



ANNASOFIA MARTIKKALA, ERKKI ISOMETSÄ

SMARTPHONE-BASED MONITORING OF MOOD DISORDERS: A REVIEW

ABSTRACT

The literature on smartphone-based monitoring in psychiatry is expanding. Data collection by utilizing smartphones can be divided into: (a) active monitoring, requiring active input from the patient, and (b) automatically generated passive monitoring. Numerous studies have investigated the potential of both active and passive monitoring in providing insights into mood disorder psychopathology. Furthermore, several intervention studies have been conducted in order to examine the utility of smartphone-based monitoring in the treatment of mood disorders. This literature review aims to provide an overview of the recent studies on using smartphones for patient monitoring among people suffering from mood disorders, and to discuss the current concerns and risks in the field. Smartphones have been demonstrated to be a valid and potentially useful tool for active monitoring of mood disorder patients. However, further research is needed to establish the validity of automatically generated passive data and effectiveness of smartphone-based interventions.

KEY WORDS: MOOD DISORDERS, MAJOR DEPRESSIVE DISORDER, BIPOLAR DISORDER, SMARTPHONES, MOBILE PHONES, MOBILE MONITORING

INTRODUCTION

NEED OF OBJECTIVE MARKERS FOR MOOD DISORDERS

Mood disorders are the most important mental disorders in terms of their public health impact, and among the leading causes of morbidity and disability worldwide (1). In Finland, over 200,000 subjects suffer from MDD annually, resulting in over 30,000 periods of sickness absence, 3,900 new disability pensions, about 500 completed suicides and annual direct costs of work disability of over 570 million euros in 2018. A significant minority of depressive patients (about 10-15% in psychiatric care) suffer from bipolar disorder, an illness involving comparable or even more marked risks for suicide and disability (2). Mood disorders are recurrent, long-term illnesses with a timescale of treatment usually lasting years.

No objective diagnostic biomarker or biological test currently exists for psychiatric diagnoses or alternating illness states. Clinical evaluations are based on interviews, and therefore, ultimately on the interviewee's ability to reflect and remember subjective experience. However, retrospective recall of variations in affective state is inaccurate, particularly if variations take place within a temporal frame of hours or days. Therefore, a great need exists for reliable objective markers of clinical state for purposes of differential diagnosis, follow-up of illness course and evaluation of treatment effectiveness.

Internet-based online mood charting tools have been available for two decades. More recent developments have been based on mobile technology and actigraphy (3). However, although thousands of applications for mental health are already available in the marketplace, very few of the applications have been systematically validated against clinical data (4). Furthermore, there is also great potential for medical harm related to poor quality of information, or self-diagnoses and uncritical self-treatment (4,5). It is vital, that responsible clinical researchers validate such measures.

REAL-TIME MONITORING IN PSYCHIATRY

One of the methods used in psychology and psychiatry to investigate patient symptoms and behaviours in real time is called Experience Sampling Method (ESM) or, alternatively, Ecological Momentary Assessment (EMA) (6,7). The core idea of ESM is to collect information regarding the patient's existing symptoms or behaviour in their natural environment by asking the patient to complete multiple questionnaires during the day. Before the ubiquitous presence of

smartphones, ESM studies relied on different kinds of portable devices, such as pagers and programmed pocket calculators (6). ESM has been used in research for decades, and it has proven its feasibility in providing information regarding dynamic psychological processes such as mood and emotions. ESM also gives the opportunity for clinicians to examine the characteristics of the patient's environment (e.g. the time of the day for a specific event) and thus, offer context to the patient's situation and reveal links between changes in patient's state and the events of the surrounding world (6).

Mood disorders are often associated with disturbances in sleep patterns, with many patients reporting problems such as difficulties in falling asleep or staying asleep. Polysomnography (PSG), where eye movement, brain activity and muscle activity are recorded, is considered to be the "gold standard" for monitoring sleep (8,9). The downside of PSG is that it is carried out in a laboratory environment, which makes carrying out recordings over multiple nights both laborious as well as expensive. This has created a substantial need for more practical options to assess patient sleep, which in turn has led to researchers utilizing accelerometers/actigraphy for the purpose (10). These wearable physical activity monitors have been used in several studies to assess patient movement and motor activity, and thus provide information regarding both patient sleep patterns and daytime physical activity (10,11).

As smartphones have become a fundamental part of modern society and an omnipresent object people use on a daily basis, they have also become a novel way for psychiatry to receive a nearly constant longitudinal stream of data about the everyday life of a patient (12). The term "digital phenotyping" is defined as "moment-by-moment quantification of the individual-level human phenotype in situ using data from smartphones and other personal digital devices" (13). The data gathered by smartphones can be categorized under two main labels: passive and active data. Active data refers to data captured via surveys and questionnaires and thus requires active input from the patient. Correspondingly, passive data refers to the data collected without any active input from the patient. Passive data is exclusively collected by using various sensors (e.g. GPS and accelerometer) embedded into smartphones.

SEARCH STRATEGY

A systematic literature search was conducted in April 2020 using the Ovid Medline database. The objective of this

literature review is to provide an overview of the recent studies regarding smartphone-based monitoring of mood disorders. Therefore, the literature search was limited to articles published between the beginning of 2018 and the present. The following search terms were used to identify studies related to mobile monitoring and smartphones: 'mobile monitoring' OR 'mobile phones' OR 'smartphones' OR 'portable sensors'. To identify studies related to specific mental illnesses, the following keywords were used: 'mood disorder' OR 'major depressive disorder' OR 'bipolar disorder'. The results from these two search steps were then combined using the Boolean operator AND. Filters were applied to restrict the search to only articles that were in English and available in full. This literature search resulted in 38 papers, out of which letters and comments were excluded. A total of 30 abstracts were screened by the first author and 23 studies selected based on their relevance to the topic. References were reviewed to identify additional studies of importance and manual searches were conducted to include suitable studies of specific topics. A total of 54 articles were included in this literature review.

SMARTPHONE USE AND ATTITUDES TOWARDS APPS AMONG MOOD DISORDER PATIENTS

SMARTPHONE AND MENTAL HEALTH APP USAGE

Several studies have been conducted to map the use and attitudes towards mental health applications among people suffering from mental disorders.

The proportion of mental health service users that own a smartphone has risen in recent years (14). According to estimates, the development has now reached a point where smartphones are as common among people who suffer from mental illness as among the general population overall (15). However, the popularity of smartphones does not seem to translate into high rates of downloaded mental health apps. In addition, research suggests that many of those who install a mental health app never start using it. This has resulted in even lower rates of mental health app usage (14).

PATIENT ENGAGEMENT IN MOOD OR SYMPTOM MONITORING

According to a study published in 2019, the most important reason why patients fail to accurately monitor their symptoms, even though they have agreed to do so, is forgetfulness (16). Therefore, the ubiquity of smartphones and the possibility to add notifications may make adhering

to smartphone-based monitoring easier than committing to using other technological tools such as wearable devices. However, the subjective perception of the patients seems to be that wearable devices require less effort than active monitoring based on a smartphone app (16).

Another recent study found that although the participants were actively completing mood and symptom measures at the beginning of the study, the discontinuation rate was high after some weeks (17).

THE IMPACT OF ACTIVE MONITORING ON MOOD

It is yet to be discovered whether app-based mood or symptom active monitoring has an impact – positive or negative – on patient mood itself. Several studies have found that participants felt that monitoring symptoms or mood via smartphone app was useful and gave them new insight into their illness (16,17). However, electronic monitoring appears not to improve patient mood, and the possibility of daily active monitoring even reinforcing chronic depression cannot be excluded (18,19). One possible reason for this phenomenon could be that some depressed participants are dispirited by having to actively engage in monitoring (16). It also seems possible that in some cases active monitoring reinforces paranoid thinking in manic states (20). This highlights the importance of adding an option that allows the deactivation of certain features, such as the movement pattern analysis via GPS (20).

ATTITUDES TOWARDS MENTAL HEALTH APPS AND MONITORING

Several studies have mapped the concerns patients raise when asked about the use of mental health apps. The findings suggest that the key concerns are privacy and security (14,15,17). Some participants also reported that it was difficult to understand the meaning of the monitoring despite being given information about the app. This highlights the need for sufficiently educating patients about the applications they will be using (17).

In a recent study (14), application type was found to have an impact on how comfortable the patients felt using the application. The participants found using the appointment reminder apps most comfortable. In contrast, using applications with passive tracking features utilizing the phone's sensors such as the GPS were found the least comfortable (14).

Comments received from the participants in several studies revealed that the attitude towards care manager

involvement and reviewing the submitted data with a clinician was primarily positive (16,17). Getting feedback about their mood or symptoms and seeing their data in a visualized format were also seen as positive features (20).

Overall, feedback collected from patients regarding use of mental health apps seems to reveal them finding both positive and negative aspects in their use (17,20). For this reason, it may be essential to allow the patients to personalize use of the apps.

ACTIVE MONITORING: ELECTRONIC SELF-REPORTING

While EMA (Ecological Momentary Assessment or Experience Sampling Method, ESM) has already been a commonly used tool in psychiatry for decades, the rapid development of technology and current ubiquity of smartphones has made self-reporting of symptoms substantially more convenient. Importantly, unlike their predecessors, smartphones do not merely record patient data but also allow the patient to receive applicable communications or feedback.

In the early days of the smartphone, self-reporting of symptoms was mostly conducted via text messages or website interfaces. In recent years, researchers have also started to utilize mobile applications as they also allow the passive collection of background data (21). This is indeed the core difference between ESM and digital phenotyping: instead of merely sending out questionnaires, the aim of digital phenotyping is to assemble and analyse different kinds of data in order to map patient experience as well as how they interact with other people and their environment (13). In other words, data collected by active monitoring can be analysed together with data collected by passive monitoring, leading to observations and insight that would have been unattainable without one or the other.

A 2019 study, for example, utilized mobile phones to conduct questionnaires while simultaneously gathering additional data related to the process of answering itself (22). The basis of this study was a self-schema model of depression and a hypothesis according to which individuals would answer to schema-compatible information more quickly than schema-incompatible information. The participants were asked to complete questionnaires on their mobile phone while the phone also recorded the time interval between the presentation of a question and answering it. The study found preliminary evidence that individuals whose depression was

not severe enough to use a negative self-schema tended to be slower in making self-referent evaluation on experienced depressive symptoms, compared to the severely depressed and non-depressed participants. According to the study, these findings illustrate the potential of answering time to depressive symptom items as an implicit self-schema indicator for depression and reveal the potential of mobile app-based depression assessment (22).

PASSIVE MONITORING: COLLECTING OBJECTIVE BEHAVIOURAL DATA

Utilizing smartphones to passively collect objective data about the daily life of patients could enable continuous assessment of social and behavioural manifestations relevant to psychiatric illnesses and mental well-being. These manifestations can be detected through a variety of signals, including but not limited to, location, word sentiment, voice tone, social and physical activity (23). Examples of smartphone embedded sensors used in five individual studies are presented in [Table 1](#).

Table 1. Examples of smartphone embedded sensor use in passive monitoring from five different studies

Sensor	Monitored feature	Examples of recorded information
GPS	Location of the smartphone	Distance traveled (25-27) Circadian movement (regularity in 24-hour rhythm) (26) Normalized entropy (mobility between favourite locations) (26) Location variance (GPS mobility independent of location) (26)
Accelerometer	Significant phone motion	Device activity (25) Physical activity levels (27-29) Stationary time (used to estimate sleep duration) (27)
Call and SMS logs	The number and duration of incoming/outgoing calls/text messages	The amount of social communication (25)
Screen usage	Monitor screen status	Phone usage frequency and duration (26)
Light sensor	Ambient light	Ambient darkness (used to estimate sleep duration) (27)
Microphone	Ambient sound	Number and duration of conversations, how much an individual speaks within a conversation, speaking rate and variations in pitch (29) Speech duration (27) Ambient silence (used to estimate sleep duration) (27)

Source: This table is based on information presented in (23,24). The five studies these sources refer to have been presented in this table with references (25-29)

As the interest in passive monitoring has increased in recent years, consequently various systematic reviews have been conducted with an aim to summarize the published research in this field. A systematic review in 2018 (24) covered 35 papers. Of these, five were related to bipolar disorder, five to depression and three to schizophrenia, making mental health the most popular application domain for studies utilizing smartphones for passive monitoring. The most used sensors in all of the 35 publications were GPS, microphone, accelerometer and light sensor. It was also a common strategy to combine several sensors. Many of the reviewed publications regarding mental health demonstrated the usefulness of passive monitoring. However, while the number of participants in most papers was adequate to examine feasibility, it was not sufficient to determine clinical value. Some of the most common concerns mentioned in the reviewed studies were privacy issues, which were discussed in 20 publications (24).

Another systematic review in 2019 reviewed eighteen papers, discussing the usage of geolocation data in schizophrenia and bipolar disorder (30). According to the review, the most used sensor to assess geolocation was smartphone embedded GPS. Other methods used for assessing geolocation were, for example, Wi-Fi and the GSM network. The reviewed publications aimed to extract different *digital biomarkers* from geolocation data and examine various themes regarding geolocation. One example of such a theme was mobility, which means assessing patterns of movement on the map without considering the meaning of any specific location. Mobility was recorded based on digital biomarkers such as *distance travelled* and *number of changes in GSM cell IDs* (a GSM cell ID refers to a specific transceiver station within the GSM network). Some other studies included in the review aimed to extract information by analysing locations where the subject stops during the day by using biomarkers such as *number of locations visited*. *Location entropy* (a

metric for measuring the popularity of various locations) was the most popular digital biomarker for assessing the routine in a subject's daily life. One publication in the review aimed to identify different kinds of activities (e.g. sports, social activities) from the data. Numerous papers collected other information, such as self-evaluation of mood or symptoms in addition to the geolocation data. Most interestingly, several of these studies found associations between geolocation data and characteristics of serious mental illnesses (e.g. time spent outside versus self-reported mood). However, it is worth noting that the duration of many of these studies was short and the sample sizes fairly small. Therefore, these findings have to be interpreted with caution (30).

The current status of smartphone-based passive monitoring in bipolar disorder has been systematically reviewed (31). As the review pointed out, utilizing smartphones to automatically gather objective data offers a way to assess interesting behavioural activities without being intrusive or tiring out the patients. According to the review, the findings from several recent studies suggest that passively gathered smartphone data might qualify as an objective marker for illness states of bipolar disorder. Examples of these studies and their findings are presented in [Table 2](#).

Table 2. Examples of the studies investigating objective smartphone data and clinically assessed symptoms among patients with bipolar disorder

The title of the study	Study characteristics	Examples of the results regarding objective monitoring
Using Smartphones to Monitor Bipolar Disorder Symptoms: A Pilot Study (25)	Participants: 13 patients with bipolar disorder Study length: 12 months	<ul style="list-style-type: none"> An increase in clinical depressive symptoms was predicted by a decline in social communication (i.e. outgoing text messages: $\beta = -.28$, $P < .001$) and a decline in physical activity as measured by the smartphone (i.e. cell tower movements: $\beta = -.11$, $P = .03$) Higher overall levels of clinical manic symptoms were predicted by lower physical activity on the smartphone (i.e. 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 ($\beta = -.17$, $P < .001$)
Smartphone data as objective measures of bipolar disorder symptoms (32)	Participants: 17 patients with bipolar disorder Study length: 3 months	<ul style="list-style-type: none"> In the unadjusted model there was a significant correlation between lowered number of changes in cell tower ID per day and higher score on HDRS-17 ($B = -0.48$, 95% CI: -0.90; -0.070, $p = 0.020$), suggesting that for every 10 points higher score on HDRS-17 patients changed 4.8 times less between cell towers *
Smartphone data as an electronic biomarker of illness activity in bipolar disorder (33)	Participants: 61 patients with bipolar disorder Study length: 6 months	<ul style="list-style-type: none"> There was a significant positive correlation between the duration of incoming calls/day and scores on the HDRS 17 in both the unadjusted model and the model adjusted for age and sex (unadjusted model $B = 19.96$, 95% CI: 4.12–35.80, $p = 0.014$; adjusted model $B = 17.15$, 95% CI: 1.00–33.30, $p = 0.037$), indicating that for every score that increased 10 points on the HDRS 17 in the adjusted models there was an increase in the duration of incoming calls/day of 171.5 (10.0; 333.0) seconds There was a significant positive correlation between the duration of incoming calls/day and scores on the YMRS in both the unadjusted model and the model adjusted for age and sex (unadjusted model $B = 28.54$, 95% CI: 5.17–51.90, $p = 0.017$; adjusted model $B = 30.38$, 95% CI: 7.04–53.71, $p = 0.011$), indicating that for every score that increased 10 points on the YMRS in the adjusted models there was an increase in the duration of incoming calls/day of 303.8 (70.4; 537.1) seconds
Voice analysis as an objective state marker in bipolar disorder (34)	Participants: 28 outpatients with bipolar disorder Study length: 12 weeks	<ul style="list-style-type: none"> Voice features were found to be more accurate, sensitive and specific in the classification of manic or mixed states with an area under the curve (AUC) = 0.89 compared with an AUC = 0.78 for the classification of depressive states
Ecologically valid long-term mood monitoring of individuals with bipolar disorder using speech (35)	Participants: 6 patients with bipolar disorder Study length: participants were enrolled for 6 months to a year	<ul style="list-style-type: none"> The results demonstrate that we are able to detect the mood state of individuals for calls recorded during the clinical interactions. We obtain an average AUC of 0.81 ± 0.17 for hypomania and an average AUC of 0.67 ± 0.18 for depression across all participants

Source: This table is based on information presented in (25) (32-35)

*HDRS-17 = Hamilton Depression Rating Scale 17-items

**YMRS = Young Mania Rating Scale

However, despite these promising findings, Faurholt-Jepsen et al. (31) pointed out that generally speaking, the studies within the field of smartphone-based objective monitoring of patients with bipolar disorder still have various shortcomings. For example, the existing literature included mainly pilot studies, sample sizes were generally small, monitoring periods were short and the studies mostly included only participants with mild symptoms. Only very few of the studies addressed confounding factors in their analyses, which poses a significant risk of bias and numerous methodological and clinical challenges. According to Faurholt-Jepsen et al., the existing literature does not allow to make conclusions regarding which elements of smartphone-based objective data have the most significant correlation with manic and depressive symptoms (31).

THE POTENTIAL OF MOBILE MONITORING IN EVALUATION OF MOOD DISORDER PHENOMENOLOGY

DETECTING THE VARIABILITY OF SYMPTOMS

Smartphones have been found to be a valid tool for detecting daily symptoms. For example, Faurholt-Jepsen et al. found that smartphone-based active monitoring of the symptoms of patients suffering from bipolar disorder (e.g. anxiety) accurately reflected the clinical assessments (36).

Fast-paced, real-time evaluation of affect offers an opportunity to study the temporal dynamics of emotional experiences and, thus, may lead to an improved understanding of the mood disorder phenomenology. A systematic review published in 2014 suggested that using EMA techniques would be the most effective way to understand the time-dependent nature of affective instability (37). When it comes to mood disorders, affective instability is clinically important as it is seen as a significant predictor of transition to bipolar disorder in the future, and it is also frequently present in depression. Another example of a mood disorder-related oscillating phenomenon that could possibly be investigated by utilizing smartphone-based EMA is suicidal ideation (38,39). The preliminary data from an ongoing study demonstrates the feasibility of smartphone-based EMA methodology in investigating suicidal ideation, suggesting that EMA can detect the oscillation of suicidal ideation over a period of time and therefore illustrate how the phenomenon is dynamic in nature. The preliminary findings would be particularly interesting if the variability of suicidal ideation could be associated with the severity of suicidality and depression. However, the study

was unable to find such statistically significant associations, meaning more research is needed to elucidate the matter (38).

Utilizing electronic self-monitoring to examine within-person variability of symptoms related to mood disorders might also reveal how patients with mood disorders differ from healthy individuals, and from patients suffering from different mental disorders. A 2019 study found that participants diagnosed with bipolar disorder had a significantly elevated within-person variability of specific symptoms (e.g. mood and energy levels) compared to healthy controls, emphasizing further the feasibility of EMA techniques in capturing within-subject symptom variation over time (40). Another study from 2018 demonstrated, based on data collected via daily mobile monitoring, that variation in both mood and irritability is greater among people suffering from borderline personality disorder compared to patients suffering from bipolar disorder (41).

The data gathered by utilizing smartphone sensors may lead to the development of clinically useful markers that can be used to refine diagnostic processes, evaluate treatment effectiveness and improve monitoring of illness course (42). Using digital phenotyping as a diagnostic biomarker could help prevent the frequent, long time lag between mood disorder onset and diagnosis. Additionally, smartphone-based monitoring could possibly be used to investigate the inter-individual heterogeneity of mood disorders and help identify new ways to distinguish disorders that overlap in symptomatology (43). For example, mobile phones have been used to assess the association between specific dynamics of affect and individual levels of depression or anxiety. According to a study from 2019, the great instability of affect, both negative and positive, was associated with trait anxiety, whereas risk for depression was more associated with greater mean and inertia of negative affect in a non-clinical sample. However, due to the limitations of this study and lack of participants diagnosed with depression or anxiety, these results should be treated with some caution. Nevertheless, the findings demonstrate the feasibility of electronic self-monitoring in assessing temporal affective dynamics and getting valuable information about the psychopathology of mood disorders (43).

ASSESSING THE ASSOCIATIONS BETWEEN SYMPTOMS AND OUTCOMES

As mobile applications allow the examination of multiple different symptoms, events or outcomes simultaneously, they can also provide crucial information regarding how

different symptoms and outcomes are interlinked. For example, anxiety has been found to have an association with quality of life, stress and ability to function among patients suffering from bipolar disorder. Similarly, mood instability, measured by smartphone-based self-monitoring, seems to be associated with decreased functioning and quality of life as well as increased stress. Interestingly, these associations were seen despite the fact that a vast majority of participants were in partial or full remission (36,44).

Smartphone-based data, combined with data collected by utilizing wearable devices, has also been used to assess the correlation between mood variation and variation in diurnal function (quantified as activity in sleep-wake cycle variability). A study investigating patients suffering from bipolar disorder or borderline personality disorder with a control group of healthy individuals found that, for borderline personality disorder, a pattern of positive correlations was possible to detect among variation in mood, activity, sleep and heart rate (41). Furthermore, the study showed that diurnal variability might be more characteristic for patients with borderline personality disorder compared to the patients with bipolar disorder. However, given that positive correlations were seen between variability of mood and variability of sleep phases in both patient groups, the findings of this study suggest that improved sleep regularity might be a potential target for therapy in both patient groups (41).

Additionally, ESM has been used to investigate the association between subjective sleep quality and the stress individuals anticipate to have the next day. The study found that, for the non-clinical control group, anticipatory stress was negatively associated with sleep quality (45). Furthermore, when individuals suffering from major depressive disorder or social phobia experienced decreased levels of openness and engagement (described as “distancing from, and letting go of, unhelpful thoughts, beliefs and memories”), they also rated their quality of sleep lower the next morning. These findings could be interpreted to suggest that practicing openness and engagement might improve the quality of sleep (45).

THE POTENTIAL OF SMARTPHONE-BASED INTERVENTIONS

STUDIES ON TEXT MESSAGE-BASED INTERVENTIONS

In addition to providing information about the psychopathology of mood disorders, smartphone-based monitoring might have the potential to be used as a therapeutic application in the treatment of mood disorders. A

recent randomized controlled trial assessed the effectiveness of a text message-based maintenance intervention among depressed patients. According to the study, the patients who received *standardized text messages* (e.g. instructions for evidence-based emotion regulation skills) after completing CBT-based inpatient treatment had a smaller increase of depressive symptoms, compared to the group of patients who did not receive text messages. Surprisingly, a similar effect was not seen in a group of patients who received *personalized text messages* (e.g. reminders about what the patient learned during inpatient treatment) after completing the inpatient treatment (46).

Another study examined the effects of repeated attachment security priming among patients suffering from depression. The basis of the study was the attachment theory, and the hypothesis that *priming secure attachment* (reminding participants to visualize and concentrate on one of their secure relationships) results in higher levels of experienced feelings of security and a greater reduction of anxiety and depression symptoms compared to the control group. After the initial *priming* (visualization task) in the lab, the participants received three *prime text messages* on three consecutive days. According to the study, the findings suggest that security priming led to a reduction of anxiety and depression symptoms after the last prime. Furthermore, security priming led to higher levels of experienced feelings of security compared to the control group (47).

STUDIES ON MODERN SMARTPHONE-BASED INTERVENTIONS

In addition to traditional text messages, more modern approaches, such as utilizing smartphone applications, have been used in intervention studies. According to Kramer et al. (48), utilizing ESM and combining it with enhancing feedback on personalized patterns of positive affect led to a stronger decrease in depressive symptoms among patients suffering from depression compared to the control group. In contrast, in the subgroup of patients who participated in the ESM procedure but did not receive feedback, the decrease in depressive symptoms did not occur until the end of the study. These findings highlight the potential of ESM-derived feedback as a therapeutic tool in treatment of patients suffering from mood disorders (48).

Not all the results of the intervention studies have been entirely positive. Pioneering MONARCA I and MONARCA II randomized controlled trials examined the effect of smartphone-based monitoring among patients suffering from

bipolar disorder (18,19). The intervention in MONARCA I trial included daily smartphone-based self-monitoring combined with a feedback loop. The findings from MONARCA I trial suggested that there was no difference between the control group and intervention group regarding the primary outcomes (differences in manic and depressive symptoms assessed by utilizing Young Mania Rating Scale and Hamilton Depression Rating Scale) or the secondary and tertiary outcomes (perceived stress, quality of life, self-assessed manic or depressive symptoms or cognitive function). Furthermore, the subgroup analyses revealed that smartphone-based self-monitoring might sustain depressive symptoms and reduce manic symptoms. The MONARCA II trial utilized an upgraded smartphone-based monitoring system including both self-reported and objective monitoring as well as a mood prediction system used with clinical feedback. Again, the findings suggested that intervention had no significant effect on manic or depressive symptoms. However, the intervention group reported having lower levels of perceived stress and higher quality of life than the control group. Interestingly, the subgroup analyses from MONARCA II trial suggested, similarly to MONARCA I trial, that the intervention group had a higher risk of depressive episodes and reduced risk of manic episodes. The authors suggested this to potentially indicate that recognizing and treating early warning symptoms of a manic episode may be easier compared to the depressive prodromes, and that electronic monitoring of depressive symptoms may worsen those symptoms. These somewhat negative findings also highlight the importance of further research on the potential harmful effects of smartphone-based monitoring.

Smartphone applications can be used to provide psychoeducation. In a 2018 study, patients suffering from bipolar disorder received daily psychoeducational messages based on the answers the patients gave to the daily screening tests prompted by the application. According to the study, even though the attrition rate was high among the participants, the feedback received regarding the general perceived helpfulness was mainly positive (49).

Another study (50) aimed to assess the association between smartphone application engagement and mental health outcomes. The application was designed to prompt daily mood questionnaires, the results of which were then collected into a digital mood diary. Based on the findings of this study, higher app engagement ratings may predict greater decrease in depression and anxiety as well as greater increase in mental well-being. Furthermore, increase in emotional self-awareness was a mediator for these mental health outcomes

among the participants who were depressed or anxious at the time of baseline assessment, whereas no such effect was seen in a non-clinical group. This may indicate that clinically depressed or anxious self-monitoring application users can significantly benefit from improving their emotional self-awareness (50).

Smartphone-based applications may have potential as novel interventions for individuals suffering from mood disorder-related symptoms. For example, a Japanese research group aims to investigate the feasibility of a video playback application, which displays positive words through video viewing. This intervention aims to reduce depressive symptoms among people suffering from subthreshold depression (51).

Another interesting subject for research is to explore how smartphone-based interventions perform compared to more traditional treatments. Results from a randomized controlled trial, investigating interventions for patients suffering from serious mental illness, suggest that smartphone-based intervention was comparable to traditional clinic-based intervention regarding both satisfaction of the patients and the clinical outcomes. Furthermore, the rate of commencement and engagement was better in the smartphone-based intervention group. The study utilized evidence-based mobile phone intervention called FOCUS, which includes daily prompts and personalized content (52).

Another paper investigated whether specific characteristics of patients, such as severity of symptoms, would influence the effect of FOCUS. The study found a significant reduction of depressive symptomatology among patients suffering from moderate to severe depressive symptoms. In contrast, there was no such effect for patients suffering from minimal to mild depressive symptoms. In addition, the findings of the study suggest that FOCUS may be a suitable intervention for patients suffering from depressive symptoms, regardless of whether the patients are using antidepressants and regardless of whether the patients are suffering from psychotic symptoms. These findings suggest that smartphone-based interventions might be suitable for patients with a variety of characteristics (53).

COMBINING SMARTPHONE-BASED INTERVENTIONS WITH OTHER TREATMENTS

In addition to providing novel treatments, smartphones can be utilized to enhance and improve current treatments. For example, according to a systematic review published in 2018, findings from several studies provided preliminary evidence

that mobile technologies can be effective in improving adherence to prescribed medication among patients suffering from mood disorders (54). Furthermore, smartphones can be used to deliver mental health interventions such as psychotherapy treatment. Given the ubiquity of mobile phones, developing smartphone-based interventions has the potential to significantly increase treatment accessibility (55).

A randomized controlled trial published in 2017 utilized a self-help smartphone app that provides several kinds of cognitive behavioural therapy (CBT) -based sessions, such as self-monitoring and behavioural activation. The study found that, among patients suffering from antidepressant-resistant major depression, combining smartphone CBT and medication change was more effective than treating the patient by medication change alone. This highlights the potential benefits of combining smartphone-based CBT applications with other treatments (56).

The secondary analysis of this randomized controlled trial aimed to thoroughly assess which aspects of behavioural activation are the most associated with decrease in depression severity. The findings suggest that the level of *expected pleasure* when the patient is planning an activity has the highest correlation with depression severity. This means that when designing smartphone-based CBT applications, it might be more beneficial to recommend activities that the patient expects to give a high level of *pleasure*, rather than just include activities with a high level of *achieved pleasure* (57).

DETECTING THE RISK OF RELAPSE

The data collected by remote monitoring might help to detect the patients with increased risk of relapse. Both passively and actively gathered data, using smartphones and wearable devices is hoped to reflect the changes in individuals' daily life relevant to risk of relapse (e.g. changes in sleep, physical activity and mood). The objective of a current multi-site prospective cohort study is to determine the clinical utility and predictive ability of the data collected by remote monitoring (58). The objective of another randomized controlled trial was to examine if patients suffering from bipolar disorder experience longer episodes of euthymia when their treating clinicians receive feedback about the changes in patients' behaviour. During the study, a smartphone application was utilized to collect objective data regarding patients' communication (e.g. number of outgoing calls), smartphone usage (e.g. hours when smartphone inactive) and activity (e.g. steps/day). If the collected data significantly differed

from the patient's individual baseline values, the attending psychiatrist was notified and they contacted the patient. This kind of smartphone-based feedback loop is hoped to help to detect the early warning signs of upcoming mood episodes and therefore optimize the timing of suitable intervention among patients suffering from bipolar disorder (59).

Furthermore, in an ongoing study Faurholt Jepsen et al. (60) aim to assess whether smartphone-based interventions decrease the number and length of readmissions compared to traditional interventions. The smartphone-based interventions used in the study consist of several components including self-monitoring, feedback loop, passively collected behavioural data and smartphone-based cognitive behavioural therapy (60).

CURRENT CHALLENGES IN SMARTPHONE-BASED INTERVENTIONS

Despite the remarkable potential of smartphone-based monitoring of mood, several challenges have emerged. Some of the most common concerns are risks regarding privacy, confidentiality and the details regarding data security such as storage and encryption (31,61). Another challenge is the fact that although a substantial number of modern day people are accustomed to using technological solutions in their everyday life, the access to technology and level of technical skills are not the same for everybody. Patients using mobile monitoring are required to analyse how their behaviour, for example, lending their phone to somebody else, affects the quality of the collected data. In addition, the level of interest towards technology varies among the population. To summarize, smartphone-based monitoring might not be the ideal solution for everyone, which means that physicians need to evaluate the suitability of smartphone-based monitoring individually with each patient (5,62). In addition, different smartphone brands and models have unique characteristics. For example, the iOS operating system has more restrictions compared to the Android operating system (31). This means that in order to precisely collect similar kinds of data by using an application that utilizes hardware components or sensors, the application needs to be certified separately for each model (5). Furthermore, reports for health apps show high attrition rate, especially outside of research settings (62).

It is of the utmost importance to ensure that the benefits of utilizing technological solutions in psychiatry far outweigh the risks. The number of mental health-related applications

has increased rapidly but only few of those applications have been validated (5). This fact was also highlighted by a systematic review conducted in 2018, which found that out of approximately 100 papers that reported utilizing a mobile application for monitoring and/or management of mental health symptoms or illness, merely fourteen used an application with clinically validated evidence of effectiveness (63). A substantial number of developers of mental health applications are not associated with a medical centre or an academic institution. Furthermore, many of the descriptions of mental health applications do not provide sufficient information about the developers, making it more difficult to evaluate the credibility of these apps (64).

The absence of regulation raises a concern of whether some of these applications may put the user at a risk of medical harm. For instance, mobile monitoring might increase self-diagnosing and self-treatment rather than encourage patients to seek professional help (61). Unvalidated applications might promote incorrect information and they might offer unsuitable or inadequate help in the form of e.g. non-professional counsellors or chatbots (62). Another concern is that electronic monitoring might lead to medicalization of normal phenomena. For example, normal mood variation might be confused with mood disorder relapses (61,62). Considering the fact that monitoring of individuals has been previously used with criminals and that the reasoning behind mobile monitoring of mood can be easily misinterpreted by the general public, there is a notable concern that monitoring might increase the stigmatization of mental disorders (5,61).

Another important question that needs to be answered is whether mobile monitoring actually increases the symptoms (61). It is also worth noting that patients suffering from mood disorders might sometimes have unhealthy habits regarding smartphone usage, which can make smartphone-based monitoring somewhat problematic (62).

In addition to academic research, various commercial organizations have been developing algorithms based on the big data gathered from daily digital transactions, in order to predict behaviour, mental state and to profile people. It is important to remember that although identical analytic approaches might be used both in academic research and commercial profiling, the objective of commercial organizations is not helping patients but profit (5).

This field of research currently lacks a standardized way to report research results, conduct analyses and detail methods (65). Also, the researchers are not unanimous in how mood is defined and quantified and how various measurements and scales are used in different studies. This lack of consensus

in the research regarding electronic mood data makes it hard for readers to thoroughly evaluate and compare the published studies. In order to rectify this issue, Faurholt-Jepsen et al. (65) published guidelines with recommendations for how to write sections such as participant descriptions (e.g. recruitment details, demographics of participants), data collection (e.g. software details, description of the questionnaires, how often participants are prompted to complete mood ratings) and data analysis (e.g. details regarding the missing data, methods of analyses, conflict of interest).

CONCLUSIONS

The objective of this review was to summarize the recent literature regarding smartphone-based monitoring of patients suffering from mood disorders. Smartphone-based monitoring, active as well as passive, has an enormous potential to help both researchers and clinicians to understand the psychopathology of mood disorders and provide novel interventions. Smartphone-based self-monitoring of symptoms has been demonstrated to reflect clinical evaluations of symptoms, making smartphones a valid tool for symptom monitoring. However, when it comes to automatically generated objective smartphone data, further research (including studies with longer monitoring periods and larger sample sizes) is needed in order to validate the findings from previous studies. Furthermore, additional randomized controlled trials are needed to examine the potential positive, negative or neutral effects smartphone-based interventions may have on the patient. In addition, established guidelines (such as those recommended by Faurholt-Jepsen et al.) for reporting on mood data gathered by remote monitoring are necessary to facilitate accurate interpretation of future studies (65). It is also important to appreciate the diverse preferences, lifestyles and technological skills of patients and, instead of merely focusing on smartphone-based data collection, it is recommended to utilize many types of technology platforms. Finally, analysing this novel, complex longitudinal multivariate data provided by smartphone-based monitoring will require cross-industry cooperation between different experts, including researchers, clinicians, statisticians and engineers.

Author:

Annasofia Martikkala, MD
Erkki Isometsä, Professor of Psychiatry, MD, PhD

Correspondence to:

Annasofia Martikkala, MD
Department of Psychiatry
University of Helsinki
PO BOX 22 (Välskärinkatu 12)
00014 University of Helsinki
annasofia.martikkala@helsinki.fi

References

1. GBD 2015 DALYs and HALE Collaborators. *Global, regional, and national disability-adjusted life-years (DALYs) for 315 diseases and injuries and healthy life expectancy (HALE), 1990-2015: A systematic analysis for the global burden of disease study 2015*. Lancet [Internet]. 2016 10 08;388(10053):1603-58.
2. Vieta E, Berk M, Schulze TG, Carvalho AF, Suppes T, Calabrese JR, Gao K, Miskowiak KW, Grande I. *Bipolar disorders*. Nat Rev Dis Prim [Internet]. 2018 03 08;4:18008.
3. Merikangas KR, Swendsen J, Hickie IB, Cui L, Shou H, Merikangas AK, Zhang J, Lamers F, Crainiceanu C, Volkow ND, Zipunnikov V. *Real-time mobile monitoring of the dynamic associations among motor activity, energy, mood, and sleep in adults with bipolar disorder*. JAMA Psychiatry [Internet]. 2019 Feb 01;76(2):190-8.
4. Torous J, Roberts LW. *Needed innovation in digital health and smartphone applications for mental health: Transparency and trust*. JAMA Psychiatry [Internet]. 2017 05 01;74(5):437-8.
5. Bauer M, Glenn T, Monteith S, Bauer R, Whybrow PC, Geddes J. *Ethical perspectives on recommending digital technology for patients with mental illness*. Int j bipolar disord [Internet]. 2017 Dec;5(1):6.
6. Csikszentmihalyi M, Larson R. *Validity and reliability of the experience-sampling method*. J Nerv Ment Dis [Internet]. 1987 Sep;175(9):526-36.
7. Onnela J, Rauch SL. *Harnessing smartphone-based digital phenotyping to enhance behavioral and mental health*. Neuropsychopharmacology [Internet]. 2016;41(7):1691-6.
8. Baglioni C, Nanovska S, Regen W, Spiegelhalter K, Feige B, Nissen C, Reynolds CF, Riemann D. *Sleep and mental disorders: A meta-analysis of polysomnographic research*. Psychol Bull [Internet]. 2016;142(9):969-90.
9. Aledavood T, Torous J, Triana Hoyos AM, Naslund JA, Onnela J, Keshavan M. *Smartphone-based tracking of sleep in depression, anxiety, and psychotic disorders*. Curr Psychiatry Rep [Internet]. 2019 Jun 04;21(7):49.
10. Ancoli-Israel S, Cole R, Alessi C, Chambers M, Moorcroft W, Pollak CP. *The role of actigraphy in the study of sleep and circadian rhythms*. Sleep [Internet]. 2003 May 01;26(3):342-92.
11. Burton C, McKinstry B, Szentagotai Tatar A, Serrano-Blanco A, Pagliari C, Wolters M. *Activity monitoring in patients with depression: A systematic review*. J Affect Disord [Internet]. 2013 Feb 15;145(1):21-8.

12. Torous J, Staples P, Onnela J. *Realizing the potential of mobile mental health: New methods for new data in psychiatry*. Curr Psychiatry Rep [Internet]. 2015 Aug;17(8):602.
13. Torous J, Kiang MV, Lorme J, Onnela J. *New tools for new research in psychiatry: A scalable and customizable platform to empower data driven smartphone research*. JMIR Ment Health [Internet]. 2016 May 05;3(2):e16.
14. Torous J, Wisniewski H, Liu G, Keshavan M. *Mental health mobile phone app usage, concerns, and benefits among psychiatric outpatients: Comparative survey study*. JMIR Ment Health [Internet]. 2018 Nov 16;5(4):e11715.
15. Young AS, Cohen AN, Niv N, Nowlin-Finch N, Oberman RS, Olmos-Ochoa TT, Goldberg RW, Whelan F. *Mobile phone and smartphone use by people with serious mental illness*. Psychiatric Services [Internet]. 2019 Nov 20;appips201900203
16. Van Til K, McInnis MG, Cochran A. *A comparative study of engagement in mobile and wearable health monitoring for bipolar disorder*. Bipolar Disord [Internet]. 2019
17. Bauer AM, Iles-Shih M, Ghomi RH, Rue T, Grover T, Kincler N, Miller M, Katon WJ. *Acceptability of mHealth augmentation of collaborative care: A mixed methods pilot study*. Gen Hosp Psychiatry [Internet]. 2018 Mar;51:22-9.
18. Faurholt-Jepsen M, Frost M, Ritz C, Christensen EM, Jacoby AS, Mikkelsen RL, Knorr U, Bardram JE, Vinberg M, Kessing LV. *Daily electronic self-monitoring in bipolar disorder using smartphones - the MONARCA I trial: a randomized, placebo-controlled, single-blind, parallel group trial*. [Internet]. England: ; 2015. 2691 p.
19. Faurholt-Jepsen M, Frost M, Christensen EM, Bardram JE, Vinberg M, Kessing LV. *The effect of smartphone-based monitoring on illness activity in bipolar disorder: The MONARCA II randomized controlled single-blinded trial*. Psychol Med [Internet]. 2019 Apr 04;1-11
20. Daus H, Kislicyn N, Heuer S, Backenstrass M. *Disease management apps and technical assistance systems for bipolar disorder: Investigating the patients' point of view*. J Affect Disord [Internet]. 2018 03 15;229:351-7.
21. Goodday SM, Atkinson L, Goodwin G, Saunders K, South M, Mackay C, Denis M, Hinds C, Attenburrow M, Davies J, Welch J, Stevens W, Mansfield K, Suvilehto J, Geddes J. *The true colours remote symptom monitoring system: A decade of evolution*. J Med Internet Res [Internet]. 2020 Jan 15;22(1):e15188.
22. Chung K, Park JY, Joung D, Jhung K. *Response time as an implicit self-schema indicator for depression among undergraduate students: Preliminary findings from a mobile app-based depression assessment*. JMIR Mhealth Uhealth [Internet]. 2019 Sep 13;7(9):e14657.
23. Reinertsen E, Clifford GD. *A review of physiological and behavioral monitoring with digital sensors for neuropsychiatric illnesses*. Physiol Meas [Internet]. 2018 05 15;39(5):05TR01.
24. Cornet VP, Holden RJ. *Systematic review of smartphone-based passive sensing for health and wellbeing*. J Biomed Inform [Internet]. 2018;77:120-32.
25. Beiwinkel T, Kindermann S, Maier A, Kerl C, Moock J, Barbian G, Rossler W. *Using smartphones to monitor bipolar disorder symptoms: A pilot study*. JMIR Ment Health [Internet]. 2016 Jan 06;3(1):e2.
26. Saeb S, Zhang M, Karr CJ, Schueller SM, Corden ME, Kording KP, Mohr DC. *Mobile phone sensor correlates of depressive symptom severity in daily-life behavior: An exploratory study*. J Med Internet Res [Internet]. 2015 Jul 15;17(7):e175.
27. Ben-Zeev D, Scherer EA, Wang R, Xie H, Campbell AT. *Next-generation psychiatric assessment: Using smartphone sensors to monitor behavior and mental health*. [Internet]. United States: ; 2015. 218 p.
28. Osmani V, Maxhuni A, Grünerbl A, Lukowicz P, Haring C, Mayora O. *Monitoring activity of patients with bipolar disorder using smart phones*. [Internet]. 2013

29. Abdullah S, Matthews M, Frank E, Doherty G, Gay G, Choudhury T. *Automatic detection of social rhythms in bipolar disorder*. [Internet]. 05: ; 2016. 538 p.
30. Fraccaro P, Beukenhorst A, Sperrin M, Harper S, Palmier-Claus J, Lewis S, Van der Veer, Sabine N., Peek N. *Digital biomarkers from geolocation data in bipolar disorder and schizophrenia: A systematic review*. J Am Med Inform Assoc [Internet]. 2019 Nov 01;26(11):1412-20.
31. Faurholt-Jepsen M, Bauer M, Kessing LV. *Smartphone-based objective monitoring in bipolar disorder: Status and considerations*. Int j bipolar disord [Internet]. 2018 Jan 23;6(1):6.
32. Faurholt-Jepsen M, Frost M, Vinberg M, Christensen EM, Bardram JE, Kessing LV. *Smartphone data as objective measures of bipolar disorder symptoms*. [Internet]. Ireland: ; 2014. 124 p.
33. Faurholt-Jepsen M, Vinberg M, Frost M, Christensen EM, Bardram JE, Kessing LV. *Smartphone data as an electronic biomarker of illness activity in bipolar disorder*. [Internet]. Denmark: ; 2015. 715 p.
34. Faurholt-Jepsen M, Busk J, Frost M, Vinberg M, Christensen EM, Winther O, Bardram JE, Kessing LV. *Voice analysis as an objective state marker in bipolar disorder*. [Internet]. 07 19: ; 2016.
35. Karam ZN, Provost EM, Singh S, Montgomery J, Archer C, Harrington G, Mcinnis MG. *ECOLOGICALLY VALID LONG-TERM MOOD MONITORING OF INDIVIDUALS WITH BIPOLAR DISORDER USING SPEECH*. [Internet]. United States: ; 2014. 4858 p.
36. Faurholt-Jepsen M, Frost M, Christensen EM, Bardram JE, Vinberg M, Kessing LV. *The validity of daily patient-reported anxiety measured using smartphones and the association with stress, quality of life and functioning in patients with bipolar disorder*. J Affect Disord [Internet]. 2019 Oct 01;257:100-7.
37. Marwaha S, He Z, Broome M, Singh SP, Scott J, Eyden J, Wolke D. *How is affective instability defined and measured? A systematic review*. Psychol Med [Internet]. 2014 Jul;44(9):1793-808.
38. Hallensleben N, Spangenberg L, Forkmann T, Rath D, Hegerl U, Kersting A, Kallert TW, Glaesmer H. *Investigating the dynamics of suicidal ideation*. Crisis [Internet]. 2018 Jan;39(1):65-9.
39. Kleiman EM, Nock MK. *Real-time assessment of suicidal thoughts and behaviors*. Curr Opin Psychol [Internet]. 2018;22:33-7.
40. Li H, Mukherjee D, Krishnamurthy VB, Millett C, Ryan KA, Zhang L, Saunders EFH, Wang M. *Use of ecological momentary assessment to detect variability in mood, sleep and stress in bipolar disorder*. BMC Res Notes [Internet]. 2019 Dec 04;12(1):791.
41. Carr O, Saunders KEA, Tsanas A, Bilderbeck AC, Palmius N, Geddes JR, Foster R, Goodwin GM, De Vos M. *Variability in phase and amplitude of diurnal rhythms is related to variation of mood in bipolar and borderline personality disorder*. Sci rep [Internet]. 2018 01 26;8(1):1649.
42. Huckvale K, Venkatesh S, Christensen H. *Toward clinical digital phenotyping: a timely opportunity to consider purpose, quality, and safety*. [Internet]. England: ; 2019. 88 p.
43. Heller AS, Fox AS, Davidson RJ. *Parsing affective dynamics to identify risk for mood and anxiety disorders*. Emotion [Internet]. 2019 Mar;19(2):283-91.
44. Faurholt-Jepsen M, Frost M, Busk J, Christensen EM, Bardram JE, Vinberg M, Kessing LV. *Is smartphone-based mood instability associated with stress, quality of life, and functioning in bipolar disorder?*. Bipolar Disord [Internet]. 2019;21(7):611-20.
45. Block VJ, Meyer AH, Miche M, Mikoteit T, Hoyer J, Imboden C, Bader K, Hatzinger M, Lieb R, Gloster AT. *The effect of anticipatory stress and openness and engagement on subsequently perceived sleep quality-an experience sampling method study*. J Sleep Res [Internet]. 2019 Dec 18;e12957
46. Schlicker S, Ebert DD, Middendorf T, Titzler I, Berking M. *Evaluation of a text-message-based maintenance intervention for major depressive disorder after inpatient cognitive behavioral therapy*. J Affect Disord [Internet]. 2018;227:305-12.

47. Carnelley KB, Bejinaru M, Otway L, Baldwin DS, Rowe AC. *Effects of repeated attachment security priming in outpatients with primary depressive disorders*. J Affect Disord [Internet]. 2018;234:201-6.
48. Kramer I, Simons CJP, Hartmann JA, Menne-Lothmann C, Viechtbauer W, Peeters F, Schruers K, van Bommel AL, Myin-Germeys I, Delespaul P, van Os J, Wichers M. *A therapeutic application of the experience sampling method in the treatment of depression: A randomized controlled trial*. World Psychiatry [Internet]. 2014 Feb;13(1):68-77.
49. Hidalgo-Mazzei D, Reinares M, Mateu A, Nikolova VL, Bonnin CDM, Samalin L, Garcia-Estela A, Perez-Sola V, Young AH, Strejilevich S, Vieta E, Colom F. *OpenSIMLe: A real-world implementation feasibility study of a smartphone-based psychoeducation programme for bipolar disorder*. J Affect Disord [Internet]. 2018 12 01;241:436-45.
50. Bakker D, Rickard N. *Engagement in mobile phone app for self-monitoring of emotional wellbeing predicts changes in mental health: MoodPrism*. J Affect Disord [Internet]. 2018;227:432-42.
51. Kato Y, Kageyama K, Mesaki T, Uchida H, Sejima Y, Marume R, Takahashi K, Hirao K. *Study protocol for a pilot randomized controlled trial on a smartphone application-based intervention for subthreshold depression: Study protocol clinical trial (SPIRIT compliant)*. Medicine (Baltimore) [Internet]. 2020 Jan;99(4):e18934.
52. Ben-Zeev D, Brian RM, Jonathan G, Razzano L, Pashka N, Carpenter-Song E, Drake RE, Scherer EA. *Mobile health (mHealth) versus clinic-based group intervention for people with serious mental illness: A randomized controlled trial*. Psychiatr Serv [Internet]. 2018 09 01;69(9):978-85.
53. Ben-Zeev D, Buck B, Chu PV, Razzano L, Pashka N, Hallgren KA. *Transdiagnostic mobile health: Smartphone intervention reduces depressive symptoms in people with mood and psychotic disorders*. JMIR Ment Health [Internet]. 2019 Apr 12;6(4):e13202.
54. Rootes-Murdy K, Glazer KL, Van Wert MJ, Mondimore FM, Zandi PP. *Mobile technology for medication adherence in people with mood disorders: A systematic review*. J Affect Disord [Internet]. 2018;227:613-7.
55. Donker T, Petrie K, Proudfoot J, Clarke J, Birch M, Christensen H. *Smartphones for smarter delivery of mental health programs: A systematic review*. J Med Internet Res [Internet]. 2013 Nov 15;15(11):e247.
56. Mantani A, Kato T, Furukawa TA, Horikoshi M, Imai H, Hiroe T, Chino B, Funayama T, Yonemoto N, Zhou Q, Kawanishi N. *Smartphone cognitive behavioral therapy as an adjunct to pharmacotherapy for refractory depression: Randomized controlled trial*. J Med Internet Res [Internet]. 2017 11 03;19(11):e373.
57. Furukawa TA, Imai H, Horikoshi M, Shimodera S, Hiroe T, Funayama T, Akechi T, FLATT Investigators. *Behavioral activation: Is it the expectation or achievement, of mastery or pleasure that contributes to improvement in depression?*. J Affect Disord [Internet]. 2018 10 01;238:336-41.
58. Matcham F, Barattieri di San Pietro, C., Bulgari V, de Girolamo G, Dobson R, Eriksson H, Folarin AA, Haro JM, Kerz M, Lamers F, Li Q, Manyakov NV, Mohr DC, Myin-Germeys I, Narayan V, Bwih P, Ranjan Y, Rashid Z, Rintala A, Siddi S, Simblett SK, Wykes T, Hotopf M, RADAR-CNS consortium. *Remote assessment of disease and relapse in major depressive disorder (RADAR-MDD): A multi-centre prospective cohort study protocol*. BMC Psychiatry [Internet]. 2019 02 18;19(1):72.
59. Muhlbaue E, Bauer M, Ebner-Priemer U, Ritter P, Hill H, Beier F, Kleindienst N, Severus E. *Effectiveness of smartphone-based ambulatory assessment (SBAA-BD) including a predicting system for upcoming episodes in the long-term treatment of patients with bipolar disorders: Study protocol for a randomized controlled single-blind trial*. BMC Psychiatry [Internet]. 2018 10 26;18(1):349.
60. Faurholt-Jepsen M, Frost M, Martiny K, Tuxen N, Rosenberg N, Busk J, Winther O, Bardram JE, Kessing LV. *Reducing the rate and duration of re-ADMISSions among patients with unipolar disorder and bipolar disorder using smartphone-based monitoring and treatment - the RADMISS trials: Study protocol for two randomized controlled trials*. Trials [Internet]. 2017 06 15;18(1):277.
61. Gillett G, Saunders KEA. *Remote monitoring for understanding mechanisms and prediction in psychiatry*. Curr Behav Neurosci Rep 6 [Internet]. 2019:51-56.

62. Bauer M, Glenn T, Geddes J, Gitlin M, Grof P, Kessing LV, Monteith S, Faurholt-Jepsen M, Severus E, Whybrow PC. *Smartphones in mental health: A critical review of background issues, current status and future concerns*. Int j bipolar disord [Internet]. 2020 Jan 10;8(1):2.
63. Wang K, Varma DS, Prosperi M. *A systematic review of the effectiveness of mobile apps for monitoring and management of mental health symptoms or disorders*. J Psychiatr Res [Internet]. 2018;107:73-8.
64. Frank E, Pong J, Asher Y, Soares CN. *Smart phone technologies and ecological momentary data: Is this the way forward on depression management and research?* Curr Opin Psychiatry [Internet]. 2018 Jan;31(1):3-6.
65. Faurholt-Jepsen M, Geddes JR, Goodwin GM, Bauer M, Duffy A, Vedel Kessing L, Saunders K. *Reporting guidelines on remotely collected electronic mood data in mood disorder (eMOOD)-recommendations*. Transl Psychiatry [Internet]. 2019 06 07;9(1):162.