widely applicable to E-Mental Health due to its easy transferability to internet-based formats [28].

The work presented in this dissertation deals with internet- and mobile-based approaches to monitor and support mental health. It contributes directly to the research areas of prevention and therapy in E-Mental Health. The empirical basis of the dissertation is provided by a series of

studies which were conducted through the Integrated Care Division of Leuphana University's Innovation Incubator between 2011 and 2016. A pilot study on mobile-based symptom monitoring among patients with bipolar disorder addresses the field of prevention. For the field of therapy, a randomized controlled trial to evaluate the effectiveness of an internet-based program in reducing depression among adults with sickness absence was conducted. Finally, the dissertation presents a study protocol for a mobile-based intervention that proposes to combine both prevention and therapy for the development of a self-monitoring smartphone application with individualized support for subjects with psychological distress. Together, these three research articles—which are presented in Chapters 2 through 4—will contribute significantly to the base of evidence for E-Mental Health in regards to its validity, effectiveness, usability, adherence, and population uptake, in addition to providing new information on the epidemiology of mental disorders and theoretical developments in the field.

The overarching goal of this dissertation is to examine internet- and mobile-based approaches for mental health in terms of:

- *Validity of assessments:* Unlike laboratory studies, E-Mental Health allows for the acquisition of real-world data in real-time. This dissertation examines the validity of sensor measurements and daily self-reports as predictors of mental health outcomes.
- *Effectiveness of interventions*: Randomized controlled trials (RCTs) represent the "gold standard" in determining the effectiveness of interventions in terms of symptom reductions and other outcomes. This dissertation reports the results of an RCT on an E-Mental Health program for depression and discusses its implications.
- *Usability & Engagement:* From the client's perspective, the usability of the E-Mental Health delivery is highly relevant to their level of engagement and interaction with the content. This dissertation examines the participants' perspectives on the presented E-Mental Health approaches.
- *Adherence:* The extent to which individuals adhere to the content of E-Mental Health is a major concern, as low adherence may reduce its efficacy. The consequences of low adherence will be discussed.
- *Access:* Wide population access is one of the most promising qualities of E-Mental Health. This dissertation provides insight into the characteristics of the study participants and the factors that influence uptake and access to E-Mental Health programs.
- *Epidemiology:* Through the collection of longitudinal information on daily life experiences and behaviors and the ability to embed this information in social context, E-Mental Health can elucidate the epidemiology of mental disorders. In Chapter 4, the dissertation explores the use of a mobile application for epidemiological data collection.

- *Theoretical Implications:* The process of maintaining mental health can be explained using vulnerability-stress models [29]. This dissertation discusses the implications of the findings for these models.

Chapter 2 presents the results of a pilot study on monitoring symptoms of bipolar disorder. Bipolar disorder is a highly suitable candidate for self-monitoring due to the potential to predict transitions between manic and depressive illness episodes. In cooperation with the Psychiatric Clinic in Uelzen, 14 patients with bipolar disorder were recruited and provided with a smartphone for the duration of one year. As part of an early warning system, a pre-installed smartphone application, (SIMBA - Social Information Monitoring for Patients with Bipolar Affective Disorder), passively monitored the participants' social and physical activity using smartphone sensors. In addition, mood states were monitored with daily self-reports. The pilot study showed that the longitudinal assessments provided by the smartphone data were correlated with symptoms of mania and depression as rated by physicians over regular intervals in the study. This finding points to the feasibility of implementing early-warning systems through mobile-based approaches in order to prevent the onset of mental disorder.

Chapter 3 presents a randomized controlled trial on the effectiveness of an internet-based program for depression. The 12-week program, HelpID, developed by Novego AG, was evaluated in adults with mild to moderate depression and sickness absence. 180 participants were recruited in cooperation with Kaufmännische Krankenkasse (KKH), a large-scale German statutory health insurance company. The study showed that the web-based program, which was based on cognitive-behavioral therapy, combined with systemic counseling and awareness training, was more effective in reducing depression compared to a psycho-education control group. Psycho-education was also effective in reducing depression, but to a lesser degree. The findings of this study show that internet-based programs provide effective support for depression during sickness absence.

Chapter 4 presents a study protocol for a fully mobile-based randomized controlled trial to assess potential improvements in mental health through the use of a smartphone application for supported self-monitoring among subjects with psychological distress. The proposed study will combine the advantages of mobile self-monitoring (Chapter 2) with an intervention to improve mental health (Chapter 3). A sample of smartphone users from the general population with low, moderate, and high psychological distress will be recruited, covering various mental health-problems. Over the course of 4 weeks, daily self-reports of symptoms and behavior will be collected. An intervention group receiving supported self-monitoring, which will include tailored feedback based on the participants' real-time information, will be compared to a self-monitoring without feedback control group and a passive control group. The primary outcome will be improvement of mental health. Secondary outcomes will include patient activation, attitudes to

and utilization of mental health services, perceived stigma, user satisfaction, engagement, and adherence to the supported self-monitoring intervention.

Chapter 5 summarizes the results of the three preceding chapters and provides an overall discussion of this dissertation's contributions to the current state of research on prevention and therapy in the field of E-Mental Health. It also discusses the individual contributions of the presented works to the overall goals of the dissertation outlined above and gives an assessment of its methodological strengths and limitations. Finally, an outlook on the future development of E-Mental Health is given, and the need for further research will be discussed. The author expects that, as a compelling and consistently growing field, E-Mental Health will contribute significantly to the long-term sustainability of our healthcare system during the years ahead.

Abbreviations

CBT: Cognitive-Behavioral Therapy
KKH: Kaufmännische Krankenkasse
YLD: Years lived with disability
NIMH: National Institute of Mental Health
RCT: Randomized Controlled Trial
SIMBA: Social Information Monitoring for Patients with Bipolar Affective Disorder

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Chapter 2

Using Smartphones to Monitor Bipolar Disorder Symptoms: A Pilot Study

Original Paper

Using Smartphones to Monitor Bipolar Disorder Symptoms: A Pilot Study

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Abstract

Background: Relapse prevention in bipolar disorder can be improved by monitoring symptoms in patients' daily life. Smartphone apps are easy-to-use, low-cost tools that can be used to assess this information. To date, few studies have examined the usefulness of smartphone data for monitoring symptoms in bipolar disorder.

Objective: We present results from a pilot test of a smartphone-based monitoring system, Social Information Monitoring for Patients with Bipolar Affective Disorder (SIMBA), that tracked daily mood, physical activity, and social communication in 13 patients. The objective of this study was to investigate whether smartphone measurements predicted clinical symptoms levels and clinical symptom change. The hypotheses that smartphone measurements are (1) negatively related to clinical depressive symptoms and (2) positively related to clinical manic symptoms were tested.

Methods: Clinical rating scales were administered to assess clinical depressive and manic symptoms. Patients used a smartphone with the monitoring app for up to 12 months. Random-coefficient multilevel models were computed to analyze the relationship between smartphone data and externally rated manic and depressive symptoms. Overall clinical symptom levels and clinical symptom changes were predicted by separating between-patient and within-patient effects. Using established clinical thresholds from the literature, marginal effect plots displayed clinical relevance of smartphone data.

Results: Overall symptom levels and change in clinical symptoms were related to smartphone measures. Higher overall levels of clinical depressive symptoms were predicted by lower self-reported mood measured by the smartphone (beta=-.56, P<.001). An increase in clinical depressive symptoms was predicted by a decline in social communication (ie, outgoing text messages: beta=-.28, P<.001) and a decline in physical activity as measured by the smartphone (ie, cell tower movements: beta=-.11, P=.03). Higher overall levels of clinical manic symptoms were predicted by lower physical activity on the smartphone (ie, distance travelled: beta=-.37, P<.001), and higher social communication (beta=.48, P=.03). An increase in clinical manic symptoms was predicted by a decrease in physical activity on the smartphone (beta=-.17, P<.001).

Conclusions: Clinical symptoms were related to some objective and subjective smartphone measurements, but not all smartphone measures predicted the occurrence of bipolar symptoms above clinical thresholds. Thus, smartphones have the potential to monitor bipolar disorder symptoms in patients' daily life. Further validation of monitoring tools in a larger sample is needed. Conclusions are limited by the low prevalence of manic and depressive symptoms in the study sample.

Trial Registration: International Standard Randomized Controlled Trial Number (ISRCTN): 05663421; http://www.controlled-trials.com/ISRCTN05663421 (Archived by WebCite at http://www.webcitation.org/6d9wsibJB)

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KEYWORDS

smartphone; sensor technology; bipolar disorder; monitoring; phase transitions; communication patterns; activity patterns

Introduction

Bipolar disorder is a serious and disabling psychiatric condition that encompasses a broad group of disorders. International lifetime prevalence estimates indicate that bipolar disorders are present in 1-5% of the general population [1]. It involves mood, behavioral, and cognitive disruptions during episodes of depression, mania, or hypomania. The recurrent and chronic nature of bipolar disorder results in a high burden of disease [2-4] and high societal costs [5]. The suicide rate of people diagnosed with bipolar disorder is the highest among all mental disorders [4,6]. Even during periods of remission, patients experience frequent subclinical mood symptoms that impair daily functioning and increase their risk for relapse [7,8].

The heterogeneity of symptoms and individual courses of disease in bipolar disorder make it difficult to predict the course of the disorder [9]. Compared to a patient with high blood pressure who needs to maintain blood pressure below a certain threshold, no analogous guidance is currently provided for patients suffering from bipolar disorder. As a consequence, patients often do not recognize their mood changes in a timely manner and lose their insight into illness [10], leading to adverse consequences [11]. In order to prevent relapses, timely information on upcoming phase transitions must be available to patients and doctors [12]. This information could allow providers to intervene shortly after symptoms appear.

Information from patients' daily life can help provide an earlier and more reliable prediction of impending phase transitions in bipolar disorder [13-16]. It has been suggested that smartphones may be easy-to-use, low-cost devices that can be used to measure this information in the patient's daily environment. Using both self-reported information collected by the device and making use of the smartphone sensor capabilities, researchers hope to gain insight in the user's well-being and behavior. Among mental health patients, too, there is great interest in monitoring symptoms with mobile apps [17]. It has been found that daily mood and the level of physical and social activity can be measured with smartphone sensors [18-22]. These measurements are assumed to represent central aspects of bipolar disorders [23,24].

Additional research is needed to establish the relationship between smartphone measurements and clinical symptoms in bipolar disorder. In particular, a more personalized approach to capture warning signs for impending phase transitions needs to consider both the patients' overall symptom levels and the dynamic symptom changes occurring over time. The advantage of this approach is that it is able to capture the interindividual variability and heterogeneity of bipolar disorder, where symptom severity within one patient fluctuates over time [25]. While statistical methods exist to compute predictions for overall symptom levels and symptom change in smartphone data [26], previous studies did not separate between these central illness components.

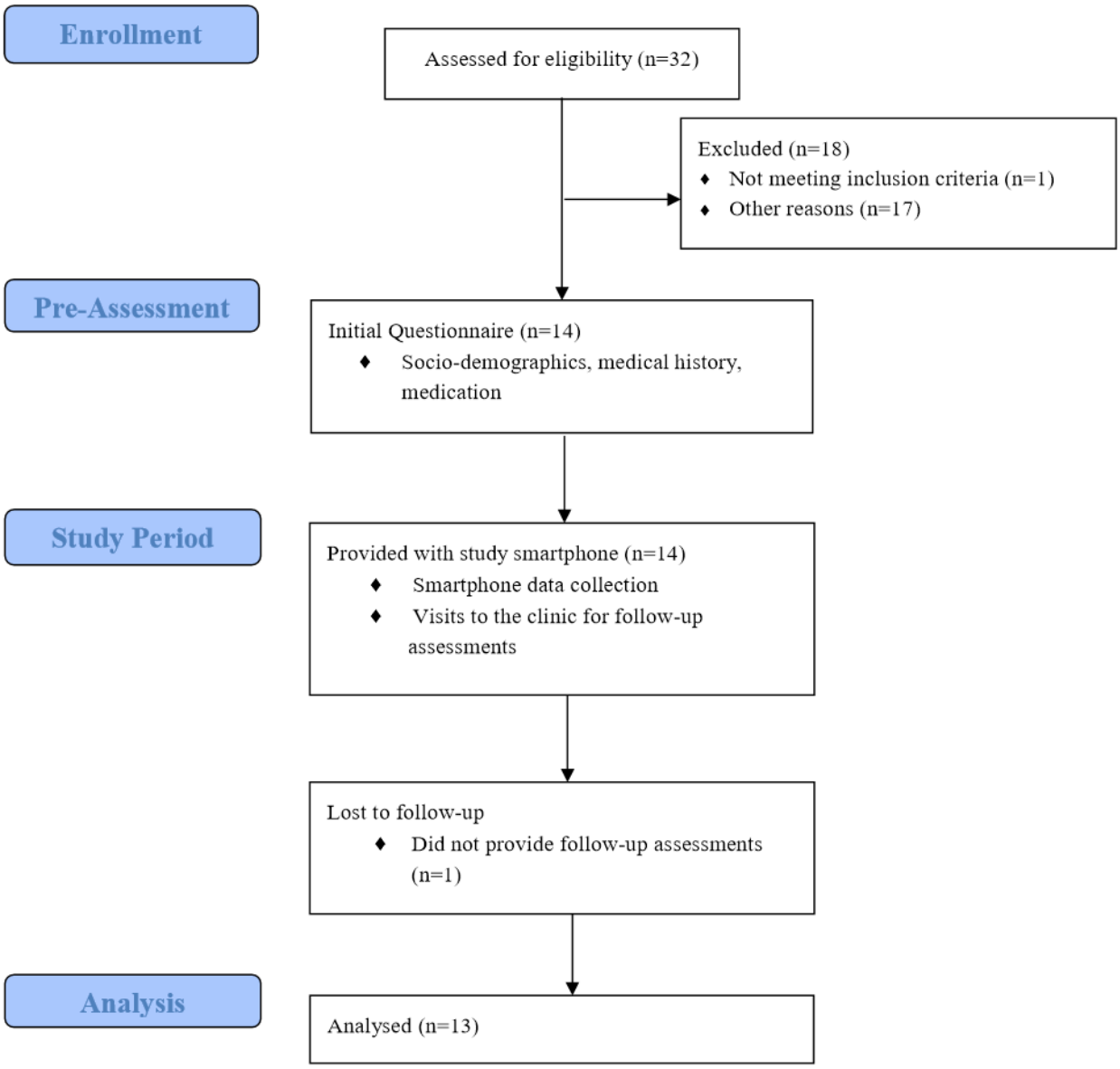
To address this research gap, a study was conducted to investigate whether smartphone data predict impending clinical symptoms in bipolar disorder. The aim of this study is twofold. First, we compare the relationship of daily self-reported mood, smartphone sensor data (ie, Global Positioning System [GPS], cell tower movements, accelerometer), and smartphone communication (ie, calls, short message service [SMS] log) with clinical symptoms. We hypothesize that for depressive symptoms, higher levels of self-reported mood, and higher levels of physical activity and social communication measured by the smartphone predict lower overall levels of depressive symptoms and temporal decreases in clinical depressive symptoms. For manic symptoms, we hypothesize that higher levels of self-reported mood and higher levels of physical activity and social communication measured by the smartphone predict both higher overall levels of clinical manic symptoms and temporal increases in manic symptoms. Second, to identify the clinical relevance of smartphone data we test the hypothesis that smartphone data predict the occurrence of overall symptoms levels above clinical thresholds.

Methods

Recruitment

Figure 1 presents the study flow chart. Participants were recruited from the outpatient department of a Psychiatric Clinic in Lower Saxony, Germany, between July 2013 and February 2014. Patients were contacted and assessed for eligibility in random order from the pool of outpatients. Inclusion criteria were diagnosis of bipolar I or bipolar II disorder according to the criteria in the *Diagnostic and Statistical Manual of Mental Disorders*, 4th edition (DSM-IV) [27], at least 18 years of age, sufficient knowledge of the German language, and basic competence in using mobile devices. Exclusion criteria were the need for inpatient treatment at the time of recruitment, suicidality, diagnosis of schizophrenia or an intellectual disability, and alcohol or drug abuse up to 6 month prior to the study. All participants provided written consent prior to participation and were loaned a smartphone for the 12-month study period. Participants were provided with an unlimited call, text, and data plan and were encouraged to use the study smartphone as their regular mobile device. The study was examined and approved by the Leuphana University Ethics Committee.

Figure 1. Study flow chart.



Measurements

Smartphone data were collected on a Sony Ericsson Xperia Neo V smartphone with Android 4.0.4. The device had the Social Information Monitoring for Patients with Bipolar Affective Disorder (SIMBA) app pre-installed. The app was developed by the authors and is based on two open source frameworks for the collection of both subjective self-report data [28] and objective sensor data [29], which are available at [30,31]. First, Open Data Kit developed at the University of Washington [28] collects subjective self-report data. Designed for socioeconomic and health surveys, Open Data Kit provides a platform to build questionnaires and to collect data on a smartphone. Its modular design allows for the implementation of questionnaires at fixed or random time points. Second, the Funf open sensing framework developed at the Massachusetts Institute of Technology (MIT) media lab [29] collects objective data using various smartphone sensors, for example, GPS, accelerometer, and screen state. It provides an extensible sensing and data processing framework for smartphones. As using smartphone sensors can drain the device battery quickly, Funf is designed to prolong battery life. The source code for the software frameworks can be found in Multimedia Appendix 1.

Three smartphone sensors were used to measure physical activity: GPS for the distance traveled per day, cell tower movement as an indicator of location changes, and accelerometer to measure the users' device activity. Both GPS and cell tower movements capture spatial movement and since the correlation between GPS and cell tower movements was low (P=.06), both measures were included. For the measurement of social communication, the number and duration of outgoing calls and the number of SMS sent per day were logged. The gathered data were cached in local storage and transferred to a secured server located at Leuphana University whenever an Internet connection was available.

Self-reported mood states were assessed once a day on the smartphone at random times with a 2-item questionnaire. When

the questionnaire was available, participants were notified via a beep and asked if the questionnaire should be answered now or if the participant wished to be notified later. Affect was assessed with the item, "On a scale of 1 (very good) to 10 (very bad), please describe your present mood," and energy was assessed with the item, "On a scale of 1 (very energetic) to 10 (not at all), how energetic do you feel at the moment?" For the purposes of this analysis, both items were reverse-coded so that higher scores reflected better mood. Due to the high correlation between the 2 items (P=.84), a single mood index was constructed.

Clinical assessments were conducted repeatedly throughout the study and served as a reference point for the smartphone data. Appointments with the treating clinician, who was blinded to smartphone data, were scheduled at approximately 8-week intervals and included assessment of manic and depressive symptoms using clinical rating scales. Manic symptoms were assessed using the German Version [32] of the Young Mania Rating Scale (YMRS) [33]. The scale is administered by a clinician and rates major relevant manic symptoms (eg, elevated mood, motoric activity) on a scale from 0-64. Values less than 5 indicate complete remission [34]. Depressive symptoms were assessed with the German Version [35] of the Hamilton Depression Scale (HAMD) [36]. The scale is based on clinician assessment and scores 17 items within a reference period of 1 week. Values greater than 7 indicate at least a mild depressive syndrome [37].

Statistical Analysis

Smartphone data were aggregated to assessment periods before each clinical appointment by computing mean scores from the daily measurements resulting in an aggregated score for each assessment period. An assessment period is the number of days between two clinical appointments. Then, the effect of the aggregated smartphone data on the clinical symptoms was assessed for each assessment period. To accommodate the nested data structure, where observations are nested within patients, multilevel models were computed according to [38] in order to obtain robust and unbiased estimates of variance components. Random coefficient models were fitted, where assessment periods were nested within patients. Smartphone data were modeled to separate between-patient effects (ie, symptom level) and within-patient effects (ie, symptom change) [26].

We estimated three separate models for self-reported data, activity data, and social data, and one full model including all smartphone data. All models were adjusted for age, sex, and length of assessment period. The total length of assessment periods was used in order to compute more precise estimates, as opposed to restricting the analysis to the shorter time frame using the reference period of HAMD and YMRS before each clinical assessment. To compare the results of the models, standardized regression coefficients are reported [39]. To provide a graphical representation of the relationship between smartphone data and clinical symptoms, the results of the full model were used to compute marginal effects, which were plotted against symptoms. The analysis was performed using the "xtmixed" command in Stata 13, where the maximum likelihood estimation method was specified [40]. Significance levels are reported at the 95% level.

Results

Sample Characteristics

Of the 14 patients who were recruited, one dropped out before clinical follow-up assessment and was thus removed from the study. Table 1 presents the sample characteristics for the 13 patients who completed the study.

Description of Dataset

Table 2 shows the available data points for self-reported data, activity data, social data, and clinical data. The compliance rate for self-reported data was 55.7%. Activity data were complete on 78.2% of days, and social data were present on 56.1% of days.

Mean Levels of Smartphone and Clinical Data

Table 3 presents mean levels and range for smartphone-collected indicators and clinical data. The average level of self-reported mood was 6.7 (SD 1.7) with a maximum of 10, indicating that average mood levels of subjects were at the upper end of the end of the scale ranging from 1 (very bad mood) to 10 (very good mood). Clinical symptom ratings revealed mean manic symptoms levels assessed by YMRS of 2.7 (SD 3.6) and depressive symptoms assessed by HAMD of 5.1 (SD 5.3), indicating low prevalence of manic and depressive symptoms in the sample.

Table 1. Sample characteristics for 13 patients.

Characteristic	N	Value
Age in years, mean (SD)	13	47.2 (3.8)
Sex, %		
Male	8	61.5
Female	5	38.5
Education, %		
Lower secondary	9	69.2
Upper secondary	4	30.8
Qualification		
None	1	7.7
Vocational	10	76.9
University level	2	15.4
Employed, %		
Yes	4	30.8
No	9	69.2
Diagnosis, %		
Bipolar I	6	46.1
Bipolar II	7	53.9
Years since first diagnosis, mean (SD)	13	9.9 (3.1)
Manic episodes, mean (SD)	13	8.6 (1.6)
Depressive episodes, mean (SD)	13	12.3 (3.0)
Total hospitalizations, mean (SD)	13	6.9 (2.8)
Currently medicated, %		
Yes	11	84.2
No	2	15.4
Study duration in days, mean (SD)	13	365.1 (31.9)
Length of assessment period, mean (SD)	13	68.6 (23.6)

Table 2. Total available data points for self-reported data, activity data, social data, and clinical data collected by 13 patients.

	N	Mean (SD)	Min/Max	Rate, %
Self-reported	2456	188.9 (83.3)	24/291	55.7
Activity	3537	272.1 (74.9)	154/362	78.2
Social	2624	201.8 (109.3)	9/339	56.1
Clinical	75	5.8 (1.4)	3/8	NA

Table 3. Mean levels, interquartile range, and range for smartphone indicators and clinical variables for 13 patients.

Variable	Mean (SD)	Interquartile Range	Min/Max
Self-reported			
Mood	6.7 (1.7)	2.0	1/10
Activity			
Distance traveled, km	10.5 (41.5)	6.3	0/732
Cell tower changes	10.5 (17.0)	10.0	0/139
Device activity, % of day	7.3 (8.2)	9.2	0/75
Social			
Number outgoing calls	2.9 (3.6)	4.0	0 /29
Duration outgoing calls, minutes	10.2 (19.6)	11.3	0/181
Outgoing SMS	1.7 (3.6)	2.0	0/54
Clinical			
YMRS	2.7 (3.6)	4.0	0/18
HAMD	5.1 (5.3)	9.0	0/18

Prediction of Clinical Symptoms

This section presents the results from the multivariate models with smartphone data as predictors for clinical symptoms. We begin with results from the between-patients analysis, representing the overall level of clinical symptoms as predicted by smartphone data. Next, we present results of the within-patient analysis, representing temporal changes in clinical symptoms as predicted by smartphone data.

Between-Patient Analysis

The combined model (Model 4) in Table 4 showed a significant negative relationship between mood level and clinical depressive symptoms (HAMD: beta=-.56, P<.001) but not on manic symptoms. This suggests that patients who reported better daily mood on the smartphone were less clinically depressed. In the activity data, distance traveled as measured by the GPS signal had a significant negative relationship with clinical manic symptoms (YMRS: beta=-.37, P<.001), indicating that patients who were more physically active experienced fewer manic symptoms. Cell tower movements and device activity were not significantly related to any clinical symptoms. In the social data, the number of calls made on the smartphone were positively related to clinical manic symptoms (YMRS: beta=.48, P=.03), suggesting that patients who made a higher frequency of calls experienced higher levels of manic symptoms. The duration of calls was not significantly related to symptoms. The number of outgoing SMS had a negative relationship with clinical depressive symptoms (HAMD: beta=-.17, P<.001), indicating that patients who sent more SMS had less severe depressive symptoms.

Table 4. Between-patient relationship of self-reported data, activity data, and social smartphone data with bipolar disorder symptoms for 13 patients based on 75 clinical ratings[a].

	Beta (*P*)			
	Self-report	Activity	Social	Combined
	Model 1 (N=74)	Model 2 (N=62)	Model 3 (N=71)	Model 4 (N=62)
Mood				
YMRS	-.09 (.45)			.05 (.79)
HAMD	-.42 (<.001)			-.56 (<.001)
Distance traveled, km				
YMRS		-.46 (.01)		-.37 (<.001)
HAMD		-.24 (.12)		-.12 (.34)
Cell tower movements				
YMRS		-.24 (.29)		-.14 (.12)
HAMD		.08 (.58)		-.04 (.82)
Device activity, %				
YMRS		.31 (.24)		.26 (.12)
HAMD		-.01 (.92)		-.06 (.80)
Number of calls				
YMRS			.19 (.38)	.48 (.03)
HAMD			.34 (.17)	.08 (.65)
Duration of calls, minutes				
YMRS			.17 (.45)	-.08 (.72)
HAMD			-.22 (.25)	.03 (.83)
Outgoing SMS				
YMRS			.03 (.72)	-.02 (.65)
HAMD			.04 (.84)	-.17 (<.001)

[a]Standardized effects of random coefficient regression models with smartphone data as predictor of depressive symptom levels (YMRS) and manic symptom levels (HAMD).

Within-Patient Analysis

Table 5 displays the within-patient relationship between change in smartphone data and change in clinical symptoms. In the full model, change in self-reported mood on the smartphone was not related to clinical symptom changes. An increase in cell tower movement was negatively related to both manic symptoms (YMRS: beta=-.17, *P*<.001) and depressive symptoms (HAMD: beta=-.11, *P*=.03), suggesting that when a patient's activity level as measured by the smartphone increased, both manic and depressive symptoms decreased. However, changes in distance traveled and device activity were not significantly related to symptom changes. In the social data, an increase in outgoing SMS was negatively related to a change in depressive symptoms (HAMD: beta=-.28, *P*<.001), which suggests that when more SMS are sent, clinical depressive symptoms are lowered.

Table 5. Within-patient relationship of change in self-report, activity, and social smartphone data with change in bipolar disorder symptoms for 13 patients[a].

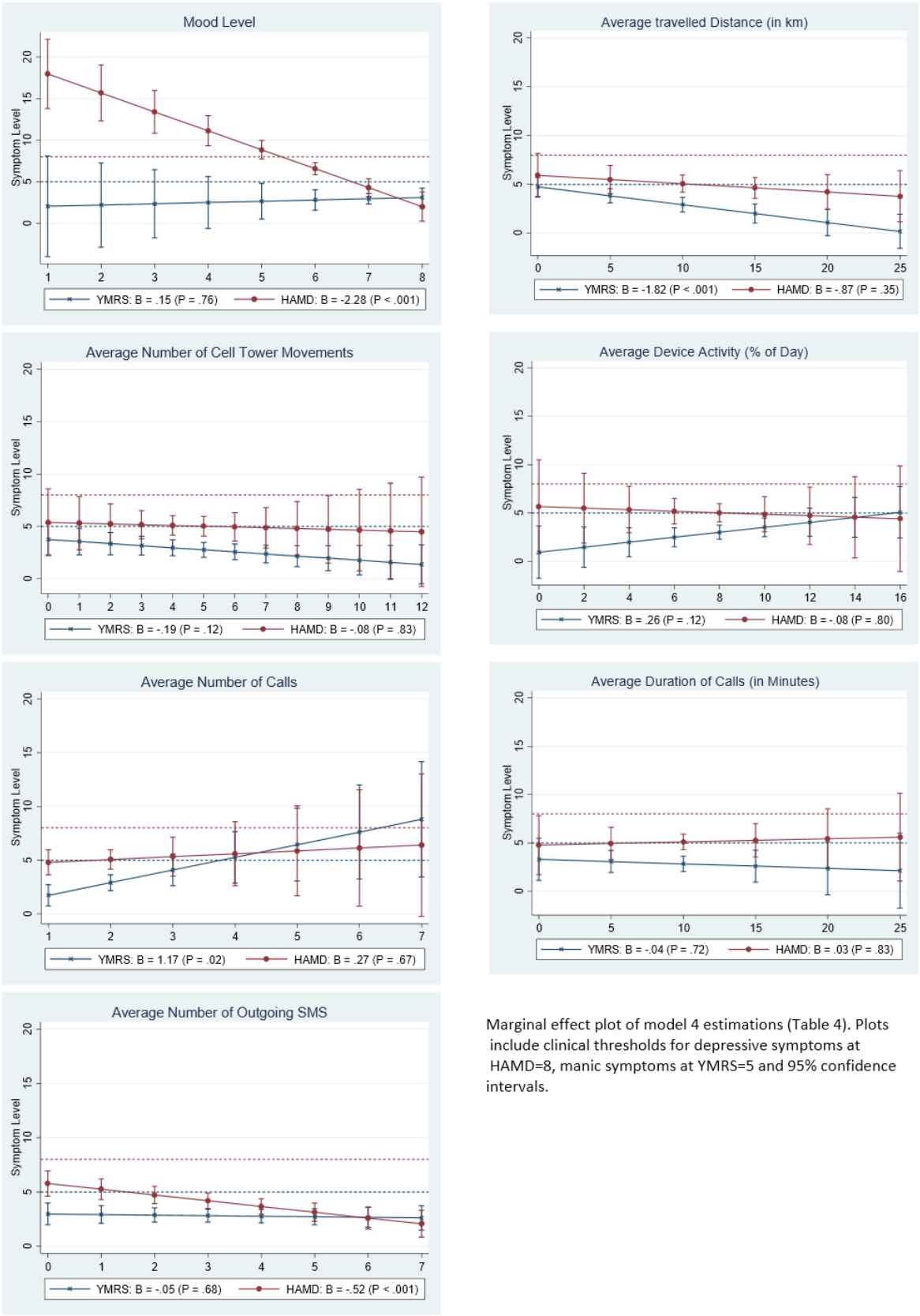
	Beta (*P*)			
	Self-report	Activity	Social	Combined
	Model 1 (N=74)	Model 2 (N=62)	Model 3 (N=71)	Model 4 (N=62)
Mood				
YMRS	-.09 (.28)			.03 (.73)
HAMD	-.18 (.10)			-.09 (.26)
Distance traveled, km				
YMRS		.03 (.40)		.01 (.85)
HAMD		.07 (.23)		.03 (.66)
Cell tower movements				
YMRS		-.10 (.03)		-.17 (<.001)
HAMD		-.17 (<.001)		-.11 (.03)
Device activity, %				
YMRS		-.11 (.17)		-.07 (.26)
HAMD		-.15 (.09)		.02 (.87)
Number outgoing calls				
YMRS			.18 (.34)	.24 (.44)
HAMD			-.07 (.60)	-.07 (.73)
Duration outgoing calls, minutes				
YMRS			-.25 (.27)	-.34 (.24)
HAMD			-.07 (.63)	-.09 (.58)
Outgoing SMS				
YMRS			-.05 (.35)	.03 (.68)
HAMD			-.30 (<.001)	-.28 (<.001)

[a]Standardized effects of random coefficient regression models with smartphone data as predictor of depressive symptom change (YMRS) and manic symptom change (HAMD).

Clinical Relevance of Smartphone Data

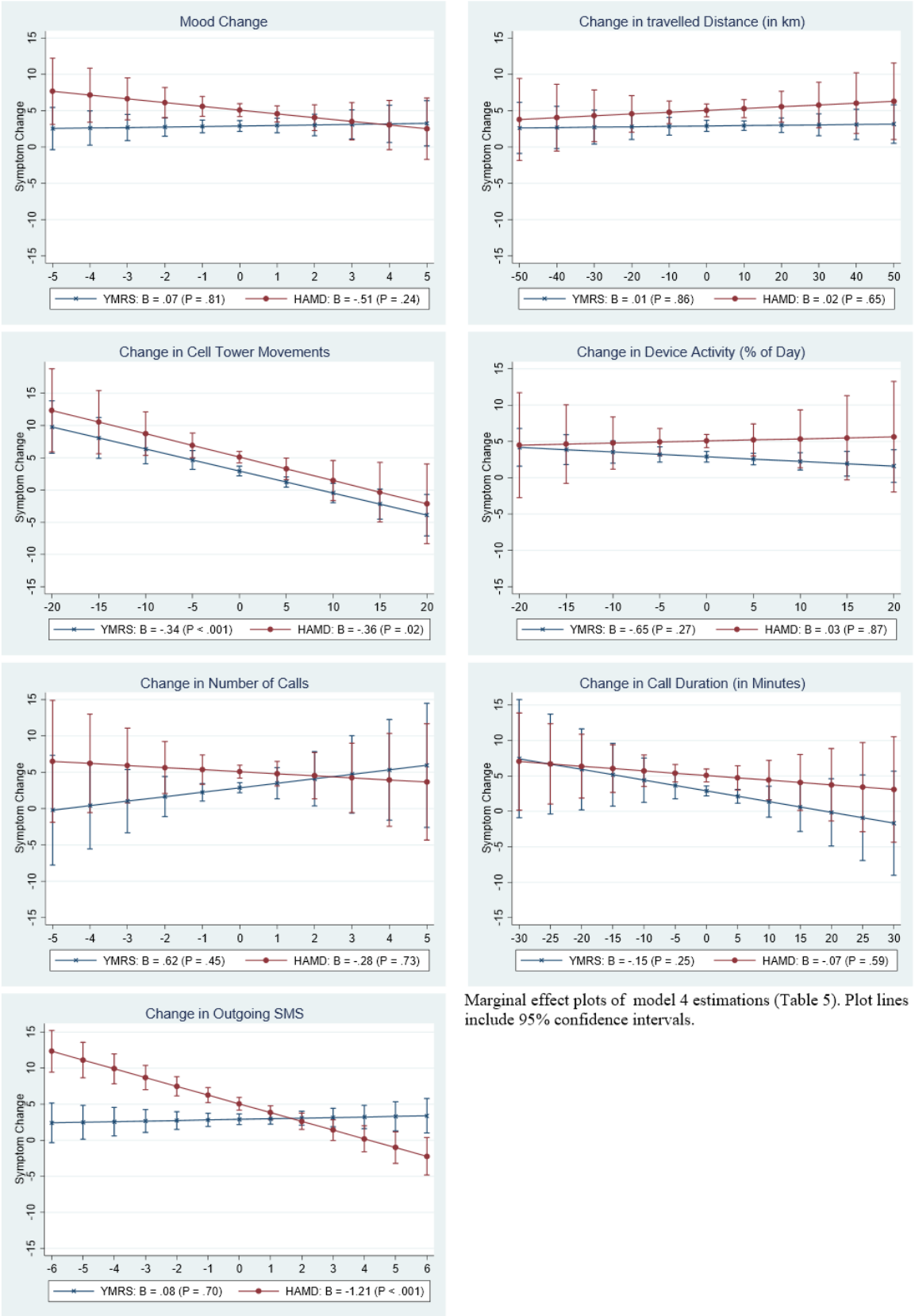
Figure 2 plots predicted symptoms levels including clinical thresholds, and Figure 3 plots predicted symptom change by smartphone data. The plots are computed from the full models in Tables 4 and 5.

Figure 2. Between-patient analysis of smartphone data and symptom levels.



Marginal effect plot of model 4 estimations (Table 4). Plots include clinical thresholds for depressive symptoms at HAMD=8, manic symptoms at YMRS=5 and 95% confidence intervals.

Figure 3. Within-patient analysis of smartphone data and symptom change.



Marginal effect plots of model 4 estimations (Table 5). Plot lines include 95% confidence intervals.

Between-Patient Analysis

Figure 2 shows that depressive symptoms above the clinical threshold are predicted when the average mood level is lower than 6 points on the 10-point mood scale. While the average number of calls had a positive effect on clinical manic symptoms (YMRS: beta=1.17, *P*=.02) and the average number of outgoing SMS had a negative relationship with clinical depressive symptoms (HAMD: beta=-.52, *P*<.001), this did not predict the occurrence of symptoms above the clinical threshold.

Within-Patient Analysis

Figure 3 visualizes the relationship between change in smartphone data and change in clinical symptoms as computed in Table 5. The negative relationship of change in cell tower movements with both clinical manic symptoms (YMRS: beta=-.34, $P<.001$) and clinical depressive symptom changes (HAMD: beta=-.36, $P<.02$), indicated that when a patient's activity as measured by the smartphone was below average, clinical symptoms were elevated and vice versa. Figure 3 shows that when a patient made 20 cell tower movements fewer than average, the model predicts an YMRS score of approximately 10 points and an HAMD score of 12 points above the patient's average. Last, Figure 3 visualizes the negative relationship between change in outgoing SMS and change in depressive symptoms (HAMD: beta=-1.21, $P<.001$), implying that when a patient sent more text messages than average, symptoms were lowered.

Discussion

Principal Results

In this pilot study, smartphone-based monitoring of mood, physical activity, and social communication was conducted in the daily life of bipolar disorder patients over the course of 12 months. The between-patient and within-patient variance of smartphone data was analyzed to present the relationship of smartphone data with both overall levels and changes in clinical symptoms. The results allow conclusions on the usefulness of smartphone measurements for the monitoring of bipolar disorder.

Higher overall levels of depressive symptoms were predicted by lower self-reported mood measured by the smartphone. An increase in depressive symptoms was predicted by a decline in social communication (ie, outgoing SMS) and a decline in physical activity (ie, cell tower movements). In contrast to our hypothesis, self-reported mood did not predict clinical manic symptoms. The overall level of manic symptoms was predicted by activity (ie, distance traveled) and social communication (ie, number of calls). In contrast to our hypothesis, an increase in clinical manic symptoms was predicted by lower physical activity (ie, cell tower movements). Other smartphone measurements (ie, device activity and the duration of calls) were related to neither symptom levels nor symptom changes.

In addition, the clinical relevance of the results was examined by investigating if smartphone measurements predicted symptom levels above clinical thresholds. This information may provide information on which smartphone measurements can be used to predict the occurrence of symptoms above clinical thresholds. Self-reported mood was found to predict depressive symptom levels above the clinical threshold but not manic symptoms. No other smartphone measurements predicted symptoms above clinical thresholds.

Comparison With Prior Work

Within the self-reported data, our data support the findings [14,20] that daily mood ratings are useful for monitoring depressive symptoms in patients who experience bipolar disorder. Similar to those studies, we could not support the hypothesis that daily mood measured by the smartphone predicts clinical manic symptoms. This is probably the result of the low prevalence of patients with severe manic symptoms in our sample (see Table 3).

Physical activity was included in the analysis as it represents a warning sign for phase transitions in bipolar disorder and can potentially be measured objectively with smartphone sensors. Similar to the approach in Faurholt-Jepsen et al [20], we used GPS sensors to track the distance traveled, patient movements across cell towers as a second measurement of physical activity, and the smartphone accelerometers to assess patients' interaction with the device. In our analysis, some within-patient and between-patient effects showed significant relationships with clinical symptoms. However, we did not expect to find that physical activity was negatively related to manic symptoms, indicating that patients with higher overall levels of physical activity (ie, as measured by distance traveled) experienced fewer manic symptoms. We also did not expect to find that declining temporal activity (ie, as measured by cell tower movements) was associated with reduced manic symptoms. These findings run counter to the literature on the early warning signs of bipolar disorder [41,42], which assumes that increased activity is a prodrome of mania. These diverging results might be explained by the low prevalence of manic symptoms in our study sample. It can be speculated that for patients with subclinical manic symptoms, as in this study, increased activity signals better patient condition, but should not be mistaken with hyperactivity in patients with severe mania.

The social data measured by the smartphones capture patients' level of interaction with their social surroundings as an early-warning sign of bipolar disorder symptoms. Both between- and within-patient effects of social communication on clinical symptoms were found in the data, implying that overall levels and dynamic changes in communication are relevant for the prediction of bipolar disorder symptoms. The overall level of text messages sent and the number of calls placed indicated levels of depression and manic symptoms, respectively, while changes in text messages sent predicted changes in depressive symptoms. As a larger number of calls, but not the duration of calls, was associated with manic symptoms it is possible that patients with increased manic symptoms have a larger activity mirrored by more calls but not the ability to concentrate on lengthier calls. Overall, our research is in line with findings from other research that highlights the role of psychosocial variables in the illness course in bipolar disorder [43]. However, a comparable study [20] did not find significant correlations between social data and clinical symptoms.

A major feature of this analysis was that the collection of smartphone data and repeated clinical measures allowed us to separate two essential components of illness activity: overall symptom levels as observed by comparing the variance between patients, and dynamic changes that occur over the course of the illness as observed by comparing the variance within one patient over time. Although this approach introduces additional assumptions to the model and can make the interpretation of results more challenging, theoretical reasons speak for the separation of between- and within-patient variance. Evidence from modern follow-up studies shows that the course of illness

in bipolar disorder is characterized by high interindividual variability and heterogeneity [25]. Symptom severity within one patient fluctuates over time and often includes the expression of major, minor, and subclinical symptoms at different stages of illness [7]. Between-patient comparisons are insufficient to analyze how symptoms develop over time as they do not capture these within-person processes. The repeat sampling rate of the smartphone data in this study offers the advantage that the dynamic nature of psychopathology can be studied in real-time and in the real world.

Limitations

This study had several limitations. The small sample size of 13 patients may have lowered the statistical power of the study, leading to type II errors in the statistical conclusions. The number of participants did not allow the inclusion of additional level 2 predictors, which might explain between-patient differences (eg, type of bipolar diagnosis). Therefore, it is necessary to replicate the study in a larger sample to validate use of smartphone data for clinical applications.

The low prevalence of clinical depressive and manic symptoms (see Table 3) in our sample may have prevented us from detecting effects that would have been present in a sample of patients who experienced more severe symptoms. The generalization of the results to patients with more severe symptoms should be made carefully. Patients who are more severely ill may show different levels of acceptance in using smartphones for symptom monitoring. It is possible that the patients recruited for this study were particularly motivated to use smartphones.

Finally, compliance with filling out self-reporting data may have affected the results. However, we did not observe a decline in compliance with self-reported mood over time, indicating that missing values were missing at random. The compliance rate (55.7%; see Table 2) in our study is comparable to a study by Depp et al [44]. The conclusions of the social data could have been limited by the fact that we were unable to assess communication over social media (eg, WhatsApp, Facebook). With communication habits moving towards social media apps, social media should be included in patient monitoring systems. We cannot exclude the possibility that patients shared the device with other people, although patients were instructed accordingly and no indication of such usage was found. Regarding the operating system, monitoring was restricted to Android smartphones and future studies should implement software for other operating systems (eg, iOS, Windows Phone) as well.

Ethical Considerations

Symptom monitoring in a patient's daily life involves the collection of sensitive health-related data including communication habits and movement patterns. Sensor-based data, such as GPS locations, need to be protected from unauthorized access. As such, concerns regarding data privacy and confidentiality issues need to be taken seriously in order to guarantee the safety of the collected personal data and to build patient trust. In this study, the encrypted and anonymized transmission of smartphone data to a protected server proved to be successful in ensuring patient data safety. From our experience, the full disclosure of the functionality of the monitoring app, as well as its potential clinical application, was also critical in fulfilling the ethical requirements.

Conclusions

Symptom monitoring is an important strategy to prevent relapses in patients with bipolar disorder. Smartphone apps are easy-to-use, low-cost tools that assist with symptom monitoring in daily life. In this pilot study, we tracked patient mood, levels of physical activity, and social communication over 12 months with an Android-based monitoring software (SIMBA). To our knowledge, this is the first study that successfully embedded a smartphone-based monitoring strategy in patients' daily life over such a long time frame. The study provides encouraging results concerning the feasibility, data analytic approaches, and clinical relevance of smartphone-based monitoring for bipolar disorder. With further clinical validation of smartphone data, it may be possible to provide smartphone-based monitoring tools for routine care, which may benefit patients and doctors.

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Authors' Contributions

TB analyzed the data, TB and SK wrote the manuscript, AM and CK contributed analysis tools, JM, WR, and GB obtained access to the dataset, and all authors contributed to the text and critically revised the manuscript. All authors approved the final version of the manuscript.

Conflicts of Interest

None declared.

Multimedia Appendix 1

Source Code.

[ZIP File (Zip Archive), 5MB - mental_v3i1e2_app1.zip]

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Abbreviations

DSM-IV: Diagnostic and Statistical Manual of Mental Disorders, 4th edition
HAMD: Hamilton Depression Rating Scale
SIMBA: Social Information Monitoring for Patients with Bipolar Affective Disorder
YMRS: Young Mania Rating Scale

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Chapter 3

Effectiveness of a Web-Based Intervention in Reducing Depression and Sickness Absence: Randomized Controlled Trial

Original Paper

Effectiveness of a Web-Based Intervention in Reducing Depression and Sickness Absence: Randomized Controlled Trial

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Abstract

Background: Depression is highly prevalent in the working population and is associated with significant loss of workdays; however, access to evidence-based treatment is limited.

Objective: This study evaluated the effectiveness of a Web-based intervention in reducing mild to moderate depression and sickness absence.

Methods: In an open-label randomized controlled trial, participants were recruited from a large-scale statutory health insurance and were assigned to two groups. The intervention group had access to a 12 week Web-based program consisting of structured interactive sessions and therapist support upon request. The wait-list control group had access to unguided Web-based psycho-education. Depressive symptoms were self-assessed at baseline, post-treatment, and follow-up (12 weeks after treatment) using the Patient Health Questionnaire (PHQ-9) and Beck Depression Inventory (BDI-II) as primary outcome measures. Data on sickness absence was retrieved from health insurance records. Intention-to-treat (ITT) analysis and per-protocol (PP) analysis were performed.

Results: Of the 180 participants who were randomized, 88 completed the post-assessment (retention rate: 48.8%, 88/180). ITT analysis showed a significant between-group difference in depressive symptoms during post-treatment in favor of the intervention group, corresponding to a moderate effect size (PHQ-9: d=0.55, 95% CI 0.25-0.85, P<.001, and BDI-II: d=0.41, CI 0.11-0.70, P=.004). PP analysis partially supported this result, but showed a non-significant effect on one primary outcome (PHQ-9: d=0.61, 95% CI 0.15-1.07, P=.04, and BDI-II: d=0.25 95% CI −0.18 to 0.65, P=.37). Analysis of clinical significance using reliable change index revealed that significantly more participants who used the Web-based intervention (63%, 63/100) responded to the treatment versus the control group (33%, 27/80; P<.001). The number needed to treat (NNT) was 4.08. Within both groups, there was a reduction in work absence frequency (IG: −67.23%, P<.001, CG: −82.61%, P<.001), but no statistical difference in sickness absence between groups was found (P=.07).

Conclusions: The Web-based intervention was effective in reducing depressive symptoms among adults with sickness absence. As this trial achieved a lower power than calculated, its results should be replicated in a larger sample. Further validation of health insurance records as an outcome measure for eHealth trials is needed.

Trial Registration: International Standard Randomized Controlled Trial Number (ISRCTN): 02446836; http://www.isrctn.com/ISRCTN02446836 (Archived by WebCite at http://www.webcitation.org/6jx4SObnw)

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KEYWORDS

Internet; depression; absenteeism; cognitive therapy; randomized controlled trial

Introduction

Depression is highly prevalent in the working population [1]. It is estimated that over the course of one year, up to 26.7% of adults experience depressive symptoms and about 8.9% fulfill all criteria for a depressive disorder [2]. The resulting impairment and functional disability poses a substantial burden for the affected individual as well as the economy. Depressed employees have higher health care costs than those without depression [3,4], which in Europe contribute to a total estimated cost of 118 billion Euros per year [5].

Depression is linked to a high loss of work days [6]. In Germany, depression is a major driver of sickness absence and produces higher durations of sickness absence than other diagnoses of mental disorders [7]. When employees return to work after a depressive episode, distress often remains and performance is reduced [8,9]. Therefore, maintaining work capacity should be an important goal of clinical interventions. However, health promotion interventions targeting occupational health in employees with depression have been developed with mixed results [10-13]. Access to treatment remains limited, and the existing personal and structural barriers prevent those affected by depression from seeking timely, evidence-based help [14-16].

Web-based interventions are a promising tool to overcome the treatment gap in depression [17]. While generally using similar techniques as face-to-face therapy, such interventions are commonly delivered through websites and allow participants to access content at any time and work through lessons at their own pace. Web-based interventions vary in the level of therapist support [18], from entirely self-help to guided formats including regular therapist contact (eg, feedback via email). The advantages of Web-based interventions are their accessibility, a low threshold for help-seeking, relative anonymity, the patients' active role in (guided) self-help, and their low costs. However, in studies comparing Web-based interventions to usual care, risks associated with the dissemination of Web-based interventions have been reported as well [19,20]. Among the working population, Web-based interventions could especially benefit those who do not want to seek regular treatment because of negative perceptions of mental ill-health at the workplace.

The effectiveness of Web-based interventions in reducing depressive symptoms has been demonstrated repeatedly, but effect sizes vary considerably across studies [21-23]. For example, in the 19 studies that were included in the meta-analysis by Richards and Richardson [21], depression improvement in comparison with a control group ranged from no effect (d=−0.03) to strong effects (d=1.43). This heterogeneity makes it necessary to evaluate the interventions separately. Methodologically, weak control groups (eg, wait-list control instead of active control groups) and failure to employ intention-to-treat principles lead to an overestimation of the treatment effect [24]. Web-based interventions for depression have been studied among different clinical populations in Germany [25-29] but, to the best of our knowledge, no studies have yet focused on a Web-based intervention among a population with sick leave due to depression.

Participant self-reports are the primary outcome measure of eHealth trials. However, the lack of independent outcome assessments and the sole reliance on self-report measures limits this evolving field. For example, a report on the methodological quality of randomized controlled trials of Web-based interventions concluded that an increased use of independent outcome measurements is needed to improve the validity of efficacy studies [24]. To date, few studies employ independent outcomes and such attempts are limited to observer ratings of symptoms and do not extend to objective behavioral measurement of work absenteeism [30-32]. The lack of objective sickness absence measurements in research on Web-based interventions is surprising because sickness absence is frequently used as an integrated measure of health in other fields [33].

This study examined the effectiveness of a guided Web-based intervention in reducing depression and sickness absence among a high-risk population using both self-assessed depression and sickness absence assessments from health insurance records. We hypothesized that the Web-based intervention would be more effective in reducing depressive symptoms and sickness absence than the control group.

Methods

Study Design

This was a two-armed open-label randomized controlled trial. Participants were randomly assigned to either the intervention group (IG), with access to the guided Web-based intervention, or the wait-list control group (CG), with access to unguided Web-based psycho-education.

We used a computerized block randomization procedure (allocation ratio 1:1, block size 10). The researcher conducting the randomization had no information about the participants apart from their 6-digit codes and did not participate in the enrollment and assignment of the participants to study groups, which was handled by two different researchers. Outcome variables were assessed at baseline (T0) and 12 weeks after randomization (post-treatment, T1). In addition, a follow-up measurement was assessed 24 weeks after randomization (12 weeks after treatment, T2). Sample size calculation was based on expected between-group differences at follow-up. G*Power was used for sample size calculation [34]. First, we assumed a power of 0.80, an alpha level of 0.05, and a small to medium effect size (d=0.3), which results in N=357 to perform a two-sided t test for differences between two independent means. Second, adding 20% attrition rate at inclusion, post-assessment, and follow-up, we calculated that N=608 participants needed to be enrolled.

The study was approved by the ethical review board at Leuphana University of Lüneburg. The study was registered retrospectively on February 1, 2013, under the International Standard Randomized Controlled Trial Number ISRCTN02446836; http://www.controlled-trials.com/ISRCTN02446836. Despite retrospective registration, no participants were enrolled before registration.

Recruitment

Participants were recruited from a large-scale German statutory health insurance between January 2013 and April 2014, with the first participant enrolled in February 2013. We recruited members from Kaufmännische Krankenkasse (KKH), a statutory health insurance company with about 1.8 million members nationwide. First, to identify participants who were at high risk for sick leave due to depression, insurance members were screened for previous diagnosis of depression (International Classification of Disease codes F32.0, F32.1, F33.0, F33.1, and F34.1), previous sickness absence due to depression, and current sickness absence. Second, the study team sent an invitation letter to all positively screened insurance members along with study information, the informed consent form (see Multimedia Appendix 1), and a 6-digit code to login into the platform. Adults with a previous episode of mild to moderate depression (International Classification of Disease codes F32.0, F32.1, F33.0, F33.1) or dysthymia (F34.1) were included to avoid giving less intensive treatment than necessary. Before registration on the platform, a screening for exclusion criteria was performed. Participants with a score of ≥20 on the Patient Health Questionnaire (PHQ-9), indicating severe depression, were excluded. A second exclusion criterion was suicidality as measured by one item on the presence of suicidal thoughts. All participants had unrestricted access to treatment as usual during the study period, including access to the treatments and services which are typically available for depression in the German health care system (eg, psychotherapy and medication).

Intervention

The Web-based intervention "HelpID" is a 12-week, Web-based program based on cognitive-behavioral therapy, awareness training, and systemic counseling. The program was structured into 12 weekly sessions. Each lasted 30 to 45 minutes and included interactive elements, videos, and audios that explained depression-related themes (eg, symptoms and course) as well as graphs, illustrations, exercises, and guidance for awareness and relaxation. Each session was available one week after completing the prior session. Participants received weekly reminder emails when a new session was available. The program had a guided format with therapist contact upon request, that is, psychologists (bachelor level or higher) trained in the intervention approach provided feedback via email or telephone. The intervention was developed by a team of clinical psychologists headed by Dr Despina Lion, a clinical psychologist and therapist with extensive experience in systemic counseling, cognitive-behavioral therapy, and neurological psychology. It is accessible online [35] (see Multimedia Appendix 2). Since July 2016, the copyright of "HelpID" is owned by IVPNetworks GmbH, a private integrated care company. The intervention is commercially available to single users and is included in health care plans of statutory health insurances.

The intervention's psychological approach includes cognitive-behavioral therapy, mindfulness training, and systemic counseling. During the development process, current research evidence on the respective therapies was used as the basis, and special emphasis was placed on a "person-based" approach, focusing on the perspectives of the people who would use the intervention. Cognitive-behavioral therapy is the most extensively researched psychological treatment approach in Web-based interventions [36]. From cognitive-behavioral therapy, the intervention used elements of cognitive restructuring, with an emphasis on dealing with negative moods and automatic thoughts, as well as exercises for behavioral activation. Mindfulness training has been used increasingly in psychotherapy over the past years. It was shown to be effective for depressive symptoms and can be adapted to online formats [37,38]. The intervention module on mindfulness engages the user in exercises to observe the self and to practice mindfulness in daily situations. Systemic counseling is a therapeutic approach that highlights the social context surrounding the individual and its resources [39]. Specifically, systemic questioning techniques and instructions were employed to make use of the participants' social support. Systemic principles were presented in specific weekly sessions, while homework exercises on systemic therapy encouraged the participants to adopt a systemic viewpoint and behavior change in their everyday interactions.

Control Group

The control group was a wait-list plus psycho-education condition. During the 12-week study period, participants had access to text-based information on the nature of depression and its symptoms and treatment. The psycho-education content was developed by a team of trained psychologists (bachelor degree or higher) and was based upon scientific literature on depression (eg, the German S3-Guideline) [40]. This type of control condition was chosen because more active control groups (ie, psycho-education) are considered to be more methodologically valid than passive control groups (ie, wait-list conditions) [24]. There is evidence that psycho-education can reduce depressive symptoms and serve as an initial treatment in primary care [41]. The control group did not have access to therapist guidance. Participants were eligible to access the intervention after study completion, if they requested access.

Outcomes

The primary outcomes were self-assessed depressive symptoms with the Patient Health Questionnaire (PHQ-9) and the Beck Depression Inventory (BDI II). The PHQ-9 measured the severity of depressive symptoms over the preceding 2 weeks, resulting in a score between 0 to 27 points with higher values indicating more severe depression [42,43]. The PHQ-9 was shown to have good reliability and construct validity [42]. The BDI II uses 21 items to measure depression severity [44,45]. The BDI II showed good psychometric properties in German-speaking samples in regard to internal consistency, retest-reliability, and construct validity [46]. As a secondary outcome, quality of life was assessed using the Manchester Short Assessment of Quality of Life (MANSA) [47]—a 12-item

scale rating the participants' satisfaction with different life domains. The MANSA has been validated in a Swedish sample and showed satisfactory internal consistency and construct validity [48]. User satisfaction was measured at post-assessment using the item "Overall, how satisfied are you with the program?" with four answer options: 1=very good, 2=good, 3=satisfactory, and 4=poor.

Information on work absenteeism was retrieved from health insurance records. In the German health care system, such standardized health data is collected routinely. Its primary purpose is cost reimbursement and quality assurance, but it can be made available for secondary analysis. Due to the routine data collection, health insurance records are assumed to have high ecological validity. We matched health insurance records from KKH health insurance with participants' data using a 6-digit participant code as identifier. The code was generated for each positively screened insurance member and was also used for registration on the study platform. We analyzed sickness absence data that covered the 90 days before randomization (baseline) and 90 days after intervention (post-assessment). Three sickness absence measures were constructed according to Hensing et al [33]. First, the number of persons who were absent at least once, second, absence frequency as the number of times a person was absent during the 90 day period irrelevant of duration, and third, absence duration as the total number of absence days during the 90 day period. Sickness absence data was not diagnosis-specific.

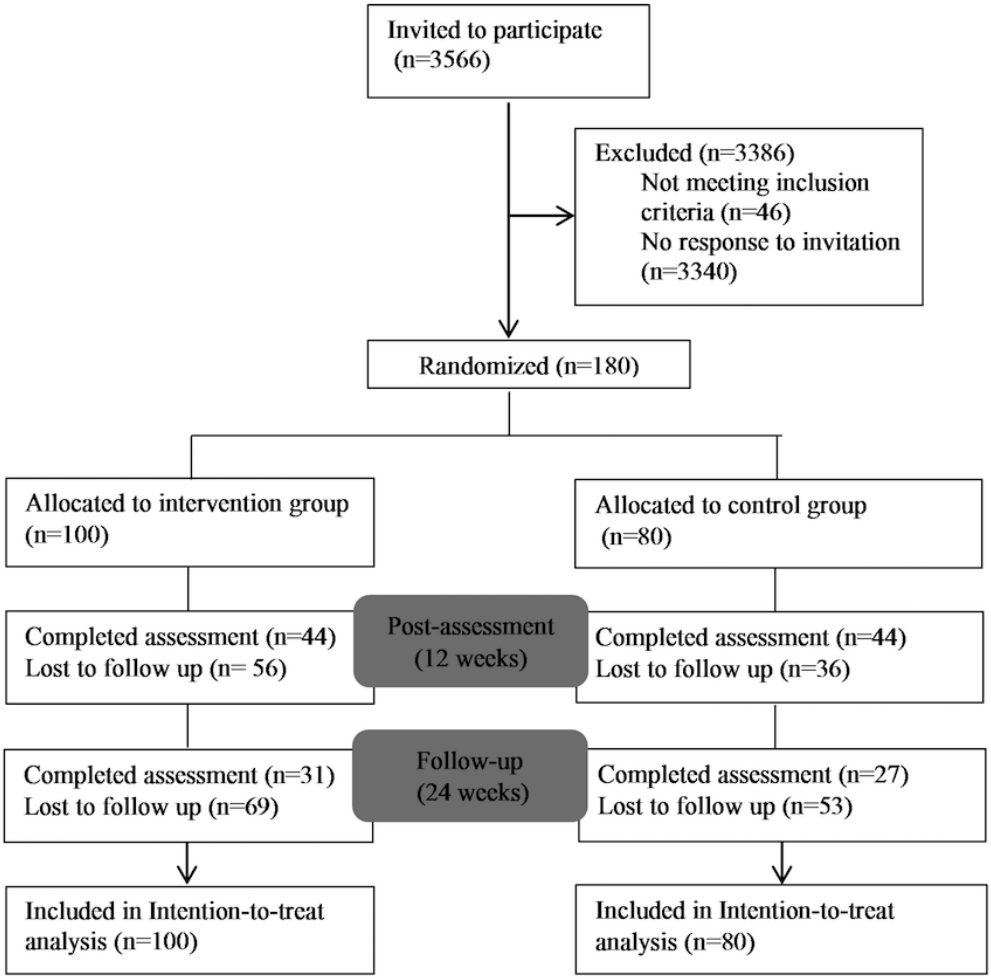
Statistical Analysis

Statistical analysis was performed on an intention-to-treat (ITT) basis according to the recommendations in the CONSORT statement [49] and its adaption for eHealth trials [50] (see Multimedia Appendix 3). Missing data at post-treatment was imputed using the Markov Chain Monte Carlo multiple imputation (missing data module in IBM SPSS version 22), where 10 estimations per missing value were specified and, besides the outcome variables, group assignment was included as an additional variable. Under the assumption that data is missing at random, multiple imputation was considered suitable to produce more precise estimates of the true intervention effect than other imputation methods, that is, last observation carried forward [51]. In addition, per-protocol (PP) analysis was performed to examine the robustness and sensitivity of the findings when including only participants who completed the post-assessment. *t* tests were used to determine differences in baseline characteristics and for within-group differences. The difference in the intervention outcomes between the intervention group and the control group at post-treatment was estimated using analysis of covariance (ANCOVA) with baseline scores as the covariate. Cohen *d* was calculated as a measure of the effect size, using pooled standard deviations [52]. For the between-group effect sizes, Cohen *d* was computed from the mean differences.

To assess clinical significance on an individual level, the reliable change index (RCI) was computed for the PHQ-9 [53]. Cronbach alpha=.89 from Kroenke et al [42] was used as an estimate of the reliability of the PHQ-9, along with pre-treatment standard deviations from the current study. Participants were classified as "responders" if they displayed a reliable positive change, or as "deteriorated" if they displayed a negative change on the RCI. A reliable positive change corresponds to less than −1.96 on the RCI and a change of PHQ-9 points to greater than −4.05. A reliable negative change corresponds to less than −1.96 on the RCI and a change in PHQ-9 points to greater than 4.05. Finally, the number needed to treat (NNT) [54] was computed.

All analysis was performed using Stata 13. The reported *P* values are two sided and in the 95% CI.

Figure 1. Study flowchart.



Results

Participant Characteristics

Figure 1 shows the flow of participants through the study. The complete pool of insurance members was screened, which resulted in 3929 positively screened insurance members who were subsequently invited to participate. Of those, 180 responded, met the inclusion criteria, provided informed consent, and were randomized. Of the 180 participants, 88 completed the post-assessment after 12 weeks (retention rate: 48.8%, 88/180), and 58 completed the follow-up assessment after 24 weeks (retention rate: 32.2%, 58/180). To estimate achieved power, a post-hoc power analysis was conducted. This revealed that with the sample of 180 participants, the achieved power to detect an effect of d=0.3 was 0.51.

Baseline characteristics between participants who completed the post-assessments and those who were lost to follow-up were tested for differences. Older participants (PHQ at T1: P=.02, BDI at T2: P=.03) and participants with higher education (PHQ at T1: P=.03, BDI at T2: P=.04) were more likely to complete the post-assessment on the primary outcome and the follow-up assessment. Participants who were not in psychotherapy during study enrollment were more likely to complete post-assessment on one of the primary outcomes (BDI at T1: P=.04) and the follow-up assessment (BDI at T2: P=.04) as compared with participants who were on a waiting list or in psychotherapy at enrollment. No other relevant differences between those who completed the post-assessments and those who were lost to follow-up were found.

Table 1 shows the participant characteristics at baseline. Participants had an average age of 48 years and were predominantly female (68%). The majority were married or had a partner (56%) and had completed secondary education or higher (85%). About half of the sample was working full-time (51%) and another 27% were working part time, while 20% of those working had an executive position. About one-fifth (21%) were not working. The majority had experienced a previous depressive episode (51%) or reported to have chronic depression (30%). During study enrollment, half of the participants were prescribed with depression medication (50%), 26% were in psychotherapy, and 13% were on a psychotherapy waiting list. Of the total number of enrolled participants, 43% had a sick leave certificate at the time. The mean baseline depressive symptoms in the sample were 11.10 points on the PHQ-9 (SD=4.45), indicating moderate depression. No clinically relevant differences in terms of any baseline characteristics were found, and we concluded that randomization was successful.

Table 1. Participant characteristics at baseline.

Characteristic	Intervention group n=100[a]	Control group n=80	Total sample n=180	*P* value
PHQ-9 Score, mean (SD)	11.53 (4.35)	10.56 (4.53)	11.10 (4.45)	.15
Age, mean (SD)	47.01 (10.36)	48.66 (11.59)	47.74 (10.92)	.31
Gender, n (%)				
Male	34 (34.0)	23 (28.7)	57 (31.7)	.45
Female	66 (66.0)	57 (71.3)	123 (68.3)	
Relationship, n (%)				
Single	24 (24.0)	18 (22.5)	42 (23.3)	.93
Married/Partner	56 (56.0)	46 (57.5)	102 (56.7)	
Divorced/Separated	15 (15.0)	14 (17.5)	29 (16.1)	
Widowed	5 (5.0)	2 (2.5)	7 (3.9)	
Education, n (%)				
Low	13 (13.3)	13 (16.2)	26 (14.6)	.38
Middle	63 (64.3)	42 (52.5)	105 (59.0)	
High	22 (22.4)	25 (31.3)	47 (26.4)	
Employment, n (%)				
Full-time	51 (52.0)	39 (50.6)	90 (51.4)	.41
Part-time	30 (30.6)	18 (23.4)	48 (27.4)	
Not working	17 (17.3)	20 (26.0)	37 (21.2)	
Executive position, n (%)				
Yes	20 (22.0)	13 (17.6)	33 (20.0)	.48
No	71 (78.0)	61 (82.4)	132 (80.0)	
Previous depression[b], n (%)				
None	18 (18.0)	14 (17.7)	32 (17.9)	.53
Episodic	54 (54.0)	38 (48.1)	92 (51.4)	
Chronic	28 (28.0)	27 (34.2)	55 (30.7)	
Depression medication, n (%)				
Yes	53 (53.0)	36 (45.6)	89 (49.7)	.33
No	47 (47.0)	43 (54.4)	90 (50.3)	
In psychotherapy, n (%)				
Yes	30 (30.0)	16 (20.3)	46 (25.7)	.15
No	57 (57.0)	52 (65.8)	109 (60.9)	
Waiting List	13 (13.0)	11 (13.9)	24 (13.4)	

[a]All values (except for *P* values) are mean (SD) or n (%).

[b]Original item: "Did you have these symptoms for the first time?" Answer options: 1. "Yes," 2. "No; I had one or multiple episodes," 3. "No; the symptoms last for several years."

Intervention Effectiveness

Table 2 shows the mean scores, standard deviations for the intervention outcomes at baseline and at post-assessment, effect sizes, and statistical significance, based on the intention-to-treat sample (imputed data). A significant between-group difference in favor of the intervention group was found for the PHQ-9 ($F_{1,179}$=15.06, P<.001), which corresponds to a medium effect size (d=0.55, CI 0.25-0.85). For those in BDI-II, a significant between-group difference at post-treatment was found ($F_{1,179}$=8.69, P=.004), which corresponds to a moderate effect size (d=0.40, CI 0.10-0.70).

Table 2. Means, standard deviations (SD), effect sizes, and statistical significance for intervention outcomes based on intention-to-treat sample (imputed data).

Outcome	Mean (SD)			Effect Size[a]	Statistical Significance[b]	
	Baseline (T0)	Post-assessment (T1)	Difference (T0−T1)	Cohen *d* (95% CI)	*F* Value	*P* value
PHQ-9						
Intervention	11.53 (4.35)	6.51 (2.87)	−5.02 (3.62)	0.55 (0.25-0.85)	15.06	<.001
Control	10.56 (4.53)	7.76 (3.63)	−2.80 (4.42)			
BDI-II						
Intervention	20.07 (7.99)	13.55 (6.46)	−6.17 (6.39)	0.41 (0.11-0.70)	8.69	.004
Control	18.78 (9.84)	15.52 (8.62)	−3.56 (6.68)			
MANSA						
Intervention	3.27 (0.72)	3.50 (0.67)	0.14 (0.71)	0,12 (−0.17 to 0.42)	0.72	.39
Control	3.30 (0.85)	3.44 (0.70)	0.22 (0.55)			

[a]Between-group effect size from mean differences.

[b]Based on ANCOVA controlling for baseline scores (T0).

In addition, both the intervention and the control group showed reductions in depressive symptoms as measured by within-group changes from baseline to post-assessment. In the intervention group, a mean reduction of 5 points on the PHQ-9 was found (t_{99}=14.28, P<.001), which corresponds to a large within-group effect size (d=1.42, CI 1.14-1.71). In the control group, a mean reduction of 2.79 points was found (t_{79}=5.82, P<.001), corresponding to a moderate effect size (d=0.65, CI 0.41-.89).

In the per-protocol analysis, we tested for differences in PHQ-9 scores between intervention completers and noncompleters at post-assessment. No significant difference was found (t_{178}=−.28, P=.78). Table 3 presents the results of the per-protocol analysis.

For the PHQ-9, a significant between-group difference in favor of the intervention group was found among completers (PHQ-9: $F_{1,77}$=8.98, P=.04), corresponding to a moderate effect size (d=0.61, CI 0.15-1.07). The mean PHQ-9 scores among completers were reduced by 5.70 points in the intervention group and by 2.24 points in the control group—this corresponds to a large effect size (d=1.72, CI 1.23-2.22) and a moderate effect size (d=0.49, CI 0.14-0.82) for within-group changes, respectively. For the BDI-II, the between-group effect failed to reach statistical significance in the per-protocol analysis ($F_{1,77}$=0.81, P=.37, d=0.25, CI −0.18 to 0.65). BDI-II within-group changes were significant in the intervention group (t_{43}=3.68, P<.001) and the control group (t_{42}=4.70, P<.001).

Table 3. Means, standard deviations (SD), effect sizes, and statistical significance for intervention outcomes based on per-protocol sample (nonimputed data).

Outcome	Mean (SD)			Effect Size[a]	Statistical Significance[b]	
	Baseline (T0)	Post-assessment (T1)	Difference (T0−T1)	Cohen *d* (95% CI)	*F* value	*P* value
PHQ-9						
Intervention	11.53 (4.35)	6.50 (3.85)	−5.03 (3.29)	0.61 (0.15-1.07)	8.98	.04
Control	10.56 (4.53)	7.95 (4.62)	−2.61 (4.61)			
BDI-II						
Intervention	20.07 (7.99)	14.86 (8.05)	−5.21 (7.59)	0.25 (−0.18 to 0.65)	0.81	.37
Control	18.78 (9.84)	15.32 (10.34)	−3.46 (6.32)			
MANSA						
Intervention	3.27 (0.72)	3.52 (0.86)	0.25 (0.64)	0.18 (−0.22 to 0.58)	0.34	.56
Control	3.30 (0.85)	3.42 (0.83)	0.12 (0.79)			

[a]Between-group effect size from mean differences.

[b]Based on ANCOVA controlling for baseline scores (T0).

Table 4. Work absence indicators at baseline and at post-assessment for 160 participants.

Indicator	Baseline (T0)[a]	Post-assessment (T1)	Difference (%)	*P* value
Absence at least once, n (%)				
Intervention	75 (85.22)	25 (28.41)	−50 (−66.67)	<.001
Control	58 (80.55)	12 (16.67)	−46 (−79.31)	<.001
Absence frequency, mean (SD)				
Intervention	1.19 (0.09)	0.39 (0.08)	−0.80 (−67.23)	<.001
Control	1.15 (0.10)	0.20 (0.06)	−0.95 (−82.61)	<.001
Absence duration, mean (SD)				
Intervention	25.60 (2.03)	24.65 (3.80)	−0.95 (−3.71)	.79
Control	27.69 (2.37)	24.04 (4.36)	−3.65 (−13.18)	.34

[a]Baseline and post-assessment cover a period of 90 days each.

Treatment Response

In the intervention group, 63% (63/100) of the participants showed a reliable symptom change from baseline to post-intervention and were thus classified as responders. In the control group, 33% (27/80) were classified as responders. The difference in reliable symptom change between intervention and control group was significant (t_{178}=3.39, P<.001). This resulted in a NNT of 4.08. One participant in the intervention group experienced symptom deterioration, and five participants in the control group experienced symptom deterioration.

Sickness Absence

Information on sickness absenteeism was available for 160 participants (Intervention group: n=88, control group: n=72). For 20 participants, sickness absenteeism could not be retrieved from insurance records, and therefore the data from these participants was unavailable.

Table 4 shows persons who were absent at least once, with absence frequency and absence duration at baseline and at post-assessment. The majority of the participants were absent at least once during the baseline period: IV: 85% (77/85), CG: 80% (58/72). Overall, significantly fewer participants were absent at least once during post-assessment (IV: 28%, CG: 16%). The within-group absence reductions were significant (IV: t_{87}=6.54, P<.001, CG: t_{71}=6.17, P<.001).

Regarding absence frequency, participants in the intervention group were absent on average 1.2 times at baseline and 0.4 times at post-assessment. In the control group, participants were absent 1.2 times at baseline and 0.2 times at post-assessment. The within-group reductions in absence frequency were significant (IV: t_{87}=7.49, P<.001, CG: t_{71}=8.59, P<.001).

Similarly, high absence durations at both baseline and post-assessment were found. From the 90 days examined at each time point, participants in the intervention group were absent from work 26 days at baseline and 25 days at post-assessment. In the control group, participants were absent 28 days at baseline and 24 days at post-assessment. However, there were no significant differences in absence duration from baseline to post-assessment (IV: t_{87}=.26, P=.79, CG: t_{71}=.95, P=.34). For all three measurements, the between-group differences at post-assessment failed to reach statistical significance (absence at least once: $F_{1,159}$=.80, P=.37, absence frequency: $F_{1,159}$=3.24, P=.07, absence duration: $F_{1,159}$=.02, P=.88).

Secondary Outcome

No significant difference in quality of life as measured by MANSA was found ($F_{1,169}$=.71, P=.40, d=0.13, CI −0.21 to 0.41).

Long-term effect

No significant between-group difference for BDI-II depression scores at 24-week follow-up was found ($F_{1,85}$=.81, P=.33). However, significant within-group changes were sustained for both the intervention and the control group. In the intervention group, there was a mean reduction from baseline to follow-up assessment of 5.46 points on the BDI-II (t_{99}=6.81, P<.001), which corresponds to a moderate effect size (d=0.68, CI 0.46-0.90). In the control group, there was a mean reduction of 4.69 points (t_{79}=4.37, P<.001), corresponding to a small effect size (d=0.48, CI 0.26-0.72).

User Satisfaction

87 participants completed the user satisfaction survey at post-assessment. In the intervention group, 13.6% (6/44) rated the program overall as very good, 68.2% (30/44) as good, and 18.2% (8/44) as satisfactory. In the control group, 4.6% (2/43) rated the program as very good, 37.2% (16/43) as good, 34.9% as satisfactory, and 23.3% (10/43) as poor. Mean satisfaction scores were 2.04 in the intervention group and 2.76 in control group. There was a significantly higher mean satisfaction in the intervention group (t_{85}=4.60, P<.001).

Discussion

Principal Findings

This study compared the effectiveness of a Web-based intervention in reducing depressive symptoms and sickness absence among adults with immediate risk for sickness absence due to mild to moderate depression. When compared with a

wait-list plus psycho-education control group, participants who used the Web-based intervention showed a significantly greater reduction in depressive symptoms. However, because of the low response and high attrition in this study, one primary outcome did not reach statistical significance among participants who completed the intervention (per-protocol analysis) and at follow-up, only within-group changes were sustained but the intervention effect was not. In terms of individual clinical significance, significantly more participants in the intervention group responded to the treatment. We used health insurance records to measure sickness absence and found that sickness absenteeism declined in both groups, but there were no statistical differences in work absence between groups. The achieved power of this trial was lower than calculated. Therefore, its results should be replicated in a larger sample.

Comparison With Prior Work

These findings are especially relevant when considering the increasing impact of mental ill-health on workforces across industrialized countries [55]. Depression is a significant cause for workday losses and produces more absence durations than other mental illnesses. To reduce the illness burden, widespread access to evidence-based treatment is needed to maintain workers' mental health before companies and individuals face more serious burdens as the illness progresses. In general, Web-based interventions provide a promising treatment tool because these interventions can be accessed at any time and at different locations at the users' own pace. Due to their relative anonymity, Web-based interventions may especially benefit employees with depression who wish to avoid the negative perceptions of being mentally ill in the workplace. However, risks associated with the dissemination of Web-based interventions in the health care system have been reported as well. According to meta-analysis, the effects of Web-based interventions vary, making it necessary to evaluate each intervention separately. If Web-based interventions that are effective in reducing depressive symptoms are more widely implemented and adopted, a positive impact on the burden and impairment caused by depression can be expected. It can also help to overcome the shortcomings of conventional treatment (eg, waiting lists).

This study contributes to the growing body of research that supports the effectiveness of Web-based interventions for depression. Within this research, a critical mass of efficacy studies is needed to identify subgroups for which these interventions work [56]. Adults who are at high risk for sick leave from work due to mild to moderate depression have not yet been targeted specifically by Web-based interventions. In terms of effect sizes, previous research has found significant heterogeneity between studies. This makes it necessary to evaluate each intervention separately. The effect sizes reported in this study are comparable to other studies evaluating guided interventions for depression, including those included in the meta-analysis by Andersson and Cuijpers [23] where a mean between-group effect size of d=0.41 is reported. The amount of therapy guidance that is necessary to increase intervention effectiveness and adherence remains a subject of debate in the field of Web-based interventions [18,57]. Considering that this intervention provided only minimal therapist support upon request and achieved similar outcomes to studies with more intense guidance, we speculate that merely having the option to contact a therapist during the intervention—versus regular therapist contact—is sufficient for the needs of many participants and works equally well. However, it is possible that the number of dropouts could have been reduced with regular guidance. The examination of support preferences was not within the scope of this study and further research on this subject is needed.

We found that health insurance records are a suitable outcome for effectiveness research in Web-based interventions. Both groups showed reductions in work absence frequency, however, no statistical difference in work absence between groups was found. Several explanations may account for this finding. First, we cannot rule out the possibility that the decline in work absence frequency over time was caused by regression toward the mean or spontaneous remission. Our sample was recruited during a period of high levels of sickness absence, as seen in the data (see Table 3). Consequently, due to statistical chance, the frequency of sickness absence tended to approach lower levels at post-assessment. A healthy control group is needed to compare baseline levels of sickness absence, which was unavailable in this study. Second, it is possible that the 90-day time period in our study was not sufficiently long to appropriately detect changes in work absence. Previous population studies on sickness absence due to mental health problems found a median absence duration of 79 days [58]. This indicates that sickness absence started or ended outside of the time period of this study. Similarly, our sample was not adequately powered to detect small differences in work loss days. Third, organizational factors (ie, high work demands, job security) could have influenced work absence in this study. Unfortunately, we could not measure organizational variables.

To disentangle these explanations, future studies on the effect of Web-based interventions on work absence should include a longer time period, information on organizational factors that may be related to sickness absence, and work absence data from a healthy control group for baseline comparisons. Integrating objective behavioral parameters (ie, sickness absence data from health insurance companies) can increase the validity of effectiveness studies and might be a valuable addition to self-reported outcome measurements.

Privacy and Data Security

In Web-based interventions, health-related information is processed and stored electronically. Therefore, data security and confidentiality issues need to be taken seriously. This study used several measures to ensure the privacy of the study participants. Person-related information and study data were stored on separate servers to ensure that individuals could not be identified. Communication between the users' Web browsers and the servers were encrypted via a Secure Sockets Layer (SSL) connection. All data were stored on servers located in Germany.

Limitations

There are several limitations to this study that must be acknowledged. First, although reporting the effect of the Web-based intervention was within the scope of our study, it remains unclear as to which specific elements and properties of

the intervention contributed to its effectiveness. Regarding the length of the intervention, evidence on the dose-response relationship in psychotherapy points to the conclusion that most progress occurs in the first few sessions of an intervention [59]. Similarly, Web-based interventions with 8 or less sessions were found to be more effective than interventions with more than 8 sessions [21]. This indicates that the present intervention with its 12 sessions could be shortened in length while maintaining its effectiveness.

A second limitation concerns the response rate. Response from the pool of positively screened insurance members was low (5.8%, 226/3929). This raises the concern that participants were particularly motivated to use a Web-based intervention when compared with nonparticipants, especially because nonparticipants were positively screened for sickness absence due to depression and thus belonged to the target group. Ideally, data from nonparticipants should have been collected as a baseline comparison group, but this data was unavailable in this study because of a lack of informed consent. When the complete pool of insurance members was screened and all positively screened insurance members were invited, recruitment was stopped. This resulted in a substantially smaller sample than was previously calculated in the power analysis (calculated N=680 vs actual N=180).

Third, attrition during the study was high. At post-assessment, 45.5% of the participants had dropped out, and at follow-up, 67.7% of participants had dropped out. In general, dropout is a common problem in Web-based interventions [60]. However, the dropout in this study was remarkably higher than the average attrition rate for Web-based interventions with therapist support, as reported in the meta-analysis by Richards and Richardson (28%) [21]. Several recent studies on Web-based interventions showed dropout rates that were remarkably lower [27,32]. One possibility for the relatively high attrition in this study is that participants who failed to complete a weekly session were reminded via email only. Comparable studies, which used telephone reminders, achieved substantially higher participant compliance. A second explanation is that therapist guidance was available upon request only. Guided interventions have lower attrition rates as compared to unguided interventions. Thus, it is possible that participants who were at risk for dropout were less likely to use therapist guidance. Despite our analysis of per protocol and imputed data showing comparable results, which indicates no difference in intervention completers versus noncompleters, the risk remains that study dropout could have biased the results. Due to the associations of several baseline characteristics (age, education, and being in psychotherapy) with the likelihood to complete the outcome assessments, the missing at random assumption could have been violated. Overall, the high attrition rates limit the conclusions drawn from this study.

Third, the positive relationship of age and education with study dropout seen here limits the generalizability of the findings to younger and less educated groups. This is supported by the composition of the study sample, where highly educated participants and those in executive positions are over-represented. Further studies with more statistical power are needed to identify effectiveness among different subgroups.

Fourth, participants had access to treatment as usual during the study, including psychotherapy and medication. Therefore we cannot exclude the possibility that within-group changes in depression scores were affected by third factor variables. Thus, within-group changes must be interpreted with caution.

Fifth, no clinical interviews were conducted to assess depression. Structured clinical interviews represent the gold standard of clinical assessment, with superior validity and reliability. Due to limited resources, this study relied solely on participants' self-reports to assess clinical symptoms.

Sixth, the amount and duration of provided therapeutic support during the study was not measured, making it difficult to compare the results with other studies on Web-based interventions that have used different levels of support, ranging from no support to more intensive and regular support. In this study, support was provided upon request, which could have prevented some participants from using support, thus lowering adherence.

Seventh, we used a wait-list plus psycho-education control group. Wait-list control groups undermine internal validity and may lead to an over-estimation of the treatment effect [24]. Thus, active control groups are considered to be less biased. To maximize participant response, we decided to inform control group participants that they could access the intervention upon request after study completion. This may have lowered expectations with regard to the control condition. Furthermore, control group participants were active during the study period as they had access to psycho-education. As a result, we observed mean symptom reductions in the control group, which is consistent with the finding that Web-based psycho-education can reduce depressive symptoms [41]. At the same time, it is possible that psycho-education has adverse effects in some participants, because it sensitizes patients to the topic of depression, leading to an over-reporting of symptom severity at follow-up. For example, a study that used a psycho-education control group found that the incidence of depression was higher than usual [32]. Our results show that reliable symptom deterioration was low overall, but occurred more frequently in the control group (6.25%, 5/80) as compared with the intervention group (1%, 1/100). This suggests that adverse effects in the control groups were present, but were unlikely to bias the treatment effect. As we did not collect data on usage and engagement with the psycho-education in the control condition, the perceived credibility of the psycho-education remains unknown.

Eighth, this was an open-label trial, where participants and researchers were aware of which group was receiving which treatment. Furthermore, only questionnaire data was assessed as a proxy of use parameters, but no uptake data was available on the actual usage of the program (eg, frequency and length of website usage). Data on how the participants interacted with the program could provide valuable insights into the effectiveness of specific intervention elements.

Conclusions

The Web-based intervention reduced depressive symptoms among adults with sickness absence. As this trial achieved a

lower power than calculated, its results should be replicated in a larger sample. Further validation of health insurance records as an outcome measure for eHealth trials is needed.

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Conflicts of Interest

This research was funded by the European Union Innovation Incubator, and one goal of the Innovation Incubator was to facilitate regional economic development by evaluating the intervention, HelpID, produced by Novego AG, a regional commercial partner within the Innovation Incubator.

Multimedia Appendix 1

Patient information informed consent form.

[PDF File (Adobe PDF File), 113KB - jmir_v19i6e213_app1.pdf]

Multimedia Appendix 2

Intervention screenshots.

[ZIP File (Zip Archive), 631KB - jmir_v19i6e213_app2.zip]

Multimedia Appendix 3

CONSORT-EHEALTH-checklist.

[PDF File (Adobe PDF File), 806KB - jmir_v19i6e213_app3.pdf]

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Abbreviations

ANCOVA: analysis of covariance
BDI-II: Beck Depression Inventory
ITT: intention-to-treat
KKH: Kaufmännische Krankenkasse
MANSA: Manchester Short Assessment of Quality of Life
PHQ-9: Patient Health Questionnaire
PP: per-protocol
RCI: Reliable Change Index

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Chapter 4

Supportive Mental Health Self-Monitoring among Smartphone Users with Psychological Distress: Protocol for a Fully Mobile Randomized Controlled Trial

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Supportive Mental Health Self-Monitoring among Smartphone Users with Psychological Distress: Protocol for a Fully Mobile Randomized Controlled Trial

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Mobile health (mHealth) could be widely used in the population to improve access to psychological treatment. In this paper, we describe the development of a mHealth intervention on the basis of supportive self-monitoring and describe the protocol for a randomized controlled trial to evaluate its effectiveness among smartphone users with psychological distress. Based on power analysis, a representative quota sample of $N = 186$ smartphone users will be recruited, with an over-sampling of persons with moderate to high distress. Over a 4-week period, the intervention will be compared to a self-monitoring without intervention group and a passive control group. Telephone interviews will be conducted at baseline, post-intervention (4 weeks), and 12-week follow-up to assess study outcomes. The primary outcome will be improvement of mental health. Secondary outcomes will include well-being, intentions toward help-seeking and help-seeking behavior, user activation, attitudes toward mental-health services, perceived stigmatization, smartphone app quality, user satisfaction, engagement, and adherence with the intervention. Additionally, data from the user's daily life as collected during self-monitoring will be used to investigate risk and protective factors of mental health in real-world settings. Therefore, this study will allow us to demonstrate the effectiveness of a smartphone application as a widely accessible and low-cost intervention to improve mental health on a population level. It also allows to identify new assessment approaches in the field of psychiatric epidemiology.

Keywords: mental health, smartphone, mobile intervention, psychological distress, self-monitoring, ambulatory assessment, randomized controlled trial

INTRODUCTION

Mental health is broadly defined as "a state of well-being in which an individual realizes his or her own abilities, can cope with the normal stresses of life, can work productively and is able to make a contribution to his or her community" (1). Thus, mental health relates not only to the absence of illness but also to positive functioning in regard to well being and social connectedness, and a sense

of control and self-efficacy. Indeed, there are strong links between mental health and work productivity, social inclusion, quality of relationships, and life opportunities in general (2–4). There is also a high comorbidity with other health conditions, where poor mental health acts as a risk factor (5). Over the lifespan, mental-health problems often take an episodic course, where relative symptom-free times alternate with more severe episodes of illness (6). Mental ill-health develops frequently in young adults and tends to become chronic in older age if not adequately treated and managed (7).

Mental ill-health is associated with a high societal burden. The most prevalent mental disorders including major depression, anxiety disorders, insomnia, somatoform disorders, and alcohol and drug dependence are among the leading causes of years lived with disability (8). The estimated cost of all mental disorders taken together amounts to up to €240 billion each year in Europe (9). As a result, these countries have made effective, accessible, and high-quality mental-health care a priority, and have called for increasing action to promote mental health in the population (10, 11).

Despite the existence of effective treatment options, improving the mental health of the population is compromised by a low detection rate and treatment-seeking of persons with mental-health problems. Community mental-health surveys indicate that up to 27% of the adult population is affected by at least one mental disorder each year (12) and up to the age of 50, 3/4 of the population has experienced some kind of mental disorder (13). But even in comprehensive health-care systems with free access to mental-health care, as, e.g., in Germany, only up to one-quarter of all persons with mental disorders receive professional help (14). Manifold barriers to help-seeking exist (15), among others also the stigma of mental disorders and self-stigmatization (16, 17). The high numbers of individuals, unaware of their mental-health problem and who consecutively do not seek treatment, lead to the conclusion that a significant amount of unmet treatment needs exist in the population.

Recently, the WHO suggested the use of mobile health (mHealth) technology to improve access to psychological treatment (18). This is referred to as mHealth. Smartphone technology is now widely available in the population, serving as an attractive, but yet under-used delivery channel for health interventions (19). This technology is suitable of repeated sampling of subjects' current behaviors and experiences in real time and in natural environments, which is referred to as Ambulatory Assessment (AA), Experience Sampling Method, or Ecological Momentary Assessment (20). It can also be combined with psychological interventions, i.e., Ecological Momentary Interventions (EMI). An EMI is a treatment "provided to people during their everyday lives (i.e., in real time) and settings (i.e., real world)" (21). A particularly promising approach for an EMI is the self-monitoring of mental health, where the user learns to keep track of his or her symptoms and behavior over time. Based on the individuals' real-time information, tailored feedback can be provided to support and reinforce positive change in mental health, and to counteract negative developments. Mobile self-monitoring could not only support mental health but could also stimulate learning about one's own mental health, and could lead to improved self-management skills and establishment of healthy attitudes and behaviors.

Self-monitoring offers several advantages. First, conducting repeated measurements of mental-health symptoms reveals insights into the dynamics of psychological processes as they naturally develop and this information can be used improve the prediction of relapses or to track treatment response. Second, by establishing short time intervals between experience and recall, or even assessing the present moment, the problem of recall bias, as in retrospective reports, can be avoided. Third, by capturing the real-world contexts, in which experiences are made or behavior occur, risk and protective factors in the psychosocial environment and their impact on mental health can be more easily identified. Fourth, self-monitoring is executed independently, without clinical supervision, which stimulates an active role of the user and empowers subjects to manage their own health. Fifth, self-monitoring can be combined with automated feedback based on the information provided by the individual, which allows for the development of interventions to support mental health and to integrate these interventions in a daily life routine, when support is mostly needed.

Supportive self-monitoring has been successfully used for a broad range of mental-health problems. It can be a feasible, well-accepted approach among patients with mental-health problems (22), and is associated with improvements in clinical outcomes (23–25). Among young adults in the early stages of depression, self-monitoring increases emotional self-awareness, which is an important first step in a stepped care approach (26). Symptom monitoring as part of a disease management program prolonged symptom-free intervals among patients with recurrent depression (27) and helps to focus on that behavior, which patients can influence themselves (28). Among untreated individuals, a motivating effect to seek health care was found (29). Over 50% of persons with mental disorders in all age groups expressed an interest in daily mental health self-monitoring (22). The available evidence on self-monitoring of mental health is limited as most studies are observational and do not employ control groups. Randomized controlled trial (RCT) are needed to investigate benefits and potential harms.

Whether supportive monitoring can be safely applied in unsupervised settings has not yet been sufficiently documented. Besides technical challenges (e.g., battery problems, availability of internet connection), issues of data security and data privacy are critical. As continuous self-monitoring is likely challenging, especially for person with mental-health symptoms, various factors such as low motivation and energy, the tolerability and desirability from the patients' perspective need to be examined. It is also unclear which subgroups of patients mostly benefit from this type of intervention. Also, the identification and timely management of crises and risk of harm during self-monitoring must be considered. Several trials have shown negative results, including more sustained symptoms as a result of self-monitoring mental health (30). This indicates that self-monitoring needs in-depth consideration and clarification before it is implemented as a clinical tool in the future.

Before this background, we aim to develop and evaluate to the best of our knowledge the first mHealth intervention for

mental health on the basis of supportive self-monitoring in the general population. A field test of mental health self-monitoring in the general population has been conducted previously and serves as the basis of this project (31). Building on a smartphone application for Android devices, the mHealth intervention can be disseminated at low cost, and can achieve broad accessibility in the population. Implementing an indicated prevention approach, we want to focus on adults from the general population with psychological distress, who display lowered productivity in day-to-day activities, but who are not seeking professional help. Examining the intervention across subgroups, subjects with low, moderate and high mental distress will be included, covering all degrees of mental-health problems. As smartphones are increasingly used not only by young people, but across all age groups, the study will include young and middle aged adults aged 18–45. We hypothesize that by using the intervention, participant's mental health and health-related behaviors will improve.

MATERIAL AND EQUIPMENT

Stepwise Procedures

A fully mobile 3-arm RCT will be conducted. The intervention will be compared toward AAs (self-monitoring without support) and a passive control group (no self-monitoring and no support). We hypothesize that using the intervention will improve mental health as compared to the control groups, where we expect no significant changes. The RCT will be registered prospectively as a clinical trial in the German registry for clinical trials (Deutsches Register Klinischer Studien).

Target Group

The target group for the mHealth intervention are 18- to 45-year-old Android smartphone users with psychological distress. We differentiate between low, moderate, and high psychological distress, as indicated by the Kessler K6 screening scale. The presence of psychological distress as measured by the K6 indicates elevated psychopathology, functional impairment, and treatment need. This was shown in several population-based studies that used the K6 scale as a screening instrument (32, 33). For high distress, a sensitivity of 0.36, specificity of 0.96, and total classification accuracy of 0.92 has been demonstrated in validation studies against structured diagnostic interviews (33). This indicates that subjects with high distress are likely to fulfill diagnostic criteria for a common mental disorder. Participants with moderate distress likely do not fulfill the diagnostic criteria for a mental disorder, but where shown to experience significant psychopathology, functional impairment, and treatment need as well (32).

The size of the target group in Germany can be roughly estimated with a combination of market data on smartphone sales (34, 35), population census data on age distribution (36), and prevalence rates of psychological distress (32). In 2015, about 63% of the German population owned a smartphone, equaling to about 44 million smartphone owners in Germany (34). The leading smartphone operating system is Android with 79.2% of sold smartphones in 2016 (35). Subtracting persons above 45 or under 18 from the 34 million Android smartphone users, we estimate a total of 12.4 million eligible persons who belong to the target group in Germany (36). From the total target group, 63.5% (7.9 million) is estimated to have low psychological distress, 27.9% (3.4 million) is estimated to have moderate psychological distress, and 8.6% (1.1 million) is estimated to have high psychological distress based on the K6 screening scale (32). These estimates indicate that a broad target group exists in the population that could benefit from the mHealth intervention.

Recruitment

We aim for a broad recruitment strategy including online and offline channels to achieve a sample that reflects the target group. Online recruitment on social media is a cost-effective approach, which can recruit large numbers of participants in short time, in particular for e-health studies (37, 38). We will place targeted advertisements on Facebook, the most popular social networking platform with 28 million active users in Germany, and Google, the most popular search engine and, with 660 million daily visitors, one of the most frequented websites. Targeted advertisements (e.g., filtered by age, gender, and smartphone usage) ensures that advertisements will reach the target group. While online recruitment is not necessarily superior to offline recruitment, the combination of both approaches was found to be optimal for achieving a representative sample (39). Therefore, efforts will be undertaken to recruit participants in the community, including placing newspaper advertisements, emails to health professionals and civic organizations, media and press releases at Charité Universitätsmedizin Berlin.

Sample Size Calculation

A power analysis was performed to detect a group difference on the primary outcome at post-assessment group. The calculation is based on the assumption that a difference between the supported monitoring group and either AA group or control group within the margin $-0.25 <$ Cohen's $d < 0.25$ can be neglected. We assume no difference between the two latter groups. Therefore, a between-group difference of $d = 0.25$ should reach statistical significance as an indicator of the general effectiveness of the intervention. The target sample size was computed using Gpower (40) for a repeated-measures analysis of variance for a within-between interaction of time and group (ANOVA). We used a targeted power of 95%, a significance level alpha of 0.05, four assessment waves, a conservative estimate of correlation between measurements ($r = 65$) and variances of the differences between groups (non-sphericity correction epsilon = 0.8). This results in a total $N = 141$. Adding 20% drop-out at T2 and T3, we will include 186 participants (62 per group).

Sample Description

Figure 1 presents the sample description in terms of gender, age, and mental distress. We aim for a quota sample of Android smartphone users from the general population. Quota sampling is a form of non-random sampling which approximates population representativeness according to a set of pre-defined criteria, while allowing for participants to self-select into the study (41). Compared to random sampling or stratified sampling, quota sampling is advantageous for the present project due to lower

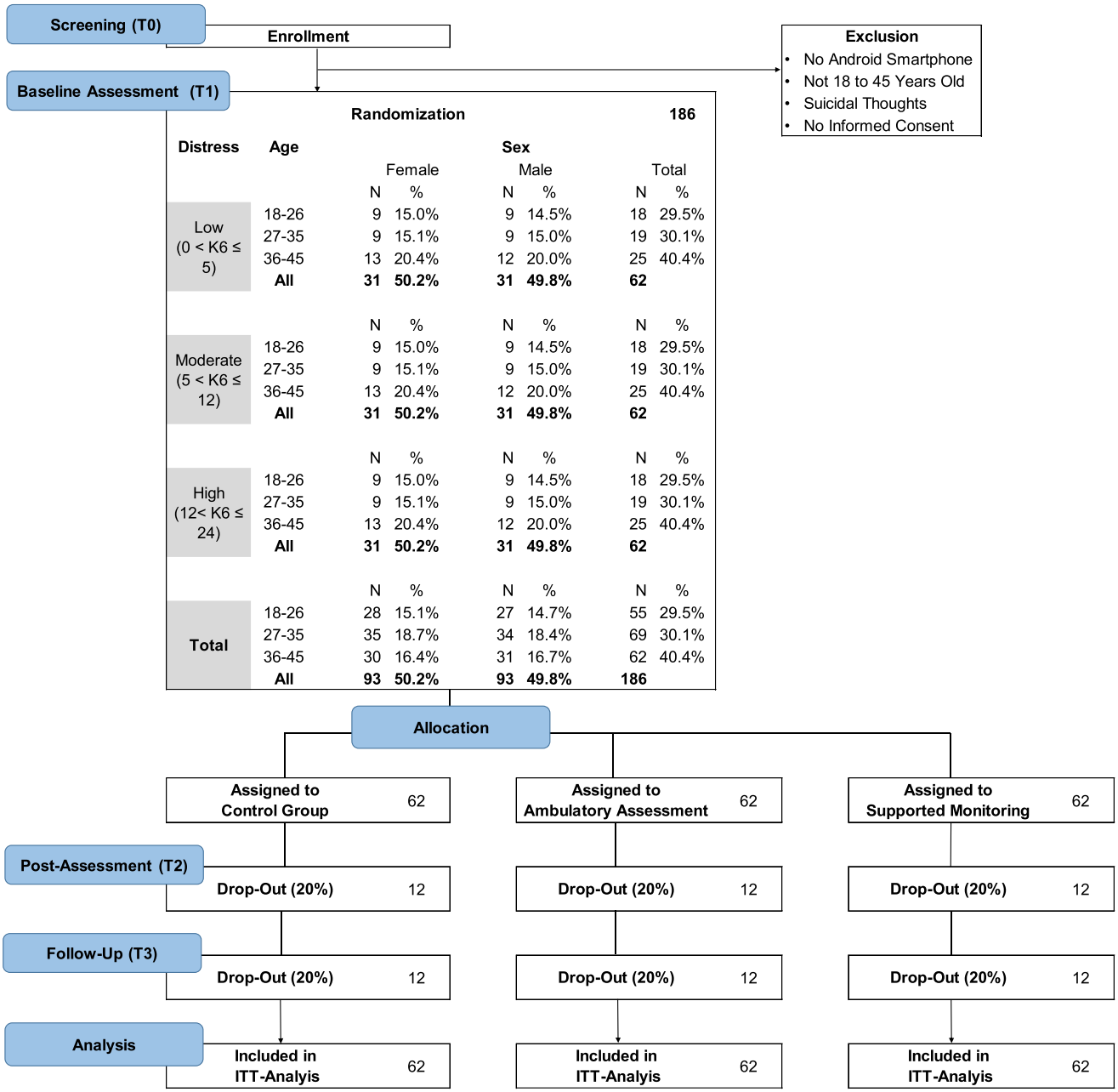

FIGURE 1 | Study flow.

costs, and because smartphone users need to be pre-screened according to psychological distress.

Three equally sized distress groups are formed, with inclusion probabilities according to prevalence estimates for the Kessler K6 screening scale (32). To achieve equally sized distress groups, participants with moderate to high distress will be over sampled. To approximate representativeness for the general adult population from 18 to 45 years, quotas for age and gender are defined according to the distribution of the latest Zensus population survey (36). Stratification by age is important to account for differential smartphone usage by age, with younger people having a higher rate of smartphone usage as compared to older people. Three age groups will be formed: Young (18–26, 29,5%), Middle (27–35, 30,1%), and Older (36–45, 40,5%). Due to a higher prevalence of mental health problems among women, groups will also be stratified by gender (49.8% male, 50.2% female).

Inclusion Criteria, Informed Consent, and Randomization

The inclusion criteria are age between 18 and 45 years and ownership of an Android smartphone (Android Version 4.0 or higher) with an active internet connection. Exclusion criteria are the

presence of suicidal thoughts as measured by one item on the presence of suicidal thoughts, and failure to provide informed consent.

Upon registration, participants will be informed about the requirements and procedure of study on the study website. Additionally, an information booklet with details on the study procedure will be available for download. Informed consent will be obtained of each participant with a written signature when first using the smartphone application. To randomize participants to study conditions, a computerized block randomization procedure will be used (Allocation ratio 1:1:1, block size 10). The researcher preparing the randomization procedure will have no information about participants and will not participate in the recruitment, enrollment of participants, or assignment of participants to study groups.

Software

Self-monitoring will be conducted on the basis of smartphone application for Android devices. A comparison of such software solutions is provided in Kubiak and Krog (42). MovisensXS will be used as a specialized software for the research methodology of AA, that has been used extensively in research studies (43). MovisensXS is designed to collect subjective self-reports of the participant in daily life and is based on the Android operating system. It consists of two components. First, a web-based portal for study administration used by the researcher. Second, a smartphone app for data collection. The application assesses self-reports throughout the day and, depending on the research question, can be triggered at random times, by the participants themselves or from context parameters.

Intervention

The intervention consists of two components: self-monitoring and support.

Self-Monitoring

During the 28-day intervention period, daily self-monitoring on the basis of AAs will be conducted. The research methodology of AA is well suited to study people in their natural environment, resulting in ecologically valid data from the persons' everyday life (44). The self-monitoring protocol should detect and monitor micro-processes of mental health and intra-individual variability, as well as the contextual factors in daily life. We aimed to design a brief, but comprehensive protocol for daily self-monitoring of mental health based on self-reports, while attempting to keep participant burden low. The most common areas of psychopathology will be included: Mood, depression, anxiety, stress, sleep, and functional impairment. In addition, physical activity, social activity, daily hassles and daily uplifts, and alcohol and drug use will be monitored as risk and protective factors of mental health. With a total length of 23 items, participants will be able to complete a daily report in under 5 min. All AAs will be time and date stamped.

Mood: To self-monitor daily mood, we will use the version of the Multidimensional Mood State Questionnaire (MDBF) from Wilhelm and Schoebi (45). The MDBF was designed specifically for daily life studies with repeated mood ratings, where a parsimonious measure that is sensitive for change is needed. It uses six items to assess the three factors calmness, valence, and energetic arousal in the present moment. Responses are indicated on three separate six-point bipolar scales with the endpoints labeled "very" ("good–bad," "awake–tired," and "calm–nervous").

Depression: depression is one of the most common mental health problems. The Patient Health Questionnaire-2 (PHQ-2) will be used to self-monitor daily depressive symptoms. The PHQ-2 uses two items to score the frequency of depressed mood and anhedonia on the present day on a 4-point scale ranging from (0) "*not at all*" to (3) "*nearly all of today*," which results in a total score ranging from 0 to 6. The PHQ-2 was originally developed as short screening scale for depression during the past 2 weeks, and will be adapted for the present project to assess depressive symptoms on the present day (46, 47). The PHQ-2 has demonstrated good sensitivity to change and its diagnostic properties were found to be comparable to longer screening instruments. Using PHQ-2 score of 3 as cut point, the authors report that the overall diagnostic accuracy of the PHQ-2 as measured as the "Area under the curve" is 0.90 for major depressive disorder (47); however, the authors also state that a cut point of 2 would enhance sensitivity, and a cut point of 4 would improve specificity.

Anxiety: anxiety disorders range over a broad spectrum of experiences related to the expression of anxiety reactions and avoidance behavior. Anxiety is among the most prevalent mental disorders with 11–20% of the population affected during their lifetime. We will use the Generalized Anxiety Disorder-2 (GAD-2) as an ultra-brief monitoring scale for anxiety disorders (48). The GAD-2 uses two items to rate the presence of core anxiety symptoms. The GAD-2 showed high sensitivity for the four most common anxiety disorders: generalized anxiety disorder, panic disorder, social anxiety disorder, and posttraumatic stress disorder. While the original version references to the past two weeks, we will adapt the reference period to the present day. A cut point of 3 on the GAD-2 was reported to be optimal (48).

Stress: we define stress as the extent to which an individual perceives that situational demands exceed their ability to cope. To measure the extent of daily stress, we will use the 4-item version of the Perceived Stress Scale (PSS-4). The PSS-4 has two positively worded items and two negatively worded items, which correspond to a two-factor structure (49). We refer to the subscale representing the negatively stated items as "Stress" and to the subscale representing the positively stated items as "Coping." The PSS uses a 5-point scale from 0 "*never*" to 4 "*very often,*" resulting in a total score of 0–8 for each subscale. As the PSS was not designed as a diagnostic instrument, no cut point is available.

Daily events: both daily hassles and daily uplifts will be monitored as risk and protective factors of mental health. Daily hassles are small, day-to-day irritations (e.g., losing things, traffic jam, arguments), while daily uplifts are small, positive events that can help reinforce a sense of well-being (50). The occurrence and appraisal of daily events will be assessed with an adapted scale from Wichers et al. (51), where respondents report the most important event of the day on a 7-point bipolar scale (−3 "very unpleasant," 0 "neutral," and 3 "very pleasant"). From this data, variables for positively appraised events (daily uplifts) and negatively appraised events (daily hassles) will be constructed by

including the range of neutral to very pleasant events (0–3) or neutral to very unpleasant events (−3–0) events.

Sleep: poor sleep quality and insomnia are widespread health problems. To monitor sleeping problems, we will use a one-item measure of sleep quality extracted from the Consensus Sleep Diary, a standardized sleep scale which was designed for self-monitoring purposes (52). The item "How would you rate the quality of your sleep?" is rated on a 5-point sale from 1: very poor–5: very good.

Physical and social activity: as a protective factor for mental health, social activity refers to daily interactions with different groups of people in the immediate social environment. It will be measured with the item: "With whom have you spend the majority of your day?" using alone, partner, friends, family, colleagues, and other as categories. Physical activity is monitored as a protective factor of mental health and will be measured with an item extracted from the International Physical Activity Questionnaire (IPAQ SA Short) (53). The item "Have you been physically active today?" uses four answer categories to assess low-, moderate- and high-intensity activities, and also no activity as an indicator for sedentary behavior. Appropriate examples for each category will be provided for instruction (e.g., low-intensity activity "walking at least 10 min a day").

Alcohol and drug use: as a risk factor for psychopathology, daily reports of drinks consumed using the categories beer, wine, liquor, and other will be collected. From this, the number of standard drinks consumed per day will be calculated. Participants will be familiarized with the concept of a standard drink and the volumes of different beverages that are equivalent to a standard drink (54). The German definition of standard drinks will be used (men: 20 g alcohol, women: 10 g alcohol). Two measures of alcohol use will be constructed: days with any drinking and days with heavy drinking (defined by five drinks for men and four drinks in for women). For drug use, the daily occurrence and frequency of any illegal substance will be assessed.

Impairment: the individuals' functioning in the context of social and occupational roles, which is assumed to be a central component of mental health will be monitored. We use a single-item scale from the PHQ-4 (55), which measures subjective impairment in work and household duties and in social relationship on the present day on a 4-point scale with the item: "How difficult have these problems made it for you to do your work, take care of things at home, or get along with other people?"

Context: contextual information on daily locations will be monitored as a risk or protective factor of mental health. For this purpose the item "Where were you the majority of the day?" will be used with the categories: at home, visiting friends or family, work or school, outbound, and other.

Support

Supportive self-monitoring is a therapeutic intervention to improve mental health, based on tailored real-time feedback on the individuals' own information collected during self-monitoring (56, 57). By self-monitoring mental health, it is expected that the user gains insights into his or her own mental health, learns to improve self-management skills and establishes healthy attitudes and behaviors. Tailored feedback based on the individuals' information is provided in real time, to support and reinforce positive change in mental health, and to counteract negative developments. **Figure 2** displays the supportive monitoring process.

1. *Self-Monitoring*: participants will be able to self-monitor mental health by visual inspection of the time course for each symptom (mood, anxiety, depression, stress, sleep, impairment). This will be achieved by displaying line plots of symptom scores on the *y*-axis, and time (in days) on the

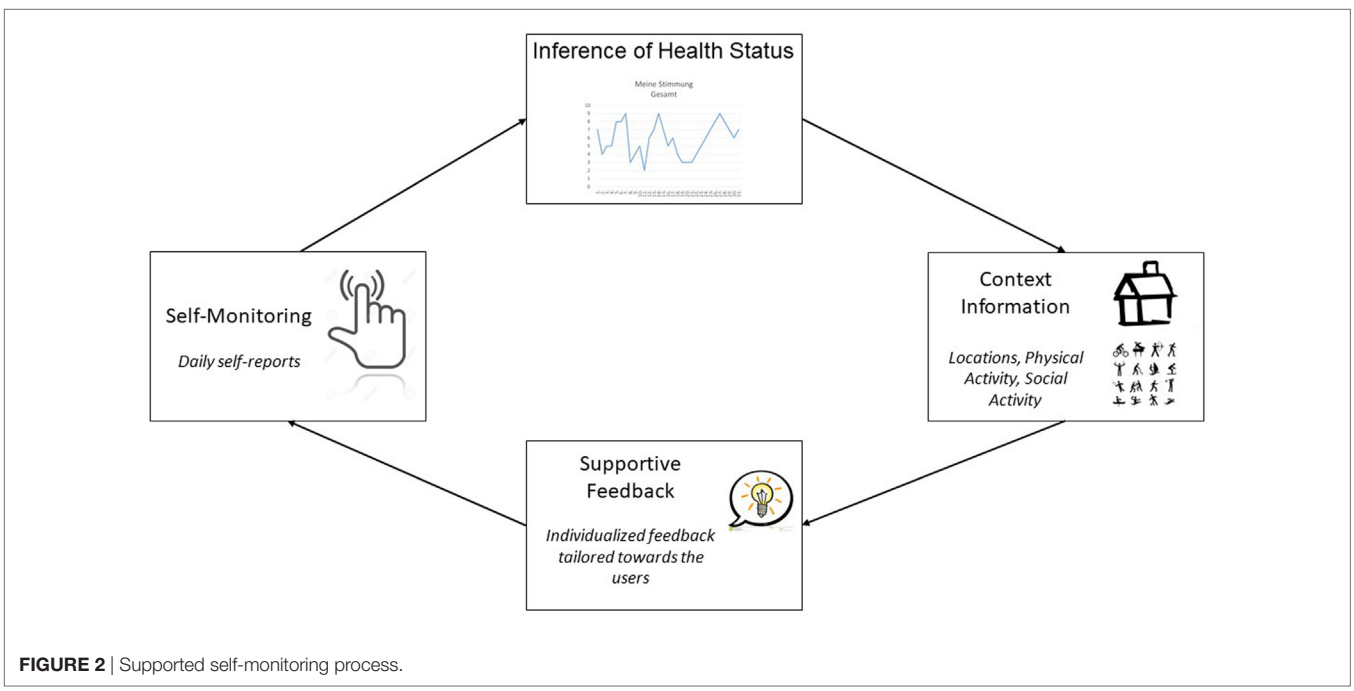

FIGURE 2 | Supported self-monitoring process.

x-axis. Participants can select the last week or the total self-monitoring period as time frame. There will be an option to display the time course of multiple symptoms simultaneously by adding or removing symptoms from the menu.

2. *Inference of Health Status:* weekly health reports will provide text-based feedback on the user's personal health status and symptoms. The participants' personalized weekly health status will be derived from the mean level for each symptom during the past week. Severity categories (low, moderate, high) will be computed by using established cut points, whenever available. For example, the established PHQ-4 cut points for symptom severity of depression (47) and anxiety (48) will be used. If no cut points are available, the scales will be divided into low, moderate, and high scores according to the tertiles of the frequency distribution. The health status will also be displayed in terms of deviations from the within person-mean. Thus, the participants' deviation of his or her mean in terms of improvements or worsening of symptoms will be displayed. As a relatively stable mean requires several days of collected data, the latter feature will be available after 1 week of use. Users will be notified whenever a new weekly health report is available with a pop-up message and an icon next to the appropriate section.
3. *Context information:* the influence of social contexts on mental health will be displayed to the user. The context-specific health status will be displayed on a text basis, allowing the users to compare the symptoms and health in each setting. For this purpose, each of seven symptoms will be grouped by its daily context/setting. Six different contexts will be available: 1. days with daily hassles, 2. days with daily uplifts, 3. days with physical activity, 4. days with social activity, 5. days spent alone, and 6. days in company (partner or friends, family, colleagues, others). Alternatively, users may group symptoms by five different locations (1. days at home, 2. days visiting friends or family, 3. days at work or school, 4. trips/outbound, and 5. other). Thus, the user can inspect his or her mental health problems within a total range of 210 possible combination, allowing for a rich and detailed inspection of symptoms by context.
4. *Supportive Feedback*: personalized supportive feedback will be given, based on the data collected by the participant. Feedback will presented in the form of daily health tips which can be accessed from within the application or as Android system notification. The feedback will include tips for the self-management of mental health and mental health micro-interventions (e.g., behavioral activation, problem solving, coping strategies) based on psychoeducation and cognitive–behavioral therapy (CBT) for low mood, anxiety, depression, stress, substance abuse, and sleep problems (58–60). The feedback will be adapted to the severity of each symptom within the last week (low, moderate, high). In the case of low to moderate severity, tips for the self-management of mental health and mental health micro-interventions will be displayed. Participants with moderate symptom severity will also be directed toward available evidence-based self-help programs (61, 62). In the case of severe symptoms, participants will be encouraged to seek help from a professional mental health service and will be provided with corresponding contact information on these services (e.g., hotlines, addresses, and websites of professional organizations). For each mental health problem and degree of severity, at least 10 different feedback messages will be developed, resulting in a total of at least 180 feedback messages (10 messages × 6 mental health problems × 3 degrees of severity). Additionally, a total of 40 feedback messages will be developed for the presence of daily life risk factors for mental ill-health (low social activity, low physical activity, daily hassles, and functional impairment). Users will be able to dismiss feedback messages that they do not wish to be presented again or to select feedback messages that they wish to be reminded of. All content will be developed on the basis of evidence-based guidelines or treatment manuals for the respective mental health problems (63–67).

Content. Psychoeducation: Psychoeducation aiming at educating the user about the nature and treatment of mental health problems was found to be an effective and easy-to-implement intervention for depression, anxiety, and psychological distress (59). Psychoeducation can also help to reduce perceived stigmatization (68), and to enhance mental health literacy (69), beliefs in the efficacy of treatment options (70), and help-seeking behavior (71). As psychoeducation is most effective when the content is perceived as relevant for a persons' problem, the intervention will offer relevant information on mental health problems adapted toward the user. This includes psychopathology from self-monitoring (mood, depression, anxiety, stress, sleep, and functional impairment) as well as risk and protective factors. The total educational content will be accessible *via* a knowledge base section within the smartphone application, and supportive feedback (daily health tips) will direct the users toward appropriate educational content, when indicated by self-monitoring information. Psychoeducation within the application will be limited to brief texts and visualizations, and links to further educational websites and resources will be provided for further reference.

Cognitive–behavioral therapy: Cognitive–behavioral therapy is one of the most extensively researched forms of psychological treatment. It aims toward improving mental health by challenging negative automatic thoughts and dysfunctional beliefs, and at changing behavioral patterns, including risk and protective factors related to mental health. CBT was found to be effective for a broad variety of mental health problems, including depression, anxiety, and stress (72–74). CBT is also a prevention technique which helps to prevent mental-health problems from maintaining, and is suitable for managing both clinical and subclinical mental health problems (75). CBT is also the recommended therapeutic principle for mHealth interventions, as it is feasible for self-administration by the user (76). In the context of mHealth, CBT has the advantage that its techniques are well suited for a text-based operationalization, allowing CBT to be converted into a short, structured format. Thus, CBT will be the basis for supportive feedback (daily health tips) in the intervention.

Coping skills training: as part of CBT-based practices, coping skills training refer to a persons' perceived ability to effectively cope with adversity and distress, by using adaptive (constructive) coping strategies in stressful situations or during conflicts.

Developing active, good coping skills is associated with improved mental health including depression (77), anxiety (78), and psychological distress (79). Improvements in coping skills are also associated with less engagement in avoidance behavior toward potentially anxiety-inducing situations, which in turn leads to increased participation in social activities as a protective factor for the maintenance of mental health (80).

Behavioral activation: aiming toward breaking the "vicious cycle" of low mood and inactivity, behavioral activation is a CBT-technique that encourages the user to engage in physically activating and rewarding activities, e.g., by planning of activities, setting goals, and engaging in pleasurable activities. Behavioral activation is associated with improvements in depression (81) and anxiety (82). As part of the daily health tips, we will select short, tangible, and universal activities to maximize user engagement with behavioral activation. By encouraging reflection on the experience after performing an activity, the tips will stimulate reflective learning.

Design. To facilitate the adoption and ease of use of the intervention, the smartphone application will be designed toward usability (user-centered design) (83, 84). For example, a tutorial will explain the features and navigation upon initial start of the application. Based on process evaluations, four usability themes for the development of smartphone applications will be considered: design, feedback, navigation, and terminology (85). Design refers to the applications' interface layout, taking into account consistency, location of icons, and functions on each screen (e.g., the size, color, and esthetics of visual elements). Feedback refers to the applications' ability to provide appropriate feedback, aimed toward assisting and guiding the user during completion of tasks (e.g., indicating sync status by color when submitting self-monitoring data). Navigation refers to optimizing the way a user navigates throughout the application, so that users know where they are in the application at all times and how to get back to where they came from (e.g., clear icons, tab views, and buttons). Terminology means that the user is able to identify and understand the language used within the application (e.g., avoidance of technical terms).

Control Groups

The intervention will be compared to two control groups: first, the active control group will complete daily AAs (self-monitoring without support). Second, there will be a passive control group (no self-monitoring and no intervention).

Pilot Test

Prior to recruitment, a pilot test of will be conducted among a sample of 30 students at Charité Universitätsmedizin Berlin, who will receive either course credit or 20€ compensation. All study procedures will be pilot tested.

Participant Incentives

To enhance adherence with the study protocol, participants who complete all outcome assessments will receive an incentive of 25€.

Potential "gaming" needs to be avoided, which refers to a situation where research participants fraudulently enroll in a study for the purpose of acquiring research payment. A first measure to prevent gaming is that the eligibility survey will be locked in case of participants trying to change submitted answers. A second measure is that study links will only be available for one user/device. Third, IP addresses will be tracked to prevent duplicate enrollment.

Data Storage and Privacy

All data will be stored and handled to fulfill the legal requirements of German data protection. Data is stored in a data center in Greifswald, Germany, which is operated by a German hosting provider ("ProfitBricks GmbH") certified according to ISO 27001 and Trusted Cloud. To prevent that the identity of the subjects is stored on the server, no person-related data will be collected together with the self-monitoring data (e.g., name). Additionally, a numerical pseudonym label will be assigned, the so-called participant identifier. Participants' study data can only be linked with person-related data by using the participant identifier. After data collection the participant identifier will be deleted. All communication between smartphone and the server, as well as communication between server and researcher will be encrypted with a 256 Bit Secure Sockets Layer encryption. Finally, to ensure that no unauthorized parties can access the participant data, e.g., in the case of losing the device, all data stored locally on the smartphone will be encrypted with Advanced Encryption Standard 256 bit technology. Each time the participant uses the application, a unique session key is generated to encrypt and securely transmit the data to the server. Only with the private key stored on the server the data can be decrypted. After data transmission from the device to the server, local data stored on the device is deleted.

Additional Procedures

Telephone reminders: to limit study drop-out, telephone reminders will be initiated in the case of failure to respond to an outcome assessment or failure to download the smartphone application. The study team will constantly supervise enrollment, downloads of application, and compliance with the study protocol, and will initiate telephone calls to participants that need to be reminded.

Application reminders: to increase adherence and to stimulate user engagement with the intervention, push notifications on the Android device will remind participants to complete the daily self-monitoring report and will remind users to engage with intervention content, e.g., by displaying a notification that a new daily health tip is available.

Outcomes

Study outcomes are assessed at four time points: screening (T0), baseline (T1), post-assessment (T3) and follow-up (T4). While the screening (T0) relies on self-assessments collected during participant registration on the study website, structured telephone interviews are conducted at T1, T2, and T3 to assess the primary outcome. The telephone interviews will be conducted by the Academic Survey Lab at the University of Hamburg. Trained interviewers who are blinded to the study condition will conduct the interviews, resulting in an independent outcome assessment to avoid confounding with the self-monitoring data. The

secondary outcomes will be self-assessed on the smartphone for all three groups.

Primary Outcome

Mental health: we will use the extent of psychological distress as a measure of mental health. Psychological distress relates to unspecific behavioral, emotional, cognitive, and psychophysiological components of mental health. The Kessler K6 screening scale will be used (33). The K6 has been extensively used in the World Mental Health Survey and has been validated and translated to German. It consists of six items for the measurement of distress during the past 30 days, resulting in a total score ranging between 0 and 24 points. K6 respondents can be classified into three severity groups, with 0–4 points indicating no distress, 4–12 points moderate distress, and 13–24 points high distress (32).

Secondary Outcomes

Well-being: the last item from the EUROQOL EQ-5D will be used to measure well-being (86). Participants are asked to rate their well-being on a Likert scale ranging from 0 to 100, where 0 represents the worst state and 100 the best state: "*What number between 0 and 100 best describes your well-being today?*"

Intentions toward help-seeking: The intention to seek help for a mental health problem will be measured with the General Help-Seeking Questionnaire (GHSQ) (87). The GHSQ asks: "*If you were having a mental health problem, how likely is it that you would seek help from the following source?"* with two help source options: 1. informal source (friend or family) and 2. professional source (general practitioner, mental health service, educational health service). Respondents rate the likelihood of seeking help from each source on a 7-point Likert scale ranging from "extremely unlikely" to "extremely likely."

Help-seeking behavior: help-seeking is defined as the behavior of actively seeking assistance, regardless of whether the source is informal or formal. The Actual Help-Seeking Questionnaire (AHSQ) will be used to measure help-seeking for a mental health problem within the past 4 weeks (88). The AHSQ first asks whether or not any help had been sought for a mental health problem during the reference period. Second, if help had been sought, whether it was sought from an informal source or from a professional source (identical to the help source options of the GHSQ). For each item, a score of one indicates that help had been sought and a score of 0 that help had not been sought.

User activation: we refer to user activation as the degree of perceived knowledge, skill, and confidence for the active self-management of one's mental health condition. The Patient Activation Measure (PAM) will be used, a reliable and validated measure for the degree of activation. The PAM rates the agreement to 13 items on a 4-point scale (89). Respondents are scored on four levels, with a higher score indicating higher activation.

Attitudes toward mental health services: Attitudes about the effectiveness of mental health services influence the likelihood of seeking professional help. The Attitudes Toward Seeking Professional Psychological Help Scale-SF (ATSPPH-SF) will be used to measure attitudes toward mental health services (90). The ATSPPH-SF has 10 items rated on a 4-point scale, resulting in a total score ranging from 0 to 30, where higher values represent more positive attitudes. It has shown good validity and reliability (91).

Perceived stigmatization: to measure the extent to which participants perceive to be stigmatized due to a mental health problem, we will adapt the stigma domain of the Caregiver Burden Scale (CBS). The CBS was originally developed to assess four domains of stigma among caregivers of family members with mental illness (92). We only use the domain of stigma which has two items: 1: "*having a mental health problem makes my family feel ashamed*" and 2: "*having a mental health problem makes me feel ashamed*." Respondents rate the items on a 5-point scale (1 = never, 5 = always). Higher scores indicate a higher level of perceived stigma. A composite measure of the stigma perceived will be constructed from the total of the scores for these two questions.

Smartphone app quality: to measure the degree to which the smartphone app meets quality criteria from a user perspective, we will use the Mobile App Rating Scale (MARS) from Stoyanov, Hides (93). The MARS has 23 items and rates smartphone app quality along five dimensions: Engagement, functionality, esthetics, information quality, and subjective quality. It has demonstrated excellent internal consistency and inter-rater reliability. The assessment of smartphone app quality will be conducted at post-intervention among all participants who have used one of the study apps.

Expectations: to measure credibility of the smartphone application and the user's expectations toward it, the credibility and expectation questionnaire (CEQ) will be used. The CEQ consists of six items and has demonstrated good psychometric properties (94).

The following objective usage parameters are automatically collected by smartphone application during the study period.

Engagement: the extent to which participants are exposed to the intervention and engage with it will be measured by usage metrics of the smartphone application. This includes a date and time-stamped log of when participants open the application and the length of each session. From this information, the number of and length of user interactions with the application will be computed for the 30-day monitoring period. In the intervention group, the users' engagement with the supportive feedback content will be assessed by tracking the number of received feedback and user ratings of each feedback message (dismiss/remind).

Adherence: adherence with outcome assessments will be measured, and in the groups that use self-monitoring, adherence with self-monitoring will be measured. The number of completed daily self-monitoring will be assessed as defined by completion of the last page of an assessment and can range between 0 and 28.

Other Assessments

Personality: personality traits will be assessed with the 10 Item Big Five Inventory (BFI-10). The BFI-10 is a short scale to assess the five-factor model as the predominant model for describing personality along the dimensions openness to experience, conscientiousness, extraversion, agreeableness, and neuroticism. The BFI-10 has shown satisfactory psychometric properties (95).

Optimism/pessimism: optimisim/pessimism is defined as expectations toward future events in all life domains, with

"optimists" having the expectation that mostly good things will happen and "pessimists" having the expectation that mostly bad things will happen. The personality trait optimisim/pessimism will be assessed with the scale Optimism-Pessimism-2 (SOP2). The SOP2 has been validated among the general population and has shown good reliability and validity (96).

Social support: the Oslo 3-items social support scale (OSS-3) will be used to measure the extent of available social support. The OSS-3 has been developed as part of a large-scale mental health survey and has been used in European comparative research, where its feasibility and predictive validity with respect to mental health has been confirmed (97).

Socio-demographics: core social variables (age, gender, nationality, ethnicity, income, employment status, marriage/relationship status, and education) will be collected on the basis of the recommended measures from the Federal Statistical Office (98).

Patient history: past and current intake of medication for mental-health problems, and past use of psychotherapy and similar health services will be assessed. Past use of health services will assess the number and duration of health service usage.

Statistical Analysis

Before analysis, data will be prepared and cleaned according to the guidance in Ref. (99). Data will then be analyzed according to the recommendations in the CONSORT statement for evaluation of e-health interventions, as well as the mHealth evidence reporting and assessment checklist from the WHO mHealth Technical Evidence Review Group (100, 101). Intention-to-treat analysis (ITT) and additional per-protocol analysis (PP) will be performed, the former including the data of all participants randomized and the latter using only the subset of participants who complete all assessments (T0, T1, T2, T3).

Multilevel models are an appropriate data-analytic strategy for smartphone data, involving daily measurements, resulting in repeated observations nested within individuals (102). These models are well suited to test the general effectiveness of supported monitoring among smartphone users, but also its differential effectiveness and its conditional effectiveness. Models include analysis of both within-person and between-person variance. Missing data will be replaced using Markov Chain Monte Carlo multiple imputation, which is considered to produce more precise estimates of the true intervention in the ITT analysis compared other imputation methods, i.e., last observation carried forward (103).

General effectiveness: to test for changes in the outcome variable from before to after the intervention period, repeated-measures analysis of variance (RM-ANOVA) will be conducted for each intervention outcome (104). In the RM-ANOVA, the within-person effect of time is used as an index of general intervention effectiveness. For the analysis of between-person variance, the model can be extended to multivariate analysis of variance (MANOVA). In this case, a between-subjects factor for group membership is added (Supported monitoring group vs. AA group vs. control group). If there is an interaction between the time factor and the group factor, we will conclude that the intervention was effective.

Differential effectiveness: to examine person-level moderators of the intervention effect, a between-person factor is added to the MANOVA. This results in a three-way interaction (person factor × time × group). However, as only categorical person variables can be included in the MANOVA, multivariate multilevel models for fixed occasions will also be performed to allow for continuous variables as moderators (105). The between-person moderators to be included in the analysis of differential effectiveness include gender, age, and baseline distress severity (low, moderate, high).

Conditional effectiveness: to examine whether time-varying characteristics of the situation (e.g., days spent at work) or the individual (e.g., being physically active) might moderate the intervention effect, multivariate multilevel models will be extended with a continuous or categorical day-level variable. To estimate the pure within-person effect of the time-varying moderator, continuous day-level variables will be centered on the person-mean.

Effect sizes: Cohen's d will be calculated as a measure of the effect size, where $d = 0.8$ or more is classified as a large effect, $d = 0.5$–0.8 is classified as a moderate effect, and $d = 0.2$–0.5 is classified as a small effect. According to Feingold (106), the raw score standard deviation of the outcome variable at baseline assessment will be used to compute Cohen's d.

Treatment response: changes in mental health on an individual level will be examined with the widely used Reliable Change Index (RCI) by Jacobson and Truax (107). Participants with an RCI greater than 1.96 will be classified as "responders," and those with an RCI below −1.96 will be classified as "deteriorated." To assess the average number of persons who need to be treated to prevent one additional bad outcome, the number needed-to-treat (NNT) will be calculated. Additionally, the number-needed-to-harm (NNH) will be calculated, indicating the number of responders in the intervention group for one extra person to have a symptom deterioration. To set the benefits of the intervention in relation to its risk, the benefit-risk ratio will be calculated by dividing the NNT through the NNH (108).

Daily life data: we will compute Cox proportional hazards models to investigate daily life behavior as risk and protective factors of mental health. Cox proportional hazards models are a type of survival model that allows for the estimation of the hazard (or risk) of an event of interest given prognostic variables. We will model changes in mental health as measured by K6 as the outcome event (i.e., improved, maintained, and deteriorated), and separate models will be computed for well-being, intentions to seek help, and help-seeking behavior as outcome event. As risk and protective factors, we will include daily life measures. Risk factors include alcohol and substance use, the frequency of daily hassles, low social activity, and low physical activity. Protective factors include coping behavior, social support, and physical activity. Furthermore, the instability or variability of daily symptoms over the 30-day monitoring period will also be examined as a risk factor by computing within-person variances, first-order autocorrelation, the mean square successive differences, and the probability of acute change according to Jahng et al. (109). Discrimination ability (the ability of the model to separate individuals who develop the event from those who do not) will be assessed with the C statistic. Model calibration, that measure how accurately model predictions match overall observed event rates, will be evaluated with a version of the goodness of fit (110).

Internal model validation will be carried out. For all daily life analysis, data from the AA group will be used ($N = 62$).

Access: we will describe access to the intervention in terms of population characteristics (sample representativeness), demographics, clinical characteristics, and sample comorbidities using the appropriate descriptive statistics.

Engagement: to assess participant engagement, we will examine the proportion of study drop-outs and the proportion of enrolled individuals who respond to the outcome assessments at each time point, and the proportion of daily life assessments filled out during the 30-day interval.

Trial Status

The trial is in preparation and recruitment will commence after funding has been obtained, approximately in 2018.

ANTICIPATED RESULTS

This fully mobile RCT will evaluate supportive mental health self-monitoring among smartphone users with psychological distress. Users with moderate to high distress will be oversampled to include all degrees of mental health problems. It compares the intervention toward AAs (self-monitoring without feedback) and a passive control group (no self-monitoring and no intervention). We hypothesize that using the intervention will improve mental health as compared to the control groups, where we expect no significant changes. We will not only test the general effectiveness of the intervention, but also its differential effectiveness (i.e., person-level moderators) and its conditional effectiveness (i.e., time-varying moderators). As the potential risks of using mHealth interventions have not been studied sufficiently, the study will also examine the safety of supportive mental health self-monitoring in regard to detrimental effects on mental health after or during using the application. Finally, the study will provide short-term evidence directly after using the app as well as the long-term sustainability of changes in mental health outcomes. Following current recommendations for evaluating mHealth interventions (100, 101), this study will result in high-quality evidence, allowing for a complete and transparent evaluation of supported self-monitoring on the basis of a smartphone application.

From an epidemiological viewpoint, this study will add important insights into the early development of mental disorders. The existing epidemiological mental health surveys provide good estimates of incidence, prevalence rates, and correlates of mental disorders (111, 112). However, due to their retrospective design, these surveys are limited to a "snapshot" of psychopathology and its correlates. It was found that the time intervals between assessment waves are so long, that there are potentially serious flaws concerning the recall bias (13). Daily life data, as collected during self-monitoring, opens new perspectives for psychiatric epidemiology by capturing the dynamic nature of psychopathology in real-world contexts. Thus, it minimizes the problem of recall bias and maximizes likewise the ecological validity (113). This is especially relevant, considering that mental disorders below clinical thresholds are responsible for a considerable share of the total burden of mental disorders (114), even for more rare mental disorders like psychotic disorders (115). Thus, self-monitoring has the advantage that it is not merely a psychological intervention, but also provides detailed information on the development of mental health over time, related behavior, and the situational context. This information will be used in the proposed study for a comprehensive analysis on risk and protective factors of mental health in daily life.

DISCUSSION

Despite the substantial burden of mental ill-health on the individual and the economy, there is a significant amount of unmet treatment need in the population. Only about 25% of persons with mental health problems currently receive adequate professional help. To address this treatment gap in mental health care, broadly accessible and evidence-based interventions to monitor and support mental health in daily life are needed. Recently, the use of mHealth technology to improve access to psychological treatment has been suggested. Supportive self-monitoring of mental health in daily life could be a particularly promising mHealth approach. However, additional research is needed to establish supportive self-monitoring as a clinical tool to improve population health in the future.

This study aims to develop and evaluate the first mHealth intervention for mental health on the basis of supportive self-monitoring in the general population. This project will benefit from several lessons learned during previous pilot testing of a smartphone application for mental health self-monitoring (39). The pilot test indicated that mental health self-monitoring is feasible even over longer time periods, if self-monitoring is designed toward minimal participant burden. Pilot testing showed that due to the widespread availability of smartphones in the population, the proposed project does not need proprietary devices to deliver the intervention, rather, the intervention will be available to download on the user's own Android device. This enables easy access and low-cost distribution. As reaching the target group of smartphone users with psychological distress will be crucial for the present study, a comprehensive, online- and offline-based recruitment campaign will facilitate inclusion. Additional telephone reminders will minimize drop-out during the trial. Blinded outcome assessments by trained telephone interviewers will be conducted, avoiding confounding bias of the intervention outcomes with self-monitoring data, thus providing high-quality data on intervention effectiveness. Additionally, the present study will use objective usage parameters on interaction and engagement with the app to enhance validity. Overall, the proposed project will not only provide new perspectives for psychiatric epidemiology, it also can contribute substantially to the provision of mental health care in the field of early detection and treatment at low costs.

The study has implications for vulnerability-stress models. Vulnerability-stress models seek to explain the onset and development of mental ill-health as a combination of predisposed vulnerability together with acute stress from life experiences (116). Such models highlight the role of environmental stressors, who are assumed to trigger the onset of mental disorders among vulnerable persons. Environmental stressors include the lack of social support or meaningful activities. Vulnerability includes,

for example, genetic factors, as well as early life experiences that predispose a person to be more susceptible to a mental disorder. A defining characteristic of vulnerability-stress models is the adoption of a dynamic perspective on the development of mental ill-health, including the investigation of causal factors. Researchers who wish to examine this dynamic perspective empirically cannot achieve this with cross-sectional data, but require longitudinal data. In this context, daily life data collected with mobile-based approaches for self-monitoring of mental health can be used to test different hypothesis derived from vulnerability-stress-models.

Analyzing the time course of daily life data from self-monitoring has the advantage, specific hypothesis on the process of development of mental ill-health can be tested. The "Additity hypothesis" within vulnerability-stress models states a straightforward, linear, dose–response relationship between the accumulated effects of stress at a given time and the sum of vulnerability of a person. Thus, the combined effects of stress and vulnerability are assumed to lead to mental disorder. In contrast, the "Ipsative Hypothesis" states an inverse relationship between the two factors. The greater the presence of one factor, the less of the other is needed to facilitate the onset of mental ill-health. As an outcome for vulnerability-stress models, changes in mental health over the 4-week self-monitoring period could be modeled.

Limitations

The proposed study has several limitations. First, short screening scales for mental health will be used (self-reports on the device and assessed by telephone interview), but due to feasibility limitations and to minimize participant burden, no diagnostic interview on mental disorders can be conducted (e.g., according to DSM-V).

Second, as participants will self-select themselves into the study, there is potential selection bias. We cannot exclude the possibility that the participants who enroll in the study have certain characteristics that differentiate them from the target group. This means that the generalizability of results is limited to smartphone users who select themselves into using the intervention. However, quota sampling according to age and gender will ensure that the sample will be representative for the population in regard to these characteristics.

Third, potential low response and loss to follow-up present a challenge for this study. Low response/retention rates would reduce the statistical power and can generate a selection bias which affects the generalization of the results. This risk needs to be carefully considered during designing and planning of the study. We will conduct telephone reminders to enhance response. To prevent systematic low response and follow-up loss among hard-to-reach populations, study staff will carefully monitor recruitment rates according to the sample composition in **Figure 1**: Study flow. Sup-populations showing low response during recruitment will be targeted specifically (e.g., older subjects, male subjects). Using flexible online advertisements, we will place ads that will be shown only to certain sub-populations to enhance response and ensure a representative composition of the sample.

Fourth, potential "gaming" needs to be avoided, which refers to a situation where research participants fraudulently enroll in a study for the purpose of acquiring research payment. Procedures to prevent gaming will include locking the registration procedure in case of participants trying to change submitted answers, availability of study links only for one user/device, and tracking of IP addresses to prevent duplicate enrollment.

Fifth, the event needs to be considered that symptom self-monitoring could have detrimental effects on participants. Appropriate safety measures need to be implemented to counteract participant harm. The study team will consist of a trained staff that can be contacted in the case of a participant experiencing potential detrimental effects. The study team will be available by mail and during telephone hours to provide support, and to forward participants to appropriate mental health-care services.

Conclusion

mHealth could be widely used in the population to improve access to psychological treatment. This project will not only contribute to the psychiatric epidemiology, but will also allow us to demonstrate the effectiveness of a smartphone application as a widely accessible and low-cost supportive mHealth intervention.

ETHICS STATEMENT

Ethics approval will be obtained from Charité—Universitéts medizin Berlin.

AUTHOR CONTRIBUTIONS

TB drafted the manuscript, WR, SH, and OB contributed to the text and critically revised the manuscript. All authors approved the final version of the manuscript.

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SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at http://journal.frontiersin.org/article/10.3389/fpubh.2017.00249/full#supplementary-material.

FIGURE S1 | Mock-up of smartphone app.

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Chapter 5: General Discussion

General Discussion

Mental health has substantial consequences for the quality of life of individuals and the well-being of society, making it a global challenge of the 21st century. The existing mental health care systems offer effective treatment options for those affected by mental ill-health, but a significant amount of unmet treatment need persists in the population. Only about 25% of people with mental health problems currently receive adequate professional help [1]. To address this treatment gap in mental health care, broadly accessible and evidence-based interventions to monitor and support mental health are needed. In this context, the increasing use of digital technology across the population offers an opportunity for the widespread delivery of E-Mental Health through internet- and mobile-based approaches. While E-Mental Health was found to be generally effective for a broad variety of mental health problems [2], there are several areas that must be addressed in this emerging field of research.

This dissertation has presented a series of work on internet- and mobile-based approaches to monitor and support mental health. It contributes to the further integration of E-Mental Health in daily life by aiming to improve early prevention and treatment of mental ill-health with the use of digital technology. As E-Mental Health is a relatively new and innovative field, having only emerged within the past 20 years, its future development depends critically on strengthening its evidence-base in a number of areas. The effectiveness of E-Mental Health as a treatment tool has been shown repeatedly, but there is less evidence on the potential of E-Mental Health for the prevention of mental ill-health. Any further development of E-Mental Health for early prevention should contribute to the sustainability of the mental health care system in the future. With the current fast-paced technological advancements in mobile devices and the Internet, E-Mental Health will also constantly need to develop and evolve in order to meet scientific standards and fulfill its promise to improve the lives of people with mental ill-health.

Summary of Results

In Chapter 2, the results from a pilot study on symptom monitoring using smartphones was presented. 13 patients with bipolar disorder were recruited and asked to use a self-monitoring smartphone application for the duration of 12 months (SIMBA). The application was designed for the self-monitoring of mood, social activity, and physical activity using a combination of daily self-reports and smartphone sensor measurements (GPS, cell tower changes, device activity, calls, SMS). The study outcome was measured using clinical rating scales, which were administered in regular assessment intervals throughout the study period to determine clinical depressive and manic symptoms. This resulted in a dataset of 75 assessment periods for each of the 13 patients. Using multilevel modeling, four separate models for within-person effects, between-person effects, manic symptoms, and depressive symptoms were computed. We hypothesized that indicators of social and physical activity derived from smartphone measurements would be positively associated with manic symptoms and negatively associated with depressive symptoms.

The between-person analysis adopted a static perspective based on levels of smartphone predictors to examine the inter-individual differences in the relationship between smartphone measurements and symptom levels. In this analysis, it was found that the number of telephone calls was positively related to manic symptoms (Beta = 0.48, P = .03). In disagreement with our hypothesis, physical activity as measured by GPS was negatively related to manic symptoms (Beta=-0.37, P<.001). Mood (Beta = -0.56 P < .001) and the number of SMS sent (Beta = -0.17 P < .001) were negatively related to depressive symptoms. The within-person analysis used a dynamic perspective based on changes in smartphone predictors to examine the intra-individual relationship between smartphone measurements and symptom changes. In the within-person analysis, decreases in physical activity as measured by cell tower movements (Beta = -0.11, P = .03) and decreases in SMS sent (Beta = -0.28, P < .001) were related to increases in depressive symptoms. In opposition to our hypothesis, decreased physical activity as measured by cell tower movements (Beta = -0.17, P < .001) was related to an increase in manic symptoms. The stated relationships between smartphone measurements and bipolar disorder symptoms leads to the conclusion that smartphones have the potential to monitor and predict bipolar disorder symptoms. However, a further validation of smartphone-based monitoring in a larger sample is needed.

In Chapter 3, the results from a randomized controlled trial on the effectiveness of an internet-based program for depression were presented. 180 participants with mild to moderate depression and sickness absence were randomized, and 88 completed the post-assessment (attrition rate: 51.1%). Intention-to-treat analysis showed a significant between-group difference in depressive symptoms at post-treatment in favor of the intervention group, corresponding to a moderate effect size (PHQ-9: d = 0.55, CI: 0.25 – 0.85, P < .001, and BDI-II: d = 0.41, CI: 0.11 – 0.70, P = .004). Per-protocol analysis partially supported this result but showed a non-significant effect on one primary outcome (PHQ-9: d = 0.61, CI: 0.15 – 1.07, P = .04, and BDI-II: d = 0.25 CI: -0.18 – 0.65, P = .37). An analysis of clinical significance using the reliable change index revealed that significantly more participants who used the web-based intervention (63%, 63/100) responded to the treatment versus the control group (33%, 27/80) (P < .001). The number needed to treat (NNT) was 4.08. Within both groups, there was a reduction in work absence frequency (Intervention Group: -67.23%, P < .001, Control Group: -82.61%, P < .001), but no statistically significant difference in sickness absence was found between groups (P = .07). It was concluded that the web-based intervention was effective in reducing depressive symptoms among adults with sickness absence. Sickness absence as measured by health insurance records can be used as an outcome of E-Mental Health trials.

Chapter 4 presented a study protocol for a fully mobile-based randomized controlled trial on supported self-monitoring among subjects with psychological distress. It proposed the recruitment of a sample of 495 smartphone users stratified by age, gender, and psychological distress (low, moderate, and high). An over-sampling of moderate to high psychological distress

will be conducted. Over a 4-week period, the intervention group will be compared to a self-monitoring without feedback group and a passive control group. Telephone interviews will be conducted at baseline, post-intervention (after 4 weeks), and 12-week follow-up. The primary outcome will be improvement of mental health. Secondary outcomes will include patient activation, attitudes to and utilization of mental health services, perceived stigma, user satisfaction, engagement, and adherence to the intervention. It was hypothesized that using the intervention will improve mental health compared to the control groups. The proposed study will not only test the general effectiveness of the intervention, but also its differential effectiveness (i.e., person-level moderators) and its conditional effectiveness (i.e., time-varying moderators). This trial will result in high-quality evidence, allowing for a complete and transparent evaluation of a supported self-monitoring intervention delivered through a smartphone application, which can be widely distributed in the population.

Discussion of Goals

Validity of assessments: The first goal of this dissertation was to examine the validity of novel assessment approaches in mental health. The validity of assessment methods is a central requirement for the evaluation of self-monitoring of mental health and its ability to detect early warning signs and to prevent mental illness in real-time and in the real-world [3]. The pilot study presented in Chapter 2 found preliminary evidence on the relationship between smartphone measurements and clinical symptoms. The study was conducted to investigate whether smartphone data can predict impending clinical symptoms in bipolar disorder. Data was collected in 13 patients over the course of 12 months using a newly developed smartphone application that combined daily self-reports and smartphone sensor data (such as GPS and cell tower changes). The hypothesis that indicators of social and physical activity derived from smartphone measurements were positively related to symptom levels and changes of mania and negatively related to symptom levels and changes of depression was partly supported. Some, but not all, smartphone measurements were related to depressive and manic symptoms, and a few smartphone measurements did not support the hypothesis (namely, cell tower movements). Thus, the smartphone application SIMBA is a potentially a valid approach for long-term symptom monitoring. However, self-monitoring on the basis of smartphone tracking warrants careful consideration before it can be implemented in the care of people with mental illness. A further validation of SIMBA would require a larger sample of participants who experience symptoms above clinical thresholds. The proposed study in Chapter 4 is designed to provide a further validation of a similar mobile-based approach for self-monitoring and addresses the methodical limitations of the pilot study. In addition, the E-Mental Health trial shown in Chapter 2 validated a second novel assessment approach, health insurance records. The study found that health insurance records can represent a suitable outcome in E-Mental Health trials.

Effectiveness of interventions: The second goal was to examine the effectiveness of E-Mental Health interventions. The effectiveness of E-Mental Health interventions in improving mental health outcomes has been demonstrated in various studies over the past several years, but no studies have yet targeted subjects on current sick leave from work due to depression. This was addressed in a randomized controlled trial presented in Chapter 3. 180 subjects with mild to moderate depression and sickness absence participated, and the study compared an Internet intervention to a psycho-education control. It was found that both Internet intervention and psycho-education were effective in reducing depression, but the effect was significantly stronger in the Internet intervention group. Thus, the intervention Help-ID was positively evaluated and is currently being distributed to health insurance subscribers in Germany. As it was found by meta-analysis that the effect sizes of internet-based interventions can vary considerably between interventions, future interventions targeted towards specific sub-groups will have to be evaluated separately. The proposed supported self-monitoring intervention presented in Chapter 4 aims at delivering tailored intervention content based on a subject's real-time information and is expected to provide crucial support in daily life situations. Therefore, this study is expected to provide new insights into effectiveness research by examining not only the general effectiveness of an E-Mental Health intervention, but also its differential effectiveness (person-level moderators) and conditional effectiveness (situation-level moderators).

Usability & Engagement: The third goal was to explore the usability of E-Mental Health, specifically the client's engagement with the approaches. User engagement can be examined with subjective ratings of the user experience at post-study or with objective usage parameters collected by the platform or application over the course of the study. The pilot study described in Chapter 2 did not include any measurement of user engagement and therefore does not allow for any formal conclusions in this regard. However, post-study informal interviews conducted by the researchers and the physician who supervised the study did provide an overall positive feedback on the smartphone application. This is consistent with studies showing that among mental health patients, there is substantial interest in using smartphone applications to monitor symptoms [4]. The randomized controlled trial presented in Chapter 3 did not employ objective usage parameters either (e.g., interaction with content on website), but included a post-study questionnaire on user satisfaction. The post-study questionnaire revealed that the majority of participants rated the intervention as either *"very good"* or *"good"*, and satisfaction ratings were significantly higher in the intervention than in the control group. This indicates that an interactive program based on cognitive-behavioral therapy that uses video, audio, and graphics is superior in terms of user experience compared to text-based psycho-education. However, due to the lack of objective usage parameters, no specific conclusions regarding the content and presentation of intervention elements are possible. Therefore, the study protocol presented in Chapter 4 proposes to include a recently developed rating scale on the quality of smartphone applications, which will allow for

the comprehensive evaluation of user experience in the dimensions of engagement, functionality, aesthetics, information quality, and subjective quality (5). In addition, similarly to other recent studies in the field of E-Mental Health, objective usage parameters will be collected on the interactions between the user and the smartphone application. It is important for the field of E-Mental Health to develop standardized instruments for the evaluation of the user experience, and to compare the user experience across different approaches. Existing theories on health service utilization, technology use, and technology adoption [6] could inform the development of E-Mental Health approaches that seek to improve user experience.

Adherence: Fourth, adherence and compliance with E-Mental Health was examined. The extent to which individuals adhere and comply with E-Mental Health content is a major concern, as low adherence may reduce its efficacy. Investigating adherence is also important because the generally lowered adherence in E-Mental Health studies in comparison to traditional mental health care (perhaps through the lack of therapeutic relationships in E-Mental Health) is often cited as an argument against E-Mental Health [7]. The pilot study in Chapter 2 examined participants' response to daily self-ratings of mood over time and found that users completed the majority of prompts (response rate: 55.7%). No decline in the response rate over time was found, indicating that long-term monitoring of mental health on the basis of self-reports is feasible. All of the initial pilot study participants except one completed the study. On the other hand, the internet-based intervention from Chapter 3 showed remarkably high drop-out. From the 180 participants that were randomized, only 88 completed the post-assessment (attrition rate: 51.1%), and 58 completed the follow-up assessment after 24 weeks (attrition rate: 67.7%). Participants were reminded via email in cases of incomplete assessments. It is possible that failure to include telephone reminders lowered adherence to the study protocol, leading to high drop-out. Another reason for the high drop-out could be the relatively longer duration of the program (12 weeks). Similar programs achieved comparable effect sizes with only 8 sessions [8], indicating that the HelpID program could be shortened in length while maintaining its efficacy. Furthermore, therapeutic guidance via email or telephone support was provided upon request only. It is likely that including compulsory weekly support instead of support on request would have increased adherence with the intervention. However, as the amount of requested support was not measured, and no usage parameters on the user's interaction with the intervention content was obtained, no specific conclusions on the reasons for the high drop-out can be drawn. Research on the influence of different guidance formats on adherence with internet-based programs shows that a significant proportion of the inter-individual difference in adherence remains unexplained [9], indicating the need for further research in this area.

Access: The fifth goal was to examine access to mobile- and internet-based approaches. Wide population access represents one of the major promises of E-Mental Health. With the increasing availability of internet access and ownership of computers and mobile devices in the population,

access to E-Mental Health approaches is assumed to be unrestricted by technological barriers among large demographic segments of the population. However, uptake and usage of E-Mental Health after the release of an intervention is generally lower than anticipated during research studies [10]. To investigate access, the randomized controlled trial in Chapter 2 examined the proportion of participants from the total pool of invited insurance members who were screened positively based on the insurance criteria (see Figure 1: Study flow chart). According to the inclusion criteria, invited insurance subscribers included all persons currently on sick leave due to mild to moderate depression during the screening period. Therefore, this pool of insurance subscribers represents the entire potential target group for the internet-based intervention. It was found that from the 3566 insurance subscribers who were invited to participate, 3340 (93%) did not respond. Thus, the response rate in this study was 7%. This low response not only reduced the achieved power of the study, which was lower than calculated, but also raised questions on the reasons for non-participation. It can be speculated that responders were more motivated to use an internet-based intervention or had higher computer literacy compared to non-responders. Unfortunately, the reasons for declining participation remain unknown, as a non-responder questionnaire was not included in the study, and health insurance records of non-responders could not be analyzed due to the lack of informed consent. Future studies should include a non-responder questionnaire, and if possible after considering data privacy statutes, should integrate the health insurance records of non-responders, which could serve as a baseline comparison group for the investigation of access.

Epidemiology: Sixth, the contribution of E-Mental Health to the epidemiology of mental disorders was examined. Existing epidemiological mental health surveys provide good estimates of incidence, prevalence, and correlates of mental disorders [11, 12]. However, due to their retrospective designs, these surveys are limited to a "snapshot" of psychopathology and its correlates. It was found that the time intervals between assessment waves are too long, such that there are potentially serious flaws regarding recall bias [13]. Mobile-based approaches are capable of collecting detailed longitudinal information on daily life experiences and behaviors in real-time, allowing for the possibility of embedding this information into social contexts. Therefore, daily life data opens new perspectives for psychiatric epidemiology by capturing the dynamic nature of psychopathology in real-world situations [14]. Daily life data minimizes the problem of recall bias and maximizes ecological validity [15]. The study presented in Chapter 4 is designed to investigate the ability of a mobile-based approach to identify risk and protective factors for mental ill-health in daily life. For this purpose, the data from 165 participants in the ambulatory assessment group (who will use a self-monitoring smartphone application over the course of 4 weeks) will be employed. Mood and mood variability, daily hassles and daily uplifts, poor sleep, physical and social activity, as well as social contexts (locations) will be included as risk and protective factors of mental health. Cox proportional hazards models will be computed to estimate

the hazard (or risk) of a change in mental health outcomes. The identification of daily life risk and protective factors of mental health will provide an epidemiological basis for targeting such factors, and will allow for new insights into modifiable mental health risks.

Theoretical Implications: The seventh goal was to explore the theoretical implications of internet- and mobile-based approaches for vulnerability-stress models. Vulnerability-stress models seek to explain the onset and development of mental ill-health as a combination of predisposed vulnerability combined with acute stress from life experiences [16]. Such models highlight the role of environmental stressors, which are likely to trigger the onset of mental disorders among the vulnerable. Environmental stressors include lack of social support or meaningful activities. Vulnerability can include genetic factors as well as early life experiences that predispose a person to be more susceptible to mental disorders. A defining characteristic of vulnerability-stress models is the adoption of a dynamic perspective on the development of mental ill-health, including investigation into causal factors. Researchers who wish to examine this dynamic perspective empirically cannot achieve this with cross-sectional data, but instead require longitudinal data. In this context, daily life data collected through mobile-based approaches for self-monitoring mental health can be used to test different hypotheses derived from vulnerability-stress models.

The pilot study presented in Chapter 2 shows preliminary evidence that a person's interaction with his or her environment temporarily precedes upcoming changes in the depressive and manic symptoms associated with bipolar disorder. In the pilot study, a dynamic perspective on the development of mental illness was adopted by analyzing the within-person effects of changes in smartphone measurements of social and physical activity on upcoming changes in depression or mania. It was shown that some, but not all, smartphone measurements were related to the level and change of bipolar disorder symptoms. A methodological advancement on the pilot study may separate within-effects and between-effect in the analysis of the predictors of symptom development [17]. Within-effects and between-effect as measures of central illness components could represent a methodological advancement that allows for the testing of the accumulative causal stress hypothesis from vulnerability-stress models.

The study protocol presented in Chapter 4 proposes to use these methodological advancements to test more specific hypotheses on the development of mental ill-health. The outcome will be modeled by computing changes in mental health over the 4 week self-monitoring period. Distinct hypotheses from vulnerability-stress models can be tested. The "*Additivity hypothesis*" within vulnerability-stress models states that a straightforward, linear, dose-response relationship exists between the accumulated effects of stress at a given time and the total vulnerability a person exhibits. Thus, the combined effects of stress and vulnerability may result in mental disorders. In contrast, the "*Ipsative Hypothesis*" states that an inverse relationship exists between the two factors. The greater the presence of one factor, the lesser of the other is required to facilitate the

onset of mental ill-health, and the effects of vulnerability or stress can be compensated by the other.

Strengths and limitations

The strength of this dissertation was that prevention and treatment of mental ill-health with E-Mental Health was thoroughly examined in a series of high-quality studies. The studies were highly innovative in regards to testing the feasibility of new E-Mental Health approaches and providing new evidence for the effectiveness of E-Mental Health interventions. The pilot study in Chapter 2 is among the first studies that report results on symptom self-monitoring in patients with bipolar disorder, and the first to conduct a long-term self-monitoring study over a 12-month duration. The randomized controlled trial in Chapter 3 provides the first evaluation of the Help-ID program, which is crucial for the ongoing dissemination of this program in Germany. The target group of persons with sickness absence due to mild to moderate depression was not previously addressed in internet-based interventions. Methodologically, the dissertation used advanced statistical methods. For example, multilevel modeling for the analysis of longitudinal data was used to separate within-person and between-person effects in Chapter 2. The randomized controlled trial in Chapter 3 was analyzed according to the latest methodological recommendations for the evaluation of E-Health trials, including intention-to-treat analysis and multiple imputation to handle missing values [18]. The study protocol in Chapter 4 proposes to further advance this research by examining not only general effectiveness of a mobile-based intervention, but also its differential and conditional effectiveness respectively to person-level and time-varying moderators of the intervention effect.

There were a number of limitations to the studies presented in this dissertation. The pilot study in Chapter 2 did not include a control group of healthy subjects or a control group of non-monitored subjects, which would enhance the validity of the results and would provide insights into the patterns of physical and social activity of patients with bipolar disorder. The generalizability of the results was limited by the small sample size and the low prevalence of manic and depressive symptoms in the sample. Thus, a further validation of the results in a larger sample of participants who experience more severe manic and depressive symptoms is necessary. The RCT in Chapter 3 achieved lower statistical power than initially calculated due to the low response among insurance members during recruitment. There was also a relatively high drop-out rate in this study, which introduced a risk for bias in this study. However, statistical analysis of both the total sample (intention-to-treat analysis) and the subset of participants who completed all assessments (per-protocol analysis) was performed to compare the influence of drop-out on the intervention effect. Finally, usage parameters were not collected in the pilot study and the RCT. Usage parameter data could provide valuable insights into how users interact with E-Mental Health content. The study protocol in Chapter 4 proposes to address these limitations by recruiting a sample of participants covering all degrees of mental health problems using online recruitment

channels, thus achieving sufficient power for the analysis of effectiveness, and by collecting usage parameters.

Outlook and future research

With the high number of individuals in the population who remain untreated for mental health problems, there is an ongoing need for widely available, evidence-based interventions to monitor and support mental health. E-Mental Health is expected to make significant contributions to improving the capacity of the health care system due to its flexibility and scalability, making it more likely that individuals in need for support are reached earlier. To evolve further, an important agenda for E-Mental Health is its integration into existing mental health care systems. This entails the development of strategies for combining E-Mental Health with the provision of services in regular care settings. For example, in stepped care approaches [19], E-Mental Health could serve the role of providing initial, low-intensity treatment, while high-intensity interventions, such as face-to-face therapy, would be reserved for more serious or complex conditions. E-Mental Health approaches for the self-monitoring of mental health, as presented in this dissertation, could serve as the first step for self-referred entry into the care system. In the case of England, the experience of implementing E-Mental Health in stepped care approaches was met with positive responses [20]. However, in many countries, including Germany, legal barriers exist for the unsupervised provision of internet-based therapy and the negative views that some providers hold towards the use of the Internet in psychotherapy need to be overcome [21, 22]. It can be expected that with the accumulating research on the effectiveness of E-Mental Health and other areas presented in this dissertation, the process of dissemination of E-Mental Health in the health care system will continue to ensure better outcomes to those affected by mental ill-health.

Abbreviations

BDI-II: Beck's Depression Inventory II
GPS: Global Positioning System
PHQ-9: Patient Health Questionnaire 9
SIMBA: Social Information Monitoring for Patients with Bipolar Affective Disorder
RCT: Randomized Controlled Trial

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Appendix

Information about the publications

Chapter 2: Using Smartphones to Monitor Bipolar Disorder Symptoms. A Pilot Study

Authors:	Till Beiwinkel, Sally Kindermann, Andras Maier, Christoper Kerl, Jörn Moock, Guido Barbian, Wulf Rössler
Author status:	First Author
Publication status:	Published (06.01.2016)
Author contributions:	TB analyzed the data, TB and SK wrote the manuscript, AM and CK contributed analysis tools, JM, WR, and GB obtained access to the dataset, and all authors contributed to the text and critically revised the manuscript. All authors approved the final version of the manuscript.
Reference:	Beiwinkel T, Kindermann S, Maier A, Kerl C, Moock J, Barbian G, Rössler W: Using Smartphones to Monitor Bipolar Disorder Symptoms: A Pilot Study. JMIR Mental Health. 2016;3(1):e2. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4720836/

Chapter 3: Effectiveness of a web-based intervention in reducing mild to moderate depression among adults with sickness absence. A randomized controlled trial

Authors:	Till Beiwinkel, Tabea Eißing, Nils-Torge Telle, Elisabeth Siegmund-Schultze, Wulf Rössler
Author status:	First Author
Publication status:	Published (15.06.2017)
Author contributions:	
Reference:	Beiwinkel T, Eißing T, Telle NT, Siegmund-Schultze E, Rössler W. Effectiveness of a Web-Based Intervention in Reducing Depression and Sickness Absence: Randomized Controlled Trial. J Med Internet

Res 2017;19(6):e213.
https://www.ncbi.nlm.nih.gov/pubmed/28619701

Chapter 4: Supportive mental health self-monitoring among smartphones users with psychological distress: Protocol for a fully mobile randomized controlled trial

Authors:	Till Beiwinkel, Stefan Hey, Olaf Bock, Wulf Rössler
Author status:	First Author
Publication status:	Published (21.09.2017)
Author contributions:	TB drafted the manuscript, WR, SH, and OB contributed to the text and critically revised the manuscript. All authors approved the final version of the manuscript.
Reference:	Beiwinkel T, Hey S, Bock O, Rössler W. Supportive mental health self-monitoring among smartphone users with psychological distress: Protocol for a fully mobile randomized controlled trial. Frontiers in Public Health (2017) 5:249.

About the Author

Till Beiwinkel was born in Mannheim and grew up in Heppenheim an der Bergstraße. His background is in Sociology. He graduated from the University of Mannheim with a B.A. in 2009 and with an M.A. in 2012. He completed part of his graduate studies at Indiana University, USA with a focus on medical sociology and public health. After graduation, he worked as a researcher in the Integrated Care division at Leuphana University's Innovation Incubator and in a joint research project with Hebrew University, Israel, funded by Volkswagen Foundation. In 2015, he started his PhD on the topic of E-Mental Health. His work aims at bridging innovative research on the Internet and mobile technology with mental health care in order to improve the lives of those affected by mental health problems. He has presented at international conferences and has published in peer-reviewed journals. In 2016, he was awarded with a prize for young scientists from the Faculty of Business & Economics for an excellent conference presentation.

Curriculum Vitae

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Aug 2015 – Juli 2017 Leuphana Universität Lüneburg, wissenschaftlicher Mitarbeiter „Niedersächsisch-israelisches Gemeinschaftsprojekt“

- Planung und Durchführung der international vergleichenden Studie „Family Stigma“ zu Stigmatisierung und Hilfesuchen bei Eltern eines Kindes mit geistiger Behinderung
- Koordination mit israelischen Projektpartnern

Okt 2012 – Mai 2015 Leuphana Universität Lüneburg, wissenschaftlicher Mitarbeiter Kompetenztandem „Vernetzte Versorgung - Grundlagen und Evaluierung der Versorgung psychisch erkrankter Menschen“

- Evaluation eines onlinebasierten Gesundheitstrainings
- Pilotstudie zur Sekundärprävention bipolarer Störungen mit einer Smartphone Applikationen
- Studienberatung in Bachelor-Studiengängen

Aug 2011 – Dez 2011 Universität Mannheim, wissenschaftliche Hilfskraft „Pairfam - nationales Beziehungs- und Familienpanel“

- Datenbankmanagement Panelstudie

Gutachtertätigkeiten

Seit April 2014 Frontiers in Public Health, Review Editor

Seit Januar 2017 Journal of Medical Internet Research, Reviewer

Praktische Erfahrungen

Jan 2012 – Juni 2012 BASF SE Ludwigshafen, Praktikum „Center of Expertise Talent Management“

- Personal- und Führungskräfteentwicklung
- Evaluation von Personalentwicklungsinstrumenten

März 2007 – Aug 2010 ISB gGmbH Heidelberg, studentische Aushilfe

- Pflegeassistenz

März 2007 – Mai 2007 Europabüro der Stadt Mannheim, Praktikum

- Bürgerberatung und Öffentlichkeitsarbeit

Aug 2005 – Juli 2006 Behindertenhilfe Bergstraße, Zivildienst

- Betreuung geistig- und körperlich eingeschränkter Menschen

Preise und Auszeichnungen

Juni 2010 DAAD Stipendium, vollfinanziertes 9-monatiges Austauschprogramm an der Indiana University, USA

November 2016 Forschungspreis für Nachwuchswissenschaftler der Fakultät Wirtschaftswissenschaften der Universität Lüneburg in der Kategorie „Hervorragende Vorträge auf offen ausgeschriebenen Tagungen“

Publikationen und Vorträge

Artikel in wissenschaftlichen Fachzeitschriften

- **Beiwinkel T**, Eißing T, Telle NT, Siegmund-Schultze E, Rössler W. Effectiveness of a Web-Based Intervention in Reducing Depression and Sickness Absence: Randomized Controlled Trial. J Med Internet Res 2017;19(6):e213 http://www.jmir.org/2017/6/e213/
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- **Beiwinkel T**, Kakarot N: Online-Trainings am Innovations-Inkubator der Leuphana Universität Lüneburg. 9. Nationale Branchenkonferenz Gesundheitswirtschaft 2013

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- **Beiwinkel T**, Eissing T, Telle N-T, Rössler W. Effectiveness of an internet intervention for adults with depression and incapacity to work: a randomized controlled trial. 4th Conference of the European Society for Research on Internet Interventions (ESRII); September 22nd - 23rd 2016, Bergen, Norway.
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